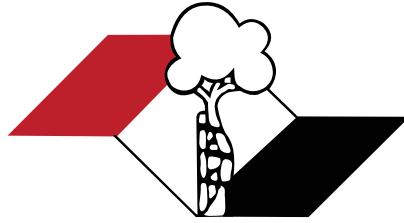


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









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





































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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.)

Level	Types of study			
	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 ^e 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 ^g	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 inconsistent 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 ^e comparative study ^g		Systematic review ^b of Level III studies	Systematic review ^b of Level III studies
	Systematic review ^b of Level III studies		Case-control study	
IV			Poor reference standard	
	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.

EDITORIAL*Olavo Pires de Camargo*DOI: <http://dx.doi.org/10.1590/1413-785220243204e050924p>**ORIGINAL ARTICLE****GENERAL**

IN-HOSPITAL MORTALITY OF OLDER ADULT PATIENT WITH PROXIMAL FEMORAL FRACTURE TREATED SURGICALLY DURING THE COVID-19 PANDEMIC**MORTALIDADE INTRA-HOSPITALAR DE PACIENTE IDOSO COM FRATURA DO FÊMUR PROXIMAL TRATADOS CIRURGICAMENTE DURANTE A PANDEMIA DE COVID-19***Giuseppe Orsi Salazar, Guilherme Grisi Mouraria, Maurício Etchebehere, Rodrigo Gonçalves Pagnano*DOI: <http://dx.doi.org/10.1590/1413-785220243204e278635>**ONE STAGE BILATERAL TOTAL HIP REPLACEMENT****ARTROPLASTIA TOTAL DO QUADRIL BILATERAL EM TEMPO ÚNICO***Fabio Stucchi Devito, Fabio Stucchi Devito Filho, Eduardo Dias Devito, Cristiane Bonvicine*DOI: <http://dx.doi.org/10.1590/1413-785220243204e278347>**KNEE**

CAN SENSORY DISTURBANCES DUE TO INJURY TO THE INFRAPATELLAR BRANCH OF THE SAPHENOUS NERVE BE PREVENTED BY AN OBLIQUE INCISION?**DISTÚRBIOS SENSITIVOS POR LESÃO DO RAMO INFRAPATELAR DO NERVO SAFENO PODEM SER EVITADOS POR UMA INCISÃO OBLÍQUA?***Julio Cesar Gali, Rodrigo de Souza Holtz, Marcello Scimini Lepispico, Enzo Barrio, João Otavio Pereira Le Senechal, Julio Cesar Gali Filho*DOI: <http://dx.doi.org/10.1590/1413-785220243204e277962>**ORTHOPEDIC TRAUMA**

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DOI: <http://dx.doi.org/10.1590/1413-785220243204e278265>

ACTA ORTOPÉDICA BRASILEIRA

15 ANOS DE JCR - JOURNAL CITATION REPORTS

OLAVO PIRES DE CAMARGO¹ 

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Abraço a todos,

Prof. Olavo Pires de Camargo
Editor Chefe

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IN-HOSPITAL MORTALITY OF OLDER ADULT PATIENT WITH PROXIMAL FEMORAL FRACTURE TREATED SURGICALLY DURING THE COVID-19 PANDEMIC

MORTALIDADE INTRA-HOSPITALAR DE PACIENTE IDOSO COM FRATURA DO FÊMUR PROXIMAL TRATADOS CIRURGICAMENTE DURANTE A PANDEMIA DE COVID-19

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ABSTRACT

Objectives: Evaluate the prevalence of hospital mortality in older adult patients with femoral fracture undergoing surgical treatment during the COVID-19 pandemic period, and to evaluate whether COVID-19 infection, clinical, and orthopedic factors interfered with mortality. **Material and Methods:** A retrospective study was conducted by reviewing medical records. Patients over 60 years of age with proximal femoral fracture undergoing surgical treatment were included. Overall mortality was calculated, as well as mortality whose primary or secondary cause was COVID-19 infection, to determine if infection influenced patient mortality. Clinical and orthopedic factors that interfered with mortality were evaluated. Categorical variables were compared using the Chi-square test or Fisher's exact test. Both unpaired t-test (parametric variables) and Mann-Whitney test (non-parametric variables) were used. The Kaplan-Meier mortality curve was constructed. **Conclusion:** The mortality of older adult patients with femoral fracture undergoing surgical treatment during the COVID-19 pandemic was 4.2%. Male sex, older age, and those who underwent blood transfusion had higher mortality rates. COVID-infected patients had ten times more chance of death and died twice as fast as the non-infected population. **Level of Evidence II, Retrospective Study.**

Keywords: Hospital mortality. Proximal Femoral Fractures. COVID-19 Serological Testing. Orthopedic Procedures.

RESUMO

Objetivos: Avaliar a mortalidade hospitalar de pacientes idosos com fratura de fêmur submetidos ao tratamento cirúrgico durante o período pandêmico de covid-19. Avaliar se a infecção pelo vírus do covid-19 e os fatores clínicos e ortopédicos interferiram na mortalidade. **Material e Métodos:** Realizou-se um estudo retrospectivo por levantamento de prontuários. Foram incluídos pacientes acima de 60 anos associados a fratura da extremidade proximal do fêmur e que submetidos a tratamento cirúrgico. Calculou-se a mortalidade geral e também aquela cuja causa principal ou secundária foi a infecção pelo covid-19 para determinar se essa influenciou na mortalidade dos pacientes. Foram avaliados se os fatores clínicos e ortopédicos interferiram na mortalidade e variáveis categóricas foram comparadas pelo teste de Qui-quadrado ou exato de Fisher, utilizando tanto o teste t não pareado (variáveis paramétricas) como o teste de Teste Mann-Whitney (variáveis não paramétricas). Por fim, construiu-se a curva de mortalidade de Kaplan-Meier. **Conclusão:** A taxa de mortalidade de pacientes idosos com fratura de fêmur submetidos ao tratamento cirúrgico durante a pandemia de Covid foi de 4,2%. Pacientes do sexo masculino, idosos e os que foram submetidos à transfusão sanguínea evoluíram com maior mortalidade. Pacientes infectados pelo Covid tiveram dez vezes mais chance de evoluir para óbito e de forma duas vezes mais rápida que a população não infectada. **Nível de Evidência II, Estudo Retrospectivo.**

Descritores: Mortalidade Hospitalar. Fraturas Proximais do Fêmur. Teste Sorológico para COVID-19. Procedimentos Ortopédicos.

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The study was conducted at Hospital Estadual de Sumaré – Dr. Leandro Franceschini, Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brazil. Correspondence: Giuseppe Orsi Salazar. Rua Vital Brasil, 80. Cidade Universitária Zeferino Vaz. Campinas, SP, Brazil, 13083888.

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INTRODUCTION

With the aging of the population, older adult's health has become a growing concern, especially when linked to mortality associated with proximal femoral fractures and when combined with infectious diseases such as COVID-19.¹⁻⁴ Such conditions hinder clinical management and worsen the prognosis of patients.^{3,5,6} In particular, the COVID-19 pandemic has caused significant disruption to health systems worldwide, particularly affecting vulnerable populations such as the older adults.^{3,6,7}

In this context, this study seeks to better understand the relation between mortality and the coexistence of proximal femoral fracture and COVID-19 infection in older adult patients during hospitalization. Although numerous studies have shown increased mortality in patients with femoral fractures and co-infection with COVID-19, there are few Brazilian studies that have evaluated the mortality of this cohort of patients. In addition, the studies focused their evaluations on the first years of the pandemic.⁸

Therefore, this study's primary objective was to evaluate the prevalence of in-hospital mortality of older adult patients with femoral fractures undergoing surgical treatment during the COVID-19 pandemic. The secondary objective was to evaluate whether infection by the COVID-19 virus, clinical, and orthopedic factors (fracture location, type of surgical treatment employed, change in hemoglobin value) interfered with mortality.

MATERIAL AND METHODS

A retrospective study was carried out based on medical records at a trauma referral hospital from January 2020 to December 2022. Inclusion criteria were patients over 60 years of age who had fractures on the proximal extremity of the femur, who underwent surgical treatment, and who had all the clinical data as well as the death record or hospital discharge.

The exclusion criteria were patients who did not have all the clinical and orthopedic data in the medical records and patients who died before undergoing surgical treatment.

Demographic data, comorbidities (Hypertension, Diabetes, Hypothyroidism, Chronic Kidney Disease, Alzheimer's, Depression, previous heart attack or previous stroke), preoperative hemoglobin value, and need for blood transfusion during hospitalization were evaluated.

Orthopedic factors evaluated were: the anatomical location of the femoral fracture (femoral neck, transtrochanteric, and subtrochanteric); types of surgical treatment used (osteosynthesis with nails, dynamic hip screw-plates, and cephalomedullary nails); variation of the pre- and postoperative hemoglobin value and, finally, the time between hospitalization and surgery.

Confirmation of COVID-19 infection was obtained by reverse transcription PCR (RT-PCR). The examination was routinely performed at the hospital during the pandemic and, therefore, symptomatic and non-symptomatic cases were diagnosed.

Overall mortality was calculated, as well as mortality in which the main or secondary cause was COVID-19 infection, to determine whether the infection influenced patient mortality. In addition, it was evaluated whether clinical and orthopedic factors interfered with patient mortality.

Categorical variables were tested by Fisher's exact or Chi-square test, and the non-categorical variables by the Kolmogorov-Smirnov test.

Thus, to study these variables, both the unpaired t-test (parametric variables) and the Mann-Whitney test (non-parametric variables) were used.

The Kaplan-Meier mortality curve was designed. A significance level of $p < 0.05$ was considered. SPSS statistics program was used.

The study was approved by the Research Ethics Committee of UNICAMP under the CAAE No. 34076720.2.0000.5404.

RESULTS

During the three years of research, 695 patients underwent surgical treatment to correct femoral fractures. However, 469 met all the inclusion criteria. There was a higher prevalence of women (64.4%). The mean age was 78.93 ± 9.1 years. The most frequent comorbidity was hypertension and type II diabetes mellitus.

The most prevalent fracture was the transtrochanteric and the most used synthesis material was the short cephalomedullary nail. Demographic data of the sample are described in Table 1.

The mean time between hospitalization and surgery was 3.03 ± 2.2 days. During the COVID-19 pandemic, seven patients were diagnosed with the disease by RT-PCR test, four of whom had respiratory complaints (symptomatic).

The overall mortality rate during hospitalization was 4.2% (20 patients). Infection with the virus influenced mortality. Infected patients were ten times more likely to die than uninfected patients (Table 2).

Male patients were twice as likely to die as female patients. In addition, older adult patients who underwent surgical treatment and died were, on average, seven years older than those who were discharged from the hospital. The presence of comorbidities (Table 1) did not influence the mortality of patients, except for those who needed to receive blood transfusions (Table 2).

The location of fracture, type of surgery (osteosynthesis or arthroplasty), difference in postoperative hemoglobin value, and the waiting time until the procedure did not influence mortality (Table 3).

Most progressions to death occurred in the first twenty days of hospitalization (Figure 1). Infection by COVID-19 determined a time acceleration for evolution to death (Figure 2).

Table 1. Demographic variables.

Variable	Values
Age (mean + sd)	78.9 + 9.1
Sex [(N° (%))]	
Male	167 (35.6%)
Female	302 (64.4%)
Location of femoral fracture[N (%)]	
Transtrochanteric	259 (55.2%)
Neck	147 (31.3%)
Subtrochanteric	57 (12.1%)
Material Used in Surgery	
Short cephalodiaphyseal nail	242 (51.5%)
Dynamic hip screw-plates	23 (4.9%)
Long cephalodiaphyseal nail	57 (12.1%)
Bipolar arthroplasty	147 (31.5%)
Comorbidities [N° (%)]	
Hypertension	287 (61.1%)
Diabetes	136 (28.9%)
Hypothyroidism	52 (11%)
Chronic Kidney Disease	45 (9.5%)
Alzheimer's disease	80 (17%)
Depression	45 (9.5%)
Previous heart attack	32 (6.8%)
Previous stroke	77 (16.4%)

Table 2. Influence of clinical variables on mortality.

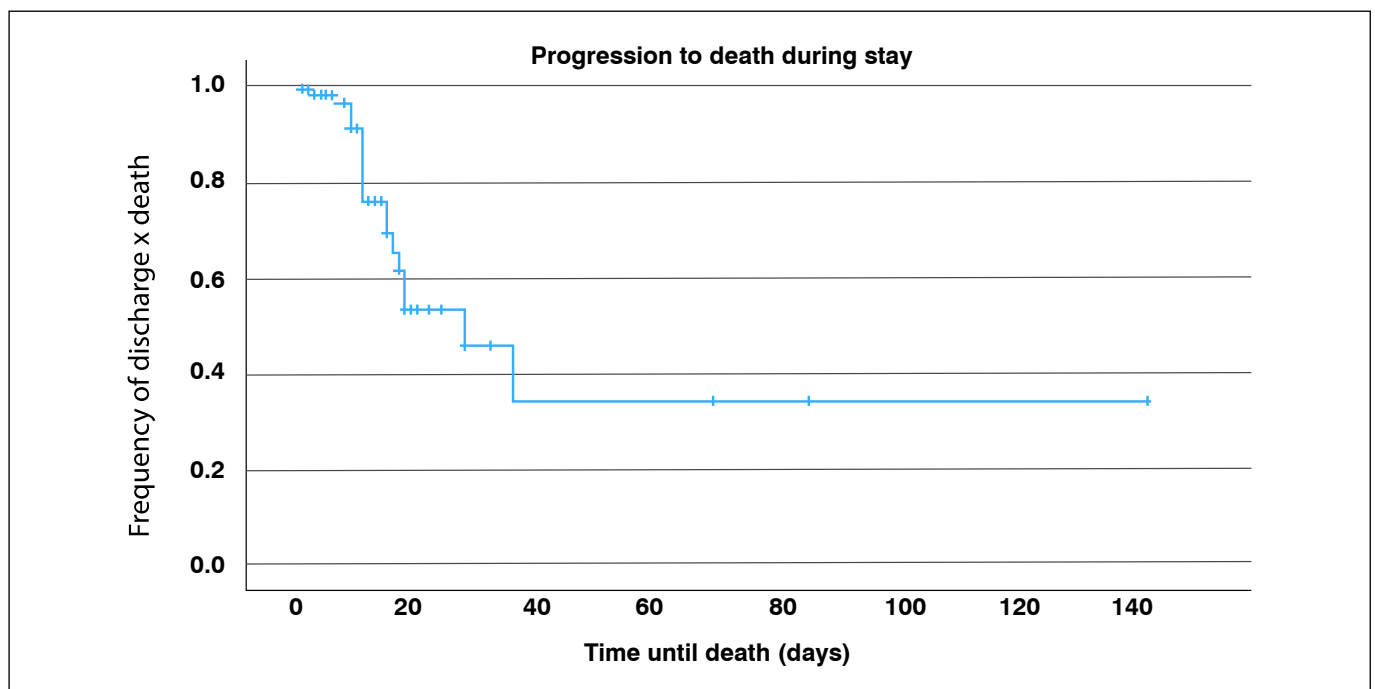
Variable	Death (n)	Hospital Discharge (n)	P value	RR*	CI
COVID-19 infection (n)					
Yes (7)	2	5	0.03 ^(a)	0.11	0.23 - 0.53
No (462)	18	444		1.09	0.94 - 1.27
Blood Transfusion (n)					
Yes (78)	9	69	< 0.01 ^(b)	0.34	0.20 - 0.58
No (391)	11	380		1.53	1.03 - 2.29
Age (mean + sd)	85.6 + 6.7	78.6 + 9.1	0.05 ^(c)	-	-
Sex (n)					
Female (315)	9	306	0.04 ^(b)	1.51	0.92 - 2.46
Male (154)	11	143		0.57	0.38 - 0.88

a = Fisher's exact test; * RR (Relative Risk Discharge/Death); b = Chi-squared; C = t-test

Table 3. Influence of orthopedic variables on mortality.

Variable	Death (n)	Hospital Discharge (n)	P value	RR*	CI
Type of Surgery (n)					
Osteosynthesis (322)	12	310	0.46 ^(a)	-	-
Arthroplasty (147)	8	139		-	-
Location of femoral fracture (n)					
Transtrochanteric (261)	9	252	0.36 ^(a)	-	-
Neck (149)	9	140	0.43 ^(a)	-	-
Subtrochanteric (59)	2	57	0.81 ^(b)		
Hemoglobin drop (Median/min-max)	0.1 (0-5)	0.1 (0-3)	0.15 ^(c)	-	-
Time until surgery (Mean + sd)	3.25±2.6	3.02±2.2	0.61 ^(d)	-	-

a = Chi-square test; * RR (Relative Risk Discharge/Death); b = Fisher's exact test; c = Mann-Whitney test; d = T-test.

**Figure 1.** Kaplan Meier curve of in-hospital mortality of patients with femoral fractures.

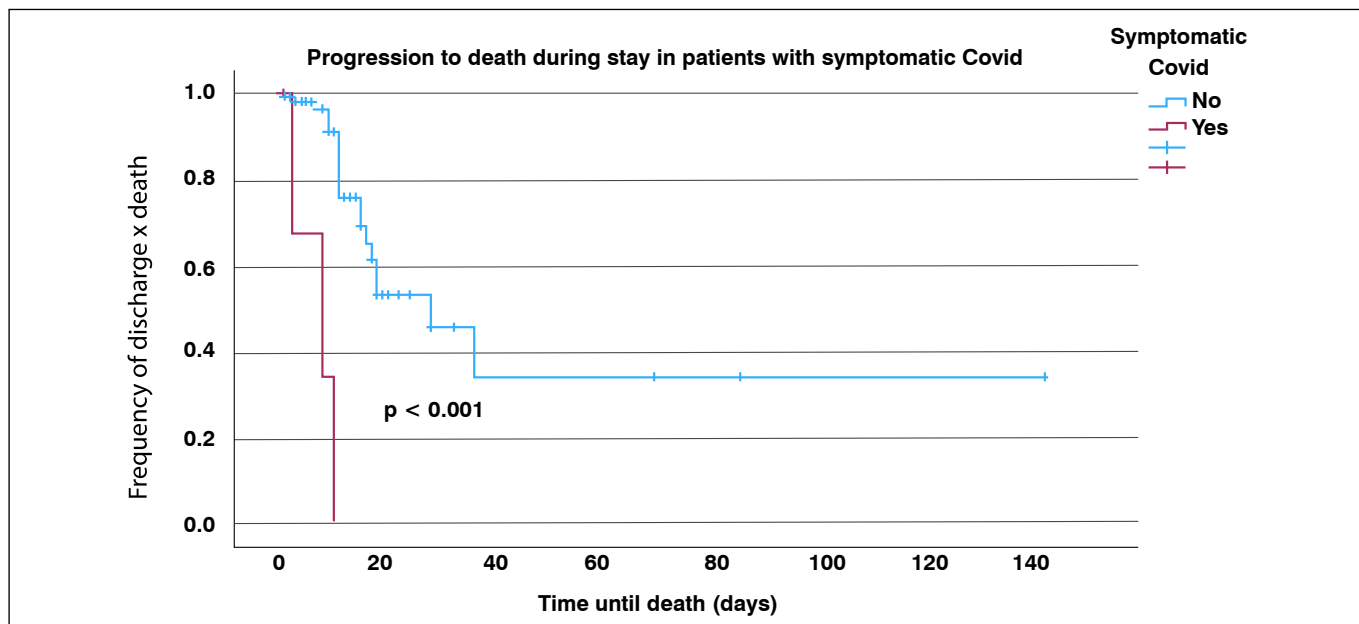


Figure 2. Kaplan Meier curve of in-hospital mortality of patients with femoral fracture associated or not with COVID-19 infection.

DISCUSSION

In this retrospective observational study, the mortality of older adult patients with proximal femoral fractures and the clinic and orthopedic factors that could influence such mortality were evaluated.

Older adult patients are known to be a vulnerable population and have numerous comorbidities.¹ Thus, during hospitalization for surgical treatment of the fracture, the presence of associated comorbidities is very frequent.⁴ Our results also show this association, since at least 61% of the population had at least one comorbidity (hypertension). The patients had a mean age of 78 years, with a higher prevalence among women. The result is similar to the international and national literature, which report greater prevalence in female patients,^{1,3,4} with an average age of 79 years.^{4,9} Several studies show that the risk of mortality from COVID-19 increases with age.⁸⁻¹⁰ However, they reported a decrease in the incidence of fracture cases at the beginning of the pandemic, suggesting that there was a reduction in the demand for health services^{11,12} due to the fear of contamination and the possibility of late sequelae related to COVID-19 infection.¹³ In our results, we observed a higher mortality among patients who underwent blood transfusion. Transfused patients were three times more likely to die than those who did not receive transfusion. However, patients who died had a similar decrease in hemoglobin values to those who were discharged from the hospital. The results restate the hypothesis that the higher mortality among transfused patients reflects a worse preoperative clinical condition than those that did not receive blood transfusion and is not related to the bleeding caused by the surgical procedure. In this context, we also observed that the type of surgery (arthroplasty or osteosynthesis) did not influence mortality.^{3,12,14,15}

The prevalence of confirmed cases of COVID-19 in our study was 7 patients, which corresponded to approximately 1.5% of the total number of patients with femoral fractures during the period. Infection with the COVID-19 virus was devastating in this population cohort, as it increased the risk of death by 10 times. Meta-analysis with 23 studies^{6,14} determined that the prevalence of COVID-19 was 13%, with a mortality rate of 35%, which corresponds to 7 times higher than those who did not have the associated infection.^{1,12,16} Thus, although the prevalence of older adults with virus infection was lower in our study when compared to the literature, there was a

high mortality rate, which may be related to worse general clinical condition of patients or a greater aggressiveness of the virus.

The highest mortality of patients occurred in the first 20 days of hospitalization, while, in those infected by COVID-19, it occurred earlier (mainly in the initial 10 days of hospitalization (Figures 1 and 2). Meta-analysis with 20 studies comparing mortality between positive and negative COVID-19 patients, observed an increase in mortality rates¹⁷ with a mean time to death of 30 days.¹² In addition, some studies point to a high rate of complications during hospitalization, such as sepsis, fluid and electrolyte imbalance.¹⁸

The mean waiting time until the surgical procedure was 3 days and did not influence patient mortality. Despite the literature pointing to an increase in waiting time for the procedure during the pandemic^{2,5,18-20}, such increase did not occur in our survey, probably because patients with fractures were prioritized over those who were hospitalized for surgical treatment of elective pathologies. The study has some limitations, mainly related to the diagnosis of COVID-19 at the beginning of the pandemic, when diagnostic tests were still being implemented. Therefore, there is a possibility that some cases have not been diagnosed. Another important limitation is also related to a possible underreporting to the medical team of patients' pre-existing comorbidities.

The study also presents some relevant aspects as it is the first national study that analyzed the mortality of patients with femoral fractures in older adult patients during the entire period of the COVID-19 pandemic and analyzed the influence of this infection on mortality. In addition, the study was conducted in a center specialized in the treatment of orthopedic trauma and that became a reference center for this disease as well during the pandemic.

CONCLUSION

The mortality of older adult patients with femoral fractures undergoing surgical treatment during the COVID-19 pandemic was 4.2%. Older male patients who underwent blood transfusion had higher mortality. Patients infected with COVID-19 were ten times more likely to die than those who were not infected. Therefore, the virus brought great morbidity to this cohort of patients, who died twice as quickly as the uninfected population.





AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. O.G.: Writing and data collection; M.G.G.: Intellectual concept of the article, data analysis, writing; E.M.: Article review; P.R.G.: Intellectual concept of the article, data analysis, article review.

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ONE STAGE BILATERAL TOTAL HIP REPLACEMENT

ARTROPLASTIA TOTAL DO QUADRIL BILATERAL EM TEMPO ÚNICO

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ABSTRACT

Introduction: One-stage bilateral total hip replacement has gained popularity due to its advantages, which include its lower cost, anesthetic time, hospitalization, and recovery. **Objective:** to show the clinical result of one-stage bilateral total hip replacement. **Methodology:** A case series of patients who underwent one-stage bilateral total hip arthroplasty. The medical records of 100 patients were evaluated from 2001 to 2022. The posterolateral route was chosen for the procedures. Of the 100 replaced prostheses, 85% were hybrid and 15 were cemented. Procedures averaged 180 minutes in length. **Results:** The average length of stay totaled three days. No deaths occurred in the 100 evaluated patients. Complications showed 1% rate of venous and pulmonary thromboembolism, one case of late dislocation (after three months. It was twice reduced and later revised), five cases of hematoma (5%. They were drained on the third postoperative day. Moreover, two occurred in both hips). **Conclusion:** One-stage bilateral total hip replacement has advantages but it must be performed on carefully selected patients and by a qualified team. **Evidence level IV, Case reports.**

Keywords: Total Hip Arthroplasty. Surgery. Hip.

