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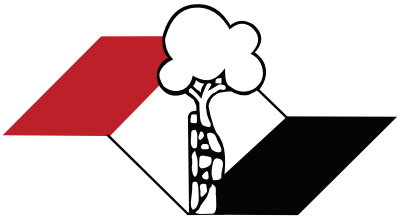

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(Reviewed January 2016)

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ACKNOWLEDGEMENTS
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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

VOLUME 27–Nº 4–2019

Original Articles

HAND

IS OBESITY A RISK FACTOR FOR FREE VASCULARIZED FIBULAR FLAP COMPLICATIONS?.....192
A OBESIDADE É FATOR DE RISCO PARA COMPLICAÇÕES DO RETALHO LIVRE DE FÍBULA VASCULARIZADA?
Raquel Bernardelli Iamaguchi, Marco Aurélio de Moraes, Gustavo Bersani Silva, Alvaro Baik Cho, Fernanda do Carmo Iwase, Teng Hsiang Wei, Marcelo Rosa de Rezende, Rames Mattar Jr
DOI: http://dx.doi.org/10.1590/1413-785220192704217444

HIP

DOES TOPICAL USE OF GENTAMICIN REDUCE THE INFECTION RATE IN PRIMARY TOTAL HIP ARTHROPLASTY?.....197
O USO TÓPICO DE GENTAMICINA REDUZ A TAXA DE INFECÇÃO NA ARTROPLASTIA TOTAL PRIMÁRIA DO QUADRIL?
Caio Luiz de Toledo Oliveira, Felipe Abrahão Elias, André dos Santos Ribacionka, Celso Hermínio Ferraz Picado, Flávio Luís Garcia
DOI: http://dx.doi.org/10.1590/1413-785220192704219177

KNEE

EXTRA-ARTICULAR RECONSTRUCTION ASSOCIATED WITH THE ANTERIOR CRUCIATE LIGAMENT IN BRAZIL....202
RECONSTRUÇÃO EXTRA-ARTICULAR ASSOCIADA AO LIGAMENTO CRUZADO ANTERIOR NO BRASIL
Camilo Partezani Helito, Carlos do Amaral Junior, Danilo Bordini Camargo, Marcelo Batista Bonadio, Jose Ricardo Pecora, Marco Kawamura Demange
DOI: http://dx.doi.org/10.1590/1413-785220192704198228

ONCOLOGY

LONG-TERM RESULTS OF EXTREMITY SOFT TISSUE SARCOMAS LIMB-SPARING SURGERY AND RADIOTHERAPYL.....207
RESULTADOS DE LONGO PRAZO DE SARCOMAS DE EXTREMIDADE: CIRURGIA E RADIOTERAPIA COM ESPUMA
Özlem Yetmen Dogan, Didem Çolpan Oksuz, Banu Atalar, Fazilet Oner Dincbas
DOI: http://dx.doi.org/10.1590/1413-785220192704217574

PEDIATRIC ORTHOPEDICS

FUNCTIONAL INDEPENDENCE OF PEDIATRIC PATIENTS WITH MUCOPOLYSACCHARIDOSES.....212
INDEPENDÊNCIA FUNCIONAL DE PACIENTES PEDIÁTRICOS COM MUCOPOLISSACARIDOSES
Paloma Silva Lopes, Diógenes Pires Serra Filho, Marcos Antônio Almeida Matos
DOI: http://dx.doi.org/10.1590/1413-785220192704187274

TRAUMA

MODIFIED STOPPA APPROACH FOR PELVIC AND ACETABULAR FRACTURE TREATMENT 216
STOPPA MODIFICADA PARA TRATAMENTO DE FRATURAS PÉLVICAS E ACETABULARES
Hong-Zhang Guo, Yu-Fang He, Wan-Qing He
DOI: http://dx.doi.org/10.1590/1413-785220192704188933

WRIST AND HAND

EVALUATION OF DISTAL FOREARM FRACTURES USING THE AO 2018 CLASSIFICATION 220
AVALIAÇÃO DAS FRATURAS DA EXTREMIDADE DISTAL DO ANTEBRAÇO PELA CLASSIFICAÇÃO AO 2018
Alysson Figueiredo Nogueira, Lucas Moratelli, Marcela dos Santos Martins, Ricardo Torres Iupi, Marcos Felipe Marcatto de Abreu, João Carlos Nakamoto
DOI: http://dx.doi.org/10.1590/1413-785220192704218467

Review Articles

FOOT

SOFT-TISSUE INJURY TO THE FOOT AND ANKLE: LITERATURE REVIEW AND STAGED MANAGEMENT PROTOCOL 223
LESÃO DE TECIDOS MOLES NO TRAUMA DO TORNOZELO E PÉ: REVISÃO DA LITERATURA E TRATAMENTO ESTAGIADO
Alexandre Leme Godoy-Santos, Tim Schepers, Soft Tissue Foot & Ankle Group
DOI: http://dx.doi.org/10.1590/1413-785220192704221240

KNEE

BRAZILIAN CONSENSUS STATEMENT ON VISCOSUPPLEMENTATION OF THE KNEE (COBRAVI).....230
CONSENSO BRASILEIRO DE VISCOSSUPLEMENTAÇÃO DO JOELHO (COBRAVI)
Gustavo Constantino de Campos, Eduardo Branco de Sousa, Paulo César Hamdan, Cyro Scala de Almeida Júnior, Antonio Martins Tieppo, Marcia Uchôa de Rezende, Adrieni Antunes do Amaral Alchaar, Carlos Bruno Pinheiro, Eduardo de Melo Carvalho Rocha, Fabiano Gonçalves Cunha, Ivan Pacheco, Mário Sérgio Rossi Vieira, Sílvio Figueira Antonio, Zartur José Barcelos Menegassi
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ORIGINAL ARTICLE

IS OBESITY A RISK FACTOR FOR FREE VASCULARIZED FIBULAR FLAP COMPLICATIONS?

A OBESIDADE É FATOR DE RISCO PARA COMPLICAÇÕES DO RETALHO LIVRE DE FÍBULA VASCULARIZADA?

Raquel Bernardelli Iamaguchi[1], Marco Aurélio de Moraes[1], Gustavo Bersani Silva[1], Alvaro Baik Cho[1], Fernanda do Carmo Iwase[1], Teng Hsiang Wei[1], Marcelo Rosa de Rezende[1], Rames Mattar Jr [1]

1. Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas (IOT/HCFMUSP), Instituto de Ortopedia e Traumatologia, Hand Surgery and Reconstructive Microsurgery Group, São Paulo, SP, Brazil.

ABSTRACT

Objective: Although our knowledge of bone reconstruction through microsurgery has increased, the vascularized fibula flap remains one of the most difficult free flap reconstructions to perform, and complications remain a challenge. The incidence of obesity is increasing and is associated with higher rates of free flap complications, which can lead to disastrous results. Since there is no consensus in literature regarding the influence of obesity on free flap outcomes in orthopedic surgeries that require segmental bone reconstruction, the objective of this study was to determine whether obesity increases the risk of post-operative complications (Clavien-Dindo grade III) after free vascularized fibular flap surgery. Methods: A cohort study was conducted in all patients undergoing free flap limb reconstructions between July 2014 and July 2018. Patients were separated in two groups based on their body mass index (BMI): non-obese and obese (BMI≥30 kg/m^2). Results: Twenty-three free vascularized fibular flaps were studied. The indications included trauma in 13, tumors in 7, and congenital pseudarthrosis of the tibia in 3. Obese patients were associated with an increase in surgical complications (p=0.038). During the final follow-up, consolidation was obtained in 17 patients (74%). Conclusion: Obesity is a risk factor for complications in free vascularized fibular flap surgery. ***Level of evidence IV, original article.***

Keywords: Microsurgery; Free tissue flaps; Tissue transplantation; Risk factors; Fibula.

RESUMO

Objetivo: Apesar do crescente conhecimento em reconstrução óssea por meio de microcirurgia, o retalho livre de fíbula vascularizada ainda permanece como uma das reconstruções mais difíceis de ser executada, e suas complicações ainda são um desafio. A incidência da obesidade tem aumentado e está associada a taxas mais altas de complicações de retalhos livres, o que pode levar a resultados desastrosos. Uma vez que não há consenso na literatura a respeito da influência da obesidade nos desfechos dos retalhos livre em cirurgias ortopédicas que requeiram reconstrução de segmento ósseo, o objetivo deste estudo foi avaliar se a obesidade aumenta o risco de complicações pós-operatórias (Clavien-Dindo grau III) após a cirurgia de retalho livre de fíbula vascularizada. Métodos: Foi realizado um estudo de coorte transversal, com a inclusão de todos os pacientes submetidos à reconstrução de membros com retalho livre de fíbula vascularizada, entre julho de 2014 e julho de 2018. Os pacientes foram separados em dois grupos, com base no índice de massa corporal: não obesos e obesos (no índice de massa corporal ≥ 30 kg/m^2). Resultados: Foram analisados 23 retalhos livres de fíbula vascularizada. As indicações foram trauma em 13 casos, tumor em sete e pseudoartrose congênita da tíbia em três. Pacientes obesos foram associados a aumento nas complicações cirúrgicas (p = 0,038). No final do acompanhamento, a consolidação óssea foi obtida em 17 pacientes (74%). Conclusão: A obesidade é um fator de risco para complicações no retalho livre de fíbula vascularizada. ***Nível de evidência IV, artigo original.***

Descritores: *Microcirurgia. Retalhos de tecido biológico.Transplante de tecidos. Fatores de risco. Fíbula.*

Citation: Iamaguchi RB, Moraes MA, Silva GB, Cho AB, Iwase FC, Wei TH, Rezende MR, Mattar Jr R. Is obesity a risk factor for free vascularized fibular flap complications? Acta Ortop Bras. [online]. 2019;27(4):192-6. Available from URL: http://www.scielo.br/aob.

INTRODUCTION

Free vascularized fibular flap is a standard technique for reconstruction of complex and long defects in lower and upper limbs, especially in traumatic and oncologic defects.

Although, the crescent knowledge in bone reconstruction with microsurgery, the fibular flap still remains one of the most difficult free flaps and complications, including the loss of viability of the vascularized bone and pseudarthrosis, remains a challenge.

With the crescent obesity in world population, the concern about complications, associated with this comorbidity, is raising. Obesity is associated with higher rates of complications in free flaps surgery and the most common is postoperative infection, which can lead to disastrous results, including total free flap loss and amputation.[1,2] Since there is no previous description in literature about the correlation of obesity with higher rates of complications in vascularized bone flaps, to our knowledge; the aim of this study it to compare

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

This work was performed at the Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas (IOT/HCFMUSP).
Correspondence: Raquel Bernardelli Iamaguchi. Rua Dr. Ovídio Pires de Campos, 333, São Paulo, SP, Brazil. 05403-010. rbiamaguchi@gmail.com

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obese and non-obese patients, according tosurgical complications rates, in free vascularized fibular flaps in orthopaedic surgeries, that requires segmental bone reconstruction.

MATERIALS AND METHODS

All consecutive patients who received a free vascularized fibular flap for upper and lower limb reconstruction forsegmental bone reconstructionat our institution, from July 2014 through July 2017, were included in a cohort study, following the strobe guidelines. No patient was excluded; informed consent was obtained from all individual participants included in the study and the minimal follow-up of one year. The study was approved by the Ethics Committee (Protocol number 42679515.2.0000.0068). Patients were separated in two groups, based on their BMI, calculated by dividing the weight in kilograms (kg) by height in meters (m) squared: non-obese (BMI< 30 kg/m^2) and obese (BMI≥30 kg/m^2) and according to the World Health Organization (WHO) definition of obesity.

Patient demographics (age, gender and comorbidities), location and size of bone defect, operative technique, including the type of fixation of bone flap, and intraoperative or postoperative surgical complications were studied. The ischemia time of the free flap was studied, which was defined as the time between the section of the pedicle in the donor area and the release of clamps of the artery and at least 1 vein (in cases in which more than 1 vein was anastomosed) and perfusion of the flap was observed.

The surgical complications withgrade III (complications requiring surgical intervention) of Clavien-Dindo classification,[3,4] observed were: dehiscence, partial or total skin island flap loss, thrombosis with absence of vascular flow in vascularized fibula with anastomoses revision and infection.

Consolidation was established on standard clinical and radiological parameters in consecutive radiographs and was not considered a Clavien-Dindo complication as it is a late complication in follow-up of vascularized fibular flap. It was studied the occurrence of pseudarthrosis and need for further surgeries to obtain consolidation. After consolidation, it was analyzed the final functional result and the use of orthotic or ambulatory aid were assessed.

Statistical Analysis

Statistical analyses were performed with SPSS 20.0 (SPSS Inc ®, Chicago, IL, EUA). All tests were two-tailed, and statistical significance was defined as $p < 0.05$. Qualitative data were analyzed by Pearson chi-square test or Fisher exact test. Mann-Whitney U-test was used for quantitative nonparametric data. Multinomial logistic regression was then conducted on the variables that were significant by univariate analysis or with a P-value < 0.20. The backward algorithm was used.

RESULTS

A total of 23 free vascularized fibular flaps were performed in 23 patients. Of these, 14 patients were male and 9 female. The indications for bone reconstruction were defects cause by: trauma in 13 patients, tumor in 7 patients and congenital pseudarthrosis of the tibia in three patients. (Figure 1) The type of bone tumor were: giant cell tumor in three cases, osteosarcoma in two cases, B-cell lymphoma in one case and adamantinoma in one case. (Figure 2)

Patients were divided in two groups according to the BMI: 18 patients were non-obese and 5 patients obese (BMI ≥ 30kg/m^2). Age, indications, wound location and size of bone defect were similar in both groups (obese versus non-obese).

The most common anatomical area of bone lesion was leg in eight cases, followed by forearm in six cases. (Figure 3)

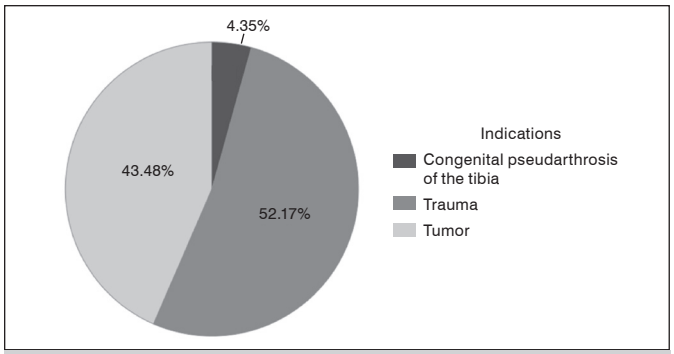

Figure 1. Indications of free vascularized fibular flap.

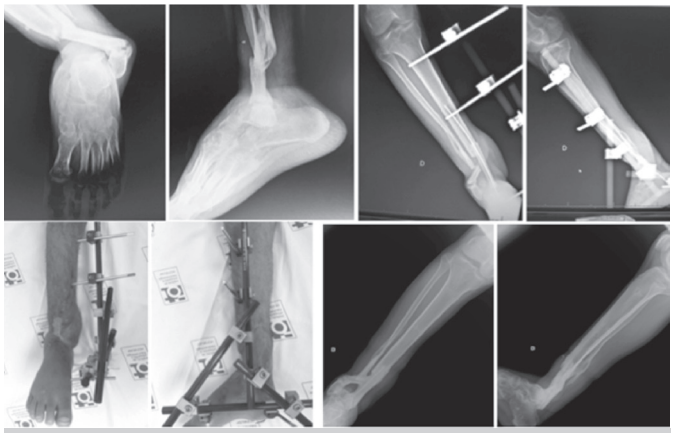

Figure 2. Male, 30 years old, motorcycle accident with open fracture of the distal leg with chronic traumatic wound. Submitted to free vascularized fibular flap for bone and soft tissue reconstruction. Final results with bone consolidation and satisfactory ambulation without bracing or crutches after two years.

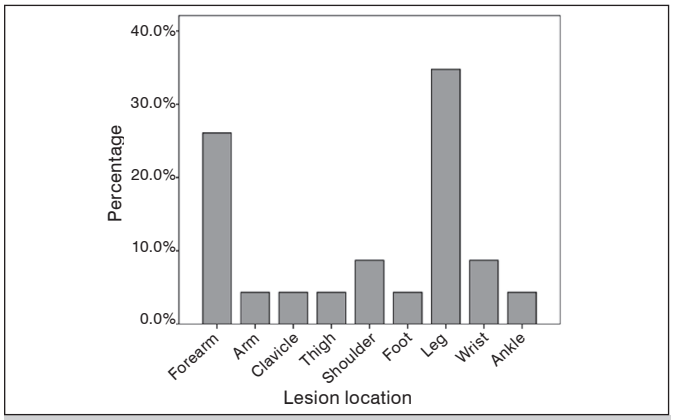

Figure 3. Description of anatomical area of the bone lesion.

The method of fixation was: plate and screw for 11 patients, K-wire and cast for 3 patients and a combination of external fixator, screw and/or K-wire for 9 patients.

The average intraoperative ischemia time of free vascularized fibular flap was 133,2 minutes (SD 42,8) for non-obese patients and 195,6 minutes (SD 71,4) for obese patients (p=0,08).

Twelve patients had surgical complications, including: 1 dehiscence, that required a local flap for coverage); 1 loss of skin island that required a local flap for coverage of fibular flap; 2 cases of post-operative infection that required surgery and treatment with

antibiotics, with complete resolution of infection, but one case lost the skin island flap and the other had pseudarthrosis of fibular flap, that was submitted to bone graft and plate with screw fixation, with final consolidation; 8 cases had signs of vascular compromise of the skin island and were submitted to reexploration, of these, two cases had thrombosis of the anastomoses and were successfully revised; two cases lost only the skin island flap without vascular compromise; one patient required hematoma drainage without thrombosis; and 3 patients had thrombosis with absence of flow in vascularized fibula, one of these patients had congenital pseudarthrosis of the tibia, the second patient had a traumatic defect of the foot and the other was a reconstruction after excision of humeral tumor. The avascular fibula was maintained after complete debridement of soft tissue. The second patient was submitted to a successful anterolateral thigh flap for coverage of the foot, but maintained a post-operative infection and at last was submitted to a Chopart amputation. Seven patients had comorbidities, including five smokers patients and comorbidities were not risk factors for complications (p=0,86). (Table 1)

At final follow-up consolidation was obtained in 17 patients (74%). Two patients had pseudarthrosis prior to final consolidation and were submitted to revision of fixation, one of these to plate and screw fixation associated to bone autograft and the other to Ilizarovexternal fixator. Among six patients without final consolidation, one patient had consolidation in proximal fixation of free vascularized fibular flap with distal pseudarthrosis but was walking with a cane; one patient had tumor recurrence and was submitted to shoulder disarticulation; and the remaining four patients, were submitted to amputation (3 transtibial and one Chopart level). In regard to gait evaluation, of the 11 patients submitted to free vascularized fibular flap transferred for the lower limb: four were submitted to amputation, five patients were walking with crutches, two patients with a cane and three patients without aid. The average defect size of patients with surgical complications was 9,7 cm and patients without complications was 12,5, no statistical difference was observed (p=0,163).

The type of fixation with plate and screw compared to other methods, did not influenced the results, regarding the surgical complications (p=0,855) or consolidation rates (p= 0,640). Obesity did not influenced the complication rates (p=1,0).

All obese patients had complications (grade III Clavien-Dindo) when compared with non-obese patients (44%) and obesitywas significantly associated with an increase in surgical complications rates of grade III Clavien-Dindo classification (p= 0,038). (Figure 4)

Table 1. Description of cases with surgical complications.

Patient	Age	Sex	Indication	Comorbidities	Defect location	Size defect (mm)	BMI (kg/m^2)	Complications	Type of fixation	Consolidation (Y/N)	Deambulation (Y/N)/ Amputation
#1	9	F	Tumor		Shoulder	221	19,37		Plate and screws	Y	N/A
#2	17	F	Tumor		Leg	103	18,83		Plate and screws	Y	Y
#3	51	M	Tumor		Leg and Ankle	232	26,93		External fixator and screws	N	Y - cane
#4	31	M	Trauma	Smoking; Diabetes	Leg	68	19,38		External fixator and K-wires	Y	Y
#5	42	M	Trauma	Smoking	Leg	140	25,71		External fixator and K-wires	Y	Y - crutches
#6	45	M	Tumor		Arm	56	30,46	Anastomoses revision; total flap loss	Plate and screws	N	N/A
#7	23	M	Trauma		Thigh	232	20,62	Anastomoses Revision	External fixator and K-wires	N	Amputation
#8	23	M	Trauma	Smoking	Forearm	93	24,22	Anastomoses Revision; Skin island flap loss	K-wires	Y	N/A
#9	2	F	CPT		Leg	48	15,00		External fixator and K-wires	Y	Y
#10	36	M	Trauma	Smoking	Clavicle	73	25,22	Dehiscence; Local flap for coverage	Plate and screws	Y	N/A
#11	10	F	Tumor		Shoulder	158	15,48	Anastomoses Revision; Skin island flap loss	Plate and screws	Y	N/A
#12	45	F	Trauma	Smoking; Hypertension; Hypothyroidism	Wrist	69	40,40	Anastomoses Revision	K-wires	Y	N/A
#13	24	F	Trauma		Leg	123	21,60	Partial Flap Loss; Local flap for coverage	External fixator and K-wires	Y	Y
#14	57	F	Tumor	Diabetes; Hypertension	Wrist	90	27,92		Plate and screws	Y	N/A
#15	26	M	Tumor	Cocaine use	Forearm	124	20,16		Plate and screws	Y	N/A
#16	3	M	CPT		Leg	80	19,38	Anastomoses revision; Total Flap Loss	External fixator and K-wires	N	Amputation
#17	28	M	Trauma		Forearm	86	30,31	Post-operative infection; Skin island flap loss	K-wires	Y	N/A
#18	29	F	Tumor		Forearm	111	23,78		Plate and screws	Y	N/A
#19	26	F	Trauma		Forearm	142	33,80	Post-operative infection	Plate and screws	Y	N/A
#20	10	M	CPT		Leg	82	15,03		External fixator and screws	N	Amputation
#21	40	M	Trauma		Foot	57	27,16	Anastomoses revision; Total flap loss	Plate and screws	N	Amputation
#22	38	M	Trauma		Ankle	79	22,94		External fixator, screws and K-wires	Y	Y
#23	31	M	Trauma		Forearm	43	30,02	Anastomoses Revision; Hematoma drainage	Plate and screws	Y	N/A

CPT (congenital pseudarthrosis of the tibia).

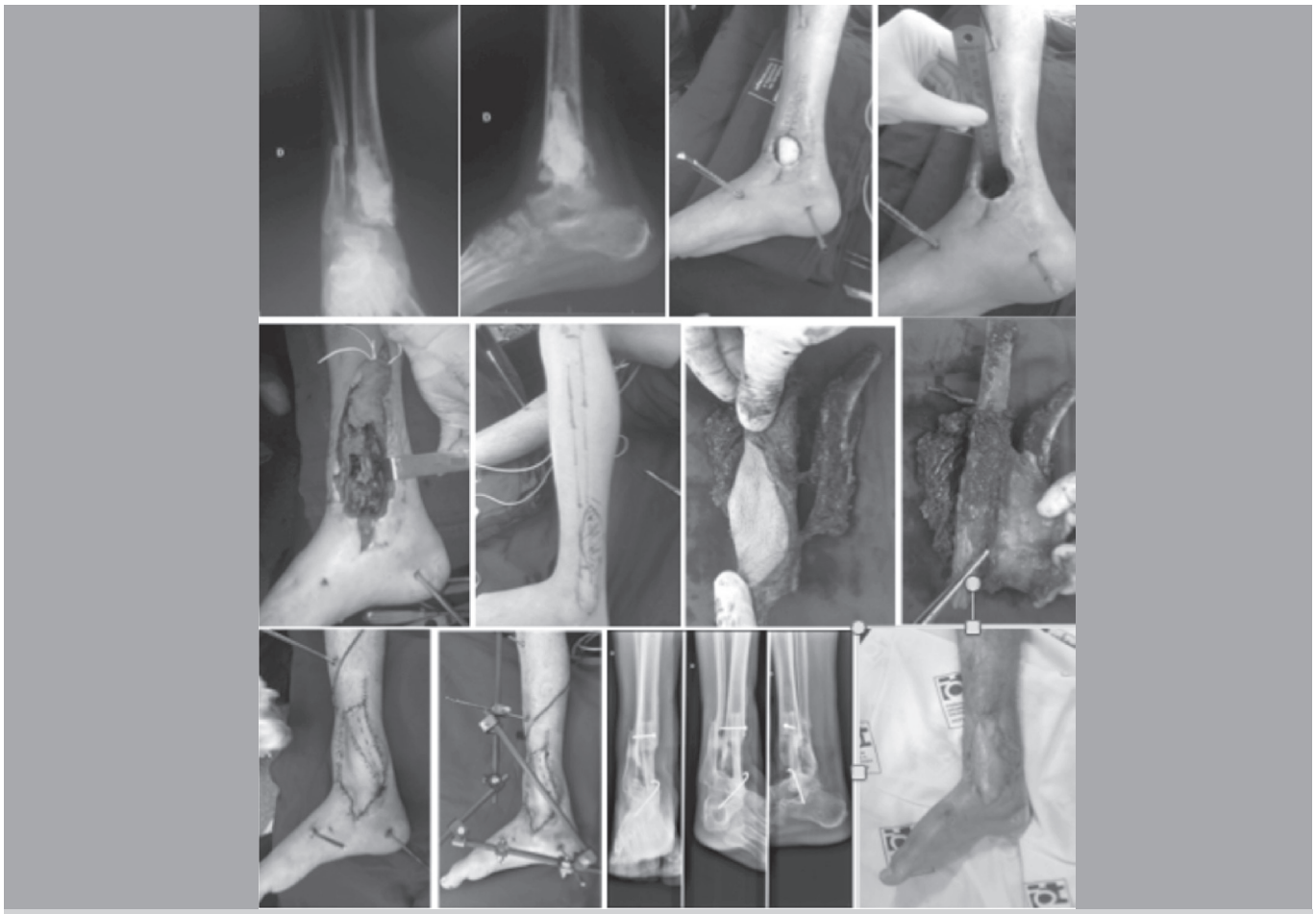

Figure 4. Male, 38 years, postoperative infection after internal fixation after an ankle sprain, forwarded with bone and soft tissue wound of the ankle. Submitted to free vascularized fibular flap for bone and soft tissue reconstruction. Final result after 15 months, achieving satisfactory ambulation, without aid.

DISCUSSION

The free vascularized fibular flap is a reliable technique for reconstruction of bone defects, usually larger than 6 cm, and indications includes: limb reconstruction after tumor, trauma, infection and congenital deformities.[5,6,7] Taylor et al 4 describes 38 free vascularized fibular flaps for tibial reconstruction, observing that, stress fractures before consolidation, occurs in most cases and obtain an overall success rate of 95%, with vascularized bone flaps. The complications described to vascularized fibular flaps includes: thrombosis of vessels anastomoses, infection, pseudarthrosis and inadequate graft hypertrophy, and can lead to limb amputation in these severe cases.[8]

The type of bone fixation of the vascularized fibular flap varies according to the recipient site, location in long bones defects, age of patients and the preference of the surgeon. Inadequate fixation is one of the causes of pseudarthrosis,[9] in our study, we could not observe difference in consolidation rates or surgical complications with different types of fixation, and bone union was obtained in 74% of cases, similar to literature.[10,11]

Obesity is a common risk factor studied for free flaps complications.[12,13] For our knowledge, there is no description of obesity influencing specifically vascularized bone flaps. Obesity may lead to difficulties during harvest and inset of free flap, prolonging operative time, increasing the risk of post-operative deep surgical site infection,[14] intraoperative total blood loss and free flap loss.[15] We observed that obese patients, with BMI $> 30\ kg/m^2$, had an increase in complications rates, with statistically significant difference. The average intraoperative ischemia time of free vascularized fibular flap was longer in obese patients, this fact may be justified by the greater difficulty in the surgical access no neurovascular structures and in the donor and recipient area dissection, although it was not statistically significant wich can be justified by the number of patients included in this study. When performing surgeries in obese patients, they should be aware of the increased risk.

Although a high rate of complications, our overall success rates are similar to those in the literature, with 13% total flap loss.

The limitation of the study is the small number of patients, which can lead to a type II error. Another important bias is the choice of bone fixation that can influence in consolidation results.

CONCLUSION

Obesity is a risk factor for complication in free vascularized fibular flap.

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REFERENCES

1. Cleveland EC, Fischer JP, Nelson JA, Wink JD, Levin LS, Kovach SJ. Free flap lower extremity reconstruction in the obese population: Does weight matter. J Reconstr Microsurg. 2014;30(4):263-70.
2. Khouri RK, Cooley BC, Kunselman AR, Landis JR, Yeramian P, Ingram D, et al. A prospective study of microvascular free-flap surgery and outcome. Plast Reconstr Surg. 1998;102(3):711-21.
3. Clavien PA, Barkun J, Oliveira ML, Vauthey N, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications. Five-year experience. Ann Surg. 2009;250(2):187-96.
4. Moreira LF, Pessôa MCM, Mattana DS, Schmitz FF, Volkweiss BS, Antoniazzi JL, et al. Cultural adaptation and the Clavien-Dindo surgical complications classification translated to Brazilian Portuguese. Rev Col Bras Cir. 2016;43(3):141-8.
5. Taylor GI, Corlett RJ, Ashton MW. The Evolution of Free Vascularized Bone Transfer: A 40-Year Experience. Plast Reconstr Surg. 2016;137(4):1292-305.
6. Repo JP, Sommarhem A, Roine RP, Sintonen H, Halonen T, Tukiainen E. Free vascularized fibular graft is reliable in upper extremity long-bone reconstruction with good long-term outcomes. J Reconstr Microsurg. 2016;32(7):513-9.
7. Iamaguchi RB, Fucs PMMB, Costa AC, Chakkour I. Vascularized fibular graft for the treatment of congenital pseudarthrosis of the tibia: long-term complications in the donor leg. Int Orthop. 2011;35(7):1065-70.
8. Bumbasirevic M, Stevanovic M, Bumbasirevic V, Lesic A, Atkinson HDE. Free vascularized fibular grafts in orthopaedics. Int Orthop. 2014;38(6):1277-82.
9. Beris AE, Lykissas MG, Korompilias AV, Vekris MD, Mitsionis GI, Malizos KN, et al. Vascularized fibula transfer for lower limb reconstruction. Microsurgery. 2011;31(3):205-11.
10. Zaretski A, Amir A, Meller I, Leshem D, Kollender Y, Barnea Y, et al. Free fibula long bone reconstruction in orthopaedic oncology: A surgical algorithm for reconstructive options. Plast Reconstr Surg. 2004;113(7):1989–2000.
11. Belt PJ, Dickinson IC, Theile DRB. Vascularized free fibular flap in bone resection and reconstruction. Br J Plast Surg. 2005;58(4):425–30.
12. Shin JY, Roh SG, Lee NH, Yang KM. Is obesity a predisposing factor for free flap failure and complications? Comparison between breast and nonbreast reconstruction: Systematic review and meta-analysis. Medicine (Baltimore). 2016;95(26):e4072.
13. De la Garza G, Militsakh O, Panwar A, Galloway TL, Joergesen JB, Ledgerwood LG, et al. Obesity and perioperative complications in head and neck free tissue reconstruction. Head Neck. 2016;38(Suppl 1):E1188-91.
14. Namba RS, Inacio MC, Paxton EW. Risk factor associated with surgical site infection in 30,491 primary total hip replacements. J Bone Joint Surg Br. 2012;94(10):1330-8.
15. Chang DW, Wang B, Robb GL, Reece GP, Miller MJ, Evans GR, et al. Effect of obesity on flap and donor-site complications in free transverse rectus abdominis myocutaneous flap breast reconstruction. Plast Reconstr Surg. 2000;105(5):1640–8.

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DOES TOPICAL USE OF GENTAMICIN REDUCE THE INFECTION RATE IN PRIMARY TOTAL HIP ARTHROPLASTY?

