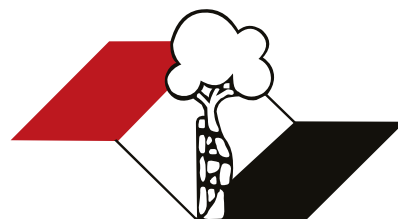


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# MINIMALLY INVASIVE HALLUX VALGUS SURGERY: LESSONS FROM 1,217 FEET OVER EIGHT YEARS AT A SINGLE CENTER

## CIRURGIA MINIMAMENTE INVASIVA PARA CORREÇÃO DO HÁLUX VALGO: EXPERIÊNCIA DE UM ÚNICO CENTRO EM 1.217 PÉS AO LONGO DE OITO ANOS

Gabriel Ferraz Ferreira<sup>1,2,3\*</sup> , JULIANA VILELA LACERDA<sup>1</sup> , Laryssa Augustinho dos Santos<sup>1</sup> , FERNANDO LEN<sup>1</sup> , Giovane Aloise Cruz<sup>1</sup> , Miguel Viana Pereira Filho<sup>1,2,3</sup> 

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### ABSTRACT

**Objective:** To document the eight-year institutional evolution of minimally invasive hallux valgus surgery at a single high-volume center, describing the sequential transitions between operative techniques and the clinical and biomechanical rationale that motivated each change. **Methods:** Retrospective analysis of prospectively collected data from January 2018 through December 2025. All feet undergoing primary minimally invasive hallux valgus surgery performed by the same team were included. Annual distributions of technique: Reverdin-Isham (RI), Minimally Invasive Chevron-Akin (MICA, 3rd-generation), metatarsal extra-articular transverse and Akin osteotomy (META, 4th-generation), and combined percutaneous exostectomy-Akin (EA), bilateral procedure rates, and surgical volume were analyzed. **Results:** A total of 1,217 feet were operated on during the study period. RI predominated in 2018-2019 (n=181), was supplanted by MICA from 2020-2021, and META became the primary institutional procedure from April 2022 onward, accounting for 51.7% (n=629) of all procedures by study end. The combined EA approach declined from 26.0% in 2019 to 0% in 2023 (p<0.001). Bilateral simultaneous procedures decreased significantly from 45.2% (2024) to 34.0% (2025) (p=0.020), driven by evidence of elevated fracture risk in bilateral cases. **Conclusion:** This study documents a continuous, evidence-driven evolution of minimally invasive hallux valgus surgery over eight years at a high-volume, single-team center. The META technique has emerged as the institutional standard due to its biomechanical safety and pedagogical advantages. These findings provide a practical framework for centers undergoing similar technical transitions. **Level of Evidence IV; Retrospective Observational Study.**

**Keywords:** Hallux Valgus; Minimally Invasive Surgical Procedures; Osteotomy; Orthopedic Procedures.

### RESUMO

**Objetivo:** Documentar a evolução institucional, ao longo de oito anos, da cirurgia minimamente invasiva do hálux valgo em um único centro de alto volume, descrevendo as transições sequenciais entre as técnicas operatórias e os fundamentos clínicos e biomecânicos que motivaram cada mudança. **Métodos:** Análise retrospectiva de dados coletados prospectivamente entre janeiro de 2018 e dezembro de 2025. Foram incluídos todos os pés submetidos à cirurgia minimamente invasiva primária do hálux valgo, realizada pela mesma equipe. Foram analisadas as distribuições anuais das técnicas: Reverdin-Isham (RI), Chevron-Akin minimamente invasiva (MICA, 3ª geração), osteotomia metatarsal transversa extra-articular associada à osteotomia de Akin (META, 4ª geração) e exostectomia percutânea combinada à osteotomia de Akin (EA), bem como as taxas de procedimentos bilaterais e o volume cirúrgico. **Resultados:** Um total de 1.217 pés foi operado durante o período do estudo. A técnica RI predominou em 2018-2019 (n=181), foi substituída pela MICA a partir de 2020-2021, e a META tornou-se o principal procedimento institucional a partir de abril de 2022, correspondendo a 51,7% (n=629) de todos os procedimentos ao final do estudo. A abordagem combinada EA diminuiu de 26,0% em 2019 para 0% em 2023 (p<0,001). Os procedimentos bilaterais simultâneos diminuíram significativamente de 45,2% (2024) para 34,0% (2025) (p=0,020), em razão de evidências de maior risco de fratura nos casos bilaterais. **Conclusão:** Este estudo documenta uma evolução contínua, orientada por evidências, da cirurgia minimamente invasiva do hálux valgo ao longo de oito anos em um centro de alto volume, com atuação de uma única equipe. A técnica META consolidou-se como o padrão institucional em razão de sua segurança biomecânica e de suas vantagens no ensino da técnica cirúrgica. Esses achados fornecem um referencial prático para centros que estejam passando por transições técnicas semelhantes. **Nível de Evidência IV; Estudo Observacional Retrospectivo.**

**Descritores:** Hallux Valgus; Procedimentos Cirúrgicos Minimamente Invasivos; Osteotomia; Procedimentos Ortopédicos.

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## INTRODUCTION

Hallux valgus is among the most prevalent forefoot deformities requiring surgical intervention, with an estimated global prevalence approaching 23% of adults.<sup>1</sup> Furthermore, the volume of scientific publications on hallux valgus has increased substantially in recent years, with continued growth expected.<sup>2</sup>

Its surgical management has historically relied on open osteotomy techniques; however, minimally invasive approaches have undergone a significant renaissance over the past two decades, driven by advances in dedicated burrs, fluoroscopic guidance, and internal fixation hardware that permit reproducible correction through incisions of only a few millimeters.<sup>2-7</sup>

The evolution of minimally invasive hallux valgus surgery can be understood as a succession of technical generations, each addressing the limitations of its predecessor.<sup>8</sup>

First-generation techniques, including the Reverdin-Isham (RI) osteotomy, offered technical simplicity and low implant burden but relied on dressing-based stabilization without rigid internal fixation.<sup>9-12</sup>

Second-generation minimally invasive hallux valgus surgery, typified by the Bösch technique, used a percutaneous subcapital transverse osteotomy stabilized with an intramedullary Kirschner wire under fluoroscopic guidance.<sup>13,14</sup>

Third-generation techniques, most prominently the Minimally Invasive Chevron-Akin (MICA) procedure as refined by Redfern and Vernois, introduced stable dual-screw fixation with extreme lateral translation of the metatarsal head, demonstrating outcomes comparable to open Scarf-Akin procedures.<sup>7,15,16</sup>

More recently, the fourth-generation Metaphyseal Extra-Articular Transverse Akin (META) osteotomy was introduced, substituting a straight transverse for the chevron-shaped cut at the distal metaphysis.<sup>17</sup> This modification eliminates the risk of creating a long lateral wing without adequate cortical purchase, a recognized pitfall of the chevron configuration, and offers a shallower learning curve for trainees.

Despite the expanding literature on individual techniques, longitudinal data documenting the institutional rationale and timing of each transition within a stable surgical team are scarce.

The present study reports our eight-year experience (2018-2025) at a single high-volume center in São Paulo, Brazil, capturing the sequential adoption of minimally invasive techniques and the observations that drove each change.

## METHODS

### Study Design

This was a retrospective observational study analyzing the evolution of minimally invasive hallux valgus techniques and surgical volume at a single center. The study was conducted at The study was conducted at Instituto Prevent Senior, São Paulo, Brazil, where all clinical evaluations and surgical procedures were performed following standardized institutional protocols.

### Ethical Approval

The study was approved by the local ethics committee and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

### Participants

All consecutive feet with primary symptomatic hallux valgus treated at our institution between January 1, 2018, and December 31, 2025, were eligible for inclusion if they underwent minimally invasive correction using one of the techniques adopted during the study period: first-generation Reverdin-Isham osteotomy, third-generation

MICA, fourth-generation META, or the combined percutaneous exostectomy-Akin procedure. All operations were performed by the same surgical team in a day-hospital setting. Revision cases and feet with incomplete institutional records were excluded. A minimum of six months of failed conservative treatment was required before surgical indication.

### Surgical Techniques

- Reverdin-Isham (RI) osteotomy. A first-generation subcapital percutaneous technique involving a subchondral medial-closing osteotomy and concomitant Akin osteotomy of the proximal phalanx, without internal fixation.<sup>18</sup> Correction is maintained entirely by dressing immobilization.
- Minimally Invasive Chevron-Akin (MICA, 3rd-generation). An extracapsular chevron (V-shaped) osteotomy at the distal metaphysis of the first metatarsal using a 2.0 mm Shannon burr, as described by Redfern and Vernois.<sup>6,7</sup> After extreme lateral translation of the metatarsal head, correcting varus, pronation, and sagittal imbalance under fluoroscopic guidance, the osteotomy is fixed with two beveled cannulated screws. Concomitant Akin osteotomy of the proximal phalanx was performed in all cases.<sup>19,20</sup>
- META osteotomy (4th-generation). The META technique employs a straight transverse osteotomy at the distal metaphysis of the first metatarsal using the same Shannon burr and dual-screw fixation principle as MICA.<sup>17,21</sup>
- Combined percutaneous exostectomy and Akin osteotomy (EA). Employed for very mild hallux valgus, involving medial eminence percutaneous excision and proximal phalangeal closing wedge osteotomy without fixation (Akin osteotomy).

### Postoperative Protocol

Immediate full weight-bearing was permitted in all cases using rigid-sole orthopaedic footwear. Perioperative analgesia followed a uniform institutional protocol consisting of ankle or Mayo block with ropivacaine.<sup>22,23</sup> Postoperative wound management differed according to technique.

For patients treated with the Reverdin-Isham osteotomy, surgical dressings were changed weekly by the operating team for six weeks, with orthopaedic footwear maintained throughout this period. For patients treated with MICA or META, weekly dressing changes were performed by the surgical team during the first four weeks; following the final dressing change, patients were instructed to initiate active mobilization of the hallux to reduce the risk of postoperative stiffness. Transition to conventional footwear was authorized at six weeks contingent on satisfactory radiographic osseous healing.

### Data Collection

Patient data were recorded using anonymized numerical identifiers and managed through Research Electronic Data Capture (REDCap). REDCap is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for data integration and interoperability with external sources.<sup>24</sup>

### Statistical Analysis

Descriptive statistics included absolute counts, proportions, and annual totals. Differences in bilateral procedure rates between selected years and in aggregate exostectomy-Akin proportions between selected periods were evaluated using Pearson chi-square tests with continuity correction. Significance was set at  $p < 0.05$ . All analyses were conducted using R version 4.4.0.<sup>25</sup>

## RESULTS

### Surgical Volume

Between January 2018 and December 2025, a total of 1,217 feet underwent minimally invasive surgery for hallux valgus at our institution (Figure 1).

Annual volume ranged from 51 feet in 2021, the nadir imposed by COVID-19 pandemic restrictions on elective surgery, to 243 feet in 2024. Following the recovery of full institutional activity in 2022, annual volume exceeded 100 feet in each subsequent year, with 240 feet operated in 2025. The consistent high volume across the study period reflects the center's role as a specialized referral unit supported by a stable, dedicated surgeon team.

### Technique Distribution

The annual distribution of operative techniques is illustrated in Figure 2.

The RI osteotomy predominated in 2018 ( $n=87$ ; 53.4%) and 2019 ( $n=94$ ; 40.0%). Transition to MICA began during 2019. MICA became the dominant technique in 2020 ( $n=61$ ; 81.3%) and 2021 ( $n=47$ ; 92.2%), with near-complete abandonment of RI. In April 2022, META became the primary institutional procedure.

By 2023, META accounted for 97.0% of procedures ( $n=98/101$ ), a proportion maintained in 2024 (95.9%;  $n=233/243$ ) and 2025 (92.1%;  $n=221/240$ ). Only a few RI cases were performed from 2024 onward ( $n=4$  in 2024 and  $n=5$  in 2025).

### Exostectomy-Akin (EA) for Mild Deformity

The combined percutaneous EA procedure was performed in 129 feet (10.6% of the total sample), with highest use in 2019

( $n=61$ ; 26.0%). Its use declined thereafter, reaching 5.9% in 2021, 1.8% in 2022, and 0% in 2023, before limited reintroduction in selected cases in 2024 ( $n=6$ ; 2.5%) and 2025 ( $n=14$ ; 5.8%). The difference in overall proportions between 2018-2019 and 2022-2023 was significant (chi-square,  $p<0.001$ ).

### Bilateral Simultaneous Procedures

Bilateral surgery was performed in 37.4% of cases in 2018 and peaked at 45.2% in 2024, reflecting a growing institutional preference for addressing both feet in a single anesthetic episode. A significant decline was observed in 2025 (34.0% vs. 45.2% in 2024; chi-square  $p=0.020$ ). Bilateral procedure proportions are shown in Figure 3.

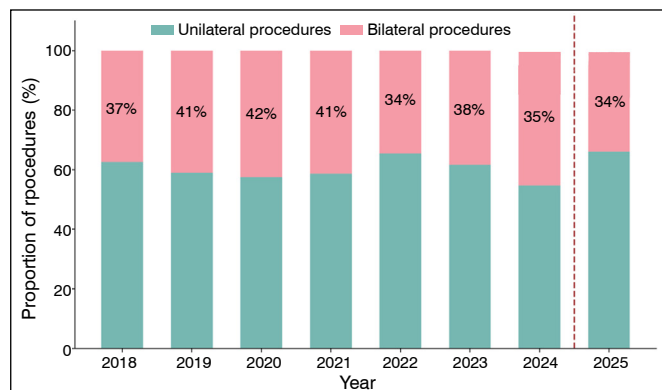


**Figure 3.** Proportion of unilateral versus simultaneous bilateral minimally invasive hallux valgus procedures by year (2018-2025).

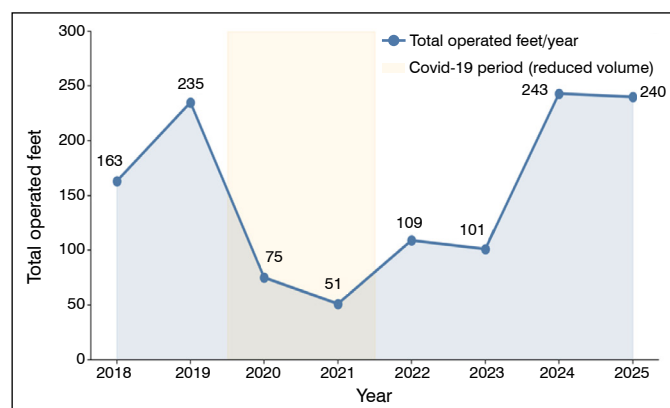


**Figure 1.** Annual surgical volume of minimally invasive hallux valgus procedures (2018-2025).

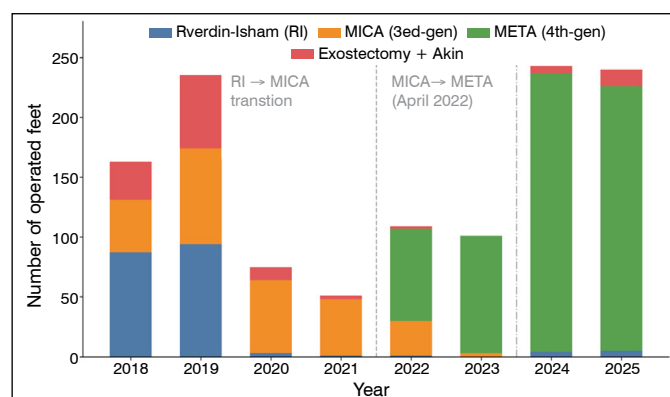


**Figure 2.** Annual distribution of minimally invasive hallux valgus techniques (2018-2025).

## DISCUSSION

The present study documents an eight-year trajectory of minimally invasive hallux valgus surgery at a single high-volume center, capturing the sequential transitions between operative techniques and the clinical and biomechanical evidence that motivated each change. To our knowledge, this represents one of the longest continuously documented single-team series of minimally invasive hallux valgus surgery in the literature, comprising 1,217 feet operated on across eight consecutive years by the same surgical partnership.

The initial institutional predominance of the RI osteotomy in 2018-2019 is consistent with the historical learning trajectory of percutaneous surgery programs internationally, in which first-generation techniques often served as accessible training platforms.<sup>18</sup>

In our practice, however, utilization of the RI technique declined progressively and was largely discontinued over time. This shift reflected a combination of factors observed during follow-up, including postoperative digital stiffness and a higher-than-acceptable rate of deformity recurrence, as well as the steep learning curve imposed on residents and fellows in training. This transition was accompanied by adoption of the MICA technique and was further supported by the two-year outcomes reported by Lewis and colleagues.<sup>7,26</sup>

Our institutional MICA experience between 2019 and early 2022 encompassed 264 feet and yielded outcomes consistent with the published literature. In a series of 69 feet with a mean follow-up of 27 months, mean AOFAS scores improved by 36.9 points and hallux valgus angle was corrected by a mean of 30.8°. In a companion series focused on severe deformities (mean preoperative hallux valgus angle 40.1 degrees, intermetatarsal angle 16.1 degrees), statistically significant corrections were achieved across all radiographic parameters.<sup>27</sup>

The transition to META in April 2022 was underpinned by two complementary rationales. Biomechanically, the chevron configuration carries an intrinsic risk: an overly long lateral wing may lack cortical purchase for bicortical proximal screw fixation, potentially

compromising construct stability and predisposing to fracture. The straight transverse cut of META eliminates this risk entirely.<sup>17</sup> Pedagogically, the linear cut is more consistently reproducible under fluoroscopic guidance by trainees and fellows, reducing radiation exposure and operative time during supervised cases, a consideration of practical importance at a teaching institution. The 12-month outcomes published by Lewis and colleagues for META validated this institutional choice.<sup>17</sup>

Over time, both the MICA and META techniques underwent progressive technical refinement in our practice, particularly with respect to fixation strategy and intraoperative correction maneuvers. One important modification was the management of the medial bony prominence after lateral translation of the first metatarsal head.<sup>28</sup> Rather than routine contouring with a wedge burr, we progressively adopted resection with the Shannon burr, which provided more efficient handling of the cortical medial prominence and facilitated a more controlled excision. In parallel, intraoperative assessment of first metatarsal pronation also evolved, with greater emphasis on fluoroscopic evaluation and technical maneuvers aimed at achieving rotational correction before definitive fixation. Together, these refinements improved the reproducibility of deformity correction and contributed to the maturation of both MICA and META as more reliable minimally invasive procedures over time.<sup>4,21,28,29</sup>

The META technique has evolved into a more reproducible minimally invasive procedure because its straight osteotomy is technically simpler to perform and easier to standardize than Chevron-type cuts. However, despite this advantage, fixation remains a critical challenge, particularly with respect to accurate screw trajectory, maintenance of correction, and control of multiplanar alignment.

For this reason, research efforts incorporating innovation and technology have been pursued, including the development of patient-specific 3D-printed instrumentation guides. As described in a recent technical report, these customized guides were designed to assist osteotomy execution and screw placement in fourth-generation minimally invasive hallux valgus surgery, with the aim of improving precision, enhancing safety, shortening operative time, and reducing radiation exposure.<sup>30</sup> As our osteotomy-based techniques evolved, systematic longitudinal follow-up also guided changes in the treatment of milder deformities. Use of the combined percutaneous exostectomy-Akin (EA) procedure progressively declined after clinical surveillance identified progressive valgus instability in a subset of patients with very mild hallux valgus. This was followed by a marked restriction in its indication, with a significant difference between 2018-2019 and 2022-2023 ( $p < 0.001$ ). Over the same period, mild cases that had previously been treated with EA were increasingly managed with MICA and, more recently, META, although EA was still used selectively in a small number of later cases.

These observations underscore the value of structured postoperative surveillance in assessing the durability of less invasive surgical strategies. A similar process was observed in bilateral simultaneous surgery. The reduction from 45.2% bilateral cases in 2024 to 34.0% in 2025 ( $p = 0.020$ ) followed institutional recognition of a higher fracture rate in bilateral cases, a finding that was subsequently confirmed in a published case-control study.<sup>31</sup>

Age was identified as the main risk factor, independently of bone mineral density, and this finding contributed to the adoption of stricter criteria for simultaneous bilateral surgery from 2025 onward. This sequence also illustrates how high-volume centers with prospective data registries can detect clinically relevant patterns before formal publication, allowing early refinement of surgical indications based on institutional evidence.

### Limitations

This study has several limitations. First, its retrospective design precludes causal inference regarding the effect of each technical

transition on outcomes. Changes in practice occurred over time within a dynamic clinical environment and were likely influenced by multiple factors, including surgeon experience, refinement of intraoperative technique, evolving case selection, and broader institutional changes.

Second, the analysis was designed to describe institutional practice evolution rather than to compare patient-level clinical or radiographic outcomes among techniques; those outcome data have been reported separately elsewhere. Third, the experience reflects a single high-volume center with a stable surgical team and a predominantly older patient population, which may differ from the case mix, resources, and training structure of other institutions. Finally, because some treatment indications continued to evolve during the later years of the study, particularly for selected mild deformities, ongoing follow-up remains necessary.

### Interpretation

The present findings show how structured longitudinal surveillance can shape surgical practice in a meaningful way, even outside the setting of randomized trials. Over the study period, each major change in institutional strategy was driven by patterns observed during routine clinical follow-up and then incorporated into subsequent decision-making. In this sense, the study does not present technique evolution as a sequence of isolated technical preferences, but rather as a cumulative process of observation, reassessment, and refinement.

The transitions from RI to MICA, from MICA to META, the progressive restriction of EA as a routine option for mild deformity, and the restriction of simultaneous bilateral procedures all emerged from this iterative process. These data suggest that, in experienced centers with prospective registries, careful monitoring of real-world outcomes can generate practice-relevant evidence that complements the published literature and supports earlier modification of surgical indications.

### Generalizability

Although the specific timeline and technical sequence reported here reflect the experience of a single referral center, the broader lessons are likely relevant to other minimally invasive hallux valgus programs. Centers adopting these procedures may encounter similar phases of transition as they move from earlier-generation techniques toward more reproducible osteotomy-based methods and refine their indications based on observed outcomes.

At the same time, direct extrapolation of our frequencies, thresholds, or institutional preferences should be made with caution, as these may vary according to patient age, bone quality, surgeon experience, training environment, and local follow-up infrastructure. Even so, the central principle appears broadly applicable: prospective outcome monitoring within a high-volume clinical practice can serve as a practical tool for improving patient selection, refining technique, and identifying specific situations in which older procedures may still retain value.

### CONCLUSION

Over eight years and 1,217 operated feet, minimally invasive hallux valgus surgery at our center evolved from Reverdin-Isham to MICA and ultimately to META as the institutional standard. This progression was guided by continuous technical refinement and structured outcome monitoring. META emerged as the preferred technique because it improved reproducibility and simplified execution, while the exostectomy-Akin approach was no longer used routinely and bilateral indications became more restrictive based on observed postoperative outcomes. These findings illustrate how prospective surveillance in a high-volume practice can support evidence-based evolution of minimally invasive hallux valgus surgery.

## CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. GFF and MVPF: Conceptualization; Methodology; Investigation; Data curation; Formal analysis; Writing – original draft. All authors: Writing – review & editing; Validation; Approval of the final version of the manuscript.

## DATA AVAILABILITY DECLARATION

The data cannot be made publicly available.

## REFERENCES

1. Cai Y, Song Y, He M, He W, Zhong X, Wen H, et al. Global prevalence and incidence of hallux valgus: a systematic review and meta-analysis. *J Foot Ankle Res.* 2023;16(1):63. doi: 10.1186/s13047-023-00661-9.
2. Ferreira GF, Stéfani KC. A global bibliometric analysis of hallux valgus research (1999-2019). *J Foot Ankle Surg.* 2021;60(3):501-6. doi: 10.1053/j.jfas.2020.09.016.
3. Ferreira GF, Borges VQ, Moraes LVdM, Stéfani KC. Percutaneous chevron/Akin (PECA) versus open scarf/Akin (SA) osteotomy treatment for hallux valgus: A systematic review and meta-analysis. *PLoS One.* 2021;16(2):e0242496. doi: 10.1371/journal.pone.0242496.
4. Ferreira GF, Mattos e Dinato MC MCME, Santos TFD, Miziara P, Pereira Filho MV. CAN THE PERCUTANEOUS CHEVRON AND AKIN (PECA) TECHNIQUE CORRECT THE PRONATION OF THE FIRST METATARSAL IN HALLUX VALGUS?. *Acta Ortop Bras.* 2023;31(spe2):e265206. doi: 10.1590/1413-785220233102e265206.
5. Nunes GA, Ferreira GF, Baumfeld T, Filho MVP, Baumfeld D, Lam P. Minimally Invasive Chevron Akin: Locking The Metatarsal-Cuneiform Joint. *Foot Ankle Spec.* 2024;17(4):336-42. doi: 10.1177/19386400221079155.
6. Redfern D, Vernois J, Legré BP. Percutaneous surgery of the forefoot. *Clin Podiatr Med Surg.* 2015;32(3):291-332. doi: 10.1016/j.fcp.2015.03.007.
7. Vernois J, Redfern DJ. Percutaneous surgery for severe hallux valgus. *Foot Ankle Clin.* 2016;21(3):479-93. doi: 10.1016/j.fcl.2016.04.002.
8. Del Vecchio JJ, Ghioldi ME. Evolution of minimally invasive surgery in hallux valgus. *Foot Ankle Clin.* 2020;25(1):79-95. doi: 10.1016/j.fcl.2019.10.010.
9. Bauer T, Biau D, Lortat-Jacob A, Hardy P. Percutaneous hallux valgus correction using the reverdin-Isham osteotomy. *Orthop Traumatol Surg Res.* 2010;96(4):407-16. doi: 10.1016/j.otsr.2010.01.007.
10. Biz C, Belluzzi E, Crimi A, Sciarretta G, Bortolato E, Ruggieri P. The Learning Curve of Reverdin-Isham and Akin Percutaneous Osteotomies for Hallux Valgus Correction: A Bayesian Approach. *J Clin Med.* 2025;14(6):1921. doi: 10.3390/jcm14061921.
11. Sanchís-Soria V, Nieto-González E, Nieto-García E, Fernández-Ehrling N, Ferrer-Torregrosa J, Lorca-Gutiérrez R. Radiological and functional outcomes of Reverdin Isham osteotomy in moderate Hallux Valgus: a systematic review and meta-analysis. *Sci Rep.* 2024;14(1):14781.
12. Severyns M, Carret P, Brunier-Agot L, Debandt M, Odri GA, Rouvillain J. Musculoskeletal Surg. 2018;103(2):161-6. doi: 10.1007/s12306-018-0563-7.
13. Bosch P, Wanke S, Legenstein R. Hallux valgus correction by the method of Bösch: a new technique with a seven-to-ten-year follow-up. *Foot Ankle Clin.* 2000;5(3):485-98, v-vi.
14. Trnka HJ. Percutaneous, MIS and open hallux valgus surgery. *EFORT Open Rev.* 2021;6(6):432-8. doi: 10.1302/2058-5241.6.210029.
15. Lee M, Walsh J, Smith MM, Ling J, Wines A, Lam P. Hallux valgus correction comparing percutaneous chevron/Akin (PECA) and open scarf/Akin osteotomies. *Foot Ankle Int.* 2017;38(8):838-46. doi: 10.1177/1071100717704941.
16. Lai MC, Rikhras IS, Woo YL, Yeo W, Ng YCS, Koo K. Clinical and radiological outcomes comparing percutaneous chevron-Akin osteotomies vs open scarf-Akin osteotomies for hallux valgus. *Foot Ankle Int.* 2017;39(3):311-7. doi: 10.1177/1071100717745282.
17. Lewis TL, Lau B, Alkhalfan Y, Trowbridge S, Gordon D, Vernois J, et al. Fourth-Generation minimally invasive hallux valgus surgery with metaphyseal extra-Articular transverse and akin osteotomy (META): 12 month clinical and radiologic results. *Foot Ankle Int.* 2023;44(3):178-91. doi: 10.1177/10711007231152491.
18. Isham SA. The Reverdin-Isham procedure for the correction of hallux abducto valgus. A distal metatarsal osteotomy procedure. *Clin Podiatr Med Surg.* 1991;8(1):81-94.
19. Ferraz Ferreira G, Araujo Nunes G, Fiorin da Costa G, Mattos e Dinato MC, Lorchan Lewis T, Ray R, et al. Is akin fixation necessary in the percutaneous chevron and akin osteotomies (PECA) technique? A retrospective comparative study with 2-year follow-up. *Eur J Orthop Surg Traumatol.* 2025;35(1):212. doi: 10.1007/s00590-025-04316-2.
20. Ferreira GF, Nunes GA, Dorado DS, Mattos e Dinato MC, Lewis TL, Sato G, et al. Minimally invasive chevron-Akin (MICA) osteotomies without akin fixation in hallux valgus correction: a case series with 2-year follow-up. *Eur J Orthop Surg Traumatol.* 2024;34(5):2339-45. doi: 10.1007/s00590-024-03924-8.
21. Ferreira GF, Nunes GA, Dorado DS, Mattos e Dinato MC, Lewis TL, Ray R, et al. Correction of first metatarsal pronation in metaphyseal extra-articular transverse osteotomy for hallux valgus correction. *Foot Ankle Orthop.* 2023;8(3):24730114231198527. doi: 10.1177/24730114231198527.
22. Ferreira GF, de Miranda CRE, Mataréio MVdP, Sevilla D, Patriarcha VA, Lewis TL, et al. Mayo versus ankle block in minimally invasive hallux valgus surgery: A comparative study. *Foot Ankle Surg.* 2026;32(1):78-84. doi: 10.1016/j.fas.2025.06.007.
23. Stefani KC, Ferreira GF, Pereira Filho MV. Postoperative Analgesia Using Peripheal Anesthetic Block of the Foot and Ankle. *Foot Ankle Int.* 2018;39(2):196-200. doi: 10.1177/1071100717739670.
24. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010.
25. R Core Team. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2024. Available from: <https://www.R-project.org/>.
26. Lewis TL, Ray R, Miller G, Gordon DJ. Third-Generation Minimally Invasive Chevron and Akin Osteotomies (MICA) in Hallux Valgus Surgery: Two-Year Follow-up of 292 Cases. *J Bone Joint Surg Am.* 2021;103(13):1203-11. doi: 10.2106/jbjs.20.01178.
27. Nunes GA, de Carvalho KAM, Ferreira GF, Filho MVP, Baptista AD, Zambelli R, et al. Minimally invasive chevron akin (MICA) osteotomy for severe hallux valgus. *Arch Orthop Trauma Surg.* 2023;143(9):5507-14. doi: 10.1007/s00402-023-04849-3.
28. Ferreira GF, Nunes GA, Mattos e Dinato MC, Pedrosa JP, Lewis TL, Lam P, et al. Technique tip: medial prominence bone spur resection in the third-generation percutaneous chevron-Akin osteotomy technique (PECA) for hallux valgus correction. *Foot Ankle Surg.* 2022;28(4):460-3. doi: 10.1016/j.fas.2021.11.004.
29. Lewis TL, Ferreira GF, Nunes GA, Lam P, Ray R. Impact of Sesamoid Coverage on Clinical Foot Function Following Fourth-Generation Percutaneous Hallux Valgus Surgery. *Foot Ankle Orthop.* 2024;9(1):24730114241230560. doi: 10.1177/24730114241230560.
30. Ferreira GF, Nunes GA, Banca VL, Michaelis LF, Lewis TL, Ray R, et al. Minimally invasive hallux valgus surgery using 3D printed patient specific instrumentation. *Arch Orthop Trauma Surg.* 2024;144(6):2553-9. doi: 10.1007/s00402-024-05383-6.
31. Ferreira GF, Proença DS, Araujo GF, Porto RS, Sevilla D, Araujo Nunes G, et al. Risk factors for first metatarsal fracture in minimally invasive hallux valgus surgery. *Bone Joint J.* 2026;108-B(3):361-8. doi: 10.1302/0301-620x.108b3.bjj-2025-0253.r1.

# ACETABULAR RECONSTRUCTION USING CUP-ON-CUP AND CUP-CAGE TECHNIQUES IN PAPROSKY IIC, IIIA, AND IIIB DEFECTS: A CASE SERIES WITH CLINICAL AND RADIOGRAPHIC EVALUATION

## RECONSTRUÇÃO ACETABULAR PELAS TÉCNICAS CUP-ON-CUP E CUP-CAGE EM DEFEITOS PAPROSKY IIC, IIIA E IIIB: SÉRIE DE CASOS COM AVALIAÇÃO CLÍNICA E RADIOGRÁFICA

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### ABSTRACT

**Purpose:** To describe the clinical and radiographic outcomes of the cup-on-cup and cup-cage techniques in Paprosky IIC, IIIA, and IIIB acetabular defects in hip revision surgery. **Patients and methods:** Retrospective case series involving 13 patients who underwent acetabular component revision using cup-on-cup (n=7) or cup-cage (n=6), with defects classified as Paprosky IIC, IIIA, or IIIB and minimum follow-up of 24 months. The factors evaluated were range of motion, flexion strength, claudication, dysmetria, and radiographic restoration of the hip center of rotation. **Results:** Mean age was  $67.5 \pm 12.0$  years and mean follow-up  $54.2 \pm 33.6$  months. Acetabular osteolysis was present in 76.9% of cases. Center of rotation restoration was achieved in 66.7% of cup-cage cases and 42.9% of cup-on-cup group. Mean active flexion was  $91.7^\circ$  and  $85.7^\circ$ , respectively. One dislocation (7.7%) was treated with closed reduction. No periprosthetic infection or reoperation was recorded. **Conclusions:** Both techniques demonstrated satisfactory outcomes in severe acetabular defects, with no major complications. The choice of techniques should be individualized based on the severity of the defect, the surgeon's experience, and the availability of the implant. **Level of Evidence IV; Case Series.**

**Keywords:** Acetabulum; Arthroplasty, Replacement, Hip; Hip Joint; Arthroplasty, Replacement.

### RESUMO

**Objetivo:** Descrever os resultados clínicos e radiográficos das técnicas cup-on-cup e cup-cage em defeitos acetabulares Paprosky IIC, IIIA e IIIB na cirurgia de revisão da artroplastia de quadril. **Pacientes e métodos:** Série de casos retrospectiva envolvendo 13 pacientes submetidos à revisão do componente acetabular utilizando as técnicas cup-on-cup (n=7) ou cup-cage (n=6), com defeitos classificados como Paprosky IIC, IIIA ou IIIB e seguimento mínimo de 24 meses. Foram avaliados: amplitude de movimento, força de flexão, claudicação, dismetria e restauração radiográfica do centro de rotação do quadril. **Resultados:** A média de idade foi de  $67,5 \pm 12,0$  anos e o tempo médio de seguimento foi de  $54,2 \pm 33,6$  meses. Osteólise acetabular estava presente em 76,9% dos casos. A restauração do centro de rotação foi alcançada em 66,7% dos casos do grupo cup-cage e em 42,9% do grupo cup-on-cup. A flexão ativa média foi de  $91,7^\circ$  e  $85,7^\circ$ , respectivamente. Um caso de deslocamento (7,7%) foi tratado com redução fechada. Não foram registrados casos de infecção periprotética ou reoperação. **Conclusões:** Ambas as técnicas demonstraram resultados satisfatórios em defeitos acetabulares graves, sem complicações maiores. A escolha da técnica deve ser individualizada com base na gravidade do defeito, na experiência do cirurgião e na disponibilidade do implante. **Nível de Evidência IV; Série de Casos.**

**Descritores:** Acetábulo; Artroplastia de Quadril; Articulação do Quadril; Artroplastia de Substituição.

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### INTRODUCTION

Total hip arthroplasty is recognized as one of the surgical procedures with the greatest impact on the quality of life of patients with degenerative joint disease. Projections predict a 137% increase

in the volume of revision surgeries in the United States between 2005 and 2030.<sup>1</sup> Regarding revisions, acetabular reconstruction represents one of the greatest technical challenges in orthopedics,

All authors declare no potential conflict of interest related to this article.

The study was conducted at Hospital de Clínicas of the Universidade Estadual de Campinas (UNICAMP).

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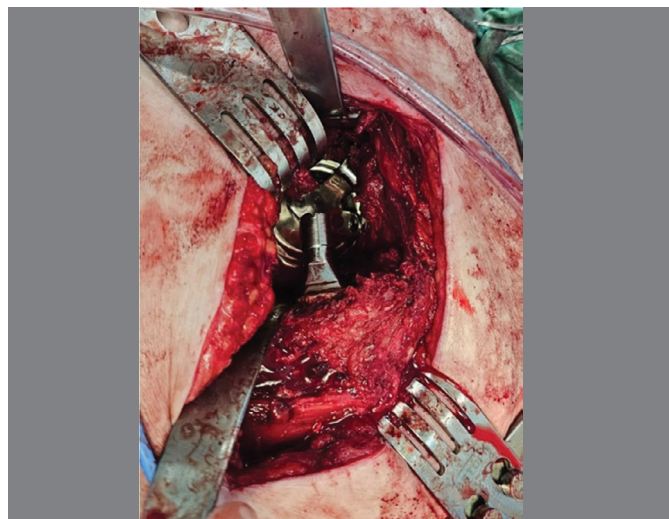


<< SUMÁRIO

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particularly when associated with extensive bone loss resulting from aseptic osteolysis, implant loosening, or septic failure.<sup>2-4</sup> Several classification systems have been proposed to stratify acetabular defects. One of the main ones is the Paprosky system, proposed in 1994, which remains the most widely used for evaluating acetabular defects in revision surgeries. It classifies bone loss based on location, extent of the defect, and integrity of the acetabular columns.<sup>5-7</sup> Defects of types IIC, IIIA, and IIIB represent a high degree of reconstruction complexity, characterized by a superiorly migrated center of rotation, extensive ischiatic osteolysis, compromise of the Köhler line, and bone-to-implant contact of less than 50% of the available acetabular surface.<sup>4,7,8</sup> The lack of consensus regarding the best surgical technique to be used in the revision of acetabular defects reflects the challenge, the surgical difficulty, and the diversity of available implants.<sup>9</sup>

Several techniques have been used to manage severe acetabular defects, including *jumbo cups*, ultra-porous cups, wedges/porous metal blocks, structural allografts, customized triflanged implants (CTAC), cup-on-cup and cup-cage techniques.<sup>4,7-11</sup> In defects classified as type III without pelvic discontinuity, the combination of a porous hemispherical cup with trabecular metal wedges currently constitutes the gold standard, with survival rates exceeding 90% at ten years.<sup>7,12</sup> In defects with pelvic discontinuity or in those where stable primary fixations cannot be achieved with a dome and wedges alone, the cup-cage technique (Figure 1, 2a and 2b) appears to be the alternative offering greater immediate stability.<sup>7,9,13,14</sup> Systematic reviews show an overall revision rate of 8% and a complication rate of 20% for this technique. Dislocation is the most frequent complication.<sup>14</sup> Series with a mean follow-up exceeding ten years report a 90% survival rate without failures due to aseptic loosening. These data corroborate the concept that the technique's success results from the combination of immediate mechanical stability and progressive biological integration, regardless of the material used.<sup>15</sup> The cup-on-cup technique represents an alternative for severe superior acetabular defects (Figures 3a and 3b). It is performed using two combined acetabular cups, which allows for flexibility in adapting to the bony defect and eliminates the need for prolonged preoperative planning.<sup>1,16,17</sup> The majority of Brazil's public orthopedic health services have limited and restricted availability of modern implants or allograft from bone banks. The two techniques described in this study can be performed by any orthopedic surgeon, as they use materials widely available.



Original image from the authors' institution.

**Figure 1.** Intraoperative image of a cup-cage surgery technique.

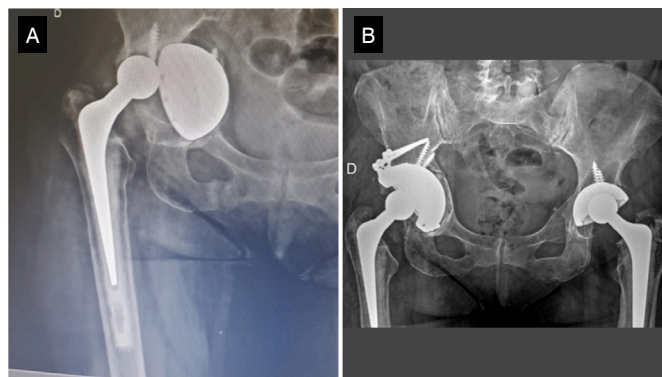


**Figure 2.** A. Preoperative radiograph of a cup-cage. B. Postoperative radiograph of a cup-cage.

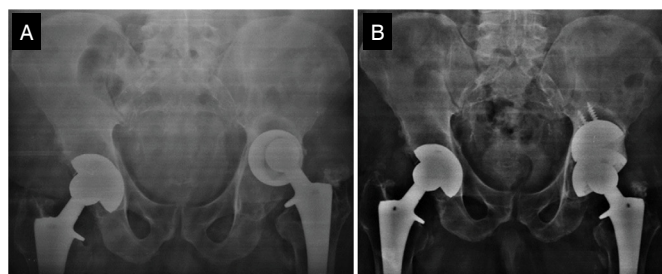


**Figure 3.** A. preoperative radiograph of a 3A acetabular defect. B. Postoperative radiograph of a cup-on-cup technique.

Despite the promising results described individually for each technique, direct comparisons between cup-on-cup and cup-cage in the same population with Paprosky defects IIC, IIIA, and IIIB remain scarce in the literature. The present study aims to describe the clinical and radiographic outcomes of these two techniques in patients undergoing acetabular revision at a hip surgery referral center.

## MATERIALS AND METHODS

This is a retrospective case series study. The surgeries were performed by orthopedic hip surgeons at the Hospital de Clínicas of the State University of Campinas (UNICAMP) between November 2017 and April 2024.

The study was approved by the Research Ethics Committee of the UNICAMP School of Medical Sciences under Opinion No. 7,094,490, CAAE: 81213724.5.0000.5404.

The authors declare that they have no conflicts of interest.

Adult patients who underwent revision of the acetabular component of total hip arthroplasty using cup-on-cup or cup-cage were included, with acetabular defects classified as Paprosky IIC, IIIA, or IIIB, and a minimum follow-up of 24 months. Patients with incomplete clinical and/or radiographic data were excluded. Ultimately, 13 cases were included in the analysis.

The bone-loss classification used for the analysis was Paprosky's, based on preoperative radiographs and confirmed intraoperatively. The criteria used to decide between cup-on-cup or cup-cage were based on intraoperative findings and the correction of specific defects. A modified cup-cage technique was used in IIC cases when jumbo cups could not provide adequate bone fixation. The cage used in the cases was made of stainless steel combined with a titanium cup. The original technique proposed by Gross, 2016 uses a titanium cage.<sup>22</sup>

The data collected were: age at surgery, year of surgery, Paprosky's classification, presence of acetabular osteolysis, presence of a contralateral prosthesis, degree of claudication, lower limb length

discrepancy (in centimeters), hip flexion strength, postoperative range of motion (active and passive flexion, extension, abduction, and adduction, in degrees), and radiographic restoration of the hip center of rotation (assessed by anteroposterior pelvic radiography in the standing position, based on the position of the femoral head relative to the interlacral line and the ilioischial line on the contralateral side).

Limping was assessed using a subscore of the Harris Hip Score (HHS), a validated and widely used instrument for evaluating hip arthroplasty outcomes: Grade 0 — normal gait, completely painless and balanced; Grade I — mild claudication, detectable only by professionals; Grade II — perceptible claudication, such as a slight pelvic drop generating abnormal movement; and Grade III — pronounced and visible claudication, accompanied by a strong lateral trunk sway.

The composite factors in the primary outcome were the clinical and radiographic results of the techniques. Postoperative complications were recorded, including dislocation, periprosthetic infection, and the need for reoperation.

Descriptive statistical analysis was used, with means, standard deviations, minimum and maximum values calculated for numerical variables, and absolute and relative frequencies for categorical variables.

## RESULTS

Thirteen cases were included with a mean age of  $67.5 \pm 12.0$  years (34–81 years). In 6 cases, the cup-cage was performed (46.2%), and in 7, the cup-on-cup (53.8%), with a mean follow-up of  $54.2 \pm 33.6$  months (24–129 months). According to Paprosky classification, three cases presented type IIC defects (23.1%), seven type IIIA defects (53.8%), and three type IIIB defects (23.1%). At 2 years postoperatively, x-ray showed acetabular osteolysis in 10 patients (76.9%), and a contralateral prosthesis was found in 2 (15.4%). The demographic and clinical data are shown in Table 1.

Cup-cage group: 6 cases, with a mean age of  $70.7 \pm 9.0$  years (60–81 years) and a mean follow-up of  $69.0 \pm 40.2$  months (24–129 months). Defects were type IIC in three cases (50.0%), IIIA in one case (16.7%), and IIIB in two cases (33.3%). No cases had a contralateral prosthesis, and acetabular osteolysis was present in 4 patients (66.7%).

Cup-on-cup group: 7 cases, with a mean age of  $64.7 \pm 14.3$  years (34–78 years) and a mean follow-up of  $41.6 \pm 22.7$  months (24–69 months). The defects were type IIIA in 6 cases (85.7%) and type IIIB in 1 case (14.3%), with no cases of type IIC. Osteolysis was identified in 6 patients (85.7%), and a contralateral prosthesis in 2 (28.6%).

## Functional results

Mean active flexion was  $88.5 \pm 17.2^\circ$  and passive flexion  $98.5 \pm 14.1^\circ$ . Extension was  $16.2 \pm 5.1^\circ$ , abduction  $27.3 \pm 4.4^\circ$ , and adduction  $30.0 \pm 7.1^\circ$ . In ten patients (76.9%), flexion strength was preserved; three (23.1%) had a deficit. According to the HHS limp subscore, Grade I was observed in six patients (46.2%), Grade II in four (30.8%), and Grade III in three (23.1%); in one of former, limping was attributed to contralateral hip arthritis and distal femur periprosthetic fracture with malunion (Figures 4a–4c). No patient was classified as Grade 0.

Lower limb length discrepancy was identified in seven patients (53.8%, six in the cup-on-cup group and one in the cup-cage), with a mean of  $0.62 \pm 0.74$  cm. Most cases had soft-tissue scars with superior migration, so limb length could not be restored. No significant association was found between the degree of limping and lower limb length discrepancy.

In the cup-cage group, mean active flexion was  $91.7 \pm 17.2^\circ$ , passive flexion  $101.7 \pm 13.3^\circ$ , extension  $16.7 \pm 5.2^\circ$ , abduction  $25.8 \pm 4.9^\circ$ ,

**Table 1.** Demographic and clinical characteristics of the overall series.

| Variable                          | Overall (n=13)  | Cup-cage (n=6)  | Cup-on-cup (n=7) |
|-----------------------------------|-----------------|-----------------|------------------|
| Age (years), mean $\pm$ SD        | 67.5 $\pm$ 12.0 | 70.7 $\pm$ 9.0  | 64.7 $\pm$ 14.3  |
| Minimum–maximum age (years)       | 34–81           | 60–81           | 34–78            |
| Follow-up (months), mean $\pm$ SD | 54.2 $\pm$ 33.6 | 69.0 $\pm$ 40.2 | 41.6 $\pm$ 22.7  |
| Min. – max. follow-up (months)    | 24–129          | 24–129          | 24–69            |
| Paprosky IIC, n (%)               | 3 (23.1%)       | 3 (50.0%)       | 0 (0%)           |
| Paprosky IIIA, n (%)              | 7 (53.8%)       | 1 (16.7%)       | 6 (85.7%)        |
| Paprosky IIIB, n (%)              | 3 (23.1%)       | 2 (33.3%)       | 1 (14.3%)        |
| Acetabular osteolysis, n (%)      | 10 (76.9%)      | 4 (66.7%)       | 6 (85.7%)        |
| Contralateral prosthesis, n (%)   | 2 (15.4%)       | 0 (0%)          | 2 (28.6%)        |

Abbreviations: n, number; COR, SD, standard deviation.

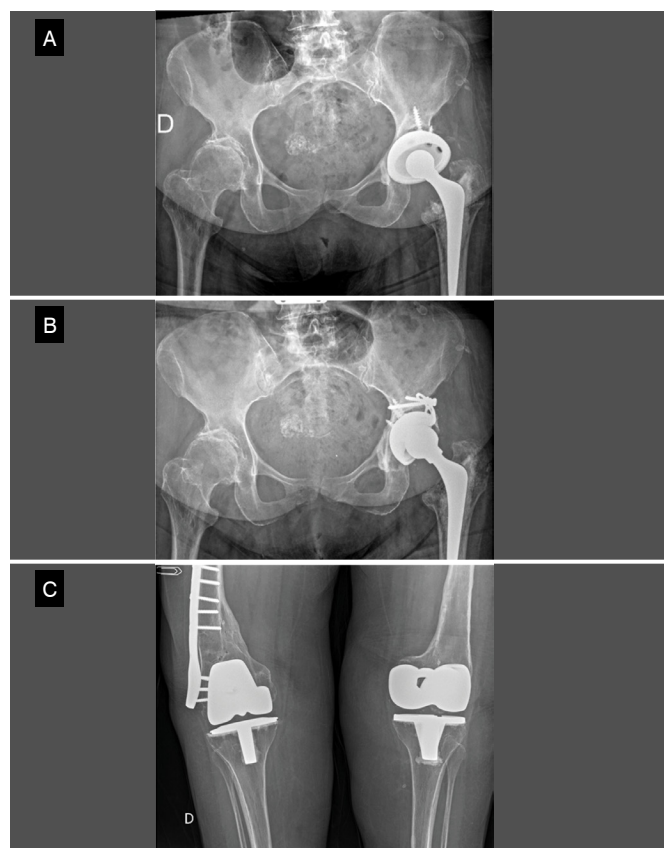


**Figure 4.** A. preoperative radiograph. B. Postoperative radiograph of a cup-cage. C. sequelae of periprosthetic femoral fracture of the knee.

and adduction  $28.3 \pm 7.5^\circ$ . Flexion strength was preserved in five cases (83.3%), and dysmetria was present in one case (16.7%), with a mean of  $0.08 \pm 0.20$  cm. In the classification of limp, Grade I was observed in 2 patients (33.3%), Grade II in 2 (33.3%), and Grade III in 2 (33.3%).