RESUMO

Introdução: O método que realiza a prótese total de quadril bilateral em um único tempo operatório (ATQB) tem ganhado popularidade por suas vantagens. **Destacam-se** menor custo, tempo anestésico reduzido, e menor período de internação e recuperação. **Objetivo:** Demonstrar o resultado clínico da ATQB em um único tempo. **Metodologia:** Estudo retrospectivo pacientes submetidos a Artroplastia total de quadril bilateral em um único tempo. Foram avaliados prontuários de 100 pacientes, durante o período de 2001 a 2022. A via escolhida foi a póstero-lateral. Das 100 próteses realizadas, 85% foram híbridas e 15 cimentadas. O tempo cirúrgico teve, em média, 180 minutos. **Resultados:** O tempo médio de internação foi de 3 dias. Não houve mortes entre os 100 pacientes avaliados; quanto às complicações, a taxa de tromboembolismo venoso e pulmonar foi de 1%, e foi relatado 1 caso de luxação tardia (após 3 meses), reduzida duas vezes e com posterior revisão. Houve cinco casos de hematoma, totalizando 5%; os mesmos foram drenados no 3º dia pós-operatório; desses, 2 aconteceram bilateralmente e 1 unilateralmente. **Conclusão:** A ATQB em um único e cirúrgico tempo apresenta vantagens, mas deve ser realizada em pacientes cuidadosamente selecionados e por uma equipe capacitada. **Nível de evidência IV, Série de casos.**

Descritores: Artroplastia Total De Quadril. Cirurgia. Quadril.

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INTRODUCTION

Total hip replacement (THR) is a surgical procedure that is widely used around the world to treat conditions such as osteoarthritis and other hip joint diseases.¹ Recent years have seen a significant increase in patients requiring bilateral hip replacement, forcing surgeons to make a crucial decision: one- or two-stage surgery. The method for bilateral total hip prosthesis involving a one-stage operative time (known as step 1) has gained popularity for its

advantages, including its lower cost,^{2,3} anesthetic time, hospital stay⁴, and rehabilitation, in addition to better limb length control.³ Bilateral single-stage prosthesis was first described by Charnley in 1971, showing excellent results since then.¹ However, several factors influence the choice between one- or two-stage surgery, including patients' age and health and surgeons' experience.³ This study aims to show the clinical outcomes of one-stage bilateral THR.

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

The study was conducted at Hospital de Base – Faculdade de Medicina de São José do Rio Preto; Austa Hospital; Hospital Padre Albino, São José do Rio Preto, SP, Brazil. Correspondence: Fabio Stuchi Devito. Torre Madri Norte – Av. Benedito Rodrigues Lisboa, 2675, Sala 501 – Jardim Bosque das Vivendas, São José do Rio Preto, SP, Brazil, 15080310. fabiosdevito@gmail.com

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MATERIALS AND METHODS

This is a retrospective observational study in which patients underwent one-stage bilateral total hip arthroplasty in the service. Medical records of 100 people were evaluated from 2001 to 2022. The ages of the 21 women and 79 men ranged from 17 to 76 years. The American Society of Anesthesiologists (ASA) physical status classification categorized patients into ASA 1 or 2.

Regarding the used route, all cases involved the posterolateral Kocher-Langenbeck route to the acetabulum.

Of the 100 prostheses performed, 85% were hybrid (non-cemented acetabular and cemented femoral components) and 15 were cemented (acetabulum and femur).

Surgeries lasted from 120 to 240 minutes, averaging 180 minutes. One gram of tranexamic acid was intraoperatively used to reduce blood loss in 78 cases, and blood transfusion ranged from zero to two bags of packed red blood cells, averaging one transfused bag. All patients needed a pneumatic pump foot for their lower limbs during hospitalization to prevent deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE).

All patients started walking on the first postoperative day, assisted by physical therapy and a gait aid. They also performed isometric and metabolic active exercises.

All cases included a suction drain that was removed 24 hours after the procedure.

Table 1. Casuistry table.

Age	17 to 76 years
Female	21
Male	79
Hybrid prosthesis	85
Cemented prostheses	15
Surgical time	120 to 240 minutes
Length of hospital stay	From 2 to 5 days

RESULTS

Mean hospital stay totaled three days, ranging from two to five days. Of the 100 evaluated patients, mortality rate totaled 0%.

Regarding thromboembolic events, the rate of DVT and PTE totaled 0.1%.

No patient showed acute dislocation, but one evinced late dislocation (after three months), which was reduced twice and necessitated later revision.

This study included five cases of hematoma (two bilateral and three unilateral ones, 5%) that were drained on the third postoperative day.

Table 2. Results

		Rate	
Mortality rate	0 cases	0%	
DVT	1 case	1%	
PTE	1 case	1%	
Acute dislocation	0 cases	0%	
Delayed Dislocation	1 case	1%	Two reductions and subsequent revision
Hematoma	5 cases	5%	Drained on the third post-op day; two bilaterally and three unilaterally drained.

DISCUSSION

Bilateral total hip replacement surgery performed simultaneously under the same anesthesia (step 1) offer excellent results, with advantages such as lower cost,^{2,3} anesthetic time, hospital stay,⁴ and rehabilitation and better control of limb length.³

This study performed Doppler ultrasound of the lower limbs and pulmonary computed tomography in patients with symptoms, finding only one case of PTE (1%). This data is similar to that in the literature, as in the 2018 study by Charity et al., which reported only two cases of PTE in 319 prostheses (0.62%). Jaffe and Charnley, in a series of 50 cases of bilateral THR in 1 step, showed two cases of pulmonary complications (4%).³

The literature shows no statistical differences in pulmonary complications between one- and two-stage bilateral THR.^{5,6,7,8} However, this technique requires care and adequate selection of patients, especially those with lung problems and lower right ventricular reserve.⁹

Regarding acute dislocation, we found no cases. As reported, only one patient had late dislocation, possibly because, when the bilateral hip prosthesis is performed in a one stage, anatomical reconstruction, gluteus medius strength, and the positioning of the prosthesis components are easier to replicate on the other side to be immediately operated. Tsiridis et al, in 2008, reported no statistical difference on the risk of acute dislocation between one- and two-stage THR.⁵ Huang et al, in 2019, in the series of 16,758 bilateral THR, reinforce the absence of statistical differences in hip dislocation,⁷ finding lower rates in other one-stage studies.¹⁰

This study found no mortality. In 2018, Charity et al. reported a 0.3% six-month mortality rate. English registries show an incidence of 0.29% in unilateral THR, evincing the similarity between step 1 and 2 incidences.

Huang et al reinforces the absence of significant differences in mortality and cardiovascular and/or infection problems.⁷

This study found no acute and/or sub-acute infection. The five patients with hematoma underwent drainage on the third postoperative day, collecting the hematoma culture and sending it to a laboratory for analysis (which tested negative for infection). In our view, a more invasive measure in the immediate postoperative period, with drainage and surgical cleaning, helps to prevent infections. In these cases that required drainage, we resumed broad-spectrum antibiotic therapy until the results of the cultures were obtained.

Micicoi et al, in 2004-2018, reported a revision rate of 2.3% for bilateral total hip replacements in a single procedure, compared to 4.1% for unilateral prostheses. Ramezani et al., on the other hand, found no significant difference between the two groups.¹⁰

The literature reinforces the data in our series: low revision rates and even lower than in two-stage periods. This suggests that the choice between step 1 and step 2 may depend on the proper selection of patients and surgeons' experience.

Partridge et al., in 2019, report the need for adequate team experience, the procedure taking place in large centers, and patient being adequately selected (involving age and comorbidity assessments).¹¹ In our view, the choice of the patient, the training of the team, the short surgical time (180 minutes for both sides), usual access route, and a surgeon used to the procedure contribute to the good result of this type of procedure. Also, the reproducibility of the previous surgery on the following side is much better, as is the adequacy of the offset to the length of the limbs.

The techniques and protocols physical therapy use to treat single-stage total hip arthroplasty vary (as in two-stage total hip

arthroplasty) but have the advantage of shorter rehabilitation time. They have important clinical efficacy proven in the literature. Patients' results after single-stage THR, such as better functionality, muscle strength, and range of motion, corroborate the results in the literature. In general, active exercises for the hip periarticular muscles provided an important functional prognosis.^{12,13,14}

CONCLUSION

Bilateral total hip arthroplasty should be performed in a single surgical procedure for carefully selected ASA 1 or 2 patients and by a trained surgical team. Our series chose the posterolateral access, but surgeons may choose other routes, depending on their preference. Rehabilitation is similar to two-stage surgery, with the advantage of a shorter recovery time.

AUTHORS' CONTRIBUTION: Each author contributed individually and significantly to the development of this article. FSD: surgeries; FSDF: drafting; EDD: data analysis; CB: article review.

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CAN SENSORY DISTURBANCES DUE TO INJURY TO THE INFRAPATELLAR BRANCH OF THE SAPHENOUS NERVE BE PREVENTED BY AN OBLIQUE INCISION?

DISTÚRBIOS SENSITIVOS POR LESÃO DO RAMO INFRAPATELAR DO NERVO SAFENO PODEM SER EVITADOS POR UMA INCISÃO OBLÍQUA?

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ABSTRACT

Objective: To evaluate the incidence of injuries to the infrapatellar branch of the saphenous nerve (IPBSN) after anterior cruciate ligament reconstruction (ACLR) with an oblique incision for hamstring graft harvesting. **Methods:** In total, 59 knees (from 57 patients) were evaluated in the follow-up of ACLR for six months. We drew a horizontal line parallel to the ground, passing through the most medial portion of the surgical incision and another, perpendicular to the first, starting at the tibial tuberosity (TT). We measured the length and angle of the cut, the distances from its most medial point to the perpendicular line, and from the TT to the horizontal line. Skin sensitivity was tested with a brush and the altered sensitivity area was measured. Patients were asked about difficulties in activities daily of living (ADL). **Results:** A total of 27 knees (45.7%) had sensory disorders, which persisted until the sixth postoperative month in 92.6% of them. The ADL were compromised in one knee (3.7%). No significant differences were found between the groups with and without changes in sensitivity regarding age, affected side, incision angle, or measured distances. The incision size was larger in the group without alteration in sensitivity. **Conclusions:** An oblique incision did not avoid IPBSN injuries. This condition rarely compromised the ADL. **Level of Evidence II, Lesser Quality Prospective Study.**

Keywords: Anterior Cruciate Ligament Reconstruction. Nervous tissue injuries. Hamstring Muscle Tendons.

RESUMO

Objetivo: Avaliar a incidência de lesões do ramo infrapatelar do nervo safeno (RIPNS) na reconstrução do ligamento cruzado anterior (RLCA), com incisão oblíqua para a coleta do enxerto dos isquiotibiais. **Métodos:** 59 joelhos (57 pacientes) foram avaliados no pós-operatório da RLCA, por seis meses. Traçamos uma linha horizontal paralela ao solo, passando pela porção mais medial da incisão cirúrgica, e outra perpendicular à esta, iniciando na tuberosidade tibial (TT). Medimos o comprimento e a angulação do corte, as distâncias do ponto mais medial do corte à linha perpendicular e outra, da TT, à linha horizontal. A sensibilidade da pele foi testada com um pincel, e a área alterada foi mensurada. Os pacientes foram questionados sobre as dificuldades nas atividades diárias da vida (ADV). **Resultados:** 27 joelhos (45,7%) apresentaram distúrbios sensitivos, persistentes até o sexto mês pós-operatório em 92,6% deles. As ADV foram comprometidas em um joelho (3,7%). Não houve diferença significativa entre os grupos com e sem alterações da sensibilidade, relativamente à idade, ao lado comprometido, ao ângulo da incisão ou às distâncias medidas. O tamanho da incisão foi maior no grupo sem alteração de sensibilidade. **Conclusões:** Uma incisão oblíqua não evitou lesões no RIPNS. Essa condição raramente comprometeu as ADV. **Nível de Evidência II, Estudo Prospectivo de Menor Qualidade.**

Descritores: Reconstrução do ligamento cruzado anterior. Tecido nervoso lesões. Tendões dos Músculos Isquiotibiais.

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INTRODUCTION

The incidence and prevalence of anterior cruciate ligament (ACL) reconstruction (ACLR) has increased significantly in recent years,

especially in women.^{1,2} Still, primary ACLR are more common in men under 30 years of age, and soccer is the sport most often linked to the rupture of this ligament.³ A survey by the ACL Study

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The study was conducted at Faculdade de Ciências Médicas e da Saúde de Sorocaba da PUC-SP, Sorocaba, SP, Brazil.

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Group showed the evolution of the graft choice for ACLR over the last three decades.⁴ In 1992, the bone-patellar tendon-bone graft was chosen for primary ACLR by about 90% of the surgeons surveyed. However, the preference for hamstring tendon grafts increased during the study period and, in 2020, flexor tendon grafts were reportedly preferred by more than 50% of those surveyed. Bertram et al.⁽⁵⁾ were the first to describe a case of infrapatellar branch of the saphenous nerve (IPBSN) neuralgia due to entrapment of the nerve branch by scar tissue. Due to its anatomical location, there is a potential risk of injury to the IPBSN during the removal of the flexor tendons for ACLR. Anatomically, the IPBSN shows an average tilt angle of $17.5^\circ \pm 6.1^\circ$ ⁶ and, theoretically, an oblique incision would exhibit a lower risk of injuring this nerve branch than a vertical incision. In another anatomical study, Wisbech Vange et al.⁷ showed that a diagonal incision can reduce risk of lesions in this branch. In fact, several authors have published that the oblique incision holds a lower risk of IPBSN injury.⁸⁻¹⁸

On the other hand, the method of evaluating skin sensitivity related to IPBSN injury is variable; some authors have used the touch of a needle,^{9,11,14,17,18} others, digital pressure measurements,¹⁰ self-reported skin sensitivity,⁸ or questionnaires.¹⁹ We believe it is important to perform skin sensitivity assessments with an atraumatic approach and prospective follow-up. This study aimed to evaluate whether using an oblique incision could prevent IPBSN injury during ACLR with hamstring tendons.

MATERIALS AND METHODS

A total of 59 knees from 57 patients were evaluated in the postoperative period of ACLR with hamstring tendon grafts, collected via oblique incision, for six months. All patients signed an informed consent form to participate in this study, which was approved by the Research Ethics Committee of the institution, under number 33453220.3.0000.5373. Patients with multiple ligament injuries, ACLR revisions, and those who had already undergone any type of previous surgical procedure in the knee region under study, as well as patients with any peripheral neurological abnormality, were excluded from this study. Patients diagnosed with anterior cruciate ligament injury by clinical examination and confirmation by magnetic resonance imaging were included. All patients were operated by the senior occupational surgeon.

In total, 52 patients were male (91.2%) and five (8.7%) were female; the age of patients ranged from 14 to 75 years [mean of 34.4 years and standard deviation (SD) of ± 11.2 years]; and 31 knees (52.5%) were right and 28 (47.4%) were left. Oblique incision was performed to remove hamstring tendons, in parallel to the IPBSN path and with blunt dissection. During this procedure, the knees were flexed and the hips externally rotated to reduce tension on the saphenous nerve.²⁰ This study did not aim to identify the IPBSN. The lateral femoral condyle was visualized through the anteromedial portal (AMP) created with a vertical incision. The femoral tunnels were then made using an accessory anteromedial portal (AAMP), also positioned with a vertical, distal, and medial incision relative to the AMP, with the knee flexed at 90° .

After closing the subcutaneous tissue, a horizontal line was drawn parallel to the ground using a sterile marker pen, passing through the most medial portion of the surgical incision. Another line was drawn perpendicular to this, starting at the tibial tuberosity (TT) and extending distally to meet the horizontal line (Figure 1). An aseptic millimeter ruler was used to measure the length of the incision and the distance from the TT to the horizontal line, termed the craniocaudal distance. Additionally, the distance from the most medial point of the incision to the perpendicular line was measured, referred to as the mediolateral distance. Intraoperative measurements were performed by the surgeon and an assistant,

who agreed on the obtained values. The “Measure Angle” tool, available on Windows, was used to obtain the cut angles from the images taken during surgeries.



Figure 1. Frontal view of a right knee showing the incision and its angle, the mediolateral distance, in green, and the craniocaudal, in red.

Follow-up was performed one, two, three, and six months postoperatively. During consultations, skin sensitivity around the incision was assessed by the same examiner, with a soft monofilament brush. Initially, the brush was applied to the patients' hands, allowing them to recognize the sensory stimulus; then, the skin sensitivity assessment around the incision was conducted with the patients with their eyes closed. Thermal and pain sensitivities were not assessed.

The boundaries of the area with altered sensitivity were marked with a sterile pen on the points of sensitivity change based on reports by the patients at intervals of 1.5 cm, thus creating a sensory map. The areas were photographed, then measured in cm^2 using the Photoshop® software (Adobe Inc., USA). At follow-up, the patients were asked about the presence of discomfort when kneeling, alteration in knee function, and difficulty in performing activities of daily living.

For the statistical analysis, the Mann-Whitney test was applied to compare the groups with and without sensory alteration, in relation to age, angle, and size of the incision, as well as craniocaudal and mediolateral distances. The Fisher's test was used to compare female and male patients, and the Chi-square test was used to compare the presence of alterations observed on the right and left side. In all tests, the index of significance (α) was set at 0.05 or 5%.

RESULTS

The mean size of the incisions was 38.7 mm, ranging from 30.0 to 50.0 mm, and SD was ± 5.20 mm; the mean angle of the cuts was 30 mm (12 to 45 mm; SD ± 6.8 mm), the mean mediolateral distance was 17.6 mm (0.0 to 30.0 mm; SD ± 6.9 mm), and the mean craniocaudal distance was 16.9 mm (0.0 to 40.0 mm; SD ± 9.6 mm). Changes in sensitivity were found in 27 knees, from 27 patients (45.7%); 32 knees did not present different sensory perception (54.2%). The two patients with bilateral ACLR had no changes in sensitivity in either knee. In the comparison between the groups with and without cutaneous dysesthesia, no significant differences were observed in relation to the age of the patients ($p = 0.52$), affected side ($p = 0.3223$), or angle of the incision ($p = 0.18$). The groups also did not differ significantly in relation to craniocaudal distance ($p = 0.4038$). However, when compared in terms of the mediolateral range, the results suggest higher values for the group with no change in sensitivity ($p = 0.0592$), even though they did not reach the significance level (0.05).

The presence of skin sensitivity alteration in females occurred in all cases (100%) and was significantly higher than that observed in males. The size of incision in the group without sensitivity alteration was significantly larger than in the group of patients who presented sensitivity alteration ($p = 0.0430$). However, the mean incision size in women was 36.0 mm, being below the mean of the group with

sensory alterations, which was 38.7 mm. In two knees (7.4%), the paresthesia observed in the first month disappeared in subsequent assessments, in the second and third month of follow-up each. In the other knees, the change in sensitivity persisted in the evaluation six months after surgery. Only one of the knees (3.7%) had functional impairment due to neurological disorder, according to the patient. In our sample, the mean area of diverse perception in the knees with altered sensitivity was 20.7 cm². The incidence of sensory neurological disturbance in the region lateral to the TT occurred in 88.8% of knees. The percentage of alterations in cutaneous perception in the region proximal to the TT was 37.0%, while in the region distal to this bony prominence, it was 62.9%. On the medial side, sensory disturbance occurred in 11.1% of the knees with sensory alteration (Table 1). Table 2 provides further information on age, sex, knee side, size and angulation of incisions, and craniocaudal and mediolateral distances obtained from patients without changes in skin sensitivity. Table 3 shows information on patients with altered sensitivity plus the affected area.

Table 1. Area of tactile sensitivity alteration.

Compromised area	Proximal to TT	Distal to TT
Medial to TT	2 (7.4%)	1 (3.7%)
Lateral to TT	8 (29.6%)	16 (59.2%)

Table 2. Information regarding age, sex, knee side, size and angulation of incisions, and craniocaudal and mediolateral distances obtained from patients without changes in skin sensitivity.

	Age	Side	Sex	Distances (mm)		Incision Size (mm)	Incision Angle (degrees)
				Craniocaudal	Mediolateral		
1	42	R	M	13	20	40	37
2	40	R	M	13	18	45	22
3	24	L	M	30	13	48	32
4	26	R	M	10	24	40	37
5	45	R	M	28	30	40	29
6	34	L	M	15	7	45	30
7	46	R	M	25	25	45	28
8	19	L	M	25	12	36	39
9	34	L	M	0	25	30	34
10	46	R	M	40	20	45	34
11	47	R	M	20	30	40	36
12	17	R	M	6	16	40	35
13	35	R	M	5	20	32	26
14	22	R	M	10	20	45	17
15	32	R	M	5	20	35	19
16	33	L	M	20	25	40	36
17	41	R	M	30	20	35	24
18	35	R	M	5	20	35	36
19	32	L	M	30	15	40	27
20	34	L	M	15	10	50	26
21	42	R	M	20	25	45	25
22	42	L	M	30	10	35	36
23	25	R	M	15	25	40	34
24	23	L	M	10	10	35	35
25	25	R	M	24	25	38	30

26	50	R	M	15	25	45	36
27	38	L	M	15	15	40	28
28	35	L	M	5	30	45	36
29	44	L	M	10	10	40	32
30	14	R	M	5	15	40	31
31	43	R	M	15	20	35	27
32	43	L	M	35	15	45	32
	34.6	R	M	17.0	19.2	40.3	30.8
	9.7	19 (59.3%)	32 (100%)	10.2	6.4	4.8	5.6
	50.0	L	F	40.0	30.0	50.0	39.0
	14.0	13 (40.6%)	0 (0%)	0.0	7.0	30.0	17.0

Table 3. Information regarding age, sex, knee side, size and angulation of incisions, craniocaudal and mediolateral distances, and altered sensitivity area obtained from patients with sensory disorders.

	Age	Side	Sex	Distances (mm)		Incision Size (mm)	Incision Angle (degrees)	Altered Sensitivity Area (cm ²)
				Craniocaudal	Mediolateral			
1	21	L	M	20	7	43	31	4
2	41	R	M	22	13	45	45	3
3	37	L	M	25	0	50	29	48
4	31	L	M	20	17	34	44	12
5	53	L	F	30	4	40	36	42
6	34	R	M	15	25	40	33	2.25
7	14	L	M	30	10	35	42	2
8	40	R	M	11	20	33	35	11.25
9	43	R	M	20	30	30	29	30
10	34	L	M	0	15	35	35	30
11	37	L	M	25	15	40	34	30
12	26	L	F	10	10	35	19	37.5
13	32	L	F	6	16	40	23	33.25
14	46	R	M	20	15	40	23	24
15	24	R	M	5	20	45	26	12.7
16	27	R	F	20	20	30	24	18
17	75	R	M	15	20	30	27	14
18	38	L	M	10	20	45	24	54
19	22	L	M	16	15	35	26	40
20	41	R	M	35	30	40	27	6.25
21	24	L	F	10	10	35	30	7.5
22	23	R	M	20	20	40	27	22.5
23	37	L	M	20	5	40	26	10
24	50	L	M	25	15	35	30	10
25	33	L	M	5	20	35	35	33
26	26	R	M	20	15	35	12	6.25
27	17	R	M	0	15	30	13	16
	34.3	R	M	16.9	15.6	37.6	29.1	20.7
	12.7	12 (44.4%)	22 (81.4%)	9.0	7.1	5.2	8.0	15.1
	75.0	L	F	35.0	30.0	50.0	45.0	54.0
	14.0	15 (55.5%)	5 (18.5%)	0.0	0.0	30.0	12.0	2.0

DISCUSSION

The main finding of our study was that an oblique incision could not prevent changes in skin sensitivity caused by IPBSN lesions. Moreover, sensory disturbances occurred in 45.7% of the knees and persisted in 92.6% of them until the sixth month of follow-up. Despite this, discomfort when kneeling and difficulties in daily activities occurred in only one of the operated knees (3.7%).

Other authors who assessed the use of oblique incision found that the IPBSN lesion occurred within 24% and 61.3% of the cases, with a mean of $37.5 \pm 13.9\%$ among their results.^{8-11,14,17,18,21,22} A possible explanation for this disparity may be the method used to assess sensory disorders.

Luo et al.⁸ asked their patients to demarcate the altered sensitivity area and Mirzatooei et al.²¹ sent a questionnaire with a diagram for the same purpose, both studies presenting very subjective methods. Sabat et al.⁹ and Sharaby et al.¹⁷ used a blunt pin; Sipahioglu et al.¹¹ used a blunt needle; and Leite et al.¹⁰ performed the assessments via digital pressure. These methods were also found to be inaccurate for measuring skin sensory changes. Mousavi et al.¹⁴ and Keyhani et al.¹⁸ used a needle for their assessments, which can be dangerous for disease transmission.

We found few articles that reported complaints of neurologically injured individuals. Sabat et al.⁹ reported that 13.5% of their cases had subjective complaints of sensitivity loss, whereas Mousavi et al.¹⁴ reported that four individuals (5%) complained of pain. On the other hand, Keyhani et al.¹⁸ reported that three patients (6.2%) reported pain at the incision site, without interfering with their activities of daily living.

In our sample, the mean size of the incisions was larger than those of other researchers, whose mean length ranged from 27 to 38 mm, with a mean of 33.2 ± 4.3 mm.^{8-11,14,17,18,21,22} We noticed that larger incisions were associated with normal sensitivity. This result is contrary to what has been published by other authors. Sharaby et al.¹⁷ found no differences between incision size and sensory loss; Mousavi et al.¹⁴ found a correlation between the patients' complaints and incision size; and Pękala et al.¹³, in a systematic review, recommended that the incision should be as small as possible to avoid IPBSN injuries.

Sensory disturbances occurred in all women in our sample, who had a mean incision size of 36.0 mm, below the mean of 38.7 mm in the general population. We found no publications addressing this datum to compare with our results.