O USO TÓPICO DE GENTAMICINA REDUZ A TAXA DE INFECÇÃO NA ARTROPLASTIA TOTAL PRIMÁRIA DO QUADRIL?

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ABSTRACT

Objective: To determine whether the topical use of gentamicin reduces periprosthetic joint infection rates in primary total hip arthroplasty (THA). Methods: We retrospectively evaluated two cohorts of patients who underwent primary THA in a university hospital, with a minimum of 1-year postoperative follow-up and full clinical, laboratory, and radiological documentation. Patients who underwent operation in the first 59 months of the study period (263 hips) received only intravenous cefazolin as antibiotic prophylaxis (Cef group), and those who underwent operation in the following 43 months (170 hips) received intravenous cefazolin plus topical gentamicin directly applied on the wound as antibiotic prophylaxis (Cef + Gen group). For the diagnosis of periprosthetic joint infection, we used the criteria of the Centers for Disease Control and Prevention. Data were analyzed using the Fisher exact test, and p values of <0.05 were considered significant. Results: Thirteen hips (4.9%) in the Cef group and eight hips (4.7%) in the Cef + Gen group presented periprosthetic joint infection. Statistical analysis revealed no difference between the infection rates (p = 1.0). Conclusion: Topical gentamicin as used in this study did not reduce periprosthetic joint infection rates in primary THA. ***Level of Evidence III, Retrospective comparative study.***

Keywords: Infection. Arthroplasty, Replacement, Hip. Clinical study. Antibiotic prophylaxis.

RESUMO

Objetivo: Determinar se o uso tópico de gentamicina reduz a taxa de infecção articular periprotética na artroplastia total primária do quadril. Métodos: Avaliamos retrospectivamente dois coortes de pacientes submetidos à artroplastia total primária do quadril em um hospital universitário, com seguimento pós-operatório mínimo de 1 ano e completa documentação clínica, laboratorial e radiológica. Os casos operados nos primeiros 59 meses do período do estudo (263 quadris) utilizaram somente a cefazolina por via endovenosa como antibioticoprofilaxia (Grupo Cef). Os casos operados nos 43 meses seguintes (170 quadris) utilizaram a cefazolina por via endovenosa associada à gentamicina tópica aspergida diretamente na ferida operatória como antibioticoprofilaxia (Grupo Cef + Gen). Para o diagnóstico de infecção articular periprotética, utilizamos os critérios do Centers for Disease Control and Prevention. Os dados foram submetidos ao teste exato de Fisher, e valor de p menor que 0,05 foi considerado significativo. Resultados: Treze quadris apresentaram infecção articular periprotética no Grupo Cef (4,9%) e oito quadris no Grupo Cef + Gen (4,7%). A análise estatística demonstrou não haver diferença entre estas taxas (p=1,0). Conclusões: O uso tópico da gentamicina, da maneira como utilizada neste estudo, não reduziu a taxa de infecção articular periprotética na artroplastia total primária do quadril. ***Nível de evidência III, Estudo comparativo retrospectivo.***

Descritores: *Infecção. Artroplastia de quadril. Estudo clínico. Antibioticoprofilaxia.*

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INTRODUCTION

Total hip arthroplasty (THA) aims to minimize pain and improve hip joint function, and is considered one of the most effective surgeries in terms of improving patients' quality of life[1]. Data published in the literature demonstrate its increasing use in the last decades, and it is estimated that this trend may grow due to its expanding indications and population aging[2].

Periprosthetic joint infection is one of the most feared complications of THA and is associated with significant morbidity and high costs of treatment. Several precautions have been proposed to reduce this complication, such as use of pulsatile lavage systems, operating rooms with laminar airflow, body exhaust suits ("space suits") and topical use of antibiotics[3-5]. In 2009, Cavanaugh et al.[6] demonstrated in an in vivo investigation a lower infection rate in

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This work was developed at the Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.
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orthopedic surgery by the combined use of parenteral cefazolin and topical gentamicin, compared to parenteral cefazolin alone. Motivated by their investigation, we started using topical gentamicin in all THA patients in our hospital.

Our aim is to determine if topical use of gentamicin reduces the periprosthetic joint infection rate in the primary THA, by comparing the infection rate in the period when we used parenteral cefazolin alone as antibiotic prophylaxis, with the most recent period when we started using topical gentamicin in addition to parenteral cefazolin.

MATERIALS AND METHODS

This is a comparative retrospective cohort study. The study was performed following the principles of the Helsinki Declaration of 1995 and was approved by the Research Ethics Committee of the institution where it was conducted (approval number 2,462,571; January 9th, 2018).

Patient selection

We included all patients who had undergone primary THA during a period of 102 months (8.5 years) in a single hospital, with a minimum postoperative follow-up time of one year and complete clinical, laboratory and radiological documentation. Of a total of 464 primary THA performed in the period, 433 met these requirements. There were no restrictions for inclusion of patients in the study with regard to age, gender, ethnicity, comorbidities, indication for arthroplasty or previous surgeries.

Patients operated on during the first 59 months of the study period used intravenous cefazolin alone as antibiotic prophylaxis (263 hips, Cef group). Patients operated on during the following 43 months of the study period used intravenous cefazolin and topical gentamicin as antibiotic prophylaxis (170 hips, Cef + Gen group).

Data collection and outcomes definition

Data collection from medical records was performed by three authors who were not involved in the treatment of patients. Collected data included patients' gender and age, indication for surgery, type of prosthesis, operative time, occurrence of periprosthetic joint infection and the germ that caused it.

The diagnosis of periprosthetic joint infection was based on the Centers for Disease Control and Prevention (CDC) criteria[7], which define that infection is present when, within one year after surgery, there is at least one of the following findings: purulent drainage from a drain that is placed through a stab wound into the joint; organisms isolated from an aseptically obtained culture of joint fluid or tissue; an abscess or other evidence of infection involving the joint on direct examination, during reoperation, or by histopathologic or radiologic examination; diagnosis of joint infection performed by a surgeon or attending physician.

Surgical technique, antibiotic prophylaxis and postoperative care

All patients were operated on by the hip surgery team of the university hospital where the study was performed, using a standardized surgical technique.

When necessary, hair removal in the incision area was performed in the operating room with an electric clipper. Skin preparation was carried out with 10% povidone-iodine-alcohol solution, and an iodine-impregnated incision drape (Ioban®, 3M, St. Paul, MN, USA) was used in the incision area. Patients were positioned in lateral decubitus and surgeries were performed by the direct lateral approach with a 12 to 15-cm long incision. The choice of implant (cemented, hybrid or uncemented) was at the discretion of the surgeon in charge and was based on criteria such as patients' age, bone quality and proximal femoral morphology. Polymethylmethacrylate bone cement used in cemented and hybrid prostheses was always standard, i.e., without antibiotics. The bearing surface used in all cases was highly cross-linked polyethylene/metallic head.

Antibiotic prophylaxis in Cef group was performed with 2g of cefazolin administered by intravenous (IV) injection approximately thirty minutes before the surgical incision and maintained in the postoperative period at a dose of 1g IV every eight hours until completing 48 hours. In Cef + Gen group, in addition to the IV cefazolin in the same protocol as described above, we sprinkled an ampoule of 80mg of liquid gentamicin with a syringe into the surgical wound, immediately before its closure (Figure 1). The postoperative rehabilitation protocol was usually initiated the day after surgery, with isometric exercises and active hip mobilization; gait training was initiated on the second postoperative day. As a general rule, patients were discharged on the third or fourth postoperative day, with information on wound care and suture removal between 10 and 14 days after surgery. Thromboprophylaxis was carried out with compressive elastic stockings and 5,000 IU of unfractionated heparin every 12 hours subcutaneously, for four weeks. All patients were followed up postoperatively for clinical and radiographic assessment at one month, two months, six months, twelve months and annually thereafter.

Statistical analysis

Data sets were evaluated by means of a descriptive statistics, in which it was possible to characterize the cohorts regarding the variables collected. Data were submitted to Fisher's exact test to evaluate the association between categorical variables, and to Student's t-test for comparison of quantitative variables.

All statistical analyses were performed using SAS® statistical software (version 9.4, SAS Institute Inc., Cary, NC, USA). Statistical significance was set at $p<0.05$.

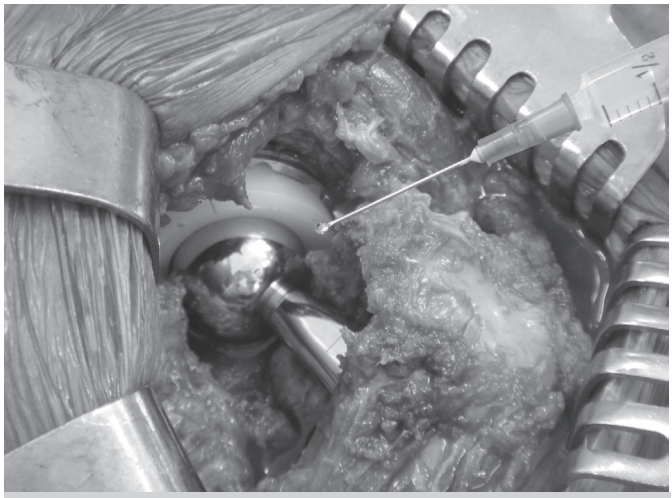

Figure 1. Liquid gentamicin sprinkled directly into the surgical wound, immediately before its closure.

RESULTS

Demographic and surgical data are presented in Table 1. Statistical analysis found that distribution of the variables gender, indication for surgery and type of prosthesis, as well as mean age were similar between the groups. Mean operative time presented a significant difference between groups, being higher in Cef group (p=0.002). Periprosthetic joint infection occurred in thirteen hips in Cef group (4.9%) and in eight hips in Cef + Gen group (4.7%). There was no significant difference between these rates (p=1.0; Table 2).

The germs that caused infections in Cef + Gen group were *S. epidermidis* (two cases), *E. cloacae* (two cases), *S. aureus*

Table 1. Demographic and surgical characteristics of patients.

Variable	Cef group	Cef + Gen group	p-value
Gender male / female (percentage)	137 / 126 (52.1% / 47.9%)	94 / 76 (55.3% / 44.7%)	p*=0.55
Mean age in years (range; SD)	64.7 (34 - 81; 6.9)	63.9 (30 - 82; 8.8)	p**=0.26
Indication for surgery			
Prim OA / Sec OA / FNF (percentage)	181 / 65 / 17 (68.8% / 24.7% / 6.5%)	108 / 50 / 12 (63.5% / 29.4% / 7.1%)	p*=0.49
Type of prosthesis			
cem / hyb / uncem (percentage)	47 / 114 / 102 (17.9% / 43.3% / 38.8%)	23 / 67 / 80 (13.5% / 39.4% / 47.1%)	p*=0.19
Mean operative time in minutes (range; SD)	135.9 (90 – 190; 17.6)	129.9 (85 – 210; 21.1)	p**=0.002

SD: standard deviation; Prim OA: primary osteoarthritis; Sec OA: secondary osteoarthritis; FNF: femoral neck fracture; cem: cemented; hyb: hybrid; uncem: uncemented; *: Fisher's exact test; **: Student's t-test.

Table 2. Periprosthetic joint infection rate in the groups.

Group	Infection		p-value*
	No	Yes	
Cef + Gen	162 (95.3%)	8 (4.7%)	1.0
Cef	250 (95.1%)	13 (4.9%)	

*: Fisher's exact test.

Table 3. Germ distribution in the groups.

Group	Germ		p-value*
	Gram-negative	Gram-positive	
Cef + Gen	5 (62.5%)	3 (37.5%)	0.39
Cef	5 (38.5%)	8 (61.5%)	

*: Fisher's exact test.

(one case), *P. aeruginosa* (one case), *A. baumannii* (one case) and *S. agalactiae* (one case). In Cef group, the germs were *S. aureus* (four cases), *S. epidermidis* (three cases), *E. coli* (two cases), *S. haemolyticus* (one case), *P. mirabilis* (one case), *E. cloacae* (one case) and *P. aeruginosa* (one case). Thus, there was a predominance of infections caused by Gram-negative germs in Cef + Gen group and a predominance of infections caused by Gram-positive germs in Cef group, but without significant difference (Table 3).

In Cef + Gen group, mean operative time for patients who developed periprosthetic joint infection was 165 minutes, but for those who did not develop periprosthetic joint infection was 128.2 minutes, demonstrating a significant difference ($p<0.0001$). The same pattern was observed in Cef group, where the mean operative times for patients who developed and did not develop periprosthetic joint infection were respectively 157.3 minutes and 134.8 minutes ($p<0.0001$). Likewise, comparison of the mean operative time for all cases who developed and did not develop periprosthetic joint infection, without distinction between groups, presented significant difference (160.2 minutes and 132.2 minutes, respectively; $p<0.0001$). The data are shown in Table 4.

There was no association between the type of prosthesis and periprosthetic joint infection, either in Cef + Gen group ($p=0.16$) or in Cef group ($p=0.75$). Analysis of this association in all cases, without distinction between groups, also did not present statistical significance ($p=0.27$). The data are shown in Table 5.

Regarding the association between indication for surgery and periprosthetic joint infection, there was no statistical significance in Cef + Gen group ($p=0.06$), but statistical significance was found in Cef group, with femoral neck fracture cases presenting a higher infection rate ($p=0.02$). Analysis of this association in all cases, without distinction between groups, also presented statistical significance and, once again, femoral neck fracture cases presented the highest infection rate ($p = 0.003$). The data are shown in Table 6.

Table 4. Association between operative time and periprosthetic joint infection.

Group	Infection	n	Mean operative time in minutes (range; SD)	Difference in minutes (95% CI)	p-value*
Cef + Gen	No	162	128.2 (85 – 175; 19.2)	36.8 (23.9 – 49.6)	<0.0001
	Yes	8	165 (130 – 210; 27.9)		
Cef	No	250	134.8 (90 – 190; 16.7)	22.5 (12.4 – 32.5)	<0.0001
	Yes	13	157.3 (120 – 190; 21.1)		
All cases	No	412	132.2 (85 – 190; 18)	28 (19.9 – 36.1)	<0.0001
	Yes	21	160.2 (120 – 210; 23.5)		

n: number of cases; SD: standard deviation; 95% CI: 95% confidence interval; *: Student's t-test.

Table 5. Association between type of prosthesis and periprosthetic joint infection.

	Cef + Gen group		Cef group		All cases	
Type of prosthesis	Infection		Infection		Infection	
	No (%)	Yes (%)	No (%)	Yes (%)	No (%)	Yes (%)
Cemented	20 (87%)	3 (13%)	44 (93.6%)	3 (6.4%)	64 (91.4%)	6 (8.6%)
Hybrid	65 (97%)	2 (3%)	108 (94.7%)	6 (5.3%)	173 (95.6%)	8 (4.4%)
Uncemented	77 (96.2%)	3 (3.8%)	98 (96.1%)	4 (3.9%)	175 (96.2%)	7 (3.8%)
	p-value*: 0.16		p-value*: 0.75		p-value*: 0.27	

*: Fisher's exact test.

Table 6. Association between indication for surgery and periprosthetic joint infection.

	Cef + Gen group		Cef group		All cases	
Indication for surgery	Infection		Infection		Infection	
	No (%)	Yes (%)	No (%)	Yes (%)	No (%)	Yes (%)
Prim OA	105 (97.2%)	3 (2.8%)	176 (97.2%)	5 (2.8%)	281 (97.2%)	8 (2.8%)
Sec OA	47 (94%)	3 (6%)	60 (92.3%)	5 (7.7%)	107 (93%)	8 (7%)
FNF	10 (83.3%)	2 (16.7%)	14 (82.4%)	3 (17.6%)	24 (82.8%)	5 (17.2%)
	p-value*: 0.06		p-value*: 0.02		p-value*: 0.003	

Prim OA: primary osteoarthritis; Sec OA: secondary osteoarthritis; FNF: femoral neck fracture; *: Fisher's exact test.

DISCUSSION

It is estimated that the cost of treatment of a periprosthetic joint infection is four to five times higher than the cost of an uncomplicated primary arthroplasty[8,9]. In addition to the direct financial impact associated to the treatment of an infected THA, there are indirect impacts related to loss of patients' productivity. Even with successful treatment, patients often require 6 to 18 months to recover the function they had before the onset of infection, and in some cases the patient may never recover the same functional levels[10].

The criteria used for the diagnosis of periprosthetic joint infection in this study were proposed by the CDC[7] in 1992 and are used in the literature until the present time[11-13]. More recently, in 2013, the Musculoskeletal Infection Society (MSIS) published an international consensus for the diagnosis of periprosthetic joint infection[14]. We did not use the MSIS criteria in this study because a significant part of our series had been operated before 2013 and, at that time, we had not yet incorporated

all the laboratory tests proposed by this international consensus for the investigation of periprosthetic joint infection. It is interesting to note that Honkanen et al.[15] recently compared the concordance between these two sets of diagnostic criteria in a tertiary orthopedic hospital and reported that 18% of the arthroplasties diagnosed as infected according to the CDC criteria were not considered infected according to the MSIS criteria, demonstrating that the old criteria may overestimate the real rate of periprosthetic joint infection or that the new criteria may underestimate it.

The periprosthetic joint infection rate in primary THA in our hospital are within the values reported by other Brazilian authors, ranging from 0.98% to 6.5%[11,16-18], but are above the rates reported by North American and European authors, ranging from 0.3% to 2.3%[4,9,19]. Besides possible factors directly related to the patient, the fact that we do not use body exhaust suits and the circulation of several persons in the operating room, typical of a teaching hospital such as ours, may be factors related to these higher rates[20].

Topical use of antibiotics in orthopedic surgeries can be accomplished by adding it to irrigation solution, bone grafts, bone substitutes, bone cement or by applying it directly to the operative wound in the form of powder or liquid, as in our case. Our results demonstrated that there was no reduction of periprosthetic joint infection rate in primary THA with topical use of gentamicin in the operative wound.

From a theoretical point of view, topical use of antibiotics in orthopedic surgeries is an interesting strategy, because it provides high concentration of the antibiotic at the surgical site, with fewer systemic adverse effects. This strategy has been studied for several years, with conflicting results. In 2011, O'Neill et al.[21] and also Sweet, Roh and Silva[22] reported a reduction in the surgical site infection rate with topical application of vancomycin powder in patients submitted to spinal arthrodesis. Parvizi et al.[4] reported that the use of antibiotic-impregnated cement reduces the rate of periprosthetic joint infection by approximately 50% in primary THA. Romanò et al.[23] in a multicenter study demonstrated a reduction in the rate of periprosthetic joint infection in THA with application of an antibiotic-loaded hydrogel coating onto the surface of the implants. Evidence on the efficacy of topical use of vancomycin[24] and gentamicin[6] to reduce the surgical site infection rate in orthopedic surgeries has also been found in animal models. On the other hand, Tubaki, Rajasekaran and Shetty[25] in 2013 found no reduction in surgical site infection rate with topical application of vancomycin powder in patients undergoing spinal surgery. Schiavone Panni et al.[26] reported in their systematic review that the use of antibiotic-loaded bone cement does not reduce the rate of periprosthetic joint infection in primary total knee arthroplasty. Finally, the CDC guideline for the prevention of surgical site infection published in 2017 declares that intraoperative antimicrobial irrigation for the prevention of surgical site infection is an unresolved issue[27].

All the demographic characteristics between groups were similar. Mean operative time was the only surgical variable that showed difference between groups (six minutes shorter in Cef + Gen group); despite the small nominal value, this difference was statistically significant (p=0.002). Therefore, even with a mean shorter operative time, Cef + Gen group did not present a lower periprosthetic joint infection rate. We can argue from a logical point of view that this finding would reinforce the hypothesis of ineffectiveness of topical gentamicin in reducing the periprosthetic joint infection rate, since the literature shows that a shorter surgical time is associated with lower infection rates[28], a fact that was also observed in our data.

We also found a higher rate of periprosthetic joint infection in patients operated due to a femoral neck fracture, and the association between these two circumstances was statistically significant in Cef group and again when patients were evaluated all together. The higher incidence of periprosthetic joint infection in patients with femoral neck fracture has been previously reported by other authors[28] and presumably occurs due to local and systemic reactions to trauma and because these surgeries are performed on an urgent basis, when patients are frequently not in the best clinical conditions.

The study has some limitations. First, it is a retrospective study based on information collected from patients' medical records, and therefore, depends on the accuracy of this information. Second, the groups were not evaluated for the presence of factors that could influence the periprosthetic joint infection rate, such as body mass index, associated systemic diseases (diabetes, autoimmune diseases), previous hip surgeries and physical status. Finally, the number of patients studied is relatively small.

CONCLUSION

Topical application of gentamicin as used in this study did not reduce the periprosthetic joint infection rate in primary THA.

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REFERÊNCIAS

1. Ethgen O, Bruyère O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. J Bone Joint Surg Am. 2004;86(5):963-74.
2. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am. 2007;89(4):780-5.
3. Block JE, Stubbs HA. Reducing the risk of deep wound infection in primary joint arthroplasty with antibiotic bone cement. Orthopedics. 2005;28(11):1334-45.
4. Parvizi J, Saleh KJ, Ragland PS, Pour AE, Mont MA. Efficacy of antibiotic-impregnated cement in total hip replacement. Acta Orthop. 2008;79(3):335-41.
5. Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: the ten-year results of the New Zealand Joint Registry. J Bone Joint Surg Br. 2011;93(1):85-90.
6. Cavanaugh DL, Berry J, Yarboro SR, Dahners LE. Better prophylaxis against surgical site infection with local as well as systemic antibiotics. An in vivo study. J Bone Joint Surg Am. 2009;91(8):1907-12.
7. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol. 1992;13(10):606-8.
8. Bozic KJ, Ries MD. The impact of infection after total hip arthroplasty on hospital and surgeon resource utilization. J Bone Joint Surg Am. 2005;87(8):1746-51.
9. Kapadia BH, Berg RA, Daley JA, Fritz J, Bhave A, Mont MA. Periprosthetic joint infection. Lancet. 2016;387(10016):386-94.
10. Malizos KN, Poultsides LA. The socio-economic burden of musculoskeletal infections. In: Meani E, Romanò C, Crosby L, Hofmann G, editors. Infection and local treatment in orthopedic surgery. Berlin: Springer-Verlag; 2007. p. 1-10.
11. Pinto CZS, Alpendre FT, Stier CJN, Maziero ECS, de Alencar PG, Cruz EDA. Characterization of hip and knee arthroplasties and factors associated with infection. Rev Bras Ortop. 2015;50(6):694-9.
12. Finkelstein R, Eluk O, Mashiach T, Levin D, Peskin B, Nirenberg G, et al. Reducing surgical site infections following total hip and knee arthroplasty: an Israeli experience. Musculoskelet Surg. 2017;101(3):219-25.
13. Baratz MD, Hallmark R, Odum SM, Springer BD. Twenty Percent of Patients May Remain Colonized With Methicillin-resistant Staphylococcus aureus

Despite a Decolonization Protocol in Patients Undergoing Elective Total Joint Arthroplasty. Clin Orthop Relat Res. 2015;473(7):2283-90.
14. Parvizi J, Gehrke T; International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty. 2014;29(7):1331.
15. Honkanen M, Jämsen E, Karppelin M, Huttunen R, Lyytikäinen O, Syrjänen J. Concordance between the old and new diagnostic criteria for periprosthetic joint infection. Infection. 2017;45(5):637-43.
16. Lima ALLM, Barone AA. Hospital infections in 46 patients submitted to total hip replacement. Acta Ortop Bras. 2001;9(1):36-41.
17. Ercole FF, Chianca TC. Surgical wound infection in patients treated with hip arthroplasty. Rev Lat Am Enfermagem. 2002;10(2):157-65.
18. von Dolinger EJ, de Souza GM, de Melo GB, Filho PP. Surgical site infections in primary total hip and knee replacement surgeries, hemiarthroplasties, and osteosyntheses at a Brazilian university hospital. Am J Infect Control. 2010;38(3):246-8.
19. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res. 2008;466(7):1710-5.
20. Picado CH, Garcia FL, Chagas MV Jr, Toquetao FG. Accuracy of intraoperative cultures in primary total hip arthroplasty. Hip Int. 2008;18(1):46-50.
21. O□Neill KR, Smith JG, Abtahi AM, Archer KR, Spengler DM, McGirt MJ, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. Spine J. 2011;11(7):641-6.
22. Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. Spine (Phila Pa 1976). 2011;36(24):2084-8.
23. Romanò CL, Malizos K, Capuano N, Mezzoprete R, D'Arienzo M, Van Der Straeten C, et al. Does an Antibiotic-Loaded Hydrogel Coating Reduce Early Post-Surgical Infection After Joint Arthroplasty? J Bone Jt Infect. 2016;1:34-41.
24. Zebala LP, Chuntarapas T, Kelly MP, Talcott M, Greco S, Riew KD. Intrawound vancomycin powder eradicates surgical wound contamination: an in vivo rabbit study. J Bone Joint Surg Am. 2014;96(1):46-51.
25. Tubaki VR, Rajasekaran S, Shetty AP. Effects of using intravenous antibiotic only versus local intrawound vancomycin antibiotic powder application in addition to intravenous antibiotics on postoperative infection in spine surgery in 907 patients. Spine (Phila Pa 1976). 2013;38(25):2149-55.
26. Schiavone Panni A, Corona K, Giulianelli M, Mazzitelli G, Del Regno C, Vasso M. Antibiotic-loaded bone cement reduces risk of infections in primary total knee arthroplasty? A systematic review. Knee Surg Sports Traumatol Arthrosc. 2016;24(10):3168-74.
27. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-91.
28. Ridgeway S, Wilson J, Charlet A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. J Bone Joint Surg Br. 2005;87(6):844-50.

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ORIGINAL ARTICLE

EXTRA-ARTICULAR RECONSTRUCTION ASSOCIATED WITH THE ANTERIOR CRUCIATE LIGAMENT IN BRAZIL

RECONSTRUÇÃO EXTRA-ARTICULAR ASSOCIADA AO LIGAMENTO CRUZADO ANTERIOR NO BRASIL

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ABSTRACT

Objective: To assess the knowledge and technical preferences of Brazilian knee surgeons in relation to the treatment of Anterior Cruciate Ligament (ACL) injuries using intra-articular reconstruction in combination with extra-articular reconstruction. Methods: A questionnaire consisting of 16 questions about intra-articular ACL reconstruction in combination with extra-articular procedures and about the Anterolateral Ligament (ALL) was applied at the 48th Brazilian Congress of Orthopedics. Results: One hundred thirty-seven surgeons answered the questionnaire. Most surgeons perform 10-30 ACL reconstructions per year, with the transtibial technique appearing as the most common. Most surgeons find some percentage of residual pivot-shift after reconstructions, but the minority performs extra-articular procedures on a routine basis. The main indications for extra-articular reconstruction are revision and profuse pivot-shift cases. Most surgeons consider the ALL a true ligament, but 46.7% with less biomechanical importance and 32.3% with greater importance in knee stability. However, 91.4% had a positive perception of the reconstruction of this structure. Conclusion: Although the preferred technique is still the transtibial procedure, combined anatomical reconstructions already make up more than 50% of cases. Extra-articular reconstructions associated with the ACL are still performed by the minority of Brazilian surgeons, but 91.4% of them report having had a positive perception with their reconstruction. ***Level of Evidence III, Descriptive Study.***

Keywords: Anterior cruciate ligament. Anterolateral ligament. Knee joint. Joint instability.

RESUMO

Objetivo: Avaliar o conhecimento e as preferências técnicas entre os cirurgiões de joelho brasileiros no tratamento das lesões do ligamento cruzado anterior, com reconstrução intra-articular associada à reconstrução extra-articular. Métodos: Foi aplicado questionário de 16 perguntas no 48° Congresso Brasileiro de Ortopedia acerca de reconstrução intra-articular do ligamento cruzado anterior associada a procedimentos extra-articulares e sobre o ligamento anterolateral. Resultados: Responderam o questionário 137 cirurgiões. A maioria faz entre 10 e 30 reconstruções de ligamento cruzado anterior por ano, sendo a técnica transtibial a mais realizada. A maioria encontrou alguma porcentagem de pivot-shift residual após as reconstruções, mas a minoria realizou procedimento extra-articular de rotina. As indicações principais de reconstrução extra-articular foram casos de revisão e pivot-shift exuberante. A maioria considera o ligamento anterolateral um ligamento verdadeiro, porém 46,7% o caraterizou com importância biomecânica menor e 32,3% com importância maior na estabilidade do joelho, mas 91,4% tiveram percepção positiva em relação à reconstrução dessa estrutura. Conclusão: Apesar da técnica de preferência ainda ser a transtibial, as reconstruções anatômicas combinadas já são mais de 50% dos casos. As reconstruções extra-articulares associadas ao ligamento cruzado anterior ainda são feitas pela minoria dos cirurgiões brasileiros, mas 91,4% deles referem ter tido uma percepção positiva com sua reconstrução. ***Nível de Evidência III, Estudo Descritivo.***

Descritores: *Ligamento cruzado anterior. Ligamento anterolateral. Articulação do joelho. Instabilidade articular.*

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INTRODUCTION

Anterior cruciate ligament (ACL) injuries are one of the most common knee injuries.[1] In the USA, for example, more than 200,000 ACL reconstructions are performed on average each year.[2] Techniques for treating anterior knee instability have made considerable progress over the past 30 years, going from open to arthroscopic procedures, and from non-anatomical to more anatomical procedures.[3]
Even with the advances in techniques, many surgeons have noted that a not inconsiderable group of patients continue to have residual

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knee instability, even after technically adequate surgery.[4,5] This instability can be measured objectively using the pivot-shift test, which ranges from minimal perceptible instability to an exacerbated degree, depending on the series used.[6] The positivity of the pivot-shift test in the postoperative period is correlated with worse functionality of these patients.[28]

Due to this residual instability, the focus has shifted back to the extra-articular area of the knee, particularly as of 2013, because of studies related to the Anterolateral Ligament, and procedures performed as monotherapy in the past are now being used in combination with intra-articular ACL reconstruction.[7-9]

Due to the high frequency of ACL injuries in sports, their social and economic impact, the considerable divergence between treatment types, and the importance of Brazilian literature, especially in articles related to the ALL and extra-articular reconstructions published in the last 5 years, it is pertinent to evaluate the perspectives and predilections of Brazilian surgeons in relation to this topic.[10-13]

Therefore, the aim of this study was to evaluate ACL reconstruction preferences among knee surgeons in Brazil, and to observe their knowledge and predilections with regards to extra-articular reconstructions and the Anterolateral Ligament.

MATERIAL AND METHODS

This is a descriptive study with the application of a questionnaire for Brazilian knee surgeons. The questionnaire was developed by the authors of this study (Appendix 1). The questionnaire, which consists of 16 questions, was applied to 137 orthopedists who perform knee surgery at the 48th Brazilian Congress of Orthopedics. The questionnaire was answered voluntarily without the signing of an Informed Consent Form.

The questions were related to the number of ACL reconstructions per year, type of technique most commonly used, clinical observations such as percentage of residual pivot-shift, percentage of association of extra-articular techniques (including ALL reconstruction) with intra-articular ACL technique, level of knowledge of ALL related studies, incidence of ALL reconstruction and criteria for indication, graft types for both ACL and ALL reconstructions, and potential complications. The objective was to gain a better insight into the preferences and degree of knowledge of new extra-articular techniques, and to enable an understanding of the predilections and perceptions of the knee surgeons. We conducted a descriptive statistical analysis of the answers obtained, based on the questionnaire, in order to characterize the sample.

This research project was approved by the Scientific Committee of the Department of Orthopedics and Traumatology of the School of Medicine of Universidade de São Paulo at a meeting, under Research Protocol IOT No. 1321.