In the cup-on-cup group, mean active flexion was  $85.7 \pm 18.1^\circ$ , passive flexion  $95.7 \pm 15.1^\circ$ , extension  $15.7 \pm 5.3^\circ$ , abduction  $28.6 \pm 3.8^\circ$ , and adduction  $31.4 \pm 6.9^\circ$ . Preserved flexion strength was found in 5 cases (71.4%), and dysmetria was present in 6 (85.7%) - mean of  $1.07 \pm 0.73$  cm. In the classification of limp, Grade I was observed in 4 patients (57.1%), Grade II in 2 (28.6%), and Grade III in 1 (14.3%).

## Restoration of the center of rotation

Restoration of the hip center of rotation was achieved in seven cases (53.8%); in the cup-cage group, it was achieved in four of six cases (66.7%); in the cup-on-cup group, it was achieved in three

of seven cases (42.9%). One dislocation occurred in the cup-cage group (16.7%), treated with closed reduction without reoperation. No periprosthetic infection, reoperation, or prosthetic loosening was recorded. Detailed functional data are presented in Tables 2 and 3.

**Table 2.** Postoperative functional results.

| Variable                          | Overall (n=13) | Cup-cage (n=6) | Cup-on-cup (n=7) |
|-----------------------------------|----------------|----------------|------------------|
| Active flexion (°), mean ± SD     | 88.5 ± 17.2    | 91.7 ± 17.2    | 85.7 ± 18.1      |
| Passive flexion (°), mean ± SD    | 98.5 ± 14.1    | 101.7 ± 13.3   | 95.7 ± 15.1      |
| Extension (°), mean ± SD          | 16.2 ± 5.1     | 16.7 ± 5.2     | 15.7 ± 5.3       |
| Abduction (°), mean ± SD          | 27.3 ± 4.4     | 25.8 ± 4.9     | 28.6 ± 3.8       |
| Adduction (°), mean ± SD          | 30.0 ± 7.1     | 28.3 ± 7.5     | 31.4 ± 6.9       |
| Normal flexion strength, n (%)    | 10 (76.9%)     | 5 (83.3%)      | 5 (71.4%)        |
| Decreased flexion strength, n (%) | 3 (23.1%)      | 1 (16.7%)      | 2 (28.6%)        |
| No asymmetry, n (%)               | 6 (46.2%)      | 5 (83.3%)      | 1 (14.3%)        |
| Asymmetry present, n (%)          | 7 (53.8%)      | 1 (16.7%)      | 6 (85.7%)        |
| Asymmetry (cm), mean ± SD         | 0.62 ± 0.74    | 0.08 ± 0.20    | 1.07 ± 0.73      |

Abbreviations: n, number; cm, centimeter.

**Table 3.** Limping and restoration of the center of rotation.

| Variable                            | Overall (n=13) | Cup-cage (n=6) | Cup-on-cup (n=7) |
|-------------------------------------|----------------|----------------|------------------|
| Limp Grade I, n (%)                 | 6 (46.2%)      | 2 (33.3%)      | 4 (57.1%)        |
| Limp Grade II, n (%)                | 4 (30.8%)      | 2 (33.3%)      | 2 (28.6%)        |
| Limp Grade III, n (%)               | 3 (23.1%)      | 2 (33.3%)      | 1 (14.3%)        |
| Restoration of the COR — Yes, n (%) | 7 (53.8%)      | 4 (66.7%)      | 3 (42.9%)        |
| COR restoration — No, n (%)         | 6 (46.2%)      | 2 (33.3%)      | 4 (57.1%)        |
| Dislocation, n (%)                  | 1 (7.7%)       | 1 (16.7%)      | 0 (0%)           |
| Periprosthetic infection, n (%)     | 0 (0%)         | 0 (0%)         | 0 (0%)           |
| Reoperation, n (%)                  | 0 (0%)         | 0 (0%)         | 0 (0%)           |

Abbreviations: n, number; COR, center of rotation.

## DISCUSSION

Treating Paprosky IIC, IIIA, and IIIB acetabular defects remains one of the greatest challenges in hip revision arthroplasty.<sup>4,7,8</sup> These defects require careful planning, surgical expertise, and specific implants. This study describes the experience of a referral center with 13 patients who underwent surgery using the cup-cage and cup-on-cup techniques, followed for a mean of 54.2 months, with 1 case of dislocation treated with closed reduction. There were no other complications or reoperations during follow-up.

Chiarlone et al. obtained similar results in their case series, with no cases of aseptic loosening or dislocation.<sup>18</sup> Systematic reviews on cup-on-cup arthroplasty report dislocation rates of around 9% and infection rates of around 4%, with an overall complication rate of 20%.<sup>14</sup> With 131 cases and 7.7 years of follow-up, Chaudhry et al. documented dislocation in 7.6% and infection in 9.1%.<sup>19</sup> In contrast, Chen et al. did not identify aseptic loosening over more than ten years of follow-up—dislocation and infection each occurred in 7% of cases.<sup>15</sup> In the study by Cano et al. involving the reconstruction of Paprosky type III acetabular defects using reconstruction rings, a similar complication profile was observed; no intraoperative complications were recorded, but there was a 17.39% rate of postoperative dislocation, all cases of which were resolved via closed reduction.<sup>20</sup>

These findings are consistent with the present study, despite the small sample size. Hip center of rotation restoration was achieved in 53.8% of cases in the overall series, with better performance in the cup-cage group (66.7%) compared to the cup-on-cup group

(42.9%). This is considered a fundamental goal of acetabular revision surgery, as it directly impacts abductor muscle function and implant stability/longevity.<sup>1,12</sup> Du et al. reported correction of superior displacement of the center of rotation from 60.9 mm to 31.7 mm in cup-on-cup cases for IIIB defects.<sup>16</sup> Webb et al., however, demonstrated a reduction from 55.7 mm to 22.5 mm in a series of 20 cases using the cup-on-cup technique.<sup>17</sup> The lower rate of satisfaction observed in the cup-on-cup group in this study may reflect the greater complexity of the defects treated in this group, predominantly IIIA (85.7%), with no cases of IIC defects, compared to the cup-cage group, where IIC defects were more frequent.

In the cup-on-cup group, there was a higher prevalence of vertical elevation of the center of rotation (85.7% of cases, mean 1.07 cm) than in the cup-cage group (16.7%, mean 0.08 cm). This difference is likely related to the greater severity of the acetabular defects treated by the cup-on-cup technique in this study, as well as to the limitations inherent in restoring femoral offset in defects with significant superior migration of the center of rotation.<sup>12,14</sup> In the study by Chaudhry et al., a significant improvement in dysmetria from 12.2 mm to 3.9 mm was documented with the cup-cage,<sup>19</sup> reinforcing that the appropriate choice of technique, guided by the severity of the defect, is crucial for correcting this parameter. Intraoperative soft-tissue contracture and superior migration due to bone loss were identified as the primary limiting factors when length discrepancy was not achieved.

Both groups exhibited very similar ranges of motion, with no significant difference between the groups. Both groups exhibited very similar ranges of motion, with no significant difference between the groups. Flexion strength remained normal in most patients, but in three (23.1%) that may be attributed to iliopsoas dysfunction, as this muscle is vulnerable in hips with significant superior migration of the center of rotation and a history of multiple previous surgical interventions.<sup>4,8</sup>

We found encouraging data in the literature regarding the cup-on-cup technique and cup-cage in studies with long-term follow-up. In a study by Chen et al., a 10-year survival rate of 90% was observed (2), and Chaudhry et al. reported a 95.5% survival rate for aseptic loosening.<sup>19</sup> For the cup-on-cup technique, follow-up data are even more limited, with a shorter average follow-up period of less than 5 years.<sup>1,16,17</sup> In one of the largest comparative studies, involving 180 cases of Paprosky IIIA and IIIB, Tarabichi et al. did not identify a statistically significant difference in survival between the techniques and implants. This study evaluated the rates of dislocation or infection among porous metal wedges, cup-cages, and custom triflanged implants, including cases with pelvic discontinuity<sup>21</sup>, suggesting that the surgeon's experience and the appropriateness of the technique to the specific defect are determining factors for outcome.

Regarding the study's limitations, we note the small sample size and the retrospective design, which preclude a more comprehensive comparative statistical analysis between the techniques. The heterogeneity in the distribution of cases across classification and technique type also limits the comparative analysis between the cup-cage and the cup-on-cup technique. The absence of functional scores, such as the Harry Hip Score, also presents an additional limitation. Future studies with larger sample sizes and longer follow-up periods are needed.

## CONCLUSION

Cases treated with cup-on-cup and cup-cage showed promising functional and radiographic outcomes. The center of rotation was restored more frequently in the cup-cage. Dysmetria, however, was more common in the cup-on-cup group, likely related to the severe bone loss defects predominant in that group. Mobility and flexion strength were preserved in most patients in both groups.

No single technique is absolutely superior to another. The choice of technique depends on the defect present, the surgeon's experience, and the implant available at the time of surgery. The techniques evaluated in this study represent good alternatives given the limitations in material availability found in most public health care systems. The study is particularly relevant in underdeveloped countries, where limited access to more expensive implants makes

"cup-on-cup" and "cup-on-cage" techniques viable alternatives, enabling the resolution of complex acetabular defects.

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## CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. STA: Conceptualization, Methodology, and Writing – original draft. SR: Data curation and investigation. PG: Data curation and investigation. MSC: Data curation and investigation. CFF: Conceptualization, Supervision, and Writing – review and editing. PRG: Conceptualization, Supervision, and Writing – review and editing.

## DATA AVAILABILITY DECLARATION

The contents underlying the research are available in the manuscript.

## REFERENCE

- Li W, Liu D, Liu X, Li X. Application of Intraoperative Individualized Cup Combination-Cup-on-Cup Technique in Severe Acetabular Defects. *Orthop Surg*. 2024;16(11):2853-61. doi: 10.1111/os.14248.
- Kumar S, Kulshrestha V, Padhi P, Datta B, Gogoi B, Sood M. "Cup-in-Cup technique" in the management of acetabular defects in hip arthroplasty: early to midterm results. *Clin Orthop Surg*. 2025;17(6):940-9. doi: 10.4055/cios25105.
- Miettinen HJ, Miettinen SS, Kettunen JS, Jalkanen J, Kröger H. Revision hip arthroplasty using a porous tantalum acetabular component. *Hip Int*. 2020;31(6):782-8. doi: 10.1177/1120700020913294.
- Ahmad AQ, Schwarzkopf R. Clinical evaluation and surgical options in acetabular reconstruction: A literature review. *J Orthop*. 2015;12(Suppl 2):S238-S243. doi: 10.1016/j.jor.2015.10.011.
- Vasios I, Makiev K, Iliopoulos E, Tilkeridis K, Drosos G. Acetabular revision with moderate-to-severe bone loss using a trabecular titanium cup-cage construct with impaction grafting. *Orthop Rev (Pavia)*. 2025;17:140718. doi: 10.52965/001c.140718.
- Loppini M, Guazzoni E, Bulgarelli A, Di Maio M, Chiappetta K, Grappiolo G. Acetabular bone defect classifications in revision total hip arthroplasty: A systematic review of the literature. *Arch Orthop Trauma Surg*. 2026;146(1):89. doi: 10.1007/s00402-026-06251-1.
- Sanghavi SA, Paprosky WG, Sheth NP. Evaluation and management of acetabular bone loss in revision total hip arthroplasty: A 10-year update. *J Am Acad Orthop Surg*. 2024;32(10):e466-e475. doi: 10.5435/jaao-d-23-00645.
- Kim Y. Acetabular cup revision. *Hip Pelvis*. 2017;29(3):155-8. doi: 10.5371/hp.2017.29.3.155.
- Pandey AK, Zuke WA, Surace P, Kamath AF. Management of acetabular bone loss in revision total hip replacement: a narrative literature review. *Ann Jt*. 2024;9:21. doi: 10.21037/aoj-23-23.
- Chiarlone F, Zanirato A, Cavagnaro L, Alessio-Mazzola M, Felli L, Burastero G. Acetabular custom-made implants for severe acetabular bone defect in revision total hip arthroplasty: a systematic review of the literature. *Arch Orthop Trauma Surg*. 2020;140(3):415-24. doi: 10.1007/s00402-020-03334-5.
- Cassar-Gheiti AJ, Mei XY, Afenu EA, Safir OA, Gross AE, Kuzyk PR. Midterm outcomes after reconstruction of superolateral acetabular defects using flying buttress porous tantalum augments during revision total hip arthroplasty. *J Arthroplasty*. 2021;36(8):2936-41. doi: 10.1016/j.arth.2021.03.040.
- Zhou B, Chan PK, Wang D. The utilisation of porous metal augments for acetabular reconstruction during revision total hip arthroplasty. *Hip Int*. 2025;36(2):151-63. doi: 10.1177/11207000251385230.
- Arvinte D, Kiran M, Sood M. Cup-cage construct for massive acetabular defect in revision hip arthroplasty- A case series with medium to long-term follow-up. *J Clin Orthop Trauma*. 2020;11(1):62-6. doi: 10.1016/j.jcot.2019.04.021.
- Wang CX, Huang ZD, Wu BJ, Li WB, Fang XY, Zhang WM. Cup-Cage solution for massive acetabular defects: A systematic review and meta-Analysis. *Orthop Surg*. 2020;12(3):701-7. doi: 10.1111/os.12710.
- Chen IH, Tzeng SC, Wang CT. Cementless titanium fiber mesh cup in cup-Cage construct for severe acetabular defect in revision total hip arthroplasty. *J Arthroplasty*. 2026;41(7):2138-45. doi: 10.1016/j.arth.2025.11.001.
- Du YQ, Liu YL, Sun JY, Ni M, Zhou YG. Reconstruction of paprosky type IIIB acetabular bone defects using a cup-on-cup technique: A surgical technique and case series. *World J Clin Cases*. 2020;8(7):1223-31. doi: 10.12998/wjcc.v8.i7.1223.
- Webb JE, McGill RJ, Palumbo BT, Moschetti WE, Estok DM. The double-Cup construct: A novel treatment strategy for the management of paprosky IIIA and IIIB acetabular defects. *J Arthroplasty*. 2017;32(9S):S225-S231. doi: 10.1016/j.arth.2017.04.017.
- Chiarlone F, Cavagnaro L, Zanirato A, Alessio Mazzola M, Lovisolo S, Mosconi L, et al. Cup-on-cup technique: a reliable management solution for severe acetabular bone loss in revision total hip replacement. *Hip Int*. 2020;30(1\_suppl):12-8. doi: 10.1177/1120700020926932.
- Chaudhry F, Daud A, Greenberg A, Braunstein D, Safir OA, Gross AE, et al. Cup-Cage construct for treatment of severe acetabular bone loss in revision total hip arthroplasty: clinical and radiographic outcomes at a mean follow-up of 7.7 years. *J Arthroplasty*. 2024;39(10):2555-60. doi: 10.1016/j.arth.2024.07.010.
- Cano JJD, Guillaumet L, Pons AP. ACETABULAR RECONSTRUCTION IN PAPROSKY TYPE III DEFECTS. *Acta Ortop Bras*. 2019;27(1):59-63. doi: 10.1590/1413-785220192701187313.
- Tarabichi S, Baker CM, Lizzano JD, Abe EA, Goh GS, Courtney PM. Porous metal augments have comparable outcomes to other constructs for severe acetabular bone loss at mid-Term follow-up. *J Arthroplasty*. 2024;39(12):3041-5. doi: 10.1016/j.arth.2024.05.089.
- Amenabar T, Rahman WA, Hetaimish BM, Kuzyk PR, Safir OA, Gross AE. Promising mid-term results with a cup-cage construct for large acetabular defects and pelvic discontinuity. *Clin Orthop Relat Res*. 2016;474(2):408-14. doi: 10.1007/s11999-015-4210-4.

# GRAFT MATURATION IN POSTOPERATIVE MAGNETIC RESONANCE IMAGING: A SYSTEMATIC REVIEW AND META-ANALYSIS OF ISOLATED VS. ANTEROLATERAL-AUGMENTED ACL RECONSTRUCTIONS

## MATURAÇÃO DO ENXERTO NA RESSONÂNCIA MAGNÉTICA PÓS-OPERATÓRIA: REVISÃO SISTEMÁTICA E METANÁLISE DE RECONSTRUÇÕES DO LCA ISOLADAS VS. COM REFORÇO ANTEROLATERAL

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### ABSTRACT

**Objectives:** This study aims to evaluate whether the association of an anterolateral extra-articular procedure (tenodesis or anterolateral ligament reconstruction) to anterior cruciate ligament reconstruction (ACLR) correlates with graft maturation time. **Methods:** We systematically searched PubMed, Embase, and the Cochrane Central for studies comparing the graft maturation time between ACLR with anterolateral augmentation (ALA) and isolated ACLR. We assessed graft maturation, via Magnetic Resonance Imaging (MRI) using the signal-to-noise quotient (SNQ). Statistical analyses were performed using Review Manager 5.4. Odds ratios (OR) and mean differences (MD) with 95% confidence intervals (CIs) were pooled using random-effects models based on heterogeneity ( $I^2$ ). **Results:** Five studies, including 450 patients, assessed graft maturation using SNQ values. No significant difference was observed between ACLR combined with ALA and isolated ACLR (MD -0.77; 95% CI -3.56–2.03;  $p=0.59$ ;  $I^2=92\%$ ), with substantial heterogeneity. **Conclusions:** The addition of ALA to ACLR does not appear to significantly enhance graft maturation. While some studies report improved stability, these benefits do not consistently translate into better ligamentization. The decision to augment ACLR should be individualized, considering population and individual characteristics. **Level of Evidence III; Systematic Review.**

**Keywords:** Anterior Cruciate Ligament Reconstruction; Tenodesis; Magnetic Resonance Imaging; Signal-To-Noise Ratio; Meta-Analysis; Joint Instability

### RESUMO

**Objetivos:** Avaliar se a associação de um procedimento extra-articular anterolateral (tenodese ou reconstrução do ligamento anterolateral) à reconstrução do ligamento cruzado anterior (ACLR) está correlacionada ao tempo de maturação do enxerto. **Métodos:** Foi realizada uma busca sistemática no PubMed, Embase e Cochrane Central por estudos comparando o tempo de maturação do enxerto entre ACLR com reforço anterolateral (ALA) e ACLR isolada. A maturação do enxerto foi avaliada por meio de Ressonância Magnética (MRI) utilizando o quociente sinal-ruído (SNQ). As análises estatísticas foram realizadas no Review Manager 5.4. Odds ratios (OR) e diferenças de médias (MD) com intervalos de confiança de 95% (CIs) foram agrupados utilizando modelos de efeitos aleatórios baseados na heterogeneidade ( $I^2$ ). **Resultados:** Cinco estudos, totalizando 450 pacientes, avaliaram a maturação do enxerto por meio dos valores de SNQ. Não foi observada diferença significativa entre ACLR combinada com ALA e ACLR isolada (MD -0.77; 95% CI -3.56–2.03;  $p=0.59$ ;  $I^2=92\%$ ), com heterogeneidade substancial. **Conclusões:** A adição de ALA à ACLR não parece melhorar significativamente a maturação do enxerto. Embora alguns estudos relatem melhora da estabilidade, esses benefícios não se traduzem consistentemente em melhor ligamentização. A decisão de associar o reforço à ACLR deve ser individualizada, considerando as características da população estudada e de cada paciente. **Nível de Evidência III; Revisão Sistemática.**

**Descritores:** Reconstrução do Ligamento Cruzado Anterior; Tenodese; Imageamento por Ressonância Magnética; Razão Sinal-Ruído; Metanálise; Instabilidade Articular.

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<< SUMÁRIO

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## INTRODUCTION

The anterior cruciate ligament (ACL) is a critical structure in knee biomechanics, primarily responsible for restraining anterior tibial translation and maintaining rotational stability.<sup>1</sup> ACL injuries are among the most common knee injuries, particularly in athletes engaged in pivoting sports, often leading to functional instability and impairing daily activities and sports participation.<sup>2</sup> The gold-standard treatment is arthroscopic anterior cruciate ligament reconstruction (ACLR) using autografts, such as hamstring or patellar tendon grafts.<sup>3</sup> Following reconstruction, these grafts undergo a complex biological process known as ligamentization, where tendon tissue gradually remodels into a structure resembling the native ACL in morphology and mechanical properties.<sup>4,5</sup> Factors interfering with this process can increase failure risk, manifesting as residual instability or re-rupture. Proper rehabilitation during this vulnerable phase is essential for successful incorporation.<sup>6</sup> While ACLR is the standard treatment for ACL deficiency, failure rates remain a concern.<sup>7-10</sup> Primary ACLR failure ranges from 3.2% to 11.1%, reaching 34.2% in high-risk populations, such as young athletes.<sup>2,11</sup> Furthermore, up to 25% of reconstructions result in residual pivot shift, indicating that this technique alone may be insufficient to fully restore knee kinematics.<sup>12,13</sup> Consequently, the role of the anterolateral complex (ALC) has gained attention. Defined as secondary rotational stabilizers, these structures, such as the anterolateral ligament (ALL), are believed to contribute to pivot shift in ACL-deficient knees and have been proposed as potential adjuncts to ACLR for improving knee stability and possibly influencing graft maturation.<sup>1,9,12,13</sup> Biomechanically, anterolateral procedures aim to limit internal rotation and reduce graft strain, potentially enhancing ligamentization and decreasing failure rates. Given these hypotheses, anterolateral augmentation is increasingly considered for high-risk populations (young, athletes, females, or those with explosive pivot-shift).<sup>6,9,13,14</sup> Combining ACLR with anterolateral augmentation (ALA), like lateral extra-articular tenodesis (LET) or anterolateral ligament reconstruction (ALLR), could reduce residual pivot shift and improve outcomes.<sup>3,8,9,15</sup> However, evidence regarding the impact of these additional procedures on graft maturation remains inconsistent. While some studies suggest improved remodeling with combined techniques<sup>16-18</sup>, others report no significant difference in ligamentization compared to isolated ACLR.<sup>11,19</sup> These conflicting findings highlight the need for a comprehensive evidence synthesis. Therefore, this meta-analysis aims to systematically evaluate whether the addition of anterolateral extra-articular augmentation to ACLR has some (positive or negative) effect on graft maturation time. By analyzing magnetic resonance imaging (MRI) to assess signal-to-noise quotient (SNQ) values, we seek to clarify the role of these combined procedures in the ligamentization process.

## METHODS

This systematic review and meta-analysis follows the guidelines of the Cochrane Collaboration Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.<sup>20,21</sup> The protocol was prospectively registered at PROSPERO on January 18, 2025 (ID: CRD 42025628492). No amendments were made to the registered protocol.

### Eligibility criteria

Inclusion was restricted to: (1) randomized clinical trials (RCT) or non-RCT or prospective/retrospective cohorts; (2) comparing ACLR with anterolateral reinforcement to ACLR isolated; and (3) evaluating graft maturation through MRI. We excluded studies with (1) no control group, (2) revision ACLR, (3) multiple ligament injuries, (4) double-bundle ACLR technique and (5) no use of signal-to-noise quotient (SNQ) to evaluate graft ligamentization.

### Search strategy and data extraction

It was systematically searched in PubMed, Embase and Cochrane Central (last searched: January 2025) the following search terms: 'ACL', 'anterior cruciate ligament', 'anterolateral ligament', 'lateral extra-articular tenodesis', 'lateral extra-articular procedure', 'LET', 'Lemaire', 'anterolateral ligament reconstruction', 'anterolateral ligament augmentation', 'extra-articular augmentation', 'lateral tenodesis', 'lateral reinforcement', 'ALL', 'MRI', 'magnetic resonance imaging', 'nuclear magnetic resonance imaging'. References from all included studies were also manually searched for any additional studies. Two authors independently extracted the data following predefined search criteria and quality assessment. Discrepancies were resolved by a third reviewer. Full search strategies for all databases are available as Supplementary Material.

### Endpoints and subgroup analyses

The primary outcome of interest was graft maturation, measured using SNQ values obtained from postoperative MRI scans. Pre-specified subanalyses included data restricted to: (1) femoral tunnel drilling technique; and (2) anterolateral augmentation technique.

#### Endpoint measurement

The primary outcome was evaluated using MRI-based SNQ values, which serve as a parameter of graft structural properties and vascularization. SNQ is calculated by subtracting the signal intensity of a reference tissue from that of the graft and dividing the result by the background noise signal. Higher SNQ values are generally associated with increased water content and vascularity, suggesting lower graft maturity. Weiller et al.<sup>22</sup> demonstrated that SNQ values inversely correlate with graft tensile strength and are associated with histological alterations and biomechanical changes during ligamentization.

### Quality assessment and publication bias

Two authors independently assessed the quality of the included studies using version 2 of the Cochrane Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) assessment tool.<sup>23</sup> Disagreements were addressed and resolved through a consensus after discussing the reasons for the discrepancy. Publication bias was evaluated by funnel-plot analysis of point estimates about study weights. As per Cochrane's recommendations, Egger's test was not performed due to the number of included studies in this meta-analysis ( $n < 10$ ).<sup>20</sup> Certainty of evidence was not formally assessed using GRADE due to the limited number of included studies ( $n=5$ ) and the observational nature of all included studies.

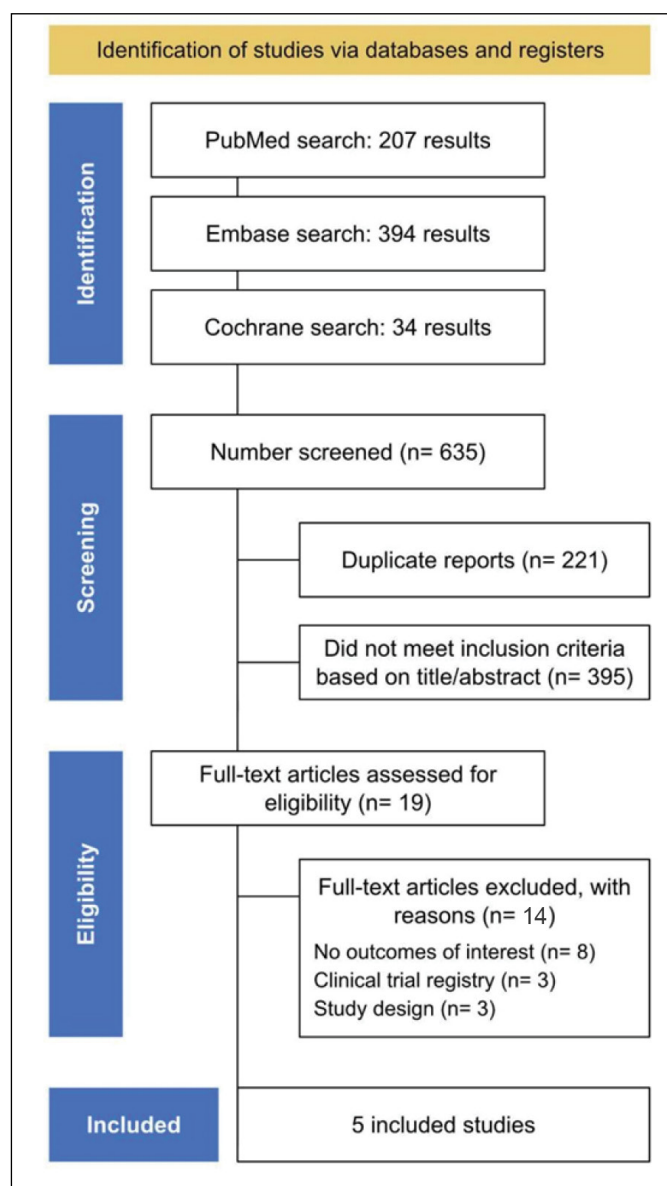
### Statistical analysis

Odds ratios (OR) with 95% confidence intervals were used to compare treatment effects for categorical outcomes, while mean differences (MD) were applied to continuous variables. Heterogeneity was classified as low when  $I^2 < 25\%$  and moderate to high when  $I^2 \geq 25\%$ . The DerSimonian-Laird random-effects model was applied when  $I^2 \geq 25\%$ . No data conversions or imputations were required. A sensitivity analysis was performed using the leave-one-out approach. All statistical analyses were conducted using Review Manager 5.4 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Results are displayed as forest plots, a risk of bias summary and a funnel plot.

## RESULTS

### Study selection and characteristics

The initial search identified 635 studies. After excluding duplicates and unrelated articles, 19 underwent a thorough review, with 5 meeting the final criteria for qualitative and quantitative analysis (Figure 1). The analysis included data from 450 patients across



The flowchart illustrates the stages of identification, screening, eligibility, and inclusion. From an initial search yielding 635 records across PubMed, Embase, and Cochrane databases, 221 duplicates were removed. After screening titles and abstracts, 19 full-text articles were assessed for eligibility, resulting in a final inclusion of 5 studies for qualitative and quantitative synthesis.

**Figure 1.** PRISMA flow diagram of study screening and selection.

5 retrospective cohort studies, of whom 187 (41.5%) underwent ACLR + ALA. Population characteristics are presented in Table 1. The studies were heterogeneous regarding graft type, surgical technique, follow-up to MRI period and baseline characteristics. We performed a subgroup analysis focusing on similarities to mitigate potential bias.

### Graft maturation and subgroup analyses

SNQ values indicated that incorporating LET or ALLR into ACLR does not result in a statistically significant difference in graft maturation (MD -0.77; 95% CI -3.56–2.03;  $p=0.59$ ;  $I^2=92\%$ ; Figure 2). However, significant heterogeneity suggests variability in the true effect. Sensitivity analysis (leave-one-out) maintained high heterogeneity across all scenarios, with no meaningful change in the overall effect estimate.

Subgroup analysis by anterolateral augmentation technique did not mitigate the observed variability. Both the ALLR group (MD -0.23;

95% CI -3.75–3.29;  $p=0.90$ ;  $I^2=90\%$ ; Figure 3a) and the LET group (MD -1.06; 95% CI -7.42–5.29;  $p=0.74$ ;  $I^2=94\%$ ; Figure 3b) exhibited very high heterogeneity. In contrast, subgroup analysis by femoral drilling technique revealed that the outside-in technique (MD -3.59; 95% CI -7.02–-0.16;  $p=0.04$ ;  $I^2=94\%$ ; Figure 4a) indicated a trend favoring the combined procedure, whereas the anteromedial portal approach (MD 3.59; 95% CI 0.50–3.56;  $p=0.009$ ;  $I^2=0\%$ ; Figure 4b) suggested a modest benefit for isolated ACLR.

### Quality assessment and publication bias

Three of the five included non-randomized studies were identified as having a serious risk of bias due to concerns on the “confounding” domain. The remaining two studies were considered to have a moderate risk of bias, primarily from potential issues related to “confounding”, “participant selection”, and “selection of the reported result”. The risk of bias for each study was assessed using the ROBINS-I tool (Figure 5).<sup>23</sup> Funnel plot asymmetry (Figure 6) suggested publication bias, indicating that studies with significant results might be more likely to be published than those with null findings. This potential bias is acknowledged as a limitation that may affect the overall interpretation of the results.

## DISCUSSION

This meta-analysis of five studies evaluating 450 patients found that adding lateral extra-articular augmentation to ACLR did not result in a statistically significant difference in imaging-based ligamentization. While the anteromedial portal technique for femoral drilling suggested a modest favorable effect on maturation for isolated ACLR, the overall results contrast with other meta-analyses, such as de Lima et al.<sup>8</sup> and Beckers et al.<sup>9</sup>, which reported clear clinical benefits for ALA in primary ACLR.

Beckers et al.<sup>9</sup> noted that combining primary ACLR with ALA significantly reduces graft rupture risk and improves rotatory stability. These objective improvements in stability do not appear to correlate consistently with enhanced graft maturation via SNQ in our analysis. This suggests that the clinical benefits of ALA might be driven by biomechanical protection rather than accelerated biological ligamentization. Therefore, rehabilitation and return-to-sport timelines should not be modified solely due to an anterolateral procedure. Similarly, de Lima et al.<sup>8</sup> found that combined ACL and ALA reconstruction achieved better postoperative clinical outcomes, especially in reducing residual pivot shift and re-rupture rates. Their analysis also indicated lower residual positive Lachman tests and better Lysholm scores in the combined group. While de Lima et al.<sup>8</sup> focused on ALA reconstruction, their findings, alongside Beckers et al.<sup>9</sup>, underscore that reduced failure rates are achievable with lateral procedures. Our results indicate these advantages are not measurable via SNQ values, reinforcing that the biological maturation rate remains independent of the extra-articular stabilization.

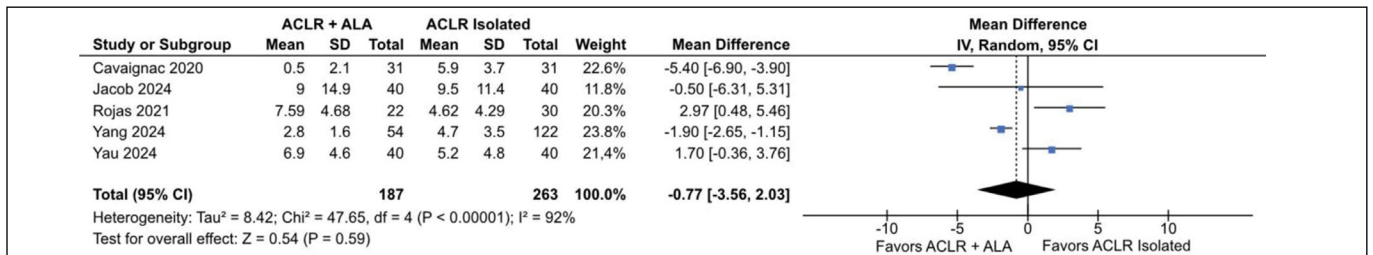
The substantial heterogeneity observed ( $I^2=92\%$ ) mirrors variability noted in clinical scores by other authors, likely stemming from differences in graft choice (semitendinosus, gracilis, or allografts), femoral drilling approaches, and fixation methods.<sup>8,9</sup> Furthermore, MRI protocols lack standardization regarding SNQ measurement techniques, reference tissues, and timing. Patient demographics, including age and concomitant injuries like meniscal tears, introduce further variability. For instance, Yang et al.<sup>18</sup> found that medial meniscal injuries were independently associated with higher SNQ values, indicating worse maturation.

Relying on SNQ as a proxy for maturation is a limitation. As an operator-dependent method, SNQ provides signal intensity data but may not fully capture the complex biological processes of ligamentization.<sup>5</sup> Nevertheless, included studies utilized multiple evaluators and assessed interobserver reliability, predominantly

**Table 1.** Baseline characteristics of included studies.

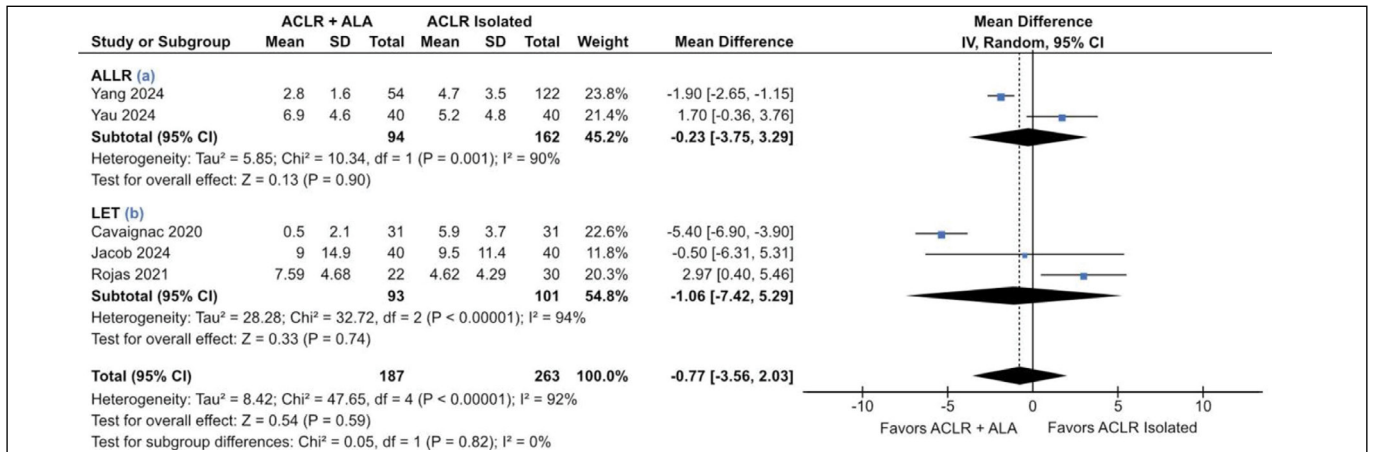
| Study                   | Country     | Study Design | Patients G1/G2 | Male (%) G1/G2 | Age (years)† G1/G2   | BMI† G1/ G2        | ALA Type | Graft Type [n° of strands reported]                                                     | ACLR Femoral Drilling G1/G2                       | ACLR Fixation              |                     | ALA Fixation             |                         | MRI                                                  |          | SNQ Measure [Ref]                       | Follow-up to MRI (mo)† |
|-------------------------|-------------|--------------|----------------|----------------|----------------------|--------------------|----------|-----------------------------------------------------------------------------------------|---------------------------------------------------|----------------------------|---------------------|--------------------------|-------------------------|------------------------------------------------------|----------|-----------------------------------------|------------------------|
|                         |             |              |                |                |                      |                    |          |                                                                                         |                                                   | Femoral                    | Tibial              | Femoral                  | Tibial                  | Machine                                              | Strength |                                         |                        |
| Cavaignac et al. (2020) | France      | Cohort       | 31/31          | 100/ 100       | 27.2±6.7/ 33.1±8.3   | 25.2±4.4/ 24.4±3.4 | LET      | G1<br>ACLR: ST [4]<br>ALLR: G [2]<br>G2<br>ACLR: ST [4]                                 | Outside-in/ Outside-in                            | TightRope (Arthrex)        | BIS (Arthrex)       | Suture anchor (ConMed)   | Spiked staple (Arthrex) | Magnetom Skyra; Siemens 15-channel volume array coil | 3.0-T    | The mean of 3 samples§ [PCL]            | 12                     |
| Jacob et al. (2024)     | Australia   | Cohort       | 40/40          | 57.5/ 57.5     | 18.7±3.8/ 18.4±3.6   | 21.9±8.4/ 24.2±3.5 | LEAT     | G1<br>ACLR: ST [4]<br>LEAT: ITB [NR]<br>G2<br>ACLR: ST [4]                              | AM portal/ AM portal                              | TightRope (Arthrex)        | TightRope (Arthrex) | PEEK SwiveLock (Arthrex) | NR                      | Magnetom Skyra; Siemens 15-channel volume array coil | 3.0-T    | The mean of 3 samples§ [PCL]            | 12                     |
| Rojas et al. (2021)     | Spain       | Cohort       | 22/30          | 45.4/ 43.3     | 31.1±6.1/ 29.7±8.2   | NR                 | MLLET    | G1<br>ACLR: ST+G [3+3]<br>MLLET: ITB [NR]<br>G2<br>ACLR: ST+G [4+3]                     | AM portal/ AM portal                              | Endobutton                 | BIS                 | BIS                      | NR                      | Signa HDxt; GE Healthcare 4-channel knee coil        | 3.0-T    | The mean of 3 samples§ [PCL]            | 10                     |
| Yang et al. (2024)      | South Korea | Cohort       | 54/122         | 81.5/ 82.0     | 26.7±10.6/ 28.7±12.0 | 25.6±3.9/ 25.6±4.1 | ALLR     | G1<br>ACLR: HS‡ [4]<br>ALLR: TA [NR]<br>G2<br>ACLR: HS‡ [4]                             | Outside-in/ Outside-in                            | TightRope (Arthrex)        | BIS                 | BIS                      | BIS                     | Magnetom Skyra; Siemens 15-channel volume array coil | NR       | The mean of 3 samples§ [PCL]            | 35                     |
| Yau et al. (2024)       | China       | Cohort       | 40/40          | 100/ 100       | 26.2±6.0/ 27.0±6.3   | 24.8±3.4/ 24.4±3.2 | ALLR     | G1<br>ACLR: ST+G [2+2]<br>ALLR: ITB [2] (n=14), ST [1] (n=26)<br>G2<br>ACLR: ST+G [2+2] | AM portal (n=14) and outside-in (n=26)/ AM portal | Cortical button. (various) | BIS                 | Suture anchor (Arthrex)  | NR                      | NR                                                   | 1.5-T    | The mean signal of the whole graft [QT] | 16                     |

Abbreviations: ACLR = anterior cruciate ligament reconstruction; ALA = anterolateral augmentation; ALLR = anterolateral ligament reconstruction; AM = anteromedial portal; BIS = bioabsorbable interference screws; HS = Hamstring; ITB = iliotibial band; G = gracilis; G1 = ACLR + anterolateral augmentation group; G2 = Isolated ACLR group; LET = lateral extra-articular tenodesis; LEAT = modified deep Lemaire anterolateral extra-articular tenodesis; MLLET = modified Lemaire anterolateral extra-articular tenodesis; MRI = magnetic resonance imaging; PCL = posterior cruciate ligament; QT = Quadriceps tendon; SNQ = signal-to-noise quotient; ST = semitendineous; T= Tesla; TA = separate fresh frozen tibialis anterior allograft; NR = no report. Notes: § = The samples were taken at a proximal, middle, and distal intra-articular portion of the graft; † = Mean ± standard deviation; ‡ = For both groups; § = Not specified.



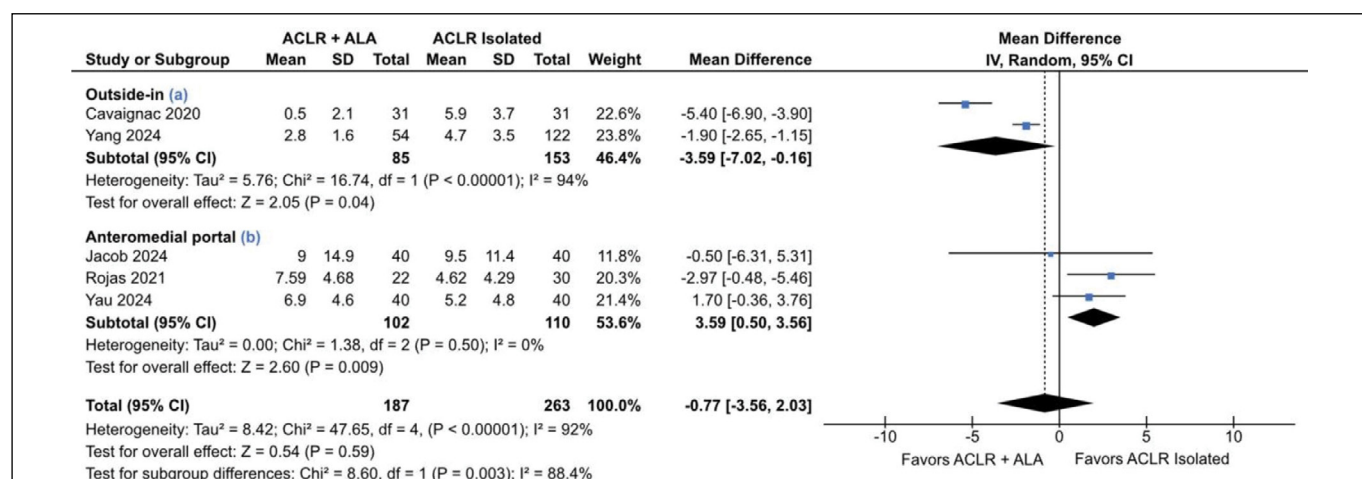
No significant difference in graft maturation between isolated ACLR and ACLR with LET/ALLR (p=0.59), considering a substantial heterogeneity between studies (I²=92%). CI = confidence interval; MD = mean difference; IV = inverse variance; ACLR = anterior cruciate ligament reconstruction; ALA = anterolateral augmentation.

**Figure 2.** Forest plot of the comparison between ACLR + ALA vs. ACLR Isolated for the primary outcome.



(a) – ALLR approach favoring ACLR with ALA (p=0.23), despite important heterogeneity (I²=94%). (b) – LET technique with no statistically significant difference, with substantial heterogeneity (I²=90%). CI = confidence interval; MD = mean difference; IV = inverse variance; ACLR = anterior cruciate ligament reconstruction; ALA = anterolateral augmentation; ALLR = anterolateral ligament reconstruction; LET = lateral extra-articular tenodesis.

**Figure 3.** Subgroup analysis based on the type of lateral procedure (LET vs. ALLR).



(a) – Outside-in technique suggesting a modest benefit for ACLR with ALLR ( $p=0.04$ ), despite important heterogeneity ( $I^2=94\%$ ). (b) – Anteromedial portal approach favoring isolated ACLR ( $p=0.009$ ), with low heterogeneity ( $I^2=0\%$ ). CI = confidence interval; MD = mean difference; IV = inverse variance; ACLR = anterior cruciate ligament reconstruction; ALA = anterolateral augmentation.

**Figure 4.** Comparison of Femoral Drilling Techniques in ACLR + ALA: Outside-in vs. Anteromedial Portal.

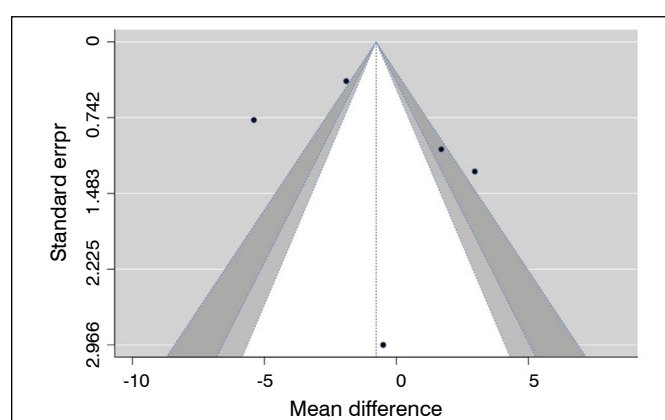


The traffic light plot illustrates the risk of bias for each study across seven domains: D1, confounding; D2, selection of participants; D3, classification of interventions; D4, deviations from intended interventions; D5, missing data; D6, measurement of outcomes; and D7, selection of the reported result. The symbols represent low risk of bias (+), some concerns (–), and high risk of bias (✗). The overall assessment indicates that the majority of studies presented high risk or significant concerns in specific domains, particularly in the D1, D2, and D7 categories.

**Figure 5.** Risk of bias assessment of the included studies.

through the Intraclass Correlation Coefficient (ICC). Reported ICC values ranged from 0.667 to 0.92, indicating moderate-to-excellent agreement.<sup>11,16-19</sup> Despite this rigor, results remain inconsistent. For instance, Cavaignac et al.<sup>16</sup> suggested better incorporation with LET, while Jacob et al.<sup>17</sup> reported less tunnel widening but no improvement in graft healing. Yang et al.<sup>18</sup> showed superior rotational stability and graft remodeling with ALLR, but there was no conclusive superiority in patient-reported outcomes. Yau et al.<sup>19</sup> also found no significant difference in graft remodeling between both groups.

Conversely, Rojas et al.<sup>11</sup> suggest that at 10 months, hamstring autografts in anatomic ACLR with LET exhibited signal intensities indicating inferior ligamentization. This raises the possibility that intra-articular maturation may even be delayed when LET is performed. Despite this, addressing anterolateral structures reduces graft rupture rates at 2 years in high-risk populations and reduces tunnel widening, suggesting clinical benefits may not reflect early MRI signal intensity improvements.<sup>7,17</sup> Additionally, Ferreti et al.<sup>24</sup> observed no statistical difference between ALLR and LET regarding maturation and functional outcomes. There is no consensus on when MRI signal intensity reflects 'normal' healing, presenting a weak correlation with clinical outcomes.<sup>25</sup>



Funnel plot of the mean differences comparing the SNQ values of ACLR isolated and ACLR with ALA. The asymmetric shape of the plot suggests the presence of publication bias. ACLR = anterior cruciate ligament reconstruction; ALA = anterolateral augmentation.

**Figure 6.** Funnel plot for the assessment of publication bias.

In skeletally immature patients, Retzky et al.<sup>26</sup> suggested LET is associated with improved maturation in young athletes, supported by Chipman et al.<sup>27</sup>, who linked ALLR to reduced signal intensity in quadriceps autografts. Perelli et al.<sup>28</sup> showed that modified Lemaire tenodesis improves stability in this population. Additionally, a pediatric study indicated that ligamentization is a prolonged process, occurring primarily between 12 and 24 months.<sup>29</sup> In contrast, studies excluding skeletally immature patients found no significant differences<sup>16,19</sup>, emphasizing that skeletal maturity may be a crucial factor when assessing the benefits of combined procedures. Patient-specific factors like sex, activity level, and comorbidities may also influence outcomes. Although sex was addressed in several studies, its impact on biological graft maturation remains inconclusive. Cavaignac et al.<sup>16</sup> excluded female participants due to concerns regarding hormonal fluctuations and their potential effect on graft incorporation, while Rojas et al.<sup>11</sup> included only males, a factor that limits the external validity of their findings. Conversely, studies that maintained a sex balance across cohorts reported no consistent differences in SNQ values, suggesting that sex may not be a primary predictor of imaging-based outcomes.<sup>17-19</sup> Patient activity level, however, played a significant role in the clinical decision-making process. High-level athletes and younger patients often demonstrate improved clinical outcomes when ALA is associated

with ACLR, likely due to the increased rotational demands.<sup>13,30</sup> Regarding comorbidities, Yang et al.<sup>18</sup> identified medial meniscal injuries as an independent risk factor for impaired graft maturation, as evidenced by significantly higher SNQ values. This highlights that the intra-articular environment and concomitant injuries may be as decisive for ligamentization as the surgical technique itself. In summary, while clinical evidence suggests that anterolateral augmentation provides superior rotational stability and reduces re-rupture rates in primary ACLR<sup>8,9</sup>, our meta-analysis focusing on MRI-based SNQ values indicates that the addition of LET or ALLR does not significantly accelerate or enhance biological graft maturation. The observed clinical benefits are likely attributable to the biomechanical reinforcement provided by the extra-articular procedure rather than a direct modulation of the intra-articular ligamentization process. The high heterogeneity regarding surgical approaches, follow-up durations, and MRI protocols underscores the urgent need for standardized assessment procedures to optimize patient selection. Therefore, the decision to perform ALA should remain individualized, targeting specific high-risk populations where mechanical stability is paramount, while acknowledging the lack of consistent evidence for improved graft maturation based on SNQ values.