When comparing our results on the altered sensitivity area with those published by other authors, we noticed a great disparity. The article by Inderhaug et al.,²³ showed a much larger area (69 cm²), whereas a smaller area was found by Luo et al.⁸ (8.4 cm²). Once again, the probable explanation for the difference was the method used for the sensitivity test. In the study by Inderhaug et al.²⁴, sensory disturbance was assessed using light touch; Luo et al.⁸ requested patients to mark the area; and Sabat et al.⁹ and Sipahioglu et al.¹¹ used a blunt needle. On the other hand, Mousavi et al.,¹⁴ as well as Keyhani et al.¹⁸ employed the needle test. In our sample, the incidence of sensory alteration occurred in the region lateral to the TT in 88.8% of the knees. The descriptions found in the literature are varied; however, as a common denominator, they compromised the region lateral to the TT.^{9-11, 18, 19,21,22}

Sensory alteration in the assessment six months after surgery remained in 92.6% of the knees in our study. This result is very different from what has been published by other authors. Mirzatooei et al.²¹ reported persistence of sensory disturbance in 48.9% of the knees, also in a six-month follow-up. With the same follow-up time, Sabat et al.⁹ and Sipahioglu et al.¹¹ reported that 32.4% and 42.8% of their patients' knees continued to have sensory alterations, respectively. For Joshi et al.²², 11.2% of the knees continued to exhibit sensory changes after 12 months. In a study by Sharaby et al., with a mean follow-up of 23.7 months, they reported sensory changes in only 5.6% of the evaluated knees. On the other hand, Inderhaug et al.,²³ at a minimum follow-up of 10 years, reported that 85% of the patients had symptoms related to ACLR injury. These authors believed that the sensory deficit was likely to be permanent. Table 4 shows the comparisons between size and angulation of the incision, percentage of patients with altered sensitivity, follow-up period, altered sensitivity area, persistence of altered sensitivity area, and main location of dysesthesia according to different authors.

Table 4. Comparisons between size and angulation of the incision, percentage of patients with altered sensitivity, follow-up period, altered sensitivity area, persistence of altered sensitivity area, and main location of dysesthesia according to different authors.

Authors and Year of Publication	Incision Length (mm)	Incision Angle (degrees)	Patients with Sensitivity Alteration (%)	Follow-up Time (months)	Area with Sensitivity Alteration (cm ²)	Persistence of Sensitivity Alteration in Follow-up	Main Location of Dysesthesia
Luo et al. 2007	33	NI	24.14	14	8.4	NI	NI
Mirzatooei et al. 2012	32	45°	48.9	6	NI	48.9%	Anterolateral superior
Sabat et al. 2013	38	50°	32.4	6	18.9	32.4%	Inferior portion of incision
Joshi et al. 2016	30	45°	16.6	12	NI	11.2%	Lateral aspect
Leite et al. 2016	30	45°	26	12	NI	NI	Inferior and superior lateral
Sipahioglu et al. 2017	38	50°	45	6	9.3	42.8%	Lateral to TT
Mousavi et al. 2018	38	45°	61.3	6	11.5	NI	NI
Sharaby et al. 2019	NI	NI	41.9	24	NI	5.6%	NI
Keyhani et al. 2020	27	45°	41.6	9	9.6	NI	Anterolateral proximal

MEAN and SD 33.2 ± 4.3 46.4 ± 2.4 37.5 ± 13.9 10.5 ± 5.9 11.5 ± 4.2 16.6 ± 17.2

As the oblique incision parallel to the IPBSN path for ACLR did not prevent injury in harvesting the hamstring tendons, other factors may have contributed to the occurrence of this condition, such as damage to a secondary branch when performing the AMP and AAMP, as described by Tifford et al.²⁴ and Plancher et al.²⁵ Our findings suggest that we should explore other methods to prevent IPBSN injury. There are some possibilities for this purpose: knowing that the incision should not be performed too medially to the TT, as found in our investigation; identifying the nerve using intraoperative ultrasound²⁶ or during surgery²¹; recognizing the 'sentinel' blood vessel adjacent to the insertion of the flexor tendons as a parameter for tendon localization, thereby allowing limited dissection of the wound²⁷; releasing the sartorius fascia before harvesting²⁸; performing tendon removal via the popliteal access^{29,30}; performing a horizontal incision when creating the AMP²⁴; and flexing the knee to 110° to create the AAMP.²⁵ There are several limitations to our research: we did not aim to identify the IPBSN during the removal of the flexor tendons; the

altered sensitivity area was delineated by the limits of the perceptual change reported by the patients, and these assessments were always performed by only one researcher, not by two members of the team. Although performed by the same person, it was not possible to control the pressure exerted at the time of the test, which may have been different between the knees examined. We only assessed tactile sensitivity; thus, thermal and pain sensitivity were not tested, as well as tactile two-point discrimination. Finally, incision angle and photographed area measurements were conducted by a single researcher; however, ideally, it should have been measured by two authors.

CONCLUSIONS

The oblique incision parallel to the IPBSN path for ACLR did not prevent injury in harvesting the hamstring tendons, especially in women. However, this condition rarely compromised the activities of daily living.

AUTHORS' CONTRIBUTION: Each author contributed individually and significantly to the development of this article. JCG: performing the surgeries, conception, interpretation, and writing of the article; RSH: review, analysis and interpretation of the data; MSL: review, analysis and interpretation of the data; EB: acquisition of data and critical review of its intellectual content; JOPLS: acquisition of data and critical review of its intellectual content; JCGF: measurements on the computer, creation of the tables, and review of the manuscript.

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EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH OPEN FRACTURES (2019 TO 2020)

PERFIL EPIDEMIOLÓGICO DOS PACIENTES COM FRATURAS EXPOSTAS (2019 A 2020)

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ABSTRACT

Objective: To evaluate the epidemiological profile of open fractures treated at the University Hospital of Lagarto in the years 2019 and 2020. **Methods:** This is an observational, retrospective study, using data from electronic medical records. **Results:** In total, 312 patients met the inclusion criteria for this research and were included. The mean age of affected patients was 36.8 years. The main segment affected were the fingers, mostly affecting males (89%) and predominantly the left side (57.62%). **Conclusions:** The male sex was the most affected by open fractures, and the most prevalent trauma mechanism was motorcycle accidents. Moreover, we found that the fundamental criteria for care in open fracture cases were not always considered by the professionals, resulting in a lack of uniformity in the adopted procedures and discrepancies with the guidelines recommended in the specific literature. **Level of Evidence III, Comparative retrospective study.**

Keywords: Fractures. Trauma. Open Fracture.

RESUMO

Objetivo: Avaliar o perfil epidemiológico das fraturas expostas atendidas no Hospital Universitário de Lagarto nos anos de 2019 e 2020. **Métodos:** Trata-se de um estudo observacional, retrospectivo, por análise de dados de prontuário médico eletrônico. **Resultados:** Foram incluídos 312 (trezentos e doze) pacientes que atenderam aos critérios de inclusão para esta pesquisa. A média de idade dos pacientes acometidos foi de 36,8 anos. O principal segmento acometido foram os dedos das mãos, conforme Tabela 1, em maior número no sexo masculino (89%) e predominando no lado esquerdo (57,62%). **Conclusões:** O gênero mais acometido por fraturas expostas foi o masculino, e o mecanismo de trauma mais prevalente foi o acidente motociclístico. **Todavia, nem sempre os critérios foram levados em conta pelos profissionais, não apresentando homogeneidade nas condutas adotadas, bem como desencontro com as condutas orientadas na literatura específica. Nível de Evidência III, Estudo Retrospectivo Comparativo.**

Descritores: Fratura. Trauma. Fratura Exposta.

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INTRODUCTION

Fracture is the result of failure of bone physical integrity and occurs when the force applied to the bone exceeds its resistance. This imbalance can occur due to the force being too great, or because the bone is weakened. An object under the action of a force undergoes deformation which, within certain limits, is reversible. However, if the force increases, the deformation reaches a critical limit at which the material will break, constituting a fracture, and the same principle applies for the bone.¹

A fracture is considered open when the soft tissue envelope ruptures over or near the fracture site in a way that the underlying bone or fracture hematoma communicates with the external environment.²

Moreover, when a fracture occurs in contaminated cavities, such as the digestive and genitourinary systems, it should be considered exposed.³ Thus, as noted by Court-Brown et al.,⁴ treating open fractures requires a multidisciplinary approach rather than relying on a single specialty to achieve better patient outcomes.

Open fractures (OF) are usually caused by high energy trauma, with car accidents being the most common.⁵ It has a preferential distribution in the age group ranging from the second to the fourth decade of life, with a higher prevalence in men.⁶ The bones located in the lower limb are the ones that suffer the most from this type of injury, with the tibia being the most affected bone.³

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

The study was conducted at Hospital Universitario de Lagarto, Lagarto, SE, Brazil.

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In some cases, diagnosing open fractures may be challenging, as observed by Filho et al.,⁷ who state that the diagnosis of OF can be difficult since the communication point of the skin lesion may be distant from the fracture focus, or even be minimal or imperceptible. Thus, whenever a tissue injury is evidenced in the fracture segment, the possibility of OF should be considered. This type of injury becomes more serious among fractures due to the various complications they can entail, with the increased risk of infection, loss of limb function, and neurovascular injuries.² However, several classifications of OF correlate the bone fracture/soft tissue binomial to evaluate prognosis and determine the most appropriate treatment.⁸ Currently, the most widespread is the Gustilo and Anderson classification, which considers the kinetic energy of the trauma, time of exposure, affected segment, severity of the soft tissue injury, characteristics of the fracture, neurovascular status, and degree of contamination.⁷

Time is paramount in relation to the clinical outcome of the fracture. Torneta III et al. (2019),² emphasizes that the ideal time from the moment of fracture to the surgical approach should not exceed six hours after the injury, considering that after this period there may be an increased risk of infection at the site. Nevertheless, antibiotic therapy should be started as early as possible, as it is the main factor in preventing infection. Moreover, Hebert et al. stated that the main goal of the treatment of open fractures is to prevent infection, obtain adequate bone union, and heal soft tissues, leading to functional recovery of the affected limb as early as possible.⁸

Based on these aspects and considering that epidemiological studies are essential to develop an understanding of the pathology and aid in therapy and preventive measures, this study aimed to evaluate the epidemiological profile of open fractures treated at the university hospital of Lagarto in the years of 2019 and 2020.

MATERIALS AND METHODS

Retrospective observational studies were conducted. Data were obtained from patients treated by the orthopedics team at the Emergency Unit of the University Hospital of Lagarto from January 1, 2019, to December 31, 2020, using the institution's database—collection conducted via electronic medical records. This study was approved by the Research Ethics Committee on Human Beings of the Federal University of Sergipe (UFSLAG/HUL), under CAAE: 61267522.1.0000.0217 and opinion number 5.823.198. Participants signed an informed consent form.

Information regarding sex, age at the time of the initial evaluation, fracture aspects (mechanism of injury, location, presence of contact with the external environment), classification according to the Gustilo and Anderson classification, and time elapsed since the first orthopedic treatment to the initial approach. Moreover, data related to the radiographic evaluation of the imaging exams present in the electronic medical records were collected from the hospital database and inserted into the study.

The study included participants over 18 years of age, undergoing orthopedic treatment for at least two months, with at least one regular weekly frequency at the hospital, and a minimum 20 minutes per workout.

The data were stored in a spreadsheet and studied using the Excel software (Microsoft). A descriptive analysis was performed using measures of central tendency (mean, median), variability (standard deviation), and position (maximum and minimum).

RESULTS

A total of 320 medical records of patients treated at the University Hospital of Lagarto of the Federal University of Sergipe (HUL-UFS) from January 1, 2019, to December 31, 2020, with possible open

fractures were analyzed. Of these, 312 met the inclusion criteria for this research. Of the eight medical records excluded, three did not present specific data defining whether the injury was a true open fracture, in two cases referred by general surgery, orthopedics ruled out open fractures, and in three cases the patients were treated in another emergency service.

The average number of open fractures treated during this period was 0.42 patients per day, i.e., about one patient every 2.4 days. The day with highest attendance was November 20, 2020, a Sunday with four cases of open fractures.

Considering the annual frequency, we found 148 cases of open fractures in 2019, with the most affected site being the fingers with 53 cases, followed by the toes with 33 cases and the tibia with 15 cases. In 2020, we found an increase in the number of OF cases in the order of 10.81% compared to 2019, totaling 164 OF cases. The most affected sites did not change, but we found a higher number of open fractures of the tibia than of the toes: fingers (65 cases), tibia (29 cases), and toes (28 cases).

Considering the studied population, we found a higher prevalence of open fractures in men 265 (85%) than in women 47 (15%). Regarding the age group, individuals in the third decade of life, from 21 to 30 years old, were the most affected, with a total of 68 patients.

The mean age of the affected patients was 36.8 years and standard deviation (SD) was 17.55 years, in a population of patients ranging from 3 to 90 years. The most affected age was 53 years, corresponding to 13 cases (4.1%).

Regarding the trauma mechanisms related to the OF, we found 12 causes, in the following order of prevalence: motorcycle accident (46.8%), cutting machine (marble saw, chaff cutting machine, chainsaw, etc.) (28.2%), white weapon injury (WWI; knife, machete, hatchet, etc.) (9%), fall from the same height (6.1%), run-over (2.9%), gunshot injury (GI; 1.9%), animal-drawn transport (cart, horse, etc.) (1.9%), bicycle accident (1.3%), fall from great height (scaffolding, ladder, tree, etc.) (1%), automobile accident (0.6%), and animal bite (0.3%).

The most affected side during open fractures was the left side. During the analyzed period, we found no bilateral open fracture.

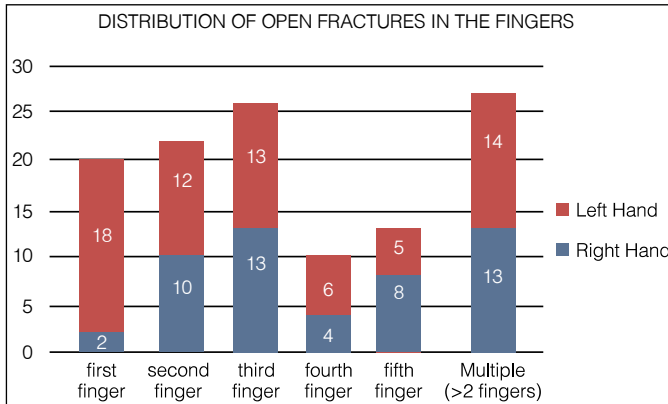
To study the location of the open fractures, it was necessary to divide them into segments, as shown in Table 1.

Table 1. Frequency of open fractures by body segment over the analyzed period.

Segment	No. OF	%
Clavicle	1	0.32
Humerus	6	1.92
Radius	17	5.45
Ulna	14	4.49
Fingers	118	37.82
Femur	6	1.92
Patella	11	3.53
Tibia	44	14.10
Fibula	3	0.96
Ankle	19	6.09
Foot	12	3.85
Toes	61	19.55
Total	312	100

Source: prepared by the authors (2024)

The most affected segment was the fingers, which showed greater numbers in men (89%) and predominantly on the left side (57.62%). Graph 1 shows the frequency of finger involvement.



Graph 1. Distribution of open fractures in the fingers.

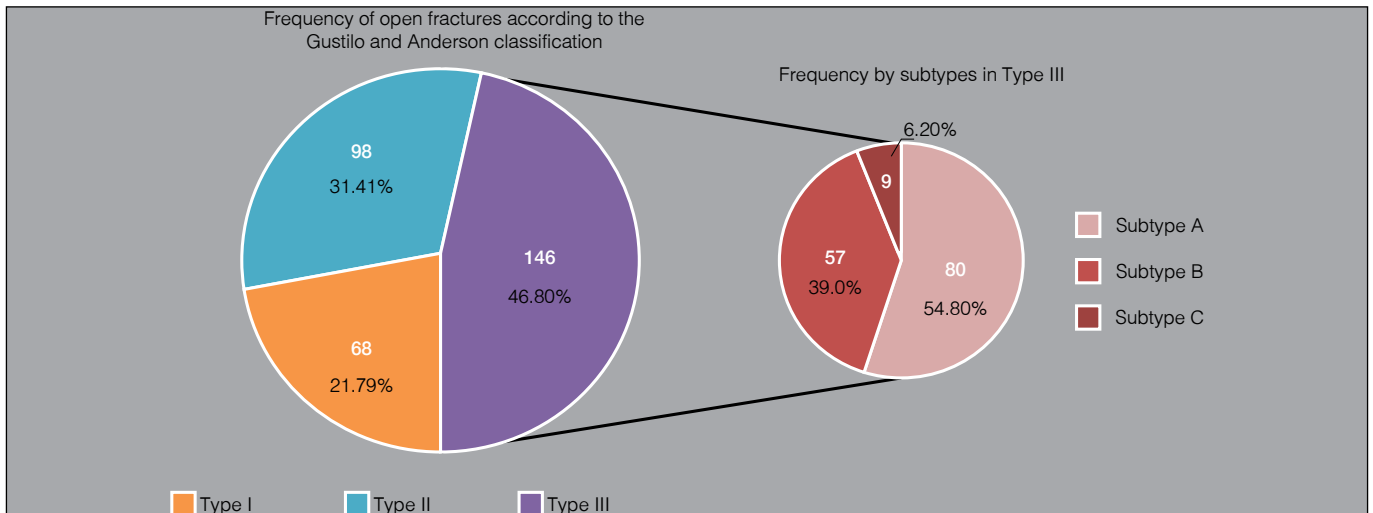
Source: prepared by the authors (2024)

The mechanisms of hand finger injuries found in order of occurrence were cutting machines (marble saw, chaff cutting machine, chainsaw, etc.) 79 cases (66.95%), white weapon injury (WWI) 26 cases (22.03%), motorcycle accident 9 cases (7.63%), gunshot injury (GI) 2 cases (1.69%), and automobile accident and animal bite each with one case (1.7%).

Regarding multiple injuries, in which there are more than two fingers affected by an open fracture, we found 27 cases. The main mechanism of trauma in this situation was accidents with cutting machines (marble saws, marble, chaff cutting machine, chainsaws, etc.), which occurred in 11 cases, representing 40.74% of the cases of multiple exposed injuries in fingers.

When considering only the long bones, the highest incidence of open fractures was in the tibia (44 cases), being more prevalent in males (37 cases) with a higher number of injuries on the right side (24 cases). The most common mechanism in this situation was motorcycle accidents, accounting for 34 cases (77.3%) of open fractures in the tibia, followed by run-overs in eight cases (18.2%). In the upper limbs, the most affected bone was the radius (17 cases), being the second most affected long bone, also with a predominance in males (12 cases) and most often injuring the left side (13 cases). In this case, the main mechanism of injury was also motorcycle accidents (9 cases), followed by falls from same height (7 cases). Using the Gustilo and Anderson classification as a basis, the most frequent open fracture was grade III (Graph 2). Graph 2 shows the distribution of open fracture types based on the Gustilo and Anderson classification.

Table 2 shows the frequency of open fractures by anatomical site according to the Gustilo and Anderson classification.



Graph 2. Frequency of open fractures according to the Gustilo and Anderson classification.

Source: prepared by the authors (2024)

Table 2. Frequency of open fractures by site according to the Gustilo and Anderson classification.

Segment	Gustilo and Anderson classification					Total
	Type I	Type II	Type III A	Type III B	Type III C	
Clavicle	1	0	0	0	0	1
Fingers	25	23	38	27	5	118
Toes	11	35	9	5	1	61
Femur	0	0	4	2	0	6
Fibula	2	1	0	0	0	3
Patella	0	9	0	2	0	11
Foot	1	4	0	7	0	12
Radius	10	4	2	1	0	17
Tibia	1	13	23	7	0	44
Ankle	9	4	3	3	0	19
Ulna	8	4	0	2	0	14
Humerus	0	1	1	1	3	6
Total	68	98	80	57	9	312

Source: prepared by the authors (2024)

DISCUSSION

In this study, we analyzed the epidemiology of 312 open fractures retrospectively in the period from January 1, 2019, to December 31, 2020, to identify the numerous aspects of this type of injury and thus reinforce our conviction that the study of these injuries is of vital importance for our institution, as well as the community. The choice to analyze data from a two-year period was due to the scarcity of other epidemiological studies in the service, hindering possible comparisons and prospective statistics. We also aimed to assess possible changes in epidemiological aspects, given that the year 2020 was atypical due to the COVID-19 pandemic.

When comparing both years, 2019 showed 148 cases (47.44%) of open fractures, while 2020 showed 164 cases (52.56%). We observed a 10.8% increase in the number of OF cases in 2020 compared to the previous year. This increase was mainly due to accidents involving motorcycles, drawing attention since it is associated with the increase in the number of delivery drivers in the pandemic peak; however, no reliable static data can prove this theory. In a study conducted by Cunha et al., an average of 4.96 cases/day was found. Our study showed an average attendance of 0.42 patients/day with open fractures, that is, about one patient every 2.4 days.⁹ Court-Brown et al. show that the frequency of open fractures in long bones is 11.5 per 100,000 inhabitants.⁴ Based on the state health plan of the government of Sergipe from 2016 to 2019, the University Hospital of Lagarto serves an estimated population of 257,633 inhabitants, so the frequency of open fractures in long bones in this service during the study period was 19.41 per 100,000 inhabitants in 2019 and 22.46 per 100,000 inhabitants in 2020. This distortion in incidence and frequency when compared to the literature may occur from region to region, depending on the characteristics of the sample, their economic activity and socio-educational conditions, means of transportation and traffic laws, and occupational safety standards and their inspection, that is, several regional variants.³ Based on these variables, Court-Brown et al. state that developing countries, such as Brazil, show higher rates of OF in long bones per 100,000 inhabitants due to a higher number of traffic accidents, especially motorcycle accidents, as well as accidents in the workplace,⁴ which corroborate our study.

As demonstrated in the study by Arruda et al., in which the left side was predominant in 59.06% patients, the greatest laterality in our study was also on the left side with 170 cases (54.48%).⁶ This datum corroborates the relationship between the lack of agility in protecting the non-dominant limb, as most participants were right-handed. Most OF occurred in male patients with a ratio of 5.5:1, in which 265 out of 312 cases occurred in this population, corresponding to 85% of the cases and corroborating other studies. Cunha et al. showed a prevalence of 84.2% of the cases being in males,⁹ as well as Arruda et al., who presented a percentage of 86.84% of males affected in their study and a sex ratio of 6.6:1.⁶ This result can be partially attributed to the greater exposure of men to various risks: the use of piercing and cutting utensils, psychological immaturity, a greater tendency to inexperience and disobedience to traffic rules, greater involvement with violence and fights, and greater labor exposure.

Patients in the third decade of life were the most affected by open fractures, accounting for 21.8% of cases (68 patients). A similar result was found by Arruda et al. and Cunha et al.,^{6,9} who found a mean age of 30 years (SD 16 years), with a mode of 21 years in the study by Arruda et al. and 25 years in the study by Cunha et al.^{6,9} In our study, the mean age of the patients was slightly higher; however, it remained close to that demonstrated in the literature, being 36.8 years of age (SD 17.55 years). Our mode, on the other hand, differed quite differently from those presented and remained

in the age of 53 years, corresponding to 4.1%, with 13 cases. This trend may have occurred due to greater recklessness in the use of machinery and sharp instruments by these patients, as they had been handling them for some years in their work activities, associated with less motor agility to deal with them compared to younger patients, affecting the fingers of the hands in greater numbers (8 cases).

The segment with the highest frequency of occurrence of open fractures in this study was the fingers (37.8%), a fact also found in the study by Cunha et al.,⁹ with OF of the bones of the hands representing 27.6% of the total open fractures.

According to Court-Brown et al., tibial shaft open fractures are the most common among long bones.⁴ This has been also found in the study by Hanciau³, in which the tibia represented 21.6% of OF cases, and by Arruda et al., in which they found 37.86% frequency in this bone segment.⁶ Therefore, if we consider only long bones, the highest percentage of involvement can be found for the tibia, representing 48.35% of the cases, which demonstrates the balance of our service with the data found in the literature.

Arruda et al. mention in their study that the use of motorcycles with greater exposure of the lower limbs contributed to the greater number of open fractures in these segments.⁶ Our research found 146 cases of open fractures caused by motorcycle accidents, accounting for 46.8%, being the most common mechanism of trauma. For Hanciau, knowledge of the trauma mechanisms that lead to OF serves as a guide to alert us to carefully look for injuries, including obscure ones.³

We found that the most common trauma mechanism for open fractures occurred on public roads, accounting for 53.52%, which is similar to the findings by Arruda et al., in which 57.30% of cases were found. These included being run over, car, motorcycle, and cycling accidents, as well as accidents involving animal traction, horses, and carts.⁶

Injuries caused by cutting machines (marble saws, marble, chaff cutting machine, chainsaws, etc.) caused open fractures and accounted for the third highest incidence, with 31 cases (9.9%), predominantly in fingers (30 cases). We believe that this fact may have occurred due to the region covered by the hospital showing an economy predominantly linked to rural areas, which use a lot of machinery of this type and where their operators have low schooling and little training to use such equipment, increasing the chances of accidents.

In our study, open fractures in the fingers were the most common (118 cases), with the third finger being the most frequently affected (26 cases, 22.03%), followed by the second finger (22 cases, 18.64%), the first finger (thumb) (20 cases, 16.95%), the fifth toe (13 cases, 11.02%), and finally, the fourth finger (10 cases, 8.47%). On the other hand, we found 27 cases (22.88%) of the lesions involving multiple fingers ($\geq 22.88\%$), which demonstrates more severe injuries due to improper handling of cutting machines. However, we did not find a relationship that could explain these numbers, believing them to be only fatalities.