RESULTS

The origin and age of the patients are shown in Tables 1 and 2. Of the 137 participants, 28.5% answered that they perform fewer than 10 ACL reconstructions per year; 29.1% perform between 10 and 30; 27.8% between 30 and 50; 12.4% between 50 and 100, and only 2.2% perform more than 100 ACL reconstructions per year (Table 1). The ACL reconstruction technique preferred by 40.9% of knee surgeons was the Single-Bundle Transtibial Technique; followed by the Single-Bundle Transportal Technique preferred by 32.1% of the participants; 18.3% prefer Single-Bundle Outside In Reconstruction; 7.3% prefer Double-Bundle Reconstruction, and the remaining 1.4% said they still perform Open ACL Reconstruction (Table 2). The incidence of residual instability determined by the pivot-shift test is described in Table 3.

Table 1. Number of Anterior Cruciate Ligament reconstructions performed per year by Brazilian surgeons who answered the questionnaire at the 48th Brazilian Congress of Orthopedics.

Number of Reconstructions/year	Number of surgeons	%
<10	39	28.5
Between 10 and 30	40	29.1
Between 30 and 50	38	27.8
Between 50 and 100	17	12.4
>100	3	2.2

Table 2. Preferred technique for Anterior Cruciate Ligament reconstructions of Brazilian surgeons who answered the questionnaire at the 48th Brazilian Congress of Orthopedics.

Preferred Technique for ACL reconstruction	No. of surgeons	%
Open	2	1,4
Arthroscopic Single-Bundle Transtibial	56	40,9
Arthroscopic Single-Bundle Transportal	44	32.1
Arthroscopic Single-Bundle Outside In	25	18.3
Double-Bundle Arthroscopic	10	7.3

ACL – Anterior Cruciate Ligament.

Table 3. Incidence of residual pivot-shift found in the post-anterior cruciate ligament reconstruction physical examination by Brazilian surgeons who answered the questionnaire at the 48th Brazilian Congress of Orthopedics.

Incidence of Residual Pivot-Shift following ACL Reconstruction	No. of Surgeons	%
Less than 5%	2	1.4
Between 5 and 10%	56	40.9
Between 10 and 15%	44	32.1
Between 15 and 20%	25	18.3
More than 20%	10	7.3

Regarding the combination of extra-articular reconstructions associated with ACL reconstruction, the majority of surgeons (73.7%) answered that they did not use this procedure in reconstructions. Among those who do, 21.2% only perform the procedure in selected cases; 1.4% use it routinely in revision cases, and 3.6% use the procedure routinely in primary and revision cases.

In an objective question about whether all the respondents were familiar with the ALL and its recent anatomical importance as well as surgical techniques for extra-articular reconstruction, 60.5% of respondents said they had only recently heard about the ALL; 32.1% said they had known about it for years, and 7.2% said they were not yet aware of the ligament.

Another question put to the surgeons concerned their opinion about the importance of the Anterolateral Knee Ligament. In the studied sample, 46.7% agree with the anatomical existence of the ligament, but believe it has little importance in the control of rotatory knee instability; only 32.3% consider the ALL important as an anatomical and functional structure in the control of rotatory instability; 9.4% regard the ALL as a lateral structure, but not a ligament, and 6.5% regard the ALL as a ligament, but without a functional role. 82.2% answered that they had not yet performed any ACL reconstruction in combination with ALL, and 17.8% had already performed the procedure at least once. Regarding the graft that would be chosen to perform Extra-articular ALL Reconstruction, 71.6% answered that they would use the Gracilis Tendon; 27.0% that they would use the Iliotibial Tract or Band, and 1.4% that they would only use Tissue Bank Tendons.

As concerns the fixation options for a potential ALL reconstruction, 55.5% said they use or would use Interference Screws; 33.5% said they prefer or would prefer to use Anchors; 5.8% would fix

the ligament using only soft tissue and transosseous sutures, and 5.2% would use Biotenodesis Screws or Anchors.

Regarding the surgical indications for ALL reconstruction, the question was open to more than one answer for the interviewees, so that 75.1% consider a high-grade pivot-shift test the main indication. The other responses are described in Table 4.

Regarding the fixation of the ALL graft, the surgeons were asked at which angle of flexion or extension they would fix this graft. 45.2% would fix it at 30° of flexion; 27.8% at 45° of flexion; 19.7% would fix the graft in extension and 4.3% would fix it at 60° of flexion. Regarding the use of a brace in extension in the postoperative period, 75.6% would not use it while 24.4% said they would. The complications found are described in Table 5. Participants could answer none, only one, or more than one complication.

Finishing with a subjective question, 91.4% answered that they had a positive perception after performing ALL reconstruction, while 8.6% answered that on the contrary, they would give the procedure a negative feedback.

Table 4. Possible indications of Anterolateral Ligament reconstruction in combination with Anterior Cruciate Ligament reconstruction by Brazilian surgeons who answered the questionnaire at the 48th Brazilian Congress of Orthopedics.

Indications for all reconstruction	%
Acl revision	63.5
High-grade pivot-shift	75.1
Sports with rotation movements	38.6
Ligament hypermobility	5.1
Age <18 years	3.6
Professional athletes	5.8
Chronic acl injuries	24.0
Lateral femoral notch	11.6
Segond fracture	36.4

Table 5. Possible complications of Anterolateral Ligament reconstruction in combination with Anterior Cruciate Ligament reconstruction found by Brazilian surgeons who answered the questionnaire at the 48th Brazilian Congress of Orthopedics.

Complications found in ALL reconstruction	%
Joint stiffness/difficulty gaining ROM	31.6
Lateral pain	33.7
Degenerative abnormalities	31.7
Postoperative infection	2.0
Problems with synthesis material	1.0

DISCUSSION

The main finding of this study is that there is still no consensus as to whether there is a need for extra-articular reconstruction combined with intra-articular reconstruction of the ACL, or on the best technique for this potential reconstruction among Brazilian knee surgeons. This controversy is also present in international literature, with groups advocating opposing viewpoints on the ALL.[14-17] Nevertheless, recent studies have shown a tendency to support the use of combined extra-articular reconstruction in selected cases.[18,19]

As regards the population that answered the questionnaire, the vast majority is in southeast Brazil, where most of the services accredited by the Brazilian Society of Knee Surgery are also located. Only about 1/6 of the sample performs more than 50 ACL reconstructions per year, a number similar to that found by Arliani et al.[20] in a study published 5 years ago, showing that few surgeons in Brazil handle a large volume of ACL reconstructions.

The transtibial isometric technique continues to be the preferred technique of most Brazilian surgeons on an individual basis, although so-called anatomical reconstructions, if analyzed in a combined manner, together with transportal and outside in reconstructions, amount to more than 50% of cases. These data show the tendency towards a change of technique in Brazil, as is the case at other international centers, albeit more slowly.

Regarding residual instability measured by the pivot-shift test, only 19.7% reported having observed this phenomenon in a few patients, which shows that it is a fairly common situation in the postoperative period. The presence of residual pivot-shift denotes some degree of rotatory instability and is related to poorer post-ACL reconstruction functional outcomes.[21] One of the advantages of extra-articular reconstruction is that it eliminates this instability. Clinical studies have already shown that the use of combined extra-articular reconstruction is able to reduce pivot-shift and the retear rate.[18,22] Rezende et al.[10] showed, in a systematic review, that the addition of extra-articular reconstruction improves both pivot-shift and anteroposterior instability in patients. Along the same lines, Ibrahim et al.[23] showed lower KT-1000 in patients who had undergone combined reconstruction.

In the questions specifically focusing on extra-articular reconstructions, the vast majority of surgeons do not perform the procedure, while those who do only perform a very limited number of procedures. Only about 5% use this practice routinely, either in primary or revision reconstructions, and only 17.8% have performed ALL reconstruction at least once. Although countries such as Italy and France use lateral reinforcement routinely, American surgeons stopped using this technique in the late 1980s, which influenced much of the world. Specifically with regards to the ALL, most surgeons appeared to have heard of this structure only recently, which is acceptable since anatomical studies focused on this structure began in 2012 with Vincent et al.,[24] and increased significantly in 2013 after the studies by Claes et al.[7] and Helito et al.[9] Only a third of interviewees, however, believe that the ALL is of significant relevance in rotatory stability of the knee. Biomechanical studies have presented considerable controversy regarding its role, without a clear consensus in the literature to date, although with a tendency to consider the ALL significant after the latest studies by Rasmussen et al.,[25] Nitri et al.[26] and Sonnery-Cottet et al.[18]

Regarding fixation techniques, most surgeons opted for the use of the gracilis tendon as a graft and fixation with interference screws in primary reconstructions, which is also the preferred technique of Sonnery-Cottet et al.[18] in the most extensive series published to date on ALL reconstruction and of the author of this article. Nevertheless, the iliotibial tract graft may be used in revision cases, especially in combination with ACL reconstruction using patellar tendon.

The indications for reconstructions presented are also consistent with the current literature.[16] Cases of reconstruction revision and patients with grosser instability based on the pivot-shift test were the most frequent indications found. Limited consensus was also achieved with respect to the fixation angle, with the majority choosing to fix at 30 and 45 degrees of flexion. Although biomechanical studies have shown that the fixation of a Lemaire tenodesis can be performed between 0 and 60 degrees without alterations in knee biomechanics, Inderhaug et al.[27] showed that ALL reconstructions should be fixed in extension.

Despite the lack of consensus among Brazilian surgeons on the vast majority of questions presented, this is also a worldwide trend in this field, with some lines of research advocating extra-articular reconstruction and others supporting only isolated intra-articular reconstruction. Knowing national trends is important to understand where we can focus our lines of research and how to guide our patients.

CONCLUSION

Although the preferred technique of the highest number of Brazilian knee surgeons (40.9%) is still the transtibial procedure, so-called combined anatomical reconstructions already represent more than 50% of cases. Combined intra- and extra-articular ACL reconstruction is still performed by the minority of Brazilian surgeons, but 91.4% of these report having had a positive perception with ALL reconstruction.

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REFERENCES

1. Bradley JP, Klimkiewicz JJ, Rytel MJ, Powell JW. Anterior cruciate ligament injuries in the National Football League: epidemiology and current treatment trends among team physicians. Arthroscopy. 2002;18(5):502-9.
2. Leroux T, Wasserstein D, Dwyer T, Ogilvie-Harris DJ, Marks PH, Bach BR Jr, et al. The epidemiology of revision anterior cruciate ligament reconstruction in Ontario, Canada. Am J Sports Med. 2014;42(11):2666-72.
3. Chambat P, Guier C, Sonnery-Cottet B, Fayard JM, Thaunat M. The evolution of ACL reconstruction over the last fifty years. Int Orthop. 2013;37(2):181-6.
4. Hussein M, van Eck CF, Cretnik A, Dinevski D, Fu FH. Prospective randomized clinical evaluation of conventional single-bundle, anatomic single-bundle, and anatomic double-bundle anterior cruciate ligament reconstruction: 281 cases with 3- to 5-year follow-up. Am J Sports Med. 2012;40(3):512-20.
5. Vadalà AP, Iorio R, De Carli A, Bonifazi A, Iorio C, Gatti A, et al. An extra--articular procedure improves the clinical outcome in anterior cruciate ligament reconstruction with hamstrings in female athletes. Int Orthop. 2013;37(2):187-92.
6. Tanaka M, Vyas D, Moloney G, Bedi A, Pearle AD, Musahl V. What does it take to have a high-grade pivot shift? Knee Surg Sports Traumatol Arthrosc. 2012;20(4):737-42.
7. Claes S, Vereecke E, Maes M, Victor J, Verdonk P, Bellemans J. Anatomy of the anterolateral ligament of the knee. J Anat. 2013;223(4):321-8.
8. Helito CP, Bonadio MB, Tirico LE, Gobbi RG, Demange MK, Angelini FJ, et al. Estudo anatômico do ligamento anterolateral do joelho. Rev Bras Ortop. 2013;48(4):368-73.
9. Helito CP, Demange MK, Bonadio MB, Tírico LE, Gobbi RG, Pécora JR, et al. Anatomy and histology of the knee anterolateral ligament. Orthop J Sports Med. 2013;1(7):2325967113513546.
10. Rezende FC, de Moraes VY, Martimbianco AL, Luzo MV, de Silveira Franciozi CE, Belloti JC. Does Combined Intra- and Extraarticular ACL Reconstruction Improve Function and Stability? A Meta-analysis. Clin Orthop Relat Res. 2015;473(8):2609-18.
11. Vieira EL, Vieira EA, da Silva RT, Berlfein PA, Abdalla RJ, Cohen M. An anatomic study of the iliotibial tract. Arthroscopy. 2007;23(3):269-74.
12. Helito CP, Bonadio MB, Gobbi RG, da Mota EARF, Pécora JR, Camanho GL, et al. Is it safe to reconstruct the knee anterolateral ligament with a femoral tunnel? Frequency of lateral collateral ligament and popliteus tendon injury. Int Orthop. 2016;40(4):821-5.
13. Helito CP, Helito PV, Leão RV, Demange MK, Bordalo-Rodrigues M. Anterolateral ligament abnormalities are associated with peripheral ligament and osseous injuries in acute ruptures of the anterior cruciate ligament. Knee Surg Sports Traumatol Arthrosc. 2017;25(4):1140-8.
14. Dombrowski ME, Costello JM, Ohashi B, Murawski CD, Rothrauff BB, Arilla FV, et al. Macroscopic anatomical, histological and magnetic resonance imaging correlation of the lateral capsule of the knee. Knee Surg Sports Traumatol Arthrosc. 2016;24(9):2854-60.
15. Rahnemai-Azar AA, Miller RM, Guenther D, Fu FH, Lesniak BP, Musahl V, et al. Structural properties of the anterolateral capsule and iliotibial band of the knee. Am J Sports Med. 2016;44(4):892-7.
16. Sonnery-Cottet B, Daggett M, Fayard JM, Ferretti A, Helito CP, Lind M, et al. Anterolateral ligament expert group consensus paper on the management of internal rotation and instability of the anterior cruciate ligament: deficient knee. J Orthop Traumatol. 2017;18(2):91-106.
17. Sonnery-Cottet B, Saithna A, Helito C, Daggett M, Thaunat M. Regarding "anterolateral ligament of the knee, fact or fiction?". Arthroscopy. 2016;32(9):1740-1.
18. Sonnery-Cottet B, Saithna A, Cavalier M, Kajetanek C, Temponi EF, Daggett M5, et al. Anterolateral Ligament Reconstruction Is associated with significantly reduced ACL graft rupture rates at a minimum follow-up of 2 Years. Am J Sports Med. 2017;45(7):1547-57.
19. Sonnery-Cottet B, Thaunat M, Freychet B, Pupim BH, Murphy CG, Claes S. Outcome of a combined anterior cruciate ligament and anterolateral ligament reconstruction technique with a minimum 2-year follow-up. Am J Sports Med. 2015;43(7):1598-605.
20. Arliani GG, Astru DC, Kanas M, Kaleka CC, Cohen M. Anterior cruciate ligament injury: treatment and rehabilitation. Current perspectives and trends. Rev Bras Ortop. 2015;47(2):191-6.
21. Sakai H, Hiraoka H, Yashiki M. Gravity-assisted pivot-shift test can predict the function of the reconstructed anterior cruciate ligament. Knee Surg Sports Traumatol Arthrosc. 2011;19(4):572-8.
22. Trojani C, Beaufils P, Burdin G, Bussière C, Chassaing V, Dijan P, et al. Revision ACL reconstruction: influence of a lateral tenodesis. Knee Surg Sports Traumatol Arthrosc. 2012;20(8):1565-70.
23. Ibrahim SA, Shohdy EM, Marwan Y, Ramadan SA, Almisfer AK, Mohammad MW, et al. Anatomic reconstruction of the anterior cruciate ligament of the knee with or without reconstruction of the anterolateral ligament. Am J Sports Med. 2017;45(7):1558-66.
24. Vincent JP, Magnussen RA, Gezmez F, Uguen A, Jacobi M, Weppe F, et al. The anterolateral ligament of the human knee: an anatomic and histologic study. Knee Surg Sports Traumatol Arthrosc. 2012;20(1):147-52.
25. Rasmussen MT, Nitri M, Williams BT, Moulton SG, Cruz RS, Dornan GJ, et al. An in vitro robotic assessment of the anterolateral ligament, part 1: secondary role of the anterolateral ligament in the setting of an anterior cruciate ligament injury. Am J Sports Med. 2016;44(3):585-92.
26. Nitri M, Rasmussen MT, Williams BT, Moulton SG, Cruz RS, Dornan GJ, et al. An in vitro robotic assessment of the anterolateral ligament, part 2: anterolateral ligament reconstruction combined with anterior cruciate ligament reconstruction. Am J Sports Med. 2016;44(3):593-601.
27. Inderhaug E, Stephen JM, Williams A, Amis AA. Biomechanical comparison of anterolateral procedures combined with anterior cruciate ligament reconstruction. Am J Sports Med. 2017;45(2):347-54.
28. Ayeni OR, Chahal M, Tran MN, Sprague S. Pivot shift as an outcome measure for ACL reconstruction: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2012;20(4):767-77.

Appendix 1. Questionnaire Applied to Knee Surgeons.

Anterolateral Ligament -48th CBOT congress

1 – Which is your area of activity?
a) North
b) Northeast
c) Midwest
d) Southeast
e) South

2 – How old are you?
a) under 35
b) 35 to 45
c) 45 to 55
d) 55 to 65
e) over 65

3 – How many ACL reconstructions do you perform per year?
a) fewer than 10
b) between 10 and 30
c) between 30 and 50
d) between 50 and 100
e) more than 100

4 – What is your preferred technique for the ACL?
a) Open reconstruction
b) Arthroscopic single-bundle transtibial reconstruction
c) Arthroscopic single-bundle transportal reconstruction
d) Arthroscopic single-bundle outside in reconstruction
e) Arthroscopic double-bundle reconstruction

5 – How often do you observe residual pivot-shift after reconstructions?
a) less than 5%
b) between 5 and 10%
c) between 10 and 15%
d) between 15 and 20%
e) more than 20%

6 – Do you perform extra-articular ACL reconstruction in combination with intra-articular reconstruction?
a) No
b) Rarely in selected cases
c) I use it routinely, more often in revision cases
d) I use it routinely, in primary and revision cases
e) I always use it in all cases

7 – Have you ever heard of the Anterolateral Ligament of the knee?
a) No
b) YES, I have know about it for several years
c) YES, but only recently

8 – What is your opinion of the Anterolateral Ligament of the knee?
a) I don't think it exists
b) I think it is a structure in the lateral region, but not a ligament
c) I think it is a ligament, but with negligible function
d) I think it is a ligament, with a minor role in controlling anterolateral knee instability
e) I think it is a ligament, with an important role in controlling anterolateral knee instability,

9 – Have you performed any anterolateral ligament reconstructions?
A) Yes
b) No

10 – With which graft did you or would you perform your reconstruction?
a) Iliotibial tract
b) Gracilis
c) Only with tissue bank tendon
d) Other (please specify_____)

11 – With which material did you or would you perform the fixation of your reconstruction?
a) I would perform fixation only with soft tissue or transosseous sutures
b) anchors
c) Interference screws
d) Biotenodesis screws/anchors

12 – Which would be your indications for Anterolateral Ligament reconstruction (mark all those you consider pertinent)
a) reconstruction revision
b) high-degree pivot-shift upon physical examination
c) sports that involve knee rotation/pivoting movements
d) Ligament hypermobility
e) Age under 18 years
f) Professional athletes
g) Chronic ACL injuries
h) Lateral femoral notch sign ("Hill-Sachs lesion of the knee")
i) Segond fracture

13 – At how many degrees of knee flexion would you perform the fixation of the anterolateral ligament graft?
a) full extension
b) 30 degrees of flexion
c) 45 degrees of flexion
d) 60 degrees of flexion
e) 90 degrees of flexion

14 – Would you tend to use a brace after combined ACL/anterolateral ligament reconstruction?
a) Yes
b) No

15 – Which complications have you experienced in anterolateral ligament reconstruction (mark all those you consider pertinent)
a) joint stiffness/difficulty gaining range of motion
b) lateral pain
c) degenerative abnormalities in the knee
d) infection
e) problems with synthesis material

16 – Generally speaking, what was your personal perception about the patients on whom you performed this procedure?
a) positive
b) negative

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LONG-TERM RESULTS OF EXTREMITY SOFT TISSUE SARCOMAS LIMB-SPARING SURGERY AND RADIOTHERAPY

RESULTADOS DE LONGO PRAZO DE SARCOMAS DE EXTREMIDADE: CIRURGIA E RADIOTERAPIA COM ESPUMA

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ABSTRACT

Objective: To assess the prognostic factors and results of limb sparing surgery and postoperative radiotherapy (PORT) in patients with non-metastatic soft tissue sarcomas (STS) of the extremities. Methods: Between 1980-2007, 114 extremity-located STS treated with PORT were analyzed retrospectively. Tumors were mostly localized in the lower extremities (71,9%). The median radiotherapy (RT) dose was 60.9 Gy. Chemotherapy was administered to 37.7% of the patients. Tumor sizes were between 3-26 cm (median 7 cm). The three most frequent histological types included undifferentiated pleomorphic sarcoma (26.3%), liposarcoma (25.4%), and synovial sarcoma (13.2%). The median follow-up for all patients was 60 months, and 81 months for survivors. Results: The 5- and 10-year local control (LC) rates were 77% and 70.4%, respectively; actuarial survival rates for 5 and 10 years were 71.8% and 69.1%, respectively. Increasing the dose above 60 Gy for all patients and the patients with positive margins demonstrated a clear benefit on 5-year LC (p=0.03 and p=0.04, respectively). Based on multivariate analysis, the addition of chemotherapy and RT dose were independent prognostic factors for LC. A recurrent presentation significantly affects the disease-free survival. Conclusions: PORT for STS of the extremities provides good long-term disease control with acceptable toxicity in a multidisciplinary approach. ***Level of evidence III, Retrospective study.***

Keywords: Soft tissue sarcomas. Extremities. Radiotherapy.

RESUMO

Objetivo: Avaliar os fatores prognósticos e os resultados da cirurgia poupadora de membro e radioterapia pós-operatória em pacientes com sarcomas de partes moles das extremidades. Métodos: Entre 1980 e 2007, 114 sarcomas de partes moles localizados em extremidades tratados com cirurgia poupadora de membro e radioterapia pós-operatória foram analisados restrospectivamente. Os tumores localizavam-se principalmente na região mais baixa (71,9%). A dose média da radioterapia foi de 60,9 Gy. A quimioterapia foi usada em 37,7% dos pacientes. Os tamanhos do tumores estiveram entre 3 e 26 cm (mediana de 7 cm). Os três tipos histológicos mais frequentes foram, respectivamente, sarcoma pleomórfico indiferenciado (26,3%), lipossarcoma (25,4%) e sarcoma sinovial (13,2%). O tempo médio de acompanhamento para todos os pacientes foi de 60 meses e 81 meses para sobrevivente. Resultados: As taxas de controle local para 5 e 10 anos foram de 77% e 70,4%, respectivamente, e as taxas de sobrevida foram de 71,8% e 69,1%. Aumentar a dose acima de 60 Gy para todos os pacientes e para aqueles com margens positivas demonstrou claro benefício no controle local de 5 anos (p = 0,03 e p = 0,04, respectivamente). Considerando a análise multivariada, a adição de quimioterapia e a dose de radioterapia foram fatores prognósticos independentes para controle local. Apresentação recorrente afetou significativamente a sobrevida livre da doença. Conclusões: A cirurgia poupadora de membro e radioterapia pós-operatória para sarcomas de partes moles das extremidades fornece bom controle da doença a longo prazo, com toxicidade aceitável na abordagem multidisciplinar. ***Nível de evidência III, Estudo retrospectivo.***

Descritores: *Sarcoma. Extremidades.Radioterapia.*

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INTRODUCTION

Soft tissue sarcomas (STS) are extremely rare neoplasms and account for < 1% of all malignancies.[1] The main goal is to preserve the extremity function with good local and distant control with satisfactory survival rates. Since the 1980's conservative surgery combined with adjuvant radiotherapy improved local control, from 78% to 91%. Many previous studies have shown that the results with limb sparing surgery and postoperative radiotherapy are similar with radical surgery- alone and with less morbidity.[2,3] Especially in high-grade sarcomas, the role of adjuvant radiotherapy in terms of conservative approach has been proven in randomized trials.[4,5]

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

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Grade is the most important predictor for both overall and disease-free survival. The other prognostic factors for survival are known to be age, tumor size and tumor location, type of surgery and resection margin.[6] The relationship between local control and survival is controversial. Some authors reported that, there is no relation between them, however, Lewis et al. found a strong correlation with local control and metastasis and tumor mortality.[7]
The present study was performed to evaluate long term results of limb-sparing surgery and post-operative radiotherapy with or without chemotherapy among patients with non-metastatic STS of the extremities and compare our results with the literature results. Acute and late radiation related toxicities were analyzed.

MATERIALS AND METHODS

Patient and tumor characteristics

Between 1980-2007, a total of 386 patients were treated with radiotherapy for soft tissue sarcomas at Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Radiation Oncology Department,Istanbul. Patients who had non-extremity STS or who received prior chemotherapy and radiotherapy to the local site or who had previous or concurrent malignancy and patients with distant metastasis and specific histologic subgroups, including, rhabdomyosarcoma, extraosseaus Ewing, primitive neuroectodermal tumor or dermatofibrosarcoma protuberans were not included in this study. Of the remaining 114 patients with extremity located soft tissue sarcomas who were treated with postoperative radiotherapy in our department, were analyzed retrospectively.
All 114 patients were treated with limb-sparing surgery followed by postoperative chemo/radiotherapy after discussed at the weekly multidisciplinary bone and STS tumor board. All the pathological specimens were received and revised by our sarcoma pathologist. Postoperative radiotherapy was performed to patients who had factors associated with an increased risk of recurrence such as high grade tumor, large tumor, close or positive surgical margins. Tumor size was divided in three groups: ≤5cm ,>5-15 cm or ≥ 15 cm. The tumor grade was defined as high; grade III, intermediate or low; grade II-I. The superficial tumor means that tumor was located above the superficial facia, and the deep tumor means that if the tumor involves the facia or located beneath the facia. Margin status was called involved; that means microscopically involved surgical margin, marginal margin; surgical margin was in pseudo-capsule or reactive zone, wide margin; tumor was in the compartmental en block resection or radical margin; tumor was in the extracompartmentalen block entire compartment.
Sixty (53%) were male, 54 (47%) were female. Median age was 44 years (range, 15-82). Tumor size was defined as the maximum diameter of the tumor during pathologic analysis. Tumor size was between 3 -26 cm (median 7cm). Tumors were mostly localized in the lower extremity 82 (71,9%).Five (4%) low grade liposarcoma patients were treated with post operative radiotherapy treatment because their tumor location was in the hand and foot with surgical margin was positive and re-excision was not possible due to location of the tumor. The tumor characteristics are summarized in Table 1.

Table 1. The characteristics of sarcomas.

	Patients (n)	(%)
Median age	44 (15-82)	
Age		
<50	68	59
≥50	46	41
Gender		
Female	54	48
Male	60	53
Median Tumor Size	7 cm	range 3-26cm
Tumor location		
Upper extremity	32	28
Lower extremity	82	72
Stage		
Ia	9	8
Ib	12	11
IIa	44	39
IIb	23	20
IIIa	10	9
IIIb	16	14
Tumor size		
≤5 cm	41	36
5-<15cm	44	39
≥ 15cm	29	25
Histopathological diagnosis		
Undifferentiated pleomorphic sarcoma	30	27
Liposarcoma	29	25
Synovialcell sarcoma	15	13
Fibrosarcoma	12	10
Others	28	25
Grade		
Grade I+II	13	11
Grade III	101	89
Surgical margin		
Involved	25	22
Marginal	72	63
Wide	12	11
Unknown	5	4

Treatment

Immobilization instruments were used for all of the patients as required. Treatment was delivered with Co^{60} machine or 4-6 MV linear accelerators. A shrinking-field technique was used. The limits of initial field margins varied but there were at least 5 cm from the tumor bed and the scar. The boost target volume was consisting of the tumor bed and incision scar with 2 cm margin. Treatment was delivered 45-50 Gy to initial field, 60-70 Gy booster dose to the tumor volume in 1.8-2Gy/fractions/day, 5 days/week. The median total tumor dose was 60,9Gy (44-70Gy).The median radiotherapy time was 49 days (31-95 days). Chemotherapy was administered to 43 (37.7%) patients with high grade and large tumors. Chemotherapy scheme was consisted of doxorubicine 75mg/m^2 (D1-3), ifosfamide 2 mg/m^2 with 2mg/m^2 mesna, and given in different combinations in 6 cycles.

Follow-up

After treatment all patients were followed regularly with a physical examination every 3 months for 2 years, every 6 months between 3 and 5 years and yearly thereafter. Recurrent disease was histologically confirmed. All patients with recurrent disease were discussed for their treatment schedule at our hospitals sarcoma board.

Prognostic Factors and Statistical methods

Prognostic factors that may influence local control, disease-free survival and overall survival were subjected to univariate and multivariate analysis. Local control, disease-free survival and overall survival rates were calculated using the Kaplan-Meier method. All time-to-failure end points were calculated from the date of diagnosis. Overall survival was measured from after the diagnosis of sarcoma to the time of last follow-up or date of death. Univariate and multivariate analysis of prognostic factors were performed using log-rank and Cox regression models, respectively. A p value < 0.05 value was accepted as statistically significant.

RESULTS

Local control

At the time of evaluation, 26 (23%) patients had local failures following postoperative radiotherapy. Of these, 14 patients died of progressive and metastatic disease; the others were still alive at last follow-up. The median time to local progression was 53 months (range of 3-270 months). The 5- and 10-year local control rates were 77%, 70% respectively. (Figure 1) On the univariate analysis; local control rate was better in patients with tumor located in the lower extremity than in upper extremity, but the difference was not significant (p=0.07). Local control rate was significantly worse in patients who received less than 60 Gy radiotherapy dose (p=0.03). The surgical margin positive patients were reanalyzed, there was a significant benefit when the dose was > 60Gy (p=0.04) (62.8%&79.4%). Patients who were treated with chemo-radiotherapy had better local control rate (p=0.08). (Table 2) In multivariate analysis, radiotherapy total dose, chemotherapy were the independent prognostic factors for local control. (Table 3)

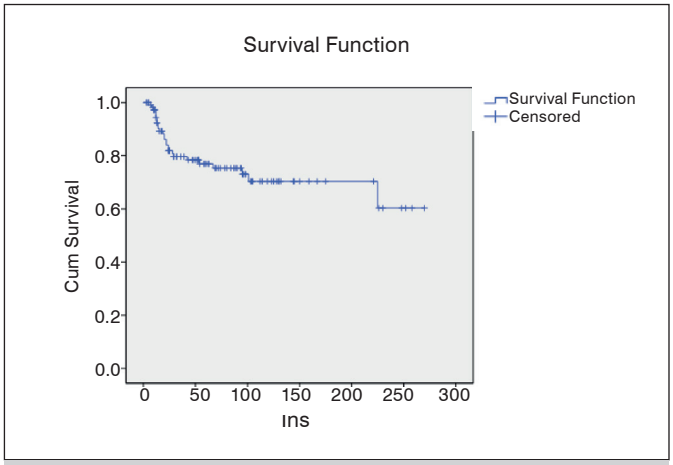

Figure 1. Five-year local control rates for all patients.

Table 2. Univariate analysis of prognostic factors for Local Control (LC), Disease-free Survival(DFS) and Actuarial Survival (ACS). (CHT: Chemotherapy; RT: radiotherapy).

