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ACTA ORTOPÉDICA BRASILEIRA

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(Reviewed April 2022)

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Levels of Evidence for Primary Research Question[a]

(This chart was adapted from material published by the Centre for Evidence-Based Medicine, Oxford, UK. For more information, please visit www.cebm.net.)

	Types of study			
Level	**Therapeutic Studies Investigating the Results of Treatment**	**Prognostic Studies – Investigating the Effect of a Patient Characteristic on the Outcome of Disease**	**Diagnostic Studies – Investigating a Diagnostic Test**	**Economic and Decision Analyses – Developing an Economic or Decision Model**
I	High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals	High quality prospective study[d] (all patients were enrolled at the same point in their disease with ≥80% of enrolled patients)	Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses
	Systematic review[b] of Level RCTs (and study results were homogenous[c])	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies
II	Lesser quality RCT (eg, < 80% followup, no blinding, or improper randomization)	Retrospective[f] study	Development of diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses
	Prospective[d] comparative study[e]	Untreated controls from an RCT	Systematic review[b] of Level II studies	Systematic review[b] of Level II studies
	Systematic review[b] of Level II studies or Level I studies with inconsis tent results	Lesser quality prospective study (eg, patients enrolled at different points in their disease or <80% followup)		
		Systematic review[b] of Level II studies		
III	Case control study[g]	Case control study[g]	Study of non consecutive patients; without consistently applied reference ''gold'' standard	Analyses based on limited alternatives and costs; and poor estimates
	Retrospective[f] comparative study[e]		Systematic review[b] of Level III studies	Systematic review[b] of Level III studies
	Systematic review[b] of Level III studies		Case-control study	
			Poor reference standard	
IV	Case series[h]	Case series		Analyses with no sensitivity analyses
V	Expert opinion	Expert opinion	Expert opinion	Expert opinion

[a] A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.
[b] A combination of results from two or more prior studies.
[c] Studies provided consistent results.
[d] Study was started before the first patient enrolled.
[e] Patients treated one way (eg, cemented hip arthroplasty) compared with a group of patients treated in another way (eg, uncemented hip arthroplasty) at the same institution.
[f] The study was started after the first patient enrolled.
[g] Patients identified for the study based on their outcome, called "cases" eg, failed total arthroplasty, are compared with patients who did not have outcome, called ''controls'' eg, successful total hip arthroplasty.
[h] Patients treated one way with no comparison group of patients treated in another way.

SUMMARY

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THE RELATIONSHIP BETWEEN FRACTURES IN PEDIATRIC POLYTRAUMA PATIENTS: EVALUATION OF CLINICAL OUTCOMES

RELAÇÃO DAS FRATURAS NO PACIENTE POLITRAUMATIZADO PEDIÁTRICO: AVALIAÇÃO DE DESFECHOS CLÍNICOS

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ABSTRACT

Objective: To evaluate children and adolescents with polytrauma and fractures of the pelvis and proximal and diaphyseal femur and correlate the impact of these conditions and clinical outcomes. Methods: Retrospective study carried out in a public hospital in Taboão da Serra (SP), with pediatric patients with polytrauma from January 2012 to December 2021. In total, 44 patients were evaluated, 70.44% boys and 29.55% girls, aged from 12 to 17 years. Results: Diaphyseal fracture of the femur affected 70.44% of the patients, mainly caused by a fall from a height (56.81%). Linear external fixation was the most used treatment (45.45%). All patients were discharged from hospital. Conclusion: We found essential sociodemographic information: 84.11% of patients did not have associated injuries; 88.63% were hospitalized from 3 to 11 days; 90.91% did not need to be admitted to an ICU, 77.27% did not need reoperation, and 22.73% underwent another surgery; 45.45% used the external fixator to stabilize injuries; 11.36% converted the external fixator to the intramedullary nail; 9.09% needed an intramedullary nail remover; 2.27% converted to a plate (bilateral) and 2.27% to a rigid nail; 2.27% had loss of reduction and revision with rod; 2.27% underwent corrective osteotomy; 2.27% had clinical hospitalization; 2.27% had osteonecrosis of the femoral head and screws removed; 2.27% removed the plate. No deaths were recorded. ***Level of Evidence II, Retrospective Study.***

Keywords: Child. Child, Hospitalized. Child Mortality. Femoral Fractures. Pelvis. Pelvic Bones.

RESUMO

Objetivo: Avaliar crianças e adolescentes politraumatizados com fraturas da pelve, proximal e diafisária do fêmur e correlacionar o impacto dessas condições e desfechos clínicos. Métodos: Estudo retrospectivo realizado em hospital público de Taboão da Serra (SP), com pacientes pediátricos politraumatizados entre janeiro de 2012 e dezembro de 2021. Avaliaram-se 44 pacientes, 70,44% meninos e 29,55% meninas, de 12 a 17 anos. Resultados: A fratura diafisária fechada do fêmur acometeu 70,44%, sendo causada principalmente por queda de altura (56,81%). A fixação externa linear foi o tratamento mais utilizado (45,45%). Todos os pacientes receberam alta hospitalar. Conclusão: Identificaram-se importantes informações sociodemográficas: 84,11% dos pacientes não apresentaram lesões associadas; 88,63% ficaram internados de 3 a 11 dias; 90,91% não necessitaram de internação em unidade de terapia intensiva (UTI), 77,27% não precisaram ser reoperados; 22,73% realizaram nova cirurgia; 45,45% utilizaram fixador externo para estabilização de lesões;11,36% converteram o fixador externo para a haste intramedular; 9,09% precisaram remover as hastes intramedulares; 2,27% converteram para placa (bilateral) e 2,27% para haste rígida; 2,27% tiveram perda de redução e revisão com haste; 2,27% realizaram osteotomia corretiva; 2,27% tiveram internação clínica; 2,27% tiveram osteonecrose da cabeça femoral e parafusos removidos; e 2,27% retiraram a placa. Não foram observados óbitos. ***Nível de Evidência II, Estudo Retrospectivo.***

Descritores: *Criança. Criança Hospitalizada. Mortalidade da Criança. Fraturas do Fêmur. Pelve. Ossos Pélvicos.*

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INTRODUCTION

Trauma is characterized by structural changes or physiological imbalances resulting from acute exposure to various forms of kinetic energy.[1] In immature skeleton, trauma injury is the leading cause of death worldwide, significantly hindering children's development.[2] According to the Committee on Trauma of the American College of Surgeons, at least 25% of all patients involved with trauma are children.[3] The countries of Southeast Asia and the Western Pacific have the highest mortality rates from pediatric trauma worldwide.[4] In Brazil, studies that stand out describing the epidemiology,

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prevalence, and potential risk factors in childhood and adolescent polytraumatism are scarce.[1]

Regarding the Brazilian population, the characteristics particular to children, as its proportions, shapes, size, volume, volume of the organs, among other peculiar ones, may increase or decrease the risk of trauma injuries.[5] Other characteristics inherent to the child should also be valued such as sex, age group, region of trauma and manner in which they occurred, especially regarding neglect and child abuse.[2]

Notably, the severity of the injury, reflected by the Injury Severity Score (ISS), is estimated based on the Abbreviated Injury Scale (AIS) and considers the three regions of the body most severely injured. Regarding the ISS, 'multiple injury occurs when its coefficient results in a value $\geq$ 16.[6,7]

The incidence of fractures of the pelvic bones in the immature skeleton varies from 2.4 to 7.5% in the reference services for trauma.[4] Although this lesion presents a low frequency, they result from accidents with high kinetic energy and represent 5% of all admissions to hospital facilities. They are also highly associated with multisystem impairments determined by a high severity score (ISS).[8,9]

The efficient and early evaluation and management of these disorders are essential to improve the evolution of patients, determining the best clinical outcomes. This would reduce the length of hospital stay, sequelae, mortality rate, inherent socioeconomic problems, and treatment costs.

Physical examination, as well as imaging techniques—such as plain radiography, ultrasonography, and computed tomography—are crucial for the early diagnoses of the individual with trauma. Moreover, laboratory analyses are essential adjunctive tools for monitoring pediatric lesions. The alteration of inflammatory markers correlates directly with post-traumatic complications, including the recognition of multiple organ failure of the human body.[1]

The seriously injured child requires interdisciplinary intervention. Although many sources of clinical information, laboratory and imaging markers can be found, the lack of prospective controlled studies concomitantly using these resources prevents the creation of safe and applicable guidelines for pediatric trauma.

Several laboratory markers have recently been described to support the early diagnosis and prognosis of severely injured children. The concomitant application of imaging techniques is essential and combining these techniques with laboratory biomarkers has reliable prognostic value and can improve the evaluation of pediatric lesions after trauma. Specific inflammatory markers may be relevant for multiple organ evaluation, especially in post-traumatic complications. Lactate concentration, blood coagulation parameters, and specific markers of organ damage are crucial clinical tools in the early identification of trauma-induced disorders.

Severe trauma is the most common cause of mortality in children whom the most frequently injured structures are the head and the chest, followed by the extremities and abdomen. The former regions are associated with a high socioeconomic burden. The efficient and early evaluation and management of these lesions are essential for better evolution of patients.

Due to the continuous efforts and studies conducted on trauma care, the rate of infant mortality and disability significantly decreased. Regarding etiology, accidents involving high kinetic energy such as road traffic injuries are the main cause of mortality and disability worldwide.

This study aimed to evaluate the clinical outcome regarding the risk of death in patients with pediatric polytrauma with fractures of the pelvis and/or femur. Furthermore, this study evaluated the length of hospital stay, need for ICU admission, and treatment methods used.

METHODS

The project of this study was initially submitted to the Research Ethics Committee of the Universidade Federal de São Paulo (UNIFESP) by the Plataforma Brasil, for the evaluation and request for exemption from the informed consent form, and was approved for implementation under CAAE number 5,612,632.

A quantitative, cross-sectional, retrospective, and documentary study was performed by descriptively analyzing the data collected. The study was conducted at the Hospital of Pirajussara, inaugurated in 1999. The hospital is a reference for about 570,187 people who live in the region, which comprises the municipalities of Embu das Artes and Taboão da Serra, in the state of São Paulo. Moreover, the hospital interacts with the Municipal Health Systems in line with the principles of universality, regionalization, and hierarchization of the Brazilian Unified Health System (SUS). All traumatic injuries of children and adolescents from these regions that require orthopedic evaluation with hospitalization and treatment are referred to the hospital.

The target population of this study consisted of all pediatric patients diagnosed with polytrauma who also had proximal femur fractures, diaphyseal femur fractures, and/or pelvic ring fractures. The study period was from January 2012 to December 2021.

After the analysis of the entire database of the hospital, a sample of 44 patients was obtained. In total, 31 (70.45%) were male and 13 (29.55%) female. When analyzing participants' ages, 11 (25.00%) individuals were aged from 1 to 7 years, 5 (11.36%) aged from 8 to 11 years, and 28 (63.64%) aged from 12 to 17 years (Tables 1 and 2). To identify the municipalities of origin of the patients, the Quantum Gis geoprocessing program (QGis) was used. QGis is a free tool licensed by General Public License (GNU), based on a Geographic Information System that allows for the creation of maps. Therefore, 22 (50.00%) participants came from Embu das Artes and 22 (50.00%) from Taboão da Serra (Table 3).

Table 1. Distribution of patients according to sex.

Sex	Patients	Percentage (%)
Male	31	70.45
Female	13	29.55
Total	44	100.00

Table 2. Distribution of patients according to age groups

Age	Patients	Percentage (%)
0–7	11	25.00
8–11	5	11.36
12–17	28	63.64

Table 3. Distribution of patients according to origin.

Origin	Patients	Percentage (%)
Embu das Artes, SP	22	50.00
Taboão da Serra, SP	22	50.00
Total	44	100.00

Data collection was based on the analysis of medical records, adding the information to a form to compile the information pertinent to this study and organizing it in Microsoft Excel spreadsheets. Subsequently, the information was exported to the Statistic Package for Social Sciences (SPSS) statistical software program version 24.0 for descriptive and inferential statistical analysis. In this study, the data were organized in 1 $\times$ c contingency tables, based on absolute and relative frequencies. Pearson's nonparametric chi-square test was used to evaluate the trend between nominal variables. A 5% significance level was used in all tests ($p < 0.05$).

<< SUMÁRIO

RESULTS

Table 4 shows the distribution of types of fracture found in our study, considering the number of patients and the percentage. Table 5 shows the mechanism of injury in our sample. Table 6 shows the distribution of patients with polytrauma and the specific types of treatment patients with polytrauma received.

Table 4. Distribution of fractures of patients with polytrauma in our study.

Type of fracture	Number	Percentage (%)
Diaphyseal fracture of the left femur	17	38.63
Diaphyseal fracture of the right femur	14	31.81
Subtrochanteric fracture of the right femur	3	6.82
Femoral neck fracture	2	4.55
Bilateral diaphyseal fracture of the femur	2	4.54
Open diaphyseal fracture of the right femur	2	4.55
Subtrochanteric fracture of the right femur	1	2.27
Fracture of the neck of the right femur + diaphyseal fracture of the right femur	1	2.27
Left femur diaphyseal fracture + iliac fracture	1	2.27
Total	44	100.00

Table 5. Distribution of injury mechanisms of patients with polytrauma in our study.

Fracture mechanism	Number	Percentage (%)
Fall from height	25	56.81
Vehicle collision	6	13.64
Run over	6	13.64
Motorcycle fall	2	4.55
Firearm projectile + run over	2	4.55
Aggression	1	2.27
Firearm projectile	1	2.27
Bicycle fall	1	2.27
Total	44	100.00

Table 6. Distribution of specific types of fracture treatment of patients with polytrauma in our study.

Treatment of fractures	Number	Percentage (%)
Linear external fastener	20	45.45
Locked intramedullary rod	9	20.45
Osteosynthesis with plate	7	15.91
In situ pinning with 2 cannulated screws of 7 mm	3	6.82
Flexible rod	3	6.82
Circular external fixator	1	2.27
Skeletal traction	1	2.27
Total	44	100.00

Table 7 shows patients' hospital length of stay, considering the intervals: up to 3 days, from 4 to 10 days, and from 11 to 17 days, with a minimum period of 3 days and a maximum of 17 days. Of these, 20 (45.45%) participants remained hospitalized from 4 to 10 days, 19 (43.18%) for up to 3 days, and 5 (11.36%) from 11 to 17 days. Of all patients, 40 (90.91%) did not need to remain hospitalized in the Intensive Care Unit (ICU), and 4 (9.08%) did (Table 8).

Table 9 shows that 36 patients (81.81%) had no other lesions, while eight (15.89%) did not (extradural hematoma + pneumomediastinum, pneumothorax + pneumocephalus, hemosinus + severe head trauma, hemopneumothorax, severe head trauma, pulmonary contusion + hemorrhagic shock, extradural hematoma, hemothorax).

Table 7. Distribution of the 44 patients according to length of hospital stay.

LENGTH OF HOSPITAL STAY	Number	Percentage (%)
Up to 3 days	19	43.18
From 4 to 10 days	20	45.45
From 11 to 17 days	5	11.36

Table 8. Distribution of the 44 patients according to admission to the ICU.

ICU ADMISSION	Number	Percentage (%)
NO	40	90.91
YES (7 DAYS)	1	2.27
YES (6 DAYS)	1	2.27
YES (4 DAYS)	1	2.27
YES (2 DAYS)	1	2.27

ICU: intensive care unit.

Table 9. Distribution of the 44 patients according to the associated lesions.

ASSOCIATED INJURIES	Number	Percentage (%)
No	37	84.11
Extradural hematoma + pneumomediastinum	1	2.27
Pneumothorax + pneumocranium	1	2.27
Hemosinus + severe head trauma	1	2.27
Hemopneumothorax	1	2.27
Severe head trauma	1	2.27
Pulmonary contusion + hemorrhagic shock	1	2.27
Extradural hematoma	1	2.27
Hemothorax	1	2.27

Table 10 shows the 44 patients according to the main outcomes. Of these, 34 (77.27%) did not need to be reoperated while 10 (22.73%) were surgically treated again. Regarding patients with femoral diaphyseal fracture, 12 (27.29%) used an external fixator to stabilize their lesions and all implants were removed during treatment; 5 (11.36%) had the conversion of the external fixator to intramedullary rod; 4 (9.09%) needed to remove the intramedullary rods; one (2.27%) required conversion to plate (bilateral); one (2.27%) had conversion to rigid rod; one (2.27%) had loss of reduction and revision with rod; one (2.27%) had to remove the fixator and an osteotomy was performed; one (2.27%) had a clinical hospitalization; one (2.27%) had osteonecrosis of the femoral head and the screws had to be removed; one (2.27%) had to remove the plate. No deaths were recorded when considering the treatments performed and the associated lesions.

Table 10. Distribution of the 44 patients according to the main outcomes.

OUTCOME	Number	Percentage (%)
No reoperation	34	77.27
Removal of the external fastener	20	45.45
Conversion to rod	5	11.36
Rod removal	4	9.09
Removal of plate	1	2.27
Conversion to rigid rod	1	2.27
Conversion to plate (bilateral)	1	2.27
Removal of the external fastener	1	2.27
Loss of reduction and revision with rod	1	2.27
Osteonecrosis of the femoral head	1	2.27
Clinical admission	1	2.27
Mortality	0	0.00

DISCUSSION

In our study, most trauma cases involved children aged from 12 to 14 years, most commonly presenting falls from heights and automobile accidents as injury mechanisms, similar to other studies in the literature.[10-12]

This etiological factor is significantly high in developing countries, as children are more exposed to this risk. We emphasize that a large circulation of vehicles, in association with a reduced socioeconomic condition, absence of education in traffic safety, and the lack of available safety equipment aggravate these risks to the population.[11,12]

The predominance of accidents involving males can be culturally justified by the activities performed by them that involve high speed, force, body impact. Thus, males are significantly more exposed to this type of accidents.

A study that aimed to evaluate the profile of pediatric hospitalizations due to external causes reported that 73% of the victims were male. Moreover, the study showed that the largest number of cases (32%) occurred in individuals aged from 10 to 12 years, followed by those aged from 4 to 6 and 7 to 9 years.[13] These findings are similar to those obtained in our study.

The primary objective of our study was to evaluate the clinical and surgical outcomes of patients diagnosed with polytrauma associated with severe fractures of the locomotor system (femur and pelvis).

We obtained essential information regarding our sample's characteristic. According to our findings, all patients were discharged from hospital. Furthermore, the most common type of fracture was the closed diaphyseal of the femur in 31 (70.44%) patients. The polytrauma correlation associated with fracture of the pelvis, proximal femur, and femoral diaphyseal showed that 37 (84.11%) patients had no associated lesions. Regarding the most common fracture mechanism, we found 25 (56.81%) falls from height, 6 (13.64%) vehicle collisions, and 6 (13.64%) run overs. Considering the length of hospital stay, 19 (43.18%) patients stayed for the minimum period of 3 days, 20 (45.45%) patients from 4 to 10 days. In total, 40 (90.91%) patients did not need to be admitted to the ICU.

Femoral diaphyseal fractures represent 1.5% of all injuries involving the immature locomotor system[14] and are related to vehicle collisions and sports accidents. These fractures require prolonged treatment in the hospital and most often surgical intervention, which socioeconomically affects the lives of children and their families.[15]

The early surgical stabilization of these fractures, in the first days after the injury, reduces the length of hospitalization and the length of ICU stay. Moreover, the surgery decreases the time required for assisted ventilation and significantly decreases the rate of complications. In this study, most patients received early surgical intervention, with a clear short time between hospitalization, treatment, and discharge, as the literature recommends.

Among many treatments available for femoral diaphyseal fractures, the evolution of implantable devices such as the use of the flexible intramedullary rod and the use of external fixators and plates and screws is remarkable.[16,17] In our casuistry, these implants were used.

Pelvic injuries in children, although unusual, result from high-energy trauma and are associated with severe multisystem injuries and high mortality rates. Few fractures are treated surgically, as most of them do not compromise the biomechanical stability of the pelvis. By improving knowledge about the repercussions of trauma to the pelvis of children and adolescents, many advances in minimally invasive surgical techniques have improved comfort, reducing complications. In our casuistry, we found only one (2.27%) patient with pelvic injury, who had an isolated and stable fracture of the iliac that did not provide anatomical, biomechanical, or hemodynamic alteration.

Polytrauma is the leading cause of mortality in adolescents and children. Smaller stature and lower body weight are determinants for the severity of the injury in children. The pattern of injury in polytrauma among children is directly dependent on age. Until school-age traumatic brain injury (TBI) is the most common injury. The extremities, chest, and abdomen are more frequently affected in older children in which, particularly thoracic and cranial trauma, are considered essential predictive factors to determine the outcomes of these patients with polytrauma.

Due to these differences in anatomy and physiology, pediatric patients with polytrauma require early diagnoses adjusted for age-specific variations. The first hour after the injury is considered the most critical in the care of polytrauma and directly determines the mortality rates. The first medical action is the evaluation whether the trauma is life-threatening or not. Then, the general picture of the patient must be stabilized.

Early estimation of the severity of the injury and the location of the affected organs is supported by the use of specific diagnostic imaging tools, including radiography, computed tomography, and whole-body ultrasound.

Markers for organ injury for severe trauma often point to involvement of the locomotor apparatus as well as internal organs. The early post-trauma inflammatory response induces secondary organ damage. Furthermore, organ damage is characterized by systemic elevation of specific biomarkers, such as in the heart, kidneys, and liver, where several well-established laboratory biomarkers determine their impairment. However, brain, lung, and splenic lesions are diagnosed by advanced imaging techniques.

Head trauma is the leading cause of mortality among adolescents and children. For pediatric management, neuroimaging is used to improve the child's clinical care. To properly estimate brain injury, CT and MRI scans are used to immediately detect hemorrhage, acute hydrocephalus, fractures, and other intraparenchymal intracranial lesions. Other than neuroimaging techniques, plasma biomarkers can be a reliable tool for the clinical evaluation of pediatric TBI.