Our research was based on the Gustilo and Anderson classification for open fractures, considering the information provided in medical records.¹⁰⁻¹² Thus, we found that the highest incidence was in Type III, with 146 cases (46.79%). This result corroborates most other studies, as according to Arruda et al., the highest incidence was also found in Type III with 45.36%, a result close to that found in the study by Cunha et al., which revealed an incidence of 54% in this type of fracture.^{6,9}

In our study, Gustilo and Anderson Type III presented the following results for its subdivision: in Type IIIa, we found the highest incidence with 80 cases (25.64%), followed by Type IIIb with 57 cases (18.27%) and Type IIIc, which showed nine cases of greater

severity (2.88%). These findings are supported, in all proportions, by the study by Cunha et al. which shows similar figures: Type IIIa 48.6%; Type IIIb 3.5%; and Type IIIc 1.9%.⁹ However, it differs from the study by Arruda et al. since they showed Type IIIa with 30%, Type IIIb with a lower incidence, only 5%, and Type IIIc with an incidence of 11%, which is justified by the fact that they conducted the study in a hospital of greater complexity which is a reference for more critical situations.⁶

Type I fractures showed an incidence of 68 (21.79%) cases, with the most prevalent being finger trauma with 25 cases, followed by toe trauma with 11 cases and radius with 10 cases. In Type II, we found 98 (31.41%) cases, with the toes being the most affected site in 35 cases, followed by fingers with 23 cases and tibia with 13 cases. Thus, we found that open fractures in our service are of a more severe nature, according to the Gustilo and Anderson classification.¹⁰⁻¹² This fact may be due to the hospital's regional status and its role as a reference center for smaller units (emergency

centers, small sized hospitals, basic health units, etc.), which results in it receiving most of the more severe injuries.

Based on what was presented, it was observed that the male sex was the most affected by open fractures, and the most prevalent trauma mechanism was motorcycle accidents. Therefore, we can conclude that a direct approach to this population group would be vital to raise awareness about the severity of the situation, aiming to reduce the incidence.

As an orthopedic emergency, open fractures must be classified and evaluated based on four fundamental criteria: type of fracture, soft tissue damage, neurovascular compromise, and contamination potential. In this study, we observed that, across various medical records and practices, the professionals did not always consider the criteria, resulting in a lack of uniformity in the adopted procedures and discrepancies with the guidelines recommended in the specific literature. This conclusion was possible based on the difficulty encountered in analyzing and quantifying the information presented in the cataloged medical records.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. RCR: literature review, scientific writing, data collection, data analysis; LVFB: literature review, scientific writing, data collection, data analysis; RCS: literature review, scientific writing, data collection, data analysis; MFV: literature review, scientific writing, data collection, data analysis; MAFC: data validation, scientific evaluation, and data analysis.

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STUDY ON THE ROLE AND MECHANISM OF MICRORNA-650/ WNT1 IN THE REPAIR OF ARTICULAR CARTILAGE INJURY

ESTUDO DO PAPEL E MECANISMO DO MICRORNA-650/WNT1 NA REPARAÇÃO DA LESÃO DA CARTILAGEM ARTICULAR

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ABSTRACT

Objectives: Osteoarthritis (OA) is a degenerative disease associated with chondrocyte injury. This study investigated the dysregulation of microRNA-650 (miR-650) in cartilage tissues of patients with OA. Its function and mechanism were also investigated in OA cell models. **Methods:** miR-650 levels were examined in 15 OA cartilage tissues and ten healthy cartilage tissues. SW1353 cells were used for cell function experiments and IL-1 β was applied to the cells to mimic OA conditions in vitro. Cell functions such as proliferation, apoptosis, and inflammation were detected. The downstream target gene of miR-650 was identified and confirmed by bioinformatic analysis and luciferase activity assay. Rescue experiments were performed to verify the mechanism. **Results:** Suppressed expression of miR-650 was tested in patients with OA and cell models. Overexpression of miR-650 increased cell proliferation but suppressed apoptosis and inflammation of SW1353. As the target gene of miR-650, WNT1 overexpression counteracted the role of miR-650 in the function of SW1353. **Conclusion:** miR-650 can protect against articular cartilage injury in OA by targeting WNT1. **Level of Evidence I, Experimental Study.**

Keywords: Osteoarthritis. microRNA. Osteocondritis.

RESUMO

Objetivos: A osteoartrite (OA) é uma doença degenerativa acompanhada de lesão dos condrocitos. Este estudo examinou a desregulação do microRNA-650 (miR-650) nos tecidos de cartilagem de doentes com OA. A sua função e mecanismo também foram explorados em modelos celulares de OA. **Métodos:** Os níveis de miR-650 foram examinados em 15 tecidos de cartilagem de OA e em 10 tecidos de cartilagem normal saudável. As células SW1353 foram utilizadas para experiências de função celular, e a IL-1 β atua sobre as células para imitar as condições da OA in vitro. Foram detectadas funções celulares, incluindo a proliferação, a apoptose e a inflamação. O gene alvo a jusante do miR-650 foi reconhecido e confirmado por meio de análise bioinformática e ensaio de atividade da luciferase. Foram efetuadas experiências de recuperação para verificação do mecanismo. **Resultados:** Foi testada uma expressão oprimida do miR-650 tanto em doentes com OA como em modelos celulares. A sobreexpressão do miR-650 aumentou a proliferação celular, mas suprimiu a apoptose e a inflamação da SW1353. Como gene alvo do miR-650, a sobreexpressão do WNT1 contrariou o papel do miR-650 na função do SW1353. **Conclusão:** O miR-650 pode proteger contra a lesão da cartilagem articular na OA através da ação sobre o WNT1. **Nível de Evidência I, Estudo de Experimental.**

Descritores: Osteoartrite. microRNA. Osteocondritis.

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INTRODUCTION

Osteoarthritis (OA) is a common degenerative disease that occurs primarily in older adults.¹ With the aging of the population, the incidence of OA has continued to increase.² Clinically, OA is characterized by arthralgia and limited mobility. The pathological features of OA include degeneration and damage to articular cartilage, subchondral sclerosis or cystic degeneration, and hyperplasia of the articular marginal bone. OA affects the joints of the knees, hips, ankles, hands, and spine, among other body

regions.³ More than half of people over the age of 65 will develop OA, which seriously reduces the quality of daily life.⁴ Various factors contribute to the onset of OA, such as age, obesity, injury, etc.⁵ The pathogenesis has not yet been elucidated.

As endogenous non-coding single-stranded RNAs, microRNAs (miRNAs) can mediate the expression of target genes at the post-transcriptional level.⁶ Recent studies have indicated that miRNAs participate in the pathogenesis of OA, affecting bone metabolism, inflammation, and cartilage homeostasis.⁷ Using miRNA microarray

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

The study was conducted at Peking University Third Hospital Qinhuaogdao Hospital in Qinhuaogdao City, Hebei Province, China.

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platform and bioinformatics, researchers have identified numerous differentially expressed miRNAs in OA samples.^{8,9} Circulating miRNAs such as miR-206, miR-140-3p, and miR-146a serve as promising biomarkers in OA pathogenesis.¹⁰⁻¹² Recently, overexpression of miR-650 has been suggested to limit proliferation and inflammation of rheumatoid arthritis fibroblast-like synoviocytes.¹³ Alterations in miR-650 expression levels in rheumatoid arthritis (RA) have implicated that it is an attractive molecule for OA progression.¹³ However, few studies have highlighted the influence of miR-650 on OA.

In this study, miR-650 levels in cartilage tissues of OA cases were examined clinically. In addition, SW1353 cells were used for cell function experiments, and IL-1 β was applied to the cells to mimic OA conditions in vitro. Functionally, the effect of miR-650 on cell proliferation, apoptosis and inflammation was investigated. In terms of mechanism, the downstream target gene of miR-650 was predicted and its functions were verified.

MATERIALS AND METHODS

Clinical sample collection

The study design was approved by the Ethics Committee of Peking University Third Hospital Qinhuangdao Hospital. All participants signed an informed consent form.

A total of 15 patients suffering from OA were selected as the case group, and their cartilage tissues were collected during total knee arthroplasty. The case group consisted of nine males and six females with a mean age of 55.60 ± 5.93 years. Another ten participants without OA were recruited as the control group. These subjects—seven males and six females—suffered from accidental injuries and required amputation. Their normal cartilage tissues were obtained during surgery. Comparison of age and gender distribution showed no obvious discrepancy between the two groups involved, which proves that they were comparable.

Ethical approval

This study complied with the guidelines of the Declaration of Helsinki and was approved by the Medical Ethics Committee of Peking University Third Hospital Qinhuangdao Hospital (No. 2021-05-16). All participants signed an informed consent form.

Cell culture and modeling

Human chondrosarcoma (SW1353) was obtained from the Cell Resource Center of Shanghai Institute of Biological Sciences (Shanghai, China). DMEM complete medium (containing 10% FBS and 1% double antibody) was used for cell culture at 37°C and 5% CO₂. Samples were divided into two groups: control group and model group. Cells in the control group maintained the routine culture in DMEM, while cells in the model group were treated with IL-1 β at the concentration of 10 ng/mL. Different time gradients were set, including 3 h, 6 h, 12 h, 24 h.

Cell transfection

To mediate the levels of miR-650 and its target gene WNT1 in SW1353, cell transfection was performed. Sequences of miR-650 mimic and its negative control (mimic-NC) were synthesized by Sangon Biotech. Sequences of WNT1 were cloned into pcDNA-3.0 vector to establish the gene overexpression plasmid, while the empty vector served as a negative control (pcDNA-3.0). After SW1353 was cultured with IL-1 β for 24 hours, the above sequences were added. After incubation for 6 hours, the normal medium was changed. Cell transfection was completed after 48 hours.

qRT-PCR

Total RNA was extracted using TRIZOL reagent, and the RNA concentration was determined. Reverse transcription was performed

using transcriptase kit (Takara Bio, Japan). SYBR Green PCRMaster Mix (Takara Bio) was used with ABI StepOnePlus real-time PCR system (Applied Biosystems, Thermo Fisher Scientific, CA) to perform qPCR. Relative values of miR-650 and WNT1 mRNA were obtained by $2^{-\Delta\Delta CT}$ based on CT values using U6 and GAPDH as internal references, respectively. The experiment was repeated three times.

CCK-8 assay

Cell proliferation was measured using the Cell Counting Kit-8 (CCK-8) assay. The prepared cell suspension was inoculated into 96-well plates to achieve 3×10^3 cells in each well. Over the course of 3 days, 10 μ L CCK-8 reagent was added to each well every 24 h (DojindoMolecular Technologies, Japan). After continuing the culture in the incubator for 3 h, cell proliferation was assessed by measuring the absorbance at 450 nm.

Flow cytometry assay

SW1353 cells were digested with pancreatic enzymes, and single cell suspension was collected and processed. After three washes with pre-cooled PBS, 10 μ L Annexin V and propyl iodide (PI) were added to the cell suspension and incubated at 4°C in the dark. FACSCalibur flow cytometry (BD Biosciences) was used to test cell apoptosis.

Elisa assay

Enzyme-linked immunosorbent assay (ELISA) was performed. The levels of cytokines TNF- α and IL-1 β in the cell culture supernatant were tested according to the ELISA instructions. The concentration was calculated based on the OD values at 450 nm.

Luciferase reporter assay

WNT1 wild-type or mutant (WT/MUT) sequences were transfected into logarithmic 293T cells with miR-650 mimic or mimic-NC. A total of 6 h after transfection, the fresh culture medium was replaced. Then, 48 h after transfection, luciferase activity was analyzed using double luciferase detection reagent.

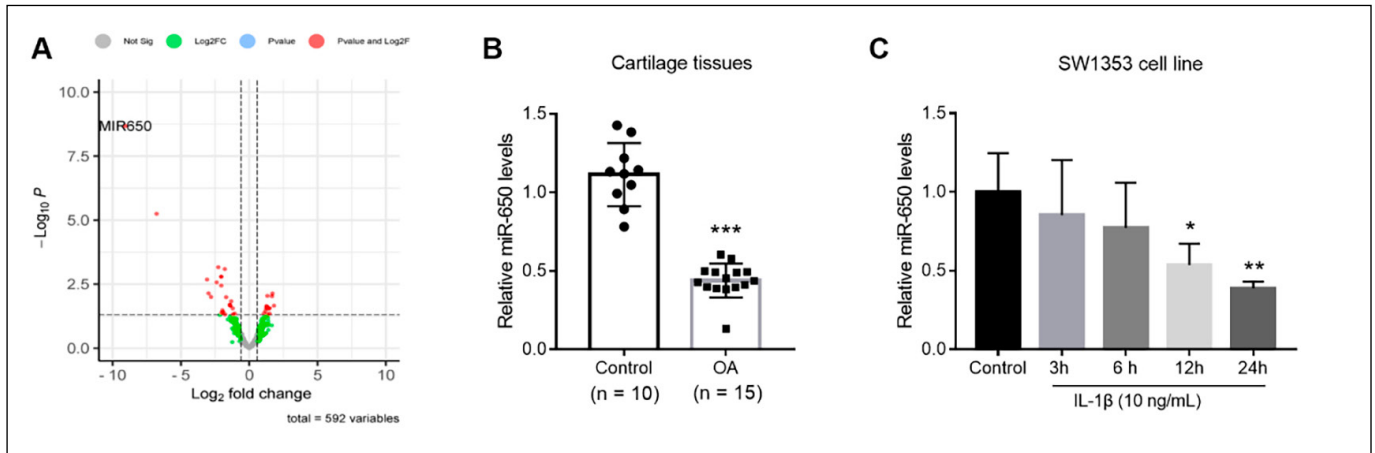
Statistical methods

SPSS 24.0 statistical software was used to process and analyze the data. Measurement data were expressed as mean \pm standard deviation (SD), and differences between groups were compared by t-test. One-way analysis of variance (one-way ANOVA) was used to compare multiple groups. Statistical significance was set at $P < 0.05$.

RESULTS

Differentially expressed miR-650 in OA

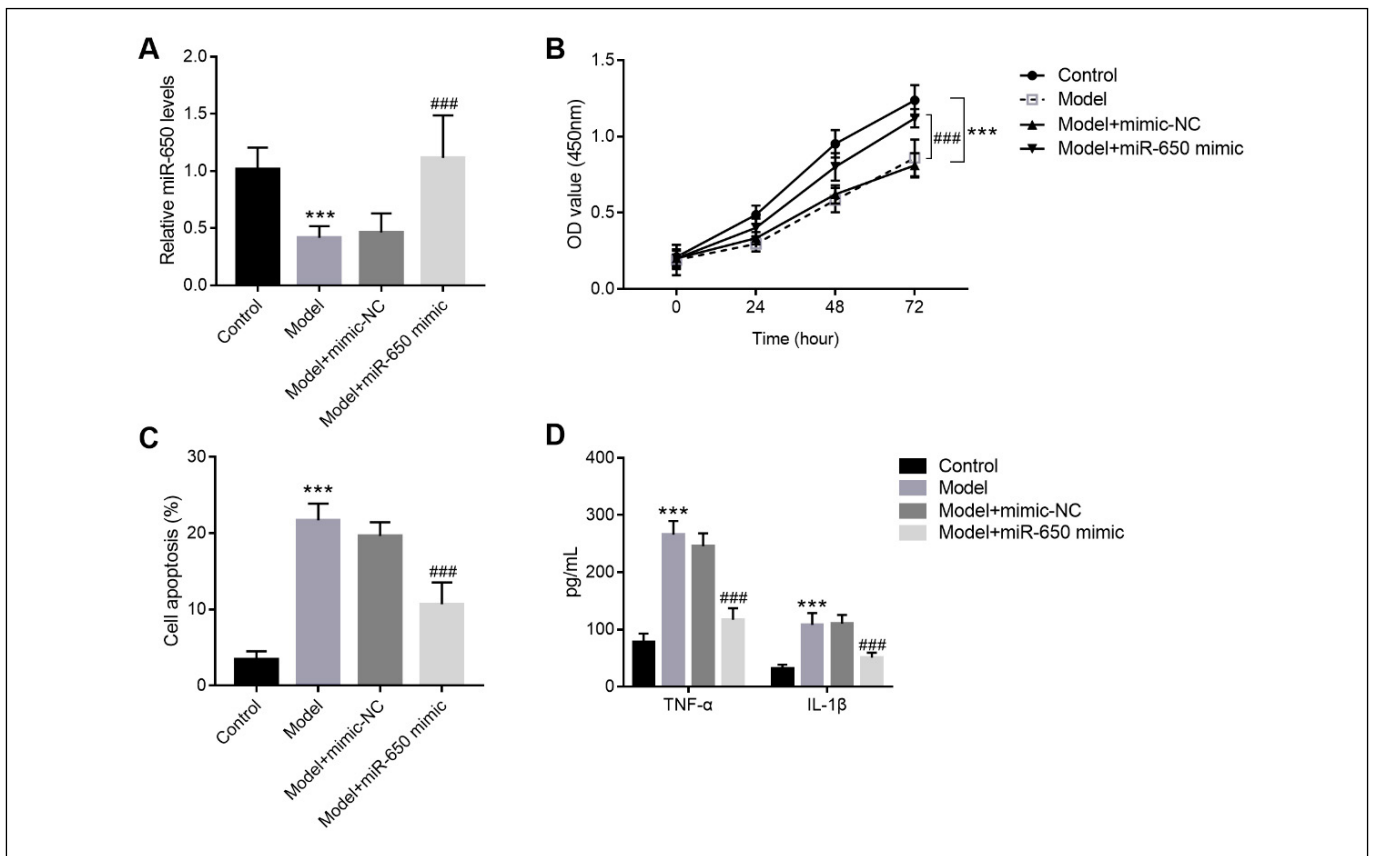
In this study, the miRNA dataset GSE213070 was downloaded from the GE database (<https://www.ncbi.nlm.nih.gov/geo/>).¹⁴ A total of 590 differentially expressed miRNAs were detected, of which 271 were downregulated and 319 were upregulated in inflamed synovial membrane after anterior cruciate ligament and/or meniscus injuries (Figure 1A). MiR-650 was ultimately selected for further experiments because it had the largest fold change and the lowest P value. Clinically, miR-650 levels in cartilage tissues of patients with OA were analyzed and compared with the controls. As shown in Figure 1B, a suppressed expression of miR-650 was identified in patients with OA ($P < 0.001$). SW1353 cells were cultured with added IL-1 β to mimic OA conditions in vitro. As shown in Figure 1C, miR-650 levels gradually decreased with increasing incubation time. After 12 hours of culture, the difference reached a significant level ($P < 0.05$).



Overexpression of miR-650 promoted cell proliferation and suppressed apoptosis of SW1353

To investigate the role of miR-650 in OA, miR-650 mimic was transfected into SW1353 to mediate its levels in vitro. As shown in Figure 2A, miR-650 levels were significantly upregulated in the miR-650 mimic transfection group ($P < 0.05$). The CCK-8 results

indicated that miR-650 overexpression enhanced the proliferation capacity of SW1353 compared with the model group (Figure 2B). The results of cell apoptosis were tested by flow cytometry assay, and it was seen that cell apoptosis was remarkably suppressed after miR-650 mimic transfection (Figure 2C). Similarly, the reduction of TNF- α and IL-1 β in SW1353 was accompanied with miR-650 mimic transfection (Figure 2D).



miR-650 directly targets WNT1 binding

The target genes of miR-650 were analyzed using the TargetScan and miRDB databases. A total of 450 target genes were identified from TargetScan, while 423 were identified from miRDB (Figure 3A). In addition, 491 OA-related targets were obtained from the GeneCards database (Figure 3A). Venn overlap analysis identified two overlapping target genes from the TargetScan, miRDB and GeneCards databases, namely IL1RN and WNT1 (Figure 3A). Based on the close association

of WNT1 with OA, WNT1 was identified as a candidate target gene of miR-650 for further analysis. Figure 3B shows the binding sequences between miR-650 and WNT1. According to the luciferase activity assay results, miR-650 overexpression weakened the luciferase activity of cells transfected with WT-MNT1, but no changes were detected in cells transfected with MUT-WNT1 (Figure 3C). Moreover, the downregulation of WNT1 mRNA levels was also tested in cells transfected with miR-650 mimic (Figure 3D).

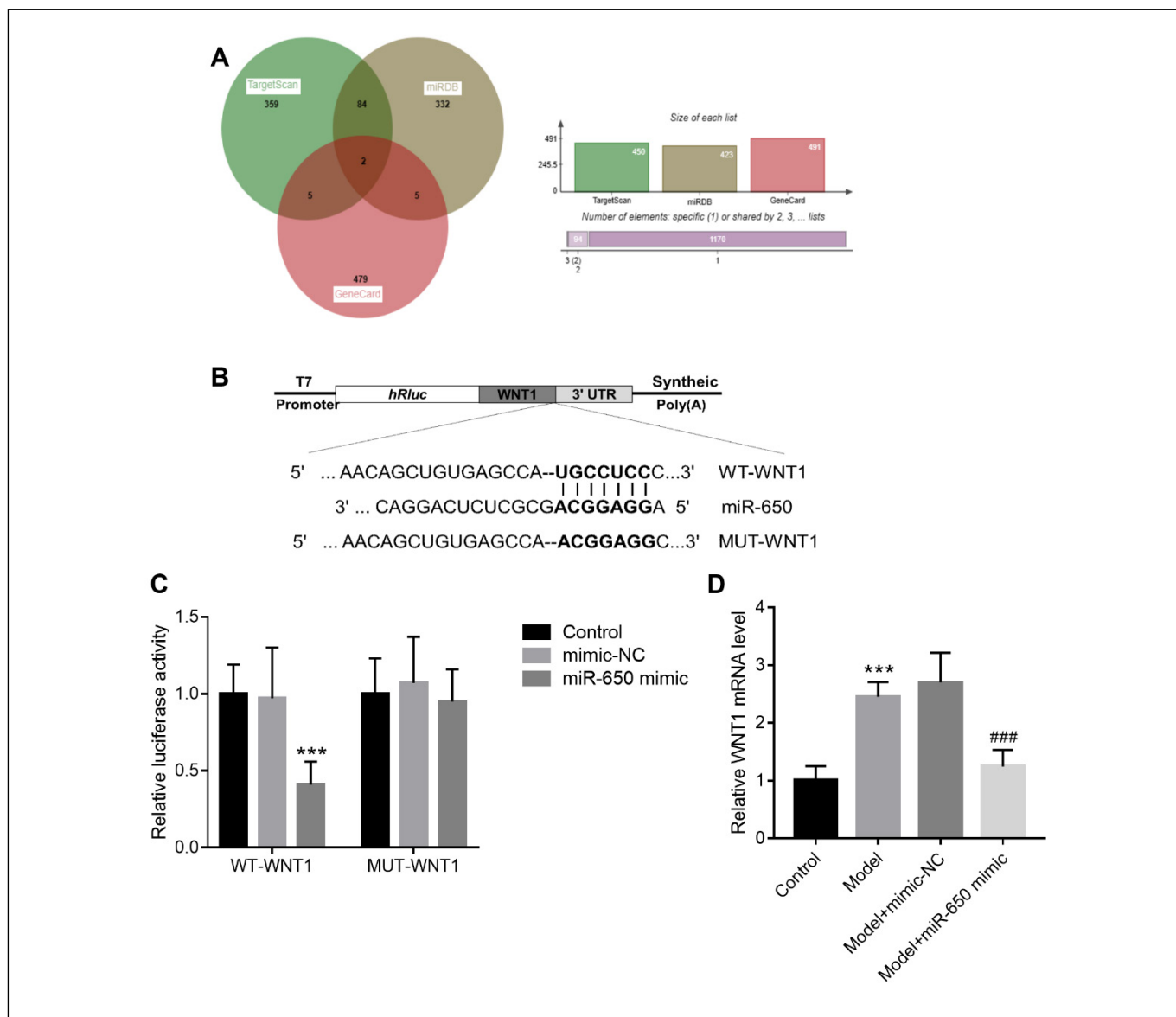


Figure 3. miR-650 directly targets WNT1 binding. Figure A: Overlapping target genes of miR-650 from the TargetScan and miRDB miRNA databases and from the GeneCards database. Figure B: Binding sequences between miR-650 and WNT1. Figure C: Luciferase activity of 293T cells transfected with miR-650 mimic or mimic-NC. Figure D: WNT1 mRNA levels in SW1353 cells. *** P < 0.001 vs. control group; ### < 0.001 vs. model group.

WNT1 overexpression counteracted the role of miR-650 in SW1353 function

The involvement of WNT1 in miR-650 was also investigated in SW1353 cells, and its expression was mediated by pcDNA 3.0-WNT1 transfection. Figure 4A shows its transfection efficiency, and an obvious increase of WNT1 mRNA levels was identified

in cells after transfection of pcDNA 3.0-WNT1. In terms of cell function, overexpression of WNT1 resulted in the suppression of cell proliferation and promotion of cell apoptosis, which counteracted the effect of miR-650 on cells (Figure 4B-C). A similar effect was found in terms of inflammation, as an excessive release of both TNF- α and IL-1 β was detected with the upregulation of WNT1 (Figure 4D).