	LC		DFS		ACS	
	5 year %	p	5 year %	p	5 year %	p
Extremity						
Upper	64.6%	0.07	57.7%	0.7	70.4%	0.4
Lower	81.5 %		60.8%		72.1%	
Dose						
<60Gy	62.2%	0.03	58.7%	0.4	76.9%	0.8
≥ 60Gy	79.4%		60.2%		75.3%	
CHT		0.08				
(-)	70.3%		54.5%	0.2	60.2%	0.2
(+)	80.8%		63.1%		77.9%	
Gender						
Male	71.6%	0.09	52.8%	0.07	64.2%	0.04
Female	83%		67.2%		81.3%	
Grade						
I	80.5%	0.3	66.4%	0.2	75.8%	0.7
II	75.1%		55.7%		77.7%	
III	63.9%		55.6%		62.2%	
Stage						
I	80.1%	0.3	65.7%	0.3	75.2%	0.7
II	76.2%		53.4%		74.8%	
III	63.9%		50.5%		62.2%	

Disease-free survival

Distant metastasis was noted in 27% of the patients; 12 of them had also local failure. The most common sites of distant metastases were the lung (20%) and the bone (5%). Disease-free survival rates for 5 and 10 years were 60% and 52% respectively. (Figure 2) The disease-free survival rates were slightly better for the female patients (p=0.07). (Table 2)

Actuarial survival

A total of 33 (28,9%) patients died during follow-up. Of these, 31 were associated with disease progression (including 3 from local-regional failure, 17 from distant metastasis and 11 from both). A further 2 patients died from an unknown cause. The median follow-up time for living patients was 81 months (12-270 months).Actuarial survival rates for 5 and 10 years were 72% and 70% respectively. (Figure 3)

Table 3. Multivariate analysisof prognostic factorsfor Local Control (LC), Disease-free Survival (DFS) and Actuarial Survival (ACS).

	LC		DFS		ACS	
	p	HR (95%CI)	p	HR(95% CI)	p	HR(95% CI)
Extremity						
Lower	0.080.488(0.218-1.092)		0.9	0.966(0.493-1.895)	0.8	0.926(0.410-2.092)
Upper	1		1		1	
Dose						
<60Gy	0.009	1	0.10.581(0.262-1.292)		0.9	1.029 (0.353-2.999)
≥ 60Gy	0.291(0.116-0.730)		1		1	
CHT						
(-)	0.03	1	1.500(0.820-2.744)		0.1	1.421(0.689-2.931)
(+)	0.423(0.191-0.935)		1		1	

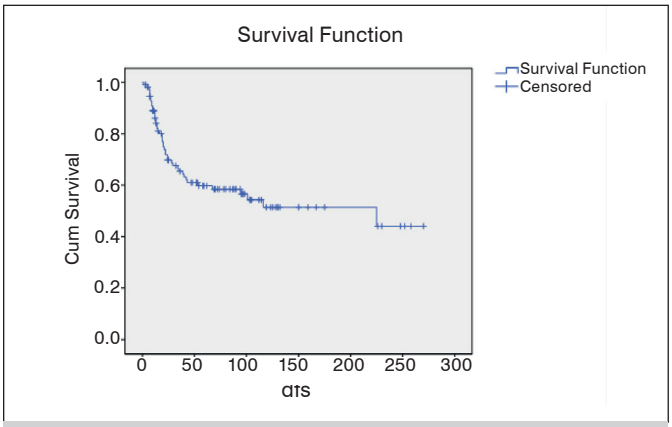

Figure 2. Five-year disease free control rates for all patients.

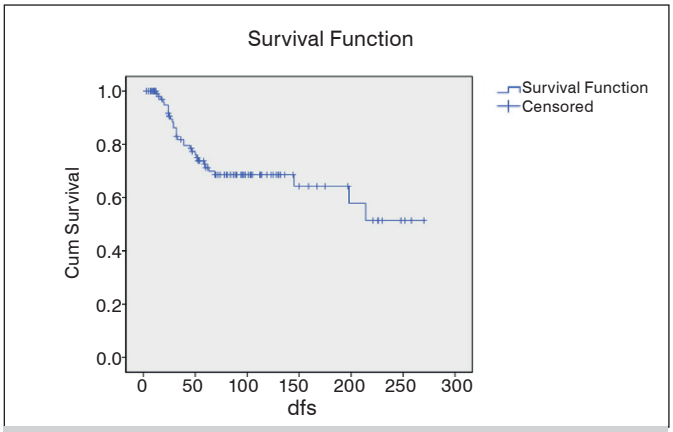

Figure 3. Five-year Actuarial control rates for all patients.

On univariate analysis, the actuarial survival rate was significantly higher in female than male patients (p=0.04). (Table 2) In addition, we did not find any independent significant prognostic factor on multivariate analysis. (Table 3)

Complications

Acute and late side effects were scored according to RTOG and EORTC criteria. Among the 92 patients, acute radiation effects were documented in 54 patients. Grade I acute skin reactions were observed in 38 patients and grade II in 16 patients. Radiation fibrosis (45.6%) was the most common late side effect. Deep vein thrombosis had occurred in one patient, 9 patients had chronic oedema, 6 patients had lymphangitis and 1 patient had bone fracture.

DISCUSSION

Nowadays, the treatment of soft tissue tumors of the extremities; except for a small rate of cases, is limb sparing therapy. The purpose is to protect quality of life and function while maintaining local control. While local control rates is not at the desired levels with limb-sparing surgery alone, adjuvant radiotherapy is offered in addition to limb sparing surgery to improve the results. The results showed that combining these two treatment methods achieved the same success with radical surgery alone.[8] The first prospective, randomized study comparing amputation with limb-sparing surgery and radiotherapy showed similar disease-free and overall survival rates.[3] These results were supported by randomized trials, especially in high-grade tumors.[9] Both pre- and post-operative radiotherapy are considered to be standard approaches for most intermediate or high grade soft tissue sarcomas. The addition of radiotherapy to surgery allows preservation of function with similar local control rates, and survival, to radical resection (i.e. compartmental excision/amputation).[8] The majority of patients with low-grade tumors will not require radiotherapy. However, it should be considered for those with large, deep tumors with close or incomplete margins of excision, in whom re-excision is not possible, especially if adjacent to vital structures that could limit further surgery in the future. Patients who have undergone a compartmental resection or amputation do not require adjuvant radiotherapy assuming that the margins are clear. If pre-operative radiotherapy is used there is a slightly higher incidence of post-operative morbidity including acute wound healing problems. Approaches which include the use of local or free flaps might be advantageous to avoid wound complications. Free flaps may reduce the risk of postoperative wound breakdown, minimize the dead space, and reconstruct the defect. A two team surgical approach (resection and reconstruction) reduces the operative time. Pre-operative radiotherapy may be less appropriate in cases where wound healing is more likely to be problematic, such as proximal thigh/groin or axillary locations. In addition, if a patient has a rapidly growing, painful tumor early surgery may be preferred. For certain radiosensitive histological subtypes, such as myxoid liposarcoma, pre-operative radiotherapy may be particularly advantageous, given the degree of tumor shrinkage that can be achieved. Pre-operative RT was significantly associated with an increased likelihood for negative surgical margins, thereby providing evidence for the underlying hypothesis that preoperative RT allows for sterilization of the surgical margins and increases the likelihood of achieving an oncological optimal resection.

Local recurrence rate varies between 9%-24% in the literature. Prognostic factors were evaluated in several studies.[10-14] The anatomic location of an extremity soft tissue tumor influences local control. Five year local control rates were shown to be significantly better in proximal localized and lower extremity tumors.[10,11] Alektiar also reported lower control rates on the upper extremity, they concluded that upper extremity localization was more difficult to obtain wide surgical margin.[12] In the present study, the number of the patients with positive surgical margin were more (44%) on the upper extremity than lower extremity (34 %) supporting the results of Alektiar et. al.The rate of local control was found to be better in patients with tumors located in the proximal lower extremity than the patients with proximal upper extremity tumors (p = 0.07).

Histological differentiation has been reported to be an important prognostic factor in several studies. Singer et. al. reported better survival rates in patients with low grade tumors than high grade tumors, although it did not influence the local control rates.[13] In addition, some studies demonstrated that high grade was the only factor found to be associated with an increased risk of metastatic recurrence.[14] In our study, patients with high grade tumors had also worse survival rates compared to patients with low grade tumors, but the difference was not statistically significant.

Most studies have agreed that surgical margin was one of the strongest negative prognostic value for local control.[9,15] Incomplete resection had found to be the most significant factor on local recurrence and survival in our previous analysis of our patients with extremity, trunk and head-neck STS treated before 1995, however this significance disappeared in the current series.[16] The adequate distance from the tumor for accepting as negative margin is variable. Helsinki University study demonstrates that surgical margins >2.5 cm from the tumor were associated with improved local control. They reported that local control rates were 89.2%,85.9% and 83.3%,respectively, when combined with adjuvant RT, with the negative margins of at least 2.5cm, 2 cm and 1 cm.[17] In addition several series agreed on that postoperative RT to the patients with close margins has improved local control.[16,18] Recently, several centers reported that higher irradiation dose should be given in order to improve local control for extremities STS patients with positive margins. Zagars et al. reported improved local control with doses $\geq$ 64 Gy for the patients with close or positive margin in the MD Anderson Cancer Center study.[15] We found similar correlation between the dose above 60Gy and local control for all patients with positive margins.

Data supporting chemotherapy for extremity STS is controversial. Patients with deeply located, high-grade and >5 cm tumors have 60% chance of developing metastatic disease.[19] Sarcoma Meta-Analysis Collaboration meta-analysis reported that adjuvant chemotherapy increases disease-free survival rate but does not affect overall survival rate.[20] In the present study, chemotherapy was given to patients with poor prognostic factors and significantly increased the local control on multivariate analysis; however, it was not reflected to the disease-free survival and actuarial survival rates.

CONCLUSION

Limb-sparing surgery with postoperative RT for extremity located STS provides excellent local control and high survival rates with acceptable toxicity and good functional outcome. In the present study although the incidence of large tumor size and marginal resections were high, local failure rate in these patients was comparable with the literature. While this is a retrospective analysis with heterogeneous patient-tumor characteristics, we found that radiotherapy dose and chemotherapy administration were the important factors to improve treatment results. Considering at the high failure rate in the patients who were previously operated in different centers, referral of these patients to the centers dealing with STS for adjuvant therapy is highly recommended.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of the manuscript. ÖYD (0000-0002-2733-0427)*: writing, revision, and data analysis; BA (0000-0001-8435-8074)*; surgeries, data analysis, and writing of articles; DÇÖ (0000-0003-4947-0428)*: statistical analysis and review of the article; FÖD (0000-0002-4764-9419)*: writing and review of manuscript and contributed the entire intellectual concept of the article. *ORCID (Open Researcher and Contributor ID).

REFERENCES

1. Liebel SA, Tranbaugh RF, Wara WM, Beckstead JH, Bovill EG, Phillips TL. Soft tissue sarcomas of the extremities: Survival and patterns of failure with conservative surgery and postoperative irradiation compared to surgery alone. Cancer. 1982;50(6):1076-83.
2. Lindberg RD, Martin RG, Romsdahl MM, Barkley HT Jr. Conservative surgery and postoperative radiotherapy in 300 adults with soft-tissue sarcomas. Cancer. 1981;47(10):2391-7.
3. Rosenberg SA, Tepper J, Gladstein E, Costa J, Baker A, Brennan M, et al. The treatment of soft tissue sarcomas of the extremities: Prospective randomized evaluations of limb sparing surgery plus radiation therapy compared with amputation and the role of adjuvant chemotherapy. Ann Surg. 1982;196(3):305-15.
4. Pisters PW, Harrison LB, Leung DH, Woodruff JM, Casper ES, Brennan MF. Long term results of a prospective randomized trial of adjuvant brachytherapy in soft tissue sarcoma. J Clin Oncol. 1996;14(3):859-68.
5. Yang JC, Chang AE, Baker AR, Sindelar WF, Danforth DN, Topalian SL, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. J Clin Oncol. 1998;16(1):197-203.
6. Toulmonde M, Le Cesne A, Mendiboure J, Blay JY, Piperno-Neumann S, Chevreau C, et al. Long-term recurrence of soft tissue sarcomas: Prognostic factors and implications for prolonged follow-up. Cancer. 2014 Oct 1;120(19):3003-6. doi: 10.1002/cncr.28836. Epub 2014 Jun 18.
7. Lewis JJ, Brennan MF. Soft tissue sarcomas. Curr Probl Surg. 1996;33(10):817-72.
8. Yang JC, Chang AE, Baker AR, Sindelar WF, Danforth DN, Topalian SL, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. J Clin Oncol. 1998;16(1):197-203.
9. Schreiber D, Rineer J, Katsoulakis E, Sroufe RL, Lange CS, Nwokedi E, et al. Impact of postoperative radiation on survival for high-grade softtissuesarcoma of the extremities after limb sparing radical resection. Am J Clin Oncol. 2012;35(1):13-7.
10. Pisters PW, Leung DH, Woodruff J, Shi W, Brennan MF. Analysis of prognostic factors in 1,041 patients with localized soft tissue sarcomas of the extremities. J Clin Oncol. 1996;14(5):1679-89.
11. Alektiar KM, Velasco J, Zelefsky MJ, Woodruff JM, Lewis JJ, Brennan MF. Adjuvant radiotherapy for margin-positive high-grade soft tissue sarcoma of the extremity. Int J Radio Oncol Biol Phys. 2000;48(4):1051-8.
12. Alektiar KM, Brennan MF, Singer S. Influence of site on the therapeutic ratio of adjuvant radiotherapy in soft-tissue sarcoma of the extremity. Int J Radiat Oncol Biol Phys. 2005;63(1):202-8
13. Singer S, Corson JM, Gonin R, Labow B, Eberlein T. Prognostic factors predictive of survival and local recurrence for extremity soft tissue sarcoma. Ann Surg. 1994;219(2):165-73.
14. Baroudi MR, Ferguson PC, Wunder JS, Isler MH, Mottard S, Werier JA, et al. Forearm soft tissue sarcoma: Tumors characteristics and oncologic outcomes following limb salvage surgery. J Surg Oncol. 2014 Nov;110(6):676-81. doi: 10.1002/jso.23686. Epub 2014 Jun 9.
15. Zagars GK, Ballo MT. Significance of dose in postoperative radiotherapy for soft tissue sarcoma. Int J Radiat Oncol Biol Phys. 2003;56(2):473-81.
16. Cakır S, Dincbas FO, Uzel O, Koca S, Okkan S. Multivariate analysis of prognostic factors in 75 patients with soft tissue sarcoma. Radiother Oncol. 1995;37(1):10-6.
17. Sampo M, Tarkkanen M, Huuhtanen R, Tukiainen E, Böhling T, Blomqvist C. Impact of the smallest surgical margin on local control in soft tissue sarcoma. Br J Surg. 2008;95(2):237-43.
18. Trovik CS, Bauer HC, Berlin O, Tukiainen E, Erlanson M,Gustafson P, et al. Local recurrence of deep-seated, high grade, soft tissue sarcoma:459 patients from the Scandinavian Sarcoma Group Register. Acta Ortop Scand. 2001;72(2):160-6.
19. Wunder JS, Healey JH, Davis AM, Brennan MF. A comparison of staging system for localized extremity soft tissue sarcomas. Cancer. 2000;88(12):2721-30.
20. Anonymous. Adjuvant chemotherapy for localized resectable soft tissue sarcoma of adults: Meta-analysis of individual data. Sarcoma Meta-analysis Collaboration. Lancet. 1997;350(9092):1647-54.

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ORIGINAL ARTICLE

FUNCTIONAL INDEPENDENCE OF PEDIATRIC PATIENTS WITH MUCOPOLYSACCHARIDOSES

INDEPENDÊNCIA FUNCIONAL DE PACIENTES PEDIÁTRICOS COM MUCOPOLISSACARIDOSES

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ABSTRACT

Objective: To measure the functional independence to perform activities of daily living of pediatric patients diagnosed with mucopolysaccharidoses. Methods: A descriptive cross-sectional study was carried out with the population of pediatric patients with a confirmed enzymatic diagnosis of mucopolysaccharidoses, enrolled in the Orthopedics outpatient clinic of a hospital in the State of Bahia. The data were collected between October 2016 and March 2017, based on the documentary analysis of the assessment forms used in the department. The variables of this study comprised sex, age, type of MPS and level of functional independence, measured by the Functional Independence Measure scale. Results: Twenty-six patients participated in the study. These were predominantly male (61.5%), with a mean age of 10 ± 4.5 years, affected by MPS VI (73.1%). In the motor domain, the mean score was 65 (± 19.9 points); the cognitive domain obtained a mean score equal to 28 (± 8.2 points); and the total FIM score was 93 (± 26.5). Conclusion: Impaired functional independence was observed among children and adolescents with mucopolysaccharidoses. Tasks related to dressing, toileting, bathing, problem solving and social interaction were those that required the most assistance and/or supervision. ***Level of Evidence IV, Case Series.***

Keywords: Mucopolysaccharidoses. Activities of daily living. Children with disabilities.

RESUMO

Objetivo: Medir a independência funcional para realização de Atividades de Vida Diária de pacientes pediátricos diagnosticados com mucopolissacaridoses (MPS). Métodos: Estudo transversal, descritivo, realizado com a população de pacientes pediátricos com diagnóstico enzimático confirmado de mucopolissacaridoses, cadastrados no ambulatório de ortopedia de um hospital no Estado da Bahia. Os dados foram coletados entre outubro de 2016 e março de 2017, a partir da análise documental das fichas de avaliação utilizadas no serviço. As variáveis deste estudo compreenderam sexo, idade, tipo de MPS e nível de independência funcional, mensurado pela escala de Medida de Independência Funcional. Resultados: Participaram do estudo 26 pacientes, que eram predominantemente do sexo masculino (61,5%), com média de idade de 10 ± 4,5 anos, acometidos por mucopolissacaridoses VI (73,1%). No domínio motor, a pontuação média foi 65 (± 19,9 pontos); o domínio cognitivo obteve escore médio igual a 28 (± 8,2 pontos); e o escore total da MIF foi 93 (±26,5). Conclusão: Foi observado comprometimento da independência funcional de crianças e adolescentes com mucopolissacaridoses. Tarefas relacionadas ao vestuário, utilização do vaso sanitário, banho, resolução de problemas e interação social foram as que demandaram maior assistência e/ou supervisão. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Mucopolissacaridoses. Atividades Cotidianas. Crianças com incapacidade.*

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INTRODUCTION

Mucopolysaccharidoses (MPS) are a group of rare hereditary metabolic diseases characterized by a defect in glycosaminoglycan metabolism, secondary to the inactivity of specific enzymes necessary for its degradation.[1,2] Intralysosomal accumulation of glycosaminoglycans, caused by enzyme deficiency, generates several chronic and progressive alterations that result in changes in the lives of affected subjects and their families.[1,3]

There are seven types of mucopolysaccharidoses described in the literature, classified on the basis of the deficient enzyme or accumulated glycosaminoglycan, and that can also vary in terms of phenotype - from attenuated to severe.[1,4] The clinical features resulting from mucopolysaccharidoses include skeletal, joint, cardiorespiratory, neurological, auditory and visual alterations that vary according to the disease type.[1,3] In patients with mucopolysaccharidoses, the somatic manifestations produce a profile marked by bone deformities, joint limitation,

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chest cavity abnormalities, short stature and hip dysplasia, as well as deformities in knee flexion and of the interphalangeal joints.[5,6] Patients may also develop obstructive respiratory disorders (such as obstructive sleep apnea and narrowing of the upper airways, caused by the accumulation of thick mucus resulting from recurrent infectious processes); or restrictive disorders due to thoracic stiffness and abdominal distension associated with thoracic deformities.[5,7] The nervous system is also commonly affected in some types of MPS, and results in the occurrence of neural and/or spinal cord compression, eventually leading to cognitive impairment.[8,9] These changes are progressive and have a significant impact on the functional independence of the individuals affected.[10]

Research on functional impairment resulting from mucopolysaccharidosis mostly originates in developed countries,[11,12] made up of populations with sociocultural characteristics that differ from the Brazilian population and supported by a better social network and health care. In Brazil and other developing countries, research on these diseases is still in the early stages.

Accordingly, the aim of this study was to measure functional independence in the performance of activities of daily living in pediatric patients diagnosed with mucopolysaccharidoses. An understanding of the functional performance of these patients may help health professionals, specifically those in the field of rehabilitation, to define the demand for necessary healthcare and improve intervention strategies for this population.

MATERIAL AND METHODS

A descriptive cross-sectional study was carried out with the population of pediatric patients with a confirmed enzymatic diagnosis of mucopolysaccharidoses, enrolled in the orthopedic outpatient clinic of a reference hospital in the city of Salvador, state of Bahia. This study is linked to the project "Clinical assessment *of* musculoskeletal features in patients with mucopolysaccharidoses". In compliance with the Guidelines and Standards for Research on Human Subjects contained in Resolution 466/2012 of the Brazilian National Board of Health, the project was submitted to the Institutional Review Board and approved under CAAE [Certificate of Submission for Ethical Consideration] no. 38746914.5.0000.5520/Opinion no. 1.672.503.

Subjects enrolled in the study were all the male and female children and adolescents aged 2-18 years who were receiving medical outpatient follow-up care between January 2012 and October 2014, except those diagnosed with another active chronic or exacerbated condition not associated with mucopolysaccharidosis, and those whose parents/guardians did not sign the Informed Consent Form. The data were collected from October 2016 to March 2017, based on the documentary analysis of the standardized assessment forms used in the department. The variables of this study included sex (stratified in female and male); age (evidenced in years); type of MPS (categorized according to the disease types described in the literature); and functional independence level measures (evidenced by numerical score, according to the specific instrument used).

To assess the level of independence, the instrument used in the abovementioned department was the Brazilian version of the Functional Independence Measure (FIM).[13,14] This is a generic assessment tool, consisting of 18 items which fall into two domains. The motor domain (13 items) evaluates four functional dimensions: self-care, sphincter control, transfer and locomotion; and the cognitive domain (5 items) evaluates two dimensions: communication and social cognition.[14] The FIM identifies how much help the individual requires to accomplish daily tasks, whether it is the assistance of another person or the use of an adaptation resource; and quantitatively measures the level of functional independence of the subject being assessed.[14]

The scoring of the items of the FIM instrument follows an ordinal scale of dependence graded at seven levels: 1 corresponds to the need for total assistance to perform the task and 7 to complete independence for the activity. The sum of points assigned to each item corresponds to the scores of the respective domains and the total score of the instrument. The motor domain ranges from 13 to 91 points; the cognitive domain, from 5 to 35 points; and the total score from 18 to 126 points. The lower the score, the greater the need for assistance to perform the task.[13,14] At the facility where this study was conducted, the FIM scale was applied by a trained professional at the time of patient admission, through an individual interview held with the parents, following the guidelines of the manual for this instrument.[13]

Following an analysis of the normal distribution of the numerical data using the Kolmogorov-Smirnov test, the continuous variables were described in mean (μ) and standard deviation ($\pm$SD), and the categorical variables in absolute and relative frequency. The analyses were carried out using version 20.0 of the statistical program IBM® SPSS® Statistics.

RESULTS

Over the study period, 26 children and adolescents diagnosed with mucopolysaccharidoses were monitored in the orthopedic department of the abovementioned hospital. Male subjects with age averaging 10$\pm$4.5 years affected by MPS type VI (73.1%) predominated (61.5%). (Table 1)

The results of the functional independence measure of the performance of activities of daily living show that in the motor domain, self-care was the subdomain with the lowest score – it reached 62% of the highest possible score (26$\pm$8.3 points). (Table 2) The activities in which the children and adolescents with MPS required most assistance or supervision in this subdomain were related to dressing, bathing and toileting. (Table 3)

Table 1. Sociodemographic and clinical characteristics of children and adolescents with MPS monitored at an Orthopedic outpatient clinic in the city of Salvador, Bahia, from January 2012 to October 2014.

Variables	N (%) or Mean SD
Sex	
Female	10 (38.5%)
Male	16 (61.5%)
Age (in years)	10 4.5
Type of MPS	
I	1 (3.8%)
II	4 (15.4%)
IV	2 (7.7%)
VI	19 (73.1%)

Caption (Table 1): MPS – Mucopolysaccharidosis; SD – Standard deviation. Source: Salvador-BA, 2017.

Table 2. Scores of the dimensions/domains and total score of the FIM scale applied to the parents of children and adolescents monitored at an Orthopedic outpatient clinic in the city of Salvador, Bahia, from January 2012 to October 2014.

Dimensions of the FIM Scale	Mean SD	(%)*
Motor Domain	65 19.9	71%
Self-care	26 8.3	62%
Sphincter control	12 3.5	86%
Transfers	17 6.6	81%
Locomotion	10 4.8	71%
Cognitive Domain	28 8.2	80%
Communication	12 3.7	86%
Social cognition	16 4.9	76%
Total Score of FIM	93 26.5	74%

Caption (Table 2): SD – Standard deviation; FIM –Functional Independence Measure; * –Percentage of the mean score obtained, in comparison to the highest possible score of the dimension/domain. Source: Salvador-BA, 2017.

In the cognitive domain, social cognition reached 76% of the highest possible score (16±4.9 points). (Table 2) Among the activities that constitute this subdomain, the subjects participating in the study needed more assistance in problem solving and social interaction. (Table 3)

DISCUSSION

The findings of this study indicated impairment of the functional independence of children and adolescents diagnosed with mucopolysaccharidoses, primarily in relation to motor function when compared to cognitive function. The most significant motor impairment was self-care activities, including dressing, bathing, and toilet hygiene.

The second lowest score was obtained in the locomotion subdomain (71% of the highest possible score), suggesting that patients with MPS develop difficulty walking, a factor that further accentuates the level of dependence among these subjects. The findings of this research project corroborate the general clinical characteristics described in the literature, regarding the significant decline in motor function evidenced in cases of mucopolysaccharidoses.[4,10,15] We believe that the alteration of hand function in patients with MPS, secondary to finger flexion deformities (claw hands) and joint stiffness, hinders the performance of daily activities, especially those that require manual ability, and has a direct impact on the functional performance of these individuals.[1,11] When studying the occurrence of carpal tunnel syndrome in children diagnosed with MPS type II, Know et al.[16] stated that this condition has a genetic etiology; and late diagnosis, due to the more severe involvement of other organs followed by skeletal dysplasia and joint stiffness, contributes to the complete loss of hand function.[16]

Since some daily activities require mobility and/or manual strength, we cogitate whether the greater the involvement of the hand, the greater the need for assistance in performing them, and consequently the greater the difficulties in self-care, since this domain includes activities that normally require the use of the upper extremities.

Cognitive status is another factor that interferes in functional performance and, consequently, in the independence to perform activities of daily living, as the integrity of this component is related to the understanding of what should be done when faced with a particular task to be performed.[17] Abnormal cognitive function is a distinct characteristic of all forms of MPS type III, and may also occur in patients with the severe form of MPS types I and II, and in MPS VII,[1] justifying the limitation in the ability of these individuals to perform their daily activities.

In this study, the prevalence of patients diagnosed with MPS VI, which does not involve cognitive impairment, may have contributed to a higher score in this domain. However, although the cognitive status of the children and adolescents participating in this research project reached a higher score than motor status, the mean of this domain was about 20% lower than the highest possible score, suggesting a certain degree of cognitive alteration in the sample studied.

In mucopolysaccharidosis, the accumulation of glycosaminoglycans in the central nervous system, the development of hydrocephalus and the presence of sleep disorders, such as obstructive apnea and sustained hypoventilation, are factors that may impair brain function and, therefore, cognitive learning, with negative repercussions on the functional state of patients.[18]

Table 3. Distribution of children and adolescents with mucopolysaccharidoses monitored at an Orthopedic outpatient clinic in the city of Salvador, Bahia, from January 2012 to October 2014, according to levels of dependence on the FIM scale.

Subdomains of the FIM Scale	SCORES†						
	1	2	3	4	5	6	7
	N (%)						
Self-care							
Eating	1 (3.8%)	2 (7.7%)		1 (3.8%)	4 (15.4%)	11 (42.3%)	7 (27%)
Grooming	3 (11.5%)		2 (7.7%)	3 (11.5%)	7 (27%)	9 (34.6%)	2 (7.7%)
Bathing	3 (11.5%)	1 (3.9%)	9 (34.6%)	3 (11.5%)	4 (15.5%)	3 (11.5%)	3 (11.5%)
Upper body dressing	3 (11.5%)	2 (7.7%)	4 (15.3%)	7 (27%)	7 (27%)		3 (11.5%)
Lower body dressing	3 (11.5%)	2 (7.7%)	2 (7.7%)	9 (34.6%)	5 (19.3%)	2 (7.7%)	3 (11.5%)
Toileting	2 (7.7%)	2 (7.7%)	6 (23%)	4 (15.4%)	6 (23.1%)	2 (7.7%)	4 (15.4%)
Sphincter control							
Bladder management	2 (7.7%)			1 (3.8%)	2 (7.7%)	3 (11.5%)	18 (69.3%)
Bowel management	2 (7.7%)	1 (3.8%)			2 (7.7%)	3 (11.5%)	18 (69.3%)
Transfers							
Bed, chair, wheelchair	2 (7.7%)	3 (11.5%)	1 (3.8%)	1 (3.8%)		2 (7.7%)	17 (65.4%)
Toilet	2 (7.7%)	2 (7.7%)	2 (7.7%)		2 (7.7%)	1 (3.8%)	17 (65.4%)
Bath, shower	3 (11.5%)	2 (7.7%)	2 (7.7%)			1 (3.8%)	18 (69.3%)
Locomotion							
Walking / wheelchair	5 (19.3%)	1 (3.8%)		3 (11.5%)		5 (19.3%)	12 (46.1%)
Stairs	7 (27%)		1 (3.8%)	4 (15.4%)		3 (11.5%)	11 (42.3%)
Communication							
Comprehension	2 (7.7%)		2 (7.7%)	2 (7.7%)	1 (3.8%)	2 (7.7%)	17 (65.4%)
Expression	2 (7.7%)		2 (7.7%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	19 (73.2%)
Social cognition							
Social interaction	1 (3.8%)	2 (7.7%)	2 (7.7%)	2 (7.7%)	4 (15.4%)	1 (3.8%)	14 (53.9%)
Problem solving	1 (3.8%)	2 (7.7%)	6 (23.1%)	3 (11.5%)	2 (7.7%)	2 (7.7%)	10 (38.5%)
Memory	2 (7.7%)	1 (3.8%)			1 (3.8%)	1 (3.8%)	21 (80.9%)

Caption (Table 3): FIM –Functional Independence Measure; †Scores: from 1 to 5 indicate the need for assistance and/or supervision, while scores from 6 to 7 indicate independence to perform the activity. Source: Salvador-BA, 2017.

In our research, we attributed the difficulty in locomotion to the susceptibility found in individuals with MPS to develop musculoskeletal deformities, joint limitations, spinal cord compression and pain - conditions that have a detrimental effect on the mobility of these patients.[1] With disease progression, individuals also develop low tolerance to physical exertion and locomotion difficulties, even when covering short distances, due to cardiorespiratory alterations.[19] Thus, we believe that this condition restricts children and adolescents in their activities and makes it impossible for them to keep up with others of the same age group, interfering in social interaction. In addition, communication difficulties, secondary to speech disorders or decreased auditory acuity, can also interfere in the interpersonal relationships of these individuals.

The main limitations of this study are related to the reduced size of the sample, which precluded a comparison of functional independence measures between the different types of MPS; and the use of a generic assessment instrument, which does not cover specific symptoms or factors of the disease in question. However, mucopolysaccharidosis is a rare disease and the majority of studies on this condition do not involve large sample groups. Regarding the instrument used, the application of the FIM in this study is justifiable due to the lack of a specific scale, validated in Brazil, to evaluate the functional independence of patients with this disease. Nevertheless, it is hoped that this research project will help us gain a better understanding of the impacts produced by mucopolysaccharidosis on the functionality of the affected subjects.

In view of the above, it can be seen that supportive therapies for the management of patients diagnosed with MPS should not aim to simply correct the anatomical and/or clinical alterations themselves, but also to improve the functional abilities of individuals, according to their specific needs. Rehabilitation programs should provide direct intervention in the condition of incapacity and/or physical limitation to perform daily activities, especially those related to self-care; mobility/transfers; locomotion; and social cognition - aspects compromised in these patients, as indicated by the findings of this study.

CONCLUSION

The functional independence of children and adolescents diagnosed with mucopolysaccharidoses is compromised. In the study population, we observed the need for assistance mainly in performing activities related to self-care and social cognition. Tasks related to dressing, toileting, bathing, problem solving and social interaction were those that required the most assistance and/or supervision.