Many laboratory markers have recently been described to support the early diagnosis and prognosis of severely injured children. However, the combination of imaging techniques and a reliable prognostic laboratory biomarker can improve the rapid and adequate assessment of pediatric injuries after trauma and improve the outcome of children with polytraumatism.

Despite the higher frequency of TBI in children, compared to orthopedic injuries in adults, the ability to recover from central nervous system injuries is much greater. The movement in the fracture focus of a long bone increases intracranial pressure, which makes it necessary to early stabilize the fracture focus, determining the use of immediate internal or external osteosynthesis, facilitating care and patient transportation. Bone instability keeps the patient immobile and interferes with the care of comorbidities and brain, thoracic, and abdominal traumas. This instability also limits the intensive care of the nursing and physical therapy service.

The direct costs of pediatric trauma exceed eight billion dollars. This estimative considers only the direct costs with the approach to pediatric patients with polytrauma, since the indirect costs that affect families and society cannot be estimated. In Brazil, according to DATASUS, the total expenditure in 2005 for the clinical surgical specialty was approximately three billion reais, which shows the economic contrast for health in our country.

Regarding patients who required hospitalization, the average amount paid per hospital stay, according to data from 2015, was $ 562.00 for the Southeast region. Considering the total number of patients,

although 19 of them had length of stay equal to or less than 3 days, 20 (45.45%) from 4 to 10 days, and 5 (11.36%) from 11 to 17 days. Considering the estimated daily value of a ward hospitalization as $ 206.87 reais, the average cost of the hospitalization period ranged from 827.48 to $ 2068.70. Regarding the costs of ICU hospitalization, the final cost is even higher. Although only four patients were admitted to an ICU, ranging from 2 to 7 days, the daily value of ICU hospitalization was estimated at $ 656.71. Thus, the values required by patients during their ICU stays ranged from 1313.42 to $ 4596.97. Thus, these values make patients with polytrauma hospitalization much more expensive.

Determining indicators in polytrauma allows for the application of prevention measures by continuing education. The orthopedist participates both in the diagnosis and in the treatment, as well as disseminating this information. The implementation of an efficient system of awareness and preventive education of the population, related to safety, based on the results of the epidemiological studies carried out, should be considered essential. Notably, based on the main trauma mechanisms found in our study, we emphasize the relevance of traffic education, the mandatory use of seat belts, the transport of young children with special vehicular devices, the transport of children in the rear seat, the mandatory use of protective helmets when traveling with a motorcycle, the use of protective items such as gloves and knee pads when riding a bicycle or skateboard, the supervision of adults, among other measures.[18] There is a need to maximize efforts in trauma prevention and improve primary care and health care services by providing high-quality trauma care.

Our study has many limitations since it was conducted in a single medical center and is retrospective. However, over 10 years, all records of patients with polytrauma associated with severe fractures were obtained, which could have determined an unfavorable outcome increasing the mortality rate.

CONCLUSION

In total, 34 (77.27%) patients did not need to be reoperated; 10 (22.73%) underwent a new surgical approach. Regarding the patients with femoral diaphyseal fracture, 20 (45.45%) used an external fixator to stabilize their lesions and all implants were removed during the treatment; five (11.36%) had the conversion of the external fixator to intramedullary rod; four (9.09%) needed to remove the intramedullary rods; one (2.27%) required conversion to plate (bilateral); one (2.27%) had conversion to rigid rod; one (2.27%) had loss of reduction and revision with rod; one (2.27%) had to remove the fixator with and perform an osteotomy; one (2.27%) had a clinical hospitalization; 1 (2.27%) had osteonecrosis of the femoral head and the screws had to be removed; one (2.27%) had to remove the plate.

No deaths were recorded when considering the treatments performed and the associated lesions.

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THE USE OF ADHESIVE RADIOPAQUE GRIDS IN GENICULAR NERVE BLOCK BY RADIOSCOPY

O USO DE MÁSCARA LOCALIZADORA NO BLOQUEIO DE NERVOS GENICULARES POR RADIOSCOPIA

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ABSTRACT

The performance of genicular nerve block requires an imaging method to guide the procedure. Radioscopy has the disadvantage of being radiation dependent. Objective: To assess whether the use of adhesive radiopaque grids reduce radiation exposure in these cases. Methods: This is a cross-sectional study conducted with 23 orthopedists in which needles were positioned in a model with and without the use of adhesive radiopaque grids. The number of fluoroscopy shots necessary for proper positioning in three points (superior lateral, superior medial, and inferior medial) were registered. Results: A statistical difference was observed in the three blocking points studied. The number of radioscopies required for these three points were 12.1 ± 2.5 in the group without grid and 5.0 ± 1.8 in the group with grid. The superior medial point presented the greatest numerical difference and the inferior medial point the smallest. Conclusion: The use of adhesive radiopaque grids led to a statistically significant reduction in the number of radioscopies/fluoroscopies required to perform the genicular block. The use of this device increases the safety of the physician and patient by reducing radiation exposure in this procedure. ***Level of Evidence III, Level of Evidence II, Random Clinical Trial.***

Keywords: Nerve Block. Orthopedic Surgeons. Peripheral Nerves.

RESUMO

Para a realização do bloqueio de nervos geniculares é necessário guiar o procedimento por um método de imagem. A radioscopia possui a desvantagem de ser dependente de radiação. Objetivo: Avaliar se o uso de máscaras localizadoras diminui a exposição à radiação nesses casos. Métodos: Estudo transversal realizado com 23 ortopedistas, que realizaram o posicionamento de agulhas em um modelo com e sem o uso da máscara localizadora. Foi registrado o número de escopias necessárias para o posicionamento adequado em três pontos: superior lateral, superior medial e inferior medial. Resultados: Foi observada diferença estatística nos três pontos de bloqueio analisados. O número de radioscopias necessárias nos três pontos somados foi de 12,1 ± 2,5, no grupo sem máscara, e 5,0 ± 1,8, no grupo com máscara. O ponto superior medial foi o que apresentou a maior diferença numérica, e o inferior medial a menor. Conclusão: O uso da máscara localizadora reduziu de forma estatisticamente significativa o número de escopias necessárias para a realização do bloqueio genicular. O uso desse dispositivo aumenta a segurança do médico e do paciente por diminuir a exposição à radioscopia nesse procediment. ***Nível de Evidência III, Ensaio clínico randomizado aberto - Nível de recomendação B - nível de evidência 2b.***

Descritores: *Bloqueio Nervoso. Cirurgiões Ortopédicos. Nervos Periféricos.*

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INTRODUCTION

Knee osteoarthritis is a disease that affects approximately 1/3 of the global population over 65 years old, causing pain and impairment in quality of life. For the treatment of gonarthrosis, there are options such as physiotherapy, orthoses, acupuncture, pain relievers, joint injections, among others. If conservative treatment fails, total knee arthroplasty (TKA) is chosen.[1] Choi et al.,[2] in 2011, introduced the use of genicular nerve block (pharmacological or radiofrequency) as an alternative treatment for chronic knee pain. Since then, in patients with refractory pain despite conservative treatment and who are not eligible for TKA due to comorbidities, the use of genicular nerve block has been shown to be a good option. In addition, about 15 to 30% of patients who undergo TKA continue to experience pain and functional limitation in the knee, and the use of genicular nerve block has been shown to be effective in treating these residual symptoms.[1,3] Other applications of genicular

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The study was conducted at the Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas, Instituto de Ortopedia e Traumatologia IOT HCFMUSP.
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nerve block include its use in patients with rheumatoid arthritis as a method to aid in the modulation of the inflammatory process,[4] and in combination with intra-articular injection (corticosteroid or viscosupplementation) to enhance its analgesic effects.[5]

Genicular nerve block, whether pharmacological or by radiofrequency, is performed on three nerve trunks around the knee: the superior lateral, superior medial, and inferior medial genicular nerves. To perform the procedure, needles must be positioned close to these nerve trunks for medication infiltration or neurotomy. Needles can be positioned in three ways: via anatomical landmarks, which is considered a fairly imprecise method and is falling out of use; guided by ultrasound or fluoroscopy. The ultrasound-guided (USG) technique is a highly precise method for guiding the procedure, as the genicular nerve can be accurately identified, and it has the advantage of not using radiation. However, it is an examiner-dependent method that requires the availability of ultrasound equipment, which is not the reality of many medical institutions in our country. The fluoroscopy-guided method has been shown to be as effective as the ultrasound-guided method in improving pain and functionality scores in comparative studies, with the disadvantage of being a radiation-dependent method.[3,6]

In our country, due to the wide availability of fluoroscopy equipment and being a simpler and examiner independent method, the fluoroscopic method is the most commonly used for genicular nerve block. A theoretical alternative to minimize radiation exposure for both the physician and the patient is the use of adhesive radiopaque grids to guide needle positioning, aiming to use a lower number of fluoroscopy scans for proper needle placement. However, studies showing objective superiority in the use of these grids to decrease radiation exposure are scarce. The published studies on guiding needles in spine procedures using grids have shown potential benefits of this method.[7,8]

Thus, this study aimed to evaluate if the use of adhesive radiopaque grids significantly reduce the number of scopies and, consequently, radiation exposure in performing genicular blockade for the treatment of chronic knee pain. As a hypothesis of the study, we assume that the use of the grid reduces the number of attempts for the proper positioning of needles in the three points (superolateral, superomedial, and inferomedial) for performing knee blocks.

METHODS

For the execution of this study, a knee model was used and placed on a fluoroscopy device with a transparent table. Orthopedic surgeons who had already received instruction and training on how to perform genicular nerve blocks were instructed to position the needles on the knee model using fluoroscopy in the anteroposterior incidence. All participants signed the informed consent form to participate in the study processes and the article was approved in the protocol of the Ethics and Research Committee under the protocol number 5,920,389.

The points chosen for needle placement were based on the study by Sari et al.[3] for blocking the superior lateral, superior medial, and inferior medial genicular nerves (Figure 1). These points were chosen since they are the most commonly used for this type of procedure.[3]

Each surgeon was instructed to position the needles without using a grid and with the use of a grid (X-GRID radiopaque adhesive grid, Target Tape, Canada). The initial positioning with or without the grid was randomly chosen to minimize its influence on the final results. The number of attempts made to achieve the correct positioning at each point was quantified. The positioning without the grid was based only on anatomical parameters and on sequential fluoroscopy images taken during the procedure.

Figure 1. Fluoroscopy image of the anatomical model used in the study demonstrating the proper positioning of genicular block needles at the superomedial, superolateral, and inferomedial points.

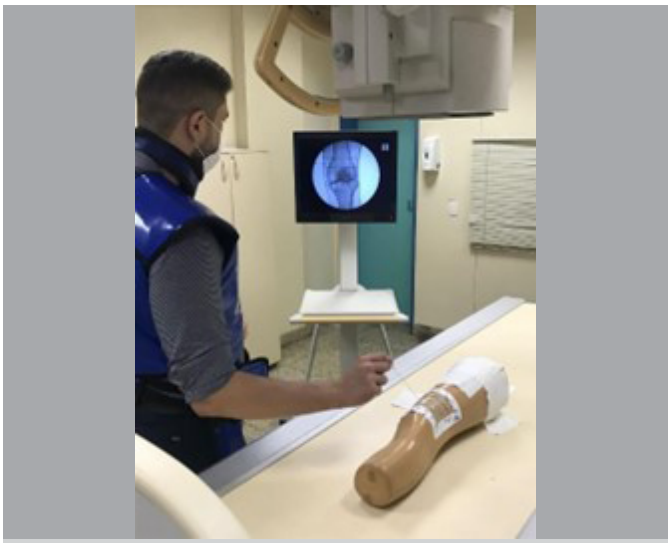

Figure 2. Orthopedist positioning the genicular block needles under fluoroscopy on the previously positioned model. It is possible to observe the adhesive radiopaque grid used in the study.

The knee model was positioned on the transparent table and fixed in the true anteroposterior position. The surgeon was not allowed to modify the position of the model. After attempts by the same surgeon, the model was repositioned if it had changed position (Figure 2).

A pilot study was conducted with five surgeons at the superior lateral genicular point, and the average number of attempts for correct positioning was 4.2 ± 0.8 attempts. Thus, considering a decrease of at least one attempt with the use of the grid, the sample was estimated for a power of 80% and $p < 0.05$ with a minimum of 14 participants.

The numerical variables were described as mean and standard deviation. Student's t-test or Mann-Whitney U test were used to compare numerical variables between groups according to the normality of the variables.

P values < 0.05 were considered significant. The SPSS 22 (IBM Corp., NY, USA) statistical software was used.

RESULTS

A total of 23 orthopedists were selected for the study. The means for each point performed without the grid were 5.4 ± 1.5; 3.6 ± 1.5; and 3.0 ± 1.3 for the superior medial, superior lateral, and inferior medial points, respectively. With the use of the grid, the means were 1.5 ± 0.8; 1.6 ± 0.6; and 1.7 ± 0.9 for the superior medial, superior lateral, and inferior medial points, respectively. The total number of fluoroscopy images performed for the group without grid in the three points studied was 12.1 ± 2.5, and for the group with grid, it was 5.0 ± 1.8.

Table 1 shows the statistical difference between the use or non-use of the safety grid found for all the points investigated. The inferior medial point showed the smallest difference between the use or non-use of the grid.

Table 1. Number of radioscopies required to achieve correct needle placement for genicular nerve block with and without the use of the adhesive radiopaque grids.

	Non-use of adhesive radiopaque grids	Use of adhesive radiopaque grids	p
Superior medial	5.4 ± 1.5 (range 3-9)	1.5 ± 0.8 (range 1-4)	< 0.0001
Superior lateral	3.6 ± 1.5 (range 1-6)	1.6 ± 0.6 (range 1-3)	< 0.0001
Inferior medial	3.0 ± 1.3 (range 1-6)	1.7 ± 0.9 (range 1-4)	0.0013
total	12.1 ± 2.5 (range 7-17)	5.0 ± 1.8 (range 3-9)	< 0.0001

DISCUSSION

The main finding of this study is that the use of the adhesive radiopaque grids reduces radiation exposure in cases of genicular nerve block. Ionizing radiation is extremely harmful to humans, being able to directly and cumulatively generate irreversible damage to DNA and the cell membrane even at low doses, especially in cells with a high replication rate, which is the initial event of carcinogenesis. Indirectly, ionizing radiation can also form free radicals that ultimately lead to cell death.[9,10] Therefore, the use of adhesive radiopaque grids significantly increased the safety of the procedure.

Due to the recurrent use of fluoroscopy in orthopedic procedures, it has been demonstrated that orthopedists have an increased risk of neoplasia/metaplasia compared to other professionals who do not use this tool in their clinical/surgical practice. Among the exposed tissues, the most sensitive to radiation are the eyes, with cataracts being the first sign of chronic radiation exposure; the thyroid, with 85% of papillary carcinomas being induced by radiation; and the hands and gonads, which increase the risk of infertility.[9,10]

To minimize the risk of radiation exposure, the International Commission on Radiological Protection (ICRP) established annual radiation dose limits for different tissues. The maximum allowable dose is 20 mSv for the body, 150 mSv for the thyroid and eyes, and 500 mSv for the hands. To prevent exceeding this dose limit, various protective measures are recommended, including the use of personal protective equipment (lead apron, collar, and glasses), which significantly reduces exposure to X-rays (up to 415 times the exposure to the thyroid), and distancing oneself from the fluoroscopy device at the time of image acquisition (being about 2 m away from the image intensifier minimizes radiation exposure).

However, in addition to using personal protective equipment and distancing oneself from the device, reducing the number of fluoroscopies is essential to reducing the amount of radiation to which professionals and patients are exposed. At this point, Malik et al.[11] demonstrated that the surgeon's experience led to a significant reduction in the number of fluoroscopies.[10,11]

In addition, important tools have emerged to guide the direction of surgical instruments to reduce the number of images needed to achieve the therapeutic goal.

In our study, the tool used to guide the needles for the genicular block was the adhesive radiopaque grids. It is an easy-to-use device, with a sterile radiopaque adhesive grid that acts as a guide for needle placement (Figures 3 and 4). Due to the significant anatomical variability among individuals, this tool is of great value for both less experienced professionals and those with extensive experience in the procedure. In the experimental model, an average of 12.1 (± 2.5) fluoroscopies were needed to perform an adequate genicular blockade without using the grid, whereas only an average of 5 (± 1.8) fluoroscopies were needed to perform the same procedure with the grid. This is a statistically significant reduction in the number of images needed, which leads to a reduction in radiation exposure for healthcare professionals and patient. Considering that orthopedic professionals are exposed to radiation in numerous procedures and that radiation has a cumulative effect, the long-term use of adhesive radiopaque grids can mean a significant reduction in the risk of ionizing radiation side effects.

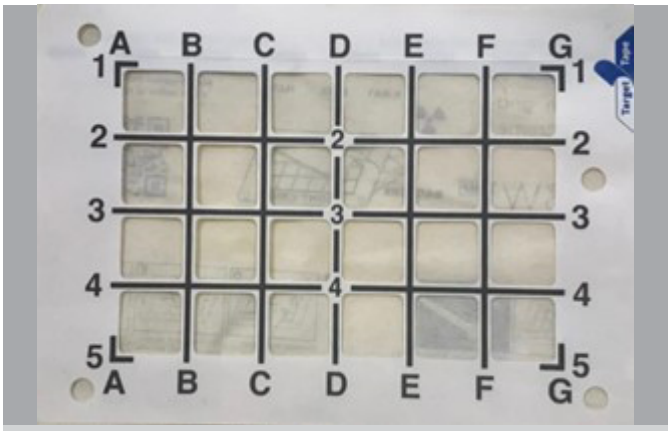

Figure 3. Adhesive radiopaque grid (X-GRID radiopaque adhesive, Target Tape, Canada) used in the study on genicular nerve block.

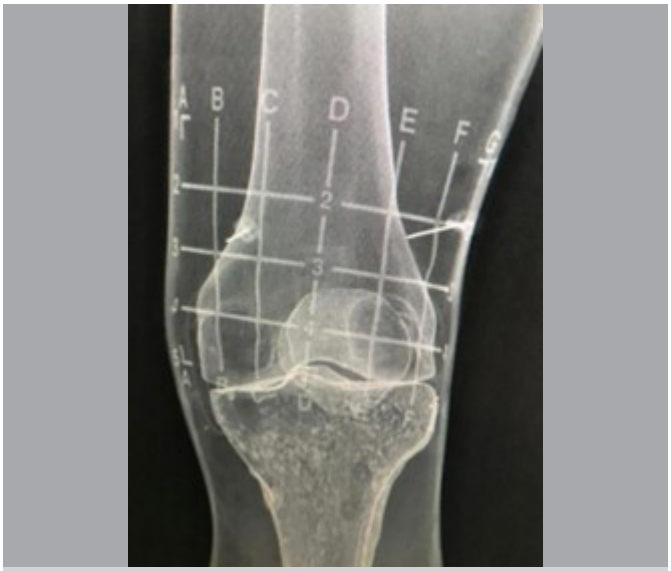

Figure 4. Fluoroscopy image of the model used in the study demonstrating the placement of needles at the superomedial and superolateral points guided by the X-Grid.

The femoral points showed the greatest difference between using or not using the grid, with the medial femoral point showing the greatest difference. This anatomical positioning is difficult since only the patella and the joint space can be used, especially in patients with thicker thighs. On the other hand, the inferior medial point had the smallest difference between the evaluated points, even so with statistical significance. The possibility of using the anterior tibial tuberosity and the medial cortex of the tibia, located more superficially, makes this point slightly easier than the femoral points.

As a study limitation, we can consider the cross-sectional design, which allows us to generate strong hypotheses about the reduction in radiation exposure, but does not allow us to evaluate the clinical outcome of greater radiation exposure without the use of the grid. Longitudinal studies with this objective are necessary to corroborate our hypothesis. Another limitation is the use of anatomical models with standard anatomy; the results could be more diverse with or without the use of the grid if clinical trials were conducted, since patients tend to have greater anatomical variability, which would make the use of the grid a more helpful tool for correctly positioning needles in these patients.

CONCLUSION

The use of adhesive radiopaque grids significantly reduced the number of fluoroscopy images required to perform the genicular nerve block in a statistically significant manner. The use of this device increases the safety of the physician and patient by decreasing the exposure to radioscopy in this procedure.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. DPL: examiner, data collection; MGLM: statistical analysis and article writing; MMA: data collection and article review; VHCG: data analysis and article review; JRP: article writing and review, as well as intellectual concept throughout the article; CPH: article writing, intellectual input throughout the article, and research project design.

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SOFT TISSUE SARCOMA – SANTA CASA DE SÃO PAULO EXPERIENCE FROM 2006 TO 2019

SARCOMA DE PARTES MOLES – EXPERIÊNCIA DA SANTA CASA DE SÃO PAULO DE 2006 A 2019

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ABSTRACT

Objective: To conduct an epidemiologic review, analyzing treatment, evolution, and survival of soft tissue sarcomas. Methods: Retrospective study based on medical records of patient with STS treated by the Orthopedic Oncology Group at the Santa Casa de São Paulo, from 2006 to 2019. Data from 121 patients were analyzed according to age, sex, histological type, tumor location, treatment, previous surgery in a non-specialized service, local recurrences, lung metastases, and survival analysis. Results: The most frequent location was the thigh. Patients who underwent surgery with a non-specialized group had higher rates of local recurrence and those with pulmonary metastasis had a lower survival rate. Conclusion: STS can occur at any age and the prevalence of the histological type depends on the patients' age group. ***Level of Evidence II, Prognostic Study.***

Keywords: Soft Tissue Neoplasms. Therapy, Soft Tissue. Epidemiology.