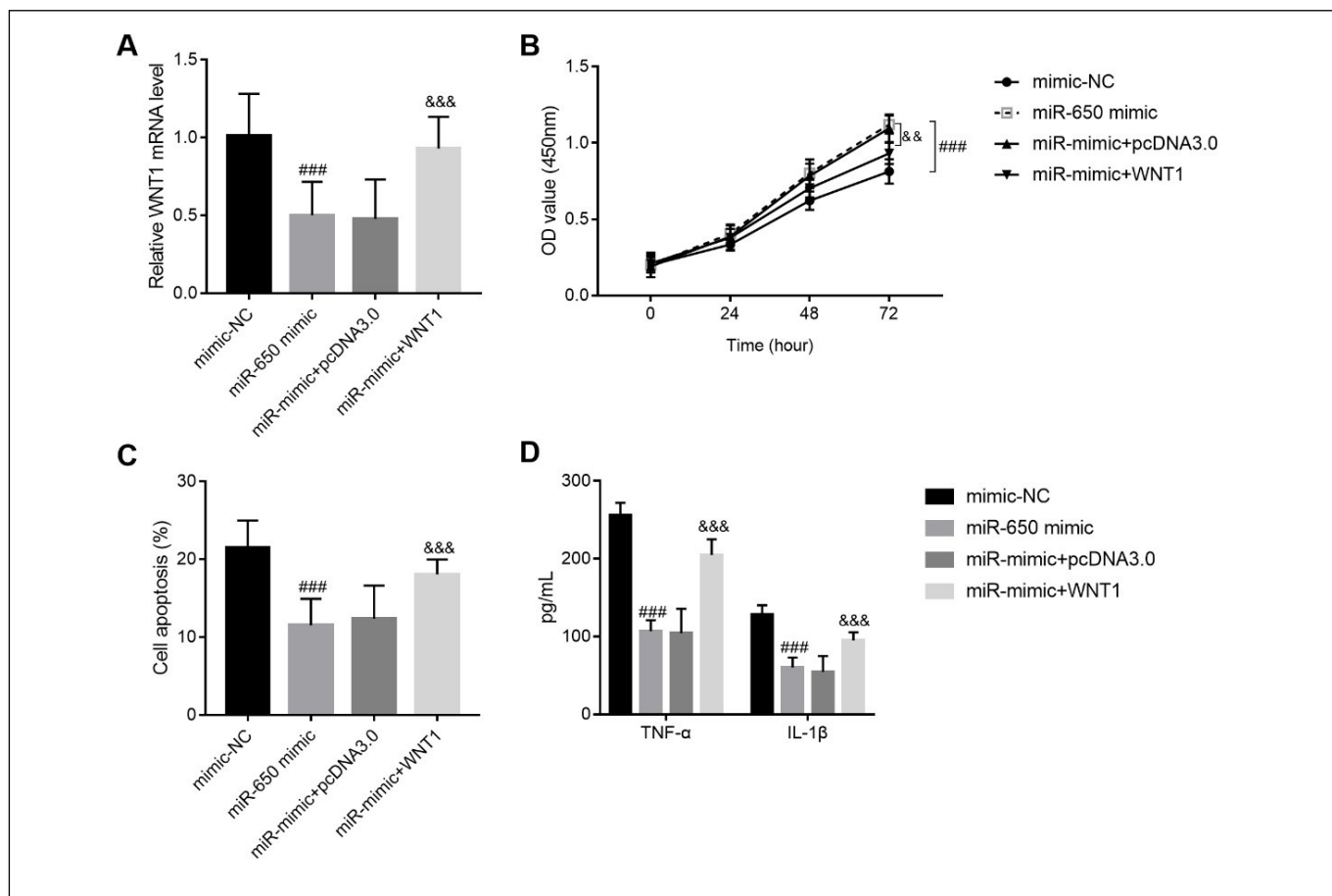


Figure 4. WNT1 overexpression counteracted the role of miR-650 in SW1353 function. Figure A: pcDNA 3.0-WNT1 transfection upregulates the mRNA level of WNT1. Figure B: Cell proliferation of OA cell models after transfection with miR-650 mimic or/and pcDNA-WNT1. Figure C: Cell apoptosis of OA cell models after transfection with miR-650 mimic or/and pcDNA-WNT1. Figure D: Concentration of TNF- α and IL-1 β in OA cell models after transfection with miR-650 mimic or/and pcDNA-WNT1. ### P < 0.001 vs. mimic-NC group; &&& P < 0.001 vs. miR-650 mimic group.

DISCUSSION

OA is the most common chronic degenerative joint disease, and its molecular mechanism is still not fully understood.¹⁵ Recent studies have confirmed that miRNAs can be involved in chondrogenesis, cartilage degradation, and OA development by regulating cellular processes such as apoptosis, proliferation, and matrix remodeling.⁸ For example, miR-17 has recently been reported to maintain cartilage homeostasis, which contributes to the prevention of OA.¹⁶ In both OA cell and mice models, reduced miR-214-3p was found to be in good agreement with unbalanced extracellular matrix (ECM) metabolism in cartilage, and this mechanism is related to the activation of the NF- κ B signaling pathway.¹⁷ In the present study, miR-650 was specifically selected because of the prominent change in its expression level in inflamed synovial membrane after anterior cruciate ligament and/or meniscus injuries, based on the GE database. Moreover, miR-650 levels were analyzed clinically in cartilage tissues of patients with OA. As expected, suppressed miR-650 was detected in these cartilage tissues. Therefore, it was concluded that miR-650 may be a factor contributing to the development of OA.

Chondrocytes are important cellular structures for maintaining the structure and function of cartilage.¹⁸ An increasing number of studies have shown that chondrocyte proliferation and apoptosis are involved in the onset of OA.¹⁹ The death of chondrocytes disrupts the balance between extracellular matrix synthesis and degradation, further aggravating OA.²⁰ In this study, SW1353 cells were used to explore cell function, and IL-1 β was applied to the cells to mimic OA

conditions in vitro. Consistent with the results of previous studies, IL-1 β treatment led to chondrocyte apoptosis and inhibition of cell proliferation. Moreover, the qRT-PCR results revealed the downregulation of miR-650 along with the prolongation of incubation time in SW1353 cells. To investigate the role of miR-650 in OA, miR-650 mimic was transfected into SW1353 to mediate its levels in vitro. As expected, miR-650 overexpression significantly promoted cell proliferation and suppressed apoptosis of chondrocytes, thereby counteracting the adverse effects of IL-1 β . Furthermore, excessive release of inflammatory cytokines was detected in chondrocyte cell models. Inflammatory response is involved in the process of cartilage destruction in OA.²¹ The in vitro experiments showed the anti-inflammatory role of miR-650 in chondrocytes, which is in agreement with the improved cell viability. It was concluded that the protective role of miR-650 against articular cartilage injury may be related to its anti-inflammatory effect. Consistently, the increase in miR-650 expression has been reported to suppress the release of inflammatory factors in the progression of rheumatoid arthritis¹³. In addition, it has been found to exert anti-inflammatory media in several other human diseases, such as ulcerative colitis.^{22,23} The previous findings support our conclusion about OA.

Subsequently, the TargetScan and miRDB databases were used to investigate the downstream targets of miR-650, and 86 overlapping target genes were identified. In addition, 491 OA-related targets from the GeneCards database were identified by Venn overlap analysis, and two overlapping target genes were identified from

the TargetScan, miRDB, and GeneCards databases. Among them, we focused on WNT family member 1 (WNT1), a key gene that plays a pivotal role in the regulation of OA.²⁴ In the progression of OA, the activation of WNT signaling can aggravate chondrocyte senescence.^{24,25} In our cell experiments, the target association was confirmed by luciferase activity assay. Furthermore, the involvement of WNT1 in the role of miR-650 was investigated in SW1353 cells. It was found that WNT1 overexpression could partially abrogate the protective influence of miR-650 induction in response to articular cartilage injury in OA cell models.

CONCLUSION

In conclusion, our results showed that miR-650 can protect against articular cartilage injury in OA by targeting WNT1. This discovery provides a new pathway for exploring the pathogenesis of OA. However, the functions and mechanisms of the miR-650/WNT1 axis in OA need to be further verified in vivo.

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ASSESSMENT OF BONE AGE AGREEMENT BETWEEN THE SAUVEGRAIN AND GREULICH AND PYLE METHODS

AVALIAÇÃO DA CONCORDÂNCIA DA IDADE ÓSSEA ENTRE OS MÉTODOS DE SAUVEGRAIN E GREULICH E PYLE

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ABSTRACT

Objective: To evaluate the intra and inter observer agreement of the Sauvegrain, Greulich and Pyle methods. **Material and methods:** This is an observational, retrospective and cross-sectional study ethically approved by opinion 6.192.391. 100 radiographic images of the elbow and 100 of the left wrist and hand were collected from children whose images were selected by a researcher who did not carry out the evaluations. The Sauvegrain, Greulich and Pyle methods were used to determine bone age. We provided a detailed explanation of each method and the evaluators received a file with the study images. After three weeks, the exams were randomized and the radiograms were reevaluated. Of the 100 patients in group A, 61 (61%) were boys and 39 (39%) were girls. In group B, 67 (67%) were boys and 33 (33%) were girls. Four statistical analyzes were used: correlation; intraclass correlation; analysis using the Bland-Altman graph; differences between groups. **Results:** Intra and interobserver agreement between groups was considered excellent. **Conclusions:** Despite the excellent agreement, group A presented a significantly better value than B. Biological ages show a greater difference compared to chronological ages in group A. In group B, skeletal and chronological ages do not show statistical difference according to the accuracy test. **Level of Evidence III, Cross-Sectional Observational Study.**

Keywords: Child. Puberty. Radiography. Evaluation Study. Age Determination by Skeleton. Observer Variation.

RESUMO

Objetivo: Avaliar a concordância intra e interobservadores dos métodos de Sauvegrain e Greulich e Pyle. **Material e métodos:** Trata-se de um estudo observacional, retrospectivo e transversal, aprovado eticamente pelo parecer 6.192.391. Foram coletadas cem imagens radiográficas do cotovelo e cem do punho e mão esquerdos de crianças, selecionadas por um pesquisador que não realizou as avaliações. Utilizou-se os métodos de Sauvegrain e Greulich e Pyle para determinar a idade óssea. Uma explicação detalhada de cada método foi realizada, e os avaliadores receberam um arquivo com as imagens do estudo. Após três semanas, os exames foram randomizados e os radiogramas reavaliados. Dos cem pacientes do grupo A, 61(61%) eram meninos e 39(39%) meninas. No grupo B, 67(67%) eram meninos e 33(33%) meninas. Quatro análises estatísticas foram utilizadas: correlação; correlação intraclasse; análise pelo gráfico de Bland-Altman; e diferenças entre grupos. **Resultados:** A concordância intra e interobservador entre os grupos foi considerada excelente. **Conclusões:** Apesar da concordância excelente, o grupo A apresentou valor significativamente melhor que o B. As idades biológicas apresentam maior diferença frente as idades cronológicas no grupo A. No grupo B, as idades esqueléticas e cronológicas não apresentam diferença estatística segundo o teste de acurácia. **Level of Evidence III, Cross-Sectional Observational Study.**

Descritores: Criança. Puberdade. Radiografia. Estudo de Avaliação. Determinação da Idade pelo Esqueleto. Variações Dependentes do Observador.

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INTRODUCTION

The practical application of determining skeletal age is widely used in pediatric orthopedics, forensic medicine, and pediatric endocrinology. Correcting length discrepancies between limbs,

deformities, and scoliosis, among other things, requires appropriate knowledge to make an assertive decision about the moment and appropriate intervention, conservative or operative.

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

The study was conducted at Hospital IFOR – Rede D'or, São Bernardo do Campo, SP, Brazil.

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Any growing skeletal structure can be used to assess biological age. When researching the medical literature, we observed that, over the years, different methods were developed for the study and clinical application of this variable, such as that of Oxford (1957), Risser (1958), Sauvegrain et al. (1962), and Greulich and Pyle (1950). Despite the typical application of these systems, there is no definition of which presents a greater degree of trust and agreement among those who use this knowledge. The scarcity of scientific works addressing this topic was decisive for this study. Bone age analysis determines developmental bone growth and maturation in ordered sequences. Any region of the skeleton that has growth is known to be usable in the pediatric population. To properly carry out these assessments, x-rays can be used and must be obtained using an appropriate technique. Such care aims to avoid and resolve errors in determining skeletal age. In this regard, poor positioning of the studied segment is considered the most common error.

Among the different systems, we have the Risser system, which uses the ossification of the iliac process and presents five stages that represent the evolution of the fusion of this structure. The interpretation of this parameter dramatically helps in choosing the appropriate treatment for scoliosis. The lower the Risser stage, the greater the patient's expected remaining growth. It is considered easy to apply and is interpreted using radiography in the anteroposterior view of the spine. On x-rays of the pelvis, other ossification centers can be visualized, such as that of the triradiate cartilage. This is directly related to the peak velocity during growth¹. The Greulich and Pyle method uses radiographs of the bones of the hand and wrist on the left side to study the ossification centers of each anatomical structure in this segment. After this investigation, a score defines the degree of skeletal maturity where the result is correlated with the chronological age of the patient involved.

The systematics of Sauvegrain et al. uses radiographs of the elbow in anteroposterior and lateral views and is more effective when applied to pediatric patients in the first two years after the onset of puberty². The pubertal period is characterized by an increase in growth speed and the emergence of secondary sexual characteristics as stipulated by Tanner's criteria. In girls between nine and 13 years old and boys between 11 and 15, the composition of the elbow is still predominantly cartilaginous. Therefore, any radiographic change is naturally recognized at this age, making supporters of this method consider it more reliable than Greulich and Pyle. In 2005, Dimeglio et al. added three intermediate scores: 3.5 for the trochlea, 6.5 for the olecranon, and 5.5 for the proximal radial epiphysis. According to the authors, this update increased the degree of reliability of this method³. Furthermore, scores in boys and girls have been documented as directly related to growth speed¹.

Naik et al.⁴ demonstrated that Sauvegrain et al.'s method is highly reproducible and allows for agreement between the assessments of three observers.

Given the above, the authors of this study aim to evaluate intra and interobserver agreement using the methods of Sauvegrain et al. and Greulich and Pyle for determining bone age.

MATERIAL AND METHODS

This is an observational, retrospective, and cross-sectional study. The project for this research was submitted for ethical consideration and approved for conduction under CAAE opinion 6,192,391.

Two groups were formed, and 100 radiographic images of the elbow and 100 radiograms of children's left wrist and hand were collected from our service's radiographic image storage bank.

These were selected by a research member who did not participate in the radiographic examination classification process. The adequate quality of the exams, strictly following the inclusion

and non-inclusion criteria determined by the study authors, was decisive in choosing the radiographs.

Inclusion criteria

- Participants between six and 16 years of age;
- Both sexes;
- Patients with a history of trauma to the left elbow, left wrist, and left hand who were assessed for suspected fracture of the upper limb but without evidence of bone injury;
- Patients with elbow radiographs in anteroposterior and lateral views of good technical quality;
- Patients with radiographs of the left wrist and left hand in the anteroposterior view of good technical quality;
- No history of previous fracture, congenital or acquired anatomical changes;
- Signature of the Informed Consent Form (ICF) by parents or guardians.

Exclusion criteria

- Not meeting the inclusion criteria.
- Not signing the TCLE.

Three different researchers applied Sauvegrain et al.'s and Greulich and Pyle's methods: the former analyzed elbow radiographs (group A), and the latter determined bone age by studying radiographic examinations of the left hand and wrist (group B).

Two hundred patients were studied, 100 from group A and 100 from group B. Of the 100 patients in group A, 61(61%) were male and 39 (39%) were female. In group B, 67 (67%) were male and 33 (33%) were female. In terms of age, group A was significantly younger than B, with ages ranging from 73 to 190 months (6 to 15 years), whereas patients in group B were between 73 and 195 months (6 to 16 years) (Table 1 and Figure 1).

Table 1. Mean and standard deviation values or absolute frequencies of ages and sexes of the 200 patients assessed.

Variable		Group A (n = 100)	Group B (n = 100)	p
Sex	Male	61	67	0.462
	Female	39	33	
Age (months)		122.5 ± 30.3	138.7 ± 32.7	< 0.001

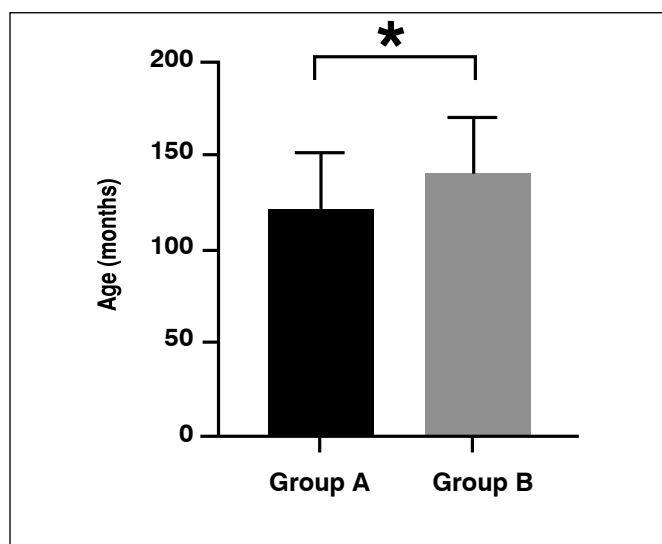


Figure 1. Means and standard deviations of the ages of 200 patients according to groups.

* p < 0.05

A detailed meeting with explanations of each system used in this work was held to minimize interpretation bias. A file with two groups of images was made available to evaluators. Each of the researchers independently and confidentially classified the radiograms. They were instructed not to discuss the results until the study was completed to avoid an erroneous correlation increase.

Each observer had the classifications as a reference, with drawings of all of them and the time needed for them to evaluate the radiographs. After three weeks, the same material was randomized and subjected to a second evaluation following the previously described method. A professional in the field of Medical Statistics carried out the statistical analysis of the results obtained. Four approaches were developed to evaluate precision and accuracy in the study: i) correlation analysis, ii) intraclass correlation (ICC) analysis, iii) analysis using the Bland-Altman graph, and IV) analysis of differences between groups. Each of these analyses complements the information of the others. In contrast, the simple correlation analysis shows the association between two measurements (the two readings of the same image by the same evaluator or the relationship between the measurement and chronological age). Intraclass correlation analysis (which can be used in intra and intraclass analyses) compares the results of two or more evaluators. It considers the general relationship and the specific agreement between the observed numerical values⁵. The Bland-Altman plot presents the relationship between the measurement size and the numerical difference between the results of the methods. This can help to understand whether there is an error pattern between the measurements. Finally, analyses of group differences present the probability that the compared values differ.

Spearman's correlation was used for correlation analyses since the data did not present a normal distribution according to the Shapiro-Wilk test. For the intraclass analysis, we chose to use the two-way mixed-effect model with the option of an absolute agreement relationship (since there is an interest in obtaining equal numerical values between the two measurement methods or between the evaluators). Differences between groups were evaluated using non-parametric Wilcoxon and Friedman tests, depending on the number of groups evaluated. In these assessments, the absolute values of

estimated ages or obtained points were compared between different observers or times, and the difference between observations was assessed if it was significantly different from zero.

Ages between groups were compared using the Mann-Whitney test, and the sex ratio using Fisher's exact test.

The comparison between the correlation coefficients and ICC used the method proposed by Eid et al. (2010).

Diagnostic randomization systems were used to analyze general patterns and accuracy, to not smooth out errors by using mean values.

The scoring data were transformed into chronological age in months, as recommended by the method of Sauvegrain et al.² to evaluate the accuracy of group A.

Statistical analyses and graphs were developed using the R program, considering a significance level of 5% ($\alpha = 0.05$).g

RESULTS

Intraobserver assessment

The data demonstrate that the methods used present excellent internal agreement for groups A and B. This can be observed by:

- Lack of significant differences between the absolute values at the different time points evaluated.
- High significant correlations between.
- Lack of significant difference between the measurement differences and the zero value
- Significant high ICC values.

This pattern of results was constant for both group A (Table 2) and B (Table 3). Importantly, all correlation values were positive and above 0.75, which characterizes them as directly proportional and robust. For ICC, it is possible to use the interpretation proposed by Koo and Li (2016): values below 0, 5 show low agreement, between 0.5 and 0.75, moderate agreement, from 0.75 to 0.9, good agreement, and above 0.9, excellent agreement.

When comparing the ICC correlation coefficients between the groups, it was possible to observe a significant statistical difference with higher values for group A (Table 4).

Table 2. Significance, correlation, and ICC values of 100 patients assessed according to group A by three evaluators at two different time points.

Evaluator	Absolute values*	Correlation between time points		Difference from 0**		ICC	
	p	r	p	p	ICC	p	
1	0.984	0.98	< 0.001	0.901	0.986	< 0.001	
2	0.829	0.98	< 0.001	0.321	0.983	< 0.001	
3	0.821	0.98	< 0.001	0.245	0.988	< 0.001	
General	0.900	0.96	< 0.001	0.869	0.991	< 0.001	

* Comparisons between the absolute values of the two time points evaluated

** Comparison between the differences concerning the two time points and the zero value

Table 3. Significance, correlation, and ICC values of 100 patients assessed according to group B by three evaluators at two different time points.

Evaluator	Absolute values*	Correlation between time points		Difference from 0**		ICC	
	p	r	p	p	ICC	p	
1	0.623	0.97	< 0.001	0.623	0.968	< 0.001	
2	0.279	0.89	< 0.001	0.279	0.913	< 0.001	
3	0.424	0.96	< 0.001	0.424	0.979	< 0.001	
General	0.408	0.98	< 0.001	0.388	0.982	< 0.001	

* Comparisons between the absolute values of the two time points evaluated

** Comparison between the differences concerning the two time points and the zero value

Table 4. Correlation coefficient and intraclass correlation in 200 patients assessed according to groups.

Measure	Group A	Group B	p
Correlation	0.964	0.978	0.061
ICC	0.991	0.982	0.008

INTEROBSERVER ASSESSMENT

The analyses of interclass differences showed that, in both groups, the agreement between the evaluators was relatively high, with no significant difference between the coefficients (Table 5).

Table 5. Interclass correlation coefficient values in two different groups in 200 patients assessed.

Group	ICC	p
A	0.985	< 0.001
B	0.982	< 0.001
p*	0.261	

* p-value associated with the comparison between ICC of different anatomical locations

The accuracy assessment showed a moderate relationship between chronological age and the estimates generated by the assessment of group A (Table 6), with values even significantly different between the estimates and absolute values.

Table 6. Significance, correlation, and ICC values of 100 patients assessed according to estimates and chronological ages for group A.

Evaluator	Absolute values*	Correlation between estimate and actual value		Difference from 0**	ICC	p
	p	r	p	p		
1	< 0.001	0.88	< 0.001	< 0.001	0.721	0.004
2	< 0.001	0.89	< 0.001	< 0.001	0.678	0.017
3	< 0.001	0.83	< 0.001	< 0.001	0.648	0.007
General	< 0.001	0.87	< 0.001	< 0.001	0.669	0.010

* Comparisons between absolute values of chronological age and estimate

** Comparison between the differences concerning the two measurements (estimate and chronological) and the zero value

The Bland-Altman plot for accuracy analysis showed that for group A, the values were far from zero, with a large part of the estimates above the chronological value. This pattern was constant across all evaluators and overall assessment (Figure 2). For group B, it was possible to demonstrate a balanced distribution of ages above and below the chronological variable, with few values outside the confidence interval (Figure 3).

Accuracy concerning group B showed results with strong, simple correlations and excellent ICC. However, in one of the evaluators, there was a significant discrepancy between the differences in estimates and the value of chronological age, reducing the confidence in this result (Table 7).

There was a significant difference in accuracy between groups, with higher values for group B (Table 8).

While both groups presented excellent results in the intraobserver agreement, group A (elbow) presented a significantly better value than group B (wrist), possibly due to using a point scale. In this case, there is variation, and different ages receive the same value. Regarding interobserver agreement, both groups presented excellent values without significant differences.

Accuracy was moderate for group A and excellent for group B, with significant differences (Table 9).

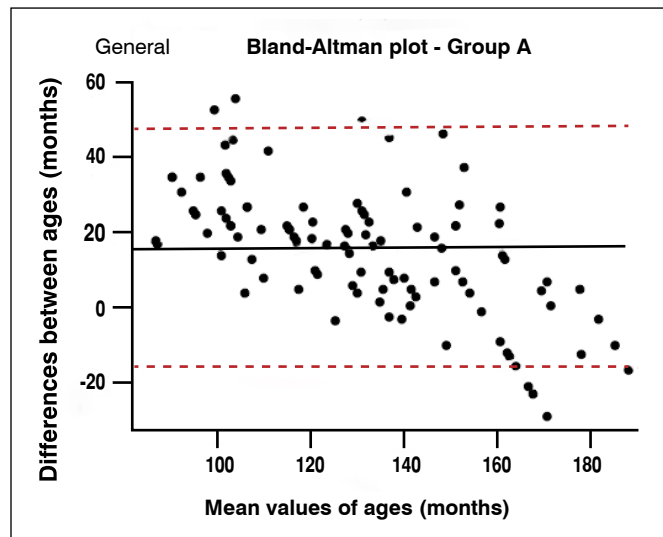


Figure 2. Bland-Altman plot for chronological age accuracy in group A assessments in 100 patients.

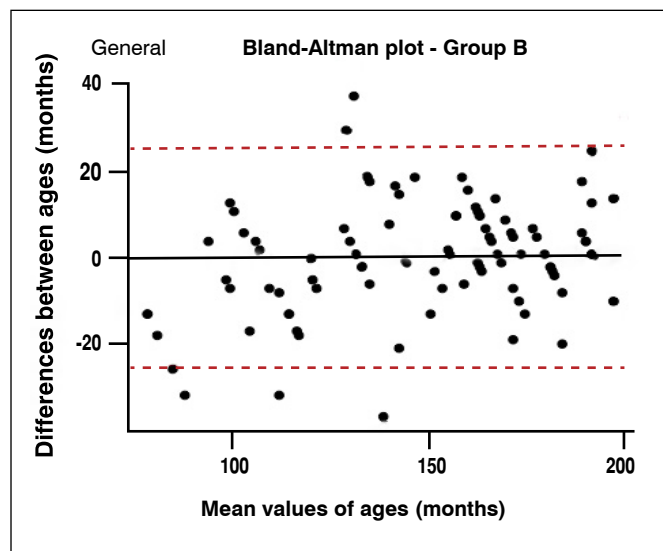


Figure 3. Bland-Altman plot for chronological age accuracy in group B assessments in 100 patients.