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REFERENCES

1. Muenzer J. Overview of the mucopolysaccharidoses. Rheumatology (Oxford). 2011;50(Suppl. 5):4–12.
2. Brands MM, Güngör D, van den Hout JM, Karstens FP, Oussoren E, Plug I, et al. Pain: a prevalent feature in patients with mucopolysaccharidosis. Results of a cross-sectional national survey. J Inherit Metab Dis. 2015;38(2):323–31.
3. Guffon N, Heron B, Chabrol B, Feillet F, Montauban V, Valayannopoulos V. Diagnosis, quality of life, and treatment of patients with Hunter syndrome in the French healthcare system: a retrospective observational study. Orphanet J Rare Dis. 2015;10(43):1–13.
4. Chan MO, Sen ES, Hardy E, Hensman P, Wraith E, Jones S, et al. Assessment of musculoskeletal abnormalities in children with mucopolysaccharidoses using pGALS. Pediatr Rheumatol Online J. 2014;12(32):1–9.
5. Lehman TJ, Miller N, Norquist B, Underhill L, Keutzer J. Diagnosis of the mucopolysaccharidoses. Rheumatology (Oxford). 2011;50(Suppl. 5):41–8.
6. White KK. Orthopaedic aspects of mucopolysaccharidoses. Rheumatology (Oxford). 2011;50(Suppl. 5):26–33.
7. Giugliani R, Federhen A, Rojas MV, Vieira TA, Artigalás O, Pinto LL, et al. Mucopolysaccharidosis I, II, and VI: brief review and guidelines for treatment. Genet Mol Biol. 2010;33(4):589–604.
8. Ru MH, Teunissen QG, van der Lee JH, Beck M, Bodamer OA, Clarke LA, et al. Capturing phenotypic heterogeneity in MPS I: results of an international consensus procedure. Orphanet J Rare Dis. 2012;7(1):22.
9. Peck SH, Casal ML, Malhotra NR, Ficicioglu C, Smith LJ. Pathogenesis and treatment of spine disease in the mucopolysaccharidoses. Mol Genet Metab. 2016;118(4):232–43.
10. Matos MA, Prado A, Schenkel G, Barreto R, Acosta AX. Energy expenditure during gait in patients with mucopolysaccharidosis. Acta Ortop Bras. 2013;21(2):116–9.
11. Kato T, Kato Z, Kuratsubo I, Ota T, Orii T, Kondo N, et al. Evaluation of ADL in patients with Hunter disease using FIM score. Brain Dev. 2007;29(5):298–305.
12. Yasuda E, Suzuki Y, Shimada T, Sawamoto K, Mackenzie WG, Theroux MC, et al. Activity of daily living for Morquio A syndrome. Mol Genet Metab. 2016;118(2):111–22.
13. Riberto M. Orientação funcional para utilização da MIF - Medida de Independência Funcional. 2004. [acesso em 26 mar 2016]. Disponível em: https://toneurologiaufpr.files.wordpress.com/2013/03/manual-mif.pdf
14. Riberto M, Miyazaki MH, Jucá SS, Sakamoto H, Potiguara P, Pinto N, et al. Validação da Versão Brasileira da Medida de Independência Funcional. Acta Fisiatr. 2004;11(2):72–6.
15. Valayannopoulos V, Nicely H, Harmatz P, Tuberville S. Mucopolysaccharidosis VI. Orphanet J Rare Dis. 2010;5(5).
16. Kwon JY, Ko K, Sohn YB, Kim SJ, Park SW, Kim SH, et al. High prevalence of carpal tunnel syndrome in children with mucopolysaccharidosis type II (Hunter syndrome). Am J Med Genet A. 2011;155A(6):1329–35.
17. Amaral IA, Omena Filho RL, Reis Neto JA, Reis MC. Avaliação da capacidade funcional de adolescentes portadores de Mucopolissacaridose do tipo II. Cad Bras Ter Ocup. 2017;25(2):297–303.
18. Berger KI, Fagondes SC, Giugliani R, Hardy KA, Lee KS, McArdle C, et al. Respiratory and sleep disorders in mucopolysaccharidosis. J Inherit Metab Dis. 2013;36(2):201–10.
19. Hendriksz CJ, Lavery C, Coker M, Ucar SK, Jain M, Bell L, et al. Burden of disease in patients with Morquio A syndrome: results from an international patient-reported outcomes survey. Orphanet J Rare Dis. 2014;9(32):1–8.

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ORIGINAL ARTICLE

MODIFIED STOPPA APPROACH FOR PELVIC AND ACETABULAR FRACTURE TREATMENT

STOPPA MODIFICADA PARA TRATAMENTO DE FRATURAS PÉLVICAS E ACETABULARES

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ABSTRACT

Objective: A retrospective review aims to investigate the operative methods and therapeutic effects of the modified Stoppa approach for treating pelvic and acetabular fractures. Methods: 18 patients with acetabular fracture of the anterior column and pelvic anterior ring fracture underwent surgical treatment using the modified Stoppa approach. Some of the treatment was combined with the iliac fossa approach or rear K-L approach. Fracture reduction and postoperative function were evaluated using the Matta scoring standard and the Majeed scoring system. The Oxford Centre for Evidence-Based Medicine system was used to grade the literature review and create graded B recommendations. Results: Incision length was 6-12 cm (mean, 10 cm), operative duration was 50-150 minutes (mean, 85 minutes), and intraoperative blood loss volume was 400-1,000 ml (mean, 500 ml). 18 patients were followed up for 12-36 months post-operation. In the results of X-ray films, 12 cases were anatomical reductions and the remaining cases were satisfactory reductions. According to Majeed standard, 13 patients were excellent and five patients were good. Conclusions: Treatment using the modified Stoppa approach was suitable for anterior approaches, in which pelvic and acetabular fractures were sufficiently exposed, the fracture was conveniently reduced, less complications occurred, and curative effect was satisfactory. ***Level of evidence III, Retrospective comparative study.***

Keywords: Acetabulum. Fracture. Modified. Pelvic. Result. Stoppa.

RESUMO

Objetivo: Uma revisão retrospectiva tem como objetivo investigar os métodos operatórios e efeitos terapêuticos da abordagem modificada de Stoppa para o tratamento de fraturas pélvicas e acetabulares. Métodos: 18 pacientes com fratura acetabular da coluna anterior e fratura do anel anterior pélvico foram submetidos a tratamento cirúrgico utilizando a abordagem de Stoppa modificada. Parte do tratamento foi feita em conjunto com a abordagem da fossa ilíaca ou com a abordagem pelo acesso posterior de K-L. A redução da fratura e a função pós-operatória foram avaliadas pelo padrão de pontuação de Matta e o sistema de pontuação de Majeed. O sistema do Oxford Centre for Evidence-Based Medicine foi usado para classificar a revisão de literatura e criar as recomendações de grau B. Resultados: O comprimento da incisão foi de 6 a 12 cm (média de 10 cm), a duração da cirurgia foi de 50 a 150 minutos (média de 85 minutos) e o volume de perda sanguínea intraoperatória foi de 400 a 1.000 ml (média de 500 ml). 18 pacientes foram acompanhados por 12-36 meses após a operação. Nos resultados dos filmes radiográficos, 12 casos foram de reduções anatômicas e os demais casos foram de reduções satisfatórias. De acordo com o padrão de Majeed, 13 pacientes foram considerados excelentes e cinco pacientes foram considerados bons. Conclusões: O tratamento que utilizou a abordagem de Stoppa modificada foi adequado para abordagens anteriores, nas quais as fraturas pélvicas e acetabulares estavam suficientemente expostas, a fratura foi convenientemente reduzida, ocorreram menos complicações e o efeito curativo foi satisfatório. ***Nível de evidencia III, Estudo retrospectivo comparativo.***

Descritores: *Acetábulo. Fratura. Modificado. Pélvico. Resultado. Stoppa.*

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INTRODUCTION

In recent years, with the rapid developments of industry and the transportation and shipping industry, the incidence rate of pelvic and acetabular fractures resulted from high energy injuries such as those caused by traffic accidents, high falling injury and crush by heavy objects have significantly increased, especially for pelvic fracture caused by traffic accidents. This type of fracture can lead to unmanageable complications such as bleeding; and in the short term, the conditions of these injuries are complex and prognosis is poor. For displaced pelvic and acetabular fractures, it is usually advocated by aggressive surgical treatment;[1] and proper operative approach is very important for fracture exposure and reduction. There are many defects in the traditional ilioinguinal approach such as complicated anatomy, severe trauma, limited reduction and fixation spaces of fracture, and more complications. Since the application of the Stoppa incision approach was applied in the

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treatment of complicated hernia repair surgery and the treatment of pelvic and acetabular fractures by Hirvensalo et al.,[2,3] the Stoppa approach and its modified approaches have became alternative approaches for traditional ilioinguinal approach due to advantages of slight trauma, replacement of the quadrilateral body fracture could be performed in direct vision,[4] and less complications. Hence, the use of this approach has continuously increased. From November 2008 to September 2012, 18 cases of pelvic and acetabular fractures were treated by the modified Stoppa approach; and the curative effect was satisfactory. The report is as follows.

MATERIALS AND METHODS

General data

A total of 18 pelvis and acetabulum fracture patients who were admitted from November 2008 to September 2012 were enrolled into this study. All participants in the study provided written the free and informed consent in accordance with the Gansu Provincial Hospital of TCM Local Ethics Committee. Among these patients, 14 were males and four were females; and the age of these patients ranged between 19-62 years old, with an average age of 38.2 years old. Reasons of injuries: traffic accident injury (10 patients), falling injury (five patients), and crush injury (three patients). Time interval from injury to surgery was 6-18 days, with an average six days. All patients underwent three position- Judet Pelvic X-ray film photography, pelvis CT scans and two- or three-dimensional reconstructions. Among patients with pelvic fractures, Tile classification were as follows: two patients were[5] B2 type, four patients were B3 type, and two patients were C2 type. Among the 10 patients with acetabulum fractures, according to Letournel-Judet classification:[6] three patients had anterior column fractures, three patients had anterior column combined with posterior hemi-transverse shaped fractures, one patient had a T-type fracture, and one patient had a double column fracture. There was no vessel, nerve, or pelvic organ injury in preoperative patients. These patients were treated in accordance with the damage control principle of surgical treatment after admission. These preoperative examinations were improved. For Tile C-type fractures, 8-10 kg of weight traction was given on the condyles of the femur; and these were reviewed by X-ray films. Patients were operated after the pelvic vertical shift was corrected. For the remaining patients, when their conditions were stable, operation should be performed as early as possible; in which incision fracture reduction and internal fixation with steel plate and screw based on the Stoppa approach was performed. Among these patients, three were treated combined with the iliac fossa approach , and one was combined with the rear Kocher-Langenbeck (K-L) approach.

Surgical methods

Surgery was performed under general anesthesia. After successful anesthesia, the patients were placed in the supine position, and a triangular pillow was placed under the knees to place the patients in the genuflex and hip flexion posture. Treatments for double column fracture patients were combine with the posterior K-L approach, draped in accordance with the floating position, routine disinfection was performed, and a longitudinal incision of approximately 6-10 cm in length was made from the synchondrosis pubis to the navel. After the skin and subcutaneous tissue were incised, the linea alba was longitudinally incised, the rectus abdominis was pulled to both sides, and the ending point of the rectus abdominis was retained. Then, lower abdominal wall muscles, external iliac blood vessels, femoral nerves, and iliac and lumbar muscles were pulled forward anterolaterally, and extraperitoneal pelvic organs were pushed posteromedially. During the exposure process, surgeons should pay attention to the abnormal vascular extraperitoneal communication branches; which is the true pelvic brim from the synchondrosis pubis to the joints sacroiliaca, and could be exposed. In this group, arterial anastomotic branches between the inferior abdominal artery and obturator artery, as well as accompanying veins, were found in five patients; wherein the “corona mortis” vessel should be isolated and cut off. The iliopectineal fascia was incised, and the subperiosteal was dissected to expose the fractures. The fractures were reduced with apparatuses such as bucking bars and pelvic fracture reduction forceps, and were combined with lower limb traction. The fracture could be first fixed with screws and Kirschner wires, the steel plate was placed at the inner edge of the true pelvis entrance after plasticity, and the steel plate could be placed in the arcuate line and fossa iliaca after plasticity when necessary. During the operation, fracture reduction and the position and length of the screws in the steel plate were observed through C-arm fluoroscopy; and it was ensured that these screws would not enter into the acetabulum. The joints sacroiliaca or ilium fractures were reduced and fixed, and combined with the iliac fossa approach. For the case of double column fractures, the rear K-L approach was performed to reduce and fix the posterior column fracture in the floating posture, after the anterior column fracture was reduced by the improved Stoppa approach. The integrity of the peritoneum was checked, and a negative pressure drainage tube was placed at the retropubic space, the inner side or the posterior of the acetabulum. Then, the fascia recta was closely sutured, and then the skin was sutured.

Postoperative treatment

All post-operative patients received a subcutaneous injection of low-molecular-weight calciparine at the dose of 5,000 U for 12 days. Antibiotics were used at postoperative 24 hours to prevent infection. The negative pressure drainage were extracted within 24-48 hours post-operation, exercised the ankle joint of the affected limbs postoperatively woke up from the anesthesia. Hip joint functions combined with active and passive motions were exercised at two days after the operation, ground activities and partial weight-bearing were started 4-6 weeks post-operation, and the time of initiating full weight-bearing exercises depended on the review of the X-ray films.

RESULTS

In this study, operative incision length was 6-12 cm (average, 10 cm) with the modified Stoppa approach, operative time duration was 50-150 minutes (average, 85 minutes), and the volume of intraoperative blood loss was 400-1,000 ml (average, 500 ml). Among these 18 patients, 12 patients revealed anatomical reductions in postoperative X-rays; and the remaining were satisfactory reduction. According to the Matta standard,[7] all 18 cases were satisfactory reduction. Curative effects were evaluated according to the Majeed standard:[8] 13 patients were excellent, and five patients were good. These patients were postoperatively followed-up for 12 to 36 months, fracture healing time was 10-12 weeks, postoperative fat liquefaction of the abdominal wall incision occurred in one patient, and the wound healed two weeks after changing the dressing. No complications such as nonunion, heterotopic ossification, lower extremity deep vein thrombosis, or ureter bladder injuries occurred. Typical cases are shown in Figures 1-4.

DISCUSSION

Selection of pelvic and acetabular fracture approaches

The purpose of surgeries for pelvic and acetabular fractures are to correct deformities and restore pelvic ring structure stability, well-reduce acetabular fractures, and provide reliable fixations; in order to facilitate early functional exercise, and prevent the occurrence of traumatic arthritis of the hip. There are two main types of surgical approachs: one is the pelvic external rear K-L approach and the extended iliac approach, and the other is the pelvic internal ilioinguinal approach

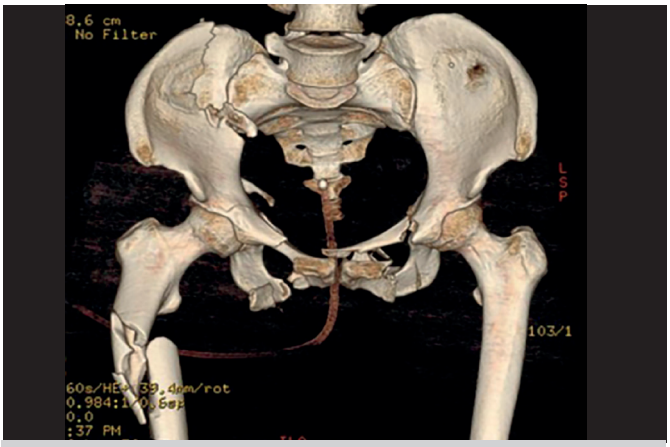

Figure 1. Via de acesso anterior de Russe para abordagem de pseudoartrose do escafoide.

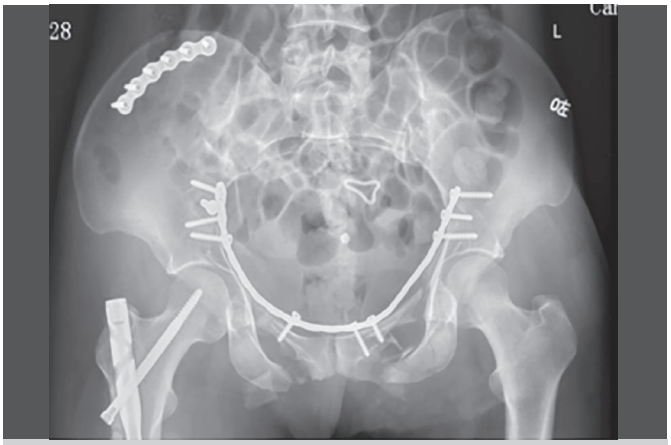

Figure 4. Female, 51 years old, pelvic fracture caused by falling from the high place, anteroposterior view radiographs of pelvic after surgery.

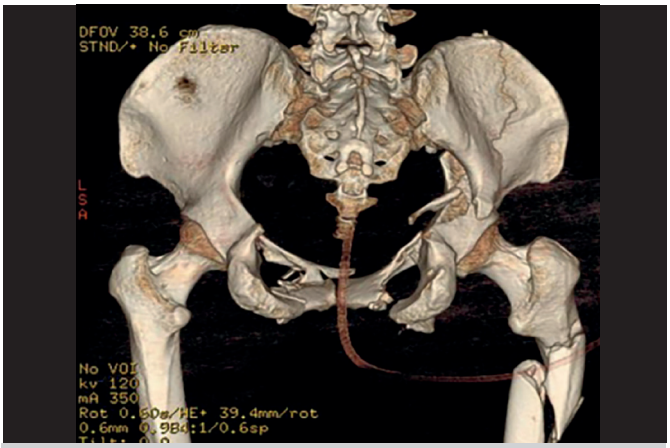

Figure 2. Female, 51 years old, pelvic fracture caused by falling from the high place, posteroanterior position showed by three dimensional rebuild CT image before surgery.

Figure 3. Female, 51 years old, pelvic fracture caused by falling from the high place, modified stoppa cut with right iliac fossa cut after surgery.

and the Pfannenstiel approach. The K-L approach was used for posterior fractures, while the ilioinguinal approach was used in anterior fractures. Anterior combined with posterior approaches, as well as the extended ilioinguinal approach, were used in double column fractures and other complex fractures. The ilioinguinal approach was used for the treatment of acetabular fractures by Letournel[9] and Matta.[10] This approach has advantages, in which the whole anterior ring of the pelvis, as well as the anterior acetabular fractures and transverse fracture, can be well revealed; reducing the incidence of heterotopic ossification and sciatic nerve injury. However, the anatomy of the ilioinguinal approach is complex; and the fractures need to be exposed in three windows of tissue spaces: the external iliac lymph vascular bundle, the femoral nerve, and the spermatic cord or the fallopian arch. The surgical trauma was great, technical requirements were high, the learning curve was steep, and it could easily cause damages to important tissues and other defects. Especially for fractures of the bilateral pelvic anterior ring and bilateral acetabulum, if the bilateral ilioinguinal approach was selected, greater trauma would be caused. In addition, the design of the ilioinguinal approach determined that this approach for the treatment of acetabular fractures is just like standing on the roof to repair the walls of a house; but the quadrilateral body fracture could not be treated under the direct vision. Furthermore, the Pfannenstiel approach reveals a limited range, which is generally limited to the treatment of synchondrosis pubis injury.

Advantages of the Stoppa and modified Stoppa approaches

The Stoppa approach[11] was initially applied for the treatment of abdominal wall hernia. Hirvensalo et al applied this approach in pelvic fractures[12] and achieved good results. Subsequently, this approach was used for acetabular fractures after being improved by Cole and Bolhofner:[13] early transverse incision, cutting off the ending points of the rectus abdominal were modified by abdominal median longitudinal incisions and the end-points of the rectus abdominal were reserved; which reduced the occurrence of abdominal wall hernias. This approach enters from the linea alba of the medial rectus abdominal. It does not need to be exposed, and stimulate the femoral artery and vein, femoral nerve, femoral lateral cutaneous nerve and other important tissues; and it is a soft tissue-friendly surgical approach.[14] The surgeon should obtain a more open field of vision at the healthy lateral of the pelvis, and the synchondrosis pubis, quadrilateral body, and anterior of the articulationes sacroiliaca were extraperitoneally exposed. Furthermore, the ischial ramus could be partly exposed when the obturator fascia and fascia iliopectinea were stripped. Through measurement, a 79% scope of the inner true pelvis could be revealed; in particular, 80% of the surface of the quadrilateral body could be directly revealed.[15] This was similar to stand inside the house to repair the wall. It had significant advantages of exposure and reduction, as well as the fixation of fractures, when compared with the ilioinguinal approach.[16-18] Compared with the ilioinguinal approach, the modified Stoppa approach could reduce blood loss, reduce the amount of blood transfusion, and shorten operation time.[19]

Furthermore, the ilioinguinal approach can easily cause injuries to the iliac vein and the lateral femoral cutaneous nerve.[20,21] There were no requirements of exposure and traction on the above tissues in the modified Stoppa approach, and no damages would be caused to these. In this study, there were no injuries occurred in iliac vessels, lateral femoral cutaneous nerves and femoral nerves.

Application experience of the modified Stoppa approach and matters that need attention

The modified Stoppa approach was applied to: anterior pelvic ring fractures, especially for unstable bilateral pubic ramus fractures, with or without pubic symphysis injury; anterior column and anterior wall fractures of the acetabulum, combined with the posterior half of the transverse fracture and T shape of the fracture, in which posterior column fracture displacement was not worse, and could be operated by a single modified Stoppa approach. The combination of the rear K-L approach could be applied to the complex fractures combined with posterior column and posterior wall fractures which were difficult to be reduced. This kind of operation model was applied to one of our patients. The injury in this operation model was significantly reduced compared with that of the ilioinguinal combined with the K-L approach, and postoperative recovery was faster. Acetabular quadrilateral body fracture combined with central femoral head dislocation could be treated *via* the modified Stoppa approach in a direct field of vision, which could significantly improve the quality of reduction, compared with the ilioinguinal approach.[22] Since the modified Stoppa approach induces less trauma, good results had been obtained in elderly patients with unstable pelvic ring fractures, compared with the application of the ilioinguinal approach.[23]

Contraindications

The modified Stoppa approach is unfavorable when used[24] in the following patients: patients with previous history of peritonitis and pelvic inflammatory disease; patients with a history of lower abdomen and pelvic cavity surgeries, and there were abdominal wall and peritoneal adhesion in these patients. Furthermore, this approach could not be replaced by the ilioinguinal approach. Patients who are too obese, patients injured for more than three weeks, and patients with serious displacement of double column fractures and iliac crest fractures are not suitable to be treated with this approach.

Some experiences

(1) Preoperative placement of a bolster under the knees, and the posture of the genuflex and hip flexion could effectively improve the exposure and reduction process during operation. (2) Care should be taken in protecting the iliac vessels bundles with a wet gauze when these were anterolaterally stretched, must not perform excessive traction; prevent damage to the external iliac vein to avoid serious consequences, perform intraoperative indwell catheterization, and attention should be given in protecting the bladder. (3) The obturator vascular nerve bundles must not be excessively retracted inward posteriorly to avoid injury. (4) If the length of the drill bit is not enough, the 3.0 mm Kirschner wire could be used instead; wherein the Kirschner wire can be used to drill a hole in a certain radian, which is conducive for adjusting the direction of the screw. (5) Since the fixation was performed in the inner walls of the pubic branch and quadrilateral body, we can make full use of the pressing and pulling effects produced by the combination of steel plate and screw to reduce the fracture. (6) The combined application of the iliac fossa approach could be used in the acetabular fracture combined with the iliac wing fracture and high anterior column fractures.

CONCLUSION

The modified Stoppa approach for the treatment of pelvic and acetabular fractures has advantages of less trauma, adequate and rapid exposure, convenient and effective fracture reduction and fixation, less complications and better postoperative recovery. Furthermore, this could be used as an alternative approach of the ilioinguinal approach. However, the clinical value of this approach remains to be verified by large sample cases due to the small number of cases and short follow-up time in this study.

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REFERENCES

1. Min BU, Nam SY, Kang CS. Complications of surgical treatment in patients with acetabular fractures. J Korean Hip Soc. 2000;12(3):253-60.
2. Hirvensalo E, Lindahl J, Böstman O. A new approach to the internal fixation of unstable pelvic fractures. Clin Orthop Relat Res. 1993;(297):28-32.
3. Hirvensalo E, Lindahl J, Kiljunen V. Modified and new approaches for pelvic and acetabular surgery. Injury. 2007;38(4):431-41.
4. Collinge CA, Lebus GF. Techniques for reduction of the quadrilateral surface and dome impaction when using the anterior intrapelvic (modified Stoppa) approach. J Orthop Trauma. 2015;29 Suppl 2:S20-4.
5. Tile M, Helfet DL, Kellam JF. Fractures of the acetabulum, ed 3. Philadelphia: Lippincott, Williams & Wilkins; 2003.
6. Letournel E, Judet R. Fractures of the acetabulum[M]. 2nd ed. New York: Springer-Verlag; 1993.
7. Matta JM, Tornetta P 3rd. Internal fixation of unstable ring injuries. Clin Orthop Relat Res. 1996;(329):129-40.
8. Majeed SA. Grading the outcome of pelvic fractures. J Bone Joint Surg (Br). 1989;71(2):304-6.
9. Letournel E. Acetabulum fractures: classification and management. Clin Orthop Relat Res. 1980;(151):81-106.
10. Matta JM. Operative treatment of acetabular fractures through the ilioinguinal approach: A 10 year perspective. J Orthop Trauma. 2016;20(1 Suppl):S20-9.
11. Stoppa RE, Rives JL, Warlaumont CR, Palot JP, Verhaeghe PJ, Delattre JF. The use of Dacron in the repair of hernias of the groin. Surg Clin North Am. 1984;64(2):269-85.
12. Rives J, Stoppa R, Fortesa L, Nicaise H. Dacron patches and their place in surgery of groin hernia: 65 cases collected from a complete series of 274 hernia operations. Ann Chir. 1968;22(3):159-71.
13. Cole JD, Bolhofner BR. Acetabular fracture fixation via a modified Stoppa limited intrapelvic approach: description of operative technique and preliminary treatment results. Clin Orthop Relat Res. 1994;(305):112-23.
14. Lehmann W, Fensky F, Hoffmann M, Rueger JM. The stoppa approach for treatment of acetabular fractures. Z Orthop Unfall. 2014;152(5):435-7.
15. Bible JE, Choxi AA, Kadakia RJ, Evans JM, Mir HR. Quantification of bony pelvic exposure through the modified Stoppa approach. J Orthop Trauma. 2014;28(6):320-3.
16. Sagi HC, Afsari A, Dziadosz D. The anterior intra-pelvic (modified rives-stoppa) approach for fixation of acetabular fractures. J Orthop Trauma. 2010;24(5):263-70.
17. Elmadag M, Guzel Y, Aksoy Y, Arazi M. Surgical Treatment of Displaced Acetabular Fractures Using a Modified Stoppa Approach. Orthopedics. 2016;39(2):e340-5.
18. Keel MJ, Bastian JD, Büchler L, Siebenrock KA. Anterior approaches to the acetabulum. Unfallchirurg. 2013;116(3):213-20.
19. Ma K, Luan F, Wang X, Ao Y, Liang Y, Fang Y, et al. Randomized, controlled trial of the modified Stoppa versus the ilioinguinal approach for acetabular fractures. Orthopedics. 2013;36(10):e1307-15.
20. Letournel E. The treatment of acetabular fractures through the ilioinguinal approach. Clin Orthop Relat Res. 1993;(292):62-76.
21. Judet R, Judet J, Letournel E. Surgical treatment of recent fractures of the acetabulum: apropos of 46 operated cases. Mem Acad Chir (Paris). 1962;88:369-77.
22. Casstevens C, Archdeacon MT, d'Heurle A, Finnan R. Intrapelvic reduction and buttress screw stabilization of dome impaction of the acetabulum: a technical trick. J Orthop Trauma. 2014;28(6):e133-7.
23. Bastian JD, Ansorge A, Tomagra S, Siebenrock KA, Benneker LM, Büchler L, et al. Anterior fixation of unstable pelvic ring fractures using the modified Stoppa approach: mid-term results are independent on patients' age. Eur J Trauma Emerg Surg. 2016;42(5):645-60.
24. Kim HY, Yang DS, Park CK, Choy WS. Modified Stoppa approach for surgical treatment of acetabular fracture. Clin Orthop Surg. 2015;7(1):29-38.

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ORIGINAL ARTICLE

EVALUATION OF DISTAL FOREARM FRACTURES USING THE AO 2018 CLASSIFICATION

AVALIAÇÃO DAS FRATURAS DA EXTREMIDADE DISTAL DO ANTEBRAÇO PELA CLASSIFICAÇÃO AO 2018

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ABSTRACT

Objective: Distal forearm fractures are among the most common upper limb fractures in all ages, and many classifications have been proposed to describe them. Recently, a new version of AO/OTA classification was proposed. The aim of this study is to use the AO/OTA 2018 classification to report the epidemiology of distal forearm fractures in adults treated at a single center. Methods: A retrospective analysis of the initial radiographs obtained from cases of distal forearm fractures in an orthopedic emergency room at a single tertiary hospital. Results: Three hundred twenty-two cases were studied, aged 50.35 ± 18.98 years, 55.3% were female and 44.7% were right-sided. Type 2R3A, 2R3B and 2R3C fractures corresponded to 32.3%, 18.0% and 48.4% of the cases, respectively. Distal ulnar fracture was present in 41.9%. There was a correlation between age and sex: 78.3% of the subjects aged under 30 years were male, and 80.6% of those aged over 60 years were female ($p<0.001$). Conclusion: The most common type of radial fractures was 2R3C, and the most common type of ulna fracture was 2U3A1.1. There was a correlation between age and sex. ***Level of evidence IV, Case-series.***

Keywords: Radius Fractures. Ulna Fractures. Wrist Injuries.

RESUMO

Objetivo: As fraturas distais do antebraço são uma das mais comuns do membro superior em todas as idades, e muitas classificações foram propostas para descrevê-las. Atualmente, uma nova versão da classificação AO/OTA foi proposta. O objetivo deste estudo foi utilizar a classificação AO/OTA 2018 para descrever a epidemiologia das fraturas distais do antebraço no adulto tratadas em um único centro. Métodos: Estudo retrospectivo, em que se avaliaram as radiografias obtidas no primeiro atendimento dos casos de fraturas da extremidade distal do antebraço de esqueletos maduros, atendidas no pronto-socorro ortopédico de um único hospital terciário. Resultados: Foram estudados 322 casos, com média da idade de 50,35 ± 18,98 anos, 55,3% do sexo feminino e 44,7% do lado direito. As fraturas do tipo 2R3A, 2R3B e 2R3C corresponderam a 32,3%, 18,0% e 48,4%, respectivamente. A ulna distal foi envolvida em 41,9%. Houve correlação entre a idade e o sexo, de modo que, no grupo etário com idade até 30 anos, 78,3% eram do sexo masculino e, acima dos 60, 80,6% do sexo feminino ($p<0,001$). Conclusão: As fraturas do tipo 2R3C foram as mais comuns do rádio, e as 2U3A1.1 foram as mais comuns da ulna. Houve correlação entre idade e sexo. ***Nível de evidência IV, Série de casos.***

Descritores: *Fraturas do rádio. Fraturas da ulna. Traumatismos do Punho.*

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INTRODUCTION

Distal radius fracture has been described as accounting for 25% of fractures in childhood and 18% in the elderly, making it one of the most common fractures of the upper limb in all ages.[1,2]

Numerous classification systems have been proposed to describe fractures of the distal end of the forearm. The main classification criteria are the presence of deviations, the degree of comminution, the type of joint involvement, and ulnar involvement.[3–6] The classification system with the highest reproducibility was the AO classification system, when categorized up to subtypes A, B and C.[7] Computed tomography did not appear to contribute to higher reproducibility in all cases.[8]

The AO classification system is an important and widely accepted system worldwide. Until recently, few studies have described the epidemiology of fractures from the viewpoint of the new 2018 AO/OTA classification.[9] Therefore, the aim of this study is to use the 2018 AO/OTA classification to describe the epidemiology of distal fractures of the forearm managed at a single healthcare center in two distinct time periods.