RESUMO

Objetivo: Conduzir uma avaliação epidemiológica analisando tratamento, evolução e sobrevida dos sarcomas de partes moles (SPMs). Métodos: Estudo retrospectivo de prontuários de pacientes com SPM tratados pelo Grupo de Oncologia Ortopédica da Santa Casa de Misericórdia de São Paulo, no período de 2006 a 2019. Foram analisados os dados de 121 pacientes referentes a idade, sexo, tipo histológico, localização do tumor, tratamento, cirurgia prévia em serviço não especializado, presença de recidivas, metástases pulmonares e análise de sobrevida. Resultados: A localização mais frequente foi a coxa. Verificou-se que pacientes que realizaram cirurgia com grupo não especializado tiveram maiores índices de recidiva local, e aqueles com metástase pulmonar tiveram menor sobrevida. Conclusão: Os SPMs podem ocorrer em qualquer idade, e a prevalência do tipo histológico depende da faixa etária dos pacientes. ***Nível de Evidência II, Estudo Prognóstico.***

Descritores: *Neoplasias de Tecidos Moles. Terapia de Tecidos Moles. Epidemiologia.*

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INTRODUCTION

Soft Tissue Sarcomas (STS) are uncommon tumors,[1] represent less than 1% of all malignant tumors in adults, and have a great histological diversity, with more than 50 histological subtypes based on the tumor lineage.[2-7] STS rarity and diversity has hindered its study. However, collaborative studies with the formation of large databases and tissues have currently increased the understanding of this group of diseases.[2,8]

Similar to other rare and serious diseases, early diagnosis and access to specialized services directly affects the prognosis, which invariably leads to errors and delays in diagnosis[2,3] Thus, the best results occur in reference centers.[2,3]

Frequently, STS presents themselves initially as slightly painful tumors, delaying and hindering the diagnosis.[4] They can occur at any age and anatomical location, with a predominance of 75% in the limbs and especially in the thigh.[4] As in other malignant neoplasms, STS incidence increases with advancing age, especially after 65 years old.[3]

At diagnosis, 10% of patients already present metastases, mainly lung lesions.[3]

Prognostic factors related to STS are histological grade, tumor size, and microscopic margin after resection.[5,6] A better understanding of the behavior of these tumors may result in better surgical treatment and the development of new adjuvant therapies.[7,9-12]

We believe that the initial step for the development of new treatments is the understanding of the behavior of a disease by an epidemiological study. The rarity and diversity in the behavior of STS hinder the publication of new studies. Thus, we aimed to study our cases and publish our outcomes.

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

The study was conducted at the Santa Casa de Misericordia de Sao Paulo, Departamento de Ortopedia e Traumatologia.
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Therefore, this study aimed to show the epidemiological data of patients with soft tissues sarcoma in the musculoskeletal tumors service of the Departamento de Ortopedia e Traumatologia of the Hospital Geral da Santa Casa de Misericórdia de São Paulo.

METHODS

This is a retrospective study, carried out by the analysis of medical records of patients diagnosed with STS who were treated by the Orthopedic Oncology Group of Santa Casa de São Paulo, from January 2006 to December 2019 (Approval Protocol of the CAAE Ethics Committee: 76547317.6.0000.5479).

Data were collected by an evaluation instrument (Appendix 1), including the following information: sex, age, histological type of tumor, tumor size at the time of diagnosis, location, type of treatment performed (surgery, chemotherapy, radiotherapy), previous surgery with another team, presence of lung metastases, local recurrence during follow-up, and date of death.

During the study period, 169 patients with biopsy-confirmed STS diagnosis were treated, 48 patients were excluded due to incomplete information in the medical record.

The statistical analysis was performed with 121 patients in two stages: descriptive analysis and inference.

In the inference, contingency tables were constructed to study the association between qualitative variables. Chi-Square and Fisher's Exact tests were used when convenient.

In the survival analysis, the Kaplan-Meier method was used to study the relationship between factors and time.

In all tests, a 5% significance level was adopted.

RESULTS

In our sample, we observed a minimum age of 6 months and a maximum age of 85 years, mean age of 45.4 years (± 20.2 SD). The incidence peak was in the age group of 41 to 50 years (Figure 1).

Females presented a small predominance of 52% (n = 63), and males composed 48% (n = 58) of the sample.

The most frequent histological types in the extremities were synovial sarcoma with 34 cases (28.1%), undifferentiated sarcoma with 20 cases (16.5%), and liposarcoma with 20 cases (16.5). Table 1 shows the remaining histological types.

The most frequent location of STS was the thigh (n = 59;48.8%), followed by the arm (n = 14; 11.6%), the leg (n = 12; 9.9%), and the pelvic girdle (n = 9; 7.4%). The other locations are distributed by anatomical region (Table 2).

Regarding tumor size, patients were divided into groups with tumors larger, and smaller than 5 cm, 113 (93%) and eight (7%) patients, respectively.

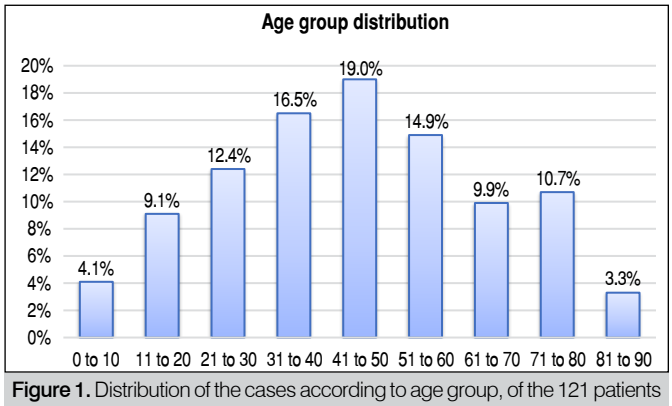

Figure 1. Distribution of the cases according to age group, of the 121 patients treated by the orthopedic oncology group from 2006 to 2019.

The treatment for patients diagnosed with STS was surgical intervention (87.6%). In total, 88 patients (67.8%) underwent tumor resection surgery with limb preservation and 24 (19.8%) underwent amputation surgery. Only 15 (12.4%) of the patients did not undergo surgical intervention due to clinical complications during chemotherapy or radiotherapy, advanced stage of the disease, or refusing the surgical treatment proposed.

In total, 72 (59.5%) patients underwent chemotherapy.

In total, 57 (47.1%) patients underwent complementary treatment with local radiotherapy, mostly, 53 (43.8%), in the postoperative period.

In our study, 24 (22.4%) patients evolved with local recurrence of the tumor. Those who underwent previous surgery in another service and/or with a non-specialized group experienced recurrence in 40.9% ($P < 0.005$) (Table 3).

During follow-up, 49 (40.5%) developed pulmonary metastasis. In total, 46 patients (38%) died during follow-up. Patients with lung metastasis had lower survival (Figure 2).

DISCUSSION

In our sample, STS is not prevalent regarding sex, as is the Memorial Sloan Kettering Cancer Center and the rest of the literature.[6,13-16]

Table 1. Distribution of the histological type of patients treated by the orthopedic oncology group from 2006 to 2019.

Histological type	(%)*	(n)
Synovial sarcoma	28.1%	34
Liposarcoma	16.5%	20
Undifferentiated sarcoma	16.5%	20
Leiomyosarcoma	8.3%	10
Neurofibrosarcoma	8.3%	10
Myxofibrosarcoma	5.8%	7
Rhabdomyosarcoma	4.1%	5
Fibromyxoid sarcoma	4.1%	5
Dermatofibrosarcoma	1.7%	2
Infantile fibrosarcoma	1.7%	2
Solitary fibrous tumor	1.7%	2
Angiosarcoma	0.8%	1
Epithelioid sarcoma	0.8%	1
Myxoinflammatory fibroblastic sarcoma	0.8%	1
Myofibroblastic sarcoma	0.8%	1

* Percentages regarding the 121 patients in the sample.

Table 2. Distribution according to tumor location of patients treated by the orthopedic oncology group from 2006 to 2019.

Location	(%)*	(n)
Thigh	48.8%	59
Arm	11.6%	14
Leg	9.9%	12
Pelvic girdle	7.4%	9
Foot	5.8%	7
Elbow	3.3%	4
Forearm	2.5%	3
Pectoral girdle	2.5%	3
Back	2.5%	3
Knee	2.5%	3
Hand	1.7%	2
Flank	0.8%	1
Chest	0.8%	1

* Percentages regarding the 121 patients in the sample.

Table 3. Distribution according to tumor location of patients treated by the orthopedic oncology group from 2006 to 2019.

		Without recurrence		With recurrence		Total		*p*-value
		N	(%)*	N	(%)*	N	(%)*	
Previous surgery	No	84	84.8	13	59.1	97	80.2	0.006
	Yes	15	15.2	9	40.9	24	19.8	

* Percentages regarding the 121 patients of the sample.

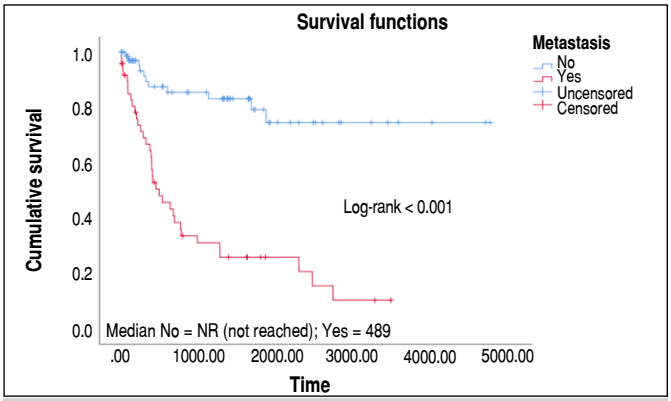

Figure 2. Kaplan-Meier survival curve for lung metastases.

The predominant age group ranged from 31 to 60 years, considering that they were treated in a general hospital that assists adults and children. Corroborating epidemiological data in the literature, the older the patients the higher the incidence of STS.[6,15-17]

We found a difference between the predominance of the histological type in patients treated at the Santa Casa de São Paulo compared to the literature. Synovial sarcoma is more prevalent in young patients, as well as the profile of patients evaluated in the general hospital within the department of orthopedics and traumatology, which assists younger patients. Moreover, these cases relate only to extremity tumors, different from the ones of the Hospital Sloan Kettering Memorial, which also includes abdominal, retroperitoneal, and thoracic tumors. The work of the Mayo Clinic, also in the United States, reveals a predominance of Liposarcoma in their cases, however, it includes cases in the retroperitoneum and abdomen.[6,15-19] We also observed that the predominance of the histological type is associated with the predominant age in each service.

The most frequent location of soft tissue sarcomas of the extremities was in the thigh, regardless of the predominance of age, sex, or histological type. Studies from the literature also reported the thigh as the most affected location among the STS of the extremities.[2,6,16,17]

Surgical treatment was chosen, an expected result since the treatment of STS is predominantly surgical. Most patients were subjected to an attempt to preserve the limb with tumor resection.[18]

Radiotherapy as treatment was associated with surgery almost exclusively in the adjuvant form. The Orthopedic Oncology Group indicates radiotherapy treatment for resection with a borderline oncologic margin, for histological types that have a low response to chemotherapy, as a complementary treatment for patients with high-grade sarcoma. This is a preference of the team regarding neoadjuvant radiotherapy to avoid complications with surgical wound.[6,15-17,20]

Some patients with STS were biopsied or initially treated in another service before being referred to a specialized service, 15 to 20% of the patients according to the literature, and with the data from our service (19%).[6,15-17] Local recurrence for these patients was statistically significant ($p \leq 0.05$) and much higher (40.9%) than for the rest of the sample.

Our global local recurrence was 22.8%, as found in the literature (20–25%).[6,15-17]

Almost half patients (40.5%) developed pulmonary metastases at some point during treatment. This finding is associated with decreased patient survival.[6,14]

Considering the nature of this study, some factors hampered data collection, namely: incorrect filling of medical records; old medical records without digitized version and with loss of information; inaccurate dates of examinations and deaths; loss of old pathological and anatomical results; difficulty contacting patients and their families; and incomplete data in medical records.

CONCLUSIONS

The predominant age group of patients with STS in our service ranged from 41 to 50 years. The most prevalent histological types were Synovial Sarcoma, followed by Undifferentiated Sarcoma and Liposarcoma. The most affected location was the thigh. The treatment was predominantly surgical with limb preservation. Those who have had previous surgery in another service have higher rates of tumor recurrence. Patients with lung metastasis have lower survival.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. BB: surgery, writing of the article, statistical analysis, intellectual concept of the article, and preparation of the entire article project; ARS: data analysis, and performance of surgeries; DGAN: surgeries and data collection; MA: data analysis, data collection, surgeries, and article review; ESY: surgeries, statistical analysis, writing and revision of the article; PMMBF: writing and revision of the article.

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APPENDIX 1

Soft Tissue Sarcoma Evaluation Protocol (Appendix 1)

Register:	
Name:	
Age:	Phone number:

Sex:
( ) M ( ) F

Histological type:

Location:

( ) Pectoral girdle	( ) Pelvic girdle
( ) Arm	( ) Thigh
( ) Forearm	( ) Knee
( ) Hand	( ) Leg
( ) Elbow	( ) Foot
( ) Wrist	( ) Ankle

Chemotherapy:			If yes:	
( ) Yes	( ) No	( ) I do not know	( ) Adjuvant	( ) Neo adjuvant

Radiotherapy:			If yes:	
( ) Yes	( ) No	( ) I do not know	( ) Adjuvant	( ) Neo adjuvant

Surgery:		If yes:
( ) Yes ( ) No ( ) I do not know		( ) Intralesional resection
		( ) Marginal resection
Date:		( ) Wide resection
		( ) Radical resection – amputation
		( ) I do not know

Tumor size:	( ) ≤ 5 cm	( ) ≥ 5 cm	( ) I do not know
Presence of metastasis:	( ) Yes	( ) No	( ) I do not know
Previous surgery by another service:	( ) Yes	( ) No	( ) I do not know
Local recurrence:	( ) Yes	( ) No	( ) I do not know
Date of diagnosis:	Date of last consultation:		
Death:	( ) Yes	( ) No	( ) I do not know
Date:			

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IMMUNOHISTOCHEMICAL ANALYSIS BY KI67 AND IDH1 IN PATIENTS WITH CHONDROSARCOMA

ANÁLISE IMUNO-HISTOQUÍMICA POR MEIO DE KI67 E IDH1 EM PACIENTES COM CONDROSSARCOMA

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ABSTRACT

Objective: To perform an immunohistochemical evaluation using the IDH1 and Ki67 markers in patients who underwent treatment for chondrosarcoma in a reference service center in Brazil. Methods: Retrospective analytical observational study using medical records of patients diagnosed with chondrosarcoma. Besides the epidemiological and clinical profile, important variables for prognosis and correlation with immunohistochemical analysis results with Ki67 and IDH1 markers were evaluated. Results: Histopathological examinations by immunohistochemistry of 56 patients were analyzed, 52% of which were women, with the age group 20-60 years being more prevalent. Grade 1 and 2 histological subtypes corresponded to most chondrosarcomas. The femur, humerus, and tibia were the most frequent anatomical sites. Most tumors (59%) were larger than 8 cm. Ki67 expression was very low (< 10%) in 98% of patients. The analysis of IDH1 was positive in 43% of the cases. The correlation between IDH1 positivity and tumor size was statistically significant, but regarding survival, we observed no significance. Conclusion: Immunohistochemical analysis using IDH1 and Ki67 markers in patients with conventional chondrosarcoma is not useful for prognostic guidance. ***Level of Evidence II, Prognostic Assessment, Results of Immunohistochemical Tests and Correlation with Survival.***

Keywords: Chondrosarcoma. Immunohistochemistry. Prognosis.

RESUMO

Objetivo: Fazer uma avaliação imuno-histoquímica usando os marcadores IDH1 e Ki67 em pacientes que fizeram tratamento para condrossarcoma em um serviço de referência no Brasil. Métodos: Estudo retrospectivo, analítico e observacional de prontuários de pacientes com diagnóstico de condrossarcoma. Além do perfil epidemiológico e clínico, foram avaliadas variáveis importantes para o prognóstico e a correlação com os resultados da análise imuno-histoquímica utilizando os marcadores Ki67 e IDH1. Resultados: Foram analisados exames histopatológicos por imuno-histoquímica de 56 pacientes, dos quais 52% eram do sexo feminino. A faixa etária mais prevalente foi entre 20 e 60 anos. Os subtipos histológicos graus 1 e 2 corresponderam à maioria dos casos. Fêmur, úmero e tíbia foram os sítios anatômicos mais frequentes. A maioria dos tumores (59%) tinha tamanho superior a 8 cm. O Ki67 teve expressão muito baixa (< 10%) em 98% dos pacientes. Já a análise do IDH1 foi positiva em 43% dos casos. A correlação entre a positividade do IDH1 e o tamanho do tumor foi estatisticamente significativa; já em relação à sobrevida, não houve significância. Conclusão: A análise imuno-histoquímica por meio dos marcadores IDH1 e Ki67 em pacientes com condrossarcoma convencional não é útil para orientação prognóstica. ***Nível de Evidência II, Avaliação Prognóstica, Resultados de Exames Imuno-Histoquímicos e Correlação com Sobrevida.***

Descritores: *Condrossarcoma. Imuno-Histoquímica. Prognóstico.*

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INTRODUCTION

Chondrosarcoma is a malignant bone tumor characterized by the formation of cartilage by tumor cells. It differs from chondroma due to its high cellularity, greater pleomorphism, and the appreciable number of pulpous cells with large or double nuclei.[1]

It presents many clinical-pathological characteristics and biological behaviors, and several distinct variants can be observed, besides the more common conventional central chondrosarcoma. They can be either primary, apparently originating from a normal bone, or secondary to some pre-existing benign cartilaginous tumor, frequently, multiple hereditary osteochondromatosis and enchondromatosis.[1]

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

The study was conducted at Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas, Instituto de Ortopedia e Traumatologia IOT HCFMUSP.
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According to the World Health Organization (WHO) classification in 2020, chondrosarcomas can be divided into eight subtypes.[2]

- Type 1 – Atypical cartilaginous tumor/chondrosarcoma, grade 1;
- Type 2 – Peripheral secondary chondrosarcoma;
- Type 3 – Central chondrosarcoma, grades 2 and 3;
- Type 4 – Secondary peripheral chondrosarcoma, grades 2 and 3;
- Type 5 – Periosteal chondrosarcoma;
- Type 6 – Clear cell chondrosarcoma;
- Type 7 – Mesenchymal chondrosarcoma;
- Type 8 – Undifferentiated chondrosarcoma.

The peak incidence of primary chondrosarcoma ranges from the fifth to seventh decades of life. Secondary chondrosarcoma affects younger individuals from the third and fourth decades of life. The clinic does not correlate with the degree or size of the lesion.[3]

Radiologically, the lesion is usually lithic and may contain points of intralesional calcification and cortical thickening. Histologically, it is one of the most difficult lesions for a pathologist to diagnose since the criterion for differentiating between low-grade chondrosarcoma and chondroma is uncertain. Diagnosis is based on the combination of clinical, imaging, and histopathological data.[4]

In most cases, biopsy only confirms it as a cartilaginous lesion. It is not entirely reliable to define the degree of malignancy of lesions *in vivo*, as the tumor may present areas with different histological grades in some cases.[5]

In the anatomopathological analysis, the routine staining used is hematoxylin eosin, and immunohistochemistry is rarely used.[5]

Treatment varies according to the histological grade, being predominantly surgical. They are tumors resistant to radiotherapy and chemotherapy, used only in high-grade cases.[6]

This study aimed to make a prognostic evaluation by immunohistochemistry using the markers IDH1 and Ki67 in patients who underwent treatment for chondrosarcoma.

METHODS

The research project was registered and approved by the Ethics and Research Committee of the Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP) and duly enrolled in Plataforma Brasil and by the Ethics Committee for the analysis of Research Projects (3,974,954).

Inclusion criteria: All patients with anatomopathological diagnosis of chondrosarcoma treated at the Orthopedic Oncology Service of the Instituto de Ortopedia e Traumatologia (IOT HCFMUSP) from January 2000 to December 2010. Available paraffin blocks. Clinical follow-up in 10 years.

Exclusion criteria: Medical records of patients with loss of outpatient follow-up. Single paraffin blocks in the laboratory, being unusable due to risk of loss. Only paraffin blocks from biopsies.

This was a retrospective analytical observational study using the medical records of patients diagnosed with chondrosarcoma, and "n" was used for convenience.

The following data were evaluated: period of diagnosis, age, gender, histological classification, tumor size, skeletal site, presence of metastases, distant disease-free survival in ten years, positivity for IDH1 and Ki67 immunohistochemistry.

The data were stored in a Windows Excel spreadsheet and later imported into the software.

Statistical analyses were performed using Epi Info version 7.2.5.0. The simple frequencies of all the variables studied were estimated. All were categorical and described by their count and relative frequency. Several associations were performed for statistical inference following the central object in the associations with IDH1 and Ki67. For the association between categorical variables, Pearson's chi-square test was used, and, when appropriate, Fisher's test or likelihood ratio test for numbers of small events observed and expected (< 10). $p \leq 0.05$ was accepted as a type error for statistically significant differences.

Positivity for IDH1 (which marks the mutation of this enzyme, with a R132H clone in this study) was correlated with the anatomical site, tumor size (we used the values of < and > 8 cm according to the study by Amin et al.),[7] gender, age group, histological subtype, types of surgery, systemic recurrence, and death.

The percentage of Ki67 was analyzed to standardize a prognostic score depending on statistical significance.

The analysis of IDH1 and Ki67 expression was performed by two pathologists "blindly."

The IDH1 test was performed using the Envision flex Dako® kit (K-800221) with the IDH1 antibody (clone: R132H) of the brand Gene AB®.

The Ki67 survey was conducted automatically, on the Dako Omnis®equipment.

RESULTS

At the end of the survey of medical records, we had 83 cases, and of these, 27 were excluded, leaving 56 patients.

Regarding gender, 29% were women, the age group 20-60 years predominated with 41%, the subtypes grade 1 and 2 totaled 45% of the cases, femur and humerus were the most common anatomical sites with 56%, and tumors larger than 8 cm were the majority with 59%.

Regarding the percentage of positivity for IDH1, 43% were obtained, whereas Ki67 was positive in only one patient (1.7%) (Figure 1).

In total, 11% of the patients had systemic recurrence.