Table 7. Significance, correlation, and ICC values of 100 patients assessed according to estimates and chronological ages for group B.

Evaluator	Absolute values*	Correlation between time points		Difference from 0**	ICC	p
	p	r	p	p		
1	0.969	0.94	< 0.001	0.815	0.929	< 0.001
2	0.362	0.89	< 0.001	0.046	0.875	< 0.001
3	0.701	0.93	< 0.001	0.745	0.922	< 0.001
General	0.556	0.94	< 0.001	0.181	0.981	< 0.001

* Comparisons between absolute values of chronological age and estimate

** Comparison between the differences concerning the two measurements (estimate and chronological) and the zero value

Table 8. Accuracy values for two anatomical locations in 200 patients assessed.

Measure	Group A	Group B	P
ICC	0.669	0.982	< 0.001

Table 9. Intra and interobserver agreement values of 100 patients for group A and group B, respectively.

Intraobserver agreement	Group A	Group B	p
Evaluator 1	98.6%	96.8%	0.002
Evaluator 2	98.3%	91.3%	< 0.001
Evaluator 3	98.8%	97.9%	0.009
General	99.1%	98.2%	0.008
Interobserver agreement	Group A	Group B	p
General	98.5%	98.2%	0.261

DISCUSSION

Skeletal maturity can be assessed in several ways, but the most frequently used methods in medical practice are Greulich and Pyle and Tanner-Whitehouse II. The latter has a higher degree of reproducibility but is time-consuming and considered difficult to apply. Roche et al., Acheson et al., and Milner et al. found that the bone ages estimated by the GP method were lower than those by the Tanner method. Waldmann et al., Roche et al., and Fry found opposite results: the values obtained by the Tanner method were higher concerning chronological age in both sexes, being higher for females⁶⁻¹⁰.

We found a study that evaluated 114 normal individuals aged 2 to 21 years, analyzed five methods: cervical vertebra (Hassel-Farman), iliac crest (Risser), hip (Oxford), knee (O'Connor), calcaneus (Nicholson) and applied to EOS. The intra and interobserver agreements were excellent, except concerning the knee method (0.865 – good). The calcaneal and cervical exams were the quickest to perform (average of 17,5 s, 33,4 s per evaluation). While the authors concluded that bone age assessment is possible with all five methods, the method proposed by Hassel-Farman proved to be easier, faster, and more reliable.

The simplicity, convenience, and speed make the Greulich and Pyle method the most commonly used reference standard for assessing skeletal age. This is widely used despite requiring a manual process that is more time-consuming than many other simple radiographic examinations. An atlas in electronic format could be developed to integrate into everyday work.

Critics of the method report a high variability of results to the detriment of defenders who point to greater reproducibility.

Knowing or not knowing chronological age before evaluating bone age radiographs does not differentially affect inter and intraobserver reliability. However, observers will likely interpret the radiograph as normal when chronological age is known.

Alternative atlases – Skeletal Development of the Hand and Wrist: Digital Bone Age Companion (DBAC) (Oxford University Press, New York) – have been developed for skeletal age estimation. However, no work has compared its applicability and comparison to the Greulich and Pyle¹¹.

DBAC is a commercially available application that accompanies a bone age reference book. Precursor images have been digitally edited so that the developmental characteristics of each bone in the left hand and wrist match Greulich and Pyle's standards.

Some authors report a potential bias when employing automated context integration by age and sex using DBAC. For example,

Berst et al.¹² observed that evaluators are more likely to interpret radiography with normal results when chronological age is known. A particular applicability of knowledge regarding bone age is in Legg-Calvé-Perthes disease, in which there is a delay in the skeletal growth of children with it and some cases of arrested skeletal development. Loder et al. document a delay in pelvic and hand bone age in children with this disease. However, for girls, the bone age of the pelvis was similar to the bone age of the hand-wrist¹³. Burwell et al. state that Legg-Calvé-Perthes disease is an acromelic disorder concerning anthropometric measurements¹⁴. The forearm and hand present more significant growth impairment than the arm, which also occurs between the foot and the tibia.

Since Risser's study in 1958, it has been widely used. More than 20 years ago, Goldberg et al. found acceptable interobserver reliability for the Risser stage (Kappa = 0.8). This author's stages are reliable radiographic parameters to assess the growth potential in children with scoliosis. In addition to acceptable interobserver agreement and clinical utility, iliac apophysis stages reflect local biology. The histological stage of iliac apophyseal chondrocytes was also inversely correlated with the Risser stages. This is a helpful indicator of growth potential in adolescent idiopathic scoliosis. The Risser should be used with other tools, such as skeletal age, chronological age, and menarche in girls.

A weakness of the Risser staging system is related to greater progression of the scoliotic curve with greater speed in height gain. While Risser Stage 4 has commonly been considered a point at which curve progression stops, the interruption of curve progression continues until Stage 5.

To improve the correlation of curve progression and the Risser staging system derived from the Sauvegrain method, Demeglio et al. proposed a simplified system that evaluates the morphological development of the olecranon to determine the growth acceleration phase^{2,3}. The simplified olecranon method was validated and proposed for patients with scoliosis to determine skeletal age and peak growth velocity, making Risser stage zero more useful.

Based on our results, Sauvegrain et al.'s method was considered advantageous compared with Greulich and Pyle's.

According to some authors, Sauvegrain et al.'s method is dynamic because the morphological changes apparent on elbow radiographs are straightforward to assess². At the beginning of puberty, the elbow still has a large amount of cartilaginous content, and after two years, the fusion of the ossification centers will be complete. The Greulich and Pyle system does not consider this critical period. This practical method allows radiographic interpretation in less than a minute and is also highly reproducible.

However, this method has limitations, as it is restricted to the period of the pubertal growth spurt and the year before this phase.

The method offers the possibility of dividing puberty into two phases: acceleration and deceleration. The acceleration in growth velocity or upward phase of pubertal growth occurs between 11 and 13 years of skeletal age in girls and between 13 and 15 years in boys. The growth centers of the elbow are open and progressively ossify during this phase. The deceleration in the growth rate or downward phase of pubertal growth occurs between 13 and 16 years of skeletal age in girls and between 15 and 18 years in boys.

In an imaging exam, the individual analysis carried out by humans is expected to add a bias in quantifying and predicting the outcomes based on its assessment. Indeed, a growing number of studies have discussed computerized analysis methods and artificial intelligence in medical practice.

Our study was conducted with three evaluators with the same level of training and qualifications. Evaluators with different levels of training, a longer time interval for carrying out the analyses, and a more significant number of cases evaluated should not modify the

results of the analyses when the classification system is appropriate. This premise supports the idea that an ideal classification system must comply with a series of well-defined criteria, such as being easy to apply, highly reproducible, indicating the appropriate treatment to use, and providing us with a prognosis. It should also allow comparisons between the results obtained from different series to be compared. This fact is observed in our study, which demonstrated excellent inter-rater reliability.

As a limitation of the study, we point out that the sample analyzed did not reach the number of participants determined by the sample calculation.

CONCLUSIONS

While both groups presented excellent results in intraobserver agreement, group A presented a significantly better value than group B, possibly due to using a point scale. In this case, there is the same variation, and different ages receive the same value. Interobserver agreement in both groups showed excellent values without significant differences.

In individuals in group A, biological ages differ more from chronological ages. According to the accuracy test, skeletal and chronological ages do not show a statistical difference in group B.

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IMPACT OF THE COVID-19 PANDEMIC ON EMERGENCY UPPER LIMB SURGERIES IN A QUATERNARY HOSPITAL

IMPACTO DA PANDEMIA POR COVID-19 NAS CIRURGIAS DE URGÊNCIA DO MEMBRO SUPERIOR EM HOSPITAL QUATERNÁRIO

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ABSTRACT

The COVID-19 pandemic has triggered a global crisis in health systems worldwide. Emergency care services have been overloaded, and there have been different changes in the patient's profile and the most frequent diagnoses. The aim of the study was to compare the number of emergency surgeries in the Hand and Microsurgery group of the quaternary hospital (IOT-FMUSP) from March 2020 to February 2022, the pandemic period, with the previous two years, March 2018 to February 2020. Two hundred and seventy-two patients were evaluated, with a mean age of 39.54 ± 17 years (range 1 to 90 years), 12.50% ($n = 34$) women and 87.50% ($n = 238$) men. Between March 2018 and February 2020, 142 (52.21%) emergency upper limb surgeries were performed; between March 2020 and February 2022, 130 surgeries were performed (47.79%). There was a reduction in upper limb surgeries in patients between 26–45 years and blunt injury surgeries. There was also an increase in surgeries in patients over 46, amputations, fractures, re-implantation procedures, and open fracture fixation. **Level of evidence III, Retrospective Comparative Study.**

Keywords: COVID-19. Upper extremity. Orthopedic procedures. Elective surgical procedures. Emergency treatments.

RESUMO

A pandemia por COVID-19 desencadeou uma crise global nos sistemas de saúde ao redor do mundo. Serviços de atendimento de urgência sofreram sobrecarga e diferentes mudanças no perfil do paciente atendido bem como dos diagnósticos mais frequentes. O objetivo do estudo foi comparar o número de cirurgias de urgência, no grupo de Mão e Microcirurgia, do hospital quaternário (IOT-FMUSP) ocorridos de março de 2020 a fevereiro de 2022, período pandêmico; com os dois anos anteriores, de março de 2018 a fevereiro de 2020. No total foram avaliados 272 pacientes com idade média de $39,54 \pm 17$ anos (variação 1 a 90 anos), sendo 12,50% ($n = 34$) de mulheres e 87,50% ($n = 238$) de homens. Entre março de 2018 a fevereiro de 2020 foram realizadas 142 (52,21%) cirurgias de urgência em membro superior e de março de 2020 a fevereiro de 2022, 130 cirurgias foram realizadas (47,79%). Identificou-se redução do número de cirurgias em membro superior em pacientes entre 26-45 anos e do número de cirurgias por ferimentos corto contusos. Além do aumento no número de cirurgias em pacientes acima de 46 anos, número de casos de amputações, fraturas, procedimentos de reimplante e fixação por fraturas expostas. **Nível de evidência III, Estudo retrospectivo comparativo.**

Descritores: COVID-19. Membro superior. Procedimentos ortopédicos. Procedimentos cirúrgicos eletivos. Tratamento de emergência.

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INTRODUCTION

The COVID-19 pandemic generated an overload of health systems and services worldwide in relation to the structural component, need to allocate financial and personal resources and adaptation of safety protocols to minimize the coronavirus spread.^{1,2} Therefore, even when faced with serious situations, patients avoided seeking health services for fear of contracting the virus in these environments.³

The demand for orthopedic care decreased during phases of greater restrictions. This reduction affected mainly the number of elective surgeries with a large number of procedures postponed or canceled, which caused possible harm to patients' quality of life and increased the challenge of managing waiting lists.⁴ Consequently, there was an increase in the proportion of

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The study was conducted at Universidade de São Paulo, Faculdade de Medicina de Ortopedia e Traumatologia, Hospital das Clínicas, São Paulo, SP, Brazil. Correspondence: Erick Yoshio Wataya. Praça Roberto Gomes Pedrosa, Portão 1, São Paulo, SP, Brazil, 05653-070. erick.wataya@gmail.com

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emergency orthopedic surgeries, and the most serious cases in health services needed to be prioritized.⁵

Although there was a reduction in the absolute number of orthopedic consultations in the emergency setting and of the volume of surgeries performed, other services faced a real increase in demand. This was due to significant changes promoted by Brazilian states in the hospital organization, aiming to free up beds for patients with COVID-19.^{6,7} In other words, while in some areas the activity decreased, in others there was a considerable increase in pressure on orthopedic medical services.

Changes in the service model also emerged during this period around the world, such as the “single service” concept. In this model, all healthcare professionals would be concentrated in the same physical space, including with the presence of a surgical arch in the plastering room, which emerged as a strategy to promote more effective care provision, reducing unnecessary patient traffic within the hospital.⁸

Although there are some similarities in the epidemiological profile of worldwide patients with upper limb injuries who seek emergency services, the types of accidents that result in these injuries may vary according to each country’s economic profile. In Brazil, a country considered underdeveloped, there is a predominance of injuries due to occupational accidents, traffic accidents, and domestic accidents. In developed countries, there is a predominance of injuries in sporting activities, falls, and occupational traumas.^{9,10}

These upper limb injuries requiring urgent surgical procedures presented important changes in the epidemiological profile during the COVID-19 pandemic, as there was a reduction in the number of elective procedures¹¹ in some specialized centers across the globe. A change in the cause of injuries was also noted, with a predominance of acute traumatic injuries caused by domestic accidents, handiwork, and serious infections.¹²

In Brazil, it is believed that the number of emergency surgeries, mainly related to severe upper limb trauma, which result in fractures, dislocations, and amputations, for example, has also decreased due to low exposure to risk factors.

The *Hospital das Clínicas* of the *Faculdade de Medicina* [School of Medicine] of *Universidade de São Paulo* [University of São Paulo] (HC-FMUSP) is a quaternary hospital, with specialized care in trauma and complex cases.

The objective of the study is to evaluate the COVID-19 pandemic effect on the number of urgent upper limb surgeries, performed by the Hand and Microsurgery group, and the trauma patients’ epidemiological profile taking into consideration the pre-pandemic period from March 2018 to February 2020 and the pandemic period between March 2020 and February 2022.

METHODS

This is a cross-sectional observational study, with retrospective data collection from medical records of patients treated at the Institute of Orthopedics and Traumatology of Hospital das Clínicas of FMUSP (IOT-HC-FMUSP), a reference in the complex upper limb trauma care. This study was approved by the Research Ethics Committee (IOT-HC-FMUSP) under protocol number 4.914.423.

Patients of both sexes and of any age, with upper limb injuries that required emergency surgery, such as fractures/dislocations, neurovascular injuries, infections and amputations were included. Patients with incomplete data, data prior to the period, and with a diagnosis that did not involve the upper limb were excluded.

The clinical variables were gender, age, injury side, injury location, injury diagnosis, injury type, trauma mechanism, procedure performed in the emergency room, and need for re-approach during hospitalization. For the dependent variable, the pre-COVID-19 pandemic (patients seen between March 2018 and February 2020)

and the pandemic period (patients seen between March 2020 and February 2022) were considered.

Statistical analysis

The database was created using Excel version 2016. For statistical analyses, Stata 13.0 software (Stata Corp LP, College Station, TX, USA) was used. Statistical significance was established using a cutoff value of $p < 0.05$. Descriptive analyses are presented in absolute numbers (n) and relative frequencies (%), together with the mean, standard deviation, and confidence interval (95% CI). One used the Chi-square test (χ^2) or Fisher’s exact test in the bivariate analysis.

RESULTS

The sample consisted of 272 patients with a mean age of 39.54 ± 17 years (range 1 to 90 years), with 12.50% (n = 34) of women and 87.50% (n = 238) of men. Between March 2018 and February 2020, 142 (52.21%) emergency orthopedic upper limb surgeries were performed, and between March 2020 and February 2022, 130 surgeries (47.79%).

Additional data on the prevalence of injuries and surgeries in the pre-COVID-19 pandemic period and during the pandemic are presented in Table 1.

Table 1. Prevalence of surgeries according to epidemiological data and upper limb injury data, comparing the pre-COVID-19 pandemic period with the pandemic.

Variable	Total	Pre-pandemic period	Pandemic	p
Gender				0.409
Female	34 (12.50 %)	20 (14.08 %)	14 (10.77 %)	
Male	238 (87.50 %)	122 (85.92 %)	116 (89.23 %)	
Age				0.016
0 to 25	59 (21.69 %)	28 (19.72 %)	31 (23.85 %)	
26 to 45	112 (41.18 %)	70 (49.30 %)	42 (32.31 %)	
46+	101 (37.13 %)	44 (30.99 %)	57 (43.85 %)	
Injury side				0.395*
Right	113 (41.54 %)	58 (40.85 %)	55 (42.31 %)	
Left	157 (57.72 %)	84 (59.15 %)	73 (56.15 %)	
Bilateral	2 (0.74 %)	0 (0.00 %)	2 (1.54 %)	
Injury location				0.225*
Finger	223 (81.99 %)	117 (82.39 %)	106 (81.54 %)	
Hand	31 (11.40 %)	13 (9.15 %)	18 (13.85 %)	
Wrist	4 (91.47 %)	1 (0.70 %)	3 (2.31 %)	
Forearm	8 (2.94 %)	6 (4.23 %)	2 (1.54 %)	
Arm	2 (0.74 %)	1 (0.70 %)	1 (0.77 %)	
Hand and finger	3 (1.10 %)	3 (2.11 %)	0 (0.00 %)	
Wrist and finger	1 (0.37 %)	1 (0.70 %)	0 (0.00 %)	
Injury diagnosis				0.163*
Fracture	88 (32.35 %)	49 (34.51 %)	39 (30.00 %)	
Amputation	131 (48.16 %)	64 (45.07 %)	67 (51.54 %)	
Laceration-contusion injury	25 (9.19 %)	9 (6.34 %)	16 (12.31 %)	
Infection	9 (3.31 %)	6 (4.23 %)	3 (2.31 %)	
Necrosis	4 (1.47 %)	3 (2.11 %)	1 (0.77 %)	
Tendon injury	15 (5.51 %)	11 (7.75 %)	4 (3.08 %)	
Injury type				0.000*
Laceration-contusion injury	135 (49.63 %)	87 (61.27 %)	48 (36.92 %)	

Table 1. Prevalence of surgeries according to epidemiological data and upper limb injury data, comparing the pre-COVID-19 pandemic period with the pandemic.

Variable	Total	Pre-pandemic period	Pandemic	p
Crush injury	19 (6.99 %)	6 (4.23 %)	13 (10.00 %)	
Amputation	80 (29.41 %)	34 (23.94 %)	46 (35.38 %)	
Infection	13 (4.78 %)	9 (6.34 %)	4 (3.08 %)	
Fracture	22 (8.09 %)	5 (3.52 %)	17 (13.08 %)	
Tendon injury	3 (1.10 %)	1 (0.70 %)	2 (1.54 %)	
Mechanism				0.156*
Injury	196 (72.06 %)	98 (69.01 %)	98 (75.38 %)	
Fall	42 (15.44 %)	20 (14.08 %)	22 (16.92 %)	
Bite	4 (1.47 %)	3 (2.11 %)	1 (0.77 %)	
Crush injury	25 (9.19 %)	18 (12.68 %)	7 (5.38 %)	
Ring degloving	2 (0.74 %)	2 (1.41 %)	0 (0.00 %)	
Post-operative necrosis	2 (0.74 %)	1 (0.70 %)	1 (0.77 %)	
Re-implantation attempt	1 (0.37 %)	0 (0.00 %)	1 (0.77 %)	
Procedures performed in the emergency room				0.005
Fixation	52 (19.12 %)	22 (15.49 %)	30 (23.08 %)	
Surgical cleaning	23 (8.46 %)	13 (9.15 %)	10 (7.69 %)	
Regularization	46 (16.91 %)	22 (15.49 %)	24 (18.46 %)	
Re-implantation	55 (20.22 %)	21 (14.79 %)	34 (26.15 %)	
Tenorrhaphy	25 (9.19 %)	13 (9.15 %)	12 (9.23 %)	
Nail bed repair	13 (4.78 %)	12 (8.45 %)	1 (0.77 %)	
Neurorrhaphy	2 (0.74 %)	1 (0.70 %)	1 (0.77 %)	
Revascularization**	40 (14.71 %)	29 (20.42 %)	11 (8.46 %)	
Flap***	15 (5.51 %)	9 (6.34 %)	6 (4.62 %)	
Graft	1 (0.37 %)	0 (0.00 %)	1 (0.77 %)	
Need for reapproach				0.084
No	256 (94.12 %)	137 (96.48 %)	119 (91.54 %)	
Yes	16 (5.88 %)	5 (3.52 %)	11 (8.46 %)	

* Fisher's exact test, ** Revascularization + neurorrhaphy + tenorrhaphy/ Fixation + neurorrhaphy/ Tenorrhaphy + neurorrhaphy + revascularization/ Fixation + tenorrhaphy/ Regularization + neurorrhaphy + fixation + tenorrhaphy/ Nail bed repair + fixation + revascularization + regularization/ Fixation + tenorrhaphy + neurorrhaphy/ Fixation + neurorrhaphy; ***Revascularization + ulnar neurorrhaphy + tenorrhaphy / Re-implantation + tenorrhaphy + neurorrhaphy / Tenorrhaphy+ flap / Surgical cleaning + db + fixation with KW / fixation; regularization; tenorrhaphy + neurorrhaphy / Revascularization + neurorrhaphy + tenorrhaphy + fixation.

There were statistical differences in the performance of surgeries during the pandemic considering age ($p = 0.016$), injury type ($p = 0.016$) and in relation to surgical procedures performed in the emergency room ($p = 0.016$).

There was a reduction in the number of surgeries during the pandemic in patients aged between 26 and 46 years old and an increase in the number of surgeries in patients over 46 years old. Regarding the injury type, it is possible to observe a reduction in the number of surgeries due to laceration-contusion injuries and infections, an increase in the number of crush injuries, amputations, fractures, and tendon injuries.

Regarding surgical procedures performed in the emergency room, during the pandemic there was an increase in the number of regularizations, re-implantations and fixation/osteosynthesis of fractures.

Figure 1 shows the prevalence distribution of upper limb surgeries according to the injury type comparing the pre-pandemic period with the pandemic period. ($p = 0.016$), with an increase in cases of crush injuries, amputations, and fractures.

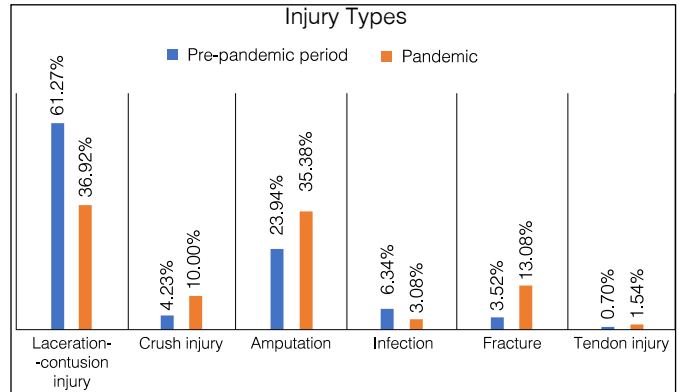


Figure 1. Prevalence of the type of upper limb surgical injuries comparing the pre-pandemic period with the pandemic period.

Figures 2 and 3 show the number of emergency surgeries month by month during the pre-pandemic period and during the pandemic period.

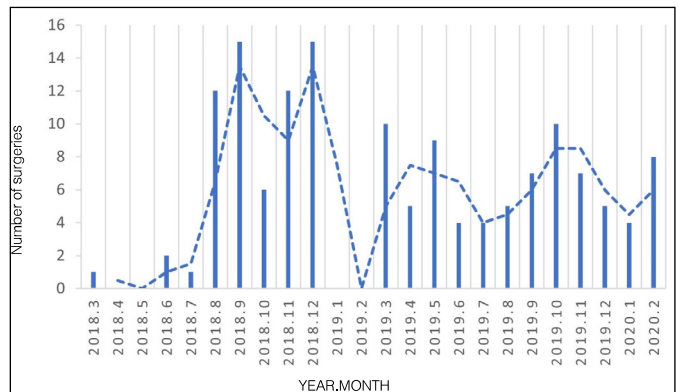


Figure 2. Total number of surgical procedures performed in the pre-COVID-19 pandemic period.

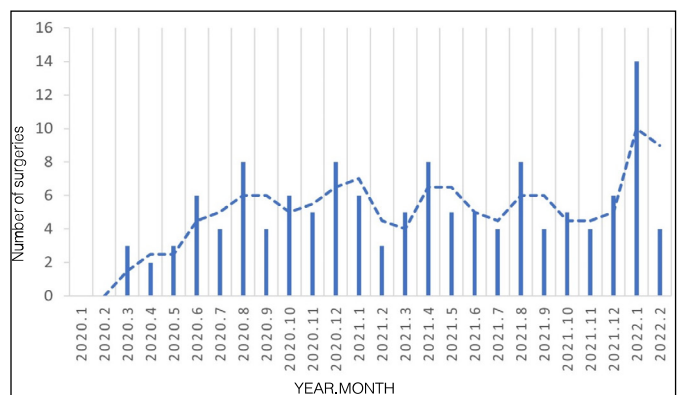


Figure 3. Total number of surgical procedures performed during the COVID-19 pandemic.

DISCUSSION

When comparing the pre-pandemic periods with the pandemic period, a decrease in the total number of emergency orthopedic upper limb surgeries was observed. During the first period, 142 surgeries (52.21%) were performed, while in the second period there were 130 surgeries (47.79%). This reduction in the number of surgeries during the pandemic may be related to several factors,

which include mobility restrictions imposed by social isolation measures, as well as greater awareness about seeking medical care only for essential cases.¹³ Similar studies have also reported decrease in the number of surgical procedures, with values ranging from 32% to 69% in emergency sectors.^{14,15,16}

There was a significantly higher prevalence of hand injuries in male patients during the pandemic and also before it, with ages ranging between 26 and 45 years. This trend was also identified by other studies,^{12,15} suggesting that males are at increased risk of suffering hand injuries, regardless of the pandemic context.