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

Work conducted by the Hand and Microsurgery Group, Hospital de Clínicas, Universidade Estadual de Campinas, Campinas, SP, Brazil.
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MATERIALS AND METHODS

This was a retrospective observational study that evaluated radiographies obtained from the orthopedic emergency center of a single tertiary care hospital providing care for patients with fractures of the distal end of the forearm. It includes both cases where the patient sough medical care spontaneously, and referred patients. The development of the study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) protocol and was approved by the Research Ethics Committee, under CAAE number 91232817.8.0000.5404.

Age, sex, side of the fracture and fracture classification were described according to the 2018 AO Foundation criteria. To avoid measurement bias, distal radius fracture was described up to sublevel "ABC", which was reported as having the highest reproducibility in the previous version of this classification. The classification was based on simple radiography of the wrist in the posterior-anterior (PA) and lateral views. For this purpose, images obtained before and after reduction were used. During the fracture classification process, the patient's demographic data were duly concealed.

Cases in which fractures of the distal end of the forearm in skeletally mature individuals were seen during two time periods (from January to December of 2014; and from January to December of 2017) were included in the study. Cases without good quality radiographs at the time of the initial treatment, and those who had received initial care at another healthcare center and therefore did not have the initial radiographic images filed in the Radiology Unit of the institution, were excluded from the study. The need to sign an informed consent form was waived by the Research Ethics Committee.

The categorical variables were analyzed by the chi-square and Fisher's exact tests, according to the type of fracture. Numerical variables were analyzed by central tendencies, and dispersions by the Student's t-test or the Mann-Whitney test, depending on the nature of distribution. The Shapiro-Wilk test was used for analysis of normality.

Descriptive and inferential analyses were obtained using the IBM® SPSS® Statistics software version 24, admitting a significance level of 5%.

RESULTS

Four hundred and twenty-nine fractures of the distal end of the forearm were identified during the period analyzed. Of these, 87 individuals were excluded because they were skeletally immature (72 cases in 2017 and 15 cases in 2014). Another 20 cases were excluded due to the poor quality of the radiographs, which made it impossible to classify the fractures. Finally, 322 cases were studied, 189 of which were managed in 2014 and 133, in 2017.

The mean patient age was 50.35 ± 18.98 years, ranging from 17 to 92 years. Female patients accounted for 55.3% of the cases and the right side was affected in 44.7% of the cases.

Distal radius fractures accounted for 98.7% of the cases. Of these, type 2R3A fractures accounted for 32.3%; type 2R3B, for 18.0%; and type 2R3C, for 48.4%. Two participants had bilateral fractures. Distal ulnar fracture occurred in 41.9%, and fracture of the tip of the styloid process was the most prevalent type (2U3A1.1), with 30.7%, followed by fractures of the base of the styloid process (2U3A1.2), with 7.1%; simple extra-articular fractures (2U3A2), with 3.5%; and multifragmentary extra-articular fractures (2U3A3), with 0.6%. The more severe the ulnar fracture, the more severe the associated radius fracture (p=0.011).

There was no difference in mean patient age according to type of fracture (p=0.077). However, there was a correlation between the age and sex of the participants. In the 30 years and under age group, 78.3% of individuals were male, while in the over 60 years age group, 80.6% were female (p<0.001). Stratifying by age, there was no correlation between type of fracture and sex (Figure 1).

Demographic data (sex and age) were similar in both periods analyzed. The rate of distal ulnar fracture was lower in 2017 than in 2014 (Table 1).

DISCUSSION

There are many different classification systems to describe distal radius fractures, but none is capable of summarize each of the descriptive characteristics in isolation, or providing guidance on treatment and inferring the prognosis.[10,11]

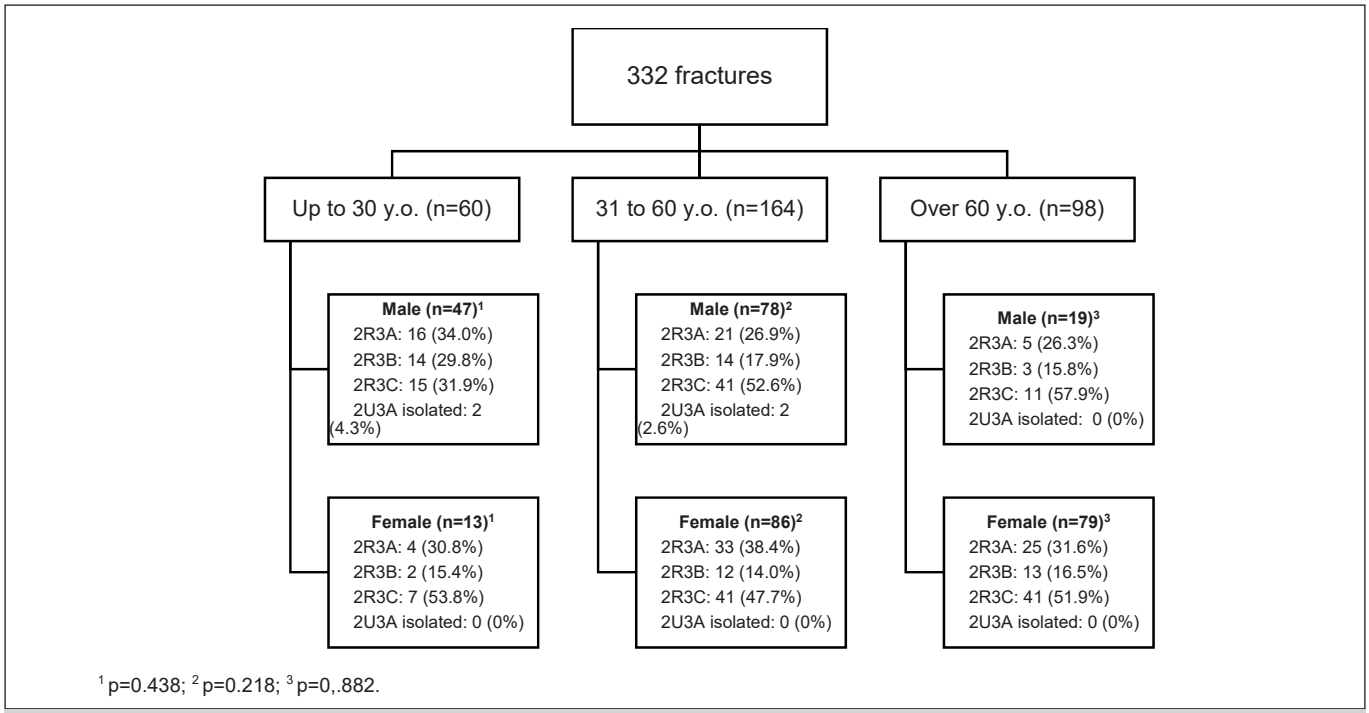

Figure 1. Correlation analysis between type of fracture and sex stratified by age.

Table 1. Demographics and fracture characteristics between 2014 and 2017.

	Year		p-value
	2014	2017	
Age			
Up to 30 y.o	33 (17.5%)	27 (20.3%)	0.675*
31 to 60 y.o.	100 (52.9%)	64 (48.1%)	
Over 60 y.o.	56 (29.6%)	42 (31.6%)	
Sex			
Male	84 (44.4%)	60 (45.1%)	0.905*
Female	105 (55.6%)	73 (54.9%)	
AO classification			
2R3A	64 (33.9%)	40 (30.1%)	0.211*
2R3B	27 (14.3%)	31 (23.3%)	
2R3C	96 (50.8%)	60 (45.1%)	
2U3A isolated	2 (1.1%)	2 (1.5%)	
Ulnar involvement			
Intact	101 (53.4%)	86 (64.7%)	0.044*
Fractured	88 (46.6%)	47 (35.3%)	

* Pearson's Chi-squared.

Koo et al. identified that males are more affected by fractures of the distal end of the forearm.[12] Although the current study observed that the majority of cases under 30 years of age were men, women were more globally affected. Furthermore, this study identified a significant increase in the proportion of women over 60 years of age who were affected. This data is described by other authors, who have identified an increasing incidence of these fractures in females over the age of 65.[13] The coexistence of fractures of the radius and distal ulna was lower than the 58% described by May et al.[14]

Among the changes observed in the 2018 AO/OTA classification, we highlight the separation between radius and ulnar fracture classifications, and the creation of a qualification to describe distal radius-ulnar joint (DRUJ) instability in type 2R3C radius fractures. These changes allowed for a larger number of combinations and enhanced the power of fracture description, which may have led to a classification of DRUJ instability. The 2018 version of the classification also includes the physical evaluation.

Ulnar styloid fractures are associated with DRUJ injuries, due to the important anatomic role of the ulna in the formation of the triangular fibrocartilage complex.[15] In view of this, some authors have recommended management of the fracture of the styloid process of the ulna, and have identified differences in functional outcomes depending on whether or not ulnar styloid fracture is concomitantly present with distal radius fracture.[16] Nevertheless, recent meta-analyses have demonstrated that there is no difference in functional outcomes between individuals with or without associated fracture of the ulna in its different presentations.[17,18] Furthermore, none of the parameters of a simple radiography was shown to be a good predictor of triangular fibrocartilage injury.[19]

Another pertinent observation concerning the new classification is that it maintains the descriptive criteria for articular fractures of the distal radius. Therefore, its high level of complexity may affect its reproducibility, as observed in the previous version of the classification.[7,20]

This study has some limitations. Since this was a descriptive study of first-aid radiographies obtained from a Radiology Image Database, it was outside the scope of this study to describe other clinical data, such as the trauma mechanism, associated lesions, type of treatment administered, and outcomes during follow-up. Finally, apart from radiography, no other diagnostic methods were used to aid in fracture classification, due to their lack of uniform availability in all cases.

CONCLUSION

The most common type of radial fractures was complete articular fractures (2R3C), and the most common type of ulna fracture was fracture of the tip of the styloid process (2U3A1.1). Males under 30 years of age are more prone to suffer these fractures, while females over 60 year of age are more prone.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. AFN (0000-0003-3249-8096)*, MSM (0000-0002-0502-586X)* and RTI (0000-0001-9573-0134)*: collected data and contributed to the concept and design of the article; LM (0000-0002-6584-5333)*: drafted the text, analyzed the data and conducted the statistical analysis; MFMA (0000-0002-9515-0540)* and JCN (0000-0003-4780-827X)*: participated in drafting and revising the text. *ORCID (Open Researcher and Contributor ID).

REFERENCES

1. Almugren TS, Al-Namlah A, Alkubaidan F, Alotaibi H, Alzimami I. Epidemiology and patterns of the hand and distal forearm fractures at King Abdul-Aziz Medical City, Riyadh, KSA. J Taibah Univ Med Sci. 2016;11(1):86-90.
2. Nellans KW, Kowalski E, Chung KC. The epidemiology of distal radius fractures. Hand Clin. 2012;28(2):113-25.
3. Frykman G. Fracture of the distal radius including sequelae--shoulder-hand-finger syndrome, disturbance in the distal radio-ulnar joint and impairment of nerve function. A clinical and experimental study. Acta Orthop Scand. 1967;Suppl 108:3+.
4. Melone CP Jr. Articular fractures of the distal radius. Orthop Clin North Am. 1984;15(2):217-36.
5. Marsh JL, Slongo TF, Agel J, Broderick JS, Creevey W, DeCoster TA, et al. Fracture and dislocation classification compendium - 2007: Orthopaedic Trauma Association classification, database and outcomes committee. J Orthop Trauma. 2007;21(10 Suppl):S1-133.
6. Fernandez DL. Distal radius fracture: the rationale of a classification. Chir Main. 2001;20(6):411-25.
7. Kreder HJ, Hanel DP, McKee M, Jupiter J, McGillivary G, Swiontkowski MF. Consistency of AO fracture classification for the distal radius. J Bone Joint Surg Br. 1996;78(5):726-31.
8. Arealis G, Galanopoulos I, Nikolaou VS, Lacon A, Ashwood N, Kitsis C. Does the CT improve inter- and intra-observer agreement for the AO, Fernandez and Universal classification systems for distal radius fractures? Injury. 2014;45(10):1579-84.
9. AO Foundation. Fracture and Dislocation Compendium-2018. J Orthop Trauma. 2018;32(1 Suppl).
10. Oliveira-Filho OM de, Belangero WD, Teles JBM. Fraturas do rádio distal: avaliação das classificações. Rev Assoc Med Bras. 2004;50(1):55-61.
11. Siripakarn Y, Niempoog S, Boontanapibul K. The comparative study of reliability and reproducibility of distal radius fracture classification among: AO frykman and Fernandez classification systems. J Med Assoc Thai. 2013;96(1):52-7.
12. Koo KOT, Tan DMK, Chong AKS. Distal radius fractures: an epidemiological review. Orthop Surg. 2013;5(3):209-13.
13. Baron JA, Karagas M, Barrett J, Kniffin W, Malenka D, Mayor M, et al. Basic epidemiology of fractures of the upper and lower limb among Americans over 65 years of age. Epidemiology. 1996;7(6):612-8.
14. May MM, Lawton JN, Blazar PE. Ulnar styloid fractures associated with distal radius fractures: Incidence and implications for distal radioulnar joint instability. J Hand Surg Am. 2002;27(6):965-71.
15. Kwon BC, Seo BK, Im H-J, Baek GH. Clinical and radiographic factors associated with distal radioulnar joint instability in distal radius fractures. Clin Orthop Relat Res. 2012;470(11):3171-9.
16. Belloti JC, Moraes VY, Albers MB, Faloppa F, Dos Santos JBG. Does an ulnar styloid fracture interfere with the results of a distal radius fracture? J Orthop Sci. 2010;15(2):216-22.
17. Mulders MAM, Fuhri Snethlage LJ, de Muinck Keizer RJO, Goslings JC, Schep NWL. Functional outcomes of distal radius fractures with and without ulnar styloid fractures: a meta-analysis. J Hand Surg Eur Vol. 2018;43(2):150-7.
18. Yuan C, Zhang H, Liu H, Gu J. Does concomitant ulnar styloid fracture and distal radius fracture portend poorer outcomes? A meta-analysis of comparative studies. Injury. 2017;48(11):2575-81.
19. Kasapinova K, Kamiloski V. The correlation of initial radiographic characteristics of distal radius fractures and injuries of the triangular fibrocartilage complex. J Hand Surg Eur Vol. 2016;41(5):516-20.
20. van Leerdam RH, Souer JS, Lindenhovius ALC, Ring DC. Agreement between Initial Classification and Subsequent Reclassification of Fractures of the Distal Radius in a Prospective Cohort Study. Hand (N Y). 2010;5(1):68-71.

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SOFT-TISSUE INJURY TO THE FOOT AND ANKLE: LITERATURE REVIEW AND STAGED MANAGEMENT PROTOCOL

LESÃO DE TECIDOS MOLES NO TRAUMA DO TORNOZELO E PÉ: REVISÃO DA LITERATURA E TRATAMENTO ESTAGIADO

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ABSTRACT

Complex trauma of the foot and ankle is characterized by fractures with severe soft tissue damage associated with neurovascular injury and joint involvement. These injuries are frequently present in the polytraumatized patient and are a predictor of unfavorable clinical outcome. In the initial approach to a patient with complex foot and ankle trauma, the decision between amputation and reconstruction is crucial. The various existing classification systems are of limited effectiveness and should serve as tools to assist and support a clinical decision rather than as determinants of conduct. In the emergency department, one of two treatment options must be adopted: early complete treatment or staged treatment. The former consists of definitive fixation and immediate skin coverage, using either primary closure (suturing) or flaps, and is usually reserved for less complex cases. Staged treatment is divided into initial and definitive. The objectives in the first phase are: prevention of the progression of ischemia, necrosis and infection. The principles of definitive treatment are: proximal-to-distal bone reconstruction, anatomic foot alignment, fusions in severe cartilage lesions or gross instabilities, stable internal fixation and adequate skin coverage. ***Level of evidence III, Systematic review of level III studies.***

Keywords: Ankle. Foot. Soft-tissue. Trauma. Fracture, Bone.

RESUMO

O trauma complexo do pé e tornozelo, caracterizado por fraturas com dano grave aos tecidos moles, associado a lesões vasculares e nervosas e com acometimento articular, está presente com frequência no paciente politraumatizado e é preditor de desfecho clínico desfavorável. Na abordagem inicial de um paciente com trauma complexo do pé e tornozelo, a decisão entre amputação ou preservação do membro é crucial. Os diversos sistemas de classificação existentes são de eficácia limitada e devem servir como ferramentas que auxiliam e fortalecem uma decisão clínica, e não como determinantes de uma conduta. No atendimento de emergência, uma das duas opções de tratamento deve ser adotada: tratamento total precoce ou tratamento estagiado. O primeiro consiste na fixação definitiva e na cobertura cutânea imediata, seja por sutura primária ou por meio de retalhos, sendo geralmente reservado a casos menos complexos. O tratamento estagiado é dividido em inicial e definitivo, e o objetivo, na primeira fase, é a prevenção da progressão da isquemia, da necrose e da infecção. Os princípios do tratamento definitivo são: reconstrução óssea de proximal para distal, alinhamento anatômico do pé, fusões nas lesões graves da cartilagem ou nas instabilidades grosseiras, fixação interna estável e cobertura cutânea adequada. ***Nível de evidência III, Revisão sistemática de estudos de nível III.***

Descritores: *Tornozelo. Pé. Trauma. Fratura Óssea.*

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INTRODUCTION

The term 'complex trauma of the foot and ankle' is reserved for fractures that involve severe soft tissue damage associated with neurovascular lesions and joint involvement, which entail a high risk for complications.[1] These injuries can also be called: mutilating injuries to the lower extremity, mangled extremity injuries and high-energy lower extremity trauma.[2]

Court-Brown and Caesar observed fractures involving the foot and ankle of approximately 12% of a total group of approximately 6000 patients over the period of one year, of which toe and metatarsal

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fractures represented 85%.[3] In a supplementary study, the authors noticed that foot fractures corresponded to 10.5% of all open fractures in almost 2400 open fractures over 15 years.[4]

The most common mechanism of injury involved in complex fractures of the foot and ankle is traffic accidents, which represent 49% of causes, followed by falls from heights and work-related trauma.[5]

The general distribution of foot and ankle fractures, observed by Shibuya et al., reveals 56% ankle, 17% hindfoot, 9% midfoot and 18% forefoot fractures.[6]

The World Health Organization reports that every year 1.2 million people die in traffic accidents and more than 50 million are injured.[7]

The literature shows a high rate of association between complex foot and ankle trauma and polytrauma or multiple injuries between 32% and 52% of the cases, making the treatment of these injuries an even greater challenge.[1,2,8-13] Complex trauma of the foot and ankle is a predictor of an unfavorable prognosis in polytraumatized patients and deserves attention and prioritized treatment like diaphyseal fractures of long bones.[14-23]

In traffic accidents, the upper part of the passenger's body is well protected, but the area of the distal third of the lower limb is vulnerable.[24,25]

Complex foot and ankle trauma is an event that affects the lives of patients, represents a high cost for healthcare systems, and has an impact on the productive activity of countries.[24-26] This form of trauma often results in some degree of disability, and is therefore a veritable treatment challenge. In this scenario, there is an area not yet adequately defined between injuries that cannot be reconstructed and those where the best outcome is amputation. In this article, we present a literature review and staged management protocol to help in decision making.

Classification Systems

Many classification systems have been reported in the literature and can be used in this scenario, such as the Gustilo-Anderson system for open (compound) fractures,[27] the Oestern and Tscherne classification for closed fractures,[28] the AO soft-tissue injury grading system – closed skin injuries (IC) / open skin injuries (IO).[29]

Zwipp et al.[1,13] designed a scoring system for ankle and foot injuries to define complex trauma (Figure 1). The foot and ankle are divided into 5 main areas. Each injured area is equal to 1 point, to which points are added based on the severity of the soft tissue injury according to the Oestern-Tscherne Classification, and a score of 5 points or more in the most affected area is considered complex trauma of the foot and ankle. In the hands of a team unused to this kind of trauma, it is more appropriate to regard the lesion as complex, even with a lower total score, and to consider referring the patient to a tertiary orthopedic trauma facility.

The MESS (Mangled Extremity Severity Score) system represents an option for deciding between reconstruction and amputation. It is based on four criteria (Table 1). When the score is 7 points or above, amputation should be considered.[30]

Other systems described in the literature are presented in Table 2. These limb-salvage scoring scales were designed to reduce subjectivity and provide guidance in the difficult therapeutic decision-making process in complex foot and ankle trauma cases. Ideally, a decision-making system in cases of severe lower limb trauma should be 100% specific and 100% sensitive; however, clinical practice and narrative findings regarding the different systems reveal specificity above 95%, yet sensitivity between 60% and 70%.[31-40]

These scoring systems are of limited use and should not be used as the sole criteria when deciding between amputation and reconstruction. They serve as a tool to facilitate and support a clinical decision.[41-43]

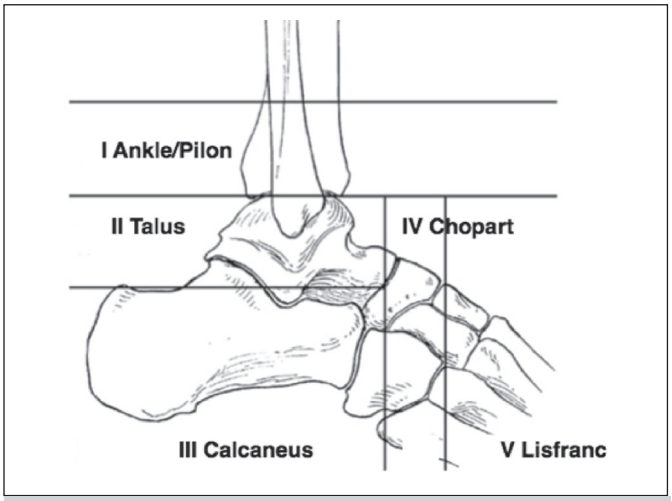

Figure 1. Scoring system for foot and ankle injuries to define complex foot and ankle trauma, according to Zwipp et al.,1,13 with division into 5 areas.

Table 1. Mangled Extremity Severity Score (MESS).

Skeletal / soft-tissue injury	score
Low energy (stab; simple fracture; pistol gunshot wound)	1
Medium energy (open or multiple fractures, dislocation)	2
High energy (high speed MVA or rifle GSW)	3
Very high energy (high speed trauma + gross contamination)	4
Limb ischemia	
Pulse reduced or absent but perfusion normal	1*
Pulseless; paresthesias, diminished capillary refill	2*
Cool, paralyzed, insensate, numb:	3*
Shock	
Systolic BP always > 90 mm Hg	0
Hypotensive transiently	1
Persistent hypotension	2
Age (years)	
< 30	0
30-50	1
> 50	2
* Double the score in cases of ischemia >6 hours	

MESS score: A score above 7 increases the chance of amputation.

Table 2. Predictive scores for limb preservation.

Score	Author and year
Abbreviated Injury Score - AIS	AAAM. 1971
Gustilo classification	Gustilo Anderson 1976; Gustilo et al 1984
Hannover Fracture Scale-97/98 - HFS-97	Tcherne. 1983
Mangled Extremity Syndrome Index - MESI	Gregory et al. 1985
Predictive Salvage Index - PSI	Howe et al. 1987
Mangled Extremity Severity Score - MESS	Johansen et al. 1990
Limb Salvage Index - LSI	Russel et al. 1991
Nerve injury, Soft-Tissue injury, Skeletal injury, Age Score - NISSSA	McNamara et al. 1994
Foot and Ankle Severity Scale - FASS	Manoli et al. 1997
The Ganga Hospital Severity Score	Rajasekaran. 2005

Treatment Principles

The objective of complex foot and ankle trauma treatment is to restore lower limb function, producing a painless, stable and functional lower limb, while avoiding infections, complications, revision surgery and hospital readmission.

First hours after trauma

In the emergency unit, a patient with a severe foot and ankle injury should be assessed for all local and systemic parameters and have the treatment algorithm defined:

1. Early total care

This type of care should be adopted in selected cases with simple fractures, clean wounds and a team trained in the definitive procedures; when both the patient's systemic condition and the local conditions are adequate to support the duration of the procedures and surgical aggression.

Soft tissue management options are:

- Primary closure
- Vacuum assisted closure device
- Fixation in combination with local or microsurgical flap
- Amputation

2. Staged treatment

- Initial treatment
- Definitive treatment

Initial Treatment

The initial approach to a complex foot and ankle injury has clear objectives and can be divided into 3 parts:

- Prevent the progression of ischemia and necrosis
- Prevent infection
- Decide between amputation and reconstruction.

Part I: Prevent the progression of ischemia and necrosis

The first step should be screening for severe trauma and when necessary resuscitation according to the principles of Advanced Trauma Life Support, both during prehospital care and afterwards during in-hospital care.[44]

In this scenario, only dislocations and fractures with major deviations that cause impairment of perfusion should be briefly treated, preferably at the site of the accident.

If there are no other life-threatening injuries that require immediate attention, or when the patient has responded adequately to systemic stabilization maneuvers, then the injury to the foot and ankle is assessed and treated.[6]

The second step is diagnosis through physical examination – the clinician should assess vascular status (palpable pulses, capillary refill, temperature, and color), neurological impairment (sensitivity, deficient), soft tissue injury (closed or open) and the conditions of bones and joints. Conventional radiographs are sufficient to determine early treatment (e.g., external fixation). Supplementary tests and computed (angio) tomography will be necessary for definitive treatment planning (span-scan-plan principle).[45]

At this stage of the treatment, compartment syndrome (CS) should be diagnosed or ruled out.

Characteristic clinical signs include:

- Tense edema – has proven the most consistent physical examination finding
- Progressive pain despite immobilization.
- Progressive increase in the need for analgesics.
- Worsening of pain with passive finger mobilization.
- Diminished discrimination of two points on the plantar aspect of the foot and toes.

The numerical diagnosis of CS occurs when muscle perfusion pressure (difference between diastolic pressure and intramuscular pressure) is less than 30 mmHg.[46]

However, if there is strong clinical suspicion and risk factors involved - hypoxia, hypovolemia, vascular injury with peripheral ischemia, high-energy trauma, severe soft tissue injury and complex fractures of the tibia –fasciotomy should be performed. Early fasciotomy is associated with lower rates of morbidity and a better outcome.[2]

A medial approach combined with two dorsal approaches over the second and fourth metatarsals is effective in releasing all 9 foot compartments.[2]

A single dorsal incision was described and termed Hannover's approach, while a single extended medial incision is known as the Henry approach.[2]

Kakadia demonstrated that the use of a vessel loop and negative pressure therapy for fasciotomy wound closure results in a higher rate of primary closure and reduces overall healing time (Figures 2A and 2B).[47]

In addition to the diagnosis and treatment of CS, this sub-phase also includes:

- Aggressive debridement using saline lavage and removal of dead tissue and loose bone fragments.
- Temporary fixation of the fracture using an external fixator or Kirschner wires to allow:

- Inspection and healing of soft tissues
- Prevention of equinus deformity
- Prevention of infection

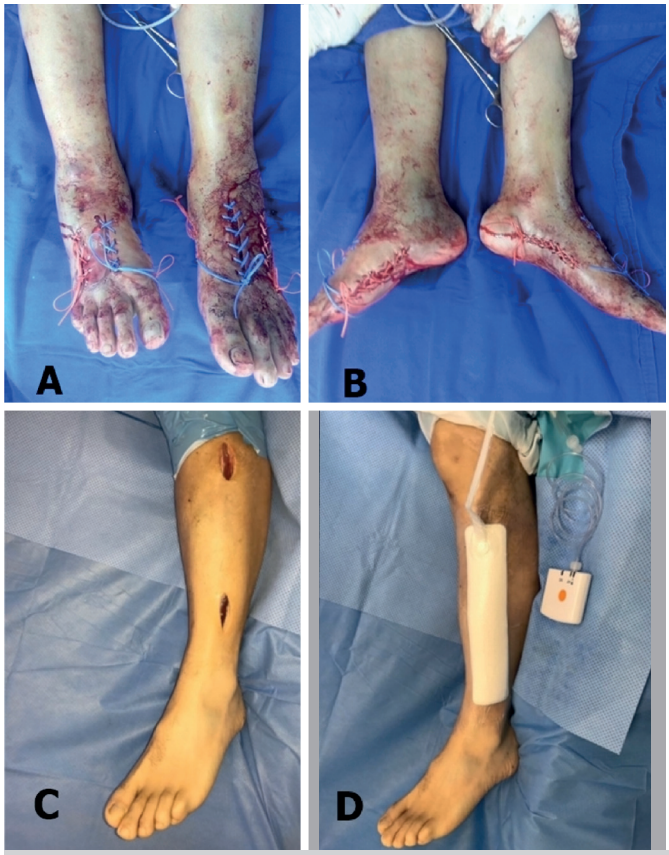

Figure 2. Adjunct soft tissue therapy in the treatment of Compartment Syndrome of the feet (A and B) and left leg (C and D). 2A. Immediate postoperative clinical presentation, dorsal view of dermofascietomies combined with the use of Vessel Loop, 2B. Immediate postoperative clinical presentation, medial view of the dermofascietomies combined with the use of the Vessel Loop. 2C. Immediate postoperative clinical presentation, lateral view of dermofascietomies, 2D. Incisional negative pressure dressing, lateral side of the dermofascietomies.

The method should permit the inspection of wounds and the application of dressings. The external fixator should be positioned on the most severely injured side in order to preserve the opposite side for the definitive surgical approach.
Indications for temporary stabilization are as follows:

- Fracture-dislocation with compromised neurovascular structures or skin at risk
- Unstable open fracture
- Fracture associated with compartment syndrome
- Gross instability of the focal point of fracture or of the joint.

Part II: Prevent infection

Open fractures should be quickly covered with sterile dressings in pre-hospital care. Less than 20% of infections in open fractures are caused by microorganisms present at the time of the trauma, and more than 90% of infections are hospital-acquired infections.[48]
Photographs must be taken to facilitate communication and patient records.
Antibiotic therapy should be initiated as soon as possible. First-generation cephalosporin is usually the first choice. Gentamicin is used in cases of gross contamination or type III open fractures. Consideration should be given to initiating tetanus prophylaxis, and definitive antibiotic therapy or a combination of antibiotics is based on the results of cultures and sensitivity tests.[10]
After debridement and initial irrigation, a new surgical approach should be adopted after 24 to 48 hours, depending on the initial contamination and the biological response of the remaining tissues.
When there are bone defects secondary to acute bone loss or removal due to infection, necrosis, or gross contamination, these may be used to fill the dead space: gentamicin-impregnated beads, antibiotic-impregnated polymethyl methacrylate or bioactive glass spacer.[49]
The use of negative pressure therapy in open fractures produces fewer infection-related complications while reducing hospital readmission and revision procedure rates.
In cases where open fracture wounds can be closed primarily following initial debridement, incisional negative pressure therapy aids the healing process (Figures 2C and 2D).
On the other hand, early soft tissue coverage has yielded lower rates of infection following complex trauma of the foot and ankle.[50]

Part III: Decide between amputation and reconstruction.

The combined rate of primary and secondary amputation is around 15% to 30%, depending on the severity of the injury. Primary amputation should be performed in extremely severe limb injuries or in life-threatening injuries, such as in multi-trauma patients with severe comorbidities[11] (Figure 3).
Whenever possible, the patient's opinion should be considered in light of the shared decision-making process. However, the final decision is based on the surgeon's experience combined with the judgment of the multidisciplinary team, who should be presenting the family and patient to sign the consent form.
The initial absence of plantar sensation is not a reliable predictor, since sensitivity returns in half of the cases. Psychological and social factors have showed themselves to be more important than scoring systems in predicting outcome. Scoring systems should not be the sole criteria on which the amputation decision is based. Everyone must keep in mind that defining reconstruction or amputation is not a prediction of outcome or of function.[43]

Amputation

The type of lower limb amputation is widely affected by the level of arterial damage, the level of viable soft tissues, and the quality and contamination of the remaining bone; amputations can be performed at different levels:

Figure 3. Decision making in amputation. 3A. Dorsal view of the soft tissue and bone injury to the left foot. 3B. Lateral view of the soft tissue injury and bone involvement of the left foot. 3C. Radiograph showing severity of the bone tissue injury. 3D. Anteroposterior radiograph of Chopart amputation, combined with primary arthrodesis. 3E. Lateral radiograph of Chopart amputation, combined with primary arthrodesis. 3F. Clinical presentation of the patient in upright position, with Chopart's disarticulation, combined with tibiotalocalcaneal arthrodesis.