## Study limitations

This meta-analysis has limitations. Potential publication bias, suggested by funnel plot asymmetry (Figure 6), may overestimate augmentation effects. High heterogeneity among included studies limits definitive conclusions. Discrepancies may be attributed to: (1) surgical variability in graft and fixation; (2) inclusion criteria differences; (3) variations in imaging timing; and (4) diverse rehabilitation protocols. Subgroup analyses were performed to identify heterogeneity sources and contextualize findings. Acknowledging these limitations, this meta-analysis provides valuable insights into the role of LET/ALLR. Future research can provide definitive evidence regarding combined procedures to guide clinical decision-making.

## CONCLUSION

This meta-analysis reveals that adding ALA to ACLR does not significantly enhance graft maturation. While some studies demonstrate improved rotational stability and reduced tunnel widening, these benefits do not consistently translate into earlier ligamentization. The decision to augment ACLR should be individualized. ALA must not modify rehabilitation and return-to-sports timelines, as it lacks a direct relationship with the biological graft maturation process.

## CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. AAC: Writing – Original Draft, Writing – Review & Editing, Methodology, Data Curation, Formal Analysis, Investigation, Project Administration, Visualization. CRB: Investigation, Methodology, Formal Analysis, Writing – Original Draft. SAGM: Conceptualization, Writing – Original Draft, Writing – Review & Editing, Methodology, Resources, Supervision. GRG: Supervision, Resources, Writing – Review & Editing. HCP: Supervision, Resources, Writing – Review & Editing. LDP: Conceptualization, Supervision, Resources, Methodology, Writing – Original Draft, Writing – Review & Editing.

## DATA AVAILABILITY DECLARATION

The contents underlying the research are available in the manuscript.

## REFERENCES

- Kennedy MI, LaPrade CM, Geeslin AG, LaPrade RF. An overview of clinically relevant biomechanics of the anterolateral structures of the knee. *Tech Orthop*. 2018;33(4):213-8. doi: 10.1097/bto.0000000000000300.
- Kemler B, Coladonato C, Sonnier JH, Campbell M, Darius D, Erickson BJ, et al. Evaluation of failed ACL reconstruction: an updated review. *Open Access J Sports Med*. 2024;15:29-39. doi: 10.2147/oajsm.s427332.
- Hewison CE, Tran MN, Kaniki N, Remtulla A, Bryant D, Getgood AM. Lateral extra-articular tenodesis reduces rotational laxity when combined with anterior cruciate ligament reconstruction: A systematic review of the literature. *Arthroscopy*. 2015;31(10):2022-34. doi: 10.1016/j.arthro.2015.04.089.
- Gupta R, Singh S, Kapoor A, Soni A, Mehta R, Kaur R, et al. Comparison of "ligamentization" process between preserved insertion hamstring tendon autograft and bone-patellar tendon-bone autograft. *J Orthop Sci*. 2024;29(4):1020-5. doi: 10.1016/j.jos.2023.06.014.
- Claes S, Verdonk P, Forsyth R, Bellemans J. The "Ligamentization" process in anterior cruciate ligament reconstruction. *Am J Sports Med*. 2011;39(11):2476-83. doi: 10.1177/0363546511402662.
- Janssen RPA, Scheffler SU. Intra-articular remodelling of hamstring tendon grafts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2013;22(9):2102-8. doi: 10.1007/s00167-013-2634-5.
- Sonnery-Cottet B, Saithna A, Cavalier M, Kajetanek C, Temponi EF, Daggett M, et al. Anterolateral ligament reconstruction is associated with significantly reduced ACL graft rupture rates at a minimum follow-up of 2 years: A prospective comparative study of 502 patients from the SANTO study group. *Am J Sports Med*. 2017;45(7):1547-57. doi: 10.1177/0363546516686057.
- de Lima DA, de Lima LL, de Souza NGR, de Moraes Perez RA, Sobrado MF, Guimarães TM, et al. Clinical outcomes of combined anterior cruciate ligament and anterolateral ligament reconstruction: a systematic review and meta-analysis. *Knee Surg Relat Res*. 2021;33(1):33. doi: 10.1186/s43019-021-00115-1.
- Beckers L, Vivacqua T, Firth AD, Getgood AMJ. Clinical outcomes of contemporary lateral augmentation techniques in primary ACL reconstruction: a systematic review and meta-analysis. *J Exp Orthop*. 2021;8(1):59. doi: 10.1186/s40634-021-00368-5.
- Ra HJ, Kim J, Lee D. Comparative clinical outcomes of anterolateral ligament reconstruction versus lateral extra-articular tenodesis in combination with anterior cruciate ligament reconstruction: systematic review and meta-analysis. *Arch Orthop Trauma Surg*. 2020;140(7):923-31. doi: 10.1007/s00402-020-03393-8.
- Rojas G, Perelli S, Ibanez M, Formagnana M, Ormazabal I, Monllau JC. Effect of modified lemaire anterolateral extra-articular tenodesis on the magnetic resonance imaging maturity signal of anterior cruciate ligament hamstring graft. *Am J Sports Med*. 2021;49(9):2379-86. doi: 10.1177/03635465211018858.
- Kernkamp WA, Li G, Van de Velde SK. The anterolateral ligament: a closed chapter?. *Ann Transl Med*. 2016;4(S1):S37. doi: 10.21037/atm.2016.09.21.
- de Lima DA, Helito CP, Lima FRA, Leite JAD. Indicações cirúrgicas para reconstrução do ligamento cruzado anterior combinada com tenodese extra-articular lateral ou reconstrução do ligamento anterolateral. *Rev Bras Ortop*. 2018;53(6):661-7. doi: 10.1016/j.rbo.2017.06.027.
- Getgood AM, Bryant DM, Litchfield R, Heard M, McCormack RG, Rezansoff A, et al. Lateral extra-articular tenodesis reduces failure of hamstring tendon autograft anterior cruciate ligament reconstruction: 2-Year outcomes from the STABILITY study randomized clinical trial. *Am J Sports Med*. 2020;48(2):285-97. doi: 10.1177/0363546519896333.
- Helito CP, Sobrado MF, Giglio PN, Bonadio MB, Pécora JR, Camanho GL, et al. Combined reconstruction of the anterolateral ligament in patients with anterior cruciate ligament injury and ligamentous hyperlaxity leads to better clinical stability and a lower failure rate than isolated anterior cruciate ligament reconstruction. *Arthroscopy*. 2019;35(9):2648-54. doi: 10.1016/j.arthro.2019.03.059.
- Cavaignac E, Mesnier T, Marot V, Fernandez A, Faruch M, Berard E, et al. Effect of lateral extra-articular tenodesis on anterior cruciate ligament graft incorporation. *Orthop J Sports Med*. 2020;8(11):2325967120960097. doi: 10.1177/2325967120960097.
- Jacob G, Lim YP, Brito CA, Parker DA. Lateral extra-articular tenodesis does not enhance ACL graft healing, however, does reduce graft tunnel widening. *Knee Surg Sports Traumatol Arthrosc*. 2024;32(11):2885-94. doi: 10.1002/ksa.12310.

18. Yang HY, Jeong WJ, Cheon JH, Seon JK. Combined anterior cruciate ligament and anterolateral ligament reconstruction shows superior graft remodeling, maturation, and stability compared with isolated anterior cruciate ligament reconstruction. *Arthroscopy*. 2024;41(8):2958-70. doi: 10.1016/j.arthro.2024.12.022.
19. Yau W, Lin W. Evaluation of graft maturation by MRI in anterior cruciate ligament reconstruction with and without concomitant anterolateral ligament reconstruction. *Orthop J Sports Med*. 2024;12(1):23259671231223976. doi: 10.1177/23259671231223976.
20. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.5 (updated August 2024). Cochrane, 2024. Available from [www.cochrane.org/handbook](http://www.cochrane.org/handbook).
21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71.
22. Weiler A, Peters G, Mäurer J, Unterhauser FN, Südkamp NP. Biomechanical properties and vascularity of an anterior cruciate ligament graft can be predicted by contrast-Enhanced magnetic resonance imaging. *Am J Sports Med*. 2001;29(6):751-61. doi: 10.1177/03635465010290061401.
23. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. doi: 10.1136/bmj.i4919.
24. Ferretti A, Carrozzo A, Saithna A, Argento G, Annibaldi A, Latini F, et al. Comparison of primary repair of the anterior cruciate ligament and anterolateral structures to reconstruction and lateral extra-articular tenodesis at 2-Year follow-up. *Am J Sports Med*. 2023;51(9):2300-12. doi: 10.1177/03635465231178301.
25. Van Dyck P, Zazulia K, Smekens C, Heusdens CH, Janssens T, Sijbers J. Assessment of anterior cruciate ligament graft maturity with conventional magnetic resonance imaging: A systematic literature review. *Orthop J Sports Med*. 2019;7(6):2325967119849012. doi: 10.1177/2325967119849012.
26. Retzky JS, Chipman DE, Mintz DN, Cordasco FA, Green DW. Association of lateral extra-Articular tenodesis with improved graft maturity on MRI 2 years after ACL reconstruction with quadriceps tendon autograft in skeletally immature athletes. *Orthop J Sports Med*. 2024;12(1):23259671231211885. doi: 10.1177/23259671231211885.
27. Chipman D, Retzky J, Cordasco F, Green D. Paper 38: addition of a lateral extra-articular tenodesis is associated with lower quadriceps tendon autograft MRI signal intensity two years following anterior cruciate ligament reconstruction in skeletally immature adolescents. *Orthop J Sports Med*. 2023;11(7\_suppl3):2325967123S00064. doi: 10.1177/2325967123S00064.
28. Perelli S, Costa GG, Terron VM, Formagnana M, Bait C, Espregueira-Mendes J, et al. Combined anterior cruciate ligament reconstruction and modified lemaire lateral extra-articular tenodesis better restores knee stability and reduces failure rates than isolated anterior cruciate ligament reconstruction in skeletally immature patients. *Am J Sports Med*. 2022;50(14):3778-85. doi: 10.1177/03635465221128926.
29. Accadbled F, Lescot T, Nicolaou N, Doumerc J, Cavaignac E, Flumian C, et al. Knee anterior laxity and graft maturation after transphyseal anterior cruciate ligament reconstruction. *J Pediatr Orthop*. 2025;45(5):281-6. doi: 10.1097/bpo.0000000000002888.
30. Carrozzo A, Monaco E, Saithna A, Annibaldi A, Guy S, Ferreira AR, et al. Clinical Outcomes of Combined Anterior Cruciate Ligament Reconstruction and Lateral Extra-articular Tenodesis Procedures in Skeletally Immature Patients: A Systematic Review From the SANTI Study Group. *J pediatr Orthop*. 2022;43(1):24-30. doi: 10.1097/BPO.0000000000002236.

# SINGLE-SHOT FEMORAL NERVE BLOCK VERSUS LOCAL INFILTRATION ANALGESIA FOR PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW AND META-ANALYSIS

## BLOQUEIO FEMORAL EM DOSE ÚNICA VERSUS ANALGESIA POR INFILTRAÇÃO LOCAL EM PACIENTES SUBMETIDOS À ARTROPLASTIA TOTAL DO JOELHO: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE

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### ABSTRACT

**Objective:** Early postoperative rehabilitation is essential for optimal outcomes after total knee arthroplasty (TKA). Femoral nerve block and local infiltration analgesia (LIA) are commonly used for postoperative pain control. However, the relative efficacy of single-shot femoral nerve block (sFNB) versus LIA remains uncertain. This meta-analysis compared both strategies in patients undergoing TKA. **Methods:** Medline, Cochrane Library, and Embase databases were searched for randomized controlled trials (RCTs) comparing sFNB and LIA in TKA patients. Outcomes included postoperative pain scores, opioid consumption, range of motion (ROM), and length of hospital stay. **Results:** Of 922 studies identified, 11 RCTs comprising 1,109 patients were included. No significant differences were observed between groups regarding early postoperative pain scores (mean difference [MD] = 0.25 points; 95% confidence interval [CI]: -0.19 to 0.69) or opioid consumption (MD = 0.55 mg; 95% CI: -3.28 to 4.38). However, the LIA group demonstrated improved ROM on postoperative day 2 (MD = -6.15 degrees; 95% CI: -9.16 to -3.14) and shorter hospital stay (MD = 0.23 days; 95% CI: 0.06 to 0.41). **Conclusions:** LIA was associated with improved ROM on the second postoperative day and shorter hospital stay compared with sFNB, without significant differences in pain scores or opioid consumption. **Level of Evidence II; Systematic review and meta-analysis of randomized clinical trials.**

**Keywords:** Arthroplasty, Replacement, Knee; Pain Management; Nerve Block. Anesthesia, Local.

### RESUMO

**Objetivo:** A reabilitação pós-operatória precoce é essencial para resultados ideais após a artroplastia total do joelho (ATJ). O bloqueio do nervo femoral e a analgesia por infiltração local (AIL) são comumente utilizados para controle da dor pós-operatória. No entanto, a eficácia relativa do bloqueio femoral em dose única (BNFu) versus AIL permanece incerta. Esta meta-análise comparou ambas as estratégias em pacientes submetidos à ATJ. **Métodos:** As bases de dados Medline, Cochrane Library e Embase foram pesquisadas em busca de ensaios clínicos randomizados (ECRs) comparando BNFu e AIL em pacientes submetidos à ATJ. Os desfechos incluíram escores de dor pós-operatória, consumo de opioides, amplitude de movimento (ADM) e tempo de internação hospitalar. **Resultados:** Dos 922 estudos identificados, 11 ECRs, compreendendo 1.109 pacientes, foram incluídos. Não foram observadas diferenças significativas entre os grupos em relação aos escores de dor pós-operatória precoce (diferença média [DM] = 0,25 pontos; intervalo de confiança [IC] de 95%: -0,19 a 0,69) ou ao consumo de opioides (DM = 0,55 mg; IC 95%: -3,28 a 4,38). No entanto, o grupo AIL demonstrou melhor ADM no segundo dia pós-operatório (DM = -6,15 graus; IC 95%: -9,16 a -3,14) e menor tempo de internação hospitalar (DM = 0,23 dias; IC 95%: 0,06 a 0,41). **Conclusões:** A AIL foi associada a melhor ADM no segundo dia pós-operatório e menor tempo de internação hospitalar em comparação ao BNFu, sem diferenças significativas nos escores de dor ou no consumo de opioides. **Nível de evidência II; Revisão sistemática e meta-análise de ensaios clínicos randomizados.**

**Descritores:** Artroplastia do Joelho; Manejo da Dor; Bloqueio Nervoso; Anestesia Local.

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<< SUMÁRIO

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## INTRODUCTION

The number of total knee arthroplasty (TKA) procedures is expected to rise significantly in the coming years, mainly due to population aging and the increasing prevalence of obesity and osteoarthritis.<sup>1</sup> Early postoperative rehabilitation in TKA, with progressive gains in range of motion (ROM), pain control, and early ambulation, is a key factor in achieving favorable outcomes.<sup>2-5</sup> Femoral nerve block (FNB) and local infiltration analgesia (LIA) are among the options for perioperative analgesia in TKA. A femoral nerve block can be administered as a single dose (sFNB) or as a continuous block (cFNB) via a catheter infusion, aiming to extend the analgesic effect of sFNB, which has been reported to last up to 24 hours.<sup>6</sup> Similarly, LIA has been reported to last 24–48 hours.<sup>7</sup>

Although reduced opioid consumption was observed in the cFNB group, previous meta-analyses comparing sFNB and cFNB did not find significant differences in the visual analog scale (VAS) at 48 hours postoperatively, nor any significant differences in length of hospital stay.<sup>8,9</sup> Therefore, despite offering benefits over sFNB, the cumulative effect of cFNB may be limited in the context of multimodal analgesic management. Since cFNB may be associated with an increased risk of falls,<sup>10-13</sup> potentially leading to major and catastrophic complications, sFNB remains a good alternative, especially in patients with other risk factors for falls.

Previous meta-analyses comparing FNB and LIA included both single-shot and continuous forms of FNB and suggested that both FNB and LIA are equally effective in controlling postoperative pain, although LIA is superior in reducing postoperative opioid consumption.<sup>14</sup> While some randomized clinical trials (RCTs) have shown lower pain scores on the first postoperative day<sup>15-17</sup> and greater range of motion on the second postoperative day in patients undergoing LIA,<sup>18-20</sup> others have demonstrated lower opioid consumption within the first 24 hours in patients undergoing single-shot femoral nerve block.<sup>21,22</sup> Additionally, some studies have failed to show any significant difference between the two methods.<sup>16,18,19,23</sup> In this context, this meta-analysis of RCTs aims to compare the efficacy of sFNB versus LIA following TKA.

## MATERIALS AND METHODS

This systematic review and meta-analysis was conducted following the guidelines outlined in the Cochrane Collaboration Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.<sup>24,25</sup> The protocol was registered in PROSPERO (CRD42024548788).

### Study Eligibility

The studies included in this meta-analysis met the following criteria: (1) RCTs; (2) comparing sFNB to LIA for the postoperative pain management in patients undergoing TKA. LIA was defined as the use of local anesthetics infiltrated into the skin and soft tissues or the knee joint capsule; sFNB was defined as the single administration of anesthetics around the nerve. Furthermore, studies were only included if they reported any of the clinical outcomes of interest, with adequately reported data, especially continuous outcomes reported as mean and standard deviation; when unavailable, methods recommended by the Cochrane Handbook were applied.<sup>24</sup> Only peer-reviewed studies were considered, without time or language restrictions.

### Literature Search, Study Selection and Data Abstraction

Medline, the Cochrane Library, and Embase were systematically searched from database inception to May 2024 using the following search terms: “knee arthroplasty”, “local infiltration analgesia”, “femoral nerve block” (the complete search strategy is available in Supplementary Material 1).

After removing duplicates, two authors independently screened titles and abstracts to identify articles that met the eligibility criteria. They then assessed full texts of the selected studies to confirm inclusion. Disagreements were resolved by consulting a third, more experienced reviewer who made the final decision.

Two authors independently extracted data from the included studies using pre-defined criteria, including study characteristics (author, local, year of publication, sample size), mean differences and number of events for outcomes of interest, and participants and intervention details (population attributes, substances, and methods used in the interventions).

### Outcomes

The primary outcome of interest was postoperative pain scores at rest and during mobilization (active or passive) measured on postoperative day 1 (POD1) and postoperative day 2 (POD2), using the VAS for pain or the Numeric Rating Scale (NRS) if VAS was unavailable. Secondary outcomes of interest include (1) opioid consumption measured in milligrams (mg) on POD1 and POD2, (2) ROM measured in degrees on POD1 and POD2, and (3) length of hospital stay measured in days after surgery.

### Data Analysis

The mean differences (MD) for continuous outcomes were pooled with the Generic Inverse-Variance method. Effect estimates were reported with 95% confidence intervals (CI), using a random-effects model with the Restricted Maximum Likelihood approach. Heterogeneity was assessed with  $I^2$  statistics, with values > 40% considered moderate.

Additionally, sensitivity analyses were performed using the leave-one-out method to investigate the impact of each study on pooled outcomes with heterogeneity greater than 40%. Subgroup analyses were conducted for (1) studies that included epinephrine in the drug cocktail, (2) morphine in the drug cocktail, (3) ketorolac in the drug cocktail.

### Risk of Bias Assessment

The risk of bias in the included studies was assessed using the Cochrane risk-of-bias tool for randomized trials (RoB 2). Each study was evaluated for potential bias across five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported result. Overall bias was classified as ‘Low,’ ‘Some concerns,’ or ‘High’ risk based on these domains. The publication bias was assessed through funnel plots and Egger’s test.

## RESULTS

### Study Selection and Baseline Characteristics

The systematic search yielded 922 results. After removing duplicate records and excluding ineligible studies, 37 studies remained for full eligibility assessment based on the inclusion criteria. A total of 11 RCTs were included in this meta-analysis (Figure 1).<sup>15-23,26,27</sup> The meta-analysis included a total of 1,109 patients, with 551 (49.7%) undergoing LIA and 558 (50.3%) receiving sFNB. Baseline characteristics of the studies are summarized in Table 1.

### Pain scores at rest

Pain scores at rest on POD1 showed no significant difference between sFNB and LIA (MD = 0.25 points; 95% CI: -0.19 to 0.69;  $p = 0.27$ ;  $I^2 = 61\%$ ; Figure 2). This analysis included eight RCTs with 944 patients. The same pattern was observed on POD2 (MD = 0.08; 95% CI: -0.30 to 0.46;  $p = 0.68$ ;  $I^2 = 41\%$ ; Supplementary Figure 1).

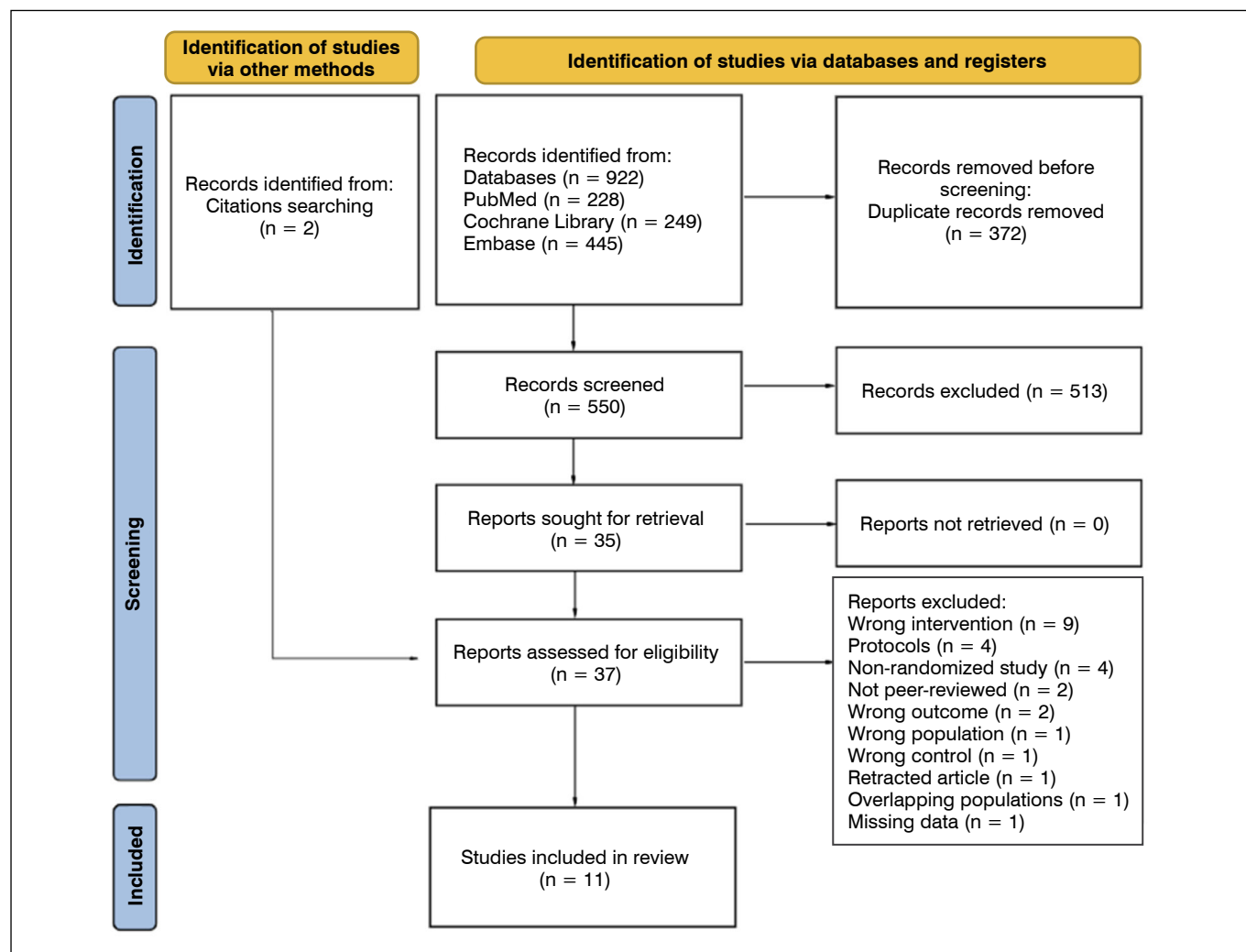


**Figure 1.** Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of the study selection.

### Pain scores during mobilization

The analysis of pain scores during mobilization also showed no significant differences between groups on POD1 (656 patients) (MD = 0.34; 95% CI: -0.66 to 1.34;  $p = 0.50$ ;  $I^2 = 81\%$ ; Figure 3) and on POD2 (467 patients) (MD = -0.04; 95% CI: -0.28 to 0.20;  $p = 0.75$ ;  $I^2 = 23\%$ ; Supplementary Figure 2).

### Opioid consumption

Eight RCTs with 955 patients evaluated opioid consumption 24 hours after surgery (MD = 0.55 mg; 95% CI: -3.28 to 4.38;  $p = 0.77$ ;  $I^2 = 85\%$ ; Figure 4). For opioid consumption on POD2, results remained non-significant (MD = -0.32 mg; 95% CI: -1.00 to 0.35;  $p = 0.35$ ;  $I^2 = 8\%$ ; Supplementary Figure 3).

### Range of motion

Three RCTs with 405 patients assessed ROM on POD1, showing no significant difference between the groups (MD = -4.53 degrees; 95% CI: -10.11 to 1.05;  $p = 0.11$ ;  $I^2 = 0\%$ ; Figure 5). For ROM on POD2, the analysis indicated a wider ROM in the LIA group (MD = -6.15 degrees; 95% CI: -9.16 to -3.14;  $p < 0.01$ ;  $I^2 = 0\%$ ; Figure 6).

### Length of hospital stay

Four RCTs with 377 patients evaluated the length of hospital stay, finding that the LIA group had a shorter duration of hospitalization (MD = 0.23 days; 95% CI: 0.06 to 0.41;  $p < 0.01$ ;  $I^2 = 0\%$ ; Figure 7).

### Subgroup Analysis

Subgroup analyses according to the use of epinephrine, morphine, or ketorolac in the LIA cocktail showed no significant differences between sFNB and LIA regarding postoperative pain scores on POD1 or opioid consumption on POD1 and POD2 (Supplementary Figures 4–12).

### Sensitivity Analysis

The leave-one-out analyses for postoperative pain score at rest on POD1 (Supplementary Figure 13) and opioid consumption on POD1 (Supplementary Figure 14) showed a trend consistent with the overall results, with no single study identified as having a predominant impact on heterogeneity.

The leave-one-out analysis for pain scores at rest on POD2 showed that omission of Fan et al<sup>23</sup> reduced the heterogeneity to unimportant, while the results remained statistically non-significant ( $I^2$  decreased from 41% to 0%; MD = 0.33; 95% CI: -0.10 to 0.77; Supplementary Figure 15).

### Quality Assessment

The quality assessment using the RoB2 tool indicated that none of the studies had an overall high risk of bias. Most studies were classified as having some concerns, while four studies<sup>16,17,19,23</sup> were rated as having a low overall risk of bias (Supplementary Figure 16).

**Table 1.** Baseline characteristics of included studies.

| Study                                         | Type of TKA | Local     | sFNB <sup>†</sup> substances                         | LIA <sup>§</sup> substances                                                                                                                                                             | Patients sFNB <sup>†</sup> /LIA <sup>§</sup> | Anesthesia method | Female, % sFNB/LIA | Age <sup>‡</sup> , y sFNB/LIA | Body Mass Index <sup>‡</sup> , kg/m <sup>2</sup> sFNB/LIA |
|-----------------------------------------------|-------------|-----------|------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------|--------------------|-------------------------------|-----------------------------------------------------------|
| Ashraf et al., 2013 <sup>15</sup>             | Primary     | England   | 30 mL of 0.2% ropivacaine                            | 150 mL 0.2% ropivacaine, 1 mL 1:1000 adrenaline, 30 mg ketorolac                                                                                                                        | 21/19                                        | Spinal            | NA                 | NA                            | NA                                                        |
| Chandrashekaraiiah et al., 2021 <sup>21</sup> | Primary     | Bahrain   | 25mL 0.5% bupivacaine (125 mgs)                      | 50 mL of 0.25% bupivacaine (125 mgs), 10 mg of morphine (1mL) and 99 mL of normal saline                                                                                                | 29/30                                        | Spinal            | 65.5/66.6          | 65.31/61.70                   | NA                                                        |
| Choi et al., 2016 <sup>16</sup>               | Primary     | Canada    | Ropivacaine 0.5% 20 mL                               | Ropivacaine 0.2% with epinephrine 10 µg/mL, 150 mL and ketorolac 30 mg                                                                                                                  | 39/41                                        | Spinal            | 49/51              | 65.2/65.9                     | 31.4/29.3                                                 |
| Craik et al., 2022 <sup>26</sup>              | Primary     | Australia | 20 mL 0.2% ropivacaine                               | 200 mL of 0.2% ropivacaine + 5 mL of 0.2% ropivacaine per hour for 24 hours                                                                                                             | 14/13                                        | Spinal            | 43/54              | 66/69                         | 31/31                                                     |
| Fan et al., 2016 <sup>23</sup>                | Primary     | China     | 20mL of ropivacaine 0.5%                             | 50 mL of cocktail mixture containing morphine (1 mL: 10 mg), ropivacaine (10 mL: 100 mg), and diprospan (1 mL: 5 mg betamethasone dipropionate and 2 mg betamethasone sodium phosphate) | 78/79                                        | General           | 79.5/86            | 68.36/67.59                   | 21.3/21.6                                                 |
| Ismail et al., 2020 <sup>17</sup>             | NA          | Egypt     | 30 mL of bupivacaine 0.25% with adrenaline 1:200,000 | 200 mg 0.5% bupivacaine, 5 mg morphine and 200 µg epinephrine mixed with sterile normal saline solution to make up a combined volume of 50 mL                                           | 65/65                                        | General           | 53.8/53.8          | 62.88/62.97                   | 27.62/27.4                                                |
| Lopes Júnior et al., 2024 <sup>18</sup>       | Primary     | Brazil    | 150 mg of ropivacaine and 150 µg of clonidine        | 150 µg of clonidine, 30 mg of ketorolac, 375 mg of ropivacaine, and 1 mg of epinephrine diluted in 50 mL of saline solution                                                             | 50/50                                        | Spinal            | 78/76              | 68.1/67.7                     | NA                                                        |
| Moghtadaei et al., 2014 <sup>27</sup>         | Primary     | Iran      | 20 mL of ropivacaine 10 mg/mL was injected           | 150 mL: 300 mg ropivacaine 1%, 30 mg ketorolac and 0.5 mg 1:100,000 epinephrine                                                                                                         | 18/18                                        | Spinal            | 33.3/27.8          | 67.4/64                       | 28/27                                                     |
| Ng et al., 2020 <sup>22</sup>                 | Primary     | England   | 20 mL 0.375% levobupivacaine                         | 40 mL 0.25% bupivacaine with adrenaline 1:200,000, diluted with 110 mL of 0.9% saline, making a total volume of 150 mL                                                                  | 79/69                                        | Spinal            | 49.3/44.9          | NA                            | NA                                                        |
| Wall et al., 2017 <sup>19</sup>               | Primary     | England   | 75 mg of 0.25% levobupivacaine hydrochloride         | 150 mg of 0.25% levobupivacaine hydrochloride, 10 mg morphine sulfate, 30 mg ketorolac trometamol and 0.25 mg of adrenaline, all diluted with 0.9% saline to make a volume of 150 ml    | 131/131                                      | Spinal or general | 61.1/58.8          | 68.2/68.7                     | NA                                                        |
| Ye et al., 2020 <sup>20</sup>                 | Primary     | China     | 0.25% ropivacaine 20 mL (89.4 mg)                    | 1% ropivacaine hydrochloride 447 mg, flurbiprofen ester 100 mg, adrenal 1 mg, and dexamethasone 5 mg were mixed in saline. A 100 mL cocktail was prepared                               | 35/35                                        | General           | 68.5/65.7          | 64.5/65.5                     | 25/23.7                                                   |

Captions: <sup>†</sup>Single Femoral Nerve Block; <sup>§</sup>Local infiltration analgesia; <sup>‡</sup>Mean.

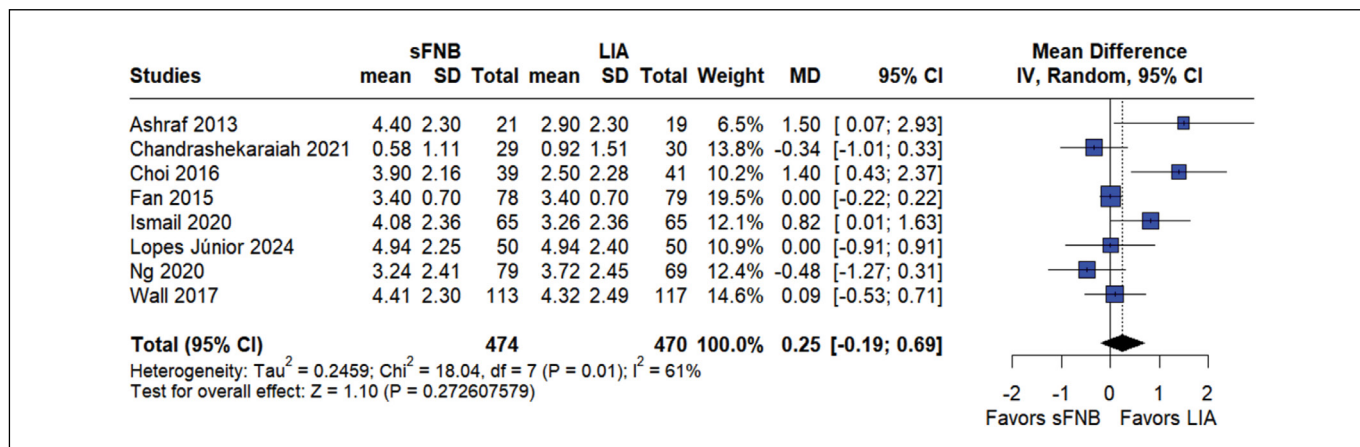


**Figure 2.** Pain scores at rest on postoperative day 1.

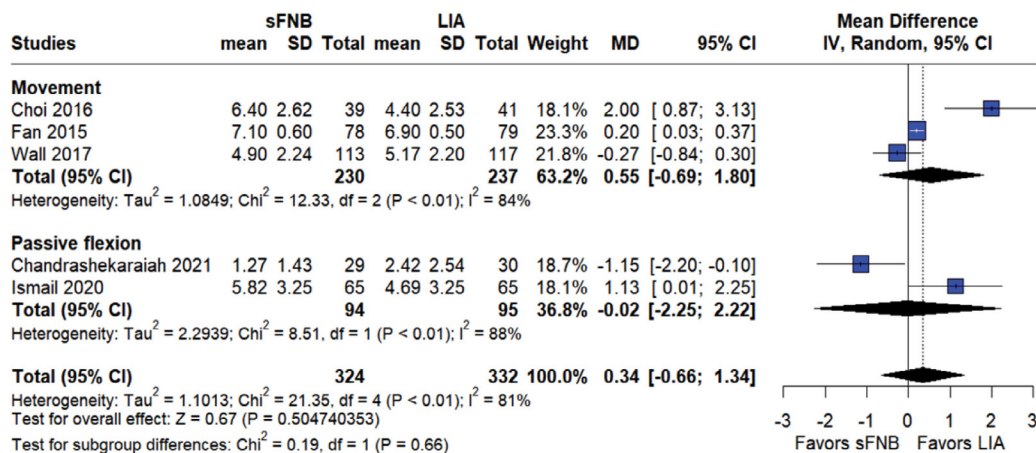


Figure 3. Pain scores during mobilization on postoperative day 1.

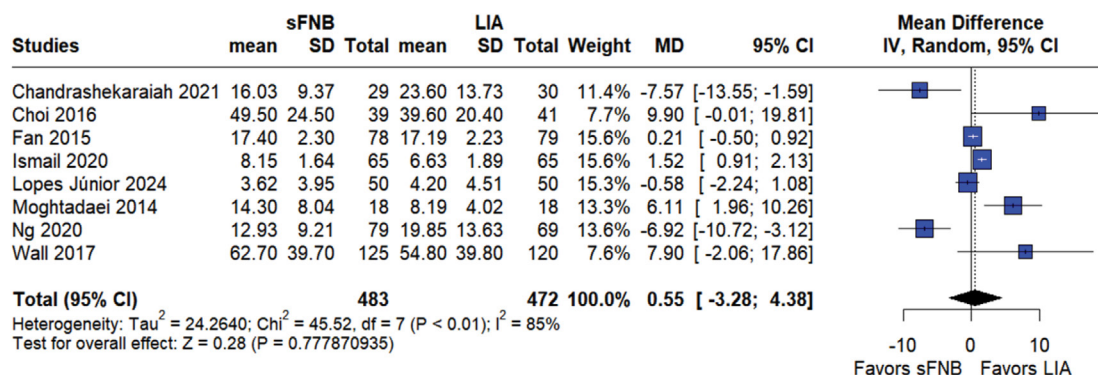


Figure 4. Opioid consumption on postoperative day 1.

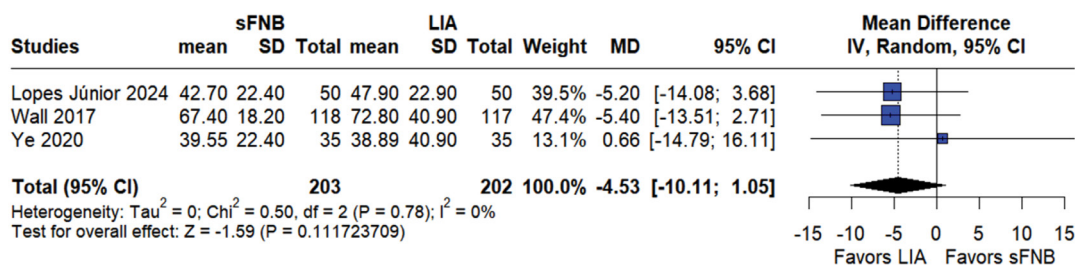


Figure 5. Range of motion on postoperative day 1.

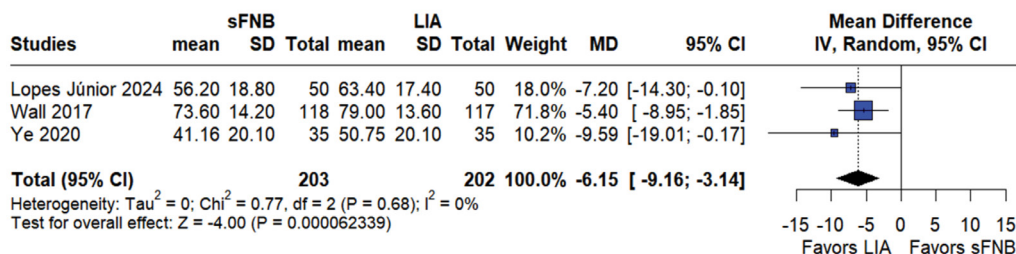


Figure 6. Range of motion on postoperative day 2.

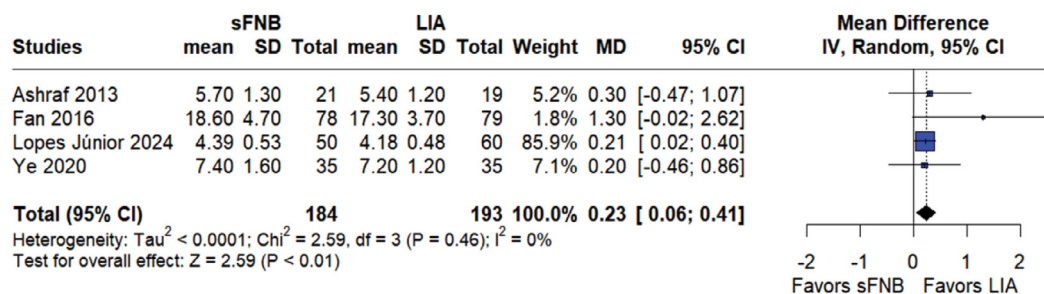


**Figure 7.** Length of hospital stay.

A funnel plot was used to assess potential publication bias for pain scores on POD1, revealing symmetry (Supplementary Figure 17), suggesting no evidence of publication bias. Additionally, an Egger's test confirmed the absence of asymmetry ( $t = 1.284$ ;  $p = 0.246$ ).

## DISCUSSION

This systematic review and meta-analysis specifically compared sFNB with LIA for postoperative pain management following TKA. Previous meta-analyses included both continuous and single-shot FNBs, potentially confounding the comparative outcomes<sup>14,28–31</sup>. The present study included 11 RCTs with a total of 1,109 patients. The main findings were: (1) there were no statistically significant differences between the two groups in terms of postoperative pain scores or opioid consumption; (2) the LIA group demonstrated a shorter hospital stay and improved range of motion on postoperative day 2; and (3) subgroup analyses involving LIA cocktails containing ketorolac, morphine, or epinephrine showed a general trend toward non-significance in pain control.

For pain at rest on POD1, our findings are consistent with those of previous meta-analyses which included both sFNB and cFNB in the analysis.<sup>14,28–31</sup> Additionally, three of them evaluated pain at rest on POD2 and also reported no significant differences between the two modalities.<sup>28,30,31</sup> Four of the previous meta-analyses assessed pain during mobilization,<sup>14,28,29,31</sup> but only the study by Mei et al.<sup>29</sup> found differences in pain scales, with the FNB group presenting lower pain scores on POD1. In neither the previous meta-analyses nor our meta-analysis—which included only sFNB—did the mean differences in pain scale values reach the minimal clinically important difference for TKA, defined as 2.26 centimeters for improvement and 2.91 centimeters for worsening on the visual analog scale.<sup>32</sup> The present study found no significant differences between sFNB and LIA regarding opioid consumption. Previous meta-analyses also found no significant differences in opioid consumption on POD1 and POD2,<sup>28,29,31</sup> nor in total opioid morphine equivalent consumption throughout the entire hospital stay.<sup>29,30</sup> Conversely, the meta-analysis by Liu et al.<sup>14</sup> found that LIA was associated with lower opioid consumption on POD1. Overall, the analgesic efficacy of sFNB and LIA seems to be comparable, and possible differences in terms of analgesia may represent a minor effect in the role of multimodal analgesia. The combination of both peripheral blocks and LIA methods is generally suggested to enhance postoperative analgesia.<sup>33</sup>

A concern with the use of FNB is the occurrence of quadriceps motor block, which could increase the risk of postoperative falls, although this remains controversial in the literature.<sup>11–13,34–37</sup> A study by Memtsoudis et al.<sup>34</sup> with a large database involving 400 hospitals and 191,570 patients in the United States found no association between inpatient falls and peripheral nerve block (PNB). Conversely, studies evaluating risk factors for falls following TKA have identified advanced age, obesity, and the use of cFNB

as being associated with an increased risk of falls.<sup>11–13,37</sup> Proprioception, ROM, and quadriceps strength were also associated with the risk of falling.<sup>35,36</sup> Regarding ROM, the present pooled analysis found no significant difference between the analgesic methods on POD1, but observed a 6.15-degree greater ROM in the LIA group on POD2. Our analysis included the studies by Lopes Júnior et al.,<sup>18</sup> Wall et al.,<sup>19</sup> and Ye et al.,<sup>20</sup> which all reported greater ROM in the LIA group, with mean differences of 7.2°, 5.4°, and 9.59°, respectively. As the reported duration of analgesic effect for LIA<sup>7</sup> is slightly longer than that of sFNB,<sup>6</sup> a possible explanation for the improved ROM on POD2 is the prolonged pain relief provided by LIA. Matsumoto et al.<sup>36</sup> investigated the correlation between falls and ROM in TKA patients between 6 and 12 months postoperatively and found that reduced postoperative knee flexion and ankle plantarflexion were factors related to falls, with patients who experienced falls demonstrating a mean knee range of motion 9.3 degrees lower than non-fallers. Among the studies included in the present meta-analysis, Choi et al.<sup>16</sup> reported no falls, Ng et al.<sup>22</sup> reported one fall in each group, and Lopes Júnior et al.<sup>18</sup> reported one fall in the sFNB group without further consequences. Due to the limited number of reported events, a pooled analysis regarding the risk of falling could not be performed.

Reducing the length of hospital stay is beneficial for minimizing clinical complications, reducing the risk of prosthesis-related infections, and lowering healthcare costs.<sup>38–40</sup> In the present study, the LIA group had a 0.23-day shorter hospital stay than the sFNB group, equivalent to approximately 6 hours. Similarly, Albrecht et al.<sup>28</sup> reported a 0.3-day shorter length of stay in the LIA group. Reported lengths of hospital stay after TKA procedures vary widely in the literature,<sup>40–45</sup> due to differences in healthcare systems, institutional protocols, hospital infrastructure, and patient-related factors such as age, smoking status, baseline comorbidities, preoperative corticosteroid use, and the American Society of Anesthesiologists (ASA) Physical Status classification.<sup>41,42</sup> El Bitar et al.<sup>41</sup> analyzed data from 1,924,432 patients in the Nationwide Inpatient Sample database in the United States and found that 74.8% of those who underwent TKA had a hospital stay of three days or less. Among the studies included, Fan et al.<sup>23</sup> reported substantially longer hospital stays than the other studies, representing an outlier within the dataset.

This study has some limitations. The primary limitation is the high heterogeneity observed in opioid consumption and postoperative pain score outcomes. To address this, we have performed subgroup analyses with studies using epinephrine, ketorolac, and morphine in the LIA cocktail. However, the subgroup results remained consistent with the overall findings, and no reduction in heterogeneity was observed, suggesting that adding these substances to LIA does not confer superiority over sFNB or significantly influence heterogeneity. Therefore, heterogeneity

may partially stem from variations in analgesia and rehabilitation protocols across studies, including different NSAIDs and analgesics, administration methods, such as patient-controlled devices and fixed opioid doses based on VAS levels. Additionally, leave-one-out analyses were performed, but heterogeneity remained high, and no single study contributed significantly to the heterogeneity in opioid consumption and postoperative pain scores.

## CONTRIBUTIONS OF THE AUTHORS

Each author made a personal and significant contribution to the development of this article. ARSOF, AGMS, DPL: Conceptualization. ARSOF, RBC, EM, VFC, DPL: Data Curation. ARSOF, RBC, EM, DPL: Formal Analysis. ARSOF, RBC, EM, VFC, CPH, AGMS, DPL: Methodology. ARSOF, CPH, AGMS, DPL: Project Administration. ARSOF, CPH, AGMS, DPL: Supervision. ARSOF, RBC, EM, VFC, CPH, AGMS, DPL: Writing – Original Draft. ARSOF, CPH, AGMS, DPL: Writing – Review & Editing.

## DATA AVAILABILITY DECLARATION

The contents are already available.