At the global level, services with surgical specialties have undergone a significant reduction in admissions and surgical volume. Blum et al. showed that there was a reduction not only in the number of elective consultations, but there was also a drop in the number of trauma surgeries (around 21.2% to 66.7%) and in the number of elective surgeries (33.3% to 100%) during the pandemic.¹⁷ In this study, emergency procedures showed an about 4.5% reduction. Relaxation of restrictive measures in the final pandemic period and the mass population vaccination may have favored the return to work and sports, which pose a risk of new accidents in the upper limb requiring urgent surgery; besides, accidents may also happen at home.

Regarding the injury mechanism, no significant differences were identified. Injuries following falls remained the most common injury type in both periods.

The performance of fixation procedures continued to predominate in urgent situations, even more so during the pandemic, compatible with the period of relaxation of restrictive measures. An increase in re-implantation cases and a reduction in the need for revascularization were also observed. Lim et al., in their systematic review, found a reduction in the total number of hand injuries and fractures, but, on the other hand, noted an increase in domestic accident injuries and occupational accidents.¹⁸ In this period of social isolation, the increase in the number of domestic accidents with circular saws may have led to more cases of amputations requiring re-implantation, as seen in Table 1.

There was a statistically significant increase in fractures that required urgent intervention for fixation. Saleh et al. also noted an increase in the number of emergency surgeries required for cleaning, surgical debridement, and extremity fixation.¹⁹

The analysis of the number of surgeries month by month during the pandemic (Figure 3) in comparison with the main events that occurred²⁰ in the same period (Figure 4) already demonstrates a low number of surgeries even before the World Health Organization declared the pandemic, in March 2020. With the beginning of the quarantine decreed in the state, some urgent cases occurred, but in smaller numbers than usual, perhaps due to domestic accidents. The beginning of the relaxation of restrictive measures in June 2020 coincides with an increase in emergency surgeries; patients were more exposed to risky situations at work, with a propensity to suffer injuries from circular saws and industrial machines, for example. From then on, the number of emergency surgeries remained relatively constant month by month. From December 2021 to January 2022, when a large part of the population was already vaccinated with at least one dose of the vaccine, there was a large increase in emergencies, reaching 14 cases in one month. At the end of January and beginning of February 2022, when the country again experienced a new outbreak with an increase in deaths from COVID-19, there was a new drop in emergency upper limb surgeries.

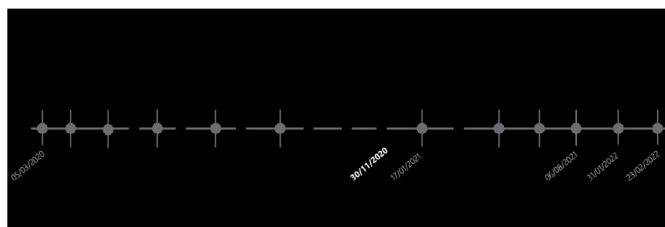


Figure 4. Timeline of the COVID-19 pandemic in the state where the study was conducted

CONCLUSION

The pandemic reduced the use of public health services in Brazil. However, emergency care continued with changes in relation to the patient's age, injury type and surgical procedures performed during the pandemic.

The social restriction and relaxation measures in force during the COVID-19 pandemic also influenced the number of emergency surgeries during this period.

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PREGABALIN AS A PREOPERATIVE ADJUVANT IN PATIENTS WITH CARPAL TUNNEL SYNDROME

AÇÃO DA PREGABALINA COMO ADJUVANTE NO PRÉ OPERATÓRIO EM PACIENTES COM SÍNDROME DO TÚNEL DO CARPO

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ABSTRACT

Objective: To evaluate the pregabalin adjuvant effect in patients with carpal tunnel syndrome (CTS) surgically treated, analyzing postoperative pain and the incidence of complex regional pain syndrome (CRPS). **Methods:** Outpatient surgical candidates with CTS were selected and followed for 12 months, divided into three groups. The Control Group received a placebo, the Pregabalin 75mg Group received a daily dose, and the Pregabalin 150mg Group received a daily dose of the medication. Patient progress was evaluated using the visual analog scale (VAS) for pain and the DN4 neuropathic pain score before surgery, one month and three months after. **Results:** The administration of pregabalin to surgical patients with CTS did not demonstrate significant differences in immediate postoperative pain relief. Additionally, there were no statistically significant variations in the incidence of complications, such as CRPS, among the groups. **Conclusion:** This study did not show a significant impact of pregabalin on postoperative pain relief or the reduction of CRPS incidence in patients undergoing surgery for CTS. These results suggest that pregabalin might not be an effective adjuvant in these surgical situations. **Level of evidence II (Oxford), Prospective Comparative Study.**

Keywords: Carpal Tunnel Syndrome. Surgical Procedures. Operative Pregabalin. Pain.

RESUMO

Objetivo: Avaliar o efeito adjuvante da pregabalina em pacientes com síndrome do túnel do carpo (STC) tratados cirurgicamente, analisando a dor pós-operatória e a incidência da síndrome da dor complexa regional (SDCR). **Métodos:** Foram selecionados pacientes com acompanhamento ambulatorial e indicação de tratamento cirúrgico para STC, sendo acompanhados ao longo de 12 meses e divididos em três grupos. O Grupo Controle recebeu placebo, o Grupo Pregabalina 75 mg tomou uma dose diária da medicação citada e o Grupo Pregabalina 150 mg também recebeu uma dose diária da medicação, em maior quantidade. A evolução dos pacientes foi avaliada mediante aplicação da escala visual analógica de dor (EVA) e escore de dor neuropática DN4 antes da cirurgia, um mês e três meses após essa. **Resultados:** A administração de pregabalina em pacientes cirúrgicos com STC não demonstrou diferenças significativas no alívio da dor pós-operatória imediata. Além disso, não houve variações estatisticamente significativas na incidência de complicações, como a SDCR, entre os grupos. **Conclusão:** Este estudo não evidenciou um impacto significativo da pregabalina no alívio da dor pós-operatória ou na redução da incidência da SDCR em pacientes submetidos a cirurgia para STC. Estes resultados sugerem que a pregabalina pode não ser um adjuvante eficaz nessas situações cirúrgicas. **Nível II de Evidência (Oxford), Estudo prospectivo comparativo.**

Descritores: Síndrome Do Túnel Do Carpo. Procedimento Cirúrgico. Pregabalina. Dor.

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The study was conducted at Grupo da Mão e Microcirurgia do Departamento de Ortopedia e Traumatologia "Pavilhão Fernandinho Simonsen", Irmandade Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil.
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INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common compressive upper limb neuropathy, affecting approximately 4% of the general population, and it is more prevalent in females and between 45 and 60 years of age.¹ The clinical status is characterized by pain and paresthesia in the territory of the median nerve, with an insidious onset and, in the most severe cases, loss of strength and atrophy of the thenar muscles is observed.² The carpal tunnel is an osteofibrous, inelastic canal, whose roof is the transverse carpal ligament, and nine tendons and the median nerve pass through it.

Surgical treatment for CTS consists of releasing the transverse ligament, leading to the nerve decompression.³ Despite being a widely performed procedure in hand surgery, with high success rates, surgery for treating CTS may present unsatisfactory results for the patient. Many complications cannot be prevented, such as the development of chronic postoperative pain.⁴

Complex regional pain syndrome (CRPS) is divided into CRPS type 1 (formerly known as reflex sympathetic dystrophy) and CRPS type 2 (formerly known as causalgia) and is a chronic pain condition with neuropathic characteristics, generally of disproportional intensity to the nociceptive stimulus. Presence of vasomotor changes may or may not be associated.⁵ There is a predominance in females and there is no evidence that risk factors predispose to the CRPS development, although immobilization for a prolonged period of time may act as a predisposing factor. Its incidence after carpal tunnel decompression surgery, regardless of the technique, is around 8%⁶ and, in some series of cases, it corresponds to half of the complications after this type of procedure.⁷

Recently, with the understanding of the central sensitization processes that lead to chronic pain, drugs from the gabapentinoid class, especially pregabalin, started being studied in order to prevent CRPS. Most of studies found in the literature analyze the reduction in pain scores and opioid consumption in knee surgeries when pregabalin was used preemptively.^{8,9} However, there is still no consensus on the dose or the length of time these medications should be used. The objective of this study is to evaluate the effectiveness of pregabalin as a preoperative adjuvant in carpal tunnel decompression surgeries.

MATERIALS AND METHODS

In this study, patients with a diagnosis of CTS, treated at the outpatient clinic of the *Grupo da Mão e Microcirurgia* at *Santa Casa de Misericórdia de São Paulo*, from June 2022 to June 2023, were evaluated and followed prospectively. The research was conducted upon approval by the Ethics and Research Committee of the aforementioned institution, following resolution 196/96 (CAAE: 69653223.9.0000.5479), and all patients signed the Informed Consent Form (ICF).

These patients were randomly subdivided into three groups:

- Patients who received placebo during the three weeks before surgery.
- Patients who received 75 mg/day of pregabalin during the three weeks before surgery.
- Patients who received 150 mg/day of pregabalin during the three weeks before surgery.

Patients of both sexes, aged between 40 and 70 years, who received a confirmed diagnosis of CTS using any of the following methods were included in this study: ultrasound, electroneuromyography, or clinical examination. In this study, surgical median nerve decompression was performed by the same surgeon, using the mini-incision surgical technique. Patients who had previous

surgeries on the same hand, other associated neuropathies, previous use of gabapentinoids, and a history of CRPS were excluded from the study.

The data were collected and analyzed by the same researcher, through the use of the Pain Visual Analogue Scale (VAS) and evaluation of the DN4 questionnaire for neuropathic pain. All patients adopted the same follow-up protocol. Patients started being given the medication or placebo three weeks before the procedure, and assessments were made in the immediate postoperative period, as well as one month and three months after surgery. All patients used an orthosis for immobilization until the surgical wound stitches were removed, which occurred two weeks after surgery. In addition, they received simple analgesia with nonsteroidal anti-inflammatory drugs (NSAIDs) and tramadol for pain relief when necessary in the first two weeks. They were also monitored by the occupational therapy team until the last assessment.

Patients were assessed before the procedure, one month and three months after surgery. The assessed quantitative characteristics were described according to groups using summary measures (means, standard deviations, medians, and quartiles) and compared between groups using analysis of variance (ANOVA) or Kruskal-Wallis test, and the qualitative characteristics were described according to groups using absolute and relative frequencies, with verification of the association by the likelihood ratio test.¹⁰

Pain scores were described according to groups throughout the moments evaluated using summary measures and compared between groups and moments using generalized estimating equations (GEE) with normal marginal distribution and identity link function, assuming a first-order autocorrelation coefficient (AR(1)) between the assessment moments.¹¹ The analyses were followed by Bonferroni multiple comparisons¹² to verify between which groups and moments the differences occurred.

The analyses were performed using IBM-SPSS for Windows version 22.0 and tabulated using Microsoft-Excel 2013; the tests were carried out with a 5% significance level.

RESULTS

Of the 45 patients diagnosed with CTS and indicated for surgical treatment, 18 patients composed group 1 (placebo during the three weeks

before surgery), 15 patients formed group 2 (pregabalin 75 mg/day during the three weeks before surgery), and 13 patients formed group 3 (pregabalin 150 mg/day during the three weeks before surgery).

Four patients were excluded from the study due to previous use of gabapentin, loss of postoperative follow-up, and non-adherence to the medication proposed before surgery.

Both VAS and DN4 showed a statistically similar average behavior of groups throughout the assessment moments (p Interaction > 0.05); VAS showed a difference between groups regardless of the assessment moment (p Group = 0.007), and VAS and DN4 showed differences on average throughout the assessment's moments regardless of group (p Moment < 0.05) (Table 1).

The VAS score was higher in the Pregabalin 75 mg group than in the placebo group regardless of the assessment moment (p = 0.006), and both VAS and DN4 decreased from the preoperative period to the other moments, regardless of the group (p < 0.001). With this kind of statistical result evaluation, it became clear that, regardless of the group, the patients presented similar results with a reduction in VAS and an improvement in DN4 in postoperative assessments. Furthermore, the occurrence of CRPS was not evident until three months after surgery in any of the three groups (Table 2).

The other demographic data can be seen in Table 3.

Table 1. Description of pain scores according to groups throughout the assessment moments and results of comparisons.

Variable/Moment	Group			P Grup	P moment	P Interaction
	Placebo	Pregabalin 75 mg	Pregabalin 150 mg			
VAS				0.007	<0.001	0.166
Pre-op						
Mean ± SD	7.9 ± 2	8.8 ± 1.8	8.4 ± 1.5			
Median (p25; p75)	8 (6.3; 10)	10 (8; 10)	9 (7; 10)			
1 month						
Mean ± SD	1.7 ± 2.4	2.9 ± 3.8	2.1 ± 1.8			
Median (p25; p75)	0 (0; 4,8)	0 (0; 6,5)	2 (0; 4)			
3 months						
Mean ± SD	0.4 ± 0.9	3.5 ± 2.8	0.8 ± 1.5			
Median (p25; p75)	0 (0; 0)	3 (1; 6,5)	0 (0; 2)			
DN4				0.375	<0.001	0.456
Pre-op						
Mean ± SD	5.3 ± 2.1	6.2 ± 1.5	6 ± 2.4			
Median (p25; p75)	4.5 (4; 7)	7 (5; 7,5)	7 (5; 8)			
1 month						
Mean ± SD	1.3 ± 1.3	1.5 ± 2	1.8 ± 2			
Median (p25; p75)	1 (0; 2)	1 (0; 2,5)	1 (0; 4)			
3 months						
Mean ± SD	0.6 ± 1.1	1.6 ± 2	0.9 ± 1.3			
Median (p25; p75)	0 (0; 1)	1 (0; 3)	0 (0; 2)			

EEG with normal distribution and identity connection function, assuming correlation matrix AR(1) between the moments

Table 2. Score comparison

Variable	Comparison	Average difference	Standard error	p	CI (95%)	
					Inferior	Superior
VAS	Placebo – Pregabalin 75 mg	-1.74	0.56	0.006	-3.09	-0.39
	Placebo – Pregabalin 150 mg	-0.45	0.59	>0.999	-1.86	0.97
	Pregabalin 75 mg – Pregabalin 150mg	1.29	0.62	0.110	-0.19	2.78
	Pre-op – 1 month	6.13	0.42	<0.001	5.12	7.14
	Pre-op – 3 months	6.76	0.48	<0.001	5.62	7.90
	1 month – 3 months	0.63	0.42	0.406	-0.38	1.64
DN4	Pre-op – 1 month	4.27	0.26	<0.001	3.66	4.89
	Pre-op – 3 months	4.78	0.32	<0.001	4.00	5.55
	1 month – 3 months	0.51	0.26	0.146	-0.11	1.12

Multiple Bonferroni Comparisons

Table 3. Epidemiological data.

Variable	Group			Total (N=40)	p
	Placebo (N=16)	Pregabalin 75 mg (N=13)	Pregabalin 150 mg (N=11)		
Age (years)					0.162**
Mean \pm SD	61 \pm 14.8	51.5 \pm 8.2	56.2 \pm 14.7	56.6 \pm 13.3	
Median (p25; p75)	60 (47.5; 75.8)	54 (47; 57.5)	52 (41.5; 71.5)	55 (41; 69)	
Gender					0.088
Female	15 (93.8)	12 (92.3)	7 (63.6)	34 (85)	
Male	1 (6.3)	1 (7.7)	4 (36.4)	6 (15)	
Side					0.031
Right	7 (43.8)	5 (38.5)	1 (9.1)	13 (32.5)	
Left	4 (25)	5 (38.5)	1 (9.1)	10 (25)	
Bilateral	5 (31.3)	3 (23.1)	9 (81.8)	17 (42.5)	
Time of symptoms (years)					0.907£
Mean \pm SD	2.7 \pm 2.5	2.6 \pm 2.4	2.5 \pm 2.5	2.6 \pm 2.4	
Median (p25; p75)	2 (1; 3)	2 (1.5; 3)	2 (0.7; 3)	2 (1; 3)	

Likelihood ratio test; ** Unpaired Student's T test; £ Kruskal-Wallis test

DISCUSSION

Pregabalin acts to modulate calcium channels present in neurons, showing proven effects as an antiepileptic and anxiolytic agent, in addition to acting as an analgesic in situations of neuropathic pain.¹³ These results supported the inclusion of such substance in this study, with the aim of reproducing and analyzing its effects on the postoperative period of patients with an already established diagnosis of CTS.

All assessed patients were already candidates for surgical treatment for CTS due to failure of clinical treatment or due to muscular hypotrophy in the thenar region, and, although gabapentinoids are approved for the treatment of chronic neuropathic pain, this medication has not yet been proven as being effective in managing CTS postoperative pain.

In a study carried out by Sadatsun,¹⁴ it was found that the use of gabapentin, an anticonvulsant with similar action to pregabalin, in a single dose of 600 mg, one hour before anesthetic induction, did not present significant results in patients with CTS. A result similar to that found in this study. Even using the medication for one month throughout the preoperative period, few patients reported improvement in symptoms before surgery with the use of the medication, not avoiding the procedure.

Other studies, however, demonstrate that the use of gabapentinoids allowed the reduction of the use of other medications, such as opioids, in the management of major surgical procedures,⁸ but this variable was not evaluated in this study, since the assessed patients maintained regular use of analgesics in postoperative follow-up.

Another aspect that must be taken into consideration in this study is that all patients already had surgical indications before the medication was administered and, as there was no statistical difference between the control group and the medication groups, we raised the hypothesis that patients who have already more severe CTS, or are refractory to conservative treatment, did not obtain any advantages when operated in association with medication, with the improvement being attributed to the surgical procedure itself. Another aspect that requires consideration in this study is that all patients already had surgical indications before the medication administration. As no statistically significant difference was found between the control group and the groups that received the medication under analysis, this situation raises the hypothesis that patients who already have a more severe CTS condition and who do not respond well to non-surgical treatment do not seem to benefit from concomitant treatment between pregabalin and the surgical procedure, with the improvement in the condition being mainly attributed to the surgery.

Regarding CRPS, although patients did not manifest this condition during the study period, the literature reports an incidence of approximately 8% of this condition in patients with CTS. Therefore, a study with a larger sample of patients could reveal other outcomes.

CONCLUSION

During the period assessed, no significant difference was found with the use of pregabalin in relation to the pain experienced by the patient upon application of the VAS and DN4, nor in terms of the occurrence of CRPS.

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COMPARISON BETWEEN FLEXIBLE NAILING AND EXTERNAL FIXATION, METHODS TO STABILIZE FEMORAL SHAFT FRACTURES IN THE IMMATURE SKELETON: A SYSTEMATIC REVIEW AND META-ANALYSIS

COMPARAÇÃO ENTRE OS MÉTODOS DE ESTABILIZAÇÃO DAS FRATURAS DIAFISÁRIAS DO FÊMUR NO ESQUELETO IMATURO, ENTRE HASTE FLEXÍVEIS E FIXADOR EXTERNO: REVISÃO SISTEMÁTICA E METANÁLISE

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ABSTRACT

Flexible intramedullary nailing and external fixation have become the main methods to surgically treat femur fractures in children. This study aimed to search the current literature and evaluate the clinical and radiographic results of surgical treatment by comparing these methods and investigating their associated complications. This systematic review was carried out following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) recommendations. Searches were carried out on the PubMed, Embase, and Web of Science databases. The search for journals in these databases was carried out from January 2023 to August 2023, retrieving 695 studies. This systematic review included 11 articles, which encompassed 718 patients who underwent surgical external fixation and flexible nailing. The most frequently observed complications referred to late or malunion, superficial and deep infections, skin irritation, angular deformity, and length discrepancy between lower limbs. Both methods of stabilization of pediatric femoral fractures can provide good clinical and radiographic results. However, the choice of treatment with flexible nails is certainly more valid and has greater acceptance than external fixation. **Level of Evidence III, Systematic Review.**

Keywords: Femur Fractures. Child. Fracture Fixation. External Fixators. Intramedullary Fracture Fixation. Systematic Review.

RESUMO

Para o tratamento cirúrgico das fraturas do fêmur em crianças, as hastes intramedulares flexíveis e os fixadores externos tornaram-se os principais métodos utilizados. Este estudo teve como objetivo pesquisar a literatura atual e avaliar os resultados clínicos e radiográficos do tratamento cirúrgico confrontando estes métodos e investigar as complicações associadas. Trata-se de uma revisão sistemática, realizada segundo as recomendações PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis), cujas buscas foram realizadas nas bases de dados (PubMed, Embase e Web of Science). A busca dos periódicos nessas bases de dados foi realizada entre janeiro de 2023 e agosto de 2023, e foram encontrados 695 estudos. Um total de 11 artigos foram incluídos nesta revisão sistemática, que engloba 718 pacientes que foram operados pelas técnicas cirúrgicas de fixação externa e haste flexível. As complicações mais frequentemente observadas foram a consolidação tardia ou viciosa, infecção superficial e profunda, irritação da pele, deformidade angular e discrepância no comprimento entre os membros inferiores. Verificou-se que ambos os métodos de estabilização das fraturas femorais pediátricas podem proporcionar bons resultados clínicos e radiográficos. No entanto, a escolha do tratamento com hastes flexíveis é certamente mais válida e tem maior aceitação, comparada à fixação externa. **Nível de evidência III, Revisão Sistemática.**

Descritores: Fraturas do Fêmur. Criança. Fixação de Fratura. Fixadores Externos. Fixação Intramedular de Fraturas. Revisão sistemática.

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INTRODUCTION

The treatment of pediatric femoral shaft fractures (FSF) is based on injury pattern and patients' age.¹

The American Academy of Orthopaedic Surgeons set guidelines updated in 2015² that provide reliable evidence to manage these lesions based on three age subgroups. For fractures in children aged up to five years, it may involve a Pavlik harness, a plaster cast, and/or skeletal traction. At school age, stabilization of these injuries by elastic stable intramedullary nailing (ESIN) constitutes the main choice. However, external fixation (EF) can be used, as in open fractures, multiple fractures, femoral fractures with severe skin lesions, and patients weighing more than 50 kg.

Complications from conservative treatment in children aged over five years include reduction loss, vicious consolidation, psychological intolerance (for the child and family), and those associated with the use of plaster casts. Historically, ESIN was introduced to treat femoral fractures by the Nancy group in 1979.³ Titanium is the most commonly used material in these implants due to its excellent biocompatibility and its elasticity, which limits the amount of permanent deformation in the nail during insertion. Its use promotes the formation of stable calluses, limiting stress. ESIN functions as an intramedullary guide that maintains the length and alignment of the fracture, thus enabling rapid mobilization. Such movements biomechanically determine callus formation and may offer a low risk of refracture.⁴

Normally, for stable-length fractures, titanium elastic nails (TEN) show high rates of consolidation and require a relatively short period of time before enabling the fractured limb to bear weight. Limited surgical dissection and reduced hospitalization guide the preference for this device. However, complication rates range from 10 to 80%⁴⁷, determining reoperations due to length discrepancy between lower limbs, implant migration, malunion, and limitation of use for adolescent patients and those weighing more than 49 kg.^{8,9} Moreover, over the past two decades, ESIN has become a popular choice to fixate femoral shaft fractures in children.⁴ The technique is based on a three-point support of the nail in the intramedullary canal so the implants occupy at least 80% of its diameter, providing stability and maintaining the reduction without violating children's growth phases.

ESIN treatment show relatively rare complications¹⁰. According to the literature, the most common complication refers to irritation at the protruding ends of the nails, which can cause pain and infect soft tissues and bone. Other complications, such as pseudoarthrosis, malunion, and one-cm limb length discrepancy, occur in 8.2% of preschool children.¹¹

Therefore, the controversy regarding the efficiency of surgical treatment concerns children aged from five to 11 years due to the variety of therapeutic options and algorithms. Thus, the main strategies for fixation use conventional dynamic compression plates, locking compression plates, limited-contact dynamic-compression plates, submuscular plates, and external fixation.^{5,10}

The use of plates is indicated, especially for patterns of unstable fractures in length or in children weighing > 49 kg, the benefits of which include decreased incidence of malunion, superior stability in axial and torsional loading, and limited exposure (if the submuscular technique is chosen).¹⁰ Comminuted fractures are unstable and thus require surgery even in children.

A biomechanical study evaluated pediatric-sized femur models with midshaft transverse fractures that had been stabilized by TEN. It then correlated the results with gait data and suggested that a maximum weight from 40 to 45 kg should serve as the cut-off point for this method of osteosynthesis. Despite such theoretical weight limit, surgeons occasionally use this type of fixation in

patients above this weight limit due to the increasing obesity in the pediatric population.^{12,13}

External fixation (EF) plays an important role in the treatment of these injuries, especially of unstable shaft fractures. However, several studies have reported significant complications such as pin-track infections, malunion, loss of reduction, and refracture.^{14,15}

Only a limited number of studies have focused on the combined use of ESIN and external fixation, such as Erturk et al.¹⁶ and Atef and El Tantawy¹⁷, who have used this combination to treat unstable open tibial fractures in adolescents. However, no studies have reported the results of this combination in children aged from five to 11 years with unstable femoral fractures.

A 2014 Cochrane review evaluated the treatment of FSF in children and adolescents and found no published randomized controlled trials on this topic in the literature. However, several observational comparative studies have been published since the release of the latest American Academy of Orthopaedic Surgeons guidelines.

We stress the current debate on whether flexible intramedullary nailing or external fixation offer the best surgical method to treat pediatric femoral fractures.¹¹ However, no consensus exist as to which would be the best method to stabilize FSF in the pediatric population.