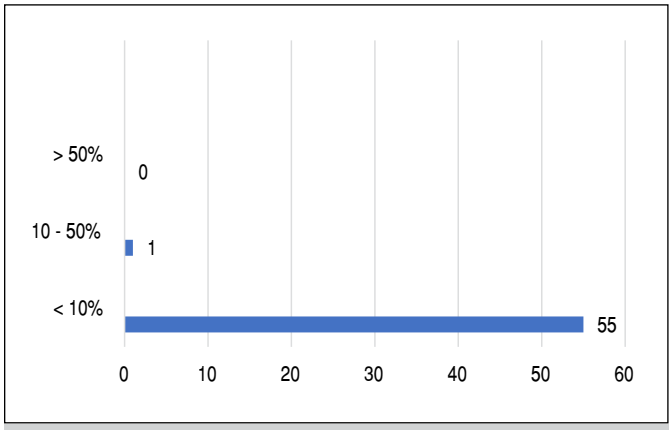

Figure 1. Total ki67 expression percentage.

Table 1. Correlation between IDH1 positivity and tumor size.

IDH1	Larger than 8 cm	Smaller than 8 cm	Total
Negative	13	19	32
Positive	19	5	24
TOTAL	32	24	56

P < 0.004.

Table 2. Correlation between IDH1 positivity and chondrosarcoma subtype.

	Chondrosarcoma subtypes					
IDH1	UD	G1	G2	G3	ME	Total
Negative	3	6	20	1	2	32
Positive	1	10	9	4	0	24
TOTAL	4	16	29	5	2	56

P = 0.108.
G: grade 1, 2, or 3; UD: undifferentiated; ME: mesenchymal.

<< SUMÁRIO

DISCUSSION

The current "gold standard" for the study of IDH1 mutations in chondrosarcoma is the genetic analysis of clones, cited by Amary et al.,[8] which is one of the limitations of this study. However, it is a high-cost method and most readily available in most reference services in Oncology. The analysis of IDH1 by immunohistochemistry is already part of the routine in several neoplasms. Positivity shows good prognosis even in tumors of the central nervous system.[8]

As for our "n" (used for convenience), which initially was 83 patients and after the exclusion criteria was 56, in the study of Vuong, Ngo, and Dunn,[9] the casuistry of most of the selected studies can be observed and, comparing with the same period, we verified that the number of cases in our study reflects the world scenario. As well as Etchebehere et al.,[10] who had a similar sample comparing the periods.

The epidemiological and clinical data corroborate almost all the included studies, especially the studies by Vuong, Ngo and Dunn,[9] and Etchebehere et al.[11]

Ki67 was suggested as a marker for analysis in our research due to its already established importance for stratification as an index of cell proliferation in sarcomas, especially in bone tumors, in which it seems to be related to biological aggressiveness and level of malignancy and may be useful in diagnosis and prognosis, such as in high-grade osteosarcoma. However, of the 56 slides, in only one the index was higher than 30% and lower than 10% in 98% of the cases, making the statistical analysis unfeasible and concluding its low expressiveness in patients with chondrosarcoma. Two studies had similar results to ours.[12,13]

The low expression of Ki67 may be useful for the differential diagnosis, especially with osteosarcoma since it often presents high proliferation rates. Scotlandi et al.,[12] show that, in bone tumors, Ki67 seems to be related to biological aggressiveness and level of malignancy and may have a useful diagnosis and prognosis, particularly in high-grade osteosarcoma.

A genetic analysis would be necessary to assess the prognosis, according to several studies: Zhu et al.,[14] analyzing IDH1 mutations, concluded that they are associated with a higher relapse- and metastasis-free survival in high-grade chondrosarcomas. Lugowska et al.,[15] showed that IDH status would be correlated with relapse-free survival without metastases in high-grade chondrosarcomas, but the effect on overall survival requires further evaluation.

Table 1 shows that the correlation between IDH1 positivity and tumor size was statistically significant. As for the subtype (Table 2), anatomical site (Table 3), and 10-year disease-free survival (Table 4), we found no significance. Nie, Lu, and Peng,[16] showed that gender, age at diagnosis, stage, grade, tumor site, surgery, and radiation are independent risk factors for survival. Amer et al.,[17] found that the only prognostic variable that had a significant effect on the survival of each subtype of nonconventional chondrosarcoma was metastatic disease at the time of diagnosis. The cases with diagnosis of undifferentiated and mesenchymal chondrosarcoma were left in this study to facilitate the analysis in future studies with our series, using the genetic isolation method. Chen et al.,[18] identified mutations in IDH1 that were important for the differential diagnosis of undifferentiated chondrosarcoma and pleomorphic sarcoma of the bone. De Andrea, San-Julian, and Bovée,[19] in an analysis of cartilaginous tumors of the bone, verified that the molecular alterations can be used for the diagnosis include alterations of IDH1 (R132C; R132H) in enchondromas, conventional chondrosarcomas,

Table 3. Correlation between IDH1 positivity and 10-year relapse-free survival.

	10-year disease-free survival		
IDH1	Yes	No	Total
Negative	30	2	32
Positive	20	4	24
Total	50	6	56

P = 0.233.

Table 4. Correlation between IDH1 positivity and the anatomical site of the tumor.

	Anatomical site of chondrosarcoma												
IDH1	Clavicle	Scapula	Phalanx	Femur	Fibula	Ischium	Mandible	Pelvis	Talus	Tibia	Humerus	Vertebra	Total
Negative	1	1	3	9	2	0	1	3	2	4	5	1	32
Positive	0	1	0	8	0	1	0	3	0	3	8	0	24
Total	1	2	3	17	2	1	1	6	2	7	13	1	56

P = 0.445.

Table 5. Correlation between anatomical site and disease-free survival in years.

	10-year disease-free survival		
Anatomical Site	YES	NO	Total
Clavicle	1	0	1
Scapula	1	1	2
Femur	14	3	17
Fibula	2	0	2
Ischium	1	0	1
Mandible	1	0	1
Pelvis	5	1	6
Talus	2	0	2
Tibia	6	1	7
Humerus	13	0	13
Vertebra	1	0	1
Total	50	6	56

P = 0.989.

Table 6. Frequency of the type of surgery performed.

Surgery	Frequency	Percentage
Amputation	4	7.14%
Wide resection without replacement	4	7.14%
Intralesional resection with replacement	24	42.86%
Wide resection and replacement by unconventional endoprosthesis	16	28.57%
Scapulectomy	2	3.57%
Hemipelvectomy	6	10.71%
Total	56	100.00%

Table 7. Correlation regarding the type of surgery and result of IDH1 analysis.

	IDH1		
Type of surgery	Negative	Positive	Total
Amputation	2	2	4
Wide resection without replacement	4	0	4
Intralesional resection with replacement	14	10	24
Wide resection and replacement by unconventional endoprosthesis	8	8	16
Scapulectomy	1	1	2
Hemipelvectomy	3	3	6
TOTAL	32	24	56

P = 0.60.

and undifferentiated chondrosarcoma. And by the HEY-NCOA2 fusion genes in mesenchymal chondrosarcoma.

The analysis of IDH1 in patients with chondrosarcoma is an essential topic, and the literature shows results that indicate the need for more prospective and comparative studies identifying factors and treatments that may influence the survival of patients with chondrosarcoma. More evidence with research could eventually lead to evidence-based treatments, avoiding the abundant exposure of patients to potentially harmful therapies, such as radiation and chemotherapy.

A greater centralization of care for patients with chondrosarcoma would be desirable and may generate opportunities for researchers to establish prospective and comparative studies.

With these results, a new analysis can be performed using clone isolation methods, multicenter studies with known metastatic cases and other statistical power analyses.

CONCLUSION

Immunohistochemical analysis using IDH1 and Ki67 markers in patients with chondrosarcoma is not useful for prognostic guidance.

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CORRELATION OF OSTEONECROSIS RATES IN THE SURGICAL TREATMENT OF PROXIMAL HUMERAL FRACTURES ACCORDING TO THE NEER AND HERTEL CLASSIFICATIONS

CORRELAÇÃO DOS ÍNDICES DE OSTEONECROSE NO TRATAMENTO CIRÚRGICO DAS FRATURAS DO ÚMERO PROXIMAL PELOS CRITÉRIOS DE NEER E HERTEL

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ABSTRACT

Objective: To predict the risk of osteonecrosis (ON) according to the Neer and Hertel et al. classification for surgically treated proximal humeral fractures after at least one year of follow-up. Methods: This is a retrospective, cross-sectional, and observational cohort study. A total of 44 patients, 16 (36.36%) men and 28 (63.63%) women, with a mean age of 61.36 years, participated in this study. Lesions were categorized according to Neer and Hertel's classifications, considering the preoperative prognosis for ON. After at least a year of follow-up, patients were reassessed. Data were evaluated using IBM SPSS Statistics®. Results: A total of three patients (6.8%) developed osteonecrosis. Comparisons showed no statistically significant difference, but we observed a superior association of osteonecrosis for the Hertel classification than that of Neer. Conclusion: Both classifications showed a similar ability to identify patients at low risk of developing ON. New studies with a greater number of participants and sample homogeneity may intensify the value of the evaluation of clinical applicability and predictive capacity of the studied classifications with greater significance and correlation. ***Level of Evidence III, Case Control Study.***

Keywords: Humeral Head. Classification. Osteonecrosis. Prognosis. Humeral Fractures.

RESUMO

Objetivo: Prognosticar o risco de osteonecrose (ON), segundo os critérios de Hertel et al. e a classificação de Neer, para fraturas do úmero proximal tratadas cirurgicamente após, pelo menos, um ano de seguimento. Métodos: Estudo de coorte retrospectiva, transversal e observacional. Foram encontrados 44 pacientes, sendo 16 (36,36%) do sexo masculino e 28 (63,63%) do feminino, com média de idade de 61,36 anos. As lesões foram categorizadas de acordo com os critérios de Neer e de Hertel et al., considerando o prognóstico pré-operatório para ON. Após pelo menos um ano de seguimento, os pacientes foram reavaliados. Os dados foram analisados por meio do programa IBM SPSS Statistics. Resultados: Três pacientes (6,8%) evoluíram com ON. As comparações não demonstraram diferença estatística significante, embora tenha sido possível observar associação superior para a classificação de Hertel et al. em comparação com a de Neer. Conclusão: As duas classificações apresentaram habilidade semelhante para identificar pacientes com baixo risco de desenvolver ON. Sugere-se a realização de novos estudos com maior número de participantes e homogeneidade da amostra para intensificar o valor da avaliação da aplicabilidade clínica e da capacidade preditiva das classificações estudadas, com aumento da significância e da correlação. ***Nível de Evidência III, Estudo Caso Controle.***

Descritores: *Cabeça do Úmero. Classificação. Osteonecrose. Prognóstico. Fraturas do Úmero.*

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INTRODUCTION

Proximal humeral fractures account for about 4 to 5% of all injuries affecting the mature skeleton. It is the second most frequent when we specifically consider upper limb trauma. In women, due to physiological osteopenia determined by natural aging, its incidence is twice as large as that of men.[1]

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The study was conducted at Rede D'Or Sao Luiz, Hospital IFOR, Serviço de Ortopedia e Traumatologia.
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Osteoporosis is directly related to the incidence of these lesions, which are becoming more common due to the increasing number of older adults in our population. Such a condition makes it difficult to fix bone damage, especially with conventional plates and screws.[1,2] To solve this issue, more appropriate systems have been developed to improve the stability of osteosynthesis systems, such as fixation with fixed angle plates and screws, blade plates, intramedullary rods, percutaneous pinning, tension band wires, and arthroplasty.[1] Among the implants available for therapeutic application, special plates with locking screws seem to have a higher mechanical stability, and several clinical studies showed favorable results regarding their function and healing.[1]

Complications from this type of injury, such as neurological damage, vascular involvement, pseudoarthrosis, and osteonecrosis (ON), are frequent. According to Neer,[3] one of the most relevant is the ON of the proximal humerus, which is influenced by age, the degree of injury (according to different fracture classification systems), the quality of reduction, implant positioning, and the energy of the trauma.[3,4]

As for outcomes, it is possible to determine the prognosis of this condition during the preoperative phase, and detecting it at this stage can affect the final result. This injury causes significant pain and, in many cases, responds poorly to non-surgical treatment. It corresponds to approximately 5% of the preoperative diagnosis of all performed shoulder arthroplasties.[4,5]

In reviewing the literature, we refer to the work of Hertel et al.,[6] who developed a binary classification system (LEGO®) with 12 possible types of proximal humeral fractures, from which, predictors of humeral head ischemia were defined as follows: length of the metaphyseal head extension < 8 mm; deviation of the medial hinge > 2 mm; basic fracture pattern (anatomical neck or epiphyseal separation); angular displacement of the head over 45°; fractures in three or four parts; the amount of displacement of tuberosities greater than 1 cm; and glenohumeral dislocation. Fractures of the anatomical neck of the humerus are associated with a "medial hinge" injury and calcar injury with metaphyseal involvement > 8 mm show 97% ON rates.

The association between proximal humeral fracture and ON is of great interest as are the orthopedic literature is yet to definitively explain several of its aspects. Such an issue instigated this group to conduct research aimed at predicting the risk of ON according to Hertel et al.[6] and Neer's[3] classifications for surgically treated proximal humeral fractures after at least one year of postoperative follow-up.

METHODS

This study was sent to the Research Ethics Committee via *Plataforma Brasil* and approved under CAEE No. 51474921.6.0000.5625 and opinion No. 4.958.341.

This is a retrospective, cross-sectional, observational cohort study that evaluated surgically treated adult proximal humeral fractures. Data collection occurred from January 2018 to January 2021.

Patients were selected from a patient database at our institution. The International Classification of Diseases (ICD 10) code S42 (fracture of shoulder and upper arm) was used. The following inclusion and exclusion criteria were determined:

Inclusion criteria:

1. Adults aged from 18 to 90 years.
2. All genders.
3. Complete medical records.
4. Diagnosis radiographs with good technical quality.
5. Postoperative radiographs with good technical quality.
6. Postoperative follow-up of at least a year.
7. Patients with no previous history of fracture and/or ON of the proximal humerus.
8. Patients with no previous history of neoplasms or oncological surgeries of the proximal humerus.
9. Patients without chronic inflammatory diseases.
10. Patients who agreed to participate in this research and signed informed consent forms.

Exclusion criterion:

1. Patients who refused either to participate in this study or to sign informed consent forms.

Therefore, 164 patients with proximal humeral fractures were found, of which 120 (73.17%) underwent conservative treatment and 44 (26.83%), surgical treatment. Of the operated patients, 16 (36.36%) were men and 28 (63.63%) were women, with an average age of 61.36 years.

All fractures were categorized according to the Neer classification.[3] For each case, the chance of ON occurrence was considered positive for types 3 and 4.

The same cases were classified according to Hertel et al.[6], and the prognosis of ON occurrence was considered on a case-by-case basis to determine the situations in which it could occur.

In the postoperative period with at least a year of follow-up, patients were evaluated for the presence or absence of ON. At this stage, our evaluation aimed to verify which had greater value to predict ON occurrence.

Statistical analysis

Data were analyzed by a professional specialized in medical statistics using the IBM SPSS Statistics®, version 21, and Microsoft Excel® 2010 (Microsoft Corporation®, San Diego, USA). Categorical data were shown as frequencies and percentages and continuous numerical data, as sample means and standard deviations. The Student's t- (for normally distributed continuous numerical data from independent samples), Chi-square test (for categorical data), and Fisher's exact tests (for cases that failed to meet Chi-square criteria) were applied. Analyses were performed to characterize the sample and identify the significant variables against the ON outcome, with statistical significance of 5%. A 2×2 table was used to evaluate the accuracy of selection and exactness of the classifications in Hertel et al.[6] and Neer[3] regarding ON. Cramer's V coefficient was used to evaluate the association between variables in non-square tables.

RESULTS

Of the patients in our series, three (6.8%) developed ON. We compared the Neer[3] and Hertel et al.[6] classifications with ON positive and negative outcome groups based on a 5% significance level. Both comparisons showed no statistically significant difference: $p = 0.467$ for the Neer classification[3] (Table 1) and $p = 0.177$ for that of Hertel et al.[6] (Table 2).

Table 1. Distribution of patients according to the Neer classification and the outcome regarding the presence or absence of osteonecrosis.

		Neer classification			p-value*
		1 part N (%)	2 parts N (%)	3 parts N (%)	
Osteonecrosis	No	10 (22.7)	26 (59.1)	5 (11.4)	0.467
	Yes	0 (0)	2 (4.5)	1 (2.3)	
	Total	10 (22.7)	28 (63.6)	6 (13.6)	

* Fisher's Exact Test.
Cramer's V 19.4%, $p = 0.438$.

Table 2. Distribution of patients according to the Hertel et al. classification and the outcome regarding the presence or absence of osteonecrosis.

		Criteria according to the Hertel et al. classification				p-value*
		0 N (%)	1 N (%)	2 N (%)	3 N (%)	
Osteonecrosis	No	10 (22.7)	16 (36.4)	14 (31.8)	1 (2.3)	0.177
	Yes	0 (0)	1 (2.3)	1 (2.3)	1 (2.3)	
	Total	10 (22.7)	17 (38.6)	15 (34.1)	2 (4.5)	

* Fisher's Exact Test.
Cramer's V 38.8%, $p = 0.085$.

Following the Neer classification,[3] we classified 10 fractures (22.7%) as type 1; 28 (63.6%), as type 2; six (13.6%), as type 3; and none (0.0%), as type 4. In this group, three cases (6.8%) developed ON, two (4.5%) of type 2 and one (2.3%) of type 3. The p-value (0.467) showed no statistically significant correlation when we compared the presence or absence of ON using this classification system.

By the Hertel et al.[6] classification, 10 fractures (22.7%) failed to meet criteria for ON risk, 17 (38.6 %) met one criterion, 15 (34.1%) met two criteria, and two (4.5%) met three criteria. The p-value (0.177) showed a higher correlation for Hertel et al.[6] than Neer.[3] However, our comparison with the positive outcome showed no statistical significance since one case (2.3%) had a positive outcome for ON and met one criterion for clinical risk according to the Hertel et al. classification,[6] one (2.3%) met two criteria, and one (2.3%) met three criteria. The Neer classification[3] showed a 19.4% Cramer's V coefficient and Hertel et al.[6], 38.8% with $p = 0.438$ and $p = 0.085$, respectively. This indicates that both classifications had no statistically positive relationship when compared to the development of ON. However, we observed a higher association for the Hertel et al.[6] classification than that of Neer,[3] although without statistical representation.

To evaluate the clinical applicability and predictive value of ON outcome of the evaluated classifications, we used 2×2 tables for high and low clinical risk: for the Neer classification,[3] we considered fractures in one and two parts as low risk and in three parts as high risk; for the Hertel et al.[6] classification, we considered fractures that met no or a criterion as low risk, and those that met two or three, as high risk for ON.

The Neer classification[3] (Table 3) showed a 33.33% sensitivity, an 87.80% specificity, a 16.66% positive predictive value, and a 94.73% negative predictive value, whereas the Hertel et al.[6] classification (Table 4), a 66.66% sensitivity, a 63.41% specificity, a 11.76% PPV, and a 96.29% NPV, indicating that both tools may be more useful to identify cases with low clinical risk and predict cases that are unable to develop into a negative outcome. When we compare both tools with our sample, the Neer[3] classification showed higher specificity and that of Hertel et al.[6], higher sensitivity. Both showed similar NPV.

Table 3. Cross table between high and low clinical risk for an osteonecrosis diagnosis according to the Neer classification.

		Osteonecrosis		Total
		Yes	No	
Neer	High risk	1	5	6
	Low risk	2	36	38
	Total	3	41	44

Fisher's exact test, p = 0.363.
Low risk: fracture in one or two parts; High risk: fracture in three parts.
Sensitivity = 1/3 = 33.33%; Specificity = 36/41 = 87.80%; PPV = 1/6 = 16.66%; NPV = 36/38 = 94.73%.

Table 4. Cross table between high and low clinical risk for an osteonecrosis diagnosis according to the Neer classification.

		Osteonecrosis		Total
		Yes	No	
Hertel	High risk	2	15	17
	Low risk	1	26	27
	Total	3	41	44

Fisher's exact test, p = 0.549.
Low risk: 0 or 1 criteria; High risk: 2 or 3 criteria.
Sensitivity = 2/3 = 66.66%; Specificity = 26/41 = 63.41%; PPV = 2/17 = 11.76%; NPV = 26/27 = 96.29%.

DISCUSSION

Understanding the circulatory anatomy of the humeral head is key to justifying the important prevalence of ON of the humeral head, specifically after three or four parts are affected. However, this condition may have its genesis in more simplified fractures.[4,7] Some studies show that unfavorable functional outcomes are frequent considering displaced proximal humeral fractures with a concomitant diagnosis of ON.[8,9]

In the early stages of this process, patients are usually asymptomatic or oligosymptomatic. Arthrofibrosis and pain progressively worsen. To minimize these impacts, these fractures should undergo anatomical reduction, which would offer satisfactory results.[4,10] Surgical treatment fails to provide superior results than conservative methods,[11,12] but arthroplasty is specifically used for patients with progressive symptoms, showing better outcomes.

However, other studies showed no better outcomes for the use of prosthesis than the surgical results of open reduction with osteosynthesis and hemiarthroplasty.[11,12]

Considering older adults, primary hemiarthroplasty seems to determine more favorable results than using it as a therapeutic alternative for ON after osteosynthesis.[9]

The Neer[3] classification system is widely known and often applied in patients with proximal humeral fractures. It states that a higher number of parts of the proximal portion determines the worst outcomes. Thus, stable reduction and osteosynthesis should be the preferred method for three-part displaced fractures and hemiarthroplasty for four-part ones. In the latter group, the method would directly relate to a greater chance of developing NO.[13,14]

Our study used the classification of this author to assess if its application would be reliable for ON prognoses, as per Neer.[3] However, we found a better tendency for the Hertel et al.[6] classification, which statistically unproven.

Our study suggests that the criteria to determine ischemia in Hertel et al.[6] may be useful to in safely anticipate NO prognoses orthopedists' daily practice. However, our small sample size prohibited a statistically significant evaluation. Proper preoperative planning should also help in choosing the best therapeutic method and osteosynthesis device.