## REFERENCES

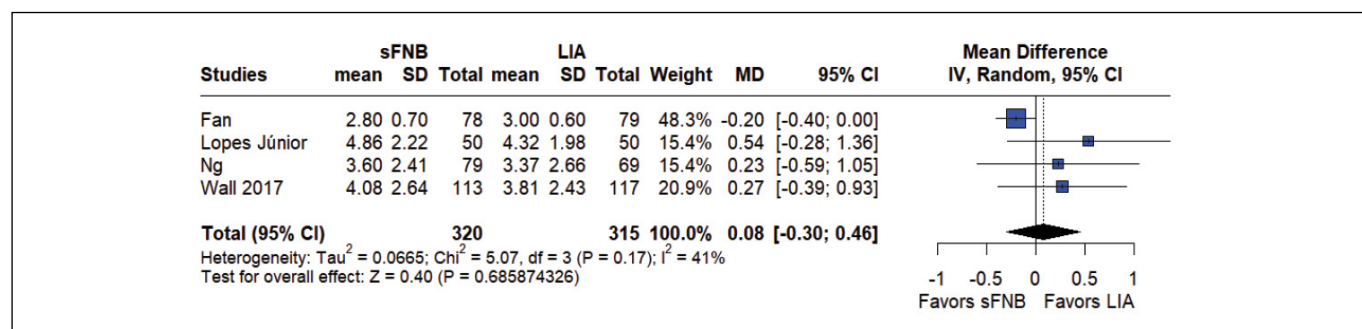
- Klug A, Gramlich Y, Rudert M, Drees P, Hoffmann R, Weissenberger M, et al. The projected volume of primary and revision total knee arthroplasty will place an immense burden on future health care systems over the next 30 years. *Knee Surg Sports Traumatol Arthrosc*. 2021;29(10):3287-98. doi: 10.1007/s00167-020-06154-7.
- Chandrasekaran S, Ariaretnam SK, Tsung J, Dickson D. Early mobilization after total knee replacement reduces the incidence of deep venous thrombosis. *ANZ J Surg*. 2009;79(7-8):526-9. doi: 10.1111/j.1445-2197.2009.04982.x.
- Hannon CP, Fillingham YA, Hamilton WG, Della Valle CJ. Multimodal Analgesia and Anesthesia: Enabling Safe and Rapid Recovery for Total Joint Arthroplasty Patients. *J Arthroplasty*. 2022;37(9):1669-70. doi: 10.1016/j.arth.2022.07.016.
- Lei YT, Xie JW, Huang Q, Huang W, Pei FX. Benefits of early ambulation within 24 h after total knee arthroplasty: a multicenter retrospective cohort study in China. *Mil Med Res*. 2021;8(1):17. doi: 10.1186/s40779-021-00310-x.
- Malviya A, Martin K, Harper I, Muller SD, Emmerson KP, Partington PF, et al. Enhanced recovery program for hip and knee replacement reduces death rate. *Acta Orthop*. 2011;82(5):577-81. doi: 10.3109/17453674.2011.618911.
- Szczukowski MJ, Hines JA, Snell JA, Sica TS. Femoral nerve block for total knee arthroplasty patients: a method to control postoperative pain. *J Arthroplasty*. 2004;19(6):720-5. doi: 10.1016/j.arth.2004.02.043.
- Seanglelur A, Vanasbodeekul P, Prapaitrakool S, Worathongchai S, Anothaisintawee T, McEvoy M, et al. The efficacy of local infiltration analgesia in the early postoperative period after total knee arthroplasty: A systematic review and meta-analysis. *Eur J Anaesthesiol*. 2016;33(11):816-31. doi: 10.1097/eja.0000000000000516.
- Li S, Zhou J, Li X, Teng X, Li Y, Du C, et al. Analgesic Impact of Single-Shot Versus Continuous Femoral Nerve Block After Total Knee Arthroplasty: A Systematic Review and Meta-Analysis. *Adv Ther*. 2020;37(2):671-85. doi: 10.1007/s12325-019-01194-z.
- Ma HH, Chou TFA, Tsai SW, Chen CF, Wu PK, Chen WM. The efficacy of continuous versus single-injection femoral nerve block in Total knee Arthroplasty: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2020;21(1):121. doi: 10.1186/s12891-020-3148-1.
- Ilfeld BM. Single-injection and continuous femoral nerve blocks are associated with different risks of falling. *Anesthesiology*. 2014;121(3):668-9. doi: 10.1097/ain.0000000000000358.
- Ilfeld BM, Duke KB, Donohue MC. The Association Between Lower Extremity Continuous Peripheral Nerve Blocks and Patient Falls After Knee and Hip Arthroplasty. *Anesth Analg*. 2010;111(6):1552-4. doi: 10.1213/ane.0b013e3181fb9507.
- Wasserstein D, Farlinger C, Brull R, Mahomed N, Gandhi R. Advanced age, obesity and continuous femoral nerve blockade are independent risk factors for inpatient falls after primary total knee arthroplasty. *J Arthroplasty*. 2013;28(7):1121-4. doi: 10.1016/j.arth.2012.08.018.
- Johnson RL, Kopp SL, Hebl JR, Erwin PJ, Mantilla CB. Falls and major orthopaedic surgery with peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth*. 2013;110(4):518-28. doi: 10.1093/bja/aet013.
- Liu Q, Wang A, Zhang J. The effects of local infiltration anesthesia and femoral nerve block analgesia after total knee arthroplasty: a systematic review and meta-analysis. *Ann Transl Med*. 2022;10(4):178. doi: 10.21037/atm-22-286.
- Ashraf A, Raut V, Canty S, McLauchlan G. Pain control after primary total knee replacement. A prospective randomised controlled trial of local infiltration versus single shot femoral nerve block. *Knee*. 2013;20(5):324-7. doi: 10.1016/j.knee.2013.04.009.
- Choi S, O'Hare T, Gollish J, Paul J, Kreder H, Thorpe K, et al. Optimizing Pain and Rehabilitation After Knee Arthroplasty: a Two-Center, Randomized Trial. *Anesth Analg*. 2016;123(5):1316-24. doi: 10.1213/ane.0000000000001469.
- Ismail TI, Elshafie MH. Patient-reported outcomes after femoral nerve block versus periarticular injections in patients undergoing total knee arthroplasty: A randomized controlled study. *Indian J Clin Anaesth*. 2020;7(4):687-94. doi: 10.18231/j.ijca.2020.123.
- Lopes Júnior O, Viana J, Carvalho J, Folle B, Kuhn V, Saggin P. Infiltração periarticular comparada ao bloqueio do nervo femoral único na artroplastia total de joelho: Um estudo prospectivo randomizado. *Rev Bras Ortop (Sao Paulo)*. 2024;59(2):e241-e246. doi: 10.1055/s-0044-1785449.
- Wall P, Parsons N, Parsons H, Achten J, Balasubramanian S, Thompson P, et al. A pragmatic randomised controlled trial comparing the efficacy of a femoral nerve block and periarticular infiltration for early pain relief following total knee arthroplasty. *Bone Joint J*. 2017;99-B(7):904-11. doi: 10.1302/0301-620x.99b7.bjj-2016-0767.r2.
- Zhang Y, Feng S, Zhang Y, Sun J, Shi S, Chen X. Early analgesic effect of cocktail periarticular injection versus femoral nerve block in total knee arthroplasty: a single-center randomized double-blind control. *Chin J Tissue Eng Res*. 2020;24(36):5800-5. doi: 10.3969/j.issn.2095-4344.2909.
- Chandrasekaraiah MM, Shah VH, Sahitya PV, Pandey VC, Butt AJ, Mohammed S, et al. Impact of Intra-Articular Local Anesthesia Infiltration versus Femoral Nerve Block for Postoperative Pain Management in Total Knee Arthroplasty. *Anesth Essays Res*. 2021;15(2):208-12. doi: 10.4103/aer.aer\_112\_21.
- Ng YM, Martin F, Waterson HB, Green A, Preece J, Robinson N, et al. A Randomised Controlled Trial of Local Infiltration Analgesia Versus Femoral Nerve Block for Postoperative Analgesia Following Total Knee Arthroplasty. *Cureus*. 2020;12(9):e10192. doi: 10.7759/cureus.10192.
- Fan L, Yu X, Zan P, Liu J, Ji T, Li G. Comparison of Local Infiltration Analgesia With Femoral Nerve Block for Total Knee Arthroplasty: a Prospective, Randomized Clinical Trial. *J Arthroplasty*. 2016;31(6):1361-5. doi: 10.1016/j.arth.2015.12.028.
- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al., editors. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6.4 (updated August 2023). *Cochrane*; 2023 [cited 2024 Aug 13].
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71.
- Craik JD, Koerber JG, Krishnan J, Wilson C. Analgesia for Total Knee Arthroplasty: A Randomized Controlled Study Comparing Local Infusion Analgesia, Femoral Nerve Block and Intrathecal Morphine. *Open Access J Biomed Sci*. 2022;4(1):1600-5. doi: 10.38125/oajbs.000403.
- Moghtadaei M, Farahini H, Faiz S, Mokarami F, Safari S. Pain Management for Total Knee Arthroplasty: single-Injection Femoral Nerve Block versus Local Infiltration Analgesia. *Iran Red Crescent Med J*. 2014;16(1):e13247. doi: 10.5812/ircmj.13247.
- Albrecht E, Guyen O, Jacot-Guillarmod A, Kirkham KR. The analgesic efficacy of local infiltration analgesia vs femoral nerve block after total knee arthroplasty: A systematic review and meta-analysis. *Br J Anaesth*. 2016;116(5):597-609. doi: 10.1093/bja/aew099.
- Mei S, Jin S, Chen Z, Ding X, Zhao X, Li Q. Analgesia for total knee arthroplasty:

## CONCLUSION

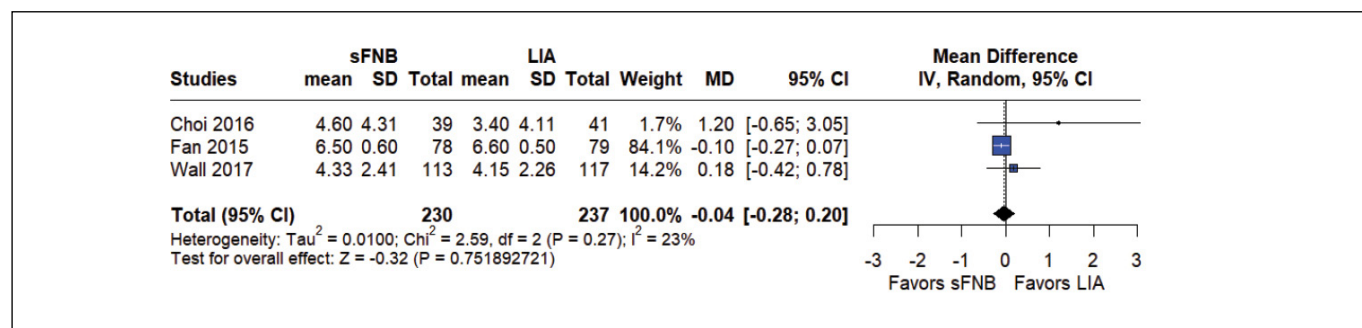
This systematic review and meta-analysis comparing local infiltration analgesia (LIA) to single-shot femoral nerve block (sFNB) for postoperative management in TKA patients indicates a 0.23-day shorter hospital stay and greater range of motion on postoperative day two in the LIA group. No statistically significant differences were observed between the two methods regarding opioid consumption or postoperative pain scores.

- a meta-analysis comparing local infiltration and femoral nerve block. *Clinics (Sao Paulo)*. 2015;70(9):648-53. doi: 10.6061/clinics/2015(09)09.
30. Zhang LK, Ma JX, Kuang MJ, Ma XL. Comparison of Periarthral Local Infiltration Analgesia With Femoral Nerve Block for Total Knee Arthroplasty: a Meta-Analysis of Randomized Controlled Trials. *J Arthroplasty*. 2018;33(6):1972-1978.e4. doi: 10.1016/j.arth.2017.12.042.
  31. Yun XD, Yin XL, Jiang J, Teng YJ, Dong HT, An LP, et al. Local infiltration analgesia versus femoral nerve block in total knee arthroplasty: A meta-analysis. *Orthop Traumatol Surg Res*. 2015;101(5):565-9. doi: 10.1016/j.otsr.2015.03.015.
  32. Danoff JR, Goel R, Sutton R, Maltenfort MG, Austin MS. How Much Pain Is Significant? Defining the Minimal Clinically Important Difference for the Visual Analog Scale for Pain After Total Joint Arthroplasty. *J Arthroplasty*. 2018;33(7S):S71-S75.e2. doi: 10.1016/j.arth.2018.02.029.
  33. Aso K, Izumi M, Sugimura N, Okanoue Y, Kamimoto Y, Yokoyama M, et al. Additional benefit of local infiltration of analgesia to femoral nerve block in total knee arthroplasty: double-blind randomized control study. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(7):2368-74. doi: 10.1007/s00167-018-5322-7.
  34. Memtsoudis SG, Danninger T, Rasul R, Poeran J, Gerner P, Stundner O, et al. Inpatient falls after total knee arthroplasty: the role of anesthesia type and peripheral nerve blocks. *Anesthesiology*. 2014;120(3):551-63. doi: 10.1097/aln.000000000000120.
  35. Levinger P, Menz HB, Wee E, Feller JA, Bartlett JR, Bergman NR. Physiological risk factors for falls in people with knee osteoarthritis before and early after knee replacement surgery. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(7):1082-9. doi: 10.1007/s00167-010-1325-8.
  36. Matsumoto H, Okuno M, Nakamura T, Yamamoto K, Hagino H. Fall incidence and risk factors in patients after total knee arthroplasty. *Arch Orthop Trauma Surg*. 2012;132(4):555-63. doi: 10.1007/s00402-011-1418-y.
  37. Sharma S, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of Femoral Nerve Block for Total Knee Arthroplasty. *Clin Orthop Relat Res*. 2010;468(1):135-40. doi: 10.1007/s11999-009-1025-1.
  38. DeMik DE, Carender CN, An Q, Callaghan JJ, Brown TS, Bedard NA. Longer Length of Stay Is Associated With More Early Complications After Total Knee Arthroplasty. *Iowa Orthop J*. 2022;42(2):53-9.
  39. Lovald ST, Ong KL, Malkani AL, Lau EC, Schmier JK, Kurtz SM, et al. Complications, mortality, and costs for outpatient and short-stay total knee arthroplasty patients in comparison to standard-stay patients. *J Arthroplasty*. 2014;29(3):510-5. doi: 10.1016/j.arth.2013.07.020.
  40. Molloy IB, Martin BI, Moschetti WE, Jevsevar DS. Effects of the Length of Stay on the Cost of Total Knee and Total Hip Arthroplasty from 2002 to 2013. *J Bone Joint Surg Am*. 2017;99(5):402-7. doi: 10.2106/jbjs.16.00019.
  41. El Bitar YF, Illingworth KD, Scaife SL, Horberg JV, Saleh KJ. Hospital Length of Stay following Primary Total Knee Arthroplasty: Data from the Nationwide Inpatient Sample Database. *J Arthroplasty*. 2015;30(10):1710-5. doi: 10.1016/j.arth.2015.05.003.
  42. Hart A, Bergeron SG, Epure L, Huk O, Zukor D, Antoniou J. Comparison of US and Canadian Perioperative Outcomes and Hospital Efficiency After Total Hip and Knee Arthroplasty. *JAMA Surg*. 2015;150(10):990-8. doi: 10.1001/jamasurg.2015.1239.
  43. Burn E, Edwards CJ, Murray DW, Silman A, Cooper C, Arden NK, et al. Trends and determinants of length of stay and hospital reimbursement following knee and hip replacement: evidence from linked primary care and NHS hospital records from 1997 to 2014. *BMJ Open*. 2018;8(1):e019146. doi: 10.1136/bmjopen-2017-019146.
  44. Styron JF, Koroukian SM, Klika AK, Barsoum WK. Patient vs provider characteristics impacting hospital lengths of stay after total knee or hip arthroplasty. *J Arthroplasty*. 2011;26(8):1418-1426.e1-2. doi: 10.1016/j.arth.2010.11.008.
  45. Long H, Zeng C, Shi Y, Wang H, Xie D, Lei G. Length of stay and inpatient charges of total knee arthroplasty in China: analysis of a national database. *Chin Med J (Engl)*. 2023;136(17):2050-7. doi: 10.1097/cm9.0000000000002220.

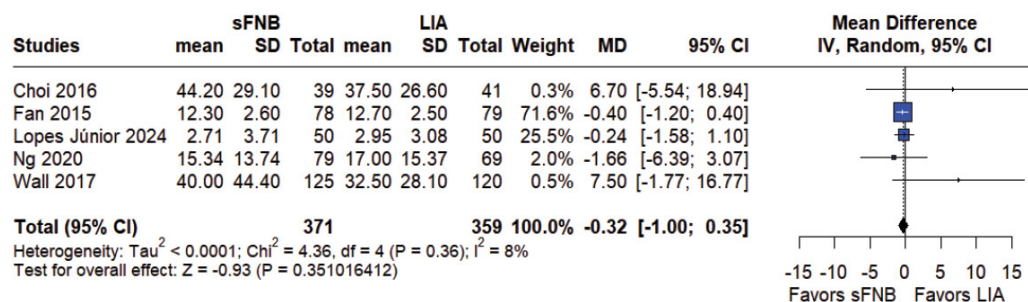
## SUPPLEMENTARY MATERIAL



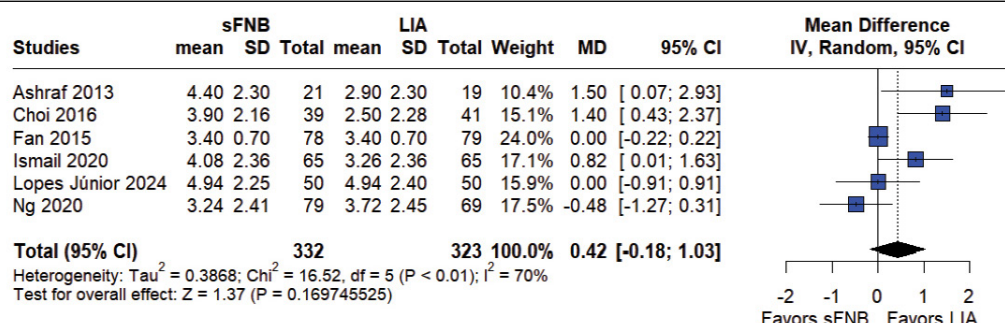
Supplementary Figure 1. Pain scores at rest on postoperative day 2.



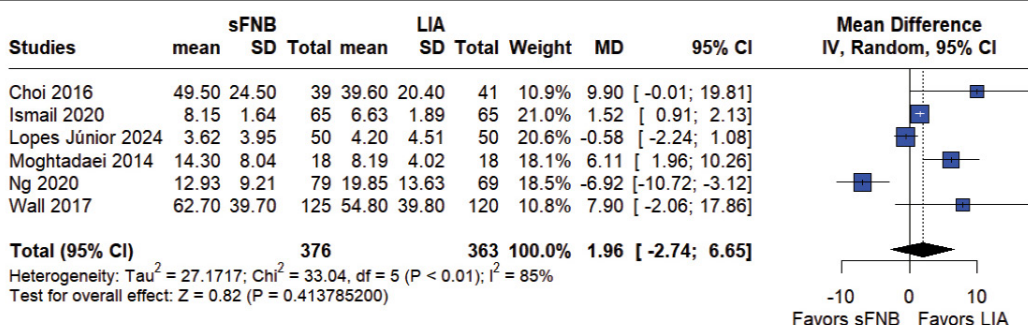
Supplementary Figure 2. Pain scores during mobilization on postoperative day 2.



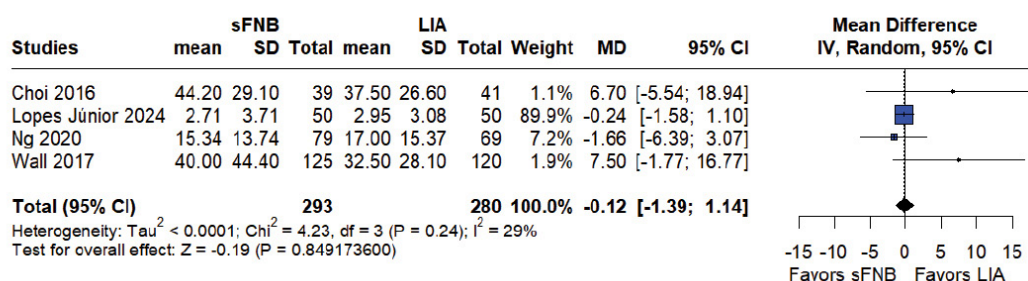
**Supplementary Figure 3.** Opioid consumption on postoperative day 2.



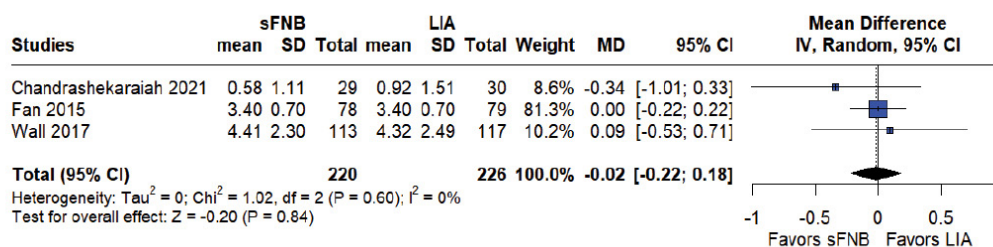
**Supplementary Figure 4.** Subgroup of studies that used epinephrine in the local infiltration analgesia cocktail for the outcome of pain scores on postoperative day 1.



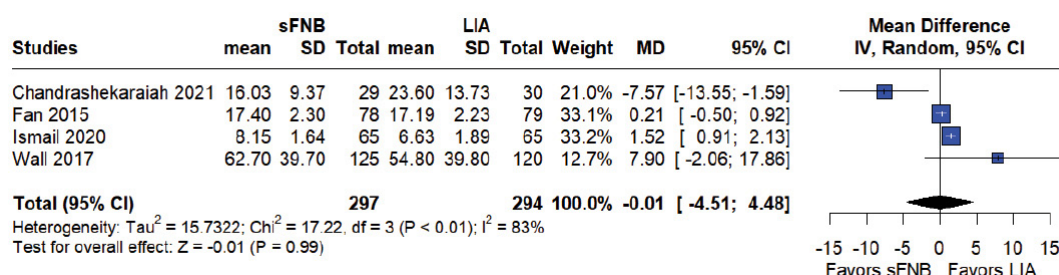
**Supplementary Figure 5.** Subgroup of studies that used epinephrine in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 1.



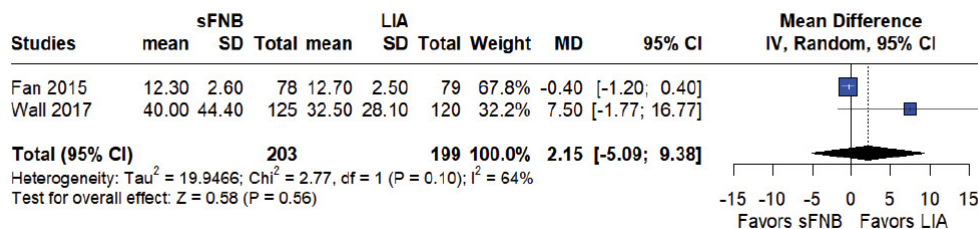
**Supplementary Figure 6.** Subgroup of studies that used epinephrine in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 2



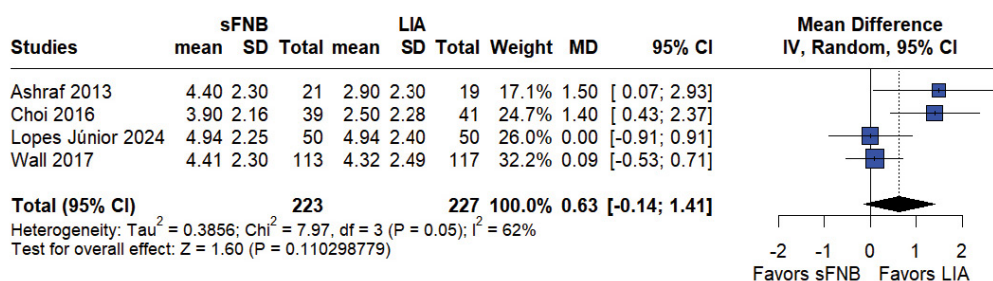
**Supplementary Figure 7.** Subgroup of studies that used morphine in the local infiltration analgesia cocktail for the outcome of pain scores on postoperative day 1



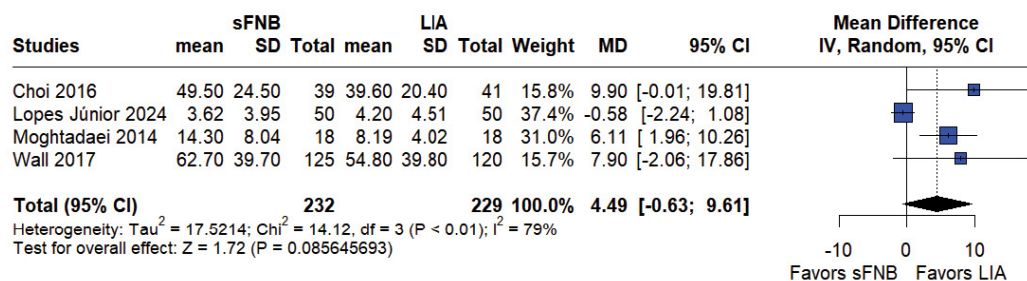
**Supplementary Figure 8.** Subgroup of studies that used morphine in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 1.



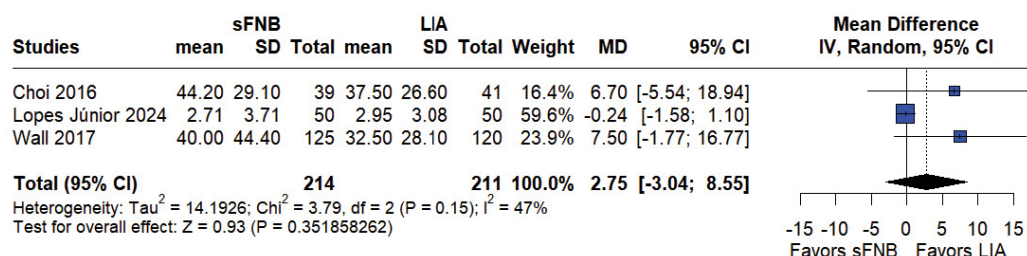
**Supplementary Figure 9.** Subgroup of studies that used morphine in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 2.



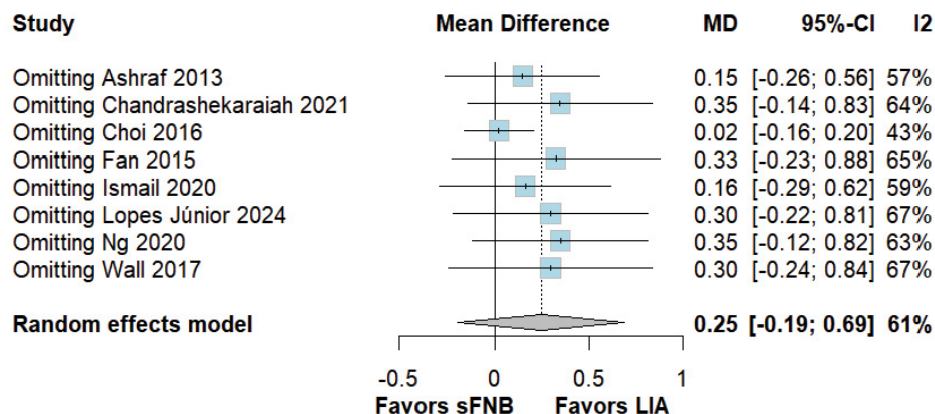
**Supplementary Figure 10.** Subgroup of studies that used ketorolac in the local infiltration analgesia cocktail for the outcome of pain scores on postoperative day 1.



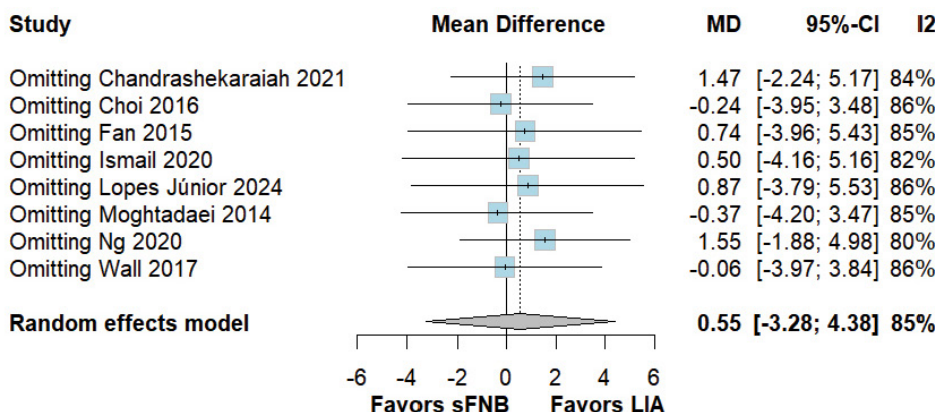
**Supplementary Figure 11.** Subgroup of studies that used ketorolac in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 1.



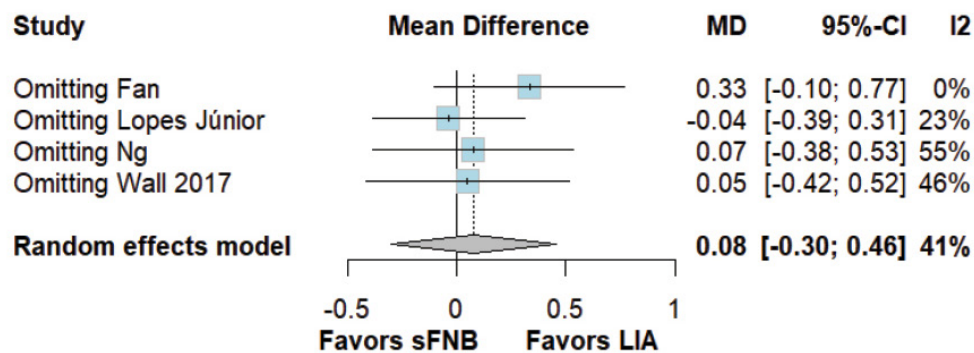
**Supplementary Figure 12.** Subgroup of studies that used ketorolac in the local infiltration analgesia cocktail for the outcome of opioid consumption on postoperative day 2.



**Supplementary Figure 13.** Leave-one-out analysis of pain scores on postoperative day 1.



**Supplementary Figure 14.** Leave-one-out analysis of opioid consumption on postoperative day 1.



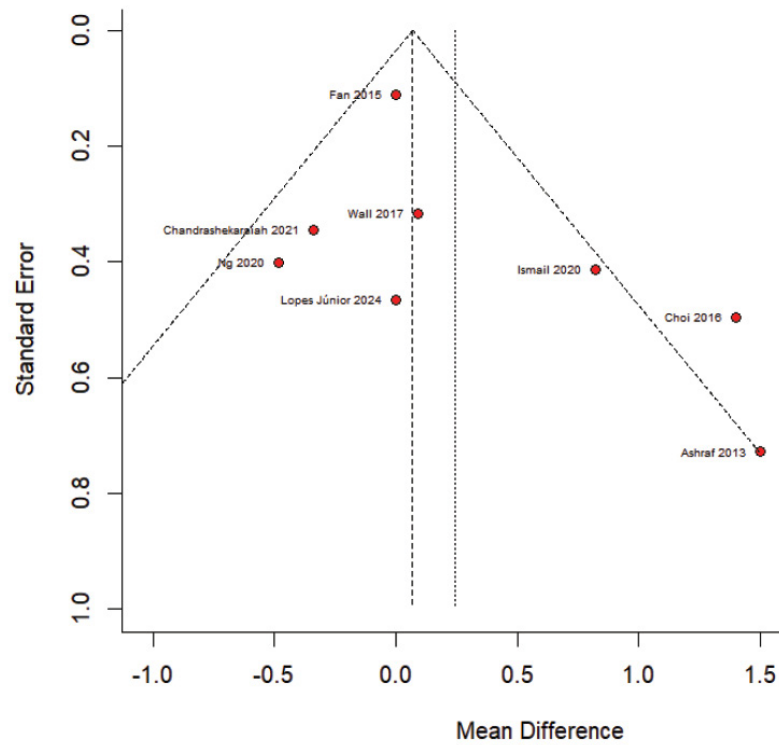
**Supplementary Figure 15.** Leave-one-out analysis of pain scores at rest on postoperative day 2.

|       |                         | Risk of bias domains |    |    |    |    |
|-------|-------------------------|----------------------|----|----|----|----|
|       |                         | D1                   | D2 | D3 | D4 | D5 |
| Study | Ashraf 2013             | +                    | -  | +  | +  | -  |
|       | Chandrashekaraiiah 2021 | -                    | +  | +  | +  | +  |
|       | Choi 2016               | +                    | +  | +  | +  | +  |
|       | Craik 2022              | +                    | +  | +  | +  | -  |
|       | Fan 2016                | +                    | +  | +  | +  | +  |
|       | Ismail 2020             | +                    | +  | +  | +  | +  |
|       | Lopes Júnior 2024       | +                    | +  | +  | +  | -  |
|       | Moghtadaei 2014         | -                    | +  | +  | +  | -  |
|       | Ng 2020                 | +                    | +  | +  | +  | -  |
|       | Wall 2017               | +                    | +  | +  | +  | +  |
|       | Ye 2020                 | +                    | +  | +  | +  | -  |
|       |                         | Overall              |    |    |    |    |
|       |                         | -                    | +  | +  | +  | -  |

Domains:  
D1: Bias arising from the randomization process.  
D2: Bias due to deviations from intended intervention.  
D3: Bias due to missing outcome data.  
D4: Bias in measurement of the outcome.  
D5: Bias in selection of the reported result.

Judgement  
- Some concerns  
+ Low

**Supplementary Figure 16.** Risk-of-bias assessment of the included studies using the Cochrane Risk of Bias 2 tool.



**Supplementary Figure 17.** Funnel plot of pain scores at rest on postoperative day 1.

# RADIOGRAPHIC UNION OVERESTIMATES BIOMECHANICAL STRENGTH: A CEILING EFFECT OF THE RUST SCORE IN RAT TIBIA MODELS

## A CONSOLIDAÇÃO RADIOGRÁFICA SUPERESTIMA A RESISTÊNCIA BIOMECÂNICA: O EFEITO TETO DA ESCALA RUST EM MODELOS DE TÍBIA DE RATO

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### ABSTRACT

**Objective:** To evaluate if the Radiographic Union Scale for Tibial Fractures (RUST) identifies bone consolidation in rat tibia osteotomies, correlating it with biomechanical parameters. **Methods:** Forty-five Wistar rats underwent right proximal tibia osteotomies, fixed with 0.8mm Kirschner wires. At 8 weeks, tibias were radiographed and underwent three-point bending tests to determine maximum force recovery (Frec). Biomechanical union was Frec > 80% of the intact side. Five blinded orthopedists scored radiographs using RUST (4-12); scores  $\geq 10$  indicated radiographic union. **Results:** Thirty-eight rats were analyzed. Spearman's correlation for non-normal data showed no significant relationship between absolute RUST scores and Frec ( $\rho = 0.09$ ;  $p = 0.58$ ). Fisher's Exact test revealed no association between RUST  $\geq 10$  and Frec > 80% ( $p = 0.50$ ). While 36 tibias (94.7%) achieved RUST  $\geq 10$ , only 16 (42.1%) reached the biomechanical threshold. **Conclusion:** At 8 weeks, RUST  $\geq 10$  overestimates structural recovery and cannot reliably predict >80% force restoration in this model. Radiographic bridging precedes complete biomechanical maturation, indicating a scoring system ceiling effect. **Level of Evidence V; Animal Experimental Study.**

**Keywords:** Tibial Fractures; Fracture Healing; Radiography; Biomechanical Phenomena; Rats, Wistar.

### RESUMO

**Objetivo:** Avaliar se a escala RUST (Radiographic Union Scale for Tibial Fractures) identifica a consolidação óssea em osteotomias de tibia de ratos, correlacionando-a com parâmetros biomecânicos. **Métodos:** Quarenta e cinco ratos Wistar sofreram osteotomia proximal da tibia direita, fixada com fio de Kirschner de 0,8 mm. Às oito semanas, as tibias foram radiografadas e submetidas a ensaio de flexão em três pontos para medir a recuperação da força máxima (Frec). Consolidação biomecânica foi Frec > 80% do lado íntegro. Cinco ortopedistas avaliaram cegamente as imagens (RUST 4-12); escore  $\geq 10$  definiu consolidação radiográfica. **Resultados:** Analisou-se 38 animais. A correlação de Spearman (dados não-normais) indicou ausência de relação significativa entre os escores absolutos de RUST e Frec ( $\rho = 0,09$ ;  $p = 0,58$ ). O Teste Exato de Fisher não evidenciou associação entre RUST  $\geq 10$  e Frec > 80% ( $p = 0,50$ ). Embora 36 tibias (94,7%) tenham atingido o critério radiográfico (RUST  $\geq 10$ ), apenas 16 (42,1%) alcançaram o limiar biomecânico. **Conclusão:** Na oitava semana, o escore RUST  $\geq 10$  superestima a recuperação estrutural e não prediz de forma confiável uma recuperação superior a 80% da força neste modelo. A ponte óssea radiográfica precede a maturação biomecânica, evidenciando um efeito teto (ceiling effect) da escala. **Nível de Evidência V; Estudo Experimental em Animais.**

**Descritores:** Fraturas da Tíbia; Consolidação da Fratura; Radiografia; Fenômenos Biomecânicos; Ratos Wistar.

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### INTRODUCTION

The assessment of bone healing is a cornerstone of both clinical practice and orthopedic research. Historically, the evaluation of fracture union relied on subjective radiographic interpretations,

leading to low inter-observer reliability. To address this, the Radiographic Union Scale for Tibial Fractures (RUST) was developed as a standardized tool to quantify healing based on the presence of bridging callus and the visibility of the fracture line across

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The study was conducted at Laboratory of Biomaterials in Orthopedics (LABIMO), Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil.

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four cortices in two orthogonal views.<sup>1</sup> The score ranges from 4 (no healing) to 12 (complete consolidation), providing a more objective measure than general clinical impression.<sup>1</sup>

In clinical settings, the RUST score has proven to be a robust prognostic marker. Mundi et al. demonstrated that RUST scores obtained in three months post-operatively are significantly associated with the risk of nonunion in tibial shaft fractures, where lower scores accurately predict the need for secondary interventions.<sup>2</sup> However, the translation of this scale to pre-clinical research is essential, as animal models remain the gold standard for testing new osteogenic therapies and fixation devices.<sup>3</sup> Tawonsawatruk et al. validated the RUST scale in rat tibial fractures, reporting excellent inter-observer and intra-observer agreement, which supports its use in small animal models.<sup>3</sup>

Despite its reliability in identifying bridging callus, the correlation between radiographic appearance and the actual physical strength of the bone remains a subject of investigation. While some studies suggest that RUST correlates with structural properties observed in micro-computed tomography (micro-CT), others point to a complex relationship with biomechanical data.<sup>4,5</sup> Alentado et al. found that radiographic scores in murine models correlate with micro-CT metrics such as bone volume fraction but emphasized that imaging alone may not fully capture the mechanical integrity of the healing callus.<sup>6</sup> Furthermore, Cooke et al. highlighted that although RUST scores generally increase with bone stiffness and strength, there is significant variability in biomechanical properties within the same RUST score group.<sup>5</sup>

Defining a clear “union” threshold is critical for experimental consistency. Litrenta et al., using a sheep model, suggested that a RUST score of 10 or higher represents a reliable threshold for biomechanical union.<sup>7</sup> However, assessing if this threshold translates universally to smaller rodents is necessary. Therefore, the present study aimed to evaluate the correlation between RUST scores and maximum force values in a rat tibia osteotomy model, specifically testing whether a categorical threshold can accurately predict biomechanically consolidated bones at 8 weeks.

## MATERIALS AND METHODS

The study protocol was approved by the Institutional Animal Care and Use Committee (CEUA-UNICAMP) under protocol numbers 6327-1/2023 and 6515-1/2024. Forty-five male Wistar rats were used in this experimental study. Each animal underwent a proximal metadiaphyseal osteotomy of the right tibia, which was stabilized using a 0.8 mm Kirschner wire. The animals were followed for a period of 8 weeks to allow for natural healing process.

At the 8-week endpoint, the animals were euthanized, and the right (operated) and left (intact) tibias were harvested. Digital radiographs were obtained in anteroposterior and lateral views with a focus-film distance of 72 cm. The radiographic images were then randomly assigned to five blinded orthopedic trauma specialists for scoring according to the RUST criteria (score 4 to 12). Consolidation was radiographically defined as a RUST score  $\geq 10$ .<sup>7</sup>

Immediately following imaging, the tibias underwent biomechanical testing using a three-point bending assay in a universal testing machine (Intermetric, model IM-100). This setup allowed for the measurement of structural properties at the osteotomy site (Figure 1). The maximum force (Fmax) supported by each bone was recorded. To standardize the results, the percentage of force recovery was calculated for each animal as Frec (Fmax operated / Fmax intact)  $\times$  100. Based on established experimental protocols, biomechanical consolidation was defined as the recovery of more than 80% of the maximum force of the intact contralateral limb.<sup>4,6</sup>

Statistical analysis began with the Shapiro-Wilk test to assess data normality. Given the non-normal ordinal distribution of the



**Figure 1.** Experimental setup for the three-point bending test of the rat tibia.

radiographic scores, the non-parametric Spearman's rank correlation coefficient ( $\rho$ ) was utilized to evaluate the relationship between absolute RUST scores and Frec. Additionally, Fisher's Exact test was employed to analyze the association between the categorical variables “radiographically consolidated” (RUST  $\geq 10$ ) and “biomechanically consolidated” (Frec  $> 80\%$ ), with significance set at  $p < 0.05$ .

## RESULTS

Thirty-eight animals were included in the final analysis after the exclusion of seven subjects due to infection or surgical complications. The biomechanical assays demonstrated a wide range of force recovery across the subjects at 8 weeks. The individual values for maximum force recovery (Frec) and absolute RUST scores for all evaluated subjects are detailed in Table 1.

Radiographic evaluation revealed that most samples presented significant bridging callus at 8 weeks. Representative images demonstrating the morphology of the tibias are shown in Figure 2. The continuous data analysis revealed the absence of a significant correlation. The Spearman's rank correlation coefficient between the absolute RUST scores and maximum force recovery was  $\rho = 0.09$  ( $p = 0.58$ ). This dispersion is visually represented in the scatter plot in Figure 3.

The categorical analysis revealed a substantial discrepancy between radiographic and biomechanical findings. Out of the 38 rats, 36 (94.7%) achieved a RUST score of 10 or higher. However, only 16 rats (42.1%) achieved the biomechanical consolidation threshold ( $> 80\%$  Frec). Fisher's Exact test revealed no significant association between achieving a RUST score  $\geq 10$  and recovering  $> 80\%$  of Frec ( $p = 0.50$ ). The overwhelming frequency of high RUST scores indicated a ceiling effect, preventing the radiographic system from effectively distinguishing between biomechanically robust and weak tibias at this time point.

## DISCUSSION

The primary finding of this study is that at 8 weeks post-osteotomy in a rat tibia model, a RUST score of 10 or higher overestimates actual structural recovery. While the scale reliably evaluates the visible presence of a bony bridge, it did not significantly predict whether the bone had recovered at least 80% of its original biomechanical strength ( $p = 0.50$ ).

**Table 1.** Maximum force results obtained in three-point bending tests for both operated and intact tibias in newton (N), maximum force recovery (Frec), and final RUST scores for each animal.

| Rat ID | F <sub>max</sub> operated (N) | F <sub>max</sub> intact (N) | Frec (%) | RUST Score |
|--------|-------------------------------|-----------------------------|----------|------------|
| 1      | 145.3                         | 182.8                       | 79.5     | 9          |
| 2      | 208.6                         | 182.7                       | 114.2    | 10         |
| 3      | 124.7                         | 169.4                       | 73.6     | 12         |
| 4      | 166.3                         | 153.8                       | 108.1    | 12         |
| 5      | 167.6                         | 218.1                       | 76.8     | 12         |
| 7      | 66.7                          | 108.7                       | 61.4     | 11         |
| 8      | 142.7                         | 181.4                       | 78.7     | 10         |
| 9      | 136.6                         | 154.7                       | 88.3     | 10         |
| 11     | 184.0                         | 198.8                       | 92.6     | 10         |
| 12     | 84.9                          | 181.7                       | 46.7     | 10         |
| 13     | 44.6                          | 186.0                       | 24.0     | 10         |
| 14     | 99.1                          | 148.2                       | 66.9     | 12         |
| 15     | 137.7                         | 168.1                       | 81.9     | 11         |
| 16     | 132.3                         | 200.6                       | 66.0     | 11         |
| 17     | 172.1                         | 244.1                       | 70.5     | 10         |
| 19     | 100.5                         | 195.8                       | 51.3     | 9          |
| 20     | 179.4                         | 196.1                       | 91.5     | 11         |
| 21     | 219.1                         | 193.4                       | 113.3    | 12         |
| 25     | 82.9                          | 212.4                       | 39.0     | 12         |
| 26     | 153.9                         | 183.3                       | 84.0     | 12         |
| 27     | 82.2                          | 245.3                       | 33.5     | 12         |
| 28     | 103.6                         | 143.9                       | 72.0     | 11         |
| 30     | 94.6                          | 190.3                       | 49.7     | 10         |
| 31     | 120.3                         | 148.8                       | 80.8     | 10         |
| 32     | 134.6                         | 139.1                       | 96.8     | 11         |
| 33     | 150.7                         | 176.5                       | 85.4     | 12         |
| 34     | 203.5                         | 199.9                       | 101.8    | 11         |
| 35     | 120.4                         | 185.5                       | 64.9     | 10         |
| 36     | 100.6                         | 167.2                       | 60.2     | 11         |
| 37     | 115.2                         | 123.8                       | 93.1     | 12         |
| 38     | 110.0                         | 169.5                       | 64.9     | 12         |
| 39     | 111.0                         | 127.9                       | 86.8     | 11         |
| 40     | 112.4                         | 184.1                       | 61.1     | 12         |
| 41     | 128.6                         | 147.8                       | 87.0     | 12         |
| 42     | 116.5                         | 153.5                       | 75.9     | 12         |
| 43     | 100.0                         | 173.3                       | 57.7     | 12         |
| 44     | 144.4                         | 167.4                       | 86.3     | 12         |
| 45     | 19.3                          | 183.9                       | 10.5     | 11         |

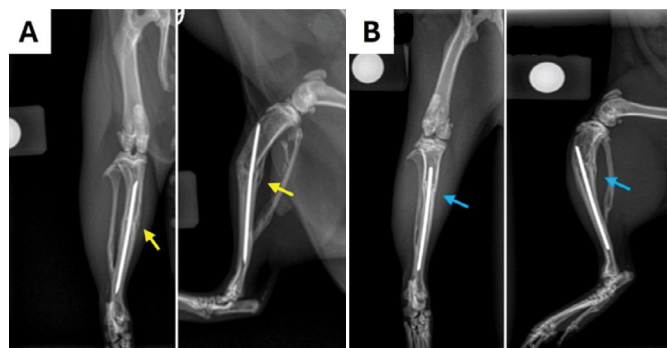
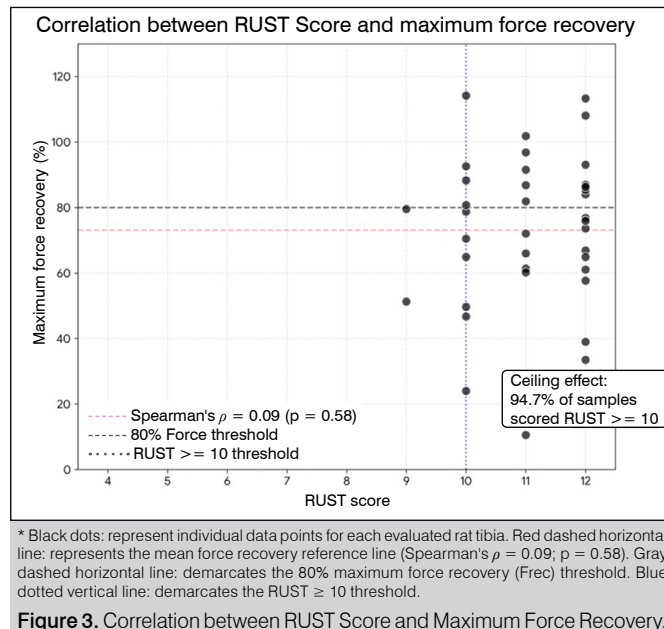


**Figure 2.** Representative radiographic images of rat tibias at 8 weeks post-osteotomy. (A) Sample with a RUST score < 10, showing persistent fracture lines (yellow arrows). (B) Consolidated sample with a RUST score  $\geq 10$ , demonstrating robust bridging callus across multiple cortices (blue arrows).



These findings illuminate a critical phenomenon in pre-clinical fracture models: radiographic union precedes biomechanical maturation. In our cohort, 94.7% of the animals exhibited sufficient cortical bridging to score a RUST of 10 or higher, yet less than half possessed the mechanical integrity to withstand 80% of the physiological load in bending. This biological discrepancy creates a “ceiling effect” for the RUST scale at 8 weeks, where numerical scores cluster at the top of the scale despite underlying structural weakness.

This lack of strong correlation ( $\rho = 0.09$ ) is consistent with the observations made by Cooke et al. regarding toughness, who reported that biological variability within each RUST score is substantial.<sup>5</sup> As they noted, mechanical properties such as ultimate strength are heavily influenced by the mineral density and mature ultra-structure of the callus, details that are not fully captured by two-dimensional plain radiographs.<sup>5</sup> Two bones with an identical RUST score of 10 may look similar regarding the *presence* of bridging but vastly differ in the *quality* of that bridge.<sup>4,5</sup>

Our results provide an important counterpoint to large-animal studies. For example, Litrenta et al. found that a RUST score of 10 correlated well with a recovery of 90% of torsional stiffness in a sheep model, successfully defining union.<sup>7</sup> However, the metabolic rate of rodents leads to a much faster initial bridging phase.<sup>4</sup> Fiset et al. demonstrated through micro-CT and torsion testing in rats that while RUST accurately reflects the initial progression of healing, actual mechanical stability is highly dependent on the later stages of remodeling.<sup>4</sup> Our data empirically validates this concept; seeing bone on an X-ray is not synonymous with functional load-bearing capacity in early-stage rodent models.

The validation of RUST in small animals remains high regarding inter-observer reliability, as shown by Tawonsawatruk et al.<sup>3</sup> and Alentado et al.<sup>6</sup> The scale is excellent for confirming that the healing cascade is successfully underway. However, researchers must be cautious. Since radiographic evaluation is nondestructive, it is tempting to use it as a standalone proxy for terminal biomechanical testing.<sup>6</sup> Our results show that relying exclusively on a RUST  $\geq 10$  threshold to define “complete union” at 8 weeks in rats will result in false positives regarding structural strength. Researchers utilizing the rat tibia model should be aware of the temporal lag between radiographic appearance and mechanical properties. While RUST is an essential tool for tracking early callus formation, biomechanical testing remains indispensable for confirming true functional consolidation.

The main strengths of this study include a robust sample size subjected to rigorous biomechanical testing and the use of a blinded panel of orthopedic specialists for image evaluation, ensuring high clinical relevance. Conversely, the limitations include the evaluation restricted to a single 8-week endpoint – which precludes longitudinal tracking of the healing timeline – and the reliance on 2D plain radiographs rather than 3D micro-CT for volumetric callus assessment.

## CONCLUSION

In this experimental rat model, neither absolute RUST scores nor the categorical threshold of  $\geq 10$  successfully predicted the recovery of

$> 80\%$  maximum force at 8 weeks. Radiographic bridging occurs faster than full biomechanical maturation, leading to a ceiling effect where plain radiographs overestimate structural strength. Consequently, a RUST score  $\geq 10$  should not be used as an isolated surrogate marker for functional load-bearing consolidation in this specific pre-clinical time point.

## ACKNOWLEDGEMENTS

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## CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. ALPR: surgical procedures, image acquisition and processing, data collection, and data analysis. RMS: data analysis, preparation of figures and tables, drafting of the manuscript, and critical revision. ISC: critical revision of the manuscript. NAB: study conceptualization, and critical revision of the manuscript. JRLM: study conceptualization, and critical revision of the manuscript. ALLA: surgical design and execution, data analysis, and critical revision of the manuscript. WDB: study conceptualization, project administration, supervision of the experimental procedures, and critical revision of the manuscript.

## DATA AVAILABILITY DECLARATION

The contents are already available.