Transtibial (below-knee), Syme, Pirogoff, Chopart with tibiotalocalcaneal fusion (Figures 3D, 3E and 3F), Chopart combined with transfer of the tibialis anterior tendon to the neck of the talus neck and with percutaneous calcaneus tendon lengthening, and finally, transmetatarsal amputation preserving all the principal tendon insertions around the foot and ankle.
The main objective is survival while the secondary objective is to provide the best quality of life possible.
The principles of an amputation are:

- Identification and adequate treatment of nerves and vessels.
- Stable myodesis, guaranteeing robust soft tissue coverage.
- Preserve the balance of muscles and tendons.
- Preserve the length of the limb when feasible
- Multidisciplinary team approach throughout the treatment period

Reconstruction

The timing of definitive treatment with reconstruction depends on the systemic state of the patient and the soft tissues.

The principles of the reconstruction procedure are:
- First bone tissue

- From proximal to distal
- When the patient has a fracture of the talus and distal tibia – first talus before the tibial pilon or ankle.

- Anatomical reconstruction of axial alignment and functional columns of the foot.
- Primary fusions for severe cartilage injury or gross instability
- Stable internal fixation
- Early and stable soft tissue coverage

Early flaps for soft tissue reconstruction allow lower rates of infection following open fractures and functional rehabilitation.

The selection of the flap should take into account: minimal morbidity in the donor area, needs of the recipient area and familiarity of the surgeon (Figure 4).

The most commonly used flaps for the treatment of complex foot and ankle are:

1. anterolateral thigh flap
2. dorsalis major
3. rectus abdominus
4. gracilis

The outcome expectation consists of 6 aspects:

- final function of the locomotor system
- local aesthetics and remaining volume
- pain and loss of sensitivity
- total treatment time
- costs of hospitalization
- emotional factors

Functional results - locomotor system

A prospective multicenter study investigated the functional outcomes of 569 patients with severe lower limb injuries, resulting in reconstruction or amputation. In two years of follow-up, there was no significant difference between the amputation and reconstruction groups for the scores and time to return to work. The patients who underwent reconstruction had a higher rate of hospital readmission.[34]

Quality of life in post-traumatic amputees in comparison to limb reconstruction was evaluated in a meta-analysis. The authors demonstrated that lower limb reconstruction is more psychologically acceptable for patients with severe trauma as compared to amputation, although the physical outcome for both treatment options is the same.[51]

A prospective longitudinal study determined the outcome of complex foot and ankle injuries undergoing limb reconstruction surgery requiring free flaps compared to a similar group of patients who underwent early amputation at the level of the proximal tibia. The authors concluded that the patients requiring free flap transfer had significantly worse scores than the amputees.[52]

An amputation usually involves a shorter hospital stay, fewer surgical procedures, and faster total rehabilitation. The costs of the prosthesis are higher and the rehabilitation process more lengthy, depending on the patient's age at the time of the injury.[53]

In the US, the prevalence is 80,000 new amputees/year, with a treatment cost per amputee in the first two years of US$ 91,106, vs US$ 81,316 per patient treated with reconstruction. The cost of lifetime medical care per amputee is US$ 509,275 vs US$ 163,282 per patient treated with reconstruction.[53]

Two comparative cohort studies, one made up of civilian patients and the other of military patients, evaluated severe isolated injuries of the foot and showed inferior functional results in the groups undergoing reconstruction in both studies. The groups of authors observed higher rates of complications and need for revision surgery, as well as longer hospitalization and rehabilitation times in the groups undergoing reconstruction.[54,55]

Consideration must be given to an important bias in this area of knowledge. While the amputation technique has been performed and improved over the last 300 years, reconstructive surgery for complex foot and ankle injuries has been under development for the past 3 decades.

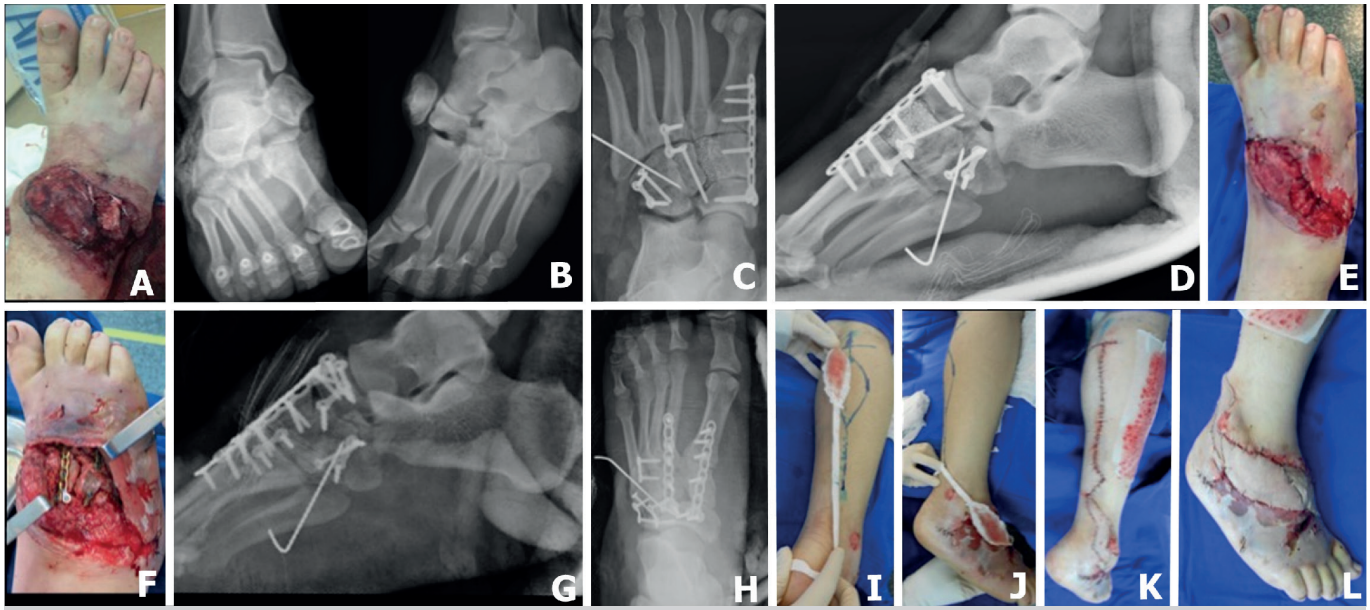

Figure 4. Example of foot reconstruction in complex injuries. 4A. Initial clinical image of the soft tissue injury, 4B. Initial AP radiograph of the ankle and oblique x-ray of the foot, showing tarsometatarsal dislocation-fracture with extrusion of the intermediate cuneiform, 4C. Anteroposterior radiograph after debridement, stabilization of the first, third and fifth radial bones, disimpactation of the cuboid and bone fragment interposition using an antibiotic-impregnated cement spacer in the intermediate cuneiform topography, 4D. Lateral radiograph after debridement, stabilization and bone fragment interposition using an antibiotic-impregnated cement spacer in the intermediate cuneiform topography, 4E. Immediate postoperative clinical presentation following debridement, stabilization and approximation of soft tissues for application of negative pressure dressing, 4F. Intraoperative clinical presentation - 72 hours after the first procedure – filling of bone fragment with autologous bone graft (iliac crest) and definitive fixation of the second radial bone, 4G. Lateral radiograph after definitive treatment 4H. Anteroposterior radiograph after definitive treatment, 4I. Planning of sural rotation flap posterior view, 4J. Planning of rotation flap lateral view, 4K. Final clinical presentation of skin coverage with rotation flap posterior view, 4L. Final clinical presentation of skin coverage with rotation flap lateral view.

FINAL CONSIDERATIONS

There have been considerable developments in the treatment of complex foot and ankle injuries over the last three decades. The final functional outcome needs to be projected right from the start of the treatment. Although saving the limb may be psychologically better in principle, a stiff, painful and/or insensitive, nonfunctional foot may represent a much worse outcome with the need for secondary interventions and prolonged hospitalization and rehabilitation.

Treatment should be individualized based on patient characteristics and local conditions. If the necessary tools are not available, referral to a specialized service should be considered. If the surgeon opts for ankle and foot reconstruction, stable internal fixation and early soft tissue coverage followed by an aggressive rehabilitation protocol and appropriate footwear modifications should be implemented to achieve maximum functional recovery. Complex foot injuries are hard to treat and may require an extended follow-up period with specialist care.

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REFERENCES

1. Zwipp H, Dahlen C, Randt T, Gavlik JM. Complex trauma of the foot. Orthopade [in German]. 1997;26(12):1046–56.
2. Schepers T, Rammelt S. Complex Foot Injury: Early and Definite Management. Foot Ankle Clin. 2017;22(1):193-213.
3. Court-Brown CM, Caesar B. Epidemiology of adult fractures: a review. Injury. 2006;37(8):691–7.
4. Court-Brown CM, Bugler KE, Clement ND, Duckworth AD, McQueen MM. The epidemiology of open fractures in adults. A 15-year review. Injury. 2012;43(6):891–7.
5. Eberl R, Ruttenstock EM, Singer G, Brader P, Hoellwarth ME. Treatment algorithm for complex injuries of the foot in paediatric patients. Injury. 2011;42(10):1171-8.
6. Shibuya N, Davis ML, Jupiter DC. Epidemiology of foot and ankle fractures in the United States: an analysis of the National Trauma Data Bank (2007 to 2011). J Foot Ankle Surg. 2014;53(5):606-8.
7. World Health Organization. Public health round-up. Bull World Health Organ. 2013;97(3):240–1.
8. Ahrberg AB, Leimcke B, Tiemann AH, Josten C, Fakler JK. Missed foot fractures in polytrauma patients: a retrospective cohort study. Patient Saf Surg. 2014;8:10.
9. Tadros AM, Eid HO, Abu-Zidan FM. Epidemiology of foot injury in a high--income developing country. Injury. 2010;41(2):137-40.
10. Kinner B, Tietz S, Muller F, Prantl L, Nerlich M, Roll C. Outcome after complex trauma of the foot. J Trauma. 2011;70(1):159–68.
11. Rammelt S, Biewener A, Grass R, et al. Foot injuries in the polytraumatized patient [in German]. Unfallchirurg. 2005;108(10):858–65.
12. Ferreira RC, Sakata MA, Costa MT, Frizzo GG, Santin RA. Long-term results of salvage surgery in severely injured feet. Foot Ankle Int. 2010;31(2):113–23.
13. Zwipp H. Severe foot trauma in combination with talar injuries. In: Tscherne H, Schatzker J, editors. Major fractures of the pilon, the talus and the calcaneus. Berlin: Springer Verlag; 1993. p.123–35.
14. Holbrook TL, Anderson JP, Sieber WJ, Browner D, Hoyt DB. Outcome after major trauma: discharge and 6-month follow-up results from the Trauma Recovery Project. J Trauma. 1998;45(2):315–23.
15. Holbrook TL, Anderson JP, Sieber WJ, Browner D, Hoyt DB. Outcome after major trauma: 12- month and 18-month follow-up results from the Trauma Recovery Project. J Trauma. 1999;46(5):765–71.
16. Probst C, Richter M, Lefering R, Frink M, Gaulke R, Krettek C, Hildebrand F. Incidence and significance of injuries to the foot and ankle in polytrauma patients–an analysis of the Trauma Registry of DGU. Injury. 2010;41(2):210–5.
17. Stalp M, Koch C, Ruchholtz S, et al. Standardized outcome evaluation after blunt multiple injuries by scoring systems: a clinical follow-up investigation 2 years after injury. J Trauma. 2002;52(6):1160–8.
18. Tran T, Thordarson D. Functional outcome of multiply injured patients with associated foot injury. Foot Ankle Int. 2002;23(4):340–3.
19. Turchin DC, Schemitsch EH, McKee MD, Waddell JP. Do foot injuries significantly affect the functional outcome of multiply injured patients? J Orthop Trauma. 1999;13(1):1-4.
20. von Ruden C, Woltmann A, Rose M, Wurm S, Ruger M, Hierholzer C, et al. Outcome after severe multiple trauma: a retrospective analysis. J Trauma Manag Outcomes. 2013;7:4.
21. Weninger P, Aldrian S, Koenig F, Vécsei V, Nau T. Functional recovery at a minimum of 2 years after multiple injury-development of an outcome score. J Trauma. 2008;65(4):799-808.
22. Zelle BA, Brown SR, Panzica M, Lohse R, Sittaro NA, Krettek C, et al. The impact of injuries below the knee joint on the long-term functional outcome following polytrauma. Injury. 2005;36(1):169-77.
23. Heckman JD, Champine MJ. New techniques in the management of foot trauma. Clin Orthop Relat Res. 1989;(240):105-14.
24. Weninger P, Nau T, Aldrian S, Vései V. Long-term results in the treatment of foot injuries in polytraumatized patients [in German]. Zentralbl Chir. 2005;130(5):485–91.
25. Myerson MS, McGarvey WC, Henderson MR, Hakim J. Morbidity after crush injuries to the foot. J Orthop Trauma. 1994;8(4):343–9.
26. Westphal T, Piatek S, Schubert S, Schuschke T, Wincker S. Quality of life after foot injuries [in German]. Zentralbl Chir. 2002;127(3):238–42.
27. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of longbones: retrospective and prospective analyses. J Bone Joint Surg Am. 1976;58(4):453-8.
28. Tscherne H, Oestern HJ. A new classification of soft-tissue damage in open and closed fractures (author's transl) [in German]. Unfallheilkunde. 1982;85(3):111-5.
29. Ruedi TP, Buckley R, Moran CG. AO Principles of Fracture Management. New York, NY, USA: Thieme Medical Publishers; 2007.
30. Johansen K, Daines M, Howey T, Helfet D, Hansen ST Jr. Objective criteria accurately predict amputation following lower extremity trauma. J Trauma. 1990;30(5):568-72.
31. Ahmed N, Sahito B, Baig N. Evaluation and reliability of Mangled Extremity Severity Scoring in traumatic amputation versus limb salvage. J Pakistan Orthop Assoc. 2013;25(2):35–40.
32. Bonanni F, Rhodes M, Lucke JF. The futility of predictive scoring of mangled lower extremities. J Trauma. 1993;34(1):99–104.
33. Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. A prospective evaluation of the clinical utility of the lower-extremity injury-severity scores. J Bone Joint Surg Am. 2001;83-A(1):3–14.
34. Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. N Engl J Med. 2002;347(24):1924-31.
35. Bosse MJ, McCarthy ML, Jones AL, Webb LX, Sims SH, Sanders RW, et al. The insensate foot following severe lower extremity trauma: an indication for amputation? J Bone Joint Surg Am. 2005;87(12):2601–8.
36. Durham RM, Mistry BM, Mazuski JE, Shapiro M, Jacobs D. Outcome and utility of scoring sys- tems in the management of the mangled extremity. Am J Surg. 1996;172(5):569-73.
37. Fodor L, Sobec R, Sita-Alb L, Fodor M, Ciuce C. Mangled lower extremity: can we trust the amputation scores? Int J Burns Trauma. 2012;2(1):51-8.
38. Helfet DL, Howey T, Sanders R, Johansen K. Limb salvage versus amputation. Prelim- inary results of the Mangled Extremity Severity Score. Clin Orthop Relat Res. 1990;(256):80-6.
39. Hoogendoorn JM, Van der Werken C. The mangled leg, decision-making based on scoring systems and outcome. Eur J Trauma. 2002;1(1):1-10.
40. Johansen K, Daines M, Howey T, Helfet D, Hansen ST Jr. Objective criteria accurately predict amputation following lower extremity trauma. J Trauma. 1990;30(5):568-72.

41. Robertson PA. Prediction of amputation after severe lower limb trauma. J Bone Joint Surg Br. 1991;73(5):816-8.
42. Busse JW, Jacobs CL, Swiontkowski MF, Bosse MJ, Bhandari M, Evidence-Based Orthopaedic Trauma Working Group. Complex limb salvage or early amputation for severe lower-limb injury: a meta-analysis of observational studies. J Orthop Trauma. 2007;21(1):70-6.
43. Brown KV, Ramasamy A, McLeod J, Stapley S, Clasper JC. Predicting the need for early amputation in ballistic mangled extremity injuries. J Trauma. 2009;66(4 Suppl):S93–7.
44. Hammerberg EM, Whitesides TE Jr, Seiler JG 3rd. The reliability of measurement of tissue pressure in compartment syndrome. J Orthop Trauma. 2012;26(1):24-31.
45. Roberts CS, Pape HC, Jones AL, Malkani AL, Rodriguez JL, Giannoudis PV. Damage control orthopaedics: evolving concepts in the treatment of patients who have sustained orthopaedic trauma. Instr Course Lect. 2005;54:447–62.
46. Dodd A, Le I. Foot compartment syndrome: diagnosis and management. J Am Acad Orthop Surg. 2013;21(11):657-64.
47. Kakagia D. How to Close a Limb Fasciotomy Wound: An Overview of Current Techniques. Int J Low Extrem Wounds. 2015;14(3):268-76.
48. Patzakis MJ, Bains RS, Lee J, Shepherd L, Singer G, Ressler R, et al. Prospective, randomized, double-blind study comparing single-agent antibiotic therapy, ciprofloxacin, to combination antibiotic therapy in open fracture wound. J Orthop Trauma. 2000;14(8):529-33.
49. Gergely I, Zazgyva A, Man A, Zuh SG, Pop TS. The in vitro antibacterial effect of S53P4 bioactive glass and gentamicin impregnated polymethylmethacrylate beads. Acta Microbiol Immunol Hung. 2014;61(2):145-60.
50. Brenner P, Rammelt S, Gavlik JM, Zwipp H. Early soft tissue coverage after complex foot trauma. World J Surg. 2001;25(5):603-9.
51. Ellington JK, Bosse MJ, Castillo RC, MacKenzie EJ; LEAP Study Group. The mangled foot and ankle: results from a 2-year prospective study. J Orthop Trauma. 2013;27(1):43-8.
52. Akula M, Gella S, Shaw CJ, McShane P, Mohsen AM. A meta-analysis of amputation versus limb salvage in mangled lower limb injuries--the patient perspective. Injury. 2011;42(11):1194-7.
53. MacKenzie EJ, Jones AS, Bosse MJ, Castillo RC, Pollak AN, Webb LX, et al. Health-care costs associated with amputation or reconstruction of a limb--threatening injury. J Bone Joint Surg Am. 2007;89(8):1685-92.
54. Demiralp B, Ege T, Kose O, Yurttas Y, Basbozkurt M. Amputation versus functional reconstruction in the management of complex hind foot injuries caused by land-mine explosions: a long-term retrospective comparison. Eur J Orthop Surg Traumatol. 2014;24(4):621-6.
55. Shawen SB, Keeling JJ, Branstetter J, Kirk KL, Ficke JR. The mangled foot and leg: salvage versus amputation. Foot Ankle Clin. 2010;15(1):63-75.

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REVIEW ARTICLE

BRAZILIAN CONSENSUS STATEMENT ON VISCOSUPPLEMENTATION OF THE KNEE (COBRAVI)

CONSENSO BRASILEIRO DE VISCOSSUPLEMENTAÇÃO DO JOELHO (COBRAVI)

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ABSTRACT

Objective: The aim of this consensus statement on viscosupplementation is to serve as a reference document based on relevant literature and clinical experience in the treatment of knee osteoarthritis using an intra-articular injection of hyaluronic acid, covering key aspects such as clinical indications, effectiveness, and tolerability. Methods: A multidisciplinary panel including two sports medicine physicians, six orthopedists, four physiatrists, and two rheumatologists were selected based on their clinical and academic experience of viscosupplementation. Sixteen statements were prepared and discussed, after which a vote was held. Each member of the panel gave a score between 0 and 10 on a Likert scale, specifying their level of agreement with the statement. Results: The panel reached a consensus on several issues. Specifically, the panel agreed that the best indication is for mild to moderate knee arthrosis; prior or concomitant use of intraarticular triamcinolone hexacetonide may optimize the effect of hyaluronic acid; viscosupplementation should not be performed as an isolated procedure but in conjunction with other rehabilitative and pharmacological measures; viscosupplementation has analgesic, anti-inflammatory, and chondroprotective effects; and viscosupplementation is cost-effective. Conclusion: This consensus statement provides clear information and guidance for both individuals and payers. ***Level of evidence V, Consensus statement.***

Keywords: Osteoarthritis. Knee. Viscosupplementation.

RESUMO

Objetivo: O Consenso Brasileiro de Viscossuplementação visa gerar uma fonte referencial e consensual, a partir de levantamentos bibliográficos relevantes, do conhecimento teórico e da experiência clínica de especialistas de áreas afins para tratamento de viscossuplementação na osteoartrite do joelho, mitigando pontos críticos desse procedimento, como via de aplicação, indicação, eficácia e tolerabilidade. Métodos: Um painel multidisciplinar foi formado com dois médicos do esporte, seis ortopedistas, quatro fisiatras e dois reumatologistas, com base nas experiências clínica e acadêmica no uso da viscossuplementação. Foram elaboradas, discutidas e votadas 16 afirmativas. Cada membro do painel deu um valor entre zero e 10, em uma escala tipo Likert, especificando seu nível de concordância com a afirmação. Resultados: O painel chegou a um consenso sobre diversos aspectos da viscossuplementação, com destaque para as seguintes afirmativas: a melhor indicação é para artrose de joelhos leve a moderada; o uso prévio ou concomitante de hexacetonido de triancinolona intra-articular pode otimizar o efeito do ácido hialurônico; a viscossuplementação não deve ser realizada como procedimento isolado no tratamento da OA, mas em conjunto com outras medidas reabilitadoras e farmacológicas; promove efeito analgésico; anti-inflamatório; condroprotetor; e é custo-efetiva. Conclusão: Este consenso traz informações claras e servirá, como guia tanto para médicos quanto para as fontes pagadoras. ***Nível de evidência V, Consenso de especialistas.***

Descritores: *Osteoartrite. Joelho. Viscossuplementação.*

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INTRODUCTION

Osteoarthritis (OA) is the most prevalent joint disease and is associated with pain and disability. It is predicted that 25% of the adult population (more than 50 million people in the US) will be affected by this disease by 2020 and that OA will be a major cause of morbidity and restricted mobility in individuals over 40 years of age.[1,2] The latest update of the 2013 Global Burden of Disease estimates that 242 million people worldwide live with symptoms and limitations due to osteoarthritis of the knees or hips.[3]

Viscosupplementation (VS) is the intra-articular injection of exogenous hyaluronic acid for the treatment of osteoarthritis.[4] Hyaluronic acid exists in several organisms, and when it is not bound to other molecules, it binds to water and becomes gelatinous. It was first isolated in 1934 by Karl Meyer.[5] Balazs popularised the name hyaluronan by using it to encompass the various forms that the molecule can take: the acid form, such as hyaluronic acid, and the salt form, such as sodium hyaluronate; Balazs is considered the pioneer in the use of this substance for the treatment of osteoarthritis.[6] Intra-articular injection of hyaluronic acid has basically three main objectives: viscosupplementation itself, i.e., improving the rheological properties of the synovial fluid, serving both as a lubricant and as a shock absorber; analgesia; and improvement of joint homeostasis by decreasing inflammation and positively stimulating chondrocytes.[4]

The clinical outcomes of VS show a benefit with regard to pain relief, which has been demonstrated in several clinical trials and meta-analyses.[7-12] It is also considered a disease-modifying drug[13,14] with benefits that have been observed over a period of 6 months to 2 years.[15] It is believed that the long-term efficacy of hyaluronic acid is attributable to its modulatory action in the inflammatory process that occurs in the osteoarthritic joint and in its interaction with the receptors of CD44 synoviocytes.[16,17] However, despite this robust evidence, the recent international guidelines are not unanimous regarding recommendations for its use.[18-21]

Thus, a multidisciplinary group was formed to generate a consensus reference document based on a review of relevant literature, theoretical knowledge and the clinical experience of specialists in areas related to viscosupplementation for knee osteoarthritis. We aimed to address critical aspects of this procedure such as injection approach, clinical indications, efficacy and tolerability. The statement is also intended to guide and support medical students, medical residents and managers of public and private health systems who seek to increase the use of this procedure and improve their medical practice to enhance the quality of life of individuals with osteoarthritis of the knees.

MATERIALS AND METHODS

A multidisciplinary panel including physicians in different specialties was formed. Participants were selected based on their clinical and academic experience in the use of viscosupplementation for the treatment of osteoarthritis. Two sports medicine physicians, 6 orthopaedists, 4 physiatrists) and 2 rheumatologists participated in the panel. Initial face-to-face meetings were held between 4 members to define the 16 statements to be discussed. Ethics approval was waived since it is an expert opinion paper.

Once the statements were defined, 1 panellist conducted a review of the relevant literature and distributed the selected articles to all panel members so that discussion and scores were based not only on personal experience but also on quality scientific evidence. The terms "viscosupplementation", "hyaluronic acid", "hylan", and "hyaluronan", in conjunction with the terms "osteoarthritis" and "knee" were used for the bibliographic search. Only articles in the English language were considered. The search was performed in the PubMed database and the articles considered most relevant were selected and distributed to all panel members. After reading the articles, all members of the panel convened for a meeting during which the statements were presented. All the statements were strongly debated before the vote. The vote was held after exhaustive debate of all questions raised regarding viscosupplementation.

Sixteen statements were prepared, discussed and voted on. For each of the statements, each panel member gave a score between 0 and 10 on a *Likert scale*, indicating their level of agreement with the statement. On this scale, the value zero meant "I completely disagree", and the value 10 meant "I completely agree". After the vote, the scores were grouped into 3 categories. Scores between 0 and 3 were classified as indicating "disagreement", scores between 4 and 6 were classified as indicating "indifference", and scores between 7 and 10 were classified as indicating "agreement". Finally, the level of agreement among panellists for each statement was summarised as "unanimously in favour" when all votes were greater than or equal to seven, "strongly in favour" when only one of the votes was not greater than or equal to seven, "moderately in favour" when only two to four votes were not greater than or equal to seven, "without consensus" when there was no category with at least four votes more than another category, "moderately against" when only two to four votes were greater than 3, "strongly against" when only one of the votes was greater than 3, and "unanimously against" when all votes were less than or equal to 3.

RESULTS

Statement 1. The best indication is for mild to moderate OA of the knee.

Agreement: 100% - unanimously in favour

Mean: 9.78 Median: 10 Score range: 8-10

The panel was unanimously in favour of the statement, as was the American group for the Appropriate Use Criteria (AUC) of hyaluronic acid for OA of the knee, which in 2017 published an article stating that there is evidence in the literature to support that viscosupplementation is an appropriate treatment for patients with mild and moderate OA.[22] Such a statement had previously been made by a consensus panel of European experts.[23] A French study focusing on evidence from "real" studies has suggested that joint infiltration with hyaluronic acid appears to be more effective when the patient has mild to moderate OA.[24] Viscosupplementationwas also recommended for patients with chronic, low-grade OA in the anterior, medial and lateral knee compartments.[25]

Statement 2. Viscosupplementation can be used as the first line of treatment.

Agreement: 92.86% - strongly in favour

Mean: 8.85 Median: 9.5 Score range: 6-10

The AMELIA study showed that repeated cycles of intra-articular hyaluronic acid infiltration improves knee OA symptoms not only during the period between treatments but also for as long as one year after the last injection.[15] Similarly, a Cochrane review conducted in 2006 and revisited in 2014 found that viscosupplementation is an effective treatment for OA of the knee, with beneficial effects on pain, function and overall assessment of the patient and over various post-treatment periods, especially between 5 and 13 weeks.[9,26] A systematic review and meta-analysis confirmed that viscosupplementation is effective within 26 weeks after infiltration in patients with OA.[27] Another meta-analysis found that there is good evidence in the literature on the efficacy of viscosupplementation in reducing pain and improving function in OA of the knee.[7] Finally, the American group for the Appropriate Use Criteria of viscosupplementation for OA of the knee has recognised that there is a need to consider injections of hyaluronic acid as primary therapy

given the expected increase in the prevalence of OA of the knee among American adults.[22]

Statement 3. Viscosupplementation may be indicated in cases of severe OA of the knee
Agreement: 85.71% - moderately in favour
Mean: 8.85 Median: 10 Score range: 5-10

Viscosupplementation improves pain and function in patients with OA of the knee.[26] Guidelines on the clinical treatment of osteoarthritis suggest that viscosupplementation is indicated for the treatment of OA of the knee either alone[18] or in combination with medications for symptomatic relief,[20] mainly in patients with mild to moderate OA (classified as Kellgren & Lawrence grades 2 and 3). However, several studies also suggest that viscosupplementation is beneficial in patients with severe OA of the knee. A recent randomised clinical trial demonstrated improvement of pain and function in patients with severe OA of the knee.[28] Waddel et al.[29] found that total knee arthroplasty was delayed by more than 7 years in 75% of 1863 knees with grade IV osteoarthritis (1342 patients) who had used viscosupplementation. The European Consensus[23] also states that viscosupplementation may be beneficial in cases of severe osteoarthritis of the knees.

Statement 4. The prior or concomitant use of intra-articular triamcinolone hexacetonide may optimise the effect of hyaluronic acid.
Agreement: 100% - unanimously in favour
Mean: 8.85 Median: 9.5 Score range: 7-10

The use of intra-articular corticosteroid in osteoarthritic knees leads to an improvement in pain and function for 2 to 4 weeks, after which the effect wanes.[8,12,30,31] Infiltration with hyaluronic acid also promotes antalgic effects and functional improvement, but with a later onset and longer duration (approximately 6 months).[7,9] Based on these findings, in 2009 Bannuru et al.[8] suggested that both medications should be used concurrently to achieve early and lasting pain control and functional improvement. This combination was studied by de Campos et al. in 2013[12] In this study, the addition of 1 ml of triamcinolone hexacetonide improved pain and function in the first week after viscosupplementation, without altering the incidence of adverse effects or even the long-term beneficial effect of viscosupplementation. This finding provides support for the effectiveness of combined corticosteroid and hyaluronic acid treatment in achieving early and lasting improvement of pain and function. Although studies on the combination of corticosteroids and hyaluronic acid consider only concomitant injection, the panel also considers it appropriate to perform the corticosteroid injection one week before the injection of the hyaluronic acid.

Statement 5. The results of VS vary according to the viscosupplementation product used.
Agreement: 85.71% - moderately in favour
Mean: 8.21 Median: 8 Score range: 6-10

The products currently on the market differ in their origin (animal or biofermented), production method, molecular weight, rheological properties, presence of crosslinks, pharmacodynamics and duration of persistence in the joint.[4] Some are still combined with anti-oxidants such as sorbitol or mannitol.[32] In the panel's view, these variations play an important role in the discrepant and unclear recommendations currently found in some systematic reviews, meta-analyses, and guidelines that attempt to aggregate evidence on viscosupplementation by considering all viscosupplements as a single class of drugs. A review in the Journal of Bone and Joint Surgery (JBJS) that carefully examined more recently published studies suggests that viscosupplementation is a safe option with a clinically important reduction of pain in patients with OA of the knee, especially when using formulations with higher molecular weights or cross-links.[33] The use of anti-oxidant substances may also potentiate the effects of viscosupplementation by reducing the rate of degradation of hyaluronic acid without increasing the risk of adverse events.[32] Similar to the European Consensus panel,[23] this panel finds that it is impossible to consider the different products as a single class. Thus, one cannot extrapolate the results from one product to another, nor perform meta-analyses by grouping results from different types of viscosupplements.