In 2015, Siebenbürger et al.[15] investigated the moment of surgery and overall complication rates in the surgical treatment of proximal humeral fractures. After analyzing 329 patients (most of classified as having two- and three-part fractures), the authors found that surgery between 48 hours to five days failed to reduce complication rates. However, surgeries performed after that period significantly decreased complication rates, such as loss of reduction, loosening of synthesis material, and ON. They noticed an ON rate of 6.4% in their cases, resembling our findings.

According to the literature, the rates of this complication after surgical reconstruction of the humeral head range from 4 to 33%. Early stable internal fixation promotes humeral head revascularization by reducing ischemia time, which would decrease ON rates.[15,16]

The glenohumeral dislocation associated with the fracture intensifies the circulatory severity of the proximal humerus as the displaced fragment has circulatory insufficiency due to the direct injury of the nutrient arteries of this segment and scarce soft tissue insertion.[17] As most fracture-dislocations occur in a younger population, orthopedic surgeons should make a major effort to restore congruence to these injuries. We consider that lower pressure determined by locked plates, the concept of biological fixation, the use of minimally invasive techniques, indirect reductions, age below 50 years, and anatomical and stable reductions provide

a substantial effect in protecting the vascular supply of the fractured humeral head.

Poor reduction and malunion seem to predispose the onset of ON. However, more research is needed to determine the causality of the relation between these factors. By analyzing the three cases of ON in our study in isolation, we observed that the poor quality of the reduction was an irrelevant factor.

This study has some limitations. Its small sample size (44 patients) and age heterogeneity (SD = 19.44) may have influenced our analysis of the correlations between the classifications to predict the outcome of interest after one year of follow-up.

CONCLUSIONS

The Neer and Hertel et al. classifications show a similar discriminative ability to identify patients at low risk for developing ON ($p = 0.467$ for the Neer classification and $p = 0.177$ for the Hertel et al. classification).

New studies with a larger number of participants and greater sample homogeneity should increase the value of evaluations of the clinical applicability and predictive capacity of the studied classifications, with greater significance and correlation considering the ON outcome. Its validity should be considered as an important support tool in the daily practice of orthopedists.

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ORIGINAL ARTICLE
SHOULDER AND ELBOW SURGERY

COMPLICATIONS AFTER SURGICAL TREATMENT OF JUPITER'S MONTEGGIA TYPE II FRACTURES

COMPLICAÇÕES APÓS TRATAMENTO CIRÚRGICO DAS FRATURAS DE MONTEGGIA TIPO II DE JUPITER

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ABSTRACT

Monteggia fracture-dislocations are rare injuries, affecting about 2–5% of the population. Jesse Jupiter subdivided Bado's Type II fractures into four types, all of which presented an associated radial head fracture. Associated chondral and ligament injuries can evolve with postoperative complications. Objective: To evaluate the incidence of complications and risk factors that may influence the postoperative outcomes of Jupiter lesions. Methods: This retrospective study was conducted with surgically treated patients. The characteristics related to fractures and surgical approaches were evaluated and these variables were correlated with radiographic and functional postoperative complications. Results: A total of 15 patients were evaluated, mostly men and with a higher prevalence of Types IIA and IID. The most frequent complications were heterotopic ossification and osteolysis around the radial head prosthesis. Postoperative instability occurred only in the lateral collateral ligament. According to MEPS functional score, 53% of the patients evolved with unfavorable outcomes. Conclusion: The studied cases evolved with high rates of postoperative complications, mainly in Jupiter's Type IID fractures and associated coronoid fractures. ***Level of Evidence III, Therapeutic Study.***

Keywords: Monteggia's Fracture. Postoperative Complications. Radial Head and Neck Fractures.

RESUMO

A fratura-luxação de Monteggia é uma lesão rara que acomete cerca de 2-5% da população. Jesse Jupiter subdividiu as fraturas tipo II de Bado em quatro tipos, todos eles associados à fratura da cabeça do rádio. As lesões condral e ligamentares associadas podem evoluir com complicações pós-operatórias. Objetivo: Avaliar a incidência das complicações e os fatores de risco que podem influenciar os resultados pós-operatórios nas fraturas de Monteggia tipo II de Jupiter. Métodos: Estudo retrospectivo com pacientes tratados cirurgicamente. Avaliaram-se as características relacionadas às fraturas e as técnicas cirúrgicas utilizadas e, em seguida, tais variáveis foram correlacionadas com complicações pós-operatórias radiográficas e funcionais. Resultados: Foram avaliados 15 pacientes, havendo predomínio do sexo masculino e maior prevalência das fraturas tipo IIA e IID. As complicações mais frequentes foram a ossificação heterotópica e a osteólise ao redor da prótese da cabeça do rádio. A instabilidade pós-operatória ocorreu somente no complexo ligamentar lateral. Funcionalmente, segundo o Mayo Elbow Performance Score, 53% dos pacientes evoluíram com resultados desfavoráveis. Conclusão: Observou-se alta taxa de complicação pós-operatória, principalmente nas fraturas tipo II-D de Jupiter e naquelas com fratura do coronoide associada. ***Nível de Evidência III, Estudo Terapêutico.***

Descritores: *Fratura de Monteggia. Complicações Pós-Operatórias. Fraturas da Cabeça e do Colo do Rádio.*

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INTRODUCTION

Monteggia fracture-dislocation is defined as a ulnar fracture associated with dislocation of the proximal radioulnar joint.[1] It is relatively rare and affects 2 to 5% of the population.[2]

Bado was the first to classify this injury into four types. He observed that in all types, the ulnar fracture and the dislocation of the radial head presented the same direction, except for Type IV, in which the radial fracture is located at the same level of the ulna.[1] Type II injuries, although theoretically associated with lower-energy trauma, can still lead to complications. The resulting chondral injury from joint fractures and associated ligament injuries can cause radiological complications, leading to heterotopic ossification, osteolysis around the prosthesis, and loosening of the prosthesis, along with pseudarthrosis

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

The study was conducted at Universidade Estadual de Campinas, Hospital Estadual Sumare Dr. Leandro Francheschini.
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as well as functional complications, such as instability, pain, and restricted elbow mobility.[3]

Jesse Jupiter observed that Bado Type II fractures (posterolateral dislocation of the radial head) could be associated with fractures at the proximal ulna, and he divided them into four types: Type IIA, which affects the proximal olecranon and the coronoid process; Type IIB, which affects the metaphyseal-diaphyseal junction and does not involve the coronoid process; Type IIC, which affects the ulnar shaft diaphysis; and Type IID, which affects the entire proximal ulna and involves the coronoid process. Every subtypes of the Jupiter classification are associated with the radial head fracture.[1,4]

Jupiter's Monteggia Type II fractures present complex surgical treatment that mainly aims to restore the ulna length and anatomic reduction of the joint. Radial head fractures can be treated with osteosynthesis, resection, or arthroplasty. Also, ligament injuries should be identified and treated. Similarly, in cases of coronoid fracture, it must be repaired for better joint stability.[5,6] Despite the adequate treatment of all lesions, postoperative complications are frequent.[7]

There are few studies that exclusively evaluate the complications of Jupiter's Monteggia Type II fractures. Most articles bring a miscellany of complex elbow injuries such as Hotchkiss' terrible triad, Monteggia, and transolecranial fractures.[2,3,5,8-11]

Objectives

This study main objective was to evaluate the incidence of postoperative and secondary radiographic and functional complications. Additionally, it aims to correlate possible risk factors that may influence the functional outcome of the elbow after surgical treatment of Jupiter's Monteggia Type II fractures.

METHODS

This is a retrospective study that reviews the medical records of participants who underwent surgery for correction of Jupiter's Monteggia Type II fractures at a Reference Hospital from 2019 to 2021.

The inclusion criteria were:

a. surgically treated Monteggia Type II fractures according to Jupiter's classification
b. a minimum follow-up time of one year after surgery
c. have pre- and postoperative radiograph images in anteroposterior and lateral views for classification of fractures and evaluation of complications
d. have preoperative tomography for classification of fractures

The exclusion criteria were:

a. patients who did not sign an informed consent form
b. patients who did not have complete information in their medical records
c. patients who had associated fractures in the ipsilateral limb or polytraumatized patients.

All participants signed an informed consent form.

The Mayo Elbow Performance Score (MEPS) was applied to assess postoperative elbow function. Moreover, demographic data were evaluated, including gender and age, along with the affected side and the specific subtype of Monteggia Type II fractures according to Jupiter's classification.

Orthopedic physicians, who did not participate in the surgical treatment, conducted the radiological evaluation using the Synapse® program. Consolidation was considered complete when the fracture line disappeared completely (primary consolidation) or when complete cortical bridging in three cortices were found (when primary consolidation was not achieved). Also, the formation of heterotopic ossification,[7] the presence of radial head subluxations or radial head prosthesis, the presence of osteolysis and/or radiographic loosening around the radial head prosthesis were evaluated. Osteolysis was considered when radiological examination identified signs of radiolucency around the prosthesis stem.[2]

Surgeries were performed with the patients in lateral decubitus position, using the global posterior approach to expose the elbow. In cases of comminuted ulnar fractures (Jupiter Type IID), the treatment procedure initially addressed radial head fracture via osteosynthesis using a 2.7 mm plate and/or Herbert screw. Arthroplasty (Metabio® prosthesis) was used as an alternative approach. Ulnar fractures were treated with a 3.5 mm reconstruction plate, and the coronoid fractures were treated with traction screws or support plates. Small coronoid fragments were fixed with transosseous sutures. After approaching the ulna and the radial head, joint stability was tested and, if there were signs of lateral or medial instability, the repair was performed with a 3.5 mm anchor.

The Monteggia Type II fractures according to Jupiter and the incidence of complications were compared by the Chi-square test or Fisher's exact test. Non-categorical variables were tested by the Kolmogorov-Smirnov test. Thus, in the study of these variables, both unpaired *t*-test (parametric variables) and Pearson's test were used. All analyses were conducted using PASW Statistics 28.0 program (SPSS Inc., Chicago, USA), adopting a 5% significance level ($p < 0.05$).

The study was approved by the local Research Ethics Committee under number 58417322.9.0000.5404

RESULTS

A total of 15 patients were evaluated after inclusion criteria. The mean age was 53 ± 15 years. The youngest patient was 29 years old and the oldest was 80 years old.

Patients' mean follow-up time was at least one year after surgery (23.2 ± 8.9 months). Most participants were men (twice higher than women) and the left side was the most affected.

Most patients who underwent radial head replacement developed signs of osteolysis around the prosthesis but none of the arthroplasties showed migration or loosening. However, all patients remained asymptomatic and, therefore, were not surgically reapproached (Figure 1).

Postoperative radiographs

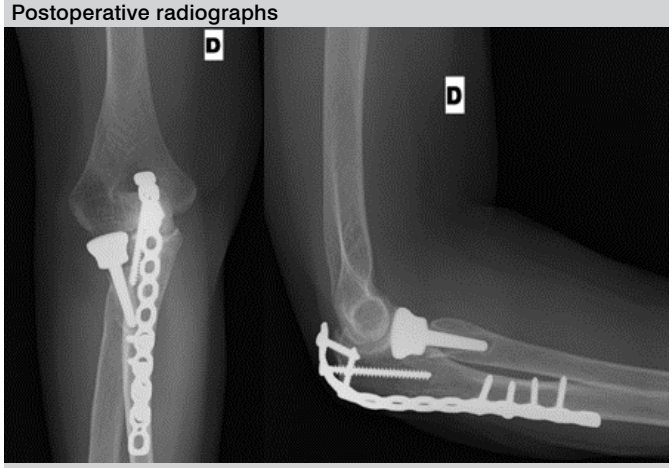

Figure 1. Osteolysis around the radial head prosthesis as a complication.

The main postoperative instability occurred in the lateral collateral ligament with evolution to posterolateral rotatory instability. One case was subjected to lateral ligament reconstruction using the ipsilateral palmaris longus tendon and two cases were subjected to prosthesis removal since it presented, in addition to instability, signs of component loosening (Figure 2).

Postoperative radiographs

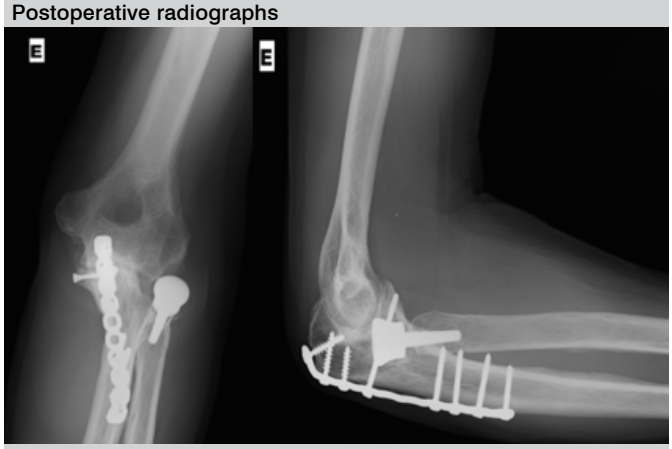

Figure 2. Posterolateral rotatory instability of the elbow as a complication.

The most prevalent fracture was Jupiter Type IIA (seven cases) followed by IID (five cases) (Table 1).
The most frequent complications were heterotopic ossification and osteolysis around the radial head prosthesis (Table 2).
The only case of pseudarthrosis evolved asymptomatically, requiring no surgical treatment.
According to the MEPS functional score: six patients had excellent results, one patient had good results, two patients had fair results, and six patients had poor results. Thus, 53% of patients evolved to an unfavorable functional outcome. Table 3 illustrates the patients' functional outcomes (Table 3).
The presence of the coronoid fracture ($p = 0.005$) and the Jupiter Type IID fracture ($p = 0.006$) evolved with functional worsening (MEPS score).

Table 1. Description of demographic data.

Characteristic	Value
Age [mean (± SD)] (years)	53.15 ± 15.0
Gender [No. (%)]	
Men	10 (66.7)
Women	5 (33.3)
Jupiter classification [No. (%)]	
IIA	7 (46.7)
IIB	2 (13.3)
IIC	1 (6.7)
IID	5 (33.3)
Affected side [No. (%)]	
Right	5 (33.3)
Left	10 (66.7)

Table 2. Incidence of postoperative complications.

Complication	Value
Heterotopic ossification (n/%)	7 (46.7)
Osteolysis around prosthesis (n/%)	7 (80)
Elbow instability	3 (20)
Pseudarthrosis	1 (6.6)

N: number; %: percentage.

Table 3. Patients' functional outcomes – Mayo Elbow Performance Score (MEPS) distribution per patient and total values (mean ± SD).

	Patient	Pain (points)	ROM (points)	Stability (points)	Daily Function (points)	Total (points)
	1	45	20	10	25	100
	2	45	15	10	0	70
	3	15	15	5	0	35
	4	15	15	10	20	60
	5	45	20	10	25	100
	6	45	20	10	25	100
	7	45	20	10	25	100
	8	30	20	10	20	80
	9	15	15	5	0	35
	10	45	20	10	25	100
	11	45	20	0	25	90
	12	15	5	0	0	20
	13	15	15	10	0	40
	14	0	5	0	10	15
	15	0	5	5	0	10
Total (mean ± SD)	15	28 ± 17.2	15.3 ± 5.6	7 ± 4	13.3 ± 11.4	63.6 ± 33.6

SD: standard deviation; ROM: range of motion.

Radial head replacement did not evolve with functional difference when compared to osteosynthesis.
Furthermore, the progression to pseudarthrosis, presence of osteolysis, whether or not associated with prosthesis loosening, and the presence of heterotopic ossification did not influence the functional outcome (Table 4).

Table 4. Correlation between the various factors and MEPS – association of MEPS with complications.

	Values according to MEPS Score (Mean ± SD)			
Characteristic	**Presence**	**Absence**	**CI**	**P-value[a]**
Osteolysis (Prosthesis)	72.14 ± 37.62	60.00 ± 34.46	–59.38–35.10	0.28
Coronoid fracture	56.25 ± 34.91	93.3 ± 11.54	10.5-63.6	0.005
Loosening (prosthesis)	50.00 ± 36.05	67.08 ± 35.25	–32.25–66.42	0.74
Jupiter Type IID	35.00 ± 22.91	78 ± 31.10	8.87–77.12	0.006
Heterotopic ossification	61.43 ± 38.0	65.63 ± 34.27	–36.68–45.07	0.41

[a] T-test; CI: confidence interval.

DISCUSSION

Jupiter's Monteggia Type II fractures are rare and can affect older patients with low bone density as a result of low-energy trauma.[8] However, such injuries can also occur due to high-energy trauma, especially with direct impact to the anterior or posterior elbow, such as a direct blow.[6] In our study, the highest prevalence was observed in young men (66.7%), which differs from some European studies that reported a higher prevalence in women.[2,3] This difference may be related to the higher incidence of traffic accidents in developing countries like Brazil.[9] High-energy traumas result in more significant chondral injuries and may have a greater potential for complications.[4]

Jupiter Type IIA (46.7%) and Type IID (33.3%) were the most prevalent fractures in our study. Laun et al.[2] and Calderazzi et al.[3] observed a higher prevalence of Type IIB, probably reflecting a demographic profile of older patients with lower-energy fractures when compared to our results.[10]

The sum of Type IIA and IID lesions found in our results represents 80% of the cases. Therefore, only 20% of patients did not have a fracture of the coronoid process associated with the presence of the coronoid fracture. The coronoid process, which is an important restrictor of the elbow, can generate joint instability when fractured. The literature diverges in whether the presence of the coronoid fracture may be a factor for worse prognosis. Our results corroborate a study by Suarez, Barquet, and Fresco,[12] who observed worse functional outcomes.[4,13] However, in the study by Chemama et al.[14] in 2010, better MEPS values were observed for patients who underwent fixation of the coronoid process compared to those who were not fixed, but the authors did not perform statistical analysis of their results.[15]

Heterotopic ossification is a common complication in joint fractures, especially around the elbow.[7,12] Although ossification occurred in 46.7% of cases, this complication did not result in functional worsening, probably because it did not lead to a decrease in the elbow range of motion. Egol et al.[16] described the development of heterotopic ossification in 22% of the patients studied and did not correlate ossification with functional worsening.

Most patients underwent radial head arthroplasty. Radial head fractures located in the articular surface of the proximal radioulnar joint or involving more than three fragments are difficult to treat with rigid osteosynthesis that allows early mobility, thus requiring prosthetic replacement.[17] According to MEPS, no disparities were found between patients who underwent arthroplasty and osteosynthesis. However, the literature presents no conclusion regarding the best approach to elbow fractures/dislocations associated with radial head fractures.[6,11,16,17] Konrad et al.[6] and Egol et al.[16] reviewed cases similar to ours and observed no differences in functional scores regardless of how the radial head replacement was conducted, corroborating our outcomes. However, Ring, Jupiter, and Simpson[18] identified 26 patients with Bado Type II fractures associated with radial head fracture. There were seven Mason II and 19 Mason III fractures, and the cases were treated with different approaches, that is, from conservative management to radial head excision, open reduction internal fixation (ORIF), and prosthetic replacement. However, the authors noted that all patients obtained unsatisfactory results.[11] Similarly, Matar et al.,[17] in their study series with 18 patients, concluded that the postoperative functional outcome of their patients did not depend on the severity of the fracture, but rather on how the fracture was surgically treated.

Osteolysis around the stem of the radial head prosthesis occurred in 80% of the patients, with 42% experiencing migration (loosening). However, it was necessary to remove or revise the component in no patient. The presence of osteolysis or prosthesis loosening was not correlated with a functional worsening. Some articles agree that radiological signs of loosening may evolve without functional changes because mobility, especially in pronation-supination, occurs in the stem of the prosthesis, which has a minimal impact on the range of motion of the elbow.[2]

Only one case evolved to ulnar pseudarthrosis, which was asymptomatic. Thus, there was no need for a additional surgical procedures. Probably, since there was no associated plate breakage, sufficient stability was achieved at the fracture site, resulting in minimal local pain. High-energy fractures, especially open fractures, can cause bone devascularization, increasing the likelihood of progressing to pseudarthrosis.[19]

The case of posterolateral instability, which did not present clinical loosening of the radial head prosthesis, underwent lateral ligament reconstruction using an ipsilateral palmaris longus tendon graft. However, there was no functional discrepancy observed between the use of the prosthesis, ORIF, or resection in the studied patients. Laun et al.,[2] did not observe any case of postoperative instability. On the other hand, Ring, Jupiter, and Simpson[18] observed that several complications required early reoperation in nine of their patients and, in one of these cases, there was persistent ulnohumeral instability. They believed, retrospectively, that this instability was due to posterolateral rotatory instability resulting from damage to the lateral collateral ligament caused by posterior displacement of the radial head and residual malalignment of the coronoid process.[18]

According to the MEPS functional score, 53% of the patients evolved with unfavorable outcomes. The mean score was 63.3 points. However, radial head replacement did not evolve with functional difference when compared to osteosynthesis. With a score value closer to that found in our study, Matar et al.[17] obtained a mean MEPS score of 76.6 points, also not showing statistical difference in the way that the radial head fracture was managed. Giannicola et al.[5] obtained a score of 98 points; however, their study encompasses a range of complex elbow injuries, not limited to Jupiter's Monteggia Type II fractures.

The presence of the coronoid fracture ($p = 0.005$) and the Jupiter Type IID fracture evolved with functional worsening (MEPS score). Egol et al.[16] mentioned that Jupiter's Type IID fractures had a higher chance of pseudarthrosis and need for a new surgical approach with worse functional outcomes. Josten and Freitag,[20] observed that patients with Type IIA fractures evolved with decreased elbow range of motion and required additional surgical procedures. Konrad et al.[6] observed that Types B and C fractures usually evolve with good or excellent results, whereas Types A and D fractures presented worse functional outcomes. Furthermore, Type IIA fractures have the worst long-term functional evolution.

Our study has some limitations such as the retrospective design and small sample size. However, most studies on this topic include various types of complex elbow fractures, rather than specifically focusing on Monteggia Type II fractures according to Jupiter's classification.