## REFERENCES

1. Kooistra BW, Dijkman BG, Busse JW, Sprague S, Schemitsch EH, Bhandari M. The radiographic union scale in tibial fractures: reliability and validity. *J Orthop Trauma*. 2010;24(Suppl 1):S81-S86. doi: 10.1097/bot.0b013e3181ca3fd1.
2. Mundi R, Axelrod D, Chaudhry H, Sahota N, Heels-Ansdell D, Sprague S, et al. Association of three-Month radiographic union score for tibia fractures (RUST) with nonunion in tibial shaft fracture patients. *Cureus*. 2020;12(5):e8314. doi: 10.7759/cureus.8314. doi: 10.7759/cureus.8314.
3. Tawonsawatruk T, Hamilton DF, Simpson AHRW. Validation of the use of radiographic fracture-healing scores in a small animal model. *J Orthop Res*. 2014;32(9):1117-9. doi: 10.1002/jor.22665.
4. Fiset S, Godbout C, Crookshank MC, Zdero R, Nauth A, Schemitsch EH. Experimental validation of the radiographic union score for tibial fractures (RUST) using micro-Computed tomography scanning and biomechanical testing in an in-Vivo rat model. *J Bone Joint Surg Am*. 2018;100(21):1871-8. doi: 10.2106/jbjs.18.00035.
5. Cooke ME, Hussein AI, Lybrand KE, Wulff A, Simmons E, Choi JH, et al. Correlation between RUST assessments of fracture healing to structural and biomechanical properties. *J Orthop Res*. 2017;36(3):945-53. doi: 10.1002/jor.23710.
6. Alentado VJ, Knox AM, Staut CA, McGuire AC, Chitwood JR, Mostardo SL, et al. Validation of the modified radiographic union score for tibia fractures (mRUST) in murine femoral fractures. *Front Endocrinol (Lausanne)*. 2022;13:911058. doi: 10.3389/fendo.2022.911058.
7. Litrenta J, Tornetta P 3rd, Ricci W, Sanders RW, O'Toole RV, Nascone JW, et al. In vivo correlation of radiographic scoring (Radiographic union scale for tibia fractures) and biomechanical data in a sheep osteotomy model: can we define union radiographically?. *J Orthop Trauma*. 2017;31(3):127-30. doi: 10.1097/bot.0000000000000753.

# FROM DONOR TO GRAFT: IMPACT OF ANTHROPOMETRY ON TENDON SIZE IN FOUR COMMON ACL ALLOGRAFTS

## DO DOADOR AO ENXERTO: IMPACTO DA ANTROPOMETRIA NO TAMANHO DO TENDÃO EM QUATRO TIPOS COMUNS DE ALOENXERTOS PARA RECONSTRUÇÃO DO LCA

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### ABSTRACT

**Objective:** Donor anthropometry may influence allograft tendon dimensions; however, its specific relationship with each of the four most common ACL graft types remains incompletely characterized. **Methods:** We retrospectively analyzed 38 cadaveric donors providing 170 tendons (Achilles  $n = 63$ , tibial  $n = 44$ , patellar  $n = 37$ , quadriceps  $n = 26$ ) from a single tissue bank (2020–2023). Pearson/Spearman correlations with false-discovery rate correction (Benjamini–Hochberg) were computed for each donor variable (height, weight, age, sex) against graft dimensions (length, width, thickness); regression models were fitted. **Results:** Height was the strongest predictor of graft length for Achilles ( $r = 0.629$ ,  $p < 0.001$ ;  $\beta = 1.80$  cm/10 cm, adj.  $R^2 = 0.39$ ) and tibial tendons ( $r = 0.608$ ,  $p < 0.001$ ;  $\beta = 1.11$  cm/10 cm, adj.  $R^2 = 0.35$ ). Male sex was the primary predictor of patellar length ( $r = 0.540$ ,  $p < 0.001$ ) and was correlated with Achilles thickness ( $r = 0.353$ ; FDR-adjusted  $q = 0.017$ ). Weight showed modest correlations with Achilles dimensions. No associations were found for quadriceps. **Conclusions:** Donor height and sex are the dominant anthropometric predictors of allograft dimensions and should guide tissue bank allocation to optimize preoperative graft planning in ACL reconstruction. **Level of Evidence IV; Retrospective Cross-Sectional Study.**

**Keywords:** Anterior Cruciate Ligament; Allograft; Tendon; Anthropometry; Tissue Bank; Graft Size.

### RESUMO

**Objetivo:** A antropometria do doador pode influenciar as dimensões dos aloenxertos tendinosos; contudo, sua relação com os quatro tipos de enxertos mais comuns na reconstrução do LCA permanece incompletamente caracterizada. **Métodos:** Analisamos 38 doadores cadavéricos fornecendo 170 tendões (Aquiles  $n = 63$ , tibial  $n = 44$ , patelar  $n = 37$ , quadricipital  $n = 26$ ) de um banco de tecidos (2020–2023). Correlações de Pearson/Spearman com controle da taxa de falsa descoberta foram calculadas para cada variável do doador (altura, peso, idade, sexo) versus dimensões do enxerto; modelos de regressão foram ajustados. **Resultados:** A altura foi o preditor mais consistente do comprimento dos enxertos Aquiles ( $r = 0,629$ ;  $\beta = 1,80$  cm/10 cm;  $R^2_{aj.} = 0,39$ ) e tibial ( $r = 0,608$ ;  $\beta = 1,11$  cm/10 cm;  $R^2_{aj.} = 0,35$ ),  $p < 0,001$ . O sexo masculino foi o principal preditor do comprimento patelar ( $r = 0,540$ ;  $p < 0,001$ ) e associou-se à espessura do Aquiles ( $r = 0,353$ ;  $q$  ajustado por FDR = 0,017). O peso correlacionou-se com o Aquiles. Sem associações para o quadricipital. **Conclusões:** Altura e sexo do doador são os principais preditores antropométricos dos aloenxertos e devem orientar a alocação nos bancos de tecidos para melhorar o planejamento pré-operatório na reconstrução do LCA. **Nível de Evidência IV; Estudo Transversal Retrospectivo.**

**Descritores:** Ligamento Cruzado Anterior; Aloenxerto; Tendão; Antropometria; Banco de Tecidos; Tamanho do Enxerto.

**Citation:** Leal DP, Machinski E, Conde RB, Mengui LAS, Silva AGM, Gobbi RG, Helito CP. From donor to graft: Impact of anthropometry on tendon size in four common ACL allografts. Acta Ortop Bras. [online]. 2026;34(6): Page 1 of 6. Available from URL: <http://www.scielo.br/aob>.

### INTRODUCTION

The use of tendons as grafts in orthopedic surgery has a well-established history. Reports of ligament substitution using autologous tissue date back to the early 20th century, most notably to Ernest Hey Groves, who in 1917 described ACL repair using a fascia lata strip.<sup>1</sup>

Widespread clinical adoption followed only after the popularization of arthroscopic techniques in the 1980s.<sup>1</sup> Autologous grafts constructs, using at the beginning only bone–patellar tendon–bone (BPTB) and hamstring and more recently incorporating the quadriceps tendon, peroneus longus<sup>2</sup> and rectus femoris,<sup>3</sup> have since become

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the reference standard for primary ACL reconstruction owing to their favorable biological integration and predictable long-term outcomes.<sup>1,4</sup> Despite their established efficacy, autologous grafts carry inherent limitations, mainly harvest-site morbidity, including post-operative pain, extensor weakness, and an extended rehabilitation period.<sup>4,5</sup> These limitations become especially consequential in revision surgery and multiligament injuries, where harvesting multiple autografts risks disproportionate functional sacrifice. In such scenarios, allografts provided by musculoskeletal tissue banks represent an important and sometimes indispensable alternative as they eliminate harvest-site morbidity, reduce operative time, and offer grafts in sizes not constrained by the recipient's own anatomy.<sup>5</sup> For tissue banks to supply grafts efficiently, particularly for size-sensitive procedures, it is important to understand whether donor anthropometrics predict graft dimensions. A recent systematic review and meta-analysis confirmed moderate-to-strong correlations between donor height, weight, and tendon length or diameter across thousands of cases.<sup>6</sup> However, graft-specific estimates for each of the four main allograft types, derived from a single cohort with uniform processing, remain scarce. The present study addresses this gap by quantifying, for each tendon type separately, the associations between donor anthropometric variables and graft dimensions using bivariate correlation and multivariable regression analyses. We hypothesized that donor height and sex would be the primary predictors of allograft length, with effect sizes varying across the four tendon types.

## METHODS

### Study Design and Ethics

This retrospective cross-sectional study was approved by the Scientific Commission of the Department of Orthopedics and Traumatology, School of Medicine, University of São Paulo (DOT/FMUSP; Protocol IOT No. 1770 / SGP: 28569). Given the de-identified nature of all records, the requirement for individual written consent was waived.

### Donor Cohort

All cadaveric donors processed at a single musculoskeletal tissue bank between January 2020 and December 2023 were eligible. Donors contributing at least one of the four target tendons, Achilles, tibial, patellar, or quadriceps, with complete dimensional records were included. Donor-level variables extracted from bank records comprised: age (years), sex (binary: male/female, coded 1/0), height (meters), and body weight (kilograms). BMI ( $\text{kg}/\text{m}^2$ ) was derived from height and weight. A total of 38 donors were identified (21 male, 17 female); the same donor may contribute multiple graft types, accounting for the larger numbers per graft group.

### Graft Measurements

For each harvested tendon, trained bank technicians recorded mean length, width, and thickness (cm) using standardized digital calipers at processing, following the bank's quality-management protocol (minimum three readings per dimension; final value = mean). For the Achilles dataset, each row represents an individual graft; for the remaining tendons, rows represent per-lot means. Patellar tendon thickness measurements were available in only 2 of 37 lots and were therefore excluded from all inferential analyses. All Tibial tendon dimensions represent per-lot means across multiple individual tendon segments.

### Statistical Analysis

All analyses were performed in R (version 4.4.0). Statistical significance was set at  $\alpha = 0.05$  (two-tailed). To address multiple comparisons (3 dimensions  $\times$  4 donor variables = 12 tests per graft type), the Benjamini–Hochberg false-discovery rate (FDR)

procedure was applied within each graft family;<sup>7</sup> FDR-adjusted p-values are reported alongside raw p-values.

For each donor variable–graft dimension pair, Pearson's  $r$  was computed with 95% confidence intervals (Fisher  $z$ -transformation) and Spearman's  $\rho$  as a non-parametric check. Point-biserial correlation (sex  $\times$  dimension) was calculated within the Pearson framework (male = 1, female = 0). Pairwise available-case analysis was used throughout, with  $n$  reported per pair.

Simple linear regression (graft length  $\sim$  donor height) was fitted for each tendon type; coefficients were rescaled to reflect change per 10 cm of height. Multiple regression (length  $\sim$  height + weight + age + sex) was subsequently fitted on complete cases. Model diagnostics included visual residual inspection, Cook's distance (threshold  $D > 1$ ), and variance inflation factors ( $VIF < 5$  considered acceptable;  $VIF$ s ranged from 1.1 to 3.2, except in the quadriceps model, where they reached 5.5).

## RESULTS

### Donor and Graft Characteristics

Thirty-eight unique donors contributed 170 tendons across the four groups. Male donors were younger ( $31.3 \pm 13.1$  vs.  $35.9 \pm 8.1$  years), substantially taller ( $1.79 \pm 0.09$  vs.  $1.62 \pm 0.07$  m), and heavier ( $85.3 \pm 17.5$  vs.  $69.7 \pm 16.5$  kg) than female donors, while mean BMI was identical ( $26.5 \text{ kg}/\text{m}^2$  in both groups). Full donor demographics are presented in Table 1, and graft-level descriptive statistics in Table 2.

### Bivariate Correlations

Statistically significant Pearson correlations, confirmed by Spearman's  $\rho$ , are summarized in Table 3. Figure 1 provides an overview of all height-to-dimension correlations as a heatmap across the four tendon types. For Achilles tendons, height showed the strongest positive correlation with graft length ( $r = 0.629$ , 95% CI 0.452–0.759;  $p = 0.568$ ;  $p < 0.001$ ) and moderately with thickness ( $r = 0.445$ ;  $p < 0.001$ ); both associations survived FDR correction. Weight correlated with Achilles length ( $r = 0.327$ ; FDR-adj  $p = 0.021$ ) and thickness ( $r = 0.344$ ; FDR-adj  $p = 0.017$ ). Male sex correlated with greater Achilles length ( $r = 0.316$ ; FDR-adj  $p = 0.023$ ) and thickness ( $r = 0.353$ ; FDR-adj  $p = 0.017$ ). No significant associations were observed for Achilles width.

For tibial tendons, height ( $r = 0.608$ ; FDR-adj  $p = 0.001$ ) and male sex ( $r = 0.525$ ; FDR-adj  $p = 0.007$ ) were robustly associated with graft length. Weight showed a nominal correlation ( $r = 0.388$ ;

**Table 1.** Donor demographic characteristics stratified by sex (mean  $\pm$  SD).

| Variable                       | Male (n = 21)   | Female (n = 17) | Total (n = 38)  |
|--------------------------------|-----------------|-----------------|-----------------|
| Age (years)                    | 31.3 $\pm$ 13.1 | 35.9 $\pm$ 8.1  | 33.4 $\pm$ 11.2 |
| Range                          | 16 – 58         | 21 – 45         | 16 – 58         |
| Height (m)                     | 1.79 $\pm$ 0.09 | 1.62 $\pm$ 0.07 | 1.71 $\pm$ 0.12 |
| Weight (kg)                    | 85.3 $\pm$ 17.5 | 69.7 $\pm$ 16.5 | 78.3 $\pm$ 18.6 |
| BMI ( $\text{kg}/\text{m}^2$ ) | 26.5 $\pm$ 4.3  | 26.5 $\pm$ 6.4  | 26.5 $\pm$ 5.3  |
| Sex, n (%)                     | 21 (55.3%)      | 17 (44.7%)      | 38 (100%)       |

**Table 2.** Descriptive statistics for each allograft type (mean  $\pm$  SD; range).

| Graft      | n  | Length (cm)               | Width (cm)                | Thickness (cm)            |
|------------|----|---------------------------|---------------------------|---------------------------|
| Achilles   | 63 | 27.7 $\pm$ 3.2 (17–35)    | 7.8 $\pm$ 1.7 (4.5–14)    | 1.72 $\pm$ 0.32 (1.0–2.0) |
| Tibial     | 44 | 24.4 $\pm$ 2.2 (20–29)    | 0.72 $\pm$ 0.20 (0.4–1.3) | 1.17 $\pm$ 0.35 (0.4–1.8) |
| Patellar   | 37 | 4.29 $\pm$ 0.73 (3.0–6.0) | 2.78 $\pm$ 0.50 (2.0–4.0) | N/A †                     |
| Quadriceps | 26 | 19.2 $\pm$ 3.0 (13–24.5)  | 3.49 $\pm$ 1.18 (2.0–6.5) | 6.5 $\pm$ 1.9 (3.0–9.0) ‡ |

† Patellar tendon thickness available for 2 lots only; excluded from analysis. ‡ Quadriceps thickness in millimeters

| Graft      | Predictor  | Outcome   | r (95% CI)            | p (Spearman) | p (FDR-adjusted q)  |
|------------|------------|-----------|-----------------------|--------------|---------------------|
| Achilles   | Height     | Length    | +0.629 [0.452, 0.759] | +0.568       | < 0.001 (< 0.001) ✓ |
|            | Height     | Thickness | +0.445 [0.222, 0.624] | +0.479       | < 0.001 (0.002) ✓   |
|            | Weight     | Length    | +0.327 [0.087, 0.532] | +0.384       | 0.009 (0.021) ✓     |
|            | Weight     | Thickness | +0.344 [0.106, 0.546] | +0.371       | 0.006 (0.017) ✓     |
|            | Sex (male) | Length    | +0.316 [0.074, 0.523] | +0.281       | 0.012 (0.023) ✓     |
|            | Sex (male) | Thickness | +0.353 [0.115, 0.552] | +0.406       | 0.005 (0.017) ✓     |
| Tibial     | Height     | Length    | +0.608 [0.345, 0.783] | +0.618       | < 0.001 (0.001) ✓   |
|            | Sex (male) | Length    | +0.525 [0.233, 0.731] | +0.540       | 0.001 (0.007) ✓     |
|            | Weight     | Length    | +0.388 [0.063, 0.639] | +0.390       | 0.021 (0.085)       |
| Patellar   | Sex (male) | Length    | +0.540 [0.261, 0.735] | +0.541       | < 0.001 (0.005) ✓   |
|            | Height     | Length    | +0.430 [0.124, 0.662] | +0.429       | 0.008 (0.031) ✓     |
|            | Sex (male) | Width     | +0.384 [0.068, 0.629] | +0.464       | 0.019 (0.051)       |
| Quadriceps | All        | All       | NS                    | NS           | all > 0.05          |

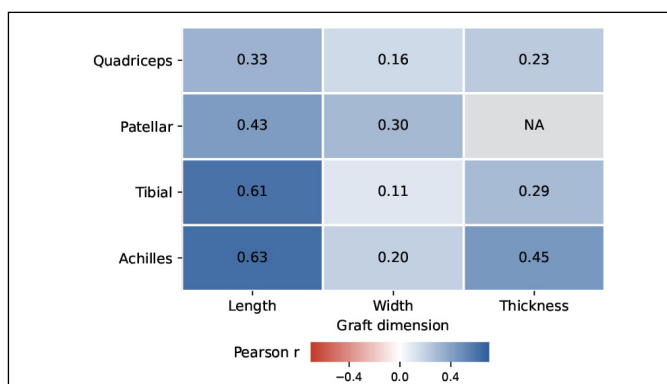


**Figure 1.** Donor height vs. graft dimension - Pearson r.

raw p = 0.021) that did not survive FDR correction (q = 0.085). No associations were significant for tibial width or thickness. For patellar tendons, male sex was the strongest predictor of length (r = 0.540; FDR-adj p = 0.005) and had a borderline association with width (r = 0.384; FDR-adj p = 0.051). Height also correlated with patellar length (r = 0.430; FDR-adj p = 0.031). For quadriceps tendons, no correlation reached statistical significance (all raw p ≥ 0.055; all FDR-adj p ≥ 0.34). The scatter plots in Figure 2 illustrate the relationship between donor height and graft length for each tendon type, with data points colored by sex. The distribution of graft length stratified by donor sex is shown in Figure 3; male donors provided longer Achilles, tibial and patellar grafts, whereas no difference was observed for quadriceps grafts (p = 0.94).

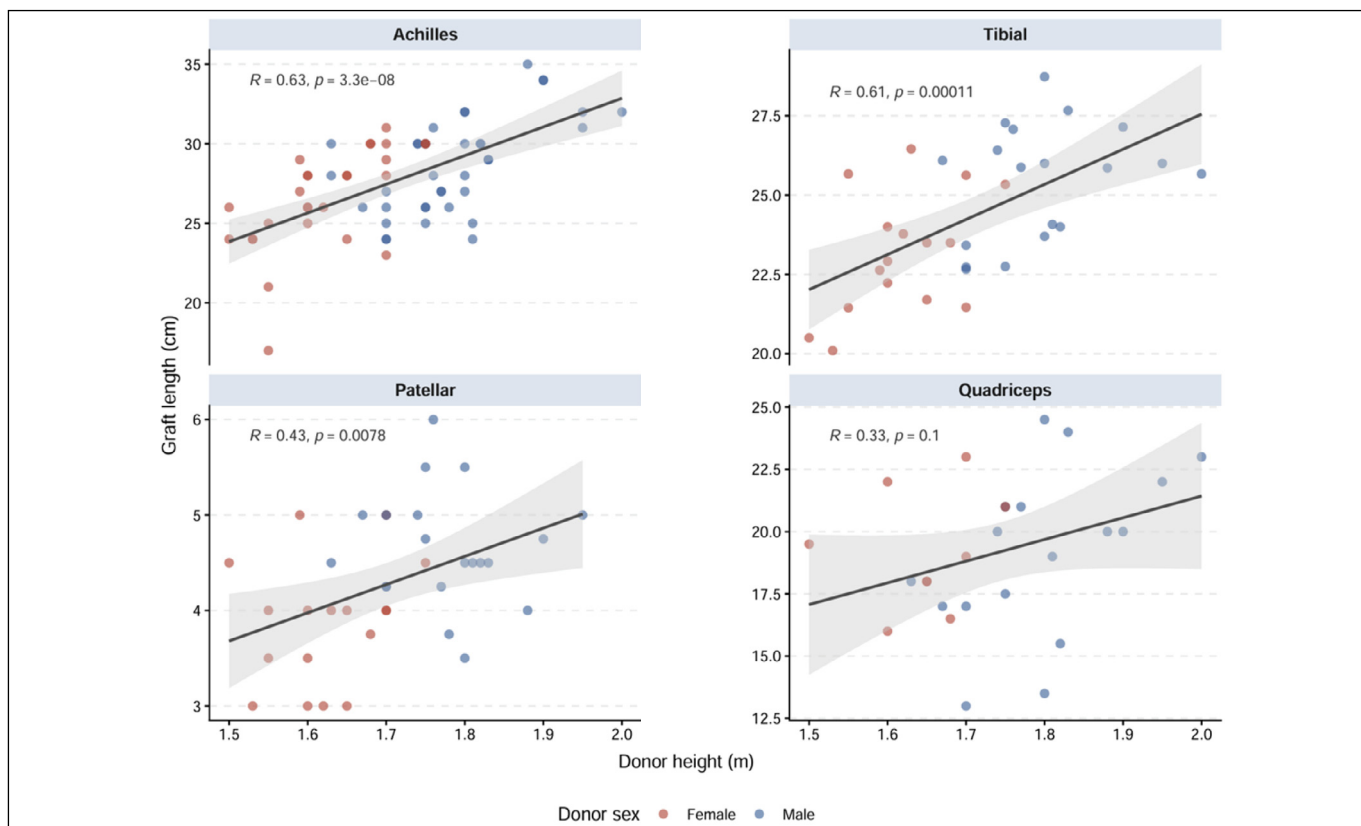


**Figure 2.** Donor height vs. allograft length.

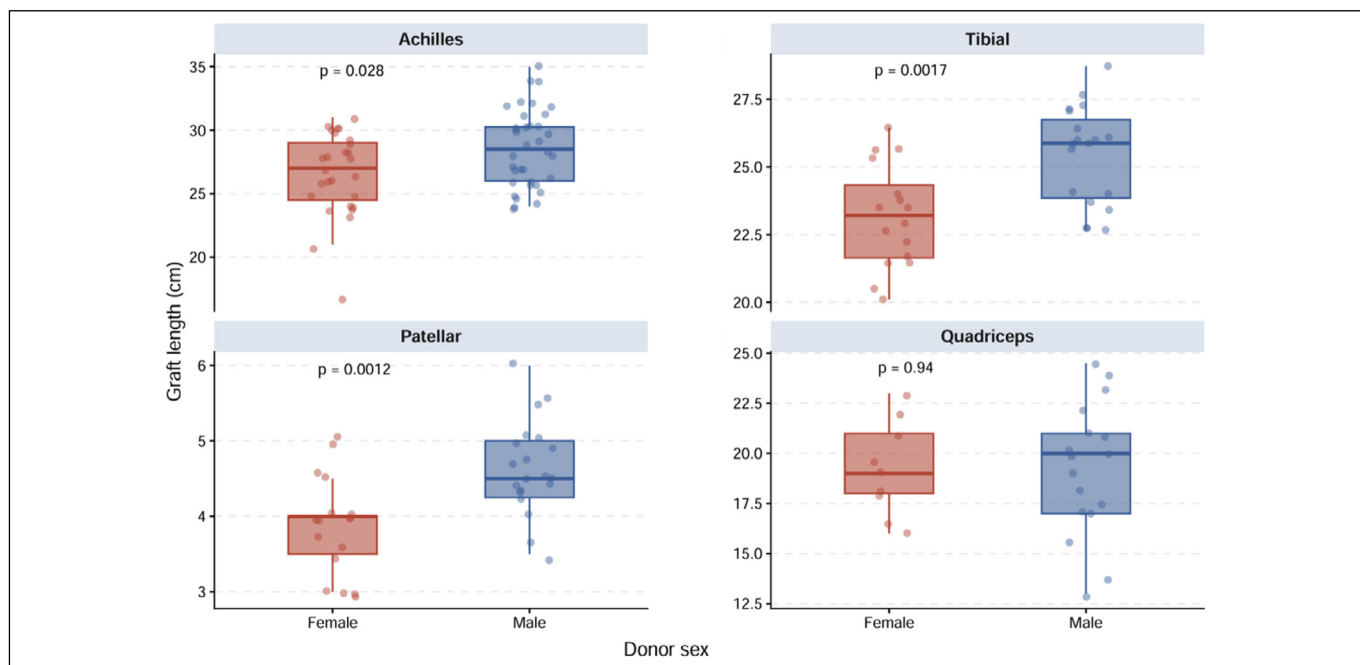


**Figure 3.** Graft length by donor sex and tendon type.

### Linear Regression Models

Regression estimates are summarized in Table 4. Figure 4 details the regression fit for the two tendons with the strongest associations, Achilles and tibial, including the regression equation and Pearson  $r$  annotation. For the Achilles tendon, each additional 10 cm of donor height predicted 1.80 cm longer grafts (95% CI 1.24–2.36; adj.  $R^2 = 0.386$ ). The multivariable model ( $n = 63$ ) was highly significant ( $F(4,58) = 11.04$ ;  $p < 0.001$ ; adj.  $R^2 = 0.393$ ); height remained the sole independent predictor ( $\beta/10 \text{ cm} = 2.39$ ;  $p < 0.001$ ), while sex showed a borderline effect ( $\beta = -1.77 \text{ cm}$  for males;  $p = 0.065$ ). Weight and age were not significant.

For tibial tendons, each 10 cm of height predicted 1.11 cm longer grafts (adj.  $R^2 = 0.351$ ;  $p < 0.001$ ). The multivariable model was significant overall ( $F(4,30) = 4.86$ ;  $p = 0.004$ ; adj.  $R^2 = 0.312$ ), with height approaching but not reaching independence ( $\beta/10 \text{ cm} = 0.91$ ;  $p = 0.058$ ), likely reflecting reduced power and collinearity with sex in this smaller subsample.

For patellar tendons, simple regression yielded  $\beta/10 \text{ cm} = 0.30$  (adj.  $R^2 = 0.162$ ;  $p = 0.008$ ). In the multivariable model ( $F(4,32) = 3.55$ ;  $p = 0.017$ ; adj.  $R^2 = 0.220$ ), sex was the only significant

**Table 4.** Linear regression: effect of donor height on graft length ( $\beta$  rescaled per 10 cm height). † Height significant in multivariable model ( $p < 0.001$ ). ‡ Sex (male) is the significant predictor in multivariable model ( $\beta = 0.68 \text{ cm}$ ,  $p = 0.039$ ). \* Overall model  $p = 0.017$ .

| Model                                 | $\beta$ per 10 cm height | 95% CI      | p-value | Adj. R     |
|---------------------------------------|--------------------------|-------------|---------|------------|
| Achilles – simple ( $n=63$ )          | 1.80 cm                  | 1.24 – 2.36 | < 0.001 | 0.386      |
| Achilles – multivariable ( $n=63$ )   | 2.39 cm †                | 1.52 – 3.27 | < 0.001 | 0.393      |
| Tibial – simple ( $n=35$ )            | 1.11 cm                  | 0.61 – 1.60 | < 0.001 | 0.351      |
| Tibial – multivariable ( $n=35$ )     | 0.91 cm                  | 0.00 – 1.82 | 0.058   | 0.312      |
| Patellar – simple ( $n=37$ )          | 0.30 cm                  | 0.09 – 0.50 | 0.008   | 0.162      |
| Patellar – multivariable ( $n=37$ ) ‡ | 0.002 cm (NS)            | —           | 0.990   | 0.220 *    |
| Quadriceps – multivariable ( $n=26$ ) | 0.22 cm (NS)             | —           | 0.852   | 0.096 (NS) |

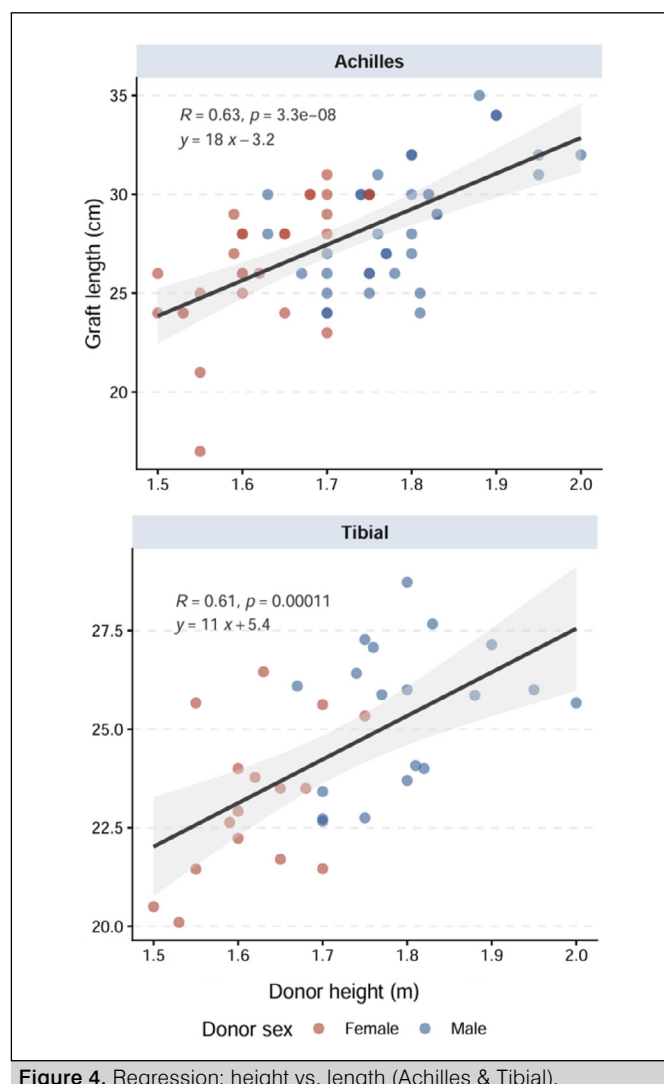


**Figure 4.** Regression: height vs. length (Achilles & Tibial).

independent predictor ( $\beta = 0.68$  cm;  $p = 0.039$ ), while height was no longer significant ( $p = 0.990$ ), suggesting that much of the height effect is mediated through or confounded by sex.

For quadriceps tendons, neither the simple regression ( $\beta/10$  cm = 0.87;  $p = 0.100$ ; adj.  $R^2 = 0.072$ ) nor the multivariable model ( $F(4,21) = 1.66$ ;  $p = 0.197$ ; adj.  $R^2 = 0.096$ ) reached significance.

## DISCUSSION

Donor height was associated with Achilles and tibial graft length, explaining approximately 35–39% of the variance in simple regression models. Height remained a significant independent predictor of Achilles length; its adjusted association with tibial length did not reach statistical significance ( $p = 0.058$ ). Donor sex was the principal correlate of patellar tendon length across both bivariate and multivariable analyses, and a secondary predictor of Achilles graft thickness. No significant anthropometric predictor was identified for quadriceps grafts. These findings have direct practical implications for tissue bank operations and preoperative ACL reconstruction planning.

The robust relationship between donor height and tendon graft length is biologically plausible: musculoskeletal structures scale proportionally with overall body size during development, and taller individuals possess longer extremity segments with correspondingly longer tendons.<sup>8,9</sup> Our estimates are clinically meaningful: a 10 cm difference in donor height translates to approximately 1.8 cm longer Achilles grafts and 1.1 cm longer tibial grafts. Situations requiring allografts, such as multiligament injuries or multiple revision ACL reconstructions, often demand long grafts; differences of this magnitude may determine whether a graft meets the length required for a given reconstruction. These findings align with and extend the pooled data reported by Salman et al.,<sup>6</sup> who demonstrated moderate-to-strong correlations between donor height and tendon length across multiple graft types in thousands of patients. Our graft-specific  $\beta$  estimates provide tissue banks with practical benchmarks: at a donor height of 1.60 m, the fitted models predict mean graft lengths of 25.7 cm (Achilles) and 23.1 cm (tibial).

Male sex was the strongest independent predictor of patellar tendon length in the multivariable model ( $\beta = +0.68$  cm;  $p = 0.039$ ), persisting even after height was controlled. This suggests that sex-related differences in patellar tendon dimensions are not entirely attributable to stature. Anatomical studies have documented sexually dimorphic differences in patellar tendon length and insertion geometry that extend beyond height-predicted values, possibly related to quadriceps angle (Q-angle), patellar height, and extensor mechanism proportions.<sup>10-12</sup> For Achilles grafts, male donors provided significantly thicker tendons ( $r = 0.353$ ;  $p = 0.005$ ), consistent with published data showing greater Achilles cross-sectional area in males even after body size normalization.<sup>13</sup> Achilles graft thickness is a key determinant of final graft diameter following tubularization and suture preparation; female donor grafts may therefore more frequently require additional preparation to achieve target diameters (typically  $\geq 8$  mm for ACL applications), or be preferentially allocated to recipients with smaller notch dimensions.

Donor weight showed modest bivariate correlations with Achilles length ( $r = 0.327$ ) and thickness ( $r = 0.344$ ), and with tibial length ( $r = 0.388$ ). However, weight did not achieve independent significance in any multivariable model. VIFs ranged from 1.1 to 3.2, except in the quadriceps model, where they reached 5.5. The lack of an independent weight effect mirrors findings from the meta-analysis of Salman et al.,<sup>6</sup> though studies using more granular body composition measures (lean mass, cross-sectional area) have reported additive associations with tendon volume.<sup>14</sup>

Donor age showed no significant association with any graft dimension in any tendon group, a finding replicated across bivariate and multivariable analyses and consistent with prior meta-analytic evidence.<sup>6</sup> Within the donor age range examined (16–58 years), macroscopic tendon length and width appear to be stable, despite well-documented age-related changes in collagen cross-linking density and tendon stiffness.

Our results support a structured anthropometry-guided allocation protocol. Donor height alone, available from routine registration data, allows banks to stratify expected graft length with reasonable accuracy for Achilles and tibial tendons. A simple decision rule, for example, routing donors taller than 1.75 m to large-graft requests (revision surgery, multiligament cases) and donors shorter than 1.60 m to standard primary reconstructions, would require no additional processing steps. For patellar grafts, incorporating sex alongside height into the allocation algorithm captures independent variance in graft length not explained by stature alone. For Achilles grafts, a sex-stratified minimum-thickness criterion at procurement could reduce downstream preparation time and graft waste.

## Limitations

This study has some limitations. First, 38 unique donors represent a relatively small cohort, and despite multiple grafts per donor the per-graft sample sizes limit power, particularly for the quadriceps group. Second, the data span a single tissue bank, potentially limiting generalizability to banks with different donor demographics or processing protocols. Third, patellar tendon thickness data were largely unavailable and had to be excluded. Future multicenter prospective studies with individual-graft measurements, standardized protocols, and matched recipient data would substantially strengthen the evidence base.

## CONCLUSION

In this analysis of 38 cadaveric donors providing 170 tendon allografts, donor height was the strongest predictor of graft length for Achilles ( $r = 0.629$ ;  $\beta = 1.80$  cm/10 cm) and tibial tendons ( $r = 0.608$ ;  $\beta = 1.11$  cm/10 cm), explaining approximately 35–39% of length variance. Donor sex was the principal independent predictor of patellar tendon length and correlated with Achilles graft thickness. No significant associations were found for quadriceps tendons, likely due to limited power. These findings support incorporating donor height and sex into tissue bank allocation algorithms to improve graft-to-recipient matching and preoperative planning efficiency in ACL reconstruction.

## CONTRIBUTIONS OF THE AUTHORS

Each author made a personal and significant contribution to the development of this article. DPL: Conceptualization, Methodology, Writing – Original Draft. EM: Data Curation, Formal Analysis, Investigation, Writing – Original Draft. RBC: Supervision, Writing – Review & Editing. LASM: Investigation, Data Curation, Writing – Review & Editing. AGMS: Investigation, Writing – Review & Editing. RGG: Resources, Supervision, Writing – Review & Editing. CPH: Conceptualization, Project Administration, Supervision, Writing – Review & Editing.

## DATA AVAILABILITY DECLARATION

The contents underlying the research are available in the manuscript.

## REFERENCES

1. D'Ambrosi R, Meena A, Arora ES, Attri M, Schäfer L, Migliorini F. Reconstruction of the anterior cruciate ligament: a historical view. *Ann Transl Med.* 2023;11(10):364-4. doi: 10.21037/atm-23-87.
2. da Silva AGM, Macedo RS, Souza MO, Giglio PN, Videira LD, Gobbi RG, et al. Combined Anterior Cruciate Ligament and Anterolateral Ligament Reconstruction Using a Single Peroneus Longus Tendon Graft. *Arthrosc Tech.* 2024;13(1):102823. doi: 10.1016/j.eats.2023.08.028
3. Barroso BG, Canuto SMdG, Helito CP, Rêgo MCF, Martins FS, Rêgo MCF. Combined anterior cruciate ligament and anterolateral ligament reconstruction using the superficial layer quadriceps tendon graft: surgical technique description. *Arthrosc Tech.* 2024;13(10):103067. doi: 10.1016/j.eats.2024.103067.
4. Thomson J, Webb M. Graft options for ACL reconstruction. *Orthop Rev (Pavia).* 2025;17:143767. doi: 10.52965/001c.143767.
5. Runer A, Keeling L, Wagala N, Nugraha H, Özbek EA, Hughes JD, et al. Current trends in graft choice for primary ACL reconstruction – Part II. *J Exp Orthop.* 2023;10(1):40. doi: 10.1186/s40634-023-00601-3.
6. Salman LA, Moghamis IS, Hatnoully AT, Khatkar H, Alebbini MM, Al-Ani A, et al. Correlation between anthropometric measurements and graft size in anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Eur J Orthop Surg Traumatol.* 2023;34(1):97-112. doi: 10.1007/s00590-023-03712-w.
7. Benjamini Y, Drai D, Elmer G, Kafkafi N, Golani I. Controlling the false discovery rate in behavior genetics research. *Behav Brain Res.* 2001;125(1-2):279-84. doi: 10.1016/s0166-4328(01)00297-2.
8. Alexander RM. Tendon elasticity and muscle function. *Comp Biochem Physiol A Mol Integr Physiol.* 2002;133(4):1001-11. doi: 10.1016/s1095-6433(02)00143-5.
9. Lieber RL. *Skeletal Muscle Structure, Function, and Plasticity.* 3rd ed. Baltimore: Lippincott Williams & Wilkins; 2009.
10. Chandrashekar N, Slaughterbeck J, Hashemi J. Sex-based differences in the anthropometry of the ACL and its relation to mechanical properties. *J Biomech.* 2006;39:2943-50.
11. Grelsamer RP, Dubey A, Weinstein CH. Men and women have similar Q angles: a clinical and trigonometric evaluation. *J Bone Joint Surg Br.* 2005;87(11):1498-501. doi: 10.1302/0301-620X.87B11.16485.
12. Aglietti P, et al. Patellar position after anterior cruciate ligament reconstruction. *Am J Sports Med.* 1993;21:717-24.
13. Kongsgaard M, et al. Mechanical properties of human patellar tendon at exercise. *J Biomech.* 2004;37:1243-52.
14. Abate M, et al. Sonographic evaluation of the Achilles tendon in patients with cardiovascular risk factors. *Int J Immunopathol Pharmacol.* 2012;25:191-6.

# TREATMENT OF RADIAL NERVE INJURY WITH DISTAL NERVE TRANSFER – CRITICAL ANALYSIS OF THE OBTAINED RESULTS

## TRATAMENTO DA LESÃO DO NERVO RADIAL COM TRANSFERÊNCIA NERVOSA DISTAL – ANÁLISE CRÍTICA DOS RESULTADOS OBTIDOS

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### ABSTRACT

**Objective:** Radial nerve injuries cause significant motor dysfunction of the upper limb, particularly affecting wrist and finger extension. The aim of this study was to evaluate motor recovery in patients who underwent distal nerve transfers for restoration of radial nerve function. **Methods:** This retrospective study included 12 patients with radial nerve injury who underwent distal nerve transfers to restore wrist and finger extension. The techniques included transfer of the flexor carpi radialis branch to the posterior interosseous nerve, associated with transfer of the flexor digitorum superficialis branch to the extensor carpi radialis brevis, or transfer of the supinator branch to the posterior interosseous nerve. Motor recovery was assessed using the Medical Research Council (MRC) muscle strength grading system. Minimum postoperative follow-up was 30 months. The mean patient age was 36 years, and the mean interval between injury and surgery was 7 months. **Results:** Satisfactory functional recovery (MRC  $\geq$  M3) for wrist and finger extension was observed in 11 patients. One patient presented unsatisfactory functional recovery. **Conclusion:** Distal nerve transfers proved to be effective in restoring wrist and finger extension, representing a reliable alternative for the treatment of radial nerve injuries. **Level of Evidence IV; Retrospective Study of the Case Series Type.**

**Keywords:** Nerve Transfer; Radial Nerve; Brachial Plexus/injuries

### RESUMO

**Objetivo:** Lesões do nervo radial causam disfunções motoras significativas do membro superior, sobretudo na extensão de punho e dedos. O objetivo deste estudo foi avaliar o ganho motor em pacientes submetidos a neurotizações distais para restauração da função do nervo radial. **Métodos:** Estudo retrospectivo com 12 pacientes portadores de lesão do nervo radial submetidos a neurotizações distais visando recuperação da extensão de punho e dedos. As técnicas incluíram transferência do ramo do flexor radial do carpo para o nervo interósseo posterior, associada ao ramo do flexor superficial dos dedos para o extensor radial curto do carpo, ou transferência do ramo do músculo supinador para o nervo interósseo posterior. O ganho motor foi avaliado pela escala do Medical Research Council (MRC). O seguimento pós-operatório mínimo foi de 30 meses. A média de idade foi de 36 anos, e o tempo médio entre a lesão e a cirurgia foi de 7 meses. **Resultados:** Ganho funcional satisfatório (MRC  $\geq$  M3) foi observado em 11 pacientes para extensão de punho e dedos. Um paciente apresentou resultado insatisfatório. **Conclusão:** As neurotizações distais demonstraram ser eficazes na restauração da extensão de punho e dedos, configurando uma alternativa confiável no tratamento das lesões do nervo radial. **Nível de Evidência IV; Estudo retrospectivo do tipo série de casos.**

**Descritores:** Transferência de Nervo; Nervo Radial; Plexo Braquial/lesões.

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### INTRODUCTION

Radial nerve injuries cause significant motor deficits in the upper limb, especially due to loss of wrist, finger, and thumb extension, in addition to reduced grip strength.<sup>1</sup> These impairments significantly affect patients' daily and professional activities. Among the most frequent causes are high-energy trauma, spiral fractures of the humerus, brachial plexus injuries, inflammatory or infectious processes, and tumors.<sup>2</sup>

When primary repair is not feasible, nerve grafting is traditionally used; however, its results may be limited due to the long distances required for axonal regeneration. Tendon transfers represent an important alternative, as they do not require reinnervation to restore movement. However, they present limitations such as loss of function of the donor tendon, absence of sensory recovery, and reduced fine motor control. The pronator teres to extensor carpi radialis brevis

All authors declare no potential conflict of interest related to this article.

The study was conducted at Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Ortopedia e Traumatologia, Grupo de Cirurgia da Mão e Microcirurgia Reconstructiva.  
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transfer, for example, restores wrist extension, but at the expense of pronation strength and with limited range of motion.<sup>3</sup>

Distal neurotizations have emerged as a promising strategy for treating radial nerve injuries, consisting of coapting a functional donor nerve to the distal branches of the recipient nerve.<sup>4</sup> Because they are performed close to the target organ, they allow earlier reinnervation and more efficient motor recovery.<sup>5</sup> Additionally, since they occur outside the scarred zone, they can be applied even in delayed cases, avoiding the problems associated with repair in previously injured areas.<sup>6</sup> The objective of this study is to evaluate motor recovery after distal neurotizations in patients with radial nerve impairment resulting from traumatic brachial plexus injuries or humeral fractures, analyzing the effectiveness of this technique as an alternative to traditional nerve reconstruction methods.

## MATERIALS AND METHODS

This study was approved by the institutional ethics committee under CAAE number: 87177825.2.0000.0068.

This is a retrospective study evaluating motor recovery in patients with radial nerve injury who underwent distal neurotizations to restore wrist and finger extension. The analysis was performed through review of medical records and surgical documentation, identifying clinical indications, techniques used, and functional outcomes obtained.

Patients underwent one of the following neurotizization techniques:

- Flexor Carpi Radialis (FCR) branch → posterior interosseous nerve (PIN)

- Flexor Digitorum Superficialis (FDS) branch → Extensor Carpi Radialis Brevis (ECRB) branch

- Supinator muscle branch → posterior interosseous nerve

Motor recovery was assessed using the Medical Research Council (MRC) muscle strength grading scale, a widely standardized method for functional analysis of specific muscle groups.

Clinical assessments were performed non-invasively during routine physical examination, with the patient seated, shoulders in neutral position, elbows flexed to 90 degrees, and forearms pronated. Patients were instructed to actively extend the wrist and fingers with and without examiner-applied resistance.

## Inclusion Criteria

- Traumatic radial nerve injury
- Minimum postoperative follow-up of 1 year
- Muscle strength  $\geq$  M4 in muscles innervated by donor nerves

## Exclusion Criteria

- Neurotizations performed for deficits due to ulnar or median nerve injuries

- Patients with extension deficits due to tetraplegia
- Postoperative follow-up < 1 year

## Surgical Technique

The following criteria were used to perform the nerve transfer: proximity between the donor nerve and the motor endplates of the target muscle; donor motor nerve that is expendable or redundant; donor nerve innervating a muscle that is synergistic to the target muscle; patient awareness of the need for motor re-education during rehabilitation.

To perform the transfer of the Flexor Digitorum Superficialis (FDS) branch to the Extensor Carpi Radialis Brevis (ECRB) branch, as well as the transfer of the Flexor Carpi Radialis (FCR) branch to the posterior interosseous nerve (PIN), a volar lazy-S incision was made in the forearm (Figure 1).

The fascia was opened, exposing the radial vascular bundle. The median nerve was then visualized, lying deep and ulnar to the radial vessels.

After releasing the deep head of the pronator teres, the median nerve was identified. Upon sectioning the fibrous arcade of the FDS, it was possible to isolate the branches of the median nerve and thus identify the donor branches. The motor branches to the FCR are located proximally, just before the branch to the palmaris longus.<sup>7</sup> The branches to the FDS are located distally to the FCR Branch. The anterior interosseous nerve is the only branch that travels radially from the median nerve (Figure 2).



**Figure 1.** Volar lazy-S incision in the forearm.

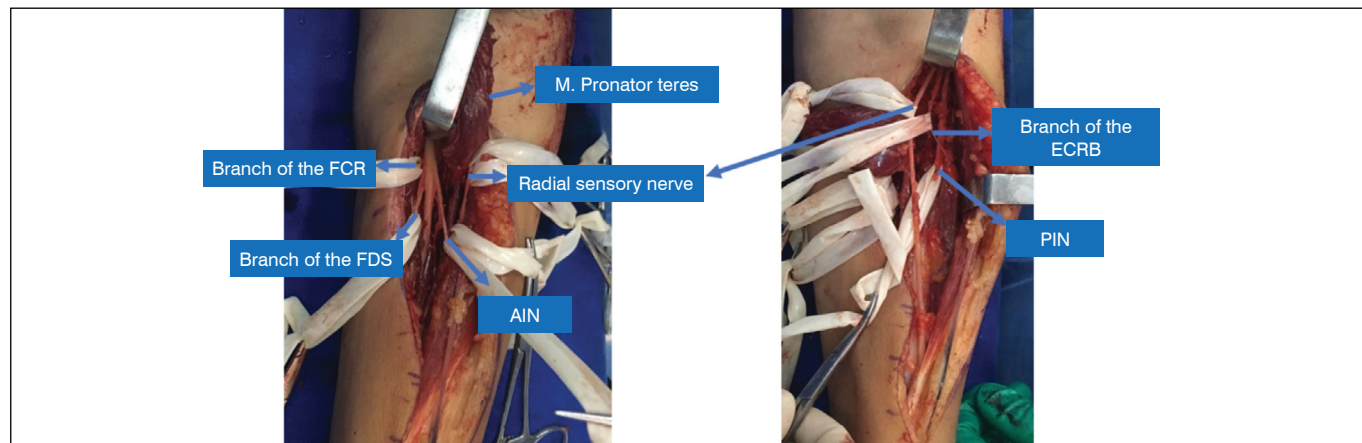


**Figure 2.** Identification of donor branches — median nerve branches to the FCR and FDS — and recipient branches — PIN and ECRB.

The radial nerve was located by identifying the superficial radial sensory nerve beneath the brachioradialis muscle. Lateral to this sensory branch lie the following branches: the branch to the Extensor Carpi Radialis Brevis (ECRB) the posterior interosseous nerve (PIN)

The PIN was identified after releasing the anterior margin of the supinator muscle (Figure 3).

In cases in which the median nerve did not have adequate donor function, but the supinator muscle was functional, the supinator motor branch was used for transfer to the PIN. Because the biceps muscle efficiently restores supination, patients do not experience functional loss even when the supinator nerve branch is used as a donor.

## RESULTS

Twelve patients were analyzed, consisting of ten male and two female individuals, with a mean age of 36 years. Of these patients, eight had traumatic brachial plexus injury due to motorcycle accidents, and four had radial nerve lesions associated with humeral fractures. Four procedures were performed on the left upper limb and eight on the right upper limb. The mean interval between injury and surgery was seven months, and the mean postoperative follow-up was 34 months (Table 1).

Regarding the procedures performed, four patients underwent transfer of the supinator motor branch to the posterior interosseous nerve. Eight patients underwent transfer of the FCR branch to the posterior interosseous nerve combined with transfer of the FDS branch to the ECRB branch. Six of these also underwent pronator teres tendon transfer to the ECRB as an adjunct procedure.

Functional recovery was considered satisfactory when extension of the wrist and fingers reached strength equal to or greater than grade 3 on the MRC scale. Eleven patients (91.6%) achieved satisfactory

results for both wrist and finger extension (Figure 4). Only one patient had an unsatisfactory outcome, showing muscle strength below grade 3 for these movements.



**Figure 4.** Preoperative image (left) and postoperative image (right) of one patient, 6 months following the transfer of the FCR branch to the PIN and FDS branch to the ECRB, demonstrating full recovery of finger, wrist and thumb extension.