Statement 6. The best access route for non-guided infiltration is the superolateral approach.
Agreement: 21.43% - no consensus
Mean: 4.5 Median: 5 Score range: 0-9

There are several non-guided techniques for knee viscosupplementation described in the literature. Most studies show that insertion points lateral to the patella are more accurate when compared to the insertion points medial to the patella.[34-36] The most cited approach in patients with associated joint effusion are the superolateral and the medial lateral patellar approaches,[34,36] which are more accurate than medial approaches. When using the superolateral and direct lateral approaches, the patient should be placed in a supine position with the knee half-extended or fully extended. For the anterolateral approach, which is similar to that used for knee arthroscopy, the patient may be in a sitting position with the knee at 90 degrees, which some professionals prefer. Although the literature favours the superolateral approach, there was no consensus among panel members in this regard. As most studies have been conducted with patients with some degree of joint effusion, the panel's opinion is that individual clinical experience should be taken into account during the procedure, especially in patients without joint effusion.

Statement 7. Viscosupplementation should not be performed as the only procedure in the treatment of OA but together with other rehabilitative and pharmacological measures.
Agreement: 100% - unanimously in favour
Mean: 9.78 Median: 10 Score range: 7-10

The consensus statement of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)[20] published in 2014 stated that patients with mild to moderate OA of the knee can be appropriately managed with a set of core measures (education, diet and exercise) combined with the use of oral analgesics (Paracetamol), slow-acting symptomatic treatment (glucosamine and chondroitin) and topical anti-inflammatories. If necessary, advanced pharmacological measures, including non-selective and selective oral anti-inflammatory drugs, intra-articular corticosteroids and hyaluronic acid, may be added. This is consistent with virtually all guidelines and opinion articles on OA treatment, which recommend a multimodal approach to OA treatment with a central core of education, weight loss and physical activity, which can be complemented with other pharmacological therapies such as, for example, viscosupplementation.

Statement 8. The number of treatments will depend on the patient's profile and the viscosupplements used.
Agreement: 92.86% - strongly in favour
Mean: 8.71 Median: 9.5 Score range: 4-10

As discussed in the Statement 5, there are various products currently on the market that differ from one another with regard to several characteristics. Some of these characteristics interfere with the longevity of viscosupplements in the joint.[37,38] Because it remains in the joint for approximately 7 days, the classic regimen for sodium hyaluronate involves weekly injections with a total of 3 to 5 treatments, which allows a total time of action in the joint of 21 to 35 days. The literature demonstrates that the presence of cross-links greatly increases the longevity of the product in the joint, probably because

it hinders resorption.[37,38] Combination with anti-oxidant substances may also delay resorption of the product.[32] The use of products with longer persistence allows for a treatment regimen with fewer injections, or even a single injection. Single-dose use was validated for high-molecular weight and cross-linked hylan in a controlled non-inferiority clinical trial.[11] However, a prospective randomised study comparing two regimens with a linear sodium hyaluronate product of intermediate molecular weight (single injection of 6 ml versus 3 weekly injections of 2 ml) demonstrated that the one-time injection did not provide the same efficacy.[39]

Statement 9. In cases of mild knee osteoarthritis, VS has a chondroprotective effect.
Agreement: 100% - unanimously in favour
Mean: 9 Median: 9 Score range: 7-10

A recent systematic review[40] found 67 articles in the literature describing chondroprotective effects conferred by intra-articular injection of hyaluronic acid. Hyaluronic acid has several beneficial effects, including reduction of chondrocyte apoptosis and increased chondrocyte proliferation,[41,42] and most of these effects are due to interaction with CD44 cell receptors. Binding to CD44 has a greater effect with viscosupplements of higher molecular weights.[43] Studies by Bagga et al. in 2006[44] and Band et al. in 2015[45] examined the synovial fluid of patients with osteoarthritis of the knee who had received hyaluronic acid injections; improvements of pain and function were observed, probably due to the chondroprotective effect of the increased hyaluronic acid concentration in the synovial fluid. Studies with more objective findings have also published. Biopsies performed before and after VS showed reconstitution of the superficial layer, better quality of the matrix and higher density of chondrocytes, with a greater number of intracellular organelles after 6 months.[13] "Second look" arthroscopies performed 1 year after starting treatment with hyaluronic acid found a better visual appearance of the articular surface compared to the placebo group.[46] Finally, Jubb et al.[47] found that treatment with hyaluronic acid significantly reduced the progression of joint space loss in patients with milder degrees of OA of the knees compared to placebo.

Statement 10. VS may be indicated in patellofemoralchondropathy.
Agreement: 85.71% - moderately in favour
Mean: 8.21 Median: 8 Score range: 6-10

There are no prospective and randomised clinical trials on viscosupplementation aimed at treating patients with chondropathy and/or patellofemoral osteoarthritis of the knee, a condition often associated with anterior knee pain, which is often disabling. An open pilot study used hylan in patients with anterior knee pain due to patellofemoral arthrosis and demonstrated a reduction of pain (particularly when climbing stairs) and overall improvement in the condition of the participating patients according to validated measures.[48] The decrease in pain was significant from week 4 and maintained until week 52.
A recent study reported improvement of pain in professional soccer players who received VS for the treatment of patellofemoral chondropathy.[49] Frosted and Dagher[50] were successful in the treatment of 25 patients with patellofemoral pain using an arthroscopic lateral release combined with viscosupplementation. Most participants in his panel recognise the potential beneficial effect of viscosupplementation in cases of patellofemoral pathology, especially when combined with non-pharmacological treatment for muscle strengthening.

Statement 11. Imaging guidance (by ultrasound, fluoroscopy, CT or other methods) is necessary to perform VS.
Agreement: 78.57% - moderately against
Mean: 2.28 Median: 2 Score range: 0-4

Hyaluronic acid (HA) may be injected in different anatomical sites, with or without imaging guidance.[34,51] However, to achieve their therapeutic benefit, hyaluronic acid derivatives should be injected directly into the space of the knee joint and not into the anterior adipose cushion or subsynovial tissues.[4] In the absence of a knee effusion, reproducible placement of the needle into the intra-articular space can be a challenge.[52] Anatomically guided injections, which rely on conventional palpation, often result in inaccurate needle positioning in the extra-articular tissue and adjacent structures. However, injections have traditionally been carried out this way and it is important to question whether the use of imaging can significantly improve the accuracy of injections. Bookman et al.[51] report an accuracy of 92.7% using ultrasound-guided infiltration of the knee joint and 77.9% using blind methods; similar results were reported by Berkooff et al.:[53] 95.8% versus 77.8%, respectively. A comparison between the effect of ultrasound-guided HA injection and blind HA injection in patients with OA of the knee was performed using clinical scores. Kianmehr et al.[52] observed better WOMAC scores in patients who underwent guided injection than in those who underwent blind injection after 6 and 12 weeks. Even so, most doctors choose to perform blind knee infiltration. The panel of experts was moderately against the need for guided puncture in viscosupplementation. Blind injections at the superolateral patellar site have good accuracy, especially if performed by an experienced professional.[54] The precision of needle placement varies from 63% to 100% with ultrasound and from 39% to 100% with conventional anatomical guidance.[53]

Statement 12. Viscosupplementation generates cost reductions for the supplementary health system, making it a cost-effective procedure.
Agreement: 92.86% - strongly in favour
Mean: 8.85 Median: 9.5 Score range: 5-10

Osteoarthritis of the knee is a great burden to society because it is extremely prevalent, it severely decreases the quality of life of the affected individuals and it generates enormous costs.[1,2,55] Thus, in addition to being effective, it is essential that any treatment for osteoarthritis be cost-effective. Several studies have studied the cost-effectiveness of viscosupplementation. A French multicentre study compared the costs and effectiveness of OA treatment with NSAIDs or hyaluronic acid and concluded that intra-articular (IA) HA treatment did not generate additional costs for the national health insurance system and was associated with functional improvement and better quality of life in patients with osteoarthritis of the knee. The cost-effectiveness analysis was in favour of VS.[56] Another study conducted in individuals of productive age (between 18 and 65 years old) concluded that the addition of high-molecular weight hyaluronic acid to the routine OA treatment is cost-effective.[57] Finally, a study carried out with the top 5 brands of hyaluronic acid on the American market concluded that viscosupplementation with any of was more cost-effective compared to routine treatment. Thus, the panel was strongly in agreement that viscosupplementation generates cost reductions for the supplementary health system and is a cost-effective procedure.[58]

Statement 13. Viscosupplementation has analgesic effects.
Agreement: 100% - unanimously in favour
Mean: 9.21 Median: 10 Score range: 7-10

VS promoted reduction of knee pain in all studies, based on both the WOMAC score and the visual analogue scale. The magnitude and duration of this pain reduction depended on the treatment used (corticosteroids, NSAIDs, placebo). The analgesic effect seems to be associated with the concentration of HA.[59] In comparison to corticosteroids, VS led to a greater reduction of pain after the 5th week, mainly between the 5th and 13th weeks, and persisted until

the 26th week.[8] It has also recently been established that VS can relieve pain beyond 12 weeks, with effects lasting up to 40 months, whereas corticosteroid use is associated with pain reduction only in the first few weeks after infiltration.[24]

In comparing VS and placebo, the evidence shows that VS can reduce knee pain starting at around the 4th week and with a peak effect at the 8th week after HA infiltration.[7,9] The effect may last up to 12 weeks,[60] up to 26 weeks,[27] or even for more than 26 weeks.[11] Finally, not many differences were found between oral NSAIDs and VS. However, VS is preferred because it does not entail the adverse effects of NSAIDs,[24,61] especially in older and high-risk patients.[20]

Statement 14. Viscosupplementation has anti-inflammatory effects.
Agreement: 100% - unanimously in favour
Mean: 8.92 Median: 9 Score range: 7-10

The anti-inflammatory effects described in the literature are observed in both preclinical and clinical studies. The main anti-inflammatory effect of hyaluronic acid is mediated by binding to CD44 receptors and consequent inhibition of IL1 beta, liposaccharides and metalloproteases.[17,40,62] According to Yasuda,[17] hyaluronic acid has an anti-inflammatory effect in cultured synovial cells of patients with rheumatoid arthritis. This effect is mediated by binding to CD44 on U937 macrophages causing secondary inhibition of PGE2, inhibition of PGE2-stimulating liposaccharides (LPS) with consequent inhibition of COX2, and down-regulation of the kappa beta nuclear factor. According to Altman,[40] viscosupplement preparations inhibit interleukin 1 (IL-1), metalloproteases (MMPs) and TNF and are thus considered to have anti-inflammatory and chondral stimulation effects. Henrontin[62] demonstrated in adults with osteoarthritis that viscosupplementation leads to a decrease in the degradation of type 2 collagen, which also supports the ability of VS to reduce the inflammatory processes associated with osteoarthritis.

Statement 15. Viscosupplementation only has biomechanical effects.
Agreement: 100% - unanimously against
Mean: 0.35 Median: 0 Score range: 0-2

The exact mechanism of action of VS is unknown. Three major effects have been proposed: mechanical effects mediated by improvement of the rheology of synovial fluid, thereby optimising mechanical properties such as viscosity and load distribution;[7] analgesic effects through the direct inhibition of nociceptive stimuli;[59] and biological effects such as stimulation of the endogenous synthesis of HA,[44] decreased inflammatory activity,[63] stimulation of the production of extracellular matrix and the proliferation of chondrocytes,[43] among others. A previous expert consensus statement published in 2015 established that when administered in early stages, VS has a chondroprotective effect.[23] A systematic review published in the same year addressed several effects of VS in the treatment of OA of the knee, including mechanical effects, chondroprotective effects, anti-inflammatory effects, analgesia and interaction with the synthesis of glycosaminoglycans and subchondral bone.[40] Therefore, the panel was unanimous in agreeing that the effect of VS is not solely mechanical.

Statement 16. VS improves quality of life in patients with OA of the knee.
Agreement: 100% - unanimously in favour
Mean: 9.57 Median: 10 Score range: 7-10

The panel of experts agreed unanimously that VS improves quality of life in patients with OA of the knee. The positive impact of HA on quality of life in patients with OA of the knee was demonstrated in several studies, which reported increased scores on quality of life questionnaires such as the SF-36 or AOKHQOL after 3 to 6 months of treatment.[56,58,64-66] The use of HA is associated with decreased pain severity, and this reflects improvements in mobility and function.[65] It has been shown that VS can increase quality-adjusted life-years in patients with symptomatic OA of the knee.[58] A recent pharmaco-economic study showed that the use of intra-articular HA did not generate additional costs for the health system and was associated with functional improvement and better quality of life in patients with OA of the knee.[56]

DISCUSSION

Viscosupplementation with intra-articular injection of hyaluronic acid has been widely used as part of the therapeutic arsenal in the conservative treatment of osteoarthritis of the knees. The literature on viscosupplementation is robust, but extremely heterogeneous and conflicting. In the face of contradictory evidence and inconclusive guidelines, physicians need other sources of information to guide their decisions and offer the best possible treatment to their patients. In this context, a consensus considering the opinion of experts in the area, including physicians in different specialties, can be highly valuable. This article constitutes the first Brazilian consensus statement on viscosupplementation and was developed by a multidisciplinary panel of two sports medicine physicians, 6 orthopaedists, 4 physiatrists and two rheumatologists.

Although it is extensive, the literature on viscosupplementation includes many studies with excessive comparisons and small samples, which does not allow adequate statistical power to draw consistent conclusions. In addition, some articles have been criticised for the involvement of the pharmaceutical industry in the design, analysis or funding of the studies. However, a careful examination of the most recently published articles indicates that viscosupplementation is a safe option with clinically important reduction of pain in patients with osteoarthritis of the knee (especially younger patients and those with less severe disease), especially in those formulations with higher molecular weights.[33]

Our panel was strongly in favour of the use of viscosupplementation as first-line treatment in osteoarthritis of the knees. The ESCEO guidelines,[20] which recommend injections of hyaluronic acid, reserve its use as a second line of treatment, referring to it as "advanced pharmacological management" indicated for patients with moderate to severe pain that do not respond to common analgesics and/or chondroprotectors. First-line use allows intervention at earlier stages of osteoarthritis, and also obviates the misconception that viscosupplementation should only be used when no other medication or procedure has been successful. The panel also agreed unanimously that viscosupplementation is best indicated for mild to moderate cases. Regarding advanced stages of knee osteoarthritis, although the use of VS as an alternative to a knee prosthesis is not an ideal indication, it can bring benefits to those patients who cannot or do not wish to undergo total knee arthroplasty surgery.[23,28]

This panel also reviewed the available literature on the various forms of action of hyaluronic acid injected into the knee. The panel unanimously agreed that the effect of viscosupplementation is not purely mechanical and that it does not simply function as an "oil change" as some physicians have said to their patients. The literature demonstrates potent biological effects, such as modulation of inflammatory activity,[16,17,63] chondrocyte stimulation[42,43] and direct analgesia with decreased nociceptive activity.[59]

Optimising the effect of hyaluronic acid requires that it is injected correctly into the joint space. The panel moderately disagreed that imaging guidance such as USG or fluoroscopy is needed for puncture of the knee joint. Although there is literature demonstrating increased efficacy with the use of a guidance method,[51-53] specialists feel comfortable with correct intra-articular positioning of the needle using only anatomical parameters. There was no consensus, however, on

the best anatomical site to perform the injection. The puncture can be performed lateral or superolateral to the patella with the patient in the supine position and the knee extended, or with an anterolateral approach with the knee at 90 degrees. The panel concluded that physicians should use the technique with which they are more accustomed and feel more confident performing.

The panel was also unanimously in favor of the prior or concomitant use of intra-articular triamcinolone hexacetonide to optimise the effect of hyaluronic acid. Antioxidants agents have been also used in combination with hyaluronic acid to decelerate degradation by the reactive oxygen species and improve its residence time into the joint. Sorbitol and mannitol which have intrinsic free radical scavenger properties have been the most studied antioxidants. The oxygen free radicals neutralization by mannitol and sorbitol can delay the degradation of HA and also provide faster analgesia without safety issues.[32]

Finally, in spite of the current reluctance of payers to cover the costs of viscosupplementation, the present panel strongly agreed that viscosupplementation generates cost reductions for the supplementary health system and is a cost-effective procedure. The literature has quality studies that demonstrate greater gain in function, increase in quality-adjusted life years, and lower use of deleterious drugs such as NSAIDs when treatment with hyaluronic acid is incorporated into routine treatment for osteoarthritis of the knee.[56-58]

CONCLUSION

This expert consensus statement provides important information on the most important aspects of viscosupplementation and may serve as a guide for both physicians and payers regarding the treatment of osteoarthritis of the knees with hyaluronic acid.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. GCC (0000-0001-7811-7354)* conceived the idea, conducted a literature search, reviewed the relevant literature, defined the statements, discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. EBS (0000-0001-8577-6403)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. PCH (0000-0002-3931-9321)* conceived the idea, defined the statements, discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. CSAJ (0000-0002-9935-9632)* conceived the idea, defined the statements, discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. AMT (0000-0001-5573-1773)* conceived the idea, defined the statements, discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. MUR (0000-0002-2020-9501)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. AAAA (0000-0002-6418-8538) discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. CBP (0000-0002-7694-4273)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. EMCR (0000-0003-2078-5450)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. FGC (0000-0002-6692-5335)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. IP (0000-0002-3109-3866)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. MSRV (0000-0002-6312-5164)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. SFA (0000-0002-0412-8306)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. ZJ BM (0000-0002-6902-0136)* discussed and voted the statements, collaborated with the manuscript, reviewed and agreed to the final manuscript. *ORCID (Open Researcher and Contributor ID).

REFERENCES

1. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis Rheum. 2008;58(1):15-25.
2. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008;58(1):26-35.
3. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(9995):743-800.
4. Rezende MU, Campos GC. Viscosuplementation. Rev Bras Ortop. 2012;47(2):160-4.
5. Meyer K, Palmer JW. The polysaccharide of the vitreous humor. J Biol Chem. 1934;107(3):629-34.
6. Balazs EA, Watson D, Duff IF, Roseman S. Hyaluronic acid in synovial fluid. I. Molecular parameters of hyaluronic acid in normal and arthritis human fluids. Arthritis Rheum. 1967;10(4):357-76.
7. Bannuru RR, Natov NS, Dasi UR, Schmid CH, McAlindon TE. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis--meta-analysis. Osteoarthritis Cartilage. 2011;19(6):611-9.
8. Bannuru RR, Natov NS, Obadan IE, Price LL, Schmid CH, McAlindon TE. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis. Arthritis Rheum. 2009;61(12):1704-11.
9. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. Cochrane Database Syst Rev. 2006;(2):CD005321.
10. Divine JG, Shaffer MD. Use of viscosupplementation for knee osteoarthritis: an update. Curr Sports Med Rep. 2011;10(5):279-84.
11. Chevalier X, Jerosch J, Goupille P, van Dijk N, Luyten FP, Scott DL, et al. Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: a randomised, multicentre, double-blind, placebo controlled trial. Ann Rheum Dis. 2010; 69(1):113-9.
12. de Campos GC, Rezende MU, Pailo AF, Frucchi R, Camargo OP. Adding triamcinolone improves viscosupplementation: a randomized clinical trial. Clin Orthop Relat Res. 2013;471(2):613-20.
13. Guidolin DD, Ronchetti IP, Lini E, Guerra D, Frizziero L. Morphological analysis of articular cartilage biopsies from a randomized, clinical study comparing the effects of 500-730 kDa sodium hyaluronate (Hyalgan) and methylprednisolone acetate on primary osteoarthritis of the knee. Osteoarthritis Cartilage. 2001;9(4):371-81.
14. Wang Y, Hall S, Hanna F, Wluka AE, Grant G, Marks P, et al. Effects of Hylan G-F 20 supplementation on cartilage preservation detected by magnetic resonance imaging in osteoarthritis of the knee: a two-year single-blind clinical trial. BMC Musculoskelet Disord. 2011;12:195.
15. Navarro-Sarabia F, Coronel P, Collantes E, Navarro FJ, de la Serna AR, Naranjo A, et al. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. Ann Rheum Dis. 2011;70(11):1957-62.
16. Wang CT, Lin YT, Chiang BL, Lin YH, Hou SM. High molecular weight hyaluronic acid down-regulates the gene expression of osteoarthritis-associated cytokines and enzymes in fibroblast-like synoviocytes from patients with early osteoarthritis. Osteoarthritis Cartilage. 2006;14(12):1237-47.
17. Yasuda T. Hyaluronan inhibits prostaglandin E2 production via CD44 in U937 human macrophages. Tohoku J Exp Med. 2010;220(3):229-35.
18. McAlindon TE, Bannuru RR, Sullivan MC, Arden NK, Berenbaum F, Bierma-Zeinstra SM, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis Cartilage. 2014;22(3):363-88.
19. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012;64(4):465-74.
20. Bruyere O, Cooper C, Pelletier JP, Branco J, Brandi ML, Guillemin F, et al. An algorithm recommendation for the management of knee osteoarthritis in Europe and internationally: a report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Semin Arthritis Rheum. 2014;44(3):253-63.
21. Jevsevar DS, Brown GA, Jones DL, Matzkin EG, Manner PA, Mooar P, et al. The American Academy of Orthopaedic Surgeons evidence-based guideline on: treatment of osteoarthritis of the knee, 2nd edition. J Bone Joint Surg. 2013;95(20):1885-6.

22. Bhadra AK, Altman R, Dasa V, Myrick K, Rosen J, Vad V, et al. Appropriate Use Criteria for Hyaluronic Acid in the Treatment of Knee Osteoarthritis in the United States. Cartilage. 2017;8(3):234-54.
23. Henrotin Y, Raman R, Richette P, Bard H, Jerosch J, Conrozier T, et al. Consensus statement on viscosupplementation with hyaluronic acid for the management of osteoarthritis. Semin Arthritis Rheum. 2015;45(2):140-9.
24. Maheu E, Rannou F, Reginster JY. Efficacy and safety of hyaluronic acid in the management of osteoarthritis: Evidence from real-life setting trials and surveys. Semin Arthritis Rheum. 2016;45(4 Suppl):S28-33.
25. Levy DM, Petersen KA, Scalley Vaught M, Christian DR, Cole BJ. Injections for Knee Osteoarthritis: Corticosteroids, Viscosupplementation, Platelet-Rich Plasma, and Autologous Stem Cells. Arthroscopy. 2018;34(5):1730-43.
26. Evaniew N, Simunovic N, Karlsson J. Cochrane in CORR(R): Viscosupplementation for the treatment of osteoarthritis of the knee. Clin Orthop Relat Res. 2014;472(7):2028-34.
27. Strand V, McIntyre LF, Beach WR, Miller LE, Block JE. Safety and efficacy of US-approved viscosupplements for knee osteoarthritis: a systematic review and meta-analysis of randomized, saline-controlled trials. J Pain Res. 2015;8:217-28.
28. Campos ALS, EAlbuquerque RSP, da Silva EB, Fayad SG, Acerbi LD, de Almeida FN, et al. Viscosupplementation in patients with severe osteoarthritis of the knee: six month follow-up of a randomized, double-blind clinical trial. Int Orthop. 2017;41(11):2273-80.
29. Waddell DD, Joseph B. Delayed Total Knee Replacement with Hylan G-F 20. J Knee Surg. 2016;29(2):159-68.
30. He WW, Kuang MJ, Zhao J, Sun L, Lu B, Wang Y, et al. Efficacy and safety of intraarticular hyaluronic acid and corticosteroid for knee osteoarthritis: A meta-analysis. Int J Surg. 2017;39:95-103.
31. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. Cochrane Database Syst Rev. 2006(2):CD005328.
32. Conrozier T. Is the addition of a polyol to hyaluronic acid a significant advance in the treatment of osteoarthritis? Curr Rheumatol Rev. 2018;14(3):226-30.
33. Johal H, Devji T, Schemitsch EH, Bhandari M. Viscosupplementation in Knee Osteoarthritis: Evidence Revisited. JBJS Rev. 2016;4(4):e11-111.
34. Telikicherla M, Kamath SU. Accuracy of Needle Placement into the Intra-Articular Space of the Knee in Osteoarthritis Patients for Viscosupplementation. J Clin Diagn Res. 2016;10(2):RC15-7.
35. Esenyel C, Demirhan M, Esenyel M, Sonmez M, Kahraman S, Senel B, et al. Comparison of four different intra-articular injection sites in the knee: a cadaver study. Knee surgery, sports traumatology. Arthroscopy. 2007;15(5):573-7.
36. Legre-Boyer V. Viscosupplementation: techniques, indications, results. Orthop Traumatol Surg Res. 2015;101(1 Suppl):S101-8.
37. Larsen NE, Dursema HD, Pollak CT, Skrabut EM. Clearance kinetics of a hylan--based viscosupplement after intra-articular and intravenous administration in animal models. J Biomed Mater Res B Appl Biomater. 2012;100(2):457-62.
38. Brown TJ, Laurent UB, Fraser JR. Turnover of hyaluronan in synovial joints: elimination of labelled hyaluronan from the knee joint of the rabbit. Exp Physiol. 1991;76(1):125-34.
39. Zoboli AA, Rezende MU, Campos GC, Pasqualin T, Frucchi R, Camargo OP. Prospective randomized clinical trial: single and weekly viscosupplementation. Acta Ortop Bras. 2013;21(5):271-5.
40. Altman RD, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. BMC Musculoskelet Disord. 2015;16:321.
41. Brun P, Panfilo S, Daga Gordini D, Cortivo R, Abatangelo G. The effect of hyaluronan on CD44-mediated survival of normal and hydroxyl radical-damaged chondrocytes. Osteoarthritis Cartilage. 2003;11(3):208-16.
42. Brun P, Zavan B, Vindigni V, Schiavinato A, Pozzuoli A, Iacobellis C, et al. In vitro response of osteoarthritic chondrocytes and fibroblast-like synoviocytes to a 500-730 kDahyaluronan amide derivative. J Biomed Mater Res B Appl Biomater. 2012;100(8):2073-81.
43. Ehlers EM, Behrens P, Wunsch L, Kuhnel W, Russlies M. Effects of hyaluronic acid on the morphology and proliferation of human chondrocytes in primary cell culture. Ann Anat. 2001;183(1):13-7.
44. Bagga H, Burkhardt D, Sambrook P, March L. Longterm effects of intraarticular hyaluronan on synovial fluid in osteoarthritis of the knee. J Rheumatol. 2006;33(5):946-50.
45. Band PA, Heeter J, Wisniewski HG, Liublinska V, Pattanayak CW, Karia RJ, et al. Hyaluronan molecular weight distribution is associated with the risk of knee osteoarthritis progression. Osteoarthritis Cartilage. 2015;23(1):70-6.
46. Listrat V, Ayral X, Patarnello F, Bonvarlet JP, Simonnet J, Amor B, et al. Arthroscopic evaluation of potential structure modifying activity of hyaluronan (Hyalgan) in osteoarthritis of the knee. Osteoarthritis Cartilage. 1997;5(3):153-60.
47. Jubb RW, Piva S, Beinat L, Dacre J, Gishen P. A one-year, randomised, placebo (saline) controlled clinical trial of 500-730 kDa sodium hyaluronate (Hyalgan) on the radiological change in osteoarthritis of the knee.Int J Clin Pract. 2003;57(6):467-74.
48. Clarke S, Lock V, Duddy J, Sharif M, Newman JH, Kirwan JR. Intra-articular hylan G-F 20 (Synvisc) in the management of patellofemoral osteoarthritis of the knee (POAK). Knee. 2005;12(1):57-62.
49. Tamburrino P, Castellacci E. Intra-articular injections of HYADD4-G in male professional soccer players with traumatic or degenerative knee chondropathy. A pilot, prospective study. J Sports Med Phys Fitness. 2016;56(12):1534-9.
50. Fosco M, Dagher E. Proposal of a therapeutic protocol for selected patients with patellofemoral knee osteoarthritis: arthroscopic lateral retinacular release followed by viscosupplementation. Musculoskelet Surg. 2016;100(3):171-8.
51. Bookman JS, Pereira DS. Ultrasound guidance for intra-articular knee and shoulder injections: a review. Bull Hosp Jt Dis (2013). 2014;72(4):266-70.
52. Kianmehr N, Hasanzadeh A, Naderi F, Khajoei S, Haghighi A. A randomized blinded comparative study of clinical response to surface anatomy guided injection versus sonography guided injection of hyaloronic acid in patients with primary knee osteoarthritis. Int J Rheum Dis. 2018;21(1):134-9.
53. Berkoff DJ, Miller LE, Block JE. Clinical utility of ultrasound guidance for intra--articular knee injections: a review. Clin Interv Aging. 2012;7:89-95.
54. Maricar N, Parkes MJ, Callaghan MJ, Felson DT, O□Neill TW. Where and how to inject the knee--a systematic review. Semin Arthritis Rheum. 2013;43(2):195-203.
55. Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. Nat Rev Rheumatol. 2014;10(7):437-41.
56. Thomas T, Amouroux F, Vincent P. Intra articular hyaluronic acid in the management of knee osteoarthritis: Pharmaco-economic study from the perspective of the national health insurance system. PLoS One. 2017;12(3):e0173683.
57. Hermans J, Reijman M, Goossens LMA, Verburg H, Bierma-Zeinstra SMA, Koopmanschap MA. Cost-Utility Analysis of High Molecular Weight Hyaluronic Acid for Knee Osteoarthritis in Everyday Clinical Care in Patients at a Working Age: An Economic Evaluation of a Randomized Clinical Trial. Arthritis Care Res (Hoboken). 2018;70(1):89-97.
58. Rosen J, Sancheti P, Fierlinger A, Niazi F, Johal H, Bedi A. Cost-Effectiveness of Different Forms of Intra-Articular Injections for the Treatment of Osteoarthritis of the Knee. Adv Ther. 2016;33(6):998-1011.
59. Gomis A, Miralles A, Schmidt RF, Belmonte C. Intra-articular injections of hyaluronan solutions of different elastoviscosity reduce nociceptive nerve activity in a model of osteoarthritic knee joint of the guinea pig. Osteoarthritis Cartilage. 2009;17(6):798-804.
60. Richette P, Chevalier X, Ea HK, Eymard F, Henrotin Y, Ornetti P, et al., Hyaluronan for knee osteoarthritis: an updated meta-analysis of trials with low risk of bias. RMD Open. 2015;1(1):e000071.
61. Campbell KA, Erickson BJ, Saltzman BM, Mascarenhas R, Bach Jr BR, Cole BJ, et al. Is Local Viscosupplementation Injection Clinically Superior to Other Therapies in the Treatment of Osteoarthritis of the Knee: A Systematic Review of Overlapping Meta-analyses. Arthroscopy. 2015;31(10):2036-45.e14.
62. Henrotin Y, Chevalier X, Deberg M, Balblanc JC, Richette P, Mulleman D, et al. Early decrease of serum biomarkers of type II collagen degradation (Coll2-1) and joint inflammation (Coll2-1 NO(2)) by hyaluronic acid intra-articular injections in patients with knee osteoarthritis: a research study part of the Biovisco study. J Orthop Res. 2013;31(6): 901-7.
63. Piuzzi NS, Midura RJ, Muschler GF, Hascall VC. Intra-articular hyaluronan injections for the treatment of osteoarthritis: perspective for the mechanism of action. Ther Adv Musculoskelet Dis. 2018;10(2):55-7.
64. Khanasuk Y, Dechmaneenin T, Tanavalee A. Prospective randomized trial comparing the efficacy of single 6-ml injection of hylan G-F 20 and hyaluronic acid for primary knee arthritis: a preliminary study. J Med Assoc Thai. 2012;95(Suppl 10):S92-7.
65. Vincent HK, Montero C, Conrad BP, Horodyski M, Connelly J, Martenson M, et al. "Functional pain," functional outcomes, and quality of life after hyaluronic acid intra-articular injection for knee osteoarthritis. PM R. 2013;5(4):310-8.
66. Rat AC, Baumann C, Guillemin F. National, multicentre, prospective study of quality of life in patients with osteoarthritis of the knee treated with hylane G-F 20. Clin Rheumatol. 2011;30(10):1285-93.