Thus, this study aimed to perform a systematic review with a meta-analysis to evaluate the outcomes of flexible nailing versus external fixator to treat femoral fractures in children and investigate the associated complications.

METHODS

Type of Study

This systematic literature review followed the methodological criteria established by Donato & Donato.⁽¹⁸⁾ This research was carried out according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) in Galvão et al.⁽¹⁹⁾

Research Strategy

The PICO strategy (P- patient, I- intervention, C- control, O- outcome) was used to establish the search criteria and elaborate the guiding question of this review: "What is the ideal intervention to surgically stabilize femoral fractures in children?" The electronic search was carried out from January 2023 to August 2023 in the following databases: Medical Literature Analysis and Retrieval System Online (Pubmed/Medline) and Science Direct. The search strategy was based on the choice of terms that were obtained from health sciences descriptors. Finally, the references in all retrieved articles were comprehensively examined for other relevant manuscripts. This search was carried out using the following terms: "*Femoral Fractures*" AND "*Child*" AND "*External Fixators*" OR "*Femoral Fractures*" AND "*Child*" AND "*Fracture Fixation, Intramedullary*."

Selection Criteria

Primary (cross-sectional, cohort, randomized, and case reports) studies that were conducted on the use of flexible nailing or external fixation in children with femoral fractures and had been published in the last 10 years (without language restrictions) were included.

Analyzed Data

The titles and abstracts of all retrieved articles were read by two reviewers using a pre-defined search strategy. They applied the inclusion criteria for this review independently. Disagreement was solved by discussion among the evaluators, and an agreement was reached in all cases to establish which studies would be included in this systematic review.

Data were then extracted from the selected studies, including information about their authors, year of publication, study design, participants' number and characteristics, type of intervention, outcomes, complications, and limitations.

The Newcastle-Ottawa scale was used to assess the quality of the studies in this review. It evaluates studies by criteria related to selection and comparability between cohorts and criteria related to study outcomes. An adapted list with five aspects of the Newcastle-Ottawa scale was also used to assess the risk of bias based on sample representativeness, exposure, presentation condition, response rate, and result determination.²⁰

Statistical analysis

For the statistical analysis, risk ratios and mean differences were estimated with a 95% confidence interval using the random effect model. Heterogeneity was classified based on I^2 values: 25%, low heterogeneity; 50%, moderate heterogeneity; and 90%, high heterogeneity.²¹ All statistical analyses were performed on R, version 4.3.1, using the meta package.

RESULTS

Description of the Search Strategy

This review screened and evaluated 391 full articles. Assessing their titles and abstracts excluded 374 articles since they failed to meet the chosen eligibility criteria. Selection and analysis rendered 11 articles as eligible to compose this systematic review. This systematic review followed the PRISMA recommendations. The 11 included studies^{12-14,22-29} evaluated 718 children (Table 1). Observational studies showed moderate quality.

Characteristics of the Included Studies

The included studies were published from 2018 to 2022. They employed retrospective (n = 9) and prospective (n = 2) designs. In total, 437 children underwent internal fixation by ESIN; 234, by EF; and 28, by the combined use of temporary external fixation and flexible intramedullary nailing. Follow-up time ranged from 12 to 24 months. Table 1 shows the epidemiological characteristics of participants.

Table 1. Article Identification.

Author/ Year	Type of Study	Sample	Type of Intervention	Follow-up Time
Frumberg et al.(22)	Retrospective Cohort	N: 6 Femur or tibia fracture Sex: 100% boys	Two flexible intramedullary nails	12 months
Li et al.(23)	Retrospective Cohort	N: 71 Fractures of the shaft of the distal third of the femur Sex: 28 girls and 43 boys	External fixation and Flexible intramedullary nailing	24 months
Ulici et al.(24)	Retrospective Study	N: 137 Femoral shaft fractures Sex: 44 girls and 93 boys	Flexible intramedullary nailing	12 months
Kirmani et al.(12)	Prospective Study	N: 45 Femoral shaft fractures Sex: 16 girls and 29 boys	Flexible intramedullary nailing	12 months
Pogorelič et al.(25)	Retrospective Study	N: 103 Dislocated femur fracture Sex: 27 girls and 76 boys	Flexible intramedullary nailing	92 months
Lu et al.(26)	Retrospective Study	N: 28 Unstable fracture of the femoral shaft Sex: 10 girls and 18 boys	Combined use of temporary external fixation and flexible intramedullary nailing Flexible intramedullary nailing	12 months
Guo; Su(14)	Retrospective Study	N: 165 Femoral shaft fractures Sex: 57 girls and 108 boys	Unilateral external fixation	19.7 months
Memeo et al.(13)	Prospective Study	N: 62 Femoral shaft fractures Sex: 22 girls and 40 boys	Flexible intramedullary nailing	12 months
Li et al.(27)	Retrospective comparative study	N: 15 Supracondylar fractures of the femur Sex: 9 girls and 6 boys	External fixation	24 months
Govindasamy et al.(28)	Retrospective Study	N: 48 Femoral shaft fractures Sex: 18 girls and 30 boys	Flexible titanium intramedullary nailing	20 months
Rollo et al.(29)	Retrospective Study	N: 38 Femoral shaft fractures Sex: 14 girls and 24 boys	Titanium flexible intramedullary nails and external fixators	14 months

Evaluation of Interventions

Table 2 data show that the chosen studies obtained good and satisfactory results. Most authors reported no significant differences between complication rates across study groups.

The most common reported complications referred to late or vicious union, superficial and deep infections, skin irritation, angular deformities, or discrepancy in length between lower limbs.

Table 2. Results of Interventions.

Author/ Year	Result	Complications
Frumberg et al. ²²	No significant differences in the rate of major complications or increases in angulation between the study and control groups.	One patient (16.7%). Occurrences: Increased anterior bowing of the femur.
Li et al. ²³	Significant reduction in pain after surgery in both groups. The rate of major complications failed to significantly differ between the two groups.	15 patients (21.1%). Occurrences: Implant irritation; Surgical site infection; Vicious consolidation; Pseudoarthrosis or loss of reduction; Angular deformity.
Ulici et al. ²⁴	21.0% of patients. Most patients were successfully treated by internal fixation with flexible nails.	29 patients (21%). Occurrences: Late consolidation; Axial deformities or discrepancies in lower extremity length.
Kirmani et al. ¹²	Results were excellent for 80% of patients.	12 patients (26.7%). Occurrences: Deep infection; Late consolidation; Superficial infection; Vicious consolidation;
	Fixation with a flexible intramedullary nail proved to be a safe method.	Limb length discrepancy; Skin irritation.
Pogorelič et al. ²⁵	All patients achieved complete radiographic cure in an average of 8.5 weeks. After the removal of the nails, all patients regained full function of their limb, with no long-term consequences.	9 patients (8.49%). Occurrences: Skin irritations at the entry site; Valgus angulation; Implant protrusion; Refracture; Varus angulation; Delayed consolidation.
Lu et al. ²⁶	All fractures healed, with no late union, malunion, or refracture. About 96.4% of the patients had excellent radiological results.	4 patients (14.3%). Occurrences: Pin-track infections; Temporary stiffness of the knee joint; 13-mm discrepancy in the lower limbs.
Guo; Su ¹⁴	About 14.5% of patients experienced refracture within one year of the removal of the external fixation.	24 patients (14.5%). Occurrence: Refracture.
Memeo et al. ¹³	All fractures healed within eight weeks after fixation, with no nonunion or delayed union. Children with transverse fractures had a shorter healing time.	24 patients (38.7%). Occurrences: Distal pain at the point of nail insertion; Superficial and deep infection; Knee stiffness; Loss of reduction; Proximal migration; Inflammatory reaction.
Li et al. ²⁷	All fractures healed without delay in consolidation. No acute or serious complications were observed.	2 patients (13.3%). Occurrences: Superficial infection of the skin in the path of the nail.
Govindasamy et al. ²⁸	All fractures healed radiologically with grade III callus formation from nine to 12 weeks. No late consolidation, nonunion, or refractures.	15 patients (31.3%). Occurrences: Limb shortening; Vicious consolidation; Infection of the protruding site of the nail; Nail migration; Skin irritation.
Rollo et al. ²⁹	The end of follow-up found no significant rotational defects	14 patients (36.8%). Occurrences: Superficial infection in the access of the nails.
	Angulation or growth for both groups. For both groups, the range of hip and knee movement was superimposable. Flexible nailing showed a greater tolerability synthesis.	

Results of the Meta-analysis

The first meta-analysis used individual proportions, combining the proportions or probabilities of an event occurring in several studies to calculate an overall proportion or probability. In total, nine studies used flexible nailing as treatment without a control group. The results of this meta-analysis (Figure 1) indicated differences between the complications in each study (RR 0.25; CI-0.07; 0,58; $p = 0.01$). They found evidence of moderate heterogeneity across studies ($I^2 = 65\%$, $\tau^2 = 0.3115$).

The second meta-analysis used individual proportions, combining the proportions or probabilities of an event occurring in multiple studies to calculate an overall proportion or probability. Overall, two studies used external fixation as treatment without a control group. The results of this meta-analysis (Figure 2-A) indicated no differences between complications in each study (RR 0.13; CI-0.09; 0,19; $p = 1.00$). Studies showed no evidence of heterogeneity ($I^2 = 0\%$, $\tau^2 = 0$).

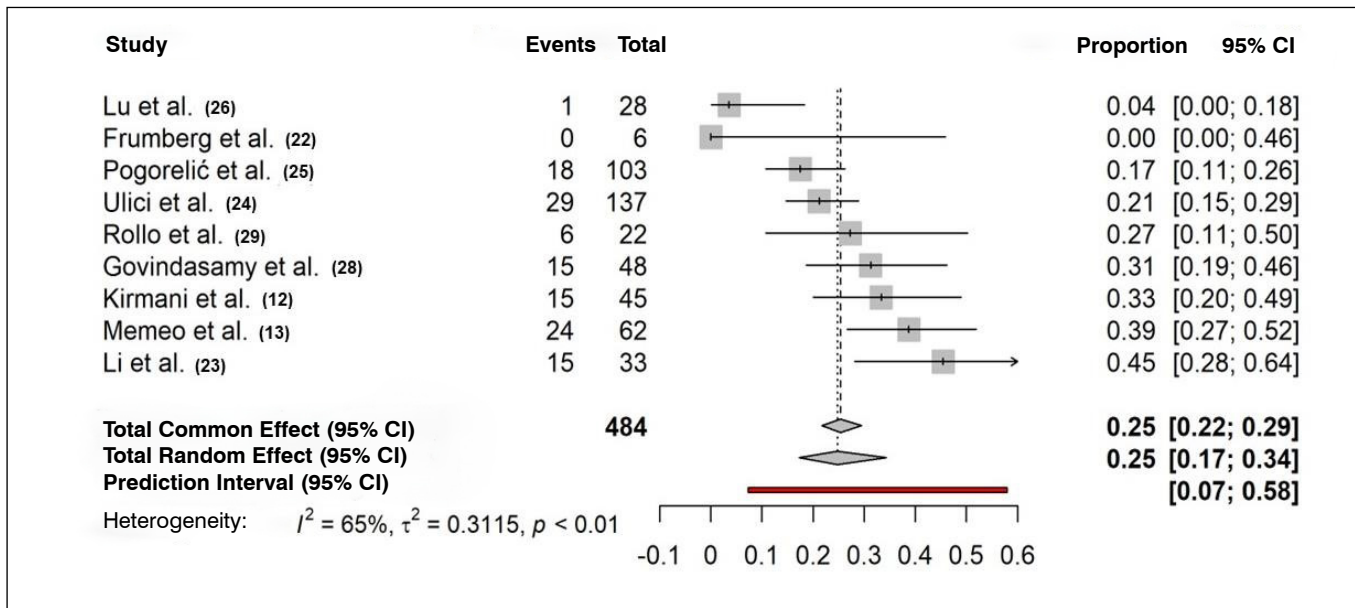


Figure 1. Forest plot showing the proportion of complications in studies that used flexible nailing without a control group.

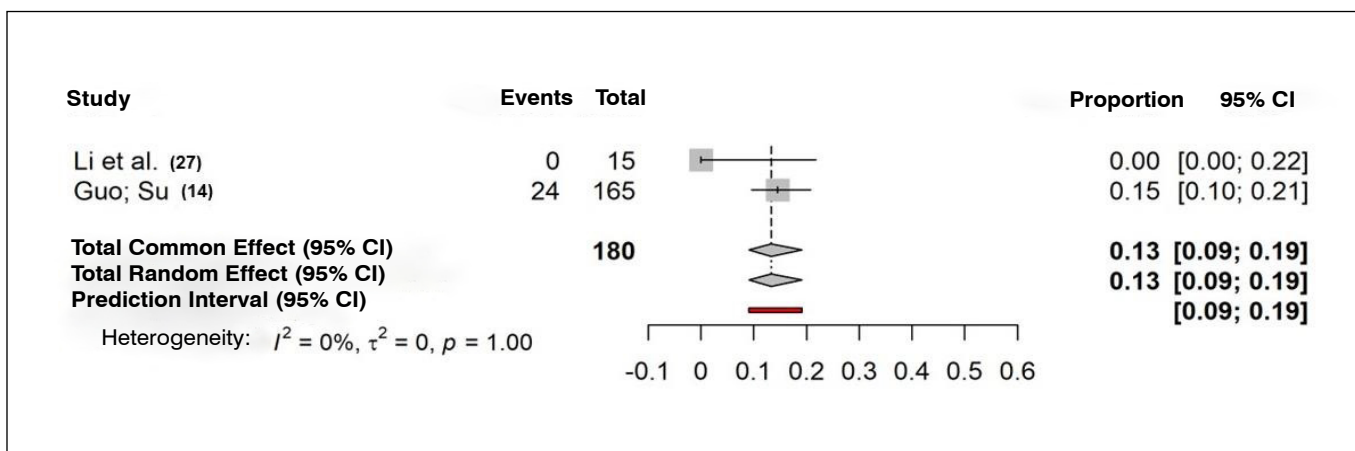


Figure 2-A

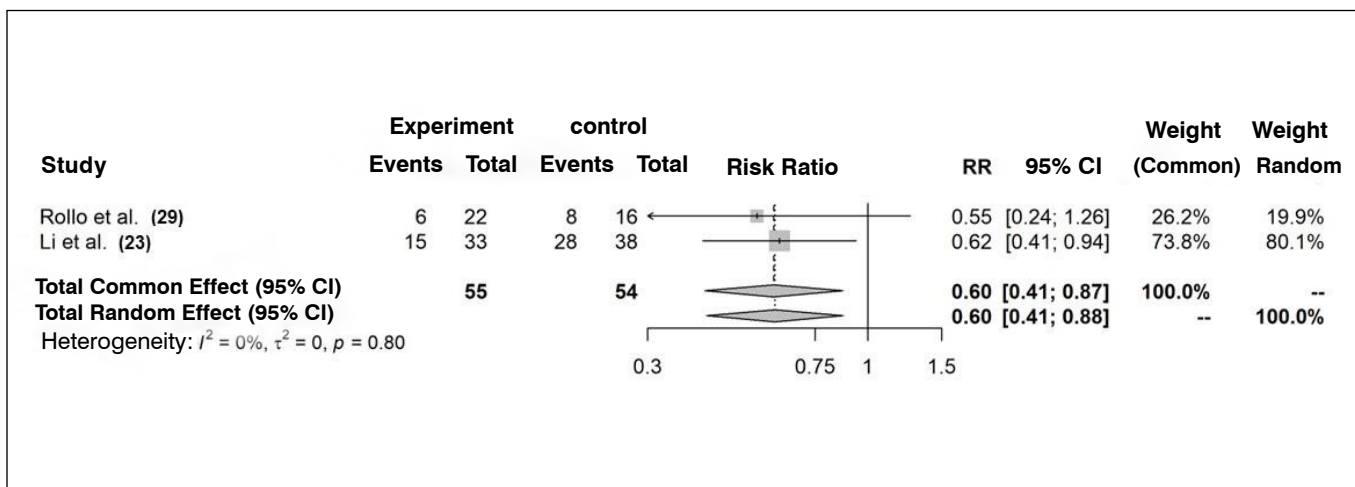


Figure 2. Forest plot showing the proportion of complications in studies that used external fixation without a control group (2-A) and studies that compared external fixation and flexible nailing in separate groups (3-B).

The third meta-analysis used a meta-analysis of binary outcomes (occurrence or absence of complications in both groups: flexible nailing and external fixation). It considered both common and random effects to obtain its risk ratio and compare studies. It used two studies that compared external fixation and flexible nailing in separate groups. Results (Figure 2-B) indicated no differences between complications across studies (RR 0.60;

CI-0.41; 0,87/0,88; $p = 0.80$). Studies showed no evidence of heterogeneity ($I^2 = 0\%$, $\tau^2 = 0$).

Evaluation of the Quality of Studies

After reading the 11 selected articles in full, this review evaluated their quality by the Newcastle-Ottawa scale¹², attributing scores from 4 to 7 to each study (Chart 1). Thus, the chosen studies¹⁴⁻²⁴ lie within the expected quality for this research.

Chart 1. Assessment of bias according to the Newcastle-Ottawa Scale.

Studies	Random sample	Unbiased sample	Sample with well-described subjects	Sample size	Unbiased evaluators	Response rate	Type of statistical test	Total
Frumberg et al.(22)	1	1	1	0	1	1	0	5
Li et al.(23)	1	1	1	0	1	1	0	5
Ulci et al.(24)	1	1	1	1	1	1	1	7
Kirmani et al.(12)	1	1	1	0	1	1	1	5
Pogorelić et al.(25)	1	1	1	1	1	1	1	7
Lu et al.(26)	0	1	1	0	1	1	0	4
Guo; Su(14)	0	1	1	1	1	1	1	6
Memeo et al.(13)	1	1	1	0	1	1	0	5
Li et al.(27)	0	1	1	0	1	1	0	4
Govindas amy et al.(28)	1	1	1	0	1	1	0	5
Rollo et al.(29)	0	1	1	0	1	1	0	4

Criteria to evaluate observational studies (maximum of 8 points): random sampling: 1 - yes, 0 - no; unbiased sampling: 1 - yes, 0 - no; sample with well-described subjects: 1 - yes, 0 - no; sample size: 1 - greater than or equal to 100 subjects, 0 - less than 100 subjects; PCAT utilization: 1 - PCATool standard version, 0 - PCATool adapted version; Unbiased evaluators: 1 - yes, 0 - no; Response rate: 1 - greater than or equal to 70%, 0 - less than 70%; Type of statistical test: 1 - T-test, 0 - other statistical tests.

DISCUSSION

This systematic review aimed to compare the results of FSF treatment by ESIN and EF in children, highlighting associated complications among the outcomes. The main finding of this systematic review and meta-analysis refers to the statistically significant difference in the incidence of complications in flexible nailing^{12,13,22,23,24,25,26,28,29} and the absence of statistical or clinical differences between the occurrence of complications for external fixation^{27,14} or the comparison between interventions.^{23,29}

The literature shows that choosing the ideal treatment for these fractures remains controversial, constantly challenging the orthopedic community. The included studies generally classified their results as good and satisfactory. Most authors reported no significant differences between complication rates across study groups. The most common reported complications for both methods referred to delayed or vicious unions, superficial and deep infections, skin irritation, angular deformities, or length discrepancy between lower limbs.

Chen et al.'s⁹ meta-analysis reported ESIN outperforming EF in the early treatment of pediatric femoral fractures, comparing the discrepancy in observed length, hospital stay duration, time to clinical improvement, time to consolidation, and complication rates. Corroborating these findings, Kirmani et al.¹² reported that TEN nails offer a safe, reliable, and effective fixation method due to its simple application, lower degree of invasion, ease of implant insertion and removal, fast union, short rehabilitation, and less psychosocial stress for patients and their families.

Similarly, Ulci et al.²⁴ found that most patients (79%) were successfully treated by closed reduction and internal flexible nailing fixation, showing no complications. However, these researchers

considered that two factors would be associated with complications: age above 11 years and/or weight above 50 kg.

Similarly, Frumberg et al.²² reported that the use of TEN can offer an excellent surgical option to fixate fractures in pediatric patients weighing less than 45 kg with FSF and stable-length tibiae. They stress that patients' weight should be carefully considered so gait forces fail to supplant the stability of the internal fixation provided by the intramedullary implant. Although ignored, this review believes that the diameter of the medullary canal and, therefore, the choice of the caliber of the intramedullary implants also configure determinant factors for obtaining adequately stable osteosynthesis. We stress that properly pre-shaping nails constitutes a fundamental step for the desired stability.

Another available resource when choosing ESIN refers to End Cap Synthes, a cap that prevents TEN from sliding backward. Its rounded shape can adequately protect soft tissues. It should be used in unstable shaft fractures of the femur and tibia.

According to Siddiqui et al.³⁰, ESIN is the preferred implant to treat FSF in children. It uses three-point fixation, providing axial, translational, and rotational stability at the fracture site. It has minimal complication rates when applied properly. Pogorelić et al.²⁵ also emphasize that this device offers excellent functional and cosmetic results and enables early functional follow-up with rapid pain reduction. These authors concluded that, due to their excellent results, surgical stabilization of femoral fractures should be recommended for pediatric patients. However, we must report that removing these implants fails to always occur easily. The incision for removal can be much larger than the one used for insertion, and the adherence of bone to titanium often hinders removal.

Lu et al.²⁶ found that femoral fractures in children aged from five to 11 years can be treated by flexible nailing with temporary external fixation. It generally shows good or excellent functional and radiographic results and complication rates that resemble that of flexible nailing or external fixation alone. They observed only one case of discrepancy in lower limb length in patients treated with external fixation. However, the literature rarely reports the combined use of these devices.

Li et al.²⁷ also reported that external fixation has potential advantages: a minimally invasive approach, less blood loss, shorter operative time, and no need for secondary surgery for hardware removal. External fixation also produces satisfactory clinical results and can be comparable to flexible intramedullary nailing.

However, about 14.5% of the patients in Guo and Su¹⁴ experienced a refracture within one year after EF removal. On the other hand, Li et al.²⁷ showed that external fixation techniques were considered the best option to treat deviated supracondylar femoral fractures in children. They found neither deformity, deep infections after surgery, nor symptoms requiring further treatment. The authors emphasize that the absence of infection should be attributed to the efficacy of prophylactic antibiotic therapy. Moreover, the external fixation group showed significantly lower amount of bleeding during the operation and the time of consolidation.

On the other hand, Li et al.²³ found that the irritation due to the implant was much greater in external fixation than in flexible intramedullary nailing due to the involvement of the thigh muscles that surround the distal femur. However, they emphasize that EF was routinely removed from seven to 12 postoperative weeks, whereas flexible nails were systematically removed from four to seven months.

On the other hand, Pogorelić et al.²⁵ found 8.49% (n: 107) of postoperative complications in patients who received flexible nailing: three skin irritations at the entry site, two valgus angulation cases, and one case of nail protrusion, refracture, varus angulation, and delayed union. All complications, except for refracture and valgus angulation, received conservative treatment, with no long-term consequences for patients after implant removal.

Moreover, Kirmani et al.¹² observed a case of deep infection in a patient with a type I open fracture, treating it with debridement and intravenous antibiotics without the need to remove the nail. They also emphasize that in open fractures with contamination, external fixation should be the preferred method of osteosynthesis to the detriment of flexible intramedullary nailing, potentially minimizing complications. On the other hand, Ulici et al.²⁴ reported that unstable femoral fractures treated with flexible intramedullary nailing and immobilization with plaster casts show no higher risk of other complications,

such as angular deformities, delayed consolidation, limb length discrepancies, or higher rates of premature ESIN removal.

Kirmani et al.¹² state that flexible intramedullary nailing should be avoided in patients weighing more than 45 kg and over 14 years of age as stability in these conditions follows failed weight bearing, leading to implant failure or malunion. Appropriate patient selection and strict adherence to basic techniques can decrease complication rates. Govindasamy et al.²⁸ also reinforce that the TEN nail offers efficacy in appropriately selected children.

Memeo et al.¹³ also report that TEN nails configure an excellent internal fixation system if used by an experienced surgeon, showing very low complication rates. However, in older children weighing more than 50 kg, the authors advise the use of alternative techniques such as plate fixation or external fixation.

According to Govindasamy et al.²⁸, the indication of ESIN continues to grow following reports of its advantages and low complication rates. They mention its immediate availability, caliber variability, and low cost as its main advantages. Complications are usually linked to improper techniques, which can be eliminated by strictly following the basic principles and technical aspects.

Corroborating these findings, Rollo et al.²⁹ show that ESIN and EF produce similar fracture consolidation and complication results. However, patients treated with a flexible nailing show a higher degree of satisfaction. Flexible nailing are currently considered the first choice for most pediatric femoral shaft fractures, offering many advantages and fewer complications. These findings agree with the results in our research.

CONCLUSION

The studies included in this systematic review found that flexible nailing and external fixation can provide good clinical and radiographic results in patients with pediatric femoral shaft fractures. However, the choice of treatment with flexible nailing receives greater acceptance than external fixation, and should be reserved for younger patients with lower age and weight, whereas treatment with external fixators remains the first choice in children aged over 11 years, weighing more than 50 kg, and showing multiple traumas or open fractures. We found that complications are usually associated with the inadequate application of the osteosynthesis technique, which can be solved by strictly following the basic principles of each technique. We stress that research with better scientific methodology, larger samples, and good-quality double-blind and randomized controlled designs can compare and confirm the efficacy of these techniques.

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