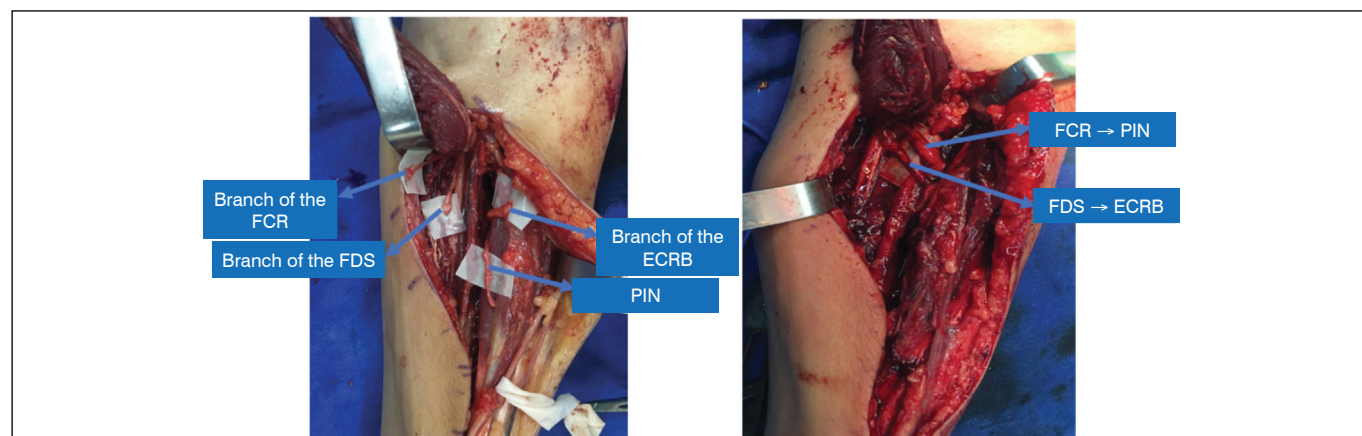


**Figure 3.** Identification of donor and recipient branches (left) and final aspect of distal neurotizations (right): branch of the Flexor Digitorum Superficialis to the Extensor Carpi Radialis Brevis and branch of the Flexor Carpi Radialis (FCR) to the posterior interosseous nerve (PIN).

**Table 1.** Epidemiological data of cases. Legend: LPB (Brachial Plexus Injury); M-R (median nerve branches neurotization to radial nerve branches).

| Sex | Id | Cause            | Time from injury to surgery | Technique | ECD | Wrist Ext. |
|-----|----|------------------|-----------------------------|-----------|-----|------------|
| M   | 42 | LPB              | 8 m                         | SPIN      | M3+ | M4         |
| M   | 30 | LPB              | 6 m                         | SPIN      | M4  | M4         |
| F   | 31 | LPB              | 6 m                         | SPIN      | M3  | M3         |
| M   | 52 | LPB              | 6 m                         | SPIN      | M3  | M3+        |
| M   | 39 | LPB              | 8 m                         | M-R       | M4  | M3         |
| M   | 58 | LPB              | 7 m                         | M-R       | M4  | M3+        |
| M   | 22 | LPB              | 7 m                         | M-R       | M4  | M3         |
| F   | 35 | LPB              | 6 m                         | M-R       | M4  | M4         |
| M   | 49 | Humerus fracture | 9 m                         | M-R       | M3- | M2         |
| M   | 19 | Humerus fracture | 8 m                         | M-R       | M3+ | M3         |
| M   | 26 | Humerus fracture | 7 m                         | M-R       | M3+ | M4         |
| M   | 30 | Humerus fracture | 6 m                         | M-R       | M4  | M4         |

## DISCUSSION

Upper-limb nerve injuries represent a challenge even for experienced surgeons and may result in significant functional deficits when not properly managed.<sup>8</sup> In the context of brachial plexus injuries, priority typically focuses on restoring shoulder and elbow function<sup>9</sup> while distal reinnervation—wrist, fingers, and hand—assumes a secondary role. However, in partial lesions involving lower roots or distal segments, reconstruction can be concentrated exclusively on the radial, median, or ulnar nerves through specific neurotization techniques for each territory.

Distal radial nerve neurotization has emerged as an effective alternative in both post-traumatic brachial plexus injuries and radial nerve lesions associated with humeral fractures.<sup>10</sup> One of the main advantages of this approach is that coaptation occurs outside the injury zone, reducing the negative impact of scar tissue on regeneration. Additionally, this technique allows individualized extension of the fingers and improved dexterity of the affected limb.

It is important to highlight that, in this technique, the proximity of the repair to the target muscle reduces denervation time, minimizing the loss of motor units and limiting irreversible muscle fibrosis<sup>11</sup> — a much greater risk when proximal neurotizations are used because of the long distance required for axonal growth. Another relevant advantage is that, unlike tendon transfers, there is no need for muscle preconditioning nor dependence on pre-existing range of motion of the donor muscle.

The greater concentration of donor nerve fibers available for the target organ also represents an advantage of distal neurotization. This point is illustrated by the less favorable results reported by Terzis and Kokkalis, who transferred the contralateral C7 posterior division to the radial nerve in 10 patients and obtained significant functional improvement in only two cases — probably due to dispersion of nerve fibers across multiple motor territories.<sup>12</sup>

Although tendon transfers are an established method for treating radial nerve injury, they present important limitations. In their review of 49 cases, Dunnet et al.<sup>13</sup> reported loss of grip strength in up to 80% of patients and reduced coordination and dexterity in 66% of cases.<sup>13</sup> Furthermore, techniques such as pronator teres transfer

to the extensor carpi radialis brevis, when used alone, have limited potential to restore wrist extension strength and amplitude, in addition to causing functional deficit of the donor muscle. Conversely, when used as a complementary procedure—as in 6 patients in this study—it can act as an “internal temporary splint,” providing support until reinnervation occurs after nerve transfer.

The results of the present study align with those in the literature. Bin Xu et al.<sup>14</sup> reported that among 10 patients submitted to supinator motor branch transfer to the posterior interosseous nerve, more than 80% recovered strength  $\geq$  M3 for finger extension.<sup>14</sup> Similarly, Mackinnon and Ray demonstrated substantial functional improvement in patients with radial nerve injuries treated with distal neurotizations using median nerve branches in a series of 19 cases. Our findings — with 91.6% satisfactory outcomes — reinforce the effectiveness of this approach.<sup>15</sup>

The only unsatisfactory result occurred in a 49-year-old patient with a 9-month interval between injury and surgery, the longest delay in the series. It is likely that the excessive denervation time, combined with comorbidities and poor adherence to rehabilitation, contributed to the inferior outcome.<sup>16</sup> This finding underscores the importance of early intervention and strict physiotherapeutic follow-up to optimize reinnervation.

The literature remains limited regarding distal neurotizations of the radial nerve due to technical complexity, ongoing procedural evolution, and the relative rarity of cases. These factors highlight the need for additional studies to expand the evidence base. Limitations of the present study include its retrospective design, lack of randomization, and the fact that surgeries were performed by different surgeons. However, the results demonstrated satisfactory functional recovery in the majority of patients, supporting the effectiveness of the techniques used.

## CONCLUSION

This study demonstrated that distal neurotization provided satisfactory functional recovery of wrist and finger extension in 91.6% of patients. Transfers using the supinator motor branch and median-nerve branches destined to the FSD and FRC proved to be effective options for restoring radial nerve extensor function.

## CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. ESSJ: Writing – original draft, review & editing, conceptualization, methodology, investigation, data curation, visualization, formal analysis, project administration. EYW: Writing – original draft, conceptualization, methodology, investigation, visualization, formal analysis. RGP: Writing – original draft, conceptualization, methodology, investigation, visualization. AISN: Writing – original draft, conceptualization, methodology, investigation, visualization. MRR: Writing – review & editing, conceptualization, methodology, investigation.

## DATA AVAILABILITY DECLARATION

The contents underlying the research are available in the manuscript.

## REFERENCES

1. Moore AM. Nerve transfers to restore upper extremity function: A paradigm shift. *Front. Neurol.* 2014;5:40. doi: 10.3389/fneur.2014.00040.
2. Brown JM, Mackinnon SE. Nerve transfers in the forearm and hand. *Hand Clin.* 2008;24(4):319-40. doi: 10.1016/j.hcl.2008.08.002.
3. Larson EL, Santosa KB, Mackinnon SE, Snyder-Warwick AK. Median to radial nerve transfer after traumatic radial nerve avulsion in a pediatric patient. *J Neurosurg Pediatr.* 2019;24(2):209-14. doi: 10.3171/2019.3.peds.18550.
4. Belzberg AJ, Dorsi MJ, Storm PB, Moriarity JL. Surgical repair of brachial plexus injury: a multinational survey of experienced peripheral nerve surgeons. *J Neurosurg.* 2004;101(3):365-76. doi: 10.3171/jns.2004.101.3.0365.
5. Tung TH. Nerve transfers. *Clin Plast Surg.* 2014;41(3):551-9. doi: 10.1016/j.cps.2014.04.002.
6. Bertelli JA, Tuffaha S, Sporer M, Seltser A, Cavalli E, Soldado F, et al. Distal nerve transfers for peripheral nerve injuries: indications and outcomes. *J Hand Surg Eur Vol.* 2024;49(6):721-33. doi: 10.1177/17531934231226169.
7. Caetano EB, Vieira LA, Sabongi Neto JJ, Caetano MBF, Picin CP, Silva Júnior LCND. Anatomical Study of the Motor Branches of the Radial Nerve in the Forearm. *Rev Bras Ortop (Sao Paulo).* 2020;55(6):764-70. doi: 10.1055/s-0040-1713403.
8. Thakkar M, Rose A, King W, Engelman K, Bednarz B. Anterior interosseous nerve to ulnar nerve transfer: A systematic review. *JPRAS Open.* 2022;32:195-210. doi: 10.1016/j.jpra.2022.02.007.
9. Cho ÁB, Ferreira CHV, Fontana RM, Montano GAÁ, Kiyohara LY, Sorrenti L. DISTAL NEUROTIZATION OF THE ANTERIOR INTEROSSEOUS NERVE TO RECOVER HAND GRASPING. *Acta Ortop Bras.* 2023;31(1):e257852. doi: 10.1590/1413-785220233101e257852.

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10. Chuang DC. NEUROTIZATION PROCEDURES FOR BRACHIAL PLEXUS INJURIES. *Hand Clin.* 1995;11(4):633-45. doi: 10.1016/s0749-0712(21)00272-9.
  11. Terzis JK, Papakonstantinou KC. The surgical treatment of brachial plexus injuries in adults. *Plast Reconstr Surg.* 2000;106(5):1097-122. doi: 10.1097/00006534-200010000-00022.
  12. Terzis JK, Kokkalis ZT. Selective contralateral C7 transfer in posttraumatic brachial plexus injuries: A report of 56 cases. *Plast Reconstr Surg.* 2009;123(3):927-38. doi: 10.1097/prs.0b013e31819ba48a.
  13. Dunnet WJ, Housden PL, Birch R. Flexor to extensor tendon transfers in the hand. *J Hand Surg Br.* 1995;20(1):26-8. doi: 10.1016/s0266-7681(05)80010-5.
  14. Xu B, Zhang C, Gu Y, Dong Z. Clinical outcome following transfer of the supinator motor branch to the posterior interosseous nerve in patients with C7-T1 brachial plexus palsy. *J reconstr Microsurg.* 2014;31(2):102-6. doi: 10.1055/s-0034-1384212.
  15. Ray WZ, Mackinnon SE. Clinical outcomes following median to radial nerve transfers. *J Hand Surg Am.* 2011;36(2):201-8. doi: 10.1016/j.jhsa.2010.09.034.
  16. Terzis JK, Saunders WB. Microreconstruction of nerve injuries. *J Pediatr Orthop.* 1987;7(4):484. doi: 10.1097/01241398-198707000-00022.

# EFFICACY AND SAFETY OF PERCUTANEOUS CRYOABLATION FOR DESMOID TUMORS: PROTOCOL FOR A SYSTEMATIC REVIEW AND META-ANALYSIS

## EFICÁCIA E SEGURANÇA DA CRIOABLAÇÃO PERCUTÂNEA PARA TUMORES DESMOIDES: PROTOCOLO DE REVISÃO SISTEMÁTICA E META-ANÁLISE

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### ABSTRACT

Desmoid tumors are rare, locally aggressive soft tissue neoplasms that may cause substantial morbidity, including chronic pain, functional limitation, and impaired quality of life, despite lacking metastatic potential. Management remains challenging and may include active surveillance, surgery, radiotherapy, systemic therapy, or image-guided ablation. Percutaneous cryoablation has emerged as a minimally invasive option for selected patients, particularly when symptom control and local disease management are priorities. However, current evidence remains heterogeneous, and its overall efficacy and safety are uncertain. This systematic review and meta-analysis will evaluate the efficacy and safety of percutaneous cryoablation in adults with desmoid tumors. Eligible studies will include randomized controlled trials and cohort studies of adult patients treated with percutaneous cryoablation, with no comparator required. The primary outcome will be local control, defined as absence of local progression or recurrence assessed radiologically or clinically. Secondary outcomes will include pain relief, major complications, retreatment rate, tumor response or size/volume reduction, symptom or functional improvement, and progression-free survival or time to local progression. Searches will be conducted in CENTRAL, Embase, PubMed, and Scopus, with risk of bias assessed using RoB-2 and ROBINS-I. **Level of Evidence II; Systematic Review.**

**Keywords:** Desmoid Tumors; Cryosurgery; Ablation Techniques; Systematic Review.

### RESUMO

Os tumores desmóides são neoplasias raras de partes moles, localmente agressivas, que podem causar morbidade significativa, incluindo dor crônica, limitação funcional e prejuízo da qualidade de vida, apesar de não apresentarem potencial metastático. Seu manejo permanece desafiador e pode incluir vigilância ativa, cirurgia, radioterapia, terapia sistêmica ou ablação guiada por imagem. Nesse contexto, a crioablação percutânea tem surgido como uma alternativa minimamente invasiva para pacientes selecionados, especialmente quando o controle dos sintomas e da doença local são prioridades. No entanto, as evidências disponíveis ainda são heterogêneas, e sua eficácia e segurança permanecem incertas. Esta revisão sistemática e meta-análise avaliará a eficácia e a segurança da crioablação percutânea em adultos com tumores desmóides. Serão incluídos ensaios clínicos randomizados e estudos de coorte envolvendo pacientes adultos tratados com crioablação percutânea, sem exigência de grupo comparador. O desfecho primário será o controle local, definido como ausência de progressão local ou recorrência, conforme avaliação radiológica ou clínica. Os desfechos secundários incluirão alívio da dor, complicações maiores, taxa de retratamento, resposta tumoral ou redução do tamanho/volume tumoral, melhora sintomática ou funcional e sobrevida livre de progressão ou tempo até progressão local. As buscas serão realizadas nas bases CENTRAL, Embase, PubMed e Scopus, e o risco de viés será avaliado por meio das ferramentas RoB-2 e ROBINS-I. **Nível de Evidência II; Revisão Sistemática.**

**Descritores:** Tumores Desmóides; Criocirurgia; Técnicas de Ablação; Revisão Sistemática.

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## INTRODUCTION

Desmoid tumors, also termed desmoid-type fibromatosis, are rare fibroblastic neoplasms that do not metastasize but may behave in a locally aggressive manner, often causing chronic pain, functional limitation, and substantial quality-of-life impairment.<sup>1,2</sup>

Historically managed with surgery and other morbid local approaches, these tumors are now understood to have a highly variable natural history, which has prompted a major shift toward individualized and less aggressive treatment strategies.<sup>1-3</sup> Accordingly, active surveillance has become the preferred initial approach for many patients, whereas systemic therapy and selected local interventions are generally reserved for progressive, symptomatic, or anatomically threatening disease.<sup>1-3</sup> Within this evolving therapeutic landscape, image-guided interventional radiology techniques - particularly percutaneous cryoablation - have emerged as promising minimally invasive options for extra-abdominal lesions.<sup>3,4</sup>

Recent literature indicates that cryoablation can provide meaningful symptom relief, tumor reduction, and local disease control, with acceptable safety profiles in carefully chosen patients with desmoid tumors.<sup>4-6</sup> Notably, retrospective comparative studies suggest that percutaneous cryoablation may achieve disease control comparable to surgical resection in selected cases, and early institutional reports document consistent clinical benefits following treatment.<sup>5,6</sup>

More recent evidence suggests that cryoablation success may depend on factors such as complete ice-ball coverage and prior exposure to tyrosine kinase inhibitors, underscoring the importance of meticulous patient selection and technical planning.<sup>7</sup>

Although recent reviews indicate that thermal ablation could be a promising treatment option for desmoid-type fibromatosis, the existing literature remains limited by significant variability in study design, patient selection, technical methods, and outcome measures.<sup>8</sup> Consequently, a dedicated systematic review and meta-analysis focusing solely on percutaneous cryoablation are necessary to deliver a clearer and more clinically relevant evaluation of its effectiveness and safety. By synthesizing the best available evidence, this review aims to assess the role of percutaneous cryoablation for adult desmoid tumors, especially regarding local control, pain relief, and treatment-related complications, addressing an important gap in the evidence-based management of this challenging condition.

## METHODS

This study will be a systematic review with a meta-analysis designed to evaluate the efficacy and safety of percutaneous cryoablation for desmoid tumors. The methodology will follow the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions,<sup>9</sup> and the reporting will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>10</sup> The protocol has been prospectively registered in the PROSPERO database under the registration number CRD420261349581. Ethics approval and informed consent are not required because this study is a systematic review protocol based exclusively on data from previously published studies.

### Eligibility criteria

The review will include studies enrolling adults ( $\geq 18$  years) with desmoid tumors (desmoid-type fibromatosis) undergoing percutaneous cryoablation. Both male and female patients will be considered, irrespective of ethnicity or geographic location. Studies exclusively involving non-adult populations, non-desmoid tumors, or patients not treated with percutaneous cryoablation will be excluded. Studies including mixed populations will also be excluded unless data for eligible adult patients with desmoid tumors can be clearly extracted. Interventions of interest will comprise percutaneous cryoablation administered for the treatment of desmoid tumors in adults. Eligible

studies may include variations in imaging guidance technique, number of probes, ablation protocol, number of treatment sessions, anesthesia approach, and prior treatment status. Studies will be required to evaluate percutaneous cryoablation as the primary intervention for desmoid tumors and to report relevant outcome data. Studies assessing only non-cryoablative interventions, non-percutaneous approaches, or interventions not primarily directed at the treatment of desmoid tumors will be excluded. Non-clinical studies, including in vitro, animal, or technical simulation studies, will also be excluded.

This review will not require a comparator group. Studies evaluating percutaneous cryoablation for the treatment of desmoid tumors in adults will be considered eligible regardless of whether a control or comparison group is present, provided that relevant outcome data are reported.

Both randomized and nonrandomized clinical study designs will be included, specifically randomized controlled trials (RCTs) and cohort studies. Eligible studies must report outcomes of interest for adults with desmoid tumors undergoing percutaneous cryoablation. Case reports, case series, case-control studies, narrative reviews, systematic reviews and meta-analyses, editorials, commentaries, letters to the editor, conference abstracts without sufficient data, in vitro studies, animal studies, and studies not reporting outcomes separately for eligible adult patients will be excluded. Studies including mixed populations will also be excluded unless data for adults with desmoid tumors can be clearly extracted.

### Search strategy

The preliminary search strategy will combine controlled vocabulary (Medical Subject Headings, MeSH) database (via: <https://www.ncbi.nlm.nih.gov/mesh/>) and free-text terms related to the condition and interventions of interest. At this stage, the core strategy includes the following: ("Desmoid Tumors" OR "Fibromatosis, Aggressive" OR "desmoid tumor" OR "desmoid tumors" OR "desmoid tumour" OR "desmoid tumours" OR "desmoid-type fibromatosis" OR "desmoid type fibromatosis" OR "aggressive fibromatosis" OR "deep fibromatosis" OR "musculoaponeurotic fibromatosis") AND ("Cryosurgery" OR "cryoablation" OR "percutaneous cryoablation" OR "image-guided cryoablation" OR "cryoablation therapy" OR "cryotherapy" OR "percutaneous cryotherapy" OR "tumor cryoablation" OR "thermal ablation").

For Embase, the search strategy will also include controlled vocabulary terms from Emtree (via: <https://www.embase.com/emtree/>), adapted to the database-specific indexing system. The preliminary Embase strategy will include the following: ('desmoid tumor'/exp OR 'aggressive fibromatosis'/exp OR 'desmoid tumor':ti,ab OR 'desmoid tumors':ti,ab OR 'desmoid tumour':ti,ab OR 'desmoid tumours':ti,ab OR 'desmoid-type fibromatosis':ti,ab OR 'desmoid type fibromatosis':ti,ab OR 'aggressive fibromatosis':ti,ab OR 'deep fibromatosis':ti,ab OR 'musculoaponeurotic fibromatosis':ti,ab) AND ('cryosurgery'/exp OR 'cryoablation':ti,ab OR 'percutaneous cryoablation':ti,ab OR 'image-guided cryoablation':ti,ab OR 'cryoablation therapy':ti,ab OR 'cryotherapy':ti,ab OR 'percutaneous cryotherapy':ti,ab OR 'tumor cryoablation':ti,ab OR 'thermal ablation':ti,ab). The main databases to be searched will include CENTRAL (Cochrane Central Register of Controlled Trials), Embase, PubMed, and Scopus. This preliminary strategy will be adapted to the syntax and indexing systems of each database during the search process and may be refined iteratively by adding additional MeSH terms, Emtree terms, synonyms, and complementary keywords, as necessary, to ensure comprehensive coverage of the literature. Boolean operators (AND, OR) will be used to structure the search queries across the selected databases.

## Studies selection

The study selection process will be conducted by two independent reviewers, who will assess all records without access to each other's evaluations. Titles and abstracts will first be screened against the pre-specified eligibility criteria, and studies deemed potentially relevant will then undergo full-text review to confirm their inclusion. In cases of disagreement, a senior reviewer will independently evaluate the articles in question and make the final decision. The Rayyan application will be employed to facilitate and streamline the screening and selection process.<sup>11</sup>

To ensure comprehensive coverage of the literature, a snowballing strategy will be applied: reference lists of relevant reviews identified through the initial search will be screened, and the reference lists of all full-text articles included in the review will likewise be examined to identify any additional eligible studies that may not have been captured by the database search.<sup>12</sup> The Cochrane Central Register of Controlled Trials (CENTRAL) will also be consulted to detect potentially relevant trials and to verify whether their results have been published.

## Outcomes

The primary outcome will be local control following percutaneous cryoablation for desmoid tumors. It is expected that this will be measured primarily as a dichotomous outcome, typically defined as the proportion of patients without local progression or recurrence, as assessed by radiologic or clinical methods and reported by each study. Outcomes will generally be extracted as binary variables reflecting achievement or non-achievement of local control. When available, quantitative measures related to tumor response or local disease status will also be extracted, and results may be stratified according to follow-up duration where appropriate.

The secondary outcomes will include several additional domains. First, pain relief will be considered, which is expected to be measured as either a continuous or dichotomous outcome, typically reported using validated pain scales such as the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS), and extracted as post-treatment values or change from baseline at the latest available follow-up. Second, major complications will be assessed as a dichotomous outcome, defined as the proportion of patients experiencing severe treatment-related adverse events, according to the classification or definition adopted in each included study. Third, retreatment rate will be evaluated as a dichotomous outcome, typically defined as the proportion of patients requiring any additional local or systemic intervention due to persistent, recurrent, or progressive disease during follow-up. Fourth, tumor response or reduction in tumor size/volume will be considered as a continuous outcome, extracted as means with standard deviations, medians with ranges, or percentage or absolute change in tumor dimensions or volume from baseline to the latest available follow-up. Fifth, symptoms or functional improvement will be assessed as either continuous scores from validated clinical or patient-reported outcome instruments, or as dichotomous improvement variables, depending on how each study reports symptom burden, functional limitation, or quality-of-life changes after treatment. Finally, progression-free survival or time to local progression, when available, will be assessed as a time-to-event or continuous outcome, reported as survival estimates, median progression-free survival, or time to recurrence or progression according to the data available in the included studies.

## Data summarization

Data will be extracted independently and in duplicate by two reviewers to ensure accuracy and reliability. A pre-designed data extraction form in Microsoft Excel® will be used to collect comprehensive information from each included study, covering study

characteristics, participant demographics, details of the intervention groups, methodological features, and outcomes assessed. Any discrepancies between the two reviewers will be resolved through consensus, and if necessary, by consultation with a senior reviewer to achieve consensus.

## Quality assessment

The risk of bias of the included studies will be assessed according to study design. Randomized controlled trials will be evaluated using the Cochrane Risk of Bias 2 (RoB-2) tool,<sup>13</sup> whereas nonrandomized studies will be assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool.<sup>14</sup> All assessments will be performed independently by at least two reviewers, and any disagreements will be resolved through a predefined process involving additional review when necessary. No additional information will be sought from study investigators if required information is unclear or unavailable in the published reports.

Since we intend to evaluate in a non-comparative way, through a single-arm meta-analysis, the assessment of publication bias will not be planned for the primary single-arm meta-analysis, as conventional methods for detecting small-study effects are of limited validity in non-comparative syntheses.<sup>15</sup>

## Statistical analysis plan

We plan to perform a meta-analysis to synthesize the data from the included studies according to the type of outcome reported. Given the expected predominance of single-arm studies, continuous outcomes with available baseline and post-intervention data will be analyzed by extracting the mean and standard deviation from each study. If studies report medians and interquartile ranges (IQR) or medians and ranges, these values will be converted into means and standard deviations using the methods described by Luo et al. (2018)<sup>16</sup> and Wan et al. (2014).<sup>17</sup> If only the standard error of the mean (SEM) is reported, it will be converted to the standard deviation (SD) using the formula  $SD = SEM \times \sqrt{n}$ , where  $n$  represents the sample size. When numerical values are available only in figures or graphs, data will be extracted using WebPlotDigitizer (via: <https://www.automeris.io>). If the same scale is used across studies, the Mean Difference (MD) will be applied as the measure of effect. If different scales are used, the Standardized Mean Difference (SMD) will be calculated. Whenever possible, SMD values will be backtransformed to the scale most used across the included studies to facilitate interpretation.

For dichotomous or proportion-based outcomes that do not involve a baseline-to-post comparison, such as local control, major complications, and retreatment rates, we will perform a single-arm proportional meta-analysis to estimate pooled event rates. To stabilize variance and improve the convergence of pooled estimates in the presence of extreme proportions, especially in studies reporting very low event rates or proportions close to zero or one, the Freeman–Tukey double arcsine transformation will be applied prior to meta-analysis.<sup>18</sup> All results will be presented with 95% confidence intervals (95% CI), and statistical significance will be defined as  $p$ -values  $< 0.05$ . Heterogeneity will be assessed using the Cochran Q test and the  $I^2$  statistic. Although  $p < 0.10$  and  $I^2 > 25\%$  will be considered indicative of significant heterogeneity, a random-effects model will be applied in all analyses regardless of the  $I^2$  value, given the anticipated clinical and methodological heterogeneity among the included studies. The random-effects model will use the REML method to estimate between-study variance, and when  $\tau^2$  is different from zero, the Hartung–Knapp–Sidik–Jonkman adjustment will be applied to estimate confidence intervals more accurately.<sup>19</sup> In addition, prediction intervals will be calculated to reflect the expected range of true effect sizes in future similar studies.<sup>20</sup>

When sufficient data are available, subgroup analyses will be performed based on clinically and methodologically relevant characteristics, including study design, tumor status, prior treatment history, tumor location, and follow-up duration. A leave-one-out sensitivity analysis will be conducted to assess the influence of each individual study on the pooled estimates.

If enough studies are available, meta-regression analyses will also be performed to explore the potential effects of moderators such as mean age, mean tumor size, follow-up duration, proportion of recurrent tumors, proportion of previously treated patients, and study quality. All statistical analyses will be conducted using RStudio v. 764.

## CONTRIBUTIONS OF THE AUTHORS

Each author made a personal and significant contribution to the development of this article. AG: Conceptualization. ESRM, AG, OPM: Data curation. AG, ESRM, CRAJ, MCCFV: Writing – original draft. ESRM, AG: Writing – review & editing. ESRM, AG, OPM: Supervision.

## DATA AVAILABILITY DECLARATION

The contents underlying the research are available in the manuscript.

## REFERENCES

1. Mangla A, Agarwal N, Schwartz G. Desmoid tumors: current perspective and treatment. *Curr Treat Options Oncol*. 2024;25(2):161-75. doi: 10.1007/s11864-024-01177-5.
2. Lee Y, Joo MW, Shin S, Hong S, Chung Y. Current treatment concepts for extra-Abdominal desmoid-Type fibromatosis: A narrative review. *Cancers (Basel)*. 2024;16(2):273. doi: 10.3390/cancers16020273.
3. Garnon J, Cazzato RL, Autrusseau P, Koch G, Weiss J, Gantzer J, et al. Desmoid fibromatosis: interventional radiology (sometimes) to the rescue for an atypical disease. *Br J Radiol*. 2024;98(1170):840-50. doi: 10.1093/bjr/tqae128.
4. Taqi K, Stockley C, Wood M, Przybojewski S, Bouchard-Fortier A, Mack L. Cryotherapy in the treatment of extra-Abdominal desmoid tumors—A review. *Curr Oncol*. 2025;32(3):137. doi: 10.3390/curroncol32030137.
5. Mandel JE, Kim D, Yarmohammadi H, Ziv E, Keohan ML, D'Angelo SP, et al. Percutaneous cryoablation provides disease control for extra-Abdominal desmoid-Type fibromatosis comparable with surgical resection. *Ann Surg Oncol*. 2021;29(1):640-8. doi: 10.1245/s10434-021-10463-7.
6. Johnston E, Alves A, Messiou C, Napolitano A, Strauss D, Hayes A, et al. Percutaneous cryoablation for desmoid fibromatosis: initial experience at a UK centre. *Clin Radiol*. 2022;77(10):784-93. doi: 10.1016/j.crad.2022.06.008.
7. Blondé P, Cazzato RL, Gantzer J, Steffen D, De Marini P, Bonnard L, et al. Determinants of morbidity and local control after cryoablation of sporadic extra-abdominal desmoid tumors. *Eur J Surg Oncol*. 2026;52(4):111456. doi: 10.1016/j.ejso.2026.111456.
8. Huang K, Hong R, Luo L, Zhao H, Wang Y, Li Y, et al. Efficacy and safety of different thermal ablative therapies for desmoid-type fibromatosis: a systematic review and meta-analysis. *Quant Imaging Med Surg*. 2023;13(10):6683-97. doi: 10.21037/qims-23-289.
9. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.5 (updated August 2024). Cochrane, 2024. Available from [www.cochrane.org/handbook](http://www.cochrane.org/handbook).
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71.
11. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4.
12. Wohlin C. Guidelines for snowballing in systematic literature studies and a replication in software engineering. In: *Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering. (EASE '14)*; 2014 May 13-14; London, United Kingdom. New York: ACM; 2014. p. 1-10. doi: 10.1145/2601248.2601268.
13. Sterne JAC, Savovi J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. doi: 10.1136/bmj.l4898.
14. Sterne JA, Hernán MA, Reeves BC, Savovi J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. doi: 10.1136/bmj.i4919.
15. Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, et al. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. *BMC Med Res Methodol*. 2021;21(1):189. doi: 10.1186/s12874-021-01381-z.
16. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res*. 2018;27(6):1785-805. doi: 10.1177/0962280216669183.
17. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135. doi: 10.1186/1471-2288-14-135.
18. Doi SA, Xu C. The freeman-Tukey double arcsine transformation for the meta-analysis of proportions: recent criticisms were seriously misleading. *J Evid Based Med*. 2021;14(4):259-61. doi: 10.1111/jebm.12445.
19. Röver C, Knapp G, Friede T. Hartung-Knapp-Sidik-Jonkman approach and its modification for random-effects meta-analysis with few studies. *BMC Med Res Methodol*. 2015;15:99. doi: 10.1186/s12874-015-0091-1.
20. Higgins JPT, Thompson SG, Spiegelhalter DJ. A re-Evaluation of random-Effects meta-Analysis. *J R Stat Soc Ser A Stat Soc*. 2009;172(1):137-59. doi: 10.1111/j.1467-985x.2008.00552.x.

# EFFICACY OF DYNAMIC MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF CERVICAL SPONDYLOTIC MYELOPATHY: SYSTEMATIC REVIEW

## EFICÁCIA DA RESSONÂNCIA MAGNÉTICA DINÂMICA NO DIAGNÓSTICO DA MIELOPATIA CERVICAL ESPONDILÓTICA: REVISÃO SISTEMÁTICA

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### ABSTRACT

**Objective:** To investigate the efficacy of Dynamic Magnetic Resonance (DMR) in diagnosing Cervical Spondylotic Myelopathy (CSM). **Methods:** Systematic review using PubMed, Embase, Scopus, Web of Science, LILACS and SciELO databases. The search terms were “cervical myelopathy”, “magnetic resonance”, and “dynamic magnetic resonance”, and two independent researchers performed the literature search and data extraction. The risk of bias was assessed using the Newcastle-Ottawa scale, and the quality of evidence was assessed using GRADE. **Results:** Four studies were included. Ancheschi et al. (2016) concluded that DMR distinguishes morphometric variations that help diagnose this condition. Jha et al. (2018) evaluated cases of cervical pain undergoing DMR and detected more significant spinal cord compression in extension, suggesting the utility of DMR. Lee et al. (2018) evaluated cervical stenosis in the neutral, flexion, and extension positions and found greater stenosis gravity in extension. Lee et al. (2019) highlighted that DMR is superior in preoperative evaluation but pointed out limitations such as lack of standardization of positioning. **Conclusion:** Observational studies show significant changes in morphometric characteristics of the cervical spinal canal in flexion and extension images, which would increase the sensitivity of DMR in diagnosing CSM, but the quality of evidence was very low. **Level of Evidence I; Systematic review.**

**Keywords:** Spine; Magnetic Resonance Imaging; Cervical Spinal Cord; Myelopathy.

### RESUMO

**Objetivo:** Investigar a eficácia da Ressonância Magnética Dinâmica (RMD) no diagnóstico da Mielopatia Cervical Espondilótica (MCE). **Métodos:** Revisão sistemática usando as bases de dados PubMed, Embase, Scopus, Web of Science, LILACS e SciELO. Os termos de busca foram “mielopatia cervical”, “ressonância magnética” e “ressonância magnética dinâmica”, e dois pesquisadores independentes realizaram a busca bibliográfica e a extração de dados. O risco de viés foi avaliado usando a escala Newcastle-Ottawa e a qualidade da evidência foi avaliada usando o sistema GRADE. **Resultados:** Quatro estudos foram incluídos. Ancheschi et al. (2016) concluíram que a RMD distingue variações morfométricas que ajudam a diagnosticar essa condição. Jha et al. (2018) avaliaram casos de dor cervical submetidos à RMD e detectaram compressão medular mais significativa em extensão, sugerindo a utilidade da RMD. Lee et al. (2018) avaliaram a estenose cervical nas posições neutra, flexão e extensão e encontraram maior gravidade da estenose na extensão. Lee et al. (2019) destacaram que a RMD é superior na avaliação pré-operatória, mas apontaram limitações como a falta de padronização do posicionamento. **Conclusão:** Estudos observacionais mostram mudanças significativas nas características morfométricas do canal vertebral cervical em imagens de flexão e extensão, o que aumentaria a sensibilidade da RMD no diagnóstico da MCE, mas a qualidade da evidência foi muito baixa. **Nível de evidência I; Revisão sistemática.**

**Descritores:** Coluna; Imagem por Ressonância Magnética; Medula Espinal Cervical; Mielopatia.

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<< SUMÁRIO

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## INTRODUCTION

Cervical spondylotic myelopathy (CSM) is a spinal cord dysfunction secondary to spinal cord compression, related to chronic, non-traumatic and progressive narrowing of the cervical spinal canal.<sup>1-5</sup> It is a multifactorial disease, with static (degenerated discs, osteophytes, thickened ligaments) and dynamic (segmental instability and cervical mobility) factors interfering in the pathophysiology and clinical presentation.<sup>1,4</sup> Occupational, behavioral, congenital, systemic and sports-related components should also be considered in evaluating the disease.<sup>5</sup> The literature is unclear regarding the incidence and prevalence of CSM, and its clinical spectrum is broad and reflects the progressive neurological dysfunction of the cervical spinal cord.<sup>1-2,5</sup> CSM is a syndrome that can manifest with paresis, paresthesia in the extremities, decreased dexterity of movements, radicular pain in the upper limb, spasticity, hyperreflexia, ataxia, urinary incontinence and fecal.<sup>6-7</sup> The diagnosis may be difficult due to the presence of associated cervical radiculopathies, vascular claudication and lumbar stenosis, and a detailed physical examination is essential in the event of symptoms suggestive of CSM.<sup>8</sup>

Despite being the most common cause of spinal cord injury, CSM is still underdiagnosed and functional disabilities inherent to the natural progression of the disease are common.<sup>9-10</sup> The diagnosis of CSM should be confirmed by imaging, with Magnetic Resonance Imaging (MRI) being the best method for assessing spinal cord involvement.<sup>3,8</sup> However, MRI has inherent limitations since the patient's cervical spine is in a neutral and static position during the examination, and it is impossible to assess dynamic factors, underestimating the risk of spinal cord injury related to spinal movements.<sup>10</sup>

Dynamic Magnetic Resonance (DMR) is a promising technique for changing this scenario because it includes images obtained in flexion and extension, making the diagnosis more accurate.<sup>11</sup> Therefore, this study aims to investigate the effectiveness of DMR in diagnosing CSM.

## MATERIALS AND METHODS

This is a systematic review, and the protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO)<sup>12</sup>, CRD42020221798, and published as an article in a scientific journal after peer review.<sup>13</sup>

This study sought to answer the research question, "Is DMR more effective than conventional MRI in diagnosing CSM?" This question was formulated based on the acronym PICO<sup>14</sup>:

- Population (P): Individuals of both sexes with CSM
- Intervention (I): Dynamic Magnetic Resonance (DMR)
- Comparator (C): Conventional Magnetic Resonance Imaging (MRI)
- Outcome (O): Diagnosis of Spondylotic Cervical Myelopathy (CSM)

The studies were searched in the MEDLINE (via PubMed), Embase, LILACS, SciELO, Scopus and Web of Science databases. The terms used in the search were: "cervical myelopathy", "magnetic resonance", and "dynamic magnetic resonance". The Boolean operators [AND] and [OR] were used. There were no restrictions on language or year of publication. The gray literature search was performed on Google Scholar.

The searches were performed by two researchers independently, following the recommendations of the Peer Review of Electronic Search Strategies (PRESS) protocol.<sup>15</sup> The results on the number of articles found in each database were recorded as a table in Microsoft Excel® software.

The selection of studies occurred independently in two phases by two researchers. In the first phase, the researchers selected the relevant studies based on the titles and abstracts. The full text of the studies selected in the previous phase was read in the second

phase. The articles chosen for full reading were evaluated according to the following eligibility criteria: individuals of both sexes, over 18 years of age, undergoing MRI for diagnostic investigation of CSM. Discordant cases were resolved by consensus with a third expert researcher on the subject, and the Mendeley® reference manager was used to avoid duplication and to facilitate file sharing among researchers.

The two researchers extracted data from the studies in pairs and independently. The Rayyan® systematic review manager, available as an online application, was used to allow better exploration of the results.

The risk of bias was verified using the Newcastle-Ottawa Scale<sup>16</sup> to assess the quality of non-randomized studies, and the quality of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system.<sup>17</sup>

The summary of the available evidence is presented in the form of a narrative synthesis, and the recommendations written in the systematic review of the PRISMA protocol.<sup>18</sup>

## RESULTS

A total of 273 records were retrieved from the database search. After evaluating the titles and abstracts of all studies, 134 were selected, of which 109 were excluded due to duplication or for not meeting the eligibility criteria. Subsequently, the 25 studies selected in the first phase were read in full, and according to the established eligibility criteria, 4 studies were selected to compose the systematic review (Figure 1) (Table 1).

Ancheschi et al. (2016)<sup>19</sup> conducted a retrospective observational study with 15 patients of both sexes, with clinical and radiological signs of CSM secondary to degenerative disease of the cervical spine. To evaluate the morphometric variations of the cervical spine, the patients underwent conventional MRI examination with the cervical spine in a neutral position and DMR evaluation, with maximum flexion and extension tolerated by the patient. The studied morphometric parameters were (1) anterior length of the spinal cord, (2) posterior length of the spinal cord, (3) diameter of the spinal canal, and (4) diameter of the spinal cord. All measurements were established on sagittal T2-weighted images in the three positions. The authors demonstrated that the evaluated parameters were

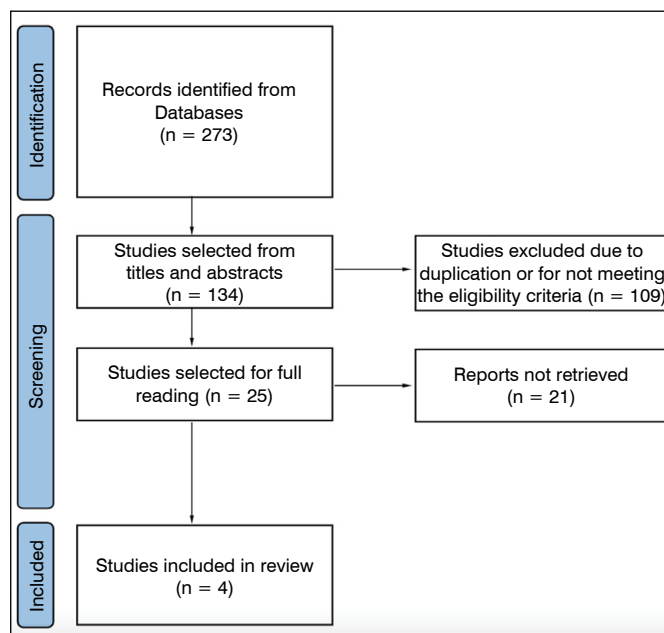


Figure 1. PRISMA flow diagram of study selection.

**Table 1.** General characteristics of the included studies.

| Study                          | Year | Country     | Journal                             | Design                      | Number of patients | Age (years old) | Diagnosis                                                                      |
|--------------------------------|------|-------------|-------------------------------------|-----------------------------|--------------------|-----------------|--------------------------------------------------------------------------------|
| Ancheschi et al. <sup>19</sup> | 2016 | Brazil      | Coluna/Columna                      | Retrospective observational | 15                 | 58,4            | Cervical spondylotic myelopathy / Degenerative disease of the cervical spine   |
| Jha et al. <sup>20</sup>       | 2018 | Japan       | Clinical Neurology and Neurosurgery | Retrospective observational | 66                 | 52,9            | Neck pain with or without mild neurological symptoms                           |
| Lee et al. <sup>21</sup>       | 2018 | South Korea | Annals of Rehabilitation Medicine   | Retrospective observational | 92                 | 57,8            | Radiculopathy / Cervical myelopathy                                            |
| Lee et al. <sup>22</sup>       | 2019 | South Korea | World Neurosurgery                  | Retrospective observational | 88                 | 68,2            | Cervical spondylotic myelopathy / Posterior longitudinal ligament ossification |

statistically longer in flexion than in the neutral and extension positions. They concluded that DMR allows the study of morphometric variations of the spinal canal. The limitations of this study include the small number of patients included, the lack of intra- and interobserver reliability, the variation in the angle of cervical flexion and extension during the DMR exams, the absence of a control group, and the lack of clinical applicability. Nevertheless, the study's objective was not to compare the morphometric changes with the symptoms presented by the patients.

The study by Jha et al. (2018)<sup>20</sup> included 66 patients with neck pain with or without mild neurological symptoms (i.e., without muscle weakness and hyperreflexia) who underwent MRI to evaluate changes in (1) spinal canal diameter; (2) anterior and posterior spinal cord length; and (3) the degree of spinal cord compression at each level from C2-C3 to C7-T1 in the flexion and extension positions of the cervical spine. The parameters were evaluated from sagittal T1- and T2-weighted images. Intra- and interobserver analysis was performed with good to excellent agreement ( $\kappa > 0.7$ ). The mean spinal canal diameter significantly decreased in flexion compared to extension at each level ( $p < 0.05$ ). The mean lengths of the anterior and posterior cervical spine and spinal cord decreased in neck extension compared with flexion ( $p < 0.05$ ). More severe stages of spinal cord compression were found in the extension position than in flexion ( $p < 0.05$ ). The article concluded that DMR may help detect etiological factors responsible for degenerative disease and cervical instability. More advanced stages of spinal cord compression were found in the extension position than in the flexion position. However, more advanced stages of spinal cord compression in the extension position did not necessarily cause severe myelopathy, and all patients were treated conservatively. The limitations of this study include the relatively small sample size, the variation in cervical flexion and extension angles during the DMR exams and the absence of a control group.

Lee et al. (2018)<sup>21</sup> conducted a retrospective observational study with 92 patients with a mean age of 57.8 years to determine the variation of cervical spinal canal stenosis according to cervical flexion and extension positions and investigate whether changes in movement angle differ according to disease severity. DMR was indicated due to clinical signs of myelopathy or cervical radiculopathy when there were no findings compatible with symptoms on conventional MRI in the neutral position. The images were evaluated in sagittal and axial sections, in T1 and T2 weightings in the neutral position, and sagittal sections in T2 weighted in the dynamic examination. The authors found that cervical extension is associated with canal narrowing, resulting in increased severity of stenosis, which was more significant in the extension position compared to the neutral and flexion positions. Furthermore, neck flexion led to a significant decrease in stenosis compared to the neutral position. The authors advise the need for caution when performing cervical extension

exercises in patients with CSM, especially in severe cases. Neck flexion may be a safer alternative for these patients. The authors also point out that these results may explain the kyphotic posture frequently observed in patients with CSM as compensation for degenerative changes. The study's limitations are related to the retrospective nature and the absence of axial images in all positions evaluated, which may have limited the assessment of stenosis in the transverse plane.

Lee et al. (2019)<sup>22</sup> conducted a study with 88 patients of both genders with symptoms of CSM but without an accurate radiological diagnosis through conventional MRI. The patients underwent DMR to assess the differences between (1) the diameter of the spinal canal and (2) the thickness of the ligamentum flavum in different cervical positions. T2 sagittal images of the dynamic exams were evaluated. Patients were divided into 66 with CSM and 22 with Ossification of the Posterior Longitudinal Ligament (OPLL). The mean diameter of the spinal canal was smaller in extension than in the neutral position at all levels measured, especially between C3-C4 and C6-C7 in the group of patients with CSM. In the OPLL group, although the canal's diameter decreased at all levels measured when passing from the neutral position to the extension, the changes were not significant. In the CSM group the thickness of the ligamentum flavum was significantly greater in extension than in the neutral and flexion positions but not in the OPLL group. Therefore, the dynamic morphometric changes were statistically significant in the CSM group. The authors suggest that DMR should be considered a better tool for the preoperative evaluation of patients with CSM, as it can provide more helpful information about the surgical levels. The retrospective nature and the relatively small sample size are highlighted as limitations, which may limit the generalization of the results. The degrees of neck movement were not standardized during DMR, and this lack of standardization may have introduced variability in the results. Furthermore, there is no description of how the diagnosis of CSM and OPLL was made to divide the patients into two groups.

## DISCUSSION

The four articles included in this systematic review explore the use of DMR in evaluating CSM. All studies have a retrospective observational design and agree that MRI, performed in flexed and extended cervical spine positions, provides valuable additional information compared to conventional MRI, performed in the neutral position. However, retrospective studies are susceptible to selection bias and may not adequately control for all confounding variables. Despite this, the examination is beneficial in patients with symptoms of CSM with inconclusive findings on conventional MRI. In general, neck extension resulted in a greater spinal canal narrowing compared with flexion. Nevertheless, it is important to remember that the use of MRI may lead to overdiagnosis of

CSM and a possible unnecessary increase in surgical interventions, and the clinical context of each patient should always be considered and not based solely on examination findings to make treatment decisions.<sup>19-22</sup>

Regarding sample size, the studies have limitations once they presented a relatively small number of patients, which may compromise the generalization of the results to the population. For ethical reasons, the four studies excluded patients with severe neurological symptoms whose diseases could be aggravated by the exams or who did not tolerate the dynamic exam from their samples.

The descriptions of the positioning of the cervical spine for performing the DMR exams were similar in the four studies included in this systematic review and also in other studies published in the literature: patients in the supine position with the chin angled anteriorly towards the chest with a cushion under the head to obtain the images in flexion; and with the chin angled posteriorly, with a cushion under the shoulders to obtain the images in extension. The patients remained comfortably or with minimal discomfort in these positions during the exams. The flexion and extension angles were not standardized, with variations according to individual limitations, constituting a measurement bias. Another point worth mentioning is that the DMR exam was performed with the patients in the supine position, which does not reflect the physiologically upright posture, and the morphometric changes and compression of the spinal cord may be different in the vertical position.

There was variation between the diagnoses justifying the symptoms of CSM in the included studies. Due to the broad spectrum of symptoms and etiologies of CSM, the literature adopts different nomenclatures, which makes it difficult to standardize terms for

similar findings.<sup>2-3,5</sup> In addition, the methods of measuring the variables differed between the studies, therefore not allowing a meta-analysis to be performed. In the study by Ancheschi et al.<sup>19</sup>, the statistical analysis was limited to describing the data with means and standard deviations. In the study by Jha et al.<sup>20</sup>, ANOVA, Tukey's test and Kappa were performed to assess interobserver agreement. In the study by Lee et al.<sup>21</sup>, repeated measures ANOVA and Pearson's correlation analysis were used to assess the relationship between the rate of variation of stenosis and the severity of stenosis. The study by Lee et al.<sup>22</sup> used the t-test, Mann-Whitney test, and linear-by-linear association test. Therefore, the lack of uniformity in the measures used makes it difficult to compare the results directly, and different statistical tests prevent the direct comparison of p-values and confidence intervals.

In addition, the studies included patients with different characteristics and degrees of severity of CSM, which may influence the results. Therefore, given the above and according to the GRADE system, the quality of the evidence found in this systematic review was considered 'very low' (Figure 2). Therefore, more research with robust methodologies and standardized measures is needed to strengthen the conclusions.