CONCLUSION

Jupiter's Monteggia Type II fractures evolved with high rates of postoperative complications. The main complications were elbow functional worsening and osteolysis around the radial head prosthesis. Jupiter's Type IID fractures and associated coronoid fractures evolved with worse functional outcomes. The main reason for reoperation was posterolateral rotatory instability of the elbow.

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REASSESSMENT OF FATTY INFILTRATION BY MAGNETIC RESONANCE TEN YEARS AFTER ROTATOR CUFF INJURY REPAIR

REAVALIAÇÃO DA INFILTRAÇÃO GORDUROSA POR RESSONÂNCIA MAGNÉTICA APÓS DEZ ANOS DE REPARO DE LESÃO DO MANGUITO ROTADOR

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ABSTRACT

Quantitative assessments of rotator cuff muscle changes after successful tendon repair are scarce. On the other hand, semi-quantitative and subjective assessments are more abundant, but their findings are controversial. One hypothesis about this divergence is that there is an immediate decrease in the proportion of fatty infiltration after surgical repair. Objective: Reassess fatty infiltration and muscle trophism of the rotator cuff after ten years of repair. Methods: Prospective comparison study. A total of 10 patients diagnosed with rotator cuff injury underwent repair of the lesion, and MRI of the affected shoulder was performed in the preoperative, immediate postoperative, and late postoperative periods (ten years). A comparative study was performed at every moment. Results: At 5% significance level, the mean of the immediate postoperative period was higher for the variable trophism and true muscle percentage. Fatty infiltration showed no difference in the three periods observed. Conclusion: Fatty infiltration does not change in the three periods evaluated and muscle trophism is greater in the immediate postoperative period. After ten years of rotator cuff repair, muscle trophism and fatty infiltration remain with statistically significantly equal results when compared to the preoperative period. ***Level of Evidence II, Prospective Comparison Study.***

Keywords: Rotator Cuff. Muscular Atrophy. Magnetic Resonance Spectroscopy.

RESUMO

Avaliações quantitativas das mudanças musculares do manguito rotador após reparos bem-sucedidos são escassas. Em contrapartida, avaliações semiquantitativas e subjetivas são mais abundantes, porém com achados controversos. Uma hipótese sobre essa discrepância é que a diminuição imediata na proporção de gordura que ocorre logo após o reparo. Objetivo: Reavaliar a infiltração gordurosa e o trofismo muscular do manguito rotador passados dez anos do reparo. Métodos: Estudo prospectivo comparativo realizado com dez pacientes diagnosticados com lesão do manguito rotador que foram submetidos a reparo da lesão e exames de ressonância magnética do ombro acometido no pré-operatório, no pós-operatório imediato e no pós-operatório tardio (dez anos), a fim de comparar as mudanças musculares em cada momento. Resultados: Ao nível de significância de 5%, a média do pós-operatório imediato foi superior para as variáveis trofismo e porcentagem muscular verdadeira. A infiltração gordurosa não apresentou diferença nos três períodos observados. Conclusão: A infiltração gordurosa não se altera nos três períodos avaliados, e o trofismo muscular é maior no pós-operatório imediato. Após dez anos do reparo do manguito rotador, o trofismo muscular e a infiltração gordurosa se mantêm com resultados estatísticos significativamente iguais quando comparados com o pré-operatório. ***Nível de Evidência II, Estudo Prospectivo Comparativo.***

Descritores: *Manguito Rotador. Atrofia Muscular. Espectroscopia de Ressonância Magnética.*

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INTRODUCTION

Rotator cuff injuries are common causes of musculoskeletal problems with a prevalence of 15 to 51% in the population, with a higher incidence in patients over 50 years.[1] After rotator cuff injury, muscle retraction occurs, causing degenerative tissue changes (fatty infiltration and atrophy),[2] which some authors consider progressive

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The study was conducted at Santa Casa de Misericordia de Sao Paulo.
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and irreversible.[3-5] Both muscle atrophy and fatty infiltration have a substantial influence on the clinical results of rotator cuff repair and on the re-rotation rate, and therefore interfere with management.[5,6] Quantitative assessments of rotator cuff muscle changes after successful tendon repair are scarce.[7] In contrast, semiquantitative and subjective assessments are more abundant, but their findings are controversial: some authors report that the degenerative changes are irreversible[5,8,9] whereas others report recovery of muscle atrophy or even fatty infiltration.[10-12] One hypothesis about this divergence is that there is an immediate decrease in the proportion of fat (in addition to an increase in the occupancy of the muscle in its fossa) soon after surgical repair. This is probably due to the traction exerted on the tendon at the time of its repair[6,13] since the muscle-tendon unit is pulled in the coronal plane of the scapula and the evaluation is usually performed in a fixed sagittal plane perpendicular to that of the traction.[14]

Precisely to study this hypothesis, in a previous study[6] we evaluated degenerative changes in the muscles of the supraspinatus comparing preoperative and immediate postoperative (POi) magnetic resonance imaging (MRI) scans of ten patients subjected to repair of rotator cuff injury, and concluded that there is an immediate increase in the muscle occupancy of the supraspinatus in its fossa. This study aims to reevaluate the same patients from the first study, approximately ten years later, and to compare the current results with the previous ones.[6] Our hypotheses are that over the course of the follow-up: (1) in cases with maintenance of repair integrity, fatty infiltration is unchanged and muscle trophism is increased; (2) in cases of loss of repair, fatty infiltration is increased and muscle trophism is decreased.

METHODS

This study was conducted from September 2011 to December 2011 in a tertiary hospital located in the city of São Paulo. A total of 10 patients (four men and six women) diagnosed with complete rotator cuff injury (MRL) were subjected to repair of the lesion, arthroscopic or open. MRI examinations of the affected shoulder were performed in the preoperative (at most one month before surgery) (Pre-op) and immediate postoperative (IPO) (at most one month after surgery). On that occasion, the area and muscle volume in the supraspinatus fossa were evaluated, comparing the pre- and immediate postoperative measurements. For this study, a new MRI was performed in a third moment, about ten years after surgery (POlate) (mean of 9.6 years, ranging from 9.5 to 10.1 years). The inclusion criteria in this study were the same: patients previously subjected to rotator cuff injury repair and evaluated in the previous study[6] with sufficient data for comparison of the preoperative, immediate postoperative, and ten years postoperative. A total of two of these 10 initial cases were excluded due to the impossibility of contact for reevaluation, plus one case that underwent a reverse total shoulder arthroplasty and another that refused to be part of the study. Thus, six patients were reassessed.

The six patients had a mean age of 71.6 years at the time of the last reassessment (65 to 75 years). They were five women and one man. In all cases, the lesions affected exclusively the supraspinatus and infraspinatus tendons. Table 1 shows other data regarding the types of lesions found and the procedures performed.

All MRI scans were performed in a high-field 1.5 Tesla equipment (Achieva, Philips Medical Systems, Holanda B.V.®). T1- and T2-weighted sagittal and coronal oblique images were obtained with reference to the glenoid cavity, as well as proton density-weighted images in the axial plane.

The MRI images were analyzed in the report program of the Department of Radiology and Diagnostic Imaging (IMPAX Agility 8.1.2 SP7.7 – Agfa Healthcare®) and evaluated by two radiologists. One of them was in the specialization phase in the area of musculoskeletal radiology and the other was already sub-specialized in the area for more than 15 years. Both evaluators had access to the patients' previous images and knew that the estimation was intended for a scientific study. There was no blinding. Each one estimated the measures only once, and the result used in this study was the average of these two measures for each variable.

Table 1. Data on patient injury and surgical procedure.

	Size of injury*	Surgical procedure	Acromioplasty	Tenotomy LHB
1	Medium	Arthroscopy	Yes	No
2	Large	Open	Yes	No
3	Medium	Arthroscopy	Yes	Yes
4	Medium	Arthroscopy	Yes	No
5	Large	Arthroscopy	No	Yes
6	Large	Arthroscopy	Yes	No

LHB: long head of the biceps brachii muscle.
*According to Cofield's classification.[15]

The T1-weighted oblique sagittal sequence, in which fat is observed with high signal and muscle with intermediate signal, was the sequence chosen for the evaluations. The chosen section was the most lateral in which the spine of the scapula is evidenced in continuity with the body, forming a "Y" (Figure 1). Once selected, the image was saved as a file and opened in Adobe Photoshop CS6®. The quick selection tool, which automatically selects areas of similar brightness, was used.

For each MRI in the entire study, three measurements were performed: area of the supraspinal fossa (called "Fossa") (Figure 2); area of the supraspinatus muscular belly (contour of muscle mass) (called "Belly") (Figure 3); and area of remaining supraspinatus muscle fibers (contour of high-signal regions on T1-weighted sequences) (called "musc") (Figure 4).

From these three measurements, two other proportions were estimated: Muscle Trophism (= Belly/Fossa) and Fatty Infiltration (= 1-[Musc/Belly]). The variation between the proportions of POlate and IPO was interpreted as a dependent variable.

The Friedman test was used to evaluate if muscle trophism, fatty infiltration, and muscle percentage changed over time, that is, if time (preoperative, postoperative, and evaluation after ten years) influenced the variables mentioned above.

This work was submitted and approved by the Research Ethics Committee under opinion: CAAE 45571621.7.0000.5479. All patients in the study signed the informed consent form.

Figure 1. Sagittal section used to assess T1-weighted fatty infiltration.

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Figure 2. Area of the supraspinatus fossa.

Figure 3. Area of the supraspinatus muscular belly.

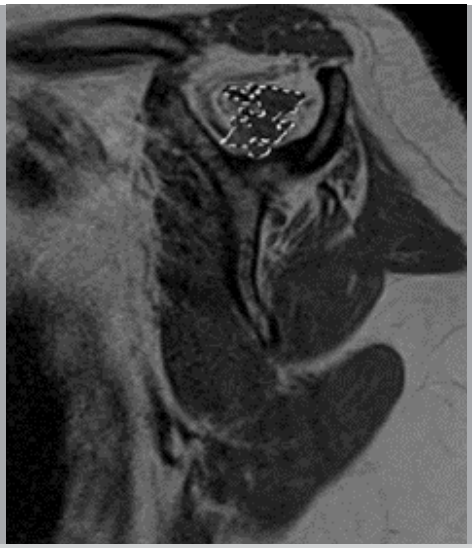

Figure 4. Area of remaining supraspinatus muscle fibers.

RESULTS

Table 2 presents the muscle percentages of the supraspinatus muscle in the suprascapular fossa and the fatty infiltration of the six patients on three occasions: preoperative, immediate postoperative, and late postoperative.

The preoperative group had a mean value of 0.315 for the true muscle percentage in the fossa, ranging from 0.173 to 0.419; the immediate postoperative group had a mean value of 0.389, ranging from 0.226 to 0.497; and the late postoperative group had a mean value of 0.286, ranging from 0.162 to 0.385.

Table 2. Muscle percentages of the supraspinatus muscle in the suprascapular fossa.

	Preoperative		Postoperative		Postoperative ten years later	
	SF	FI	SF	FI	SF	FI
1	0.323	0.94	0.355	0.84	0.162	0.84
2	0.397	0.89	0.497	0.89	0.376	0.93
3	0.269	0.72	0.319	0.79	0.253	0.79
4	0.419	0.84	0.461	0.75	0.325	0.81
5	0.173	0.78	0.226	0.75	0.218	0.85
6	0.313	0.78	0.484	0.97	0.385	0.78

SF: area of muscle occupancy in the supraspinatus fossa; FI: fatty infiltration (%muscle).

Muscle trophism

Friedman's test rejected the hypothesis that conditions did not influence trophism ($p = 0.009$).

At the 5% significance level, the mean of the variable Trophism was higher in the immediate postoperative compared with the other conditions (Figure 5).

Fatty infiltration

Friedman's test did not rejected the hypothesis that conditions did not influence trophism ($p = 0.638$).

We thus conclude that there was no difference in the infiltration variable in the three occasions observed (Figure 6).

Muscle percentage

Friedman's test rejected the hypothesis that the conditions did not influence Musc ($p = 0.009$)

At the 5% significance level, the mean of the variable Musc was higher in the immediate postoperative compared with the other conditions (Figure 7).

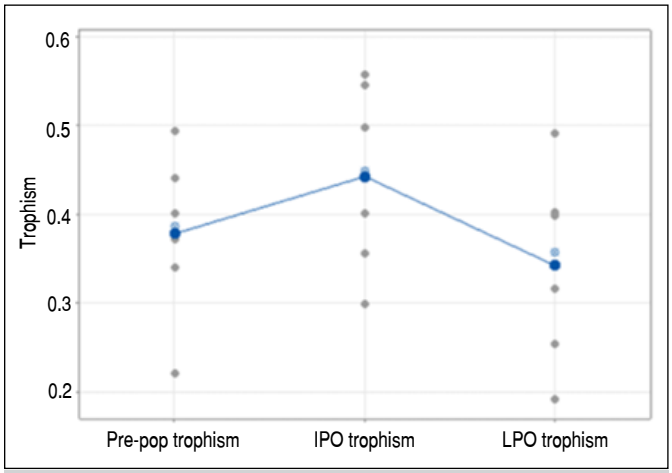

Figure 5. Graph of individual values for the trophism variable, emphasizing the means and medians.
Pre-op: preoperative; IPO: immediate postoperative; LPO: late postoperative.

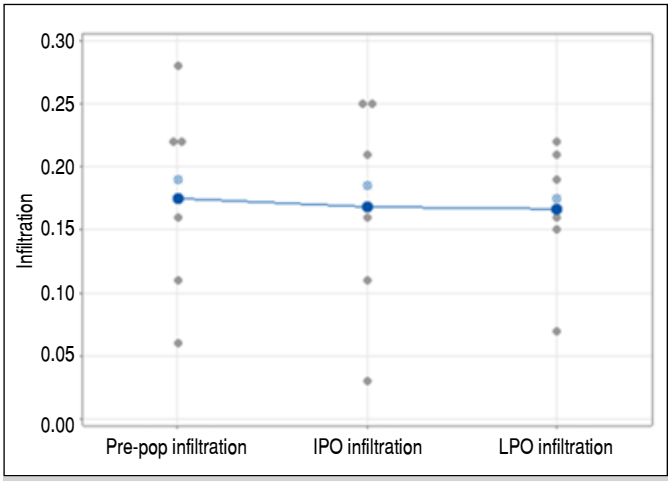

Figure 6. Graph of individual values for the infiltration variable, emphasizing the means and medians.
Pre-op: preoperative; IPO: immediate postoperative; LPO: late postoperative.

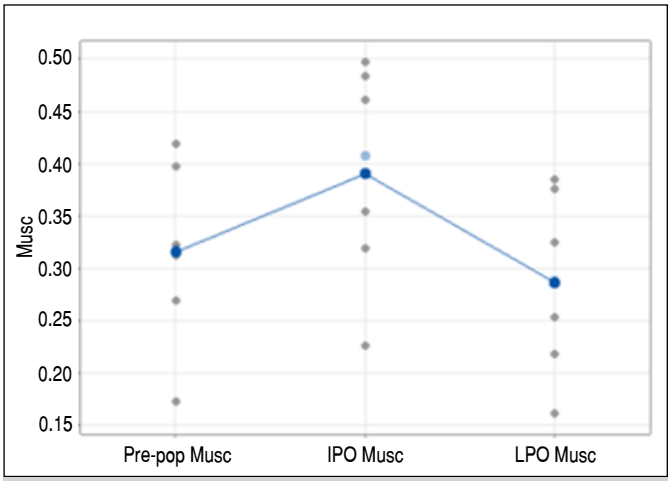

Figure 7. Graph of individual values for the Musc variable, emphasizing the means and medians.
Pre-op: preoperative; IPO: immediate postoperative; LPO: late postoperative; Musc: area of remaining supraspinatus muscle fibers.

Next, the Anderson-Darling goodness of fit tests were performed for all variables, concluding that the distributions of all variables fitted the normal distribution. Thus, to evaluate the existence of linear relationships, Pearson's correlation coefficient was used.
At 5% significance level, only IPO Trophism and Pre-op Trophism showed a linear (increasing) relationship ($p = 0.007$).
At 5% significance level, no linear correlation was significant in relation to fatty infiltration.
At 5% significance level, IPO Musc and Pre-op Musc ($p = 0.023$) and IPO Musc and LTO Musc ($p = 0.050$) showed linear (increasing) relationship.
The small sample size made it impossible to analyze the impact of the variable "reinjury" on the outcomes "Trophism," "Fatty infiltration," and "% Musc". Therefore, it was presented only descriptively (Table 3).

DISCUSSION

Muscle atrophy and fatty infiltration lead to loss of muscle elasticity and strength and are associated with outcomes of surgical rotator cuff repair.[13] Both atrophy and fatty degeneration progress with non-surgical treatments.[16] Repair results in decreased pain and functional improvement of the shoulder, but the effects of repair on muscle trophism and fatty infiltration are still controversial.[17]
In 2007, Liem et al.[5] conducted a study with 53 patients subjected to repair of rotator cuff injuries (RCI), evaluated with MRI after two years, showing an irreversibility of both trophism and fatty infiltration. These results were confirmed by Gladstone et al.[8] in the same year. In the study, the 38 patients subjected to repair and evaluated one year later with MRI showed irreversibility of trophism or fatty infiltration, even in successful repairs.
In 1997, Thomazeau et al.,[18] conducted a study with 30 patients subjected to RCI repair and reevaluated two years later: there was reversibility of muscle trophism in half of the patients in whom the repair remained intact. Gerber et al.[19] did not obtain the same result regarding trophism with patients subjected to repair of extensive lesions and evaluated two years later, but did show a significant improvement in fatty infiltration.
In 2016, Parker et al.[13] evaluated 47 patients with MRI studies, finding a small statistical improvement in trophism after 2 years of follow-up (11.3% to 13.9 %), and it was not possible to prove a statistical improvement in relation to fatty infiltration.
In this controversial scenario, Kim, Yoo and Jeong[17] conducted a study with comparative times points (preoperative; immediate postoperative [IPO] and late postoperative [LPO] at six months) to further elucidate this issue. The authors showed significant improvements in both muscle trophism and fatty infiltration in the IPO compared to the preoperative. These results are partially in line with our study, in which muscle tropism was significantly improved in IPO, but fatty infiltration was not. Kim, Yoo and Jeong[17] also compared preoperative with LPO, as well as IPO with LPO. Their results showed no significant improvement in fatty infiltration or muscle trophism comparing either the preoperative with LPO or IPO with LPO.
Our study performed a prolonged follow-up (with a LPO close to ten years) at three time points (preoperative, IPO, and LPO). It evidenced that fatty infiltration does not change at any time point and that muscle trophism and the true muscular percentage of supraspinatus are higher at IPO compared to both preoperative and LPO. It also showed no difference for any of the variables analyzed in the preoperative and the LPO.
We think that the improvement in muscle trophism in the immediate postoperative can be explained in two ways: either there is a true improvement, or there is a misinterpretation. The reduction of the tendon in the surgical procedure changes the muscle area evaluated, while the standardized scapular plane is maintained, generating a bias.[13] Another factor that alters the interpretation of the exam in cases of IPO evaluation is that the presence of saline solution in the subacromial space or local edema may hinder the evaluation.[17]
Over time, RCI in cases not treated surgically lead to the increase of muscle trophism and fatty infiltration,[16] but the outcomes of cases with surgical repair and reinjury may differ; we thus sought to evaluate, with statistical significance, the relationship of repair

Table 3. Descriptive statistics for the variables trophism, infiltration, and muscle, in the three conditions, in the groups without reinjury and with reinjury.

Variable	Pre-op trophism		IPO trophism		LPO trophism		Pre-op infiltration		IPO infiltration		LPO infiltration		Pre-op Musc		IPO Musc		LPO Musc	
Reinjury	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Medium	0.421	0.357	0.5275	0.4005	0.4465	0.2903	0.165	0.18	0.07	0.2175	0.145	0.1775	0.355	0.296	0.4905	0.3402	0.3805	0.2395

Pre-op: preoperative; IPO: immediate postoperative; LPO: late postoperative; Musc: area of remaining supraspinatus muscle fibers.

integrity and the result of the variables trophism and fatty infiltration in LPO. However, due to the low number of patients reevaluated, it was not possible. We believe that further studies with larger samples are important.

The strengths of this study were: (1) imaging studies performed with MRI; (2) standardization in the performance of the exams (3) long postoperative follow-up (approximately ten years). The limitations were: (1) small sample size (six patients) (2) lack of correlation between imaging results and functional results.

CONCLUSION

Muscle trophism and the true muscle percentage of the supraspinatus in its fossa are higher in the immediate postoperative compared to the preoperative and late postoperative (ten years). Fatty infiltration does not change.

After ten years of rotator cuff repair, muscle trophism and fatty infiltration remain statistically significantly equal when compared with the preoperative moment.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. ANM, LAS, GVS, CSC: preparation of the research project, statistical analysis, review and concept of the article; JCAM, VMM: writing of the article, concept, data collection and analysis.

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SURGICAL TREATMENT OF CLAVICLE FRACTURES: A DESCRIPTIVE ANALYSIS OF 88 CASES

TRATAMENTO CIRÚRGICO DAS FRATURAS DE CLAVÍCULA: UMA ANÁLISE DESCRITIVA DE 88 CASOS

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ABSTRACT

Clavicle fractures are one of the most common types of bone injuries in adults. Recently, the treatment protocol for these fractures has undergone changes. Objective: To better understand the epidemiological and behavioral profile of these lesions when they require surgical treatment. Methods: This is an analysis of a series of cases. Our sample included individuals undergoing surgical treatment for clavicle fractures. Results: In total, 88 subjects fulfilled the predetermined criteria. Among these, 75 (85.22%) were male; automobile accidents corresponded to the largest etiological group, reaching 48% of prevalence; there was a slight predominance of the right side, totaling 45 cases (51%); most fractures were classified as Allman type I; an infection rate was observed in 1.13% of the cases; and the development of pseudarthrosis was identified in 2.27% of the patients. Conclusion: The incidence of clavicle fracture is higher in young men, mainly caused by car accidents, being mostly located in the middle third. No statistical significance was found between the synthesis material data and the postoperative complication rate, revealing the absence of risk superiority between the different types of surgical approaches used. ***Level of Evidence IV, Case Series.***

Keywords: Fracture Fixation. Clavicle. Epidemiology.