Finally, MRI, performed in flexion and extension positions of the cervical spine, has emerged as a complementary tool to conventional MRI in evaluating CSM.<sup>23</sup> Among the advantages of DMR is the possibility of identifying the dynamic factors that cause stenosis, providing greater sensitivity in diagnosing this condition.<sup>24</sup> However, disadvantages include the low availability of the exam, which may limit its use in clinical practice, and the risk of overdiagnosis, something that should be considered in the clinical setting of patients.

| Certainty assessment                                                                                                                                             |                        |                           |                      |              |             |                                                                         | N.of patients |                  | Effect            |                   | Certainty                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------------------|----------------------|--------------|-------------|-------------------------------------------------------------------------|---------------|------------------|-------------------|-------------------|---------------------------------|
| N. of studies                                                                                                                                                    | Study design           | Risk of bias              | Inconsistency        | Indirectness | Imprecision | Other considerations                                                    | CMR           | Conventional MRI | Relative (95% CI) | Absolute (95% CI) |                                 |
| Diagnosis of Cervical Spondylotic Myelopathy                                                                                                                     |                        |                           |                      |              |             |                                                                         |               |                  |                   |                   |                                 |
| 4                                                                                                                                                                | non-randomised studies | very serious <sup>a</sup> | serious <sup>b</sup> | not serious  | not serious | all plausible residual confounding would reduce the demonstrated effect | 261/-         |                  | not estimable     |                   | ⊕○○○<br>Very low <sup>a,b</sup> |
| CI: confidence interval                                                                                                                                          |                        |                           |                      |              |             |                                                                         |               |                  |                   |                   |                                 |
| Explanations                                                                                                                                                     |                        |                           |                      |              |             |                                                                         |               |                  |                   |                   |                                 |
| a. Small number of patients, lack of intra- and interobserver reliability, absence of control group, limited the assessment of stenosis in the transverse plane. |                        |                           |                      |              |             |                                                                         |               |                  |                   |                   |                                 |
| b. The degrees of neck movement were not standardized during DMR, and this lack of standardization may have introduced variability in the results                |                        |                           |                      |              |             |                                                                         |               |                  |                   |                   |                                 |

**Figure 2.** Analysis of Quality of Evidence using *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE).

## CONCLUSION

In conclusion, observational studies showed significant changes in the morphometric characteristics of the cervical spinal canal in flexion and extension images performed in DMR, which would

increase the sensitivity of this exam in diagnosing CSM. The quality of the evidence, however, could have been higher, and its clinical usefulness remains uncertain for directing the treatment of patients with CSM.

## CONTRIBUTIONS OF THE AUTHORS

Each author made an individual and significant contribution to the development of this article. LVPG; OLPR; PMDSP: Substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; drafting the work or critically revising it for important intellectual content. STP; HCFPS: Substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; final approval of the version of the manuscript to be published.

## DATA AVAILABILITY DECLARATION

Research data are available from the corresponding author upon request.

## REFERENCES

- Yamaguchi JT, Hsu WK. Intervertebral disc herniation in elite athletes. *Int Orthop*. 2018;43(4):833-40. doi: 10.1007/s00264-018-4261-8.
- Tu J, Vargas Castillo J, Das A, Diwan AD. Degenerative cervical myelopathy: insights into its pathobiology and molecular mechanisms. *J Clin Med*. 2021;10(6):1214. doi: 10.3390/jcm10061214.

3. Nouri A, Tetreault L, Singh A, Karadimas SK, Fehlings MG. Degenerative cervical myelopathy. *Spine (Phila Pa 1976)*. 2015;40(12):E675-E693. doi: 10.1097/brs.0000000000000913.
4. Marie-Hardy L, Pascal-Moussellard H. Degenerative cervical myelopathy. *Rev Neurol (Paris)*. 2021;177(5):490-7. doi: 10.1016/j.neurol.2020.11.015.
5. Boogaarts HD, Bartels RHMA. Prevalence of cervical spondylotic myelopathy. *Eur Spine J*. 2013;24(S2):139-41. doi: 10.1007/s00586-013-2781-x.
6. Wilder FV, Fahlman L, Donnelly R. Radiographic cervical spine osteoarthritis progression rates: a longitudinal assessment. *Rheumatol Int*. 2009;31(1):45-8. doi: 10.1007/s00296-009-1216-9.
7. Lannon M, Kachur E. Degenerative cervical myelopathy: clinical presentation, assessment, and natural history. *J Clin Med*. 2021;10(16):3626. doi: 10.3390/jcm10163626.
8. Williams J, D'Amore P, Redlich N, Darlow M, Suwak P, Sarkovich S, et al. Degenerative cervical myelopathy. *Orthop Clin North Am*. 2022;53(4):509-21. doi: 10.1016/j.ocl.2022.05.007.
9. Gibson J, Nouri A, Krueger B, Lakombin N, Nasser R, Gimbel D, et al. Degenerative Cervical Myelopathy: A Clinical Review. *Yale J Biol Med*. 2018;91(1):43-8.
10. Badhiwala JH, Ahuja CS, Akbar MA, Witiw CD, Nassiri F, Furlan JC, et al. Degenerative cervical myelopathy — update and future directions. *Nat Rev Neurol*. 2020;16(2):108-24. doi: 10.1038/s41582-019-0303-0.
11. Sangondimath G, Mallepally AR, Marathe N, Mak K, Suman Salimath. Degenerative cervical myelopathy: recent updates and future directions. *J Clin Orthop Trauma*. 2020;11(5):822-9. doi: 10.1016/j.jcot.2020.07.012.
12. PROSPERO [Internet]. York: Centre for Reviews and Dissemination, University of York. Available from: <https://www.crd.york.ac.uk/PROSPERO/>.
13. Luizari VPG, Oliveira LPDR, Pontes MDS, Soeira TP, Herrero CFPDS. Efficacy of Dynamic Magnetic Resonance Imaging in the Diagnosis of Degenerative Cervical Myelopathy: Systematic Review Protocol. *Rev Bras Ortop (Sao Paulo)*. 2024;59(1):e17-e20. doi: 10.1055/s-0044-1779311.
14. Riva JJ, Malik KMP, Burnie SJ, Endicott AR, Busse JW. What is your research question? An introduction to the PICOT format for clinicians. *J Can Chiropr Assoc*. 2012;56(3):167-71.
15. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. *J Clin Epidemiol*. 2016;75:40-6. doi: 10.1016/j.jclinepi.2016.01.021.
16. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. Ottawa: Ottawa Hospital Research Institute. Available from: <https://ohri.ca/en/who-we-are/core-facilities-and-platforms/ottawa-methods-centre/newcastle-ottawa-scale>.
17. Piggott T, Morgan RL, Cuellar-Garcia CA, Santesso N, Mustafa RA, Meerpohl JJ, et al. Grading of recommendations assessment, development, and evaluations (GRADE) notes: extremely serious, GRADE's terminology for rating down by three levels. *J Clin Epidemiol*. 2020;120:116-20. doi: 10.1016/j.jclinepi.2019.11.019.
18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71.
19. Ancheschi BDC, Savarese A, Pratali RDR, Maranhão DAC, Castilha MT, Nogueira-Barbosa MH, et al. DYNAMIC MAGNETIC RESONANCE IMAGING: PRELIMINARY PRESENTATION OF A TECHNIQUE. *Coluna/Columna*. 2016;15(3):209-12. doi: 10.1590/s1808-185120161503162794.
20. Jha SC, Miyazaki M, Tsumura H. Kinetic change of spinal cord compression on flexion-extension magnetic resonance imaging in cervical spine. *Clin Neurol Neurosurg*. 2018;174:86-91. doi: 10.1016/j.clineuro.2018.09.017.
21. Lee Y, Kim SY, Kim K. A dynamic magnetic resonance imaging study of changes in severity of cervical spinal stenosis in flexion and extension. *Ann Rehabil Med*. 2018;42(4):584-90. doi: 10.5535/arm.2018.42.4.584.
22. Lee JB, Kim IS, Kwon JY, Lee JJ, Park J, Cho CB, et al. Difference of dynamic morphometric changes between in patients with ossification of posterior longitudinal ligament and patients with cervical spondylosis: assessment by cervical dynamic magnetic resonance imaging. *World Neurosurg*. 2019;123:e566-e573. doi: 10.1016/j.wneu.2018.11.213.
23. Nigro L, Donnarumma P, Tarantino R, Rullo M, Santoro A, Delfini R. Static and dynamic cervical MRI: two useful exams in cervical myelopathy. *J Spine Surg*. 2017;3(2):212-6. doi: 10.21037/jss.2017.06.01.
24. Guppy KH, Hawk M, Chakrabarti I, Banerjee A. The use of flexion-extension magnetic resonance imaging for evaluating signal intensity changes of the cervical spinal cord. *J Neurosurg Spine*. 2009;10(4):366-73. doi: 10.3171/2009.1.spine08567.

# DO CLINICAL TRIALS ON ELECTRICAL STIMULATION FOR PERIPHERAL NERVE INJURY MEASURE WHAT REALLY MATTERS? A SINGLE-ARM META-ANALYSIS AND META-REGRESSION

## ENSAIOS CLÍNICOS SOBRE ESTIMULAÇÃO ELÉTRICA PARA LESÃO DOS NERVOS PERIFÉRICOS MEDEM O QUE REALMENTE IMPORTA? META-ANÁLISE E META-REGRESSÃO DE BRAÇO ÚNICO

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### ABSTRACT

**Introduction:** Electrical stimulation (ES) has emerged as an adjunct therapy to promote nerve regeneration; however, the clinical relevance of outcomes reported in related randomized controlled trials (RCTs) remains uncertain. This study evaluated whether RCTs of ES for peripheral nerve injuries prioritize outcomes that meaningfully reflect patient benefit. **Methods:** We conducted a systematic review and meta-science single-arm meta-analysis, registered on PROSPERO (CRD420251002257). PubMed, Scopus, Embase, and Cochrane CENTRAL were searched from database inception to June 2026. Only full-text articles published in English were included; trial registries and grey literature were not searched. Outcomes were classified using the Heneghan et al. criteria into clinically relevant, surrogate, subjective, composite, complex, or lack of relevance. **Results:** Twenty-one RCTs with 823 patients were included. Clinically relevant outcomes were the most frequently reported, with a pooled proportion of 88% (95% CI: 71.65%–98.02%), calculated as the proportion of patients with evaluable data assessed using clinically relevant outcomes across trials. Surrogate and subjective outcomes were reported in 59% and 40% of cases, respectively, while composite outcomes were rare (0.53%). No outcomes were classified as complex or lack of relevance. Meta-regression showed no significant trend over time in the reporting of clinically meaningful outcomes ( $p = 0.38$ ). **Conclusion:** Most randomized controlled trials assessing electrical stimulation for peripheral nerve injuries prioritize clinically relevant outcomes. Future trials should prespecify core outcome sets, define explicit primary and secondary outcome hierarchies at trial registration, and routinely report patient-centered functional and quality-of-life measures to enhance clinical applicability. **Level of Evidence II; Systematic review of Level I studies with discrepant results.**

**Keywords:** Peripheral Nerve Injuries; Electric Stimulation Therapy; Randomized Controlled Trials as Topic; Endpoint Determination; Outcome Assessment, Health Care; Meta-Analysis.

### RESUMO

**Introdução:** A estimulação elétrica (EE) surgiu como terapia adjuvante para promover a regeneração nervosa; no entanto, a relevância clínica dos desfechos relatados nos ensaios clínicos randomizados (ECRs) sobre o tema permanece incerta. Este estudo avaliou se os ECRs de EE para lesões de nervos periféricos priorizam desfechos que refletem de forma significativa o benefício ao paciente. **Métodos:** Foi realizada uma revisão sistemática com meta-análise de braço único, em abordagem de metaciência, registrada no PROSPERO (CRD420251002257). As bases PubMed, Scopus, Embase e Cochrane CENTRAL foram pesquisadas desde a criação de cada base até junho de 2026. Foram incluídos apenas artigos em texto completo publicados em inglês; registros de ensaios clínicos e literatura cinzenta não foram pesquisados. Os desfechos foram classificados segundo os critérios de Heneghan et al. em clinicamente relevantes, substitutos, subjetivos, compostos, complexos ou sem relevância. **Resultados:** Foram incluídos vinte e um ECRs, com 823 pacientes. Os desfechos clinicamente relevantes foram os mais frequentemente relatados, com proporção agrupada de 88% (IC 95%: 71,65%–98,02%), calculada como a proporção de pacientes com dados avaliáveis analisados por meio de desfechos clinicamente relevantes nos ensaios. Desfechos substitutos e subjetivos foram relatados em 59% e 40% dos casos, respectivamente, enquanto desfechos compostos foram raros (0,53%). Nenhum desfecho foi classificado como complexo ou sem relevância. A meta-regressão não mostrou tendência significativa ao longo do tempo no relato de desfechos clinicamente importantes ( $p = 0,38$ ). **Conclusão:** A maioria dos ensaios clínicos randomizados que avaliam a estimulação elétrica para lesões de nervos periféricos prioriza desfechos clinicamente relevantes. Ensaios futuros devem pré-especificar conjuntos centrais de desfechos (core outcome sets), definir hierarquias explícitas de desfechos primários e secundários no registro do ensaio e relatar rotineiramente medidas funcionais e de qualidade de vida centradas no paciente, a fim de ampliar a aplicabilidade clínica. **Nível de Evidência II; Revisão sistemática de estudos de Nível I com resultados discrepantes.**

**Descritores:** Traumatismos dos Nervos Periféricos; Terapia por Estimulação Elétrica; Ensaios Clínicos Controlados Aleatórios como Assunto; Determinação de Ponto Final; Avaliação de Resultados em Cuidados de Saúde; Metanálise.

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<< SUMÁRIO

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## INTRODUCTION

Peripheral nerve injuries can lead to substantial impairments in patients' social and occupational functioning, with a significant impact on quality of life.<sup>1</sup> Despite considerable advances in techniques aimed at overcoming barriers to nerve regeneration, important limitations remain.

Nerve regeneration is influenced by a variety of factors, including patient age, level and extent of injury, time to surgical repair, and presence of concomitant lesions.<sup>2-4</sup> In recent years, attention has turned to adjuvant therapies that could enhance axonal regeneration. One promising approach is electrical stimulation (ES), which has demonstrated favorable effects in preclinical models.<sup>5</sup> ES has been shown to promote early regenerative processes, including neuronal survival and axonal sprouting, supporting its use as a potentially effective clinical practice.<sup>5</sup> Randomized controlled trials (RCTs) are widely considered the gold standard for evaluating the effectiveness of medical interventions, standing at the top of the evidence hierarchy.<sup>6</sup> However, RCTs are not immune to methodological flaws, including inadequate randomization, lack of allocation concealment, absence of blinding, and selective outcome reporting. Such biases can mislead readers and obscure the true impact of interventions.<sup>7</sup>

The choice of outcomes in RCTs is a critical methodological decision, as it directly influences how an intervention's effectiveness is interpreted. Depending on the trial's objective, whether to estimate the preliminary probability of benefit (as in early-phase studies) or to establish clinical utility, certain types of outcomes may be more appropriate than others.<sup>8</sup> However, the frequent use of endpoints that do not adequately reflect patients' health status in trials raises concerns about the real-world applicability of some of these studies. In peripheral nerve trials, this limitation is well illustrated when improvements in electrophysiological metrics (e.g., nerve conduction parameters) do not translate proportionally into patient-perceived symptom relief or functional recovery. For example, in carpal tunnel syndrome, neurophysiological improvements after treatment show only modest correlations with clinical outcome measures.<sup>9</sup> Similarly, after median or ulnar nerve laceration repair, agreement between clinical motor recovery and electrophysiological recovery can be only fair, with substantial discrepancies between the two assessments.<sup>10</sup> Heneghan et al. have pointed out that surrogate, composite, subjective, complex outcomes, and particularly those lacking direct clinical relevance, may make RCT results less applicable in using them to guide clinical decisions.<sup>7</sup> Considering that, our study aimed to perform a meta-science single-arm meta-analysis to assess how outcomes are being selected and reported in RCTs involving electrical stimulation for peripheral nerve injuries. By calculating the proportion of patients that have been assessed with clinically meaningful endpoints, this review tries to clarify whether the current evidence truly reflects outcomes that matter to patients and healthcare providers.

## METHODS

This systematic literature review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>11</sup> recommendations. Its objective was to determine the proportion of studies evaluating patients with peripheral nerve injuries who received electrical stimulation, based on the outcome classification criteria proposed by Heneghan et al. (2017)<sup>7</sup>. This review was registered in the International Prospective Register of Systematic Reviews (PROSPERO), under registration number CRD420251002257, with the methodology pre-defined and documented.

### Eligibility criteria

This review used the PICOS framework (Population, Intervention, Comparison, Outcomes, and Study type). Eligibility criteria included

full-text RCTs published in English, from inception up to June 2026, and available in the PubMed, Scopus, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) databases. Eligible studies were required to involve patients with peripheral nerve injuries who received electrical stimulation as an intervention. The control group could consist of any comparator, including placebo, standard care, alternative therapies, or no intervention. The assessed outcomes are described in the section below. Exclusion criteria comprised articles not available in full text on digital platforms, studies that did not assess electrical stimulation, conference abstracts, preprints, letters to the editor, case reports and series, observational studies, non-randomized trials, quasi-experimental studies, and reviews. Duplicate publications of the same study were also excluded, with only the most comprehensive report included.

### Outcomes Assessed

The outcomes assessed in this meta-science meta-analysis were classified according to the criteria proposed by Heneghan et al. (2017)<sup>7</sup>, categorizing clinical outcomes into clinically relevant, surrogate, composite, subjective, complex scales, and lack of relevance. Outcome classification was independently conducted by two orthopedic surgeons (ESRM and AG) working in consensus. Inter-rater reliability prior to consensus (e.g., Cohen's kappa) was not calculated because pre-consensus classifications were not prospectively recorded. Outcomes were classified as clinically relevant when they directly reflected patient benefit, including symptom relief, functional status, or quality of life. Outcomes were classified as subjective when they primarily represented opinion-based assessments, such as satisfaction or global impression ratings, which are more susceptible to bias. When an outcome could be considered both patient-reported and subjective, such as pain intensity measured by the Visual Analogue Scale (VAS), it was classified as clinically relevant. This decision was based on the rationale that pain intensity directly captures a clinically meaningful symptom from the patient's perspective, rather than a surrogate physiological marker or a purely opinion-based judgment. This operational rule was applied consistently across all included studies.

The artificial intelligence tool ChatGPT-4o was used to assist in classifying non-orthopedic outcome measures when existing scales were ambiguous or outside the reviewers' core expertise. AI assistance was used only to support the interpretation of unfamiliar outcome instruments (e.g., identifying what domain an instrument measures). No study results or effect estimates were provided to the AI. All AI-suggested classifications were independently reviewed by both orthopedic surgeons, and final classification decisions were made by human judgment; when possible, instrument descriptions were verified against primary sources. When outcome definitions or instruments were insufficiently described, we verified the instrument domain and scoring using primary sources (e.g., original instrument publications and/or scoring manuals) prior to classification, and any remaining uncertainty was resolved by consensus between the two orthopedic surgeons. No study authors were contacted for outcome clarification.

For each included study, the number of patients who had evaluable outcomes within each classification category was recorded, excluding those lost to follow-up. The proportion was then calculated by dividing this number by the total sample size of the study. Studies that did not report any outcome fitting a given classification were considered to have 0% reporting for that category, ensuring that all studies contributed to the full outcome spectrum. This methodological approach allowed for an indirect estimation of the prevalence of clinically relevant outcomes across randomized trials evaluating electrical stimulation for peripheral nerve injury.

## Search Strategy

The database search strategy included descriptors related to “Electrical Stimulation” and “Peripheral Nerve Injury.” The descriptors were obtained from the Medical Subject Headings (MeSH) database ([www.ncbi.nlm.nih.gov/mesh/](http://www.ncbi.nlm.nih.gov/mesh/)) and supplemented with additional relevant terms. Boolean operators *AND* and *OR* were used to structure the search queries across the selected databases, following the predefined inclusion and exclusion criteria. A complete list of descriptors and the whole search strategy for each database are provided in Supplementary Material 1.

## Selection of studies

Two reviewers (ESRB and CRAJ), who had no access to each other's assessments, evaluated the titles and abstracts of the identified articles, selecting those that met the inclusion criteria. Articles that passed the initial screening were reviewed in full text to determine their inclusion. When discrepancies arose between the two reviewers, a senior reviewer (ESRM), who had exclusive access to the conflicting articles, intervened to resolve differences. The studies were selected using the Rayyan (Rayyan QCRI, developed by the Qatar Computing Research Institute, Doha, Qatar).<sup>12</sup>

## Data summarization

Data extraction was performed independently and in duplicate (ESRB and CRAJ) to ensure accuracy and reliability. Two reviewers extracted data from the included studies using a pre-designed data extraction form created in Microsoft Excel® (version 2205). The form captured comprehensive details on study characteristics, including population size, methodological approaches, and the outcomes assessed. Any discrepancies were resolved through discussion or consultation with a senior reviewer (AG) to achieve consensus.

## Quality assessment

The risk of bias assessment was conducted using the Cochrane Risk of Bias tool for randomized trials (RoB 2)<sup>13</sup>, evaluated independently by two reviewers (ESRB and MCCFV), with discrepancies resolved through a senior reviewer (OPM). Assessment of publication bias was not performed, given the risk of introducing bias in this context and the lack of recommendations for such analysis in proportion-based meta-analyses.<sup>14</sup>

## Statistical analysis

The outcomes were analyzed using a single-arm meta-analysis, with pooled proportions (meta-proportions) and corresponding 95% confidence intervals (95% CI) calculated. In this meta-science analysis, pooled proportions represent the percentage of patients within each study who were evaluated using outcomes belonging to a given Heneghan classification<sup>7</sup> category. A proportion of zero indicates that the study did not assess or report that outcome category, rather than absence of effect. Although the original protocol specified the use of PLOGIT transformation for variance stabilization, during the analysis phase, it was observed that several studies presented extreme proportions (close to 0% or 100%). Therefore, the Freeman-Tukey double arcsine transformation was deemed more appropriate to stabilize variances under these conditions.<sup>15</sup> Inverse variance weighting was used as the pooling method, with the Hartung-Knapp correction applied to adjust confidence intervals. Heterogeneity among studies was assessed using Cochran's Q test and the I<sup>2</sup> statistic, with p-values < 0.10 and I<sup>2</sup> values > 25% indicative of significant heterogeneity. Given the anticipated methodological variability, a random-effects model was employed for all analyses, regardless of the degree of heterogeneity, as a conservative approach to result synthesis. To address heterogeneity and estimate the expected effect size in

future studies, we calculated prediction intervals (PI), which were reported to account for between-study variability, reflecting the expected range of effects in future studies.<sup>16</sup> No subgroup analyses were performed. A leave-one-out sensitivity analysis was conducted to assess the influence of individual studies on the pooled proportion estimates. Meta-regression analyses were limited to a single covariate (year of publication) and were performed in an exploratory manner to evaluate temporal trends in the reporting of clinically relevant outcomes. All statistical analyses were performed using RStudio (version 764), using the 'meta' and 'metafor' packages.

## RESULTS

The database search, applying filters based on pre-established inclusion and exclusion criteria, yielded 1,362 articles. Following the removal of duplicates, 852 articles remained. After reviewing the titles and abstracts, 28 articles were selected for full-text review. Twenty-one articles were included in the review and incorporated into the meta-analysis.<sup>17–37</sup> The exact number of disagreements was not prospectively recorded; however, all final inclusion decisions were made by consensus after review by a senior reviewer. The flowchart outlining the study selection process and reasons for exclusion is presented in Figure 1.

## Studies Characteristics

A total of 21 RCTs were included in this review, encompassing patients with various types of peripheral nerve injuries treated with electrical stimulation interventions.<sup>17–37</sup> The total population analyzed across studies was 823 patients. Considering available data, the mean age of participants was approximately 41.6 ± 9.2 years. In several studies, authors reported only the overall age of the entire sample without group stratification.<sup>24,32,34</sup> The follow-up periods ranged from acute assessments lasting minutes<sup>19</sup> to long-term evaluations up to 12 months.<sup>18,20,35</sup>

The included studies encompassed a broad range of peripheral nerve injuries. Compressive neuropathies were the most common, particularly carpal tunnel syndrome (CTS), evaluated in patients with mild to severe presentations.<sup>19,21–23,29,35</sup> Cubital tunnel syndrome was also addressed<sup>25</sup>, along with ulnar nerve entrapment<sup>32</sup>.

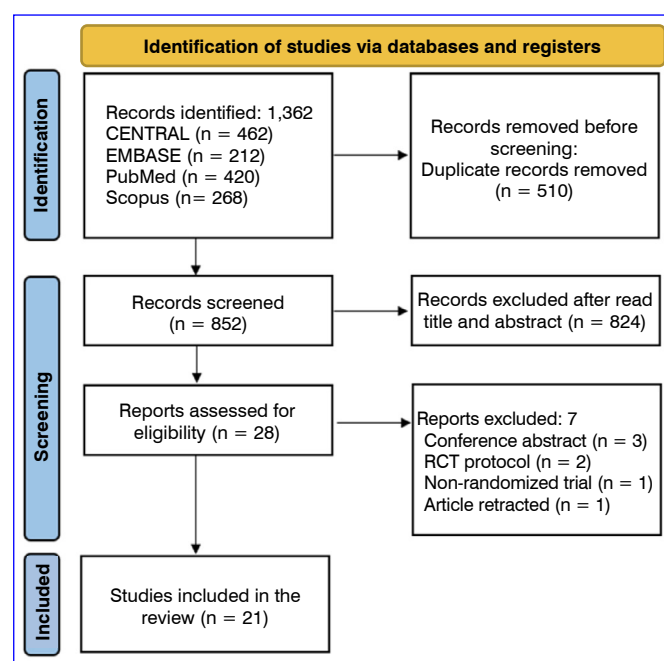


Figure 1. Flowchart of included studies.

Traumatic lesions included complete digital nerve transection<sup>27,30</sup>, and neurotmesis of the median nerve<sup>31</sup>. Peroneal nerve neuropathy following burn injuries was investigated in two studies.<sup>17,24</sup> Postoperative and iatrogenic nerve dysfunctions were also represented, such as brachial plexus motor impairment after surgery<sup>28</sup>, shoulder dysfunction due to spinal accessory nerve manipulation during oncologic surgery<sup>18</sup>, and nerve injuries evaluated during rehabilitation following surgical repair<sup>37</sup>. Idiopathic cases included facial nerve palsy (Bell's palsy).<sup>20,26</sup> Corneal hypoesthesia after LASIK and dry eye symptoms following PRK were included as ocular nerve dysfunction models.<sup>34,36</sup>

A variety of electrical stimulation (ES) techniques were applied across the included trials. Transcutaneous electrical nerve stimulation (TENS) was the most frequently used modality<sup>19,21,23,29–32</sup>, followed by neuromuscular electrical stimulation (NMES)<sup>17,24</sup> and transcutaneous electrical stimulation (TES) in ocular applications<sup>34,36</sup>. Electroacupuncture (EA) approaches were observed in

three studies.<sup>22,23,37</sup> Some studies used subthreshold or submaximal direct stimulation postoperatively<sup>25,27,35</sup>, and one applied brief intraoperative electrical stimulation to the spinal accessory nerve<sup>38</sup>. Control groups varied across studies and included sham stimulation<sup>19,25,27,30,36</sup>, standard treatments such as splinting or pharmacologic therapy<sup>20,22,26</sup>, conventional rehabilitation protocols<sup>28,31,32</sup>, and low-level laser therapy<sup>17,24</sup>. In one study, the contralateral eye served as an intraindividual control<sup>34</sup>; in others, patients underwent surgery without active stimulation<sup>18,35</sup>.

The distribution of 25 primary outcomes across the 21 studies showed that most (84%) studies used clinically important endpoints. Almost a third of the studies (30%) used a single surrogate outcome; subjective results comprised only 10% of this, based on the Heneghan et al. (2017)<sup>7</sup> detection framework. Details of outcome classification and characteristics of individual studies are reported in Table 1 and Figure 2.

**Table 1.** The main characteristics of the included studies.

| Author (year)                           | Design              | Country  | Follow-up                                                               | Nerve Injury     | Population                                                                                                                                                  | Intervention                                                                                                           | Control                                                                                         | N° of Patients Intervention (M/F) |           | Age (Years)               |                           | N° of Outcomes |
|-----------------------------------------|---------------------|----------|-------------------------------------------------------------------------|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------|-----------|---------------------------|---------------------------|----------------|
|                                         |                     |          |                                                                         |                  |                                                                                                                                                             |                                                                                                                        |                                                                                                 | Intervention                      | Control   | Intervention              | Control                   |                |
| Mattos et al. (2026) <sup>30</sup>      | RCT                 | Brazil   | 3 months                                                                | Digital nerve    | Adult patients with acute, isolated, non-segmental traumatic digital nerve injuries of the hand undergoing microsurgical neurotomy within 2 weeks of injury | Transcutaneous PES, 20 Hz, 1 hour, biphasic symmetrical current, within 24 h after surgery; followed by rehabilitation | Sham PES under identical setup, electrode positioning, and duration; followed by rehabilitation | 16                                | 16        | 36.6 (18–57) <sup>a</sup> | 34.2 (21–58) <sup>a</sup> | 4              |
| Naeser et al. (2002) <sup>24</sup>      | RCT crossover trial | Egypt    | 2 months                                                                | Common peroneal  | Patients with chronic burns involving 20–30% of TBSA, second- or third-degree, evolving to common peroneal neuropathy.                                      | NMES – 20 minutes per session, 3 times per week                                                                        | Low-intensity laser (LIL) – 20 minutes per session, 3 times per week                            | 11 (9/2)                          |           | 53.5 ± 8.8 <sup>†</sup>   |                           | 3              |
| Ghaffariyeh et al. (2009) <sup>34</sup> | RCT                 | Iran     | 3 months                                                                | Ophthalmic nerve | Patients undergoing bilateral refractive surgery (LASIK - Laser-Assisted in Situ Keratomileusis) without comorbidities                                      | TES (20 Hz, 60 min, 50–60 mA) to one eye postoperatively                                                               | Fellow eye without stimulation (intraindividual control)                                        | 20 (10/10)                        |           | 23.29 ± 2.14 <sup>†</sup> |                           | 5              |
| Gordon et al. (2010) <sup>35</sup>      | RCT                 | Canada   | 12 months                                                               | Median nerve     | Patients with CTS (≥50% motor axonal loss) and bilateral symptoms are undergoing unilateral carpal tunnel release surgery.                                  | Surgery plus median nerve stimulation (20 Hz, 1 h, immediate postoperative)                                            | Surgery without electrical stimulation                                                          | 11 (5/6)                          | 10 (3/7)  | 53 ± 18 <sup>†</sup>      | 61 ± 16 <sup>†</sup>      | 5              |
| Kara et al. (2010) <sup>19</sup>        | RCT                 | Turkey   | Single session; multiple assessments up to 35 minutes post-intervention | Median nerve     | Female patients with mild to moderate CTS, bilateral or unilateral, right-hand dominant                                                                     | Conventional TENS (100 Hz, 200 s, 30 min) over median nerve – sensory submotor intensity                               | Sham TENS with electrodes placed identically                                                    | 10 (0/10)                         | 10 (0/10) | 49.1 ± 6.7 <sup>†</sup>   | 51.8 ± 3.2 <sup>†</sup>   | 3              |
| Kumnerdee et al. (2010) <sup>22</sup>   | RCT                 | Thailand | 5 weeks                                                                 | Median nerve     | Patients with mild to moderate CTS, unilateral or bilateral (more severe side evaluated)                                                                    | EA (10 sessions, twice weekly, 1 Hz for 30 minutes)                                                                    | Neutral volar wrist splint worn at night                                                        | 30 (4/26)                         | 30 (2/28) | 50.4 ± 9.0 <sup>†</sup>   | 51.7 ± 8.9 <sup>†</sup>   | 2              |

**Table 1.** The main characteristics of the included studies.

|                                    |     |             |           |                                                                            |                                                                                                                                                                        |                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                 |                        |                                         |                              |                                                                     |   |
|------------------------------------|-----|-------------|-----------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------------------------------------|------------------------------|---------------------------------------------------------------------|---|
| Zhou et al. (2012) <sup>28</sup>   | RCT | China       | 4 months  | Brachial plexus                                                            | Patients with total or partial brachial plexus injury post-reconstruction                                                                                              | Comprehensive rehabilitation program including TENS (30 minutes twice daily), MFES (20 minutes twice daily), individualized OT, and Tuina (twice weekly), over four 30-day cycles, with a one-week interval between cycles only for TENS and MFES.                      | Home-based NMES and self-directed OT; no supervised physiotherapy or Tuina. Conducted over 4 cycles of 30 days.                                                                                                 | 21 (17/4)              | 22 (19/3)                               | 35,12 ± 2,25 <sup>†</sup>    | 32,27 ± 2,15 <sup>†</sup>                                           | 2 |
| Casale et al. (2013) <sup>29</sup> | RCT | Italy       | 3 weeks   | Median nerve                                                               | Patients with mild to moderate CTS, with clinical confirmation (positive Tinetti and/or Phalen tests) and neurophysiological confirmation.                             | High-intensity combined-wavelength LASER (830/1064 nm; 250 J/cm <sup>2</sup> , 100 s) applied over the median nerve; 15 daily sessions.                                                                                                                                 | TENS 100 Hz, 80 ms pulse width, below the muscle contraction threshold, 30 minutes per session; 15 daily sessions.                                                                                              | 10 (5/5)               | 10 (5/5)                                | 57,3 ± 12,9 <sup>†</sup>     | 56,8 ± 12,0 <sup>†</sup>                                            | 2 |
| Koca et al. (2014) <sup>21</sup>   | RCT | Turkey      | 3 weeks   | Median nerve                                                               | Patients with idiopathic mild to moderate CTS, with clinical confirmation (positive Phalen, Tinetti, or carpal compression tests) and neurophysiological confirmation. | IFC with 15 sessions (five times per week), 20 minutes each, applied to the volar forearm and hand; 4000 Hz base frequency with 20 Hz modulation.                                                                                                                       | TENS: Conventional TENS (100 Hz, 80 ms, 20 minutes per session), 15 sessions (five times weekly), electrodes placed over the transverse carpal ligament and palmar region.<br><br>Split: Neutral-position night | IFC: 21 (6/15)         | TENS: 20 (7/13)<br><br>Split: 22 (7/15) | IFC: 34,9 ± 4,8 <sup>†</sup> | TENS: 34,2 ± 5,2 <sup>†</sup><br><br>Split: 35,4 ± 4,2 <sup>†</sup> | 3 |
| He et al. (2015) <sup>37</sup>     | RCT | China       | 6 weeks   | radial, ulnar, median, fibular, tibial, sciatic nerves, or brachial plexus | Adult patients with peripheral nerve injury confirmed by electromyography, due to trauma, compression, or repetitive strain                                            | EA at Governor vessel (GV) and local meridian (LM) points of the injured nerve; 30 sessions (five times per week for six weeks), 30 minutes per session.                                                                                                                | EA applied exclusively to local meridian points (LM); 30 sessions (five times per week for six weeks), each lasting 30 minutes.                                                                                 | 15 (8/7)               | 15 (9/6)                                | 28,3 ± 9,6 <sup>†</sup>      | 28,6 ± 10,3 <sup>†</sup>                                            | 5 |
| Kim et al. (2015) <sup>20</sup>    | RCT | South Korea | 12 months | Facial nerve                                                               | Patients with Bell's palsy (House-Brackmann ≤ 4, Sunnybrook > 20), symptom onset within 7 days, without other neurological conditions.                                 | Prednisolone (1 mg/kg/day for 10 days) with or without acyclovir (1500 mg/day for 5 days) combined with continuous subthreshold electrical stimulation (20 Hz, 10 ms, average 1.4 mA) applied to facial nerve branches using adhesive electrodes, usually during sleep. | Prednisolone (1 mg/kg/day for 10 days) with or without acyclovir (1500 mg/day for 5 days), without electrical stimulation.                                                                                      | 30 (sex not specified) | 30 (sex not specified)                  | 46,5 ± 16,3 <sup>†</sup>     | 49,17 ± 18,2 <sup>†</sup>                                           | 4 |
| Wong et al. (2015) <sup>27</sup>   | RCT | Canada      | 6 weeks   | Digital nerve                                                              | Patients with complete digital nerve transection repaired with epineurial suture, operated within 14 days of trauma, and without neurological comorbidities.           | Submaximal electrical stimulation (20 Hz, up to 30 V, 0.1–0.4 ms) for 1 hour with electrodes implanted at the coaptation site immediately after nerve repair.                                                                                                           | Sham stimulation with active current (20 Hz, up to 30 V, 0.1–0.4 ms) for 5 seconds, followed by device deactivation for 55 minutes, with electrodes positioned identically.                                     | 18**                   | 18**                                    | 37,2 ± 13,3 <sup>†</sup>     | 39,3 ± 17,9 <sup>†</sup>                                            | 5 |

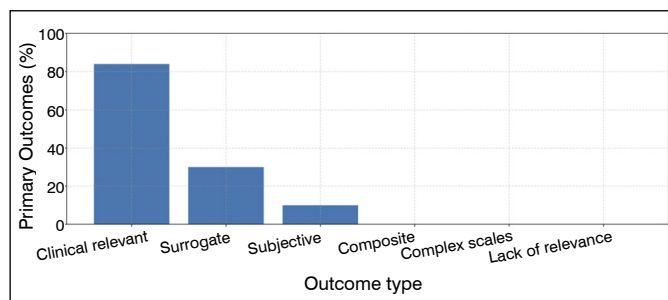
**Table 1.** The main characteristics of the included studies.

|                                    |     |             |           |                        |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                 |                                    |                                      |                                                                            |    |
|------------------------------------|-----|-------------|-----------|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|------------------------------------|--------------------------------------|----------------------------------------------------------------------------|----|
| Barber et al. (2018) <sup>18</sup> | RCT | Canada      | 12 months | Spinal accessory nerve | Patients with a new diagnosis of HNC, undergoing neck dissection including Level IIb, with shoulder dysfunction due to spinal accessory nerve injury.                                                                                              | Intraoperative BES of SAN with 60 minutes of continuous stimulation (20 Hz, 3–5 V, 0.1 ms) using a cuff electrode after neck dissection and before closure.                                                                                               | No electrical stimulation, standard skin closure.                                                                                                                                                                                                                                                                                                                                                                                                  | 27 (21/6)       | 27 (22/5)                          | 57.8 <sup>§</sup>                    | 57.9 <sup>§</sup>                                                          | 3  |
| Power et al. (2019) <sup>25</sup>  | RCT | Canada      | 3 years   | Cubital nerve          | Patients with grade 3 CuTS (McGowan-Goldberg), chronic motor axonal loss on EMG, and MUNE $\geq 2$ SD below the mean were included; patients with prior elbow surgery or associated neurological conditions were excluded.                         | Surgery (in situ decompression or transposition) with 1 hour of PES (20 Hz, <30V, 0.1 ms) applied near the ulnar nerve immediately postoperatively.                                                                                                       | Surgery with sham stimulation, with active PES for 5 seconds followed by deactivation for the remainder of the hour.                                                                                                                                                                                                                                                                                                                               | 20 (15/5)       | 11 (8/3)                           | 54 $\pm$ 12 <sup>†</sup>             | 59 $\pm$ 12 <sup>†</sup>                                                   | 5  |
| Chu et al. (2022) <sup>21</sup>    | RCT | China       | 5 weeks   | Median nerve           | Patients with complete median nerve transection treated with neurolysis, with injury duration less than 2 months and no prior history of electrical stimulation                                                                                    | Ultrasound-guided PENS with parallel needles (3 cm from lesion center), 20 Hz, 0.2 ms, 1 hour, four times per week for five weeks, combined with conventional rehabilitation.                                                                             | TENS with surface electrodes placed 3 cm from the lesion center, 20 Hz, 0.2 ms, 1 hour per session, four times weekly for five weeks, combined with conventional rehabilitation.                                                                                                                                                                                                                                                                   | 12**            | 11**                               | 36.83 $\pm$ 12.95 <sup>†</sup>       | 35.55 $\pm$ 13.06 <sup>†</sup>                                             | 5  |
| Han et al. (2022) <sup>26</sup>    | RCT | South Korea | 12 weeks  | Ophthalmic nerve       | Patients with myopia (-0.50 to -7.50 D) and astigmatism up to 3 D, without ocular or systemic diseases affecting the ocular surface, undergoing bilateral PRK, are at risk of corneal sensory dysfunction related to corneal sensory nerve injury. | TES (4–7 mA, 2 Hz, 15–30 minutes daily for 2 weeks, then once weekly until 12 weeks) was applied periorbitally with conventional post-PRK treatment.                                                                                                      | Sham TES, visually identical, used for 15–30 minutes daily for 2 weeks and then once weekly until 12 weeks, combined with conventional post-PRK treatment.                                                                                                                                                                                                                                                                                         | 12 (6/6)        | 12 (5/7)                           | 28,3 $\pm$ 4,7 <sup>†</sup>          | 26,6 $\pm$ 5,3 <sup>†</sup>                                                | 10 |
| Shoman et al. (2022) <sup>26</sup> | RCT | Egypt       | 6 weeks   | Facial nerve           | Patients with Bell's palsy, without identifiable secondary causes, with a complete clinical diagnosis confirmed by imaging.                                                                                                                        | LLLT (850 nm, 1 W/cm <sup>2</sup> ) applied to 8 facial points for 8 minutes per session (1 minute per point), twice weekly for 6 weeks, combined with prednisolone (80 mg/day for 10 days, tapered over 21 days), facial exercises, and massage therapy. | ES: Electrical stimulation (50 Hz, until visible muscle contraction, 10 minutes per session), twice weekly for 6 weeks, combined with prednisolone (80 mg/day for 10 days, tapered over 21 days), acyclovir, facial exercises, and massage therapy.<br><br>Control: Prednisolone (80 mg/day for 10 days, tapered over 21 days) and acyclovir, combined with facial exercises and massage therapy, without laser therapy or electrical stimulation. | LLLT: 15 (10/5) | ES: 15 (10/5)<br>Control: 15 (8/7) | LLLT: 34,66 $\pm$ 8,44 <sup>††</sup> | ES: 32,8 $\pm$ 8,09 <sup>†</sup><br>Control: 32,66 $\pm$ 8,86 <sup>†</sup> | 2  |

**Table 1.** The main characteristics of the included studies.

|                                                    |     |        |           |                      |                                                                                                                                                                         |                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                       |            |            |                           |                           |   |
|----------------------------------------------------|-----|--------|-----------|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|------------|---------------------------|---------------------------|---|
| Chu et al. (2023) <sup>32</sup>                    | RCT | China  | 5 weeks   | Ulnar nerve          | Patients with a history of elbow trauma and electrophysiological diagnosis of ulnar nerve injury (axonotmesis) were evaluated between 1 and 3 months after injury.      | PES (20 Hz, 0.2 ms, 1 hour per session, four times per week for five weeks) using six needles placed longitudinally along the ulnar nerve, combined with conventional rehabilitation.                                                                                | TENS with surface electrodes (20 Hz, 0.2 ms, 1 hour per session, four times weekly for five weeks), combined with conventional rehabilitation.                                                        | 13 (9/4)   | 12 (8/4)   | 38 ± 11 <sup>†</sup>      |                           | 7 |
| Lo et al. (2023) <sup>23</sup>                     | RCT | Taiwan | 6 weeks   | Median nerve         | Patients with clinical symptoms compatible with CTS and a diagnosis confirmed by electrodiagnostic testing.                                                             | ELMT applied to the PC-6, PC-7, and hand points, 15 minutes per acupoint, five times per week for six weeks, combined with tendon and nerve gliding exercises.                                                                                                       | Conventional TENS applied to the same anatomical points, 30 Hz, 70 s, 15 minutes per session, five times weekly for six weeks, combined with the same tendon and nerve gliding exercises.             | 17 (15/2)  | 17 (13/4)  | 47,4 ± 7,1 <sup>†</sup>   | 46,3 ± 11,0 <sup>†</sup>  | 3 |
| Ahmed et al. (2024) <sup>17</sup>                  | RCT | Egypt  | 2 months  | Common fibular nerve | Patients with second- or third-degree burns of the lower limbs (20–30% of total body surface area), evolving to peripheral mononeuropathy of the common peroneal nerve. | NMES (20 minutes per session, three times per week for two months), with electrodes placed over the popliteal fossa and the head of the fibula. The intensity was adjusted to elicit a visible motor response.                                                       | LILT applied in continuous mode with direct contact, 90 seconds per point across 10 points (totaling 15 minutes per region), over the lateral popliteal fossa and fibular head, three times per week. | 30 (13/17) | 30 (14/16) | 28,27 ± 4,66 <sup>†</sup> | 27,97 ± 3,92 <sup>†</sup> | 1 |
| Fernández-de-las-Peñas et al. (2023) <sup>33</sup> | RCT | Spain  | 20 months | Median nerve         | Women with unilateral CTS, with persistent clinical symptoms for at least 6 months, and a diagnosis confirmed by electrodiagnosis.                                      | Ultrasound-guided PENS applied to four points along the median nerve trajectory (arm and forearm), three sessions (one per week), 2 Hz, 250 s, with intensity adjusted to achieve a visible motor response, combined with tendon and median nerve gliding exercises. | Endoscopic carpal tunnel release surgery followed by tendon and median nerve gliding exercises.                                                                                                       | 35 (0/35)  | 35 (0/35)  | 46 ± 10 <sup>†</sup>      | 47 ± 7 <sup>†</sup>       | 1 |

Legends: M/F = Male/female; N° = Number; RCT = Randomized Controlled Trial; TBSA = Total Body Surface Area; LASIK = Laser-Assisted in Situ Keratomileusis; TES = Transcutaneous Electrical Stimulation; CTS = Carpal Tunnel Syndrome; TENS = Transcutaneous Electrical Nerve Stimulation; NMES = Neuromuscular Electrical Stimulation; MFES = Medium-Frequency Electrical Stimulation; OT = Occupational Therapy; LIL = Low-Intensity Laser; LASER = Light Amplification by Stimulated Emission of Radiation; IFC = Interferential Current; EA = Electroacupuncture; GV = Governor Vessel; LM = Local Meridian; ES = Electrical Stimulation; BES = Brief Electrical Stimulation; SAN = Spinal Accessory Nerve; CuTS = Cubital Tunnel Syndrome; MUNE = Motor Unit Number Estimation; DP = Standard Deviation; PENS = Percutaneous Electrical Nerve Stimulation; LLLT = Low-Level Laser Therapy; ELMT = Electroacupuncture-Like Magnetic Therapy; LILT = Low-Intensity Laser Therapy; HNC = Head and Neck Cancer; BCTQ = Boston Carpal Tunnel Questionnaire; NPRS = Numerical Pain Rating Scale; GROCC = Global Rating of Change. \* The studies presented only the overall mean age of the total sample, without group-specific age data. \*\* The studies did not report population data stratified by sex. <sup>a</sup> Mean (range). <sup>†</sup> Mean ± Standard Deviation. <sup>‡</sup> Mean.



Legend: Percentages represent the proportion of trials reporting at least one primary outcome within each classification category. Outcome categories are not mutually exclusive, as some randomized controlled trials reported more than one primary outcome, which were classified independently and could therefore contribute to more than one category. Consequently, the summed percentages may exceed 100%.

**Figure 2.** Distribution of primary outcome classifications according to Heneghan's criteria.

## Meta-analysis of included studies

Across the included randomized controlled trials, outcomes were classified into clinically relevant, surrogate, subjective, or composite categories, following the criteria established by Heneghan et al. (2017)<sup>7</sup>. Clinically relevant outcomes were the most frequently reported, followed by surrogate outcomes and subjective measures. Composite outcomes were rarely used, with only one study contributing data to this category. Notably, no outcomes were classified as complex scales or as lacking clinical relevance, reflecting a strong focus on pragmatic and patient-centered outcome measures throughout the included studies.

Worked example: in an RCT with a total sample size of N = 100, assume the study reports three endpoints, reoperation (classified as *clinically relevant*), assessed in n = 92 participants; strength measured by dynamometry (classified as a *surrogate*), assessed in n = 90; and pain on a VAS (classified as *subjective*), assessed

in  $n = 88$ . For each endpoint, we recorded the number of participants with evaluable data (excluding those lost to follow-up) and calculated the proportion using the total study sample size as the denominator: 92/100, 90/100, and 88/100, respectively. Categories not reported by a given study were recorded as 0%.

### Clinically relevant

Clinically relevant outcomes directly reflected improvements in patient function, symptom relief, or quality of life.<sup>7</sup> These outcomes included measures such as grip strength, motor function scores (e.g., British Medical Research Council Scale), validated functional questionnaires (e.g., Constant-Murley Score for shoulder function), and visual analogue scales (VAS) for pain or disability. Only outcomes

that captured meaningful changes in patients' clinical status, rather than surrogate physiological markers or isolated electrophysiological measurements, were classified as clinically relevant.

A total of 673 patients were evaluated for clinically relevant outcomes across the 20 randomized controlled trials included in this meta-analysis. The overall pooled proportion of patients assessed with clinically relevant outcomes was 88.61% (95% CI: 73.64% to 98.22%; PI 11.22% to 100%;  $I^2 = 96.6\%$ ) (Figure 3). A sensitivity analysis using the leave-one-out method revealed no substantial changes in the overall proportion when omitting individual studies (Figure S1).

A meta-regression analysis was conducted to assess whether the year of publication influenced the reporting of clinically relevant outcomes.