RESUMO

As fraturas de clavícula consistem em um dos tipos mais comuns de lesões ósseas na população adulta. O protocolo de tratamento dessas fraturas tem sofrido modificações. Objetivo: Compreender melhor o perfil epidemiológico e comportamental das lesões de clavícula submetidas a tratamento cirúrgico. Métodos: Análise de uma série de casos, cuja amostragem incluiu indivíduos submetidos à abordagem cirúrgica de fratura de clavícula. Resultados: No total, 88 indivíduos preencheram os critérios pré-determinados. Dentre estes, 75 (85,22%) eram do sexo masculino; o acidente automobilístico correspondeu ao maior grupo etiológico (48%); houve ligeira predominância do lado direito, totalizando 45 casos (51%); a maior parte das fraturas foi classificada como Allman tipo I; observou-se uma taxa de infecção em 1,13% dos casos; e o desenvolvimento de pseudoartrose foi identificado em 2,27% dos pacientes. Conclusão: A incidência de fratura de clavícula é maior em homens jovens, ocasionada principalmente por acidentes automobilísticos, sendo, na maioria dos casos, localizada no terço médio. Não foi encontrada significância estatística entre os dados do material de síntese e o índice de complicação pós-operatória, revelando a ausência de superioridade de risco entre os diferentes tipos de abordagem cirúrgica. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Fixação de Fratura. Clavícula. Epidemiologia.*

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INTRODUCTION

Clavicle fractures are one of the most common types of bone injuries in adults, accounting for about 2.6% of all fractures and 44.1% of fractures among the shoulder bones.[1-3] Recently, the treatment protocol for clavicle fractures has undergone changes due to the evident superiority of surgeries regarding the development of functional sequelae.[2] Moreover, several studies have reported an increase in the prevalence of clavicle fractures in recent decades and it is believed that this raise is mainly due to the increase in the practice of sports and in the use of motorcycle vehicles,[3] valuing the focus on the study of the treatment of these injuries.

The objective of this retrospective study is to better understand the epidemiological and behavioral profile of postoperative clavicle fractures subjected to surgery for a period of six years in a tertiary hospital.

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

The study was conducted at Vitoria Apart Hospital.
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METHODS

This is an observational and cross-sectional study, with a sample including both males and females, without age restriction, who have been subjected to the surgical approach of clavicle fracture from February 2014 to May 2020 in a specialized orthopedic center.

The research was approved by the Research Ethics Committee registered in the Brazil Platform under the CAAE no. 51097521.4.0000.5073, following the guidelines of resolution 446/12 of the National Health Council, Brazilian Ministry of Health.

The inclusion criteria attributed to the research were: (1) use of surgical coding 3.07.17.10-8 (Brazilian Hierarchical Classification of Medical Procedures – CBHPM) with the term "fracture and/or dislocations and/or avulsions – surgical treatment" in medical records and (2) date of care from February 2014 to May 2020. The exclusion criteria were: (1) association and/or reference to surgical approaches involving distinct structures and (2) absence of complete data in medical records.

Regarding the surgical technique used, the patients were stationed in a beach chair position, as Hoppenfeld[4] indicates, and the palpation of the clavicle was performed to locate the focus of the fracture and determine the extent of the incision. Immediately after, an S-shaped anterosuperior incision was made, starting at the medial extremity, followed by a dissection by planes of the soft parts of the subcutaneous face of the clavicle in the subperiosteal plane to expose the lesion. After this step, reduction and internal fixation (absolute or relative, depending on the fracture profile) were performed with the use of plates and screws. In cases of Allman II fracture, fixation was performed with Kirschner wires in association with anchor fixation in the coracoid or subcoracoid ligature.

In total, 88 individuals met the predetermined criteria and were included in the research. The clinical variables analyzed were: (1) age; (2) sex; (3) affected side; (4) mechanism of trauma; (5) fracture classification according to Allman's description; (6) synthesis material used in surgical treatment; (7) need for reoperation; (8) development of operative complications; and (9) associated lesions.

Demographic data were collected, organized, and tabulated using the Excel software program. All indices were expressed as mean ± standard deviation. P-values < 0.05 were considered statistically significant. Statistical analysis was performed using the GraphPadPrism program, version 7.0.

All participants signed an informed consent form. The research was approved by the Research Ethics Committee on September 10, 2021, according to substantiated opinion number 4,963,234.

RESULTS

Among the individuals included in the study, 13 (14.77%) were female and 75 (85.22%) were male, with ages ranging from 11 to 64 years (mean of 34.94 years) at the time of surgery.

Among the types of trauma mechanism identified in the study, automobile accidents corresponded to the largest etiological group, reaching 48% prevalence, while 26% were attributed to sports-related trauma, 10% to falls from one's own height, and 8% to falls from a bicycle. As for the affected side, there was a slight predominance of the right side, totaling 45 cases (51%). Most fractures were classified as Allman type I, corresponding to 72 fractures (81.81%), while 16 fractures (18.18%) were classified as Allman type II. There were no fractures classified as Allman type III.

Table 1 shows the demographic clinical characteristics of the analyzed participants segregated by sex. No significant differences were observed between the groups regarding the frequency of the etiologies 'automobile accident' and 'fall from one's own height' as trauma mechanisms, maintaining the etiologies 'sports-related traumas' and 'bicycle falls' exclusively in males. There were also no differences between the groups regarding the affected side, with a predominance, in both, of traumas involving the right shoulder and the classification of the injuries according to the Allman model.

Table 1. Main clinical and demographic characteristics of patients.

Characteristic	Female (n = 13)	Male (n = 75)	*p*
Age (years)	34.5 ± 2.0	31.3 ± 4	*0.93*
Trauma mechanism (%)			
Car accident	48.0 ± 0.5	44.1 ± 0.8	*0.49*
Sports-related traumas	-	9.3 ± 1.0	
Fall from one's own height	49.3 ± 0.7	46.8 ± 1.0	*0.85*
Bicycle fall	-	3.3 ± 0.5	
Affected side			
Right	57.3 ± 0.6	53.8 ± 0.82	*0.51*
Left	42.6 ± 0.7	46.15 ± 0.7	*0.69*
Lesion classification			
Allman Type I	15.3 ± 0.6	17.3 ± 0.5	*0.68*
Allman Type II	84.7 ± 0.8	82.6 ± 0.9	*0.54*

*Values were expressed as mean ± standard deviation.

The synthesis materials used in the osteosynthesis of fractures were 15 reconstruction plates, 46 locking clavicle plates, 11 locking reconstruction plates, 1 dynamic compression plate (DCP), 1 locking T-plate, 1 distal clavicle plate, 4 Kirschner wires, 6 Kirschner wires with anchor, and 3 Kirschner wires with ligature.

During clinical follow-up of patients undergoing surgical treatment, it was necessary to remove the synthesis material from 7 patients (7.95%). One patient (1.13%) presented evidence of postoperative infection and was subjected to the removal of the Kirschner wire with anchor; 2 individuals with a history of osteosynthesis using a locking clavicle plate evolved to pseudarthrosis (2.27%); and 4 patients opted for the removal of the material (2 locking clavicle plates, 1 DCP plate, and 1 reconstruction plate) due to local discomfort. None of the patients presented loosening of material or postoperative brachial plexus injury.

Finally, regarding associated injuries, 1 (1.13%) patient had open clavicle fracture and 2 (2.7%) presented cases with brachial plexus injury in the preoperative period.

DISCUSSION

The results obtained in our analysis are corroborated by Herteleer et al.,[5] which reported the predominance of males as the most affected by this type of injury in 2017. Regarding average age, several studies have identified a bimodal distribution,[1,2,5] while Kihlström et al.[1] observed an overall average of 48 years, affecting males at a younger mean age (43 years) and females at an older age (59 years). Conversely, in our study, we observed a general average of 34.94 years, with a average age fractionated by sex of 35.6 years in females and 58.04 years in males, which can be justified by the cultural differences in our population and the high rates of automobile accidents in younger patients.

Regarding affected side, our findings agree with the literature. Souza et al.[6] analyzed 26 osteosyntheses in 25 patients with midshaft clavicle fracture, occurring in 50% of the cases on the right, with a mean similar to that defined in our study.

Regarding fracture classification, the Allman classification was used as a descriptive criterion. Typically, midshaft clavicle fractures (Allman type I) are the most frequent, accounting for about 80% of cases, occurring mostly in young patients. Fractures located at the lateral end of the clavicle (type II) correspond to approximately 15%–25%, and, to a lesser extent, about 5% occur

in the proximal third (type III).[7] Regarding the data of this study, a higher incidence of Allman type I fractures was observed (81.81%), corroborating the literature.

Regarding mechanism of the trauma that caused the fracture, a discrepancy of probable cultural origin was observed. Our study showed a higher occurrence of clavicle fracture after motorcycle accidents (48%) and sports-related traumas (26%), while the European population-based articles, such as the one by Herteller et al.,[5] reported that the most common trauma mechanism was bicycle accidents (35.3%–20.5%) and low-energy falls (34.1%–14.5 %).[1,5]

Regarding postoperative complications, in our follow-up, a rate of infection related to the surgical site was observed in 1.13% of the cases, corresponding to an index lower than that described by Leroux et al.,[8] who found a percentage of 2.6%. The development of pseudarthrosis was identified in 2.27% of the cases studied in our database, in a proportion similar to that defined by Altamimi et al.[9] and Zlowodski et al.[10] Finally, no literature data were found that corroborate or contradict our statistical indices regarding surgical reoperation to remove synthesis material due to complaints of discomfort.

After statistical analysis of correlation, no statistical significance was found between the data of synthesis material and postoperative complication index, revealing the absence of superiority of risk between the different types of surgical approach used in our research. Similarly, Ashman et al.[11] compared the postoperative results between fixation with reconstruction plate and compression and found no difference in the clinical outcome. Despite the neutrality of the negative results, after extensive analysis in the follow-up period, we believe that the best synthesis materials for the surgical treatment of clavicle fractures are the reconstruction plate and the locking clavicle plate, considering the bone anatomy and the possibility of molding the reconstruction plates according to the individual particularity and the pre-molding of the locking clavicle plate, which provides an anatomy similar in both appearance and physiological aspect.

CONCLUSION

This study showed that the incidence of clavicle fracture is higher in young men, is mostly caused mostly by automobile accidents, and is most often located in the middle third of the clavicle.

We also observed a low rate of postoperative complications and satisfactory functional results considering the various surgical fixation materials used, with negative correlative analysis when comparing the type of approach and clinical outcomes. Thus, we recommend for detailed analyses to be conducted on the synthesis material used, considering the importance of using a low profile and molded plate, reducing the need to remove the material due to discomfort.

The data of this analysis present sampling bias since it was limited to a private tertiary hospital. Thus, we conclude that efforts should be directed in the design of large, controlled, and randomized population-based studies, to further extrapolate the results found.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. LMR: data analysis and surgery; RSO, LFN, AT: writing of the article, data analysis, and performing surgeries; FFL: data analysis and performing surgery; AD: writing and reviewing the article and performing surgeries.

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RELATIONSHIP BETWEEN PARVOVIRUS B19 AND OSTEOARTHRITIS: LITERATURE REVIEW

RELAÇÃO ENTRE PARVOVÍRUS B19 E OSTEOARTRITE: REVISÃO BIBLIOGRÁFICA

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ABSTRACT

Osteoarthritis and Parvovirus B19 infection present silent and gradual evolution, since the former is a degenerative process while the latter is often asymptomatic and may persist in the individual's body during their life. This study aims to analyze clinical studies that establish a correlation between degenerative osteoarthritis and Parvovirus B19 infection. Of the 62 studies found, 25 were chosen for reading in full. Analyzing only the studies that establish the correlation between the pathologies, seven confirm this relationship between Parvovirus B19 and Osteoarthritis, while one reports no relationship. No objective correlation could be found between the other articles studied. Our findings suggest that there is a close relationship between Parvovirus B19 and Osteoarthritis, with a higher prevalence of acquired causes, women and older adults, but it can manifest during life. However, it is essential to carry out new studies involving family history of patients with Osteoarthritis with positivity of Parvovirus B19, cohort studies between childhood and adult-old adult, so that it can elucidate this duality of congenital-acquired cause and, finally, raise treatment alternatives. ***Level of Evidence II, Systematic Review of Level II Studies.***

Keywords: Osteoarthritis. Parvovirus B19, Human. Coinfeccion.

RESUMO

Tanto a osteoartrite quanto a infecção pelo parvovírus B19 apresentam evolução muitas vezes silenciosa e gradual, uma vez que a primeira é um processo degenerativo, e a segunda é geralmente assintomática, podendo persistir no corpo do indivíduo por toda a sua vida. Esta revisão bibliográfica visa analisar estudos clínicos que estabeleceram a correlação entre a osteoartrite degenerativa e a infecção pelo parvovírus B19. Dos 62 artigos encontrados, foram eleitos 25 para leitura em sua totalidade. Analisando apenas os artigos que estabelecem a relação entre as patologias, temos sete que confirmaram essa relação, enquanto um deles afirmou que não há relação. Não houve correlação objetiva entre os demais artigos estudados. Nossos resultados sugerem que há estreita relação entre a osteoartrite e o parvovírus B19, que tende a ser uma doença de causa adquirida com maior prevalência em mulheres e idosos, porém que pode se manifestar durante toda a vida. Contudo, é crucial a realização de novos estudos envolvendo antecedentes familiares de pacientes com osteoartrite e com positividade para o parvovírus B19 e estudos de coorte entre a infância e o adulto-idoso, a fim de elucidar essa dualidade de causa congênita-adquirida e, enfim, levantar alternativas de tratamento. ***Nível de Evidência II, Revisão Sistemática de Estudos de Nível II.***

Descritores: *Osteoartrite. Parvovírus B19 Humano. Coinfecção.*

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INTRODUCTION

Human Parvovirus B19 is a single-stranded DNA virus, without membrane, and from the erythrovirus genus. This virus is responsible for a wide range of clinical manifestations still without specific antiviral therapy, only the treatment of symptoms.[1] The target cells of parvovirus B19 are erythroid progenitors in the bone marrow, which induce changes in receptors, causing cell death by both lysis and apoptosis.[2] The natural course of acute Parvovirus B19 infection is to be controlled by the immunocompetent individuals' antibodies.[3] Acute infection is characterized by skin rash, erythema infectiosum, arthralgia, fetal death, and transient aplastic crisis (TAC). However, in immunocompetent patients the pathogenesis is defined by viral symptoms: Fever, malaise, headache, nausea and sickness, and myalgia. Joint symptoms in Parvovirus B19 infection occur up to 80% in sick adults, most of them in women.

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The study was conducted at Universidade Nove de Julho.
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Osteoarthritis (OA) is a degenerative joint disease characterized by pain, especially during the morning, in at least one joint of the body,[4] as well as stiffness, crepitation, and reduction of the joint space.[5] Furthermore, OA is the most common disease of the locomotor apparatus and the major cause of disability, both in developed countries and in the so-called emerging countries.[6] The traditional focus on treatment is given to the final stages of the disease with the placement of joint prosthesis, showing good effectiveness for the treatment of symptoms; however, low effectiveness in the treatment pathology itself.[7] Currently, new treatments are emerging, aiming to replace the palliative treatment method with the preventive one, by gene-therapy and administration of intra-articular anti-inflammatory drugs seeking joint homeostasis.[8]

Thus, in this study, a medical literature search was carried out to identify the correlation between these pathologies, their pathophysiological processes, and currently used conducts.

This study aimed to analyze clinical studies that establish the correlation between Parvovirus B19 and osteoarthritis.

METHODS

This is an integrative review with data collection performed from secondary sources, by a literature survey. A literature search of studies was performed using the following descriptors: Osteoarthritis, Osteoarthritis, Pavovirus B19 and Co-infection Pavovirus B19, and Osteoarthritis, in the following databases: Google Schoolar, PubMed, SciELO, Elsevier-ScienceDirect, and Web of Science. Inclusion criteria were analyzed studies with WebQualis A1 to C1. Exclusion criteria were studies related to other diseases besides those studied.

The studies were evaluated by their titles and abstracts. After applying the inclusion and exclusion criteria, they were read in full. The analysis of the selected studies and the synthesis of their extracted data were carried out, by at least two evaluators, in a descriptive way, enabling to observe, relate, and identify the evolution of the knowledge produced about the subject explored in this study.

RESULTS

First, we found 62 studies, which were selected according to the inclusion and exclusion criteria. In total, 25 studies were eligible for reading in full. By analyzing only the studies that establish the relationship between the pathologies, we observed that seven confirmed the correlation between Parvovirus B19 and Osteoarthritis and, on the other hand, one of them reported no relationship. The other studies are about the pathologies studied and their concepts; however, without making an objective correlation.

Methods of analysis and research of the virus have become more sensitive and specific over the years, improving the samples accuracy. Among the positive studies found, other studies in the medical literature on the proposed topic are scarce, since there is no study establishing a direct relationship between Parvovirus B19 and autoimmune diseases,[9] such as Osteoarthritis. The study by Rollín et al.[10] stands out negatively regarding this correlation, since it reports that in patients with transplanted bone marrow the number of coinfected patients is insignificant to establish this relationship (Table 1).

Table 1. Analysis of studies on the correlation between parvovirus B19 and osteoarthritis.

Author	Date	Title	Correlation
Aslan et al.[11]	2008	Detection of parvovirus B19 in synovial fluids of patients with osteoarthritis.	Positive
Chen et al.[12]	2012	Significant association of past parvovirus B19 infection with cytopenia in both adult-onset Still's disease and systemic lupus erythematosus patients.	Positive
Colmegna and Alberts-Grill[13]	2009	Parvovirus B19: its role in chronic arthritis.	Positive
Kerr[14]	2000	Pathogenesis of human parvovirus B19 in rheumatic disease.	Positive
Meyer[15]	2003	Parvovirus B19 and autoimmune diseases.	Positive
Page et al.[9]	2015	Human parvovirus B19 and autoimmune diseases. Review of the literature and pathophysiological hypotheses	Positive
Rollín et al.[10]	2007	Human parvovirus B19, varicella zoster virus, and human herpesvirus-6 in mesenchymal stem cells of patients with osteoarthritis: analysis with quantitative real-time polymerase chain reaction.	Negative
Takahashi et al.[16]	1998	Human parvovirus B19 as a causative agent for rheumatoid arthritis.	Positive

DISCUSSION

This study aimed to analyze the relationship of Parvovirus B19 in individuals with osteoarthritis (OA), focusing on the pathophysiological mechanism, epidemiology, and possible conducts. The results from most of the studies reviewed showed a relationship between both pathologies; however, they lacked evidence. This study showed that Parvovirus B19 has a greater tendency to be a disease of acquired cause, with virus positivity already in late adolescence[12] and higher prevalence in older adults, especially women.[11,13] Rollín et al.[10] reinforce the acquired cause theory of the disease after obtaining a similar prevalence (16.7% and 20%) in their case-control study performed with young mesenchymal cell transplantation in patients with osteoarthritis, showing the absence of significant virus reactivation after transplantation. However, they do not specify that there is no relationship and that it cannot also be of congenital cause.

The prevalence of Parvovirus B19 in children is lower; however, it exists and has different clinical characteristics,[13] which manifest themselves in an oligoarticular and asymmetrical way, preceded by erythema infectiosum (EI) and multiarticular in the adults and older adults, with a higher prevalence of the metacarpophalangeal, proximal interphalangeal, knee, wrist, and elbow joints, respectively. On the other hand, a case-control study,[11] carried out to detect the virus in the synovial fluid in patients with osteoarthritis, reported no prevalence of involvement between the joints. There are no studies with any hypothesis as to why clinical characteristics between children and adults are different or not. Moreover, of the studies reviewed, we found no information whether people who tested positive for osteoarthritis have a previous history of PVB-19 infection; if the acquired cause is more prevalent from adolescence,[12] or if in fact all these patients started the entire infectious trajectory in childhood, with the manifestations resulting from a recurrence or exacerbation of the virus. This shows the need for further evidence to corroborate the hypotheses in question.

One of the objectives of this study was to evaluate the impact of the presence of PVB-19 on joint damage. We observed that the persistence of the virus is crucial for the arthrogenic potential, although there is no conclusive evidence about its pathophysiological mechanism, according to Chen et al.,[12] Colmegna and Alberts-Grill,[13] and Page et al.[9] The viral proteins of Parvovirus B19, VP1 and NS1, trigger an inflammatory response that controls the expression of TNF-alpha and IL-6, leading to a cytotoxic action on the joints. Over time and with the persistence of inflammation, a set of events lead to increased joint destruction and clinical worsening, such as exacerbation of bone and cartilaginous loss, increased fibrosis, formation of osteophytes, among others. This corroborates the

presence of PVB19 and IL-6 more frequently in individuals with stage 4 osteoarthritis, marked by visible deformities in the affected joint.[11] Another important aspect of PVB19 is its correlation with autoimmune diseases. Among them, the most prevalent were Systemic Lupus Erythematosus, collagenosis, vasculitis, rheumatoid arthritis, among others.[9,12,14-16] In an experimental study that showed apoptotic bodies (including autoantigens in SMITH-type autoimmunity, DNA, histone h4, and phosphatidylserine) generated by the expression of the protein PVB19-NS1 in an alternative, non-permissive cellular pathway.[9] Another study conducted to associate PVB19 with rheumatic diseases found an increase in rheumatoid factor, antinuclear antibody, mitochondrial, and smooth muscle antibody in the presence of the virus.[14] Only one study had a result without significance in the positivity between the IgG antibody of VP1 and NS1 and autoimmune diseases. However, authors still strongly believe in this relationship and that this topic needs further studies to draw a conclusion on the subject.[12]

Since PVB19 has an important role within autoimmune diseases and osteoarthritis is one of the common complications among this type of disease, there must be a close relationship between them three, so that intervention and one of the factors can reduce the effect of the others. The correct pathophysiological mechanism that induces the immune system to develop autoantibodies is unknown. Many hypotheses lead to other aspects of this discussion: one of them is that PVB19 has a terminal sequence similar to the adeno-associated adenovirus (AAV), which is not associated with human disease and can integrate and stabilize the human chromosome,[14] thus making it more difficult to be recognized and eliminated by the immune system. Authors believe that there is a kind of "looping" between the parvovirus and the autoimmune diseases, which act as a trigger, one stimulating and exacerbating the other.[12]

This may explain why the persistence and recurrence of this type of virus is so frequent in individuals with autoimmune diseases that mainly involve joint disease. Furthermore, it also questions the clinical similarity between them, as well as the difficulty regarding a treatment; however, concrete evidence on these mechanisms is scarce. Takahashi et al.[16] reported the clinical improvement of patients with rheumatoid arthritis and autoimmune hemolytic anemia associated with PVB-19 undergoing immunoglobulin therapy. However, many factors need to be interpreted: both the low sample of patients with rheumatoid arthritis examined and treated,[16] and if immunoglobulin will be efficient considering the hypothesis previously discussed by Kerr,[14] since the virus would stabilize on the human chromosome and may even act similarly to the autoantibody. If treatment would bring more benefits or harms is unknown. On the other hand, considering that this Parvovirus acts within a tripod between the virus-osteoarthritis-autoimmune disease, treating one of the causes may result in a decrease in the others. In the studies reviewed, we found no citations regarding other treatment alternatives besides immunoglobulin therapy; however, there is evidence of the use of anti-inflammatory drugs either intra-articularly, to improve isolated osteoarthritis not initially related to PVB-19,[8] or systemically, if considering the hypothesis of persistence or exacerbation of the tripod Parvovirus-osteoarthritis-autoimmune disease.