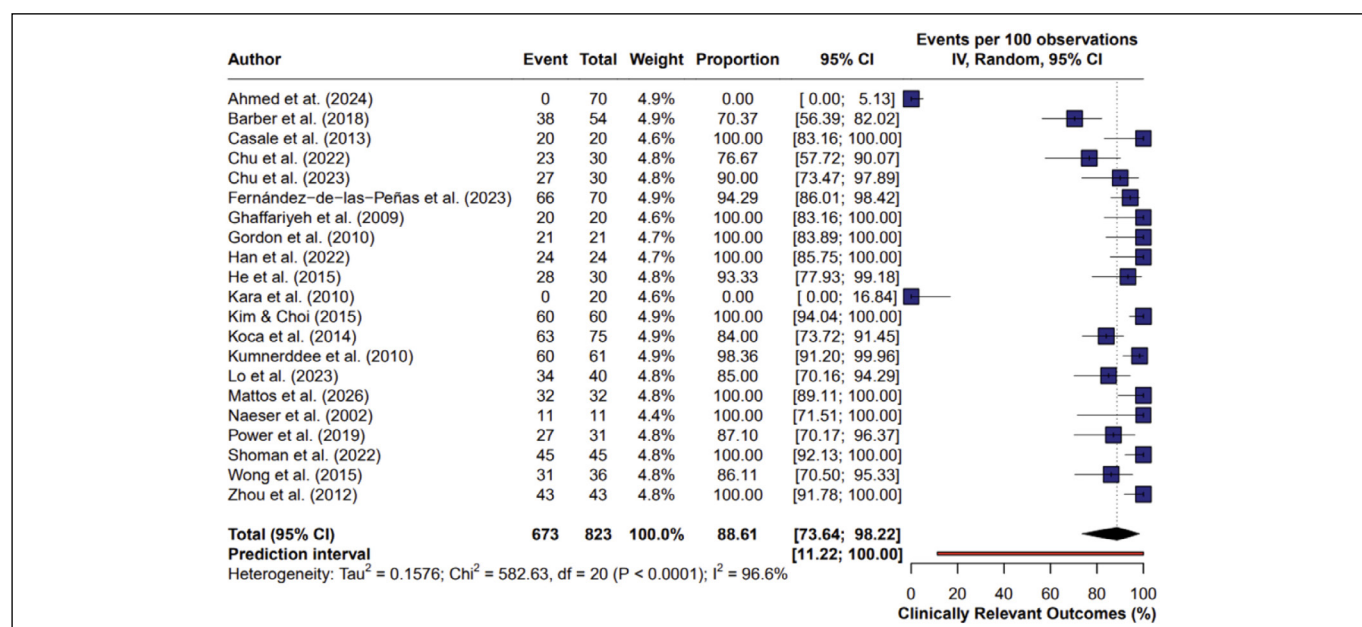


Figure 3. Forest plot of the proportion of patients assessed with clinically relevant outcomes.

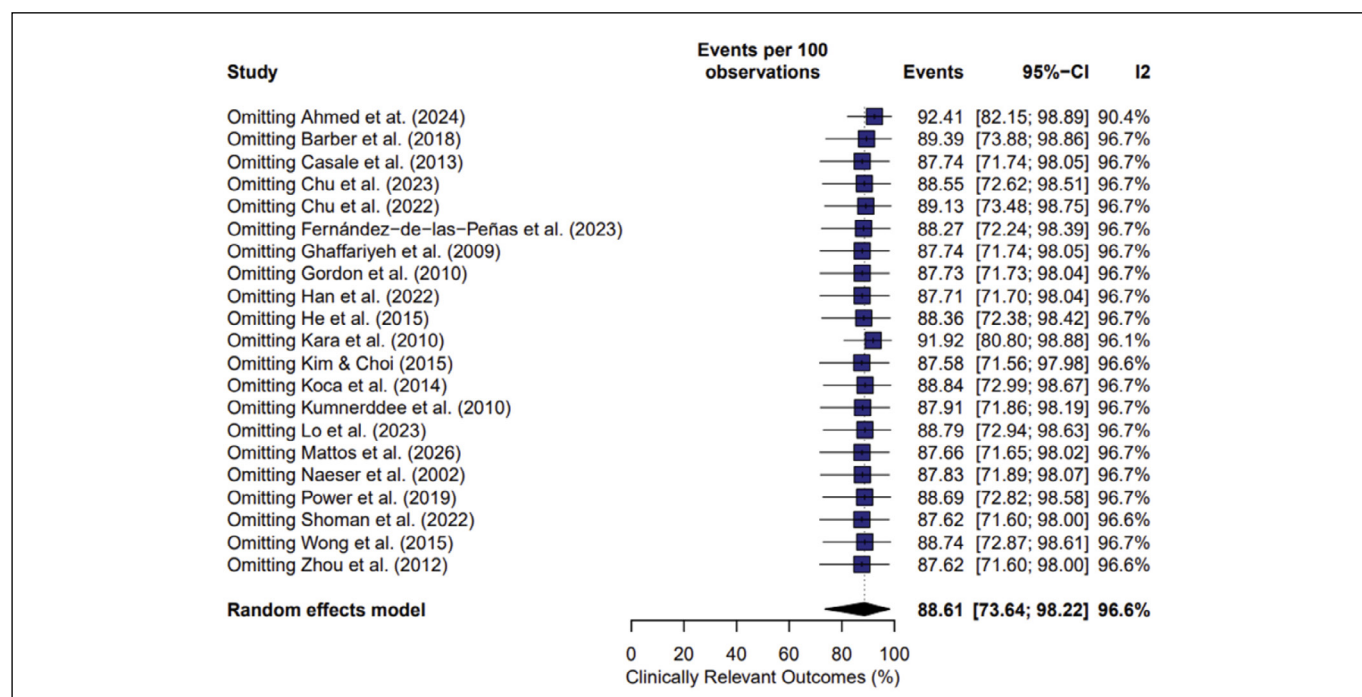


Figure S1. Leave-one-out sensitivity analysis of clinically relevant outcomes.

The results indicated no significant association between publication year and the proportion of clinically relevant outcomes ( $\beta = -0.01$ ,  $p = 0.54$ ) (Table 2; Figure S2). Residual heterogeneity remained high ( $I^2 = 96.21\%$ ,  $p < 0.0001$ ), suggesting that other unmeasured factors may have contributed to the between-study variability.

Surrogate

A total of 443 patients were evaluated for surrogate outcomes across the included randomized controlled trials. The overall pooled

**Table 2.** Meta-regression of the relationship between articles' publication year and clinically relevant outcomes.

|                  | Effect estimates | p-value | I      | Test of residual heterogeneity |
|------------------|------------------|---------|--------|--------------------------------|
| Intercept        | 19.46            | 0.52    | 96.21% | p < 0.0001                     |
| Publication year | -0.01            | 0.54    |        |                                |

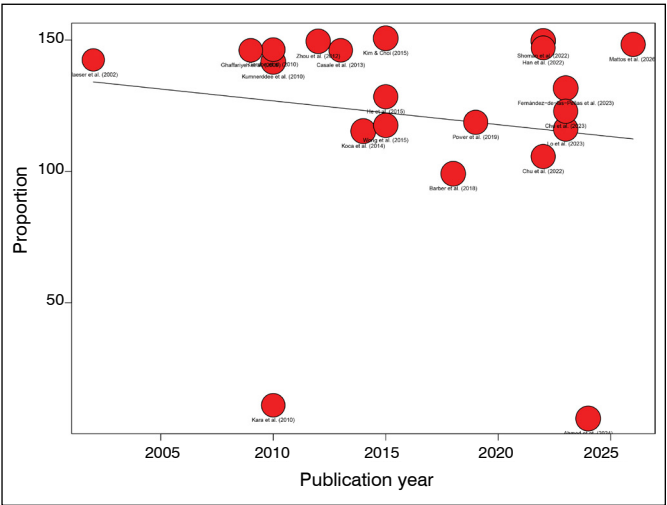


**Figure S2.** Bubble plot (Scatter Plot) illustrating the relationship between the articles' publication year and clinically relevant outcomes.

proportion of patients assessed with surrogate outcomes was 55.02% (95% CI: 29.08% to 79.65%; PI 0% to 100%;  $I^2 = 98.0\%$ ) (Figure 4). A sensitivity analysis using the leave-one-out method revealed no substantial changes in the overall proportion when omitting individual studies (Figure S3).

Subjective

A total of 324 patients were evaluated for subjective outcomes across the included randomized controlled trials. The overall pooled proportion of patients assessed with subjective outcomes was 37.57% (95% CI: 12.09% to 67.17%; PI 0% to 100%;  $I^2 = 98.4\%$ ) (Figure S4). A sensitivity analysis using the leave-one-out method revealed no substantial changes in the overall proportion when omitting individual studies (Figure S5)

Composite

A total of 23 patients were evaluated for composite outcomes across the included studies. The overall pooled proportion of patients assessed with composite outcomes was 0.48% (95% CI: 0.0% to 3.70%; PI 0% to 25.90%;  $I^2 = 82.5\%$ ) (Figure S6). No sensitivity analysis was performed for composite outcomes, as only one study contributed data to this analysis.<sup>31</sup> In that trial, the composite endpoint was the functional median nerve subscore, which combines four indicators (wrist/finger flexor strength, thumb opposition, and sensory function) into a total score (0–16), where higher scores indicate better median nerve function. By integrating motor and sensory domains, it may provide a more comprehensive assessment of functional recovery. However, aggregating distinct components may mask differential changes across domains and hinder identification of the primary driver of the observed result. Consequently, heterogeneity and potential influences from individual studies could not be assessed.

Risk of bias on included studies

The risk of bias judgments by RoB 2 domain are summarized in Figure 5.

Randomization process

Kim et al. (2015)<sup>20</sup> was classified as having a high risk of bias because randomization was based on assignment to different

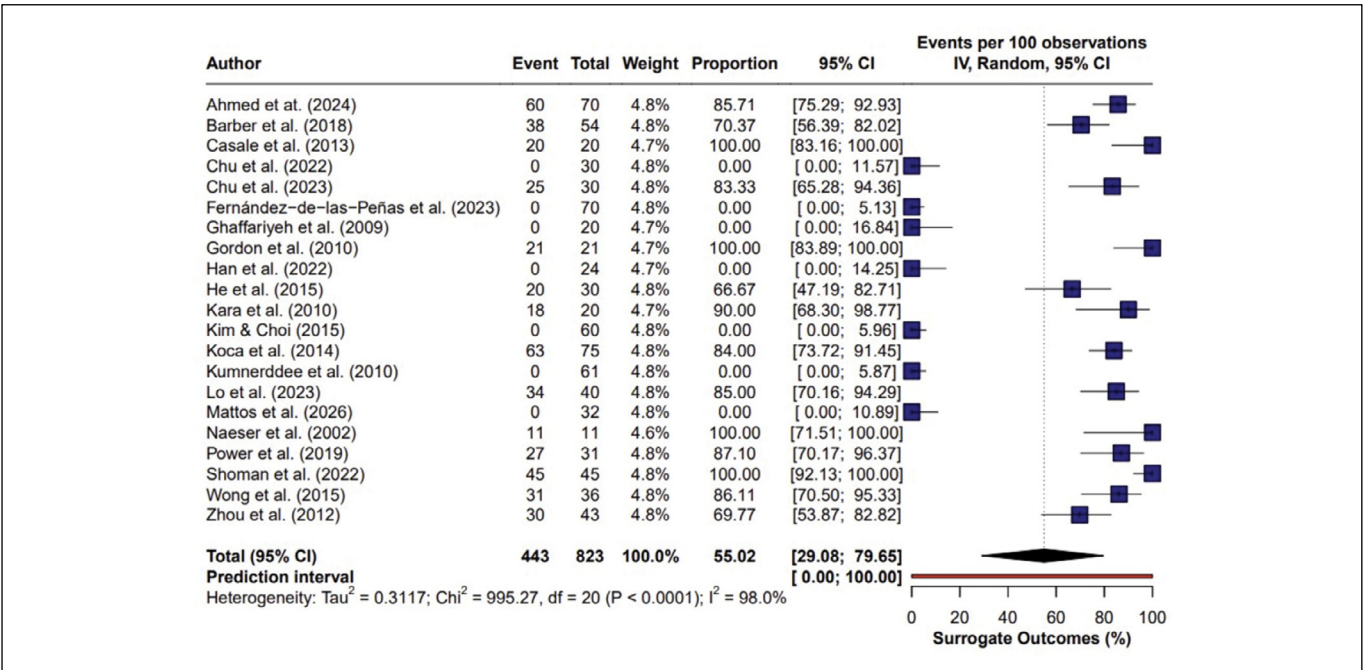


**Figure 4.** Forest plot of the proportion of patients assessed with surrogate outcomes.

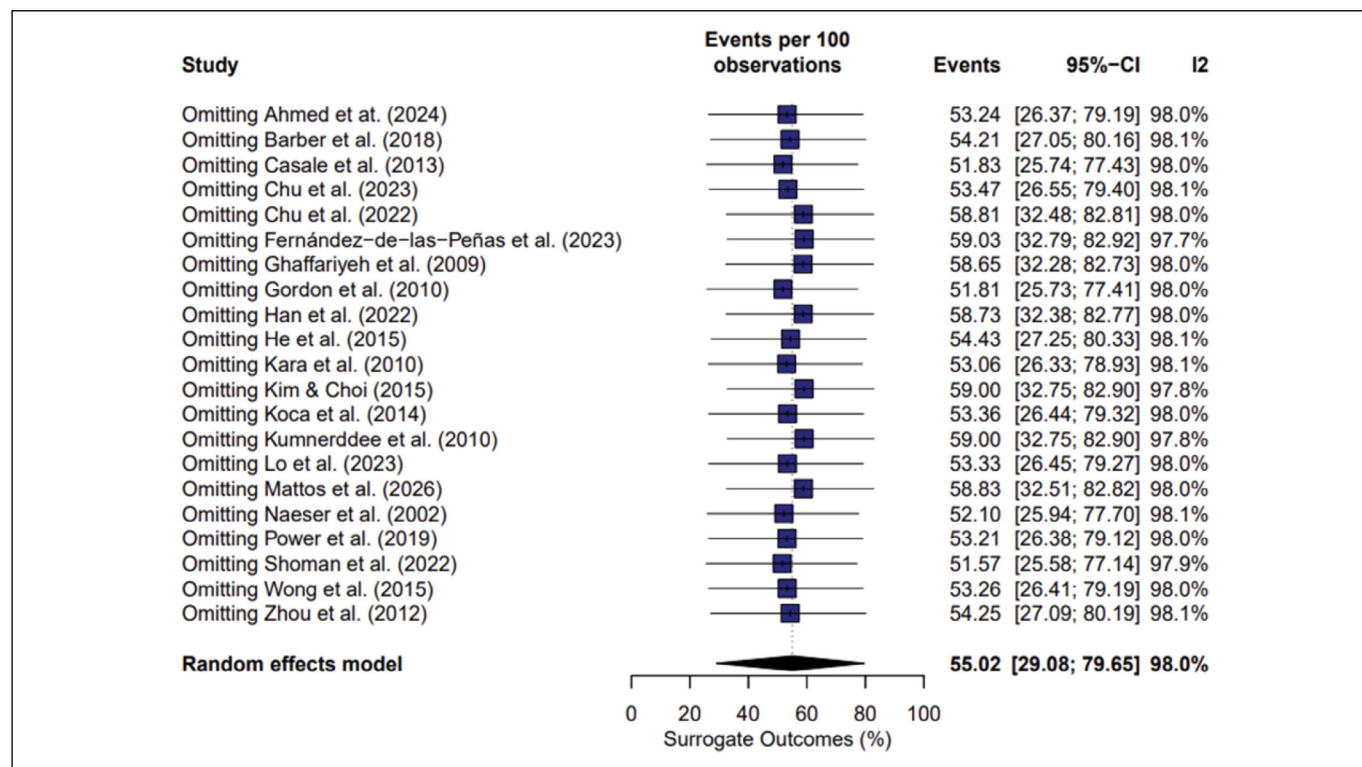


Figure S3. Leave-one-out sensitivity analysis of surrogate outcomes.

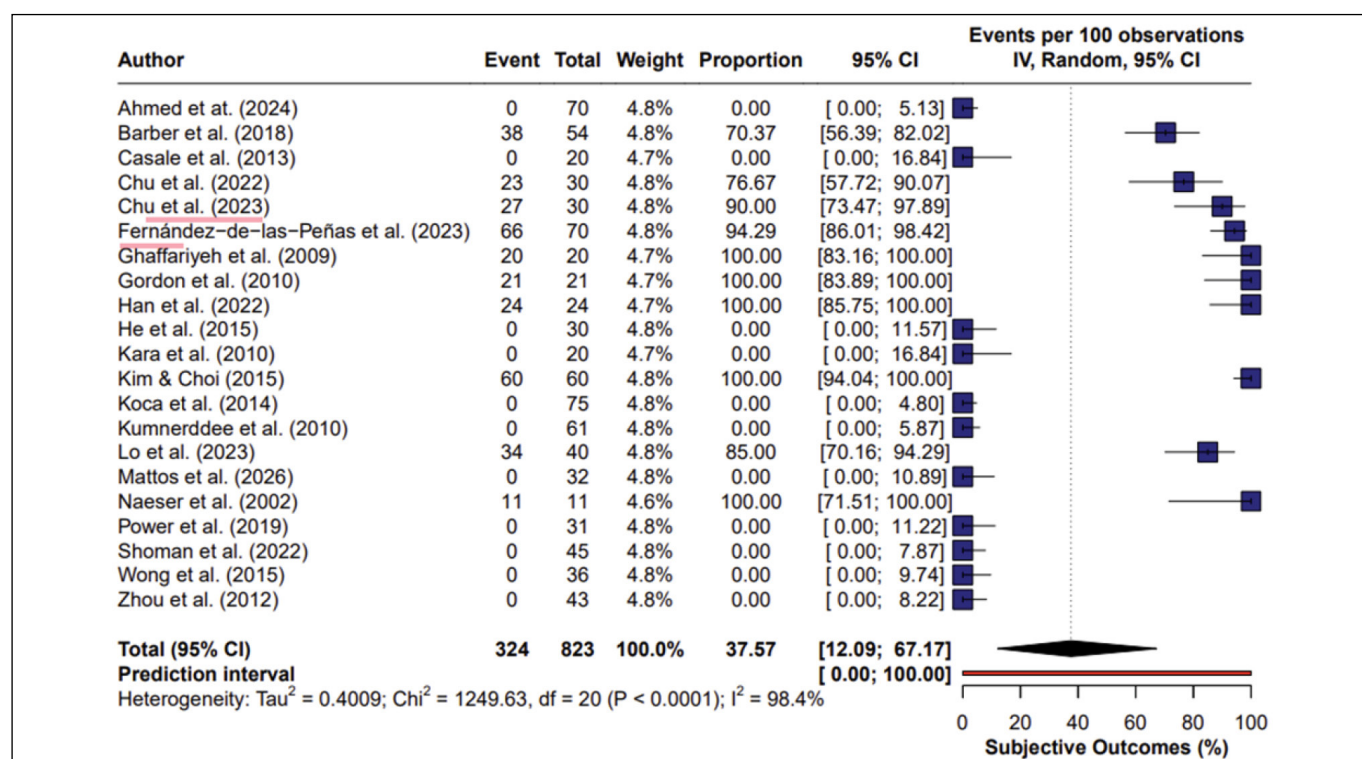


Figure S4. Leave-one-out sensitivity analysis of subjective outcomes.

treating physicians, without adequate allocation concealment or complete control over the randomization process. Koca et al. (2014)<sup>21</sup> was classified as having some concerns due to using a pseudo-randomization method (simple sequential assignment based on the order of clinic entry), although baseline characteristics between groups were comparable.

Additionally, six studies were classified as having some concerns because, although identified as randomized controlled trials (RCTs), they did not provide sufficient details regarding the randomization procedures.<sup>17,19,23,28,34,37</sup> The remaining studies were classified as having a low risk of bias for the randomization process.<sup>18,22,24–27,29,31–33,35,36</sup>

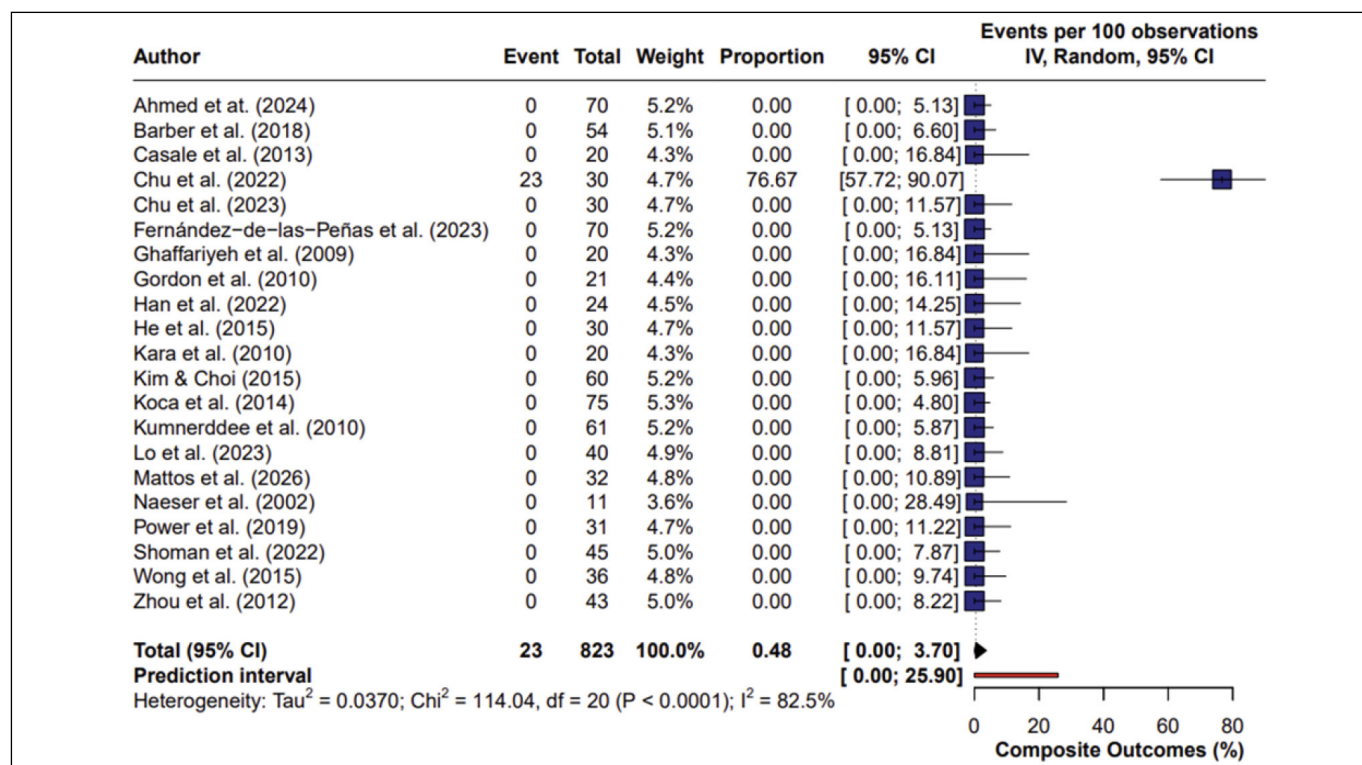


Figure S5. Forest plot of the proportion of patients assessed with composite outcomes.

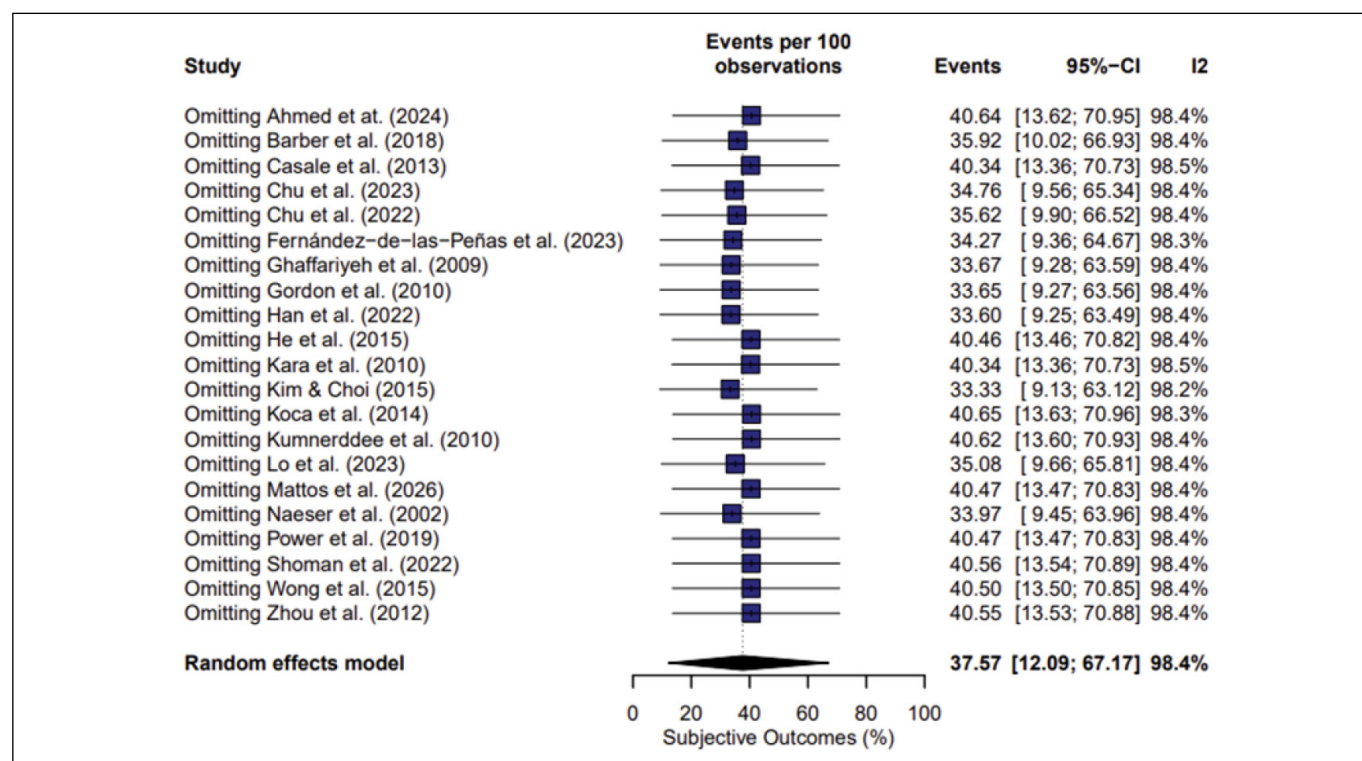


Figure S6. Forest plot of the proportion of patients assessed with composite outcomes.

#### Deviations from intended interventions

Kim et al. (2015)<sup>20</sup> was classified as having a high risk of bias because patients were aware of the additional treatment (electrical stimulator use) and there was no blinding of participants or personnel, leading to a potential risk of performance bias.

Eight studies were classified as having some concerns because they were open-label trials without participant or personnel blinding.<sup>17,22,23,28,30,34,35,37</sup> The remaining studies were classified as having a low risk of bias regarding deviations from intended interventions.<sup>18,19,21,25–27,29,31–33,36</sup>

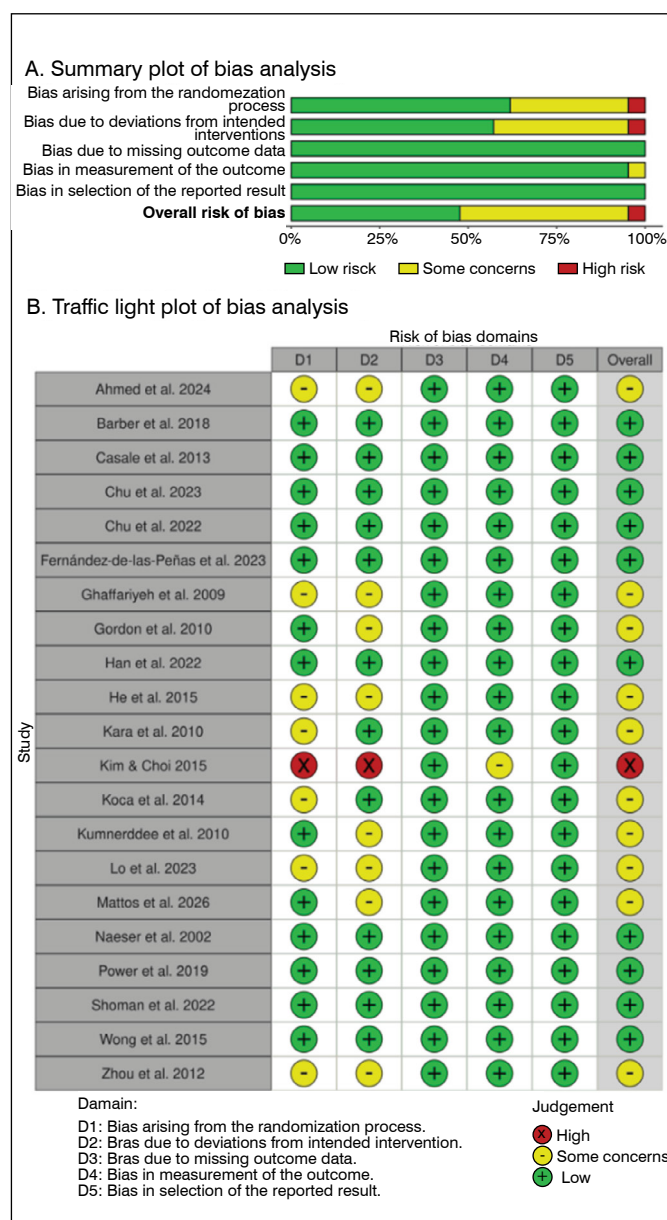


**Figure 5.** Risk of bias on included studies.

## Outcome data and measurement

Kim et al. (2015)<sup>20</sup> was classified as having a low risk of bias for missing outcome data (RoB2 Domain 3) but as having some concerns for outcome measurement (RoB2 Domain 4), as clinical outcomes (HB and SB scales) were assessed without transparent reporting on assessor blinding. All other studies were classified as having a low risk of bias in both missing outcome data and outcome measurement domains.<sup>17–19,21–37</sup>

## Selection of the reported result

All included studies were classified as having a low risk of bias for selective reporting of outcomes.<sup>17–37</sup>

## DISCUSSION

Our meta-analysis suggests that, across RCTs of electrical stimulation for peripheral nerve injuries, most trials assessed at least one clinically relevant outcome. However, estimates varied substantially across studies, consistent with the high between-study

heterogeneity observed in the pooled analyses. In this context, our findings should be interpreted as describing overall patterns of outcome selection rather than implying uniform practice across trials. This aligns with broader efforts to emphasize patient-centred outcomes that better reflect real-world intervention effectiveness.<sup>7,39</sup> The meta-regression analysis performed showed no significant relationship between the proportion of clinically relevant outcomes reported and the year of publication of the included studies. This suggests that the focus on patient-oriented outcomes is not a more recent phenomenon in the field. Although there has been an upward trend in the use of PROs in certain areas of clinical research recently<sup>39–41</sup>, our findings suggest that among studies of electrical stimulation for peripheral nerve injuries, the prioritization of clinically meaningful outcomes has remained consistent over the years covered by this review.

Although surrogate endpoints have several advantages, such as objectivity and expedited data acquisition, it is essential that their validity be based on a strong relationship with important clinical endpoints.<sup>42</sup> Evidence indicates that many surrogate markers are not very predictive of patient benefit for the endpoint that matters, which can result in misjudgments about whether treatments are effective.<sup>7</sup> A review of the FDA found that many of the surrogate outcomes were not consistently correlated with overall survival in oncology trials.<sup>43</sup> Subjective outcomes, including patient-reported measures like pain or satisfaction, are vital for capturing the patient's perspective.<sup>7</sup> Nevertheless, these studies are open to investigator bias, especially in unblinded studies, and findings cannot always be relied on. Research has shown that when blinding is not used in trials evaluating subjective outcomes, it may inflate effect estimates and make careful attention to study design a precondition.<sup>44</sup> Composite outcomes used in clinical trials are intended to improve statistical power by combining several components of an event.<sup>45</sup> However, methodological issues arise when components differ in their clinical significance, or the composite is driven by outcomes of less importance to patients. Literature emphasizes the importance of carefully selecting and validating components of composite endpoints to ensure they collectively reflect meaningful clinical benefits.<sup>46</sup> In our analysis, the minimal use of composite outcomes may reflect a cautious approach, prioritizing clarity and clinical significance in outcome measurement.

Although surrogate and composite endpoints often lack the ability to capture meaningful changes in patients' clinical status, their use should not be dismissed outright. In early-phase trials or proof-of-concept studies, these outcomes can serve a crucial function by offering preliminary evidence about the biological plausibility or potential efficacy of an intervention, thus informing the "pre-test probability" of a given hypothesis under a Bayesian framework.<sup>47,48</sup> This is particularly relevant in trials where clinically meaningful outcomes may require longer follow-up or larger samples, making initial studies with surrogate endpoints more feasible and cost-effective.<sup>7,49</sup> The observed variability in outcome selection highlights the need for outcome standardization in peripheral nerve trials. A consensus-derived core outcome set, focused on a minimum set of patient-important domains and harmonized assessment schedules, would likely improve between-study comparability. Clear prespecification of primary and secondary outcomes, instruments, and follow-up time points in trial registries should accompany such efforts to mitigate outcome switching and improve transparency.

Nonetheless, the goal of clinical research should be to generate evidence that directly improves patient care and quality of life. In this context, RCTs are expected not only to test scientific hypotheses but also to do so using endpoints that are meaningful and actionable in clinical practice.<sup>49</sup> As the highest level of evidence in the hierarchy, RCTs carry the responsibility of selecting outcomes that truly reflect

patient benefit, particularly when guiding therapeutic decisions or informing policy.<sup>6</sup> For instance, if researches are mainly based on electrophysiological improvements without translating them into functional recovery, the clinician could apply therapies that have biological optimism but do not bring any benefit to the patients' independence or quality of life.

As highlighted by Viergever et al.<sup>50</sup>, the global increase in the number of RCTs has not been accompanied by a proportional improvement in their methodological rigor or clinical impact. While RCTs sit at the top of the evidence hierarchy<sup>6</sup>, they are resource-intensive and time-consuming. Many trials, to simplify and cheapen their operations, wind up turning to outcomes that are easier to measure or more likely to be statistically significant, but are potentially confusing as to their clinical relevance.<sup>8,51</sup> This is perhaps practicable, but may undermine the purpose of clinical trials: to create evidence that unequivocally enhances patient care.

Future RCTs investigating electrical stimulation for peripheral nerve injuries should continue to prioritize clinically meaningful endpoints while improving transparency and consistency in outcome selection. Adoption of a COS and explicit trial-registry prespecification of outcomes, instruments, and assessment time points may strengthen interpretability, facilitate evidence synthesis, and better align research with patient needs and clinical decision-making.

### Study limitations

This meta-science review has several limitations that must be acknowledged. First, although efforts were made to classify outcomes rigorously using the framework by Heneghan et al.<sup>7</sup>, some outcome measures involved subjective interpretation, especially in cases where studies did not clearly define primary endpoints or used mixed outcome types. Because participants could contribute to more than one outcome category within a trial, category-specific proportions are not mutually exclusive and should not be interpreted as additive. This approach was intentional and appropriate for our descriptive objective of quantifying how frequently different outcome types were

assessed across trials. Second, several included studies did not stratify data between intervention and control groups or failed to report complete demographic details, which limited the ability to perform subgroup analyses. Third, substantial heterogeneity was observed across all pooled analyses ( $I^2 > 95\%$ ), reflecting marked variability in outcome selection, reporting practices, follow-up completeness, and study populations. While such heterogeneity limits the interpretability of pooled point estimates as precise summary measures, it was expected and inherent to the meta-scientific objective of this review, which aimed to quantify differences in outcome assessment rather than intervention effects. Accordingly, pooled proportions should be interpreted as descriptive indicators of the prevalence of outcome use rather than as definitive summary estimates applicable to individual settings. Finally, classification of some borderline or poorly described instruments inevitably required judgment; to minimize subjectivity, two orthopaedic surgeons independently reviewed classifications, resolved discrepancies by consensus, and verified instrument domains against primary sources when feasible. AI support was restricted to domain identification and did not use study results. Therefore, any residual misclassification is likely to be limited and non-systematic, although it cannot be fully excluded.

### CONCLUSION

This meta-science review revealed that most randomized controlled trials assessing electrical stimulation for peripheral nerve injuries prioritize clinically relevant outcomes, although surrogate and subjective measures remain frequent. To enhance the clinical applicability of future research, upcoming trials should adopt standardized core outcome sets, ensure prospective registration with clearly defined primary outcomes, and routinely report patient-centered measures of functional independence and quality of life. Such practices are essential to align trial design with outcomes that truly matter to patients and to strengthen the translation of evidence into clinical decision-making.

### CONTRIBUTIONS OF THE AUTHORS

Each author made a personal and significant contribution to the development of this article. ESRM: Conceptualization. ESRM, AG: Data Curation. AG, ESRB, CRAJ: Writing – Original Draft. ESRM, AG: Writing – Review & Editing. ESRM, AG, AFB, OPC: Supervision.

### DATA AVAILABILITY DECLARATION

All data generated or analyzed during this study are included in the main text and supplementary materials of the article. No additional source data was used.

### REFERENCES

- Willand MP, Nguyen MA, Borschel GH, Gordon T. Electrical Stimulation to Promote Peripheral Nerve Regeneration. *Neurorehabil Neural Repair*. 2016;30(5):490-6. doi: 10.1177/1545968315604399.
- Mattos E, Guedes A, Lessa PIF, Baptista AF. Influence of surface peripheral electrical stimulation on nerve regeneration after digital nerve neurotomy: study protocol for a randomized clinical trial. *F1000Res*. 2021;10:219. doi: 10.12688/f1000research.42120.2.
- Mattos ESR, Guedes A, Viana MS, Baptista AF. Influence of electrical stimulation on peripheral nerve regeneration: Protocol for a systematic review. *Res Soc Dev*. 2021;10(17):e230101724942. doi: 10.33448/rsd-v10i17.24942.
- Dunlop RLE, Wormald JCR, Jain A. Outcome of surgical repair of adult digital nerve injury: a systematic review. *BMJ Open*. 2019;9(3):e025443. doi: 10.1136/bmjopen-2018-025443.
- Lal D, Hetzler LT, Sharma N, Wurster RD, Marzo SJ, Jones KJ, et al. Electrical stimulation facilitates rat facial nerve recovery from a crush injury. *Otolaryngol Head Neck Surg*. 2008;139(1):68-73. doi: 10.1016/j.otohns.2008.04.030.
- Murad MH, Asi N, Alsawas M, Alahdab F. New evidence pyramid. *Evid Based Med*. 2016;21(4):125-7. doi: 10.1136/ebmed-2016-110401.
- Heneghan C, Goldacre B, Mahtani KR. Why clinical trial outcomes fail to translate into benefits for patients. *Trials*. 2017;18(1):122. doi: 10.1186/s13063-017-1870-2.
- Lonn E. The use of surrogate endpoints in clinical trials: focus on clinical trials in cardiovascular diseases. *Pharmacoeconom Drug Saf*. 2001;10(6):497-508. doi: 10.1002/pds.654.
- Schrijver HM, Gerritsen AAM, Strijers RLM, Uitdehaag BM, Scholten RJ, de Vet HC, et al. Correlating Nerve Conduction Studies and Clinical Outcome Measures on Carpal Tunnel Syndrome: Lessons From a Randomized Controlled Trial. *J Clin Neurophysiol*. 2005;22(3):216-21.
- van de Kar THJ, Jaquet JB, Meulstee J, Molenaar CBH, Schimsheiner RJ, Hovius SER. Clinical Value of Electrodiagnostic Testing Following Repair of Peripheral Nerve Lesions: A Prospective Study. *J Hand Surg Br*. 2002;27(4):345-9. doi: 10.1054/jhsb.2002.0778.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71.
- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4.

13. Higgins JPT, Altman DG, Gotzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. doi: 10.1136/bmj.d5928.
14. Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, et al. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. *BMC Med Res Methodol*. 2021;21(1):189. doi: 10.1186/s12874-021-01381-z.
15. Abdulmajeed J, Chivese T, Doi SAR. Overcoming challenges in prevalence meta-analysis: the case for the Freeman-Tukey transform. *BMC Med Res Methodol*. 2025;25(1):89. doi: 10.1186/s12874-025-02527-z.
16. Higgins JPT, Thompson SG, Spiegelhalter DJ. A Re-Evaluation of Random-Effects Meta-Analysis. *J R Stat Soc Ser A Stat Soc*. 2009;172(1):137-59. doi: 10.1111/j.1467-985x.2008.00552.x.
17. Ahmed BR, Mowafy ZME, Kenawy AM, Khalil ESW. Effect of Neuromuscular Electrical Stimulation Versus Low-Intensity Laser in Relation to Motor Conduction Velocity of the Neuropathic Common Peroneal Nerve Post Burn. *Afr J Biol Sci (Cape Town)*. 2024;6(4):1-9. doi: 10.48047/AFJBS.6.Si4.2024.1551-1559.
18. Barber B, Seikaly H, Ming Chan K, Beaudry R, Rychlik S, Olson J, et al. Intraoperative Brief Electrical Stimulation of the Spinal Accessory Nerve (BEST SPIN) for prevention of shoulder dysfunction after oncologic neck dissection: A double-blinded, randomized controlled trial. *J Otolaryngol Head Neck Surg*. 2018;47(1):7. doi: 10.1186/s40463-017-0244-9.
19. Kara M, Özçakar L, Gökçay D, Özçelik E, Yörübulut M, Güneri S, et al. Quantification of the Effects of Transcutaneous Electrical Nerve Stimulation With Functional Magnetic Resonance Imaging: A Double-Blind Randomized Placebo-Controlled Study. *Arch Phys Med Rehabil*. 2010;91(8):1160-5. doi: 10.1016/j.apmr.2010.04.023.
20. Kim J, Choi JY. The effect of subthreshold continuous electrical stimulation on the facial function of patients with Bell's palsy. *Acta Otolaryngol*. 2016;136(1):100-5. doi: 10.3109/00016489.2015.1083121.
21. Koca I, Boyacı A, Tutoglu A, Ucar M, Kocaturk O. Assessment of the effectiveness of interferential current therapy and TENS in the management of carpal tunnel syndrome: a randomized controlled study. *Rheumatol Int*. 2014;34(12):1639-45. doi: 10.1007/s00296-014-3005-3.
22. Kummerddee W, Kaewtong A. Efficacy of acupuncture versus night splinting for carpal tunnel syndrome: a randomized clinical trial. *J Med Assoc Thai*. 2010;93(12):1463-9.
23. Lo SF, Chou LW, Chung H, Lin HC. Clinical efficacy of electroacupuncture-like magnetic therapy compared to conventional transcutaneous electrical nerve stimulation in individuals with carpal tunnel syndrome. *Sci Rep*. 2023;13(1):20134. doi: 10.1038/s41598-023-46916-0.
24. Naeser MA, Hahn KAK, Lieberman BE, Branco KF. Carpal tunnel syndrome pain treated with low-level laser and microamperes transcutaneous electric nerve stimulation: A controlled study. *Arch Phys Med Rehabil*. 2002;83(7):978-88. doi: 10.1053/apmr.2002.33096.
25. Power HA, Morhart MJ, Olson JL, Chan KM. Postsurgical Electrical Stimulation Enhances Recovery Following Surgery for Severe Cubital Tunnel Syndrome: A Double-Blind Randomized Controlled Trial. *Neurosurgery*. 2020;86(6):769-77. doi: 10.1093/neuros/nyz322.
26. Shoman A, Hassan A, Kassab A. A Study on the Effect of 850 nm Low-Level Diode Laser versus Electrical Stimulation in Facial Nerve Regeneration for Patients with Bell's Palsy. *ORL J Otorhinolaryngol Relat Spec*. 2022;84(5):370-7. doi: 10.1159/000521789.
27. Wong JN, Olson JL, Morhart MJ, Chan KM. Electrical stimulation enhances sensory recovery: A randomized controlled trial. *Ann Neurol*. 2015;77(6):996-1006. doi: 10.1002/ana.24397.
28. Zhou JM, Gu YD, Xu XJ, Zhang SY, Zhao X. Clinical research of comprehensive rehabilitation in treating brachial plexus injury patients. *Chin Med J (Engl)*. 2012;125(14):2516-20.
29. Casale R, Damiani C, Maestri R, Wells CD. Pain and electrophysiological parameters are improved by combined 830-1064 high-intensity LASER in symptomatic carpal tunnel syndrome versus Transcutaneous Electrical Nerve Stimulation. A randomized controlled study. *Eur J Phys Rehabil Med*. 2013;49(2):205-11.
30. Mattos ESR, Guedes A, Zana Y, Lessa PIF, Antunes Júnior CR, Barreto ESR, et al. Effects of transcutaneous electrical stimulation on peripheral nerve regeneration after digital neurotomy: A randomized clinical trial. *F1000Res*. 2026;14:1222. doi: 10.12688/f1000research.169801.3.
31. Chu XL, Song XZ, Li YR, Wu ZR, Li Q, Li Q, et al. An ultrasound-guided percutaneous electrical nerve stimulation regimen devised using finite element modeling promotes functional recovery after median nerve transection. *Neural Regen Res*. 2023;18(3):683-8. doi: 10.4103/1673-5374.350215.
32. Chu X, Song X, Li R, Li Q, Gu X, et al. Multielectrode Array-Based Percutaneous Nerve Stimulation Strategy With Ultrasound Guidance for Ulnar Nerve Injury. *IEEE Trans Neural Syst Rehabil Eng*. 2023;31:1502-10. doi: 10.1109/tnsre.2023.3247164.
33. Fernández-de-las-Peñas C, Ortega-Santiago R, De-la-Llave-Rincón AI, Cleland JA, Pareja JA, Fahandezh-Saddi-Díaz H, et al. Ultrasound-guided percutaneous electrical nerve stimulation versus surgery for women with unilateral carpal tunnel syndrome: A randomized parallel-group trial. *Eur J Pain*. 2023;27(7):860-70. doi: 10.1002/ejp.2117.
34. Ghaffariyeh A, Peyman A, Puyan S, Honarpisheh N, Bagheri B, Peyman M. Evaluation of transcutaneous electrical stimulation to improve recovery from corneal hypoesthesia after LASIK. *Graefes Arch Clin Exp Ophthalmol*. 2009;247(8):1133-8. doi: 10.1007/s00417-009-1079-5.
35. Gordon T, Amirjani N, Edwards DC, Chan KM. Brief post-surgical electrical stimulation accelerates axon regeneration and muscle reinnervation without affecting the functional measures in carpal tunnel syndrome patients. *Exp Neurol*. 2010;223(1):192-202. doi: 10.1016/j.expneurol.2009.09.020.
36. Han G, Lim DH, Yoo YS, Shin EH, Park JY, Kim D, et al. Transcutaneous Electrical Stimulation for the Prevention of Dry Eye Disease after Photorefractive Keratectomy. *Ophthalmol Sci*. 2023;3(2):100242. doi: 10.1016/j.xops.2022.100242.
37. He GH, Ruan JW, Zeng YS, Zhou X, Ding Y, Zhou GH. Improvement in acupoint selection for acupuncture of nerves surrounding the injury site: electroacupuncture with Governor vessel with local meridian acupoints. *Neural Regen Res*. 2015;10(1):128. doi: 10.4103/1673-5374.150720.
38. Lange M, Lee CW, Knisely T, Perla S, Barber K, Kia M. Efficacy of Intravenous Acetaminophen in Length of Stay and Postoperative Pain Control in Laparoscopic Roux-en-Y Gastric Bypass Surgery Patients. *Bariatric Surg Pract Patient Care*. 2018;13(3):103-8. doi: 10.1089/bari.2018.0005.
39. Spece H, Kurtz MA, Piuze NS, Kurtz SM. Patient-reported outcome measures offer little additional value two years after arthroplasty. *Bone Joint J*. 2025;107-B(3):296-307. doi: 10.1302/0301-620x.107b3.bjj-2024-0910.r1.
40. Balitsky AK, Rayner D, Britto J, Lionel AC, Ginsberg L, Cho W, et al. Patient-Reported Outcome Measures in Cancer Care. *JAMA Netw Open*. 2024;7(8):e2424793. doi: 10.1001/jamanetworkopen.2024.24793.
41. Park J, Chang MJ, Kim TW, Lima DD, Kim H, Han HS. Serial changes in patient-reported outcome measures and satisfaction rate during long-term follow-up after total knee arthroplasty: a systematic review and meta-analysis. *Knee Surg Relat Res*. 2024;36(1):43. doi: 10.1186/s43019-024-00241-6.
42. Johnson KR, Freemantle N, Anthony DM, Lassere MND. LDL-cholesterol differences predicted survival benefit in statin trials by the surrogate threshold effect (STE). *J Clin Epidemiol*. 2009;62(3):328-36. doi: 10.1016/j.jclinepi.2008.06.004.
43. Walia A, Haslam A, Prasad V. FDA validation of surrogate endpoints in oncology: 2005-2022. *J Cancer Policy*. 2022;34:100364. doi: 10.1016/j.jcpo.2022.100364.
44. Hróbjartsson A, Gøtzsche PC. Is the Placebo Powerless? *N Engl J Med*. 2001;344(21):1594-602. doi: 10.1056/nejm200105243442106.
45. Pogue J, Devereaux PJ, Thabane L, Yusuf S. Designing and Analyzing Clinical Trials with Composite Outcomes: Consideration of Possible Treatment Differences between the Individual Outcomes. *PLoS One*. 2012;7(4):e34785. doi: 10.1371/journal.pone.0034785.
46. Carneiro AV. Composite outcomes in clinical trials: uses and problems. *Rev Port Cardiol*. 2003;22(10):1253-63.
47. Fleming TR, DeMets DL. Surrogate End Points in Clinical Trials: Are We Being Misled? *Ann Intern Med*. 1996;125(7):605-13. doi: 10.7326/0003-4819-125-7-199610010-00011.
48. Rescorla M. Bayesian modeling of the mind: From norms to neurons. *Wiley Interdiscip Rev Cogn Sci*. 2021;12(1). doi: 10.1002/wcs.1540.
49. Pedrazzi V, Figueiredo FAT, Adami LE, Furlaneto F, Palioto DB, Messoria MR. Surrogate endpoints: when to use and when not to use? A critical appraisal of current evidences. *Braz Oral Res*. 2020;34(Suppl 2):e074. doi: 10.1590/1807-3107bor-2020.vol34.0074.
50. Viergever RF, Li K. Trends in global clinical trial registration: an analysis of numbers of registered clinical trials in different parts of the world from 2004 to 2013. *BMJ Open*. 2015;5(9):e008932. doi: 10.1136/bmjopen-2015-008932.
51. Evans SR. Fundamentals of clinical trial design. *J Exp Stroke Transl Med*. 2010;3(1):19-27. doi: 10.6030/1939-067x-3.1.19.