CONCLUSION

Our results suggest that there is a close relationship between Parvovirus B19 and osteoarthritis. However, the lack of a specific study for the correlation is highlighted, since it prevents a statistical deepening on the subject. We established an association that behaves predominantly as an acquired cause, with a higher prevalence among women and older adults, however, they can manifest during any age group. Although this study was unable to establish a specific causal relationship, there are plausible hypotheses that may justify the possible mechanisms of action and recurrence of the virus, which may act as a foundation for the discovery of new treatments. This subject should be further explored, with more studies involving family history of patients with osteoarthritis with positivity of Parvovirus B19, cohort studies between childhood and adult-old adults. Thus, it would be possible to elucidate this duality of congenital-acquired cause and, finally, raise treatment alternatives for this relationship.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. GLM: writing of the article and collection and analysis of data; FCSS, TSD, RTSM, FCJN: interpretation and critical review of the study data; GGF: analysis and critical review of the work data and final approval of the manuscript.

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HETEROTOPIC OSSIFICATION AFTER SPINAL CORD INJURY: PREVENTION AND TREATMENT – A SISTEMATIC REVIEW

OSSIFICAÇÃO HETEROTÓPICA NO LESADO MEDULAR: PREVENÇÃO E TRATAMENTO – REVISÃO SISTEMÁTICA

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ABSTRACT

Trauma configures the main cause of spinal cord injuries. Patients with traumatic spinal cord injury often develop severe and debilitating outcomes that require multidisciplinary care to adapt patients to their new reality. Heterotopic ossification (HO) is one of the frequent comorbidities in these patients but it still lacks well-established treatments or a gold standard one. Thus, this systematic review aimed to search the current literature for HO treatment and prevention. This study was conducted following PRISMA recommendations (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) and searches were conducted in three databases (PubMed, Embase, and Web of Science). A total of 193 articles were found in an initial search. After screening following the established criteria, eight articles were included in this review; of these, two reported prevention and the others, treatments. Based on data analysis, the use of non-steroidal anti-inflammatory drugs in the acute post-traumatic period proved to be the best method of prevention. In cases of mature HO or accompanied by ankylosis, surgical resection proved to be the most effective treatment despite the high rate of postoperative infections. ***Level of Evidence III, Systematic Review.***

Keywords: Spinal Cord Injuries. Ossification, Heterotopic. Therapeutics.

RESUMO

A principal causa de lesão medular é o trauma. O paciente com trauma raquimedular frequentemente evolui com incapacidades graves e debilitantes, fazendo com que necessite de cuidado multiprofissional para se adaptar a uma nova realidade. A ossificação heterotópica (OH) é uma comorbidade comum nesses pacientes, mas que ainda não tem tratamentos bem estabelecidos ou considerados padrão-ouro. Esta revisão sistemática teve como objetivo buscar formas de tratamento e prevenção da OH na literatura atual. O estudo seguiu a recomendação Principais Itens para Relatar Revisões Sistemáticas e Meta-Análises (PRISMA) e realizou buscas em três bases de literatura (PubMed, Embase e Web of Science). Foram encontrados 193 artigos inicialmente, e, após triagem considerando os critérios estabelecidos, oito foram eleitos para o trabalho final. Dois trabalhos abordaram a prevenção; e os demais, tratamentos. Pela análise dos dados, o uso de anti-inflamatórios não esteroidais (AINEs) no período agudo pós-traumático se mostrou como o melhor método de prevenção. Já em relação ao tratamento, nos casos de OH maduras ou com anquilose, a ressecção cirúrgica revelou-se como o método mais efetivo, a despeito da grande taxa de infecção pós-operatória. ***Nível de Evidência III, Revisão Sistemática.***

Descritores: *Traumatismos da Medula Espinal. Ossificação Heterotópica. Terapêutica.*

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INTRODUCTION

Spinal cord injuries (SCI) constitute an important economic and public health problem, mostly affecting the younger population. Its annual worldwide incidence revolves around 15 to 40 cases per million population. Motor vehicle accidents, violence, recreational activity, and falling from heights feature among the causes of this injury.[1]

The United States showed an incidence of traumatic spinal cord injury in 2017 of about 54 per million people per year and a prevalence of 280,000 survivors.[2]

Population aging increases the mean age of patients at the time of trauma but plays no proportional role in their survival due to the high morbidity and mortality of this patient group, especially after 60 years.[3]

Such an event becomes more devastating due to the chronic and irreversible changes it brings to survivors,[4] including musculoskeletal changes, especially heterotopic ossification and disuse osteoporosis.

Heterotopic ossification (HO) configures an anomalous bone deposition in periarticular soft tissues. It occurs mainly in the hips[5] and

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The study was conducted at Universidade Estadual de Campinas.
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affects more than half of those with spinal cord injuries, with an average onset of three months after the injury.[6]
The most common clinical picture include reduced range of motion of the joint with periarticular edema. It may also be associated with pain, erythema, localized increased temperature (when sensitivity is preserved), and low-grade fever.[7]
The literature still lacks a consensus of a gold standard to treat neurogenic HO, mentioning non-steroidal anti-inflammatory drugs (NSAIDs), bisphosphonates, radiotherapy (RT), and resection surgery.[8,9]
Therefore, we find a growing demand for the best treatment and prevention of these chronic changes in people with spinal cord injuries, aiming at a better quality of life and possible increased survival. This review aimed to search the current literature for proposals to treat and prevent HO.

METHODS

Search strategy

This review was conducted following PRISMA (Main items to report Systematic Reviews and Meta-analyses) guidelines.[10]
To design our search strategy, the PICO framework (Patient, Intervention, Control, Outcome) was initially used to construct a suitable guiding question. "What is the optimal treatment or prevention for heterotopic ossification in patients with spinal cord injuries?" Then, the following descriptors and Boolean operators were selected for our search strategy: "Spinal cord injuries" AND; "Ossification, heterotopic" AND (Therapeutics OR Prevention), with the selection filter set for articles published in the last 10 years. Searches were conducted in three databases: PubMed, Embase, and Web of Science.

Selection criteria

Our inclusion criterion consisted of 1) original articles dealing with treatment or prevention of neurogenic heterotopic ossification of traumatic origin, whereas our exclusion criteria, of 1) non-neurogenic heterotopic ossification; 2) review articles; 3) articles that aren't mainly focused on treating or preventing HO; and 4) case reports.

Analyzed data

The following data were extracted: author and year of publication, study design, sample size, intervention, incidence of HO solution/recurrence rate, and intervention-related complications.

RESULTS

Search results

We found 125 Studies on PubMed, 68 in Embase, and zero in Web of Science, totaling 193 articles (Figure 1) from the research we conducted on 05/31/2022. We found no duplicates.
We excluded studies by title and abstract in the first screening phase. The first and second reviewers independently excluded 170 studies, totaling 23 selected articles, 11 of which showed conflicts. The conflict was resolved by a third reviewer. We chose 22 for our second review stage, in which we were to fully read them. Then, we chose eight articles for this study, excluding 14 according to our selection criterion.

Characteristics of the included studies

All articles were retrospective studies, five of which were cohort studies and three, case controls. From these, two studies dealt with HO prophylaxis (one with bisphosphonate and the other with NSAIDs) and the others, with treatment (surgical resection, radiotherapy, and combinations of techniques). Table 1 shows further details.

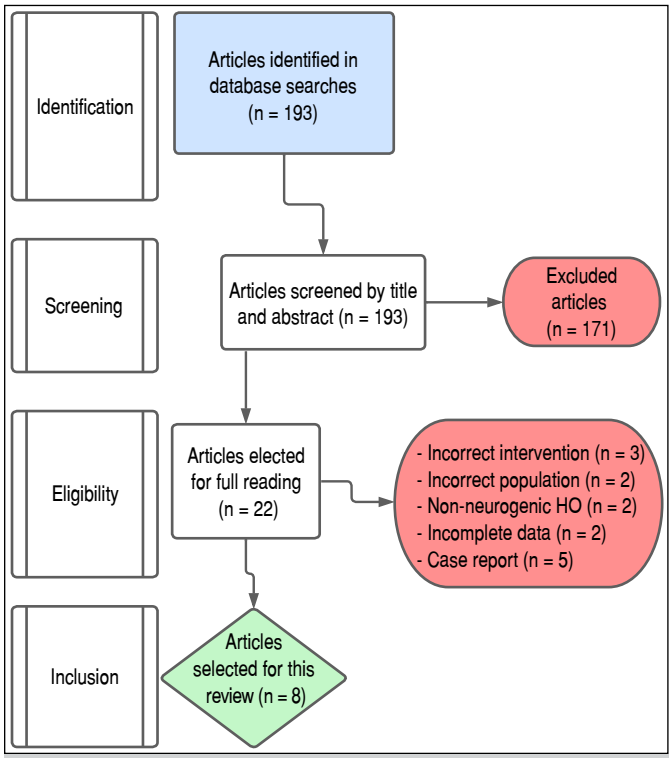

Figure 1. Flowchart.
HO: heterotopic ossification.

Evaluation of interventions

We found that four studies dealt with surgical resection but only two evaluated it as a main treatment intervention, one of which with the association of NSAIDs for four weeks.[11,16] The others mainly evaluated the action of radiotherapy (RT) as an adjuvant.[13,14] Cases of surgical resection, mainly associated with the use of NSAIDs, showed low or even null recurrence rates, but had high rates of postoperative complications, infections being their main cause. Specifically, Honore et al.[14] observed no statistical difference in HO recurrence between the group with resection associated with RT and that with resection only, but found significant infection rates in the group that performed RT (case group). Therefore, the study was unable to recommend this association, especially in cases of complicated recurrent HO, as were the majority (78.9%) of the case group — unlike the control group (5.3%).
Of the analyzed studies, three addressed RT as the main treatment, two in isolation[15,16] and one associated with etidronate.[13] Recurrence rates were also low but generally higher than surgical resection (Figure 2). The study with the highest recurrence rate was the one that associated resection with etidronate. A patient showed disease progression, a high percentage due to their small sample. The advantage of RT is the near absence of complications, but all studies had short follow-ups. Furthermore, two studies on isolated RT performed early treatments due to ultrasound screening diagnoses (an institutional protocol) rather than by patients' clinics.
Of the total, two studies addressed HO prevention methods, one on the use of alendronate and another on NSAIDs (celecoxib or indomethacin). They found no statistical difference in the use of alendronate to prevent HO. However, a reduction in alkaline phosphatase (ALP) was observed, which was high in the group that developed HO.[12]
In the study with NSAIDs, occurrence decreased by 28.4% after at least 15 days of treatment during the acute period after trauma.[15]
Table 2 shows further details on the outcomes of the studies.

Table 1. Identification of articles.

ID	Author and year	Study design	Population	Control	Intervention	Intervention details
1	de l'Escalopier et al., 2019[11]	Retrospective cohort	377 (104 SCI)		Surgical resection	Surgical resection in symptomatic patients. Minimal resection to achieve functional ROM. Post-procedure physical therapy and pre-procedure ATB
2	Ploumis et al., 2015[12]	Retrospective control case	125	174	Alendronate	Administration of alendronate 70 mg per week, averaging 38.17 ± 57.89 weeks. The patients were followed for an average of 626.72 ± 620.49 days.
3	Ester et al., 2022[13]	Retrospective cohort	3 SCI and 1 CCT		Radiotherapy (8 Gy) + resection + NSAIDs Radiotherapy (8 Gy) + etidronate	Irradiated 3 hips, post resection, with 8 Gy, followed by 6 weeks of 25 mg of indomethacin, 3 times/day. Three hips and 2 elbows were irradiated + etidronate, no surgery.
4	Honore et al., 2020[14]	Retrospective control case	11 SCI and 8 CCT	76 (SCI or CCT)	Radiotherapy (7.5 Gy)	RT was performed with 7.5 Gy perioperatively to prevent recurrence.
5	Zakrasek et al., 2019[15]	Retrospective control case	27	81	NSAIDs	Use of NSAIDs (indomethacin 25 mg 3 times/day or celecoxib 200 mg/day) for 15 days or more. Followed up for an average of 63 days, being evaluated an average of 21 days after trauma.
6	Romero-Muñoz et al., 2018[16]	Retrospective cohort	20		Surgical resection + NSAIDs	Surgical resection of HO in 16 cases and Girdlestone in 4 cases. Goal of surgery: gain 90° of flexion and 20° of abduction. Physical therapy + celecoxib 200 mg/day for 4 weeks after the procedure.
7	Müseler et al., 2017[17]	Retrospective cohort	244		Radiotherapy (7 Gy)	Single radiation dose of 7 Gy in patients detected with HO (via biweekly US screening). After an average of 4.9 days after diagnosis, treatment was performed, which was on average 63.2 days after SCI.
8	Citak et al., 2016[18]	Retrospective cohort	13		Single radiation dose (7 Gy, 6 Gy in two cases)	Single radiation dose in patients with HO (via biweekly US screening).

HO: heterotopic ossification; SCI: spinal cord injury; ROM: range of motion ATB: antibiotic; CCT; craniocerebral trauma; NSAIDs; Non-steroidal anti-inflammatory drugs; US: ultrasound.

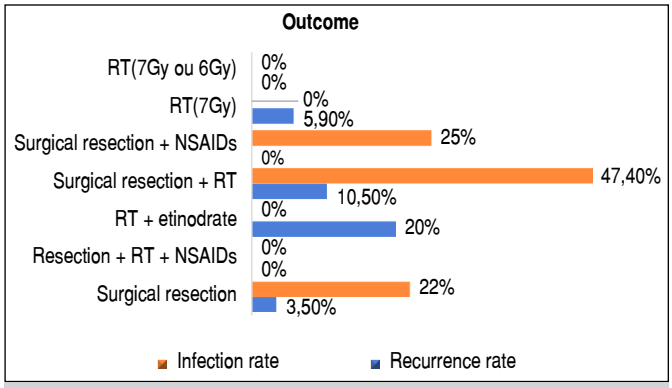

Figure 2. Outcome by intervention.

RT: radiotherapy; NSAIDs: non-steroidal anti-inflammatory drugs.

DISCUSSION

This systematic review aimed to investigate methods to prevent and treat neurogenic HO in people with spinal cord injuries.

The analyzed studies (all retrospective) ranged from level 3 to 4 of evidence. The main problem in most studies referred to their short post-treatment follow-up. HO may have recurred after these periods.

Resection surgery effectively treated HO, despite high infection rates. Romero-Muñoz's[16] patients felt satisfied with their outcome (including those who had complications, such as operative wound infections). Infection occurs particularly often in patients with SCI, as it disrupts neuroimmune regulation, causing a deficiency of peripheral immunity. Furthermore, constant vasodilation due to sympathetic denervation causes chronic inflammation in these patients, delaying their healing, especially in cases with pressure ulcers.[19,20]

Radiotherapy has also shown promise, but it should be followed up for longer. The reviewed studies had short follow-ups. HO could have reoccurred in the medium term, as could have adverse effects in the long term. As mentioned, HO diagnosed by ultrasound screening received early treatment. This was an institutional protocol and patients may have had no complaint or clinic. Thus, we were unable to extrapolate this positive effect to more mature HO, chronic HO, or HO that developed ankylosis. The peak incidence of HO occurs in the first two to three months after SCI,[21] configuring the window of opportunity to institute screening protocols and thus enable treatment with RT, which has a lower complication rate than surgery. Radiotherapy associated with surgery in complicated cases of HO, such as those with recurrence or higher risk factors associated with recurrence, has shown to ineffectively prevent HO and increase the risk of local infections. Patients with spasticity, complete spinal cord injury (AIS A), urinary tract infections, pneumonia, and pressure ulcers were associated with a higher risk of developing HO.[22,23] In the presence of these factors, it is of paramount importance to treat possible comorbidities. These patients are also the greatest candidates for screening, enabling early treatment.

Regarding the studies on HO prevention, the use of NSAIDs proved to be effective, despite short follow-ups.[15] Banovac et al.[24] showed in 2001 the positive effects of using indomethacin to prevent HO in the first two months following the SCI. Later, in 2004, the use of rofecoxib (a selective COX-2 inhibitor)[25] corroborated that positive result. The use of alendronate failed to prevent HO but it reduced ALP levels. Its heterogeneous study group and divergent protocols may have

Table 2. Outcomes of the interventions.

ID	Outcome	Complications	Limitations
1	Recurrence: 3.5%.	Intraoperative hemorrhage; femoral neck fracture, local infection (10.3% overall, 22% in those with spinal cord injuries)	
2	No statistical difference was observed for the prevention of HO. However, patients who developed HO had altered serum ALP levels, and the group taking alendronate was positively correlated with normal ALP levels.	No reported complications	Inhomogeneous group; no exact protocol for the treatment beginning and duration
3	Efficacy rate of 87.5% in total; 1 patient progressed to HO in the etidronate group.	Grade 2 dermatitis in a patient	The effect of radiation alone has not been proven. Small sample, short follow-up (11 weeks), unknown effect and long-term toxicity.
4	Case group: 10.5% of recurrence, 47% with postoperative complications. Control group: 5.3% of recurrence, 23.3% with postoperative complications. There was no statistical difference in the recurrence of HO between groups but a higher rate of postoperative complications in the study group.	Main complication: postoperative sepsis, especially in the case group.	Patients undergoing RT tended to recurrence (inhomogeneous groups). A total of 78.9% of case patients had HO recurrence, while only 5.3% in the control group.
5	A total of 28.4% reduction in the rate of occurrence of HO in patients who used NSAIDs for 15 days or more in the acute phase of rehabilitation after SCI. (indomethacin 75 mg/day or celecoxib 200 mg/day) $p < 0.006$.	No observed adverse effects or complications	Non-randomized choice and non-blinded patients. Average follow-up of only 60 days. Non-standardization of days of use of NSAIDs and date of introduction.
6	Recurrence: 0% Important ROM gain. Flexion 90°, abduction 20°, IR 20°, and ER of 40° on average. All patients were satisfied with the postoperative outcome, even those with complications. Minimum follow-up of 1 year.	Complication in 30%: Deep infections (3 cases); retained bruises (2 cases); intraoperative deep femoral lesion (1 case)	Small sample
7	Recurrence: 13 patients (5.3%), of which, 26 hips (5.9%). A further dose was repeated in these patients, in which only 1 patient developed ankylosis. On average, patients were followed for 89.4 days.	No observed complications	The lower recurrence rate may stem from two reasons: short follow-up and early treatment due to screening. Recurrence cases were based on clinical pictures, which allows for underdiagnosis.
8	Average follow-up: 88.8 days. ROM gain: 92.1° flexion, 94.5° abduction, 26.4° external rotation. Recurrence: 0%	No observed complications	Only screened people with symptoms, there may be underdiagnosis of HO recurrence. Short follow-up time.

HO: heterotopic ossification; ALP: alkaline phosphatase; NSAIDs; non-steroidal anti-inflammatory drugs; SCI: spinal cord injury; ROM: range of motion; RT: radiotherapy; ER: external rotation; IR: internal rotation.

generated a bias. Thus, prospective studies with well-established protocols on the use of oral bisphosphonates could show positive results, considering the association found with ALP levels. However, the meta-analysis in Yolcu et al.[26] in 2020 showed no preventive effect with the use of bisphosphonates, although NSAIDs obtained positive effects.

Our research found several case reports, which we excluded due to our exclusion criteria. However, they showed the benefits of extracorporeal shock therapy to reduce pain and improve range of motion, with promising results.[27,28]

The inclusion of heterogeneous studies with small samples and retrospective studies are limitations of this study.

As strengths, we highlight the opportunity to gather the various methods of treatment and prevention in a single, carefully researched work to facilitate and guide the treatment of these cases.

CONCLUSION

By analyzing the data in this systematic review, the use of NSAIDs proved to be the best method of prevention, if administered in the acute period after spinal cord injury.

For the already established HO treatment, the best method was surgical resection, being more effective if associated with the use of NSAIDs for four weeks after resection. But because of the high rate of postoperative complications, it is recommended to restrict this method to patients with a significant functional limitation, such as the inability to transfer from bed to wheelchair. Radiotherapy is promising in treating cases of HO detected early but not in association with surgical resection or in cases of recurrence.

Therefore, a good follow-up for these patients may include treating associated risk factors, such as urinary tract infection, tracheostomy care, and pressure injury, instituting NSAIDs protocols for the acute phase of SCI, and screening these patients at risk in the acute phase, as well as radiotherapy for early cases and resection for cases of ankylosis.

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