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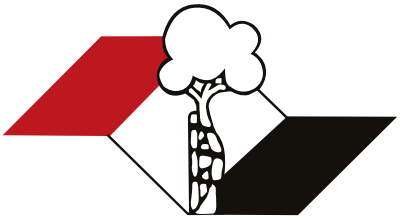

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ASSESSMENT OF ISOMETRIC AND ISOKINETIC ANKLE STRENGTH MEASURES: A PILOT STUDY

AVALIAÇÃO DE MEDIDAS DE FORÇAS ISOMÉTRICAS E ISOCINÉTICAS DE TORNOZELO: ESTUDO PILOTO

Carolina Lins[1], Andreza Ribeiro Batista de Oliveira[2], Marina Squarizi Simões Chagas[1], Felippe Ribeiro[3], Alberto Cliquet Junior[1], Rodrigo Gonçalves Pagnano[1]

1. Universidade Estadual de Campinas (UNICAMP), Faculdade de Ciencias Medicas, Departamento de Ortopedia, Reumatologia e Traumatologia, Campinas, Sao Paulo, SP, Brazil.
2. Centro de Reabilitacao Fisica Monica Cristina Blanco, Hortolandia, Sao Paulo, SP, Brazil.
3. Instituto Wilson Mello, Campinas, Sao Paulo, SP, Brazil.

ABSTRACT

Objective: To evaluate isometric and isokinetic ankle strength in of dorsiflexion (DF), plantar flexion (PF), inversion (INV), and eversion (EVE) in healthy individuals. Methods: A cross-sectional study was conducted with individuals aged 18 to 60 years, of both sexes. The Lafayette® isometric manual dynamometer was used to evaluate isometric strength, the Humac Norm® isokinetic dynamometer to evaluate isokinetic strength, and the IPAQ questionnaire (International Physical Activity Questionnaire) for the level of physical activity. Statistical analysis compared sex, dominance, and physical activity level with isometric and isokinetic strengths using the Spearman coefficient and the Mann-Whitney test. Results: There was a difference between genders for dominant and non-dominant limbs in isokinetic strength and not in isometric strength. There was a difference between isokinetic strength variables and physical activity levels. The isokinetic strength of dominant PF (p=0.0153), non-dominant (p=0.0287), and non-dominant INV (p=0.0183) demonstrated that very active individuals have a higher torque peak than irregularly active and sedentary individuals. Conclusion: The results demonstrated greater isokinetic strength in men than in women and active individuals compared to sedentary ones. However, it was not possible to establish an association between isometric and isokinetic ankle measurements. ***Level of Evidence IV, Cross-Sectional Study.***

Keywords: Ankle; Rehabilitation; Muscle Strength Dynamometer.

RESUMO

Objetivo: Avaliar forças isométricas e isocinéticas de dorsiflexão (DF), flexão plantar (FP), inversão (INV) e eversão (EVE) do tornozelo em indivíduos saudáveis. Métodos: Estudo transversal com indivíduos entre 18 e 60 anos, de ambos os sexos. Foram utilizados o dinamômetro manual isométrico Lafayette® para avaliar a força isométrica, o dinamômetro isocinético Humac Norm® para avaliar a força isocinética e o questionário IPAQ (Questionário Internacional de Atividade Física) para o nível de atividade física. A análise estatística comparou sexo, dominância e nível de atividade física com forças isométricas e isocinéticas por meio do coeficiente de Spearman e do teste de Mann-Whitney. Resultados: Houve diferença entre gêneros para membros dominantes e não dominantes nas forças isocinéticas e não na força isométrica. Houve diferença entre variáveis de força isocinética e níveis de atividade física. Força isocinética de FP dominante (p=0,0153), não dominante (p=0,0287) e INV não dominante (p=0,0183) demonstraram que indivíduos muito ativos apresentam pico de torque maior que os irregularmente ativos e sedentários. Conclusão: Os resultados demonstraram maior força isocinética em homens do que em mulheres, assim como em indivíduos ativos em comparação aos sedentários. No entanto, não foi possível estabelecer uma associação entre as medidas isométricas e isocinéticas do tornozelo. ***Nível de Evidência IV, Estudo Transversal.***

Descritores: *Tornozelo; Reabilitação; Dinamômetro de Força Muscular.*

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INTRODUCTION

Various treatment modalities are used in foot and ankle tendinopathies, both conservative and surgical, with the assessment of muscle strength (MS) being an important component in the rehabilitation process of these cases. Various methods are used to achieve this, such as manual strength testing, manual dynamometers and isokinetic dynamometers.[1,2]

The manual strength test is the most common, based on a subjective grading system, which consists of performing movement against resistance applied by the examiner or resistance against gravity

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

The study was conducted at Universidade Estadual de Campinas (UNICAMP) and the orthopedic clinic Instituto Wilson Mello, located at Rua Tessalia Vieira de Camargo, 126, Cidade Universitaria, Sao Paulo, SP, Brazil. 13083-887.
Correspondence: Carolina Lins. 126, Rua Tessália Vieira de Camargo, Cidade Universitaria, Sao Paulo, SP, Brazil.13083-887. linsc@unicamp.br

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applied during the test.[3,4] The isokinetic dynamometer is the most accurate instrument for evaluating MS, however its disadvantages are the high cost of the equipment and the need for a qualified professional to carry out the test.[5] The third method, isometric dynamometry, preserves the efficiency and adaptability of the manual strength test, promoting a more accurate and objective assessment of MS.[6] Among the portable isometric dynamometry devices is the Lafayette® Hand-Held-Dynamometer. Researchers report the usefulness of manual dynamometers in rehabilitation services due to the benefit and objectivity for both the evaluator and the patient.

There are studies that compare the effectiveness, reproducibility and reliability of these devices in evaluating the knee and shoulder joints.[7,8] However, there are few consistent studies on the application of manual dynamometers and there is no definitive protocol for evaluating isometric and isokinetic strength of the ankle joint in the sagittal and frontal plane. This study aims to evaluate isometric and isokinetic forces of dorsiflexion (DF), plantar flexion (PF), inversion (INV) and eversion (EVE) of the ankle in healthy individuals.

MATERIALS AND METHODS

Cross-sectional study, approved by the FCM-Unicamp Research Ethics Committee, fulfilling the requirements of resolution 466/2012 CNS/MS and complementary requirements in the preparation of the protocol and in obtaining this Informed Consent Form. The recruitment and data collection process took place at the Universidade Estadual de Campinas (UNICAMP) and at an orthopedic clinic Wilson Mello Institute.

Population

25 volunteers of both genders, aged between 18 and 60 years old, were selected. Initially, all individuals received explanations about the study and, upon agreeing, signed the free and informed consent form. Firstly, the subjects were interviewed to collect personal data, age, anthropometric data, dominance of the lower limbs, goniometry, investigation of previous lower limb dysfunctions and the IPAQ questionnaire for level of physical activity. The inclusion criteria were healthy female and male individuals, aged between 18 and 60 years, who agreed to participate in the study, signing the free and informed consent form. The exclusion criteria were subjects with previous lower limb injuries or surgeries or presenting severe or decompensated systemic diseases.

Instruments and Procedures

Instruments

Participants answered the IPAQ physical activity questionnaire (short version) that assesses the individual's daily physical capacity, classifying them as very active, active, irregularly active (A and B) and sedentary. Activities carried out at work, going from one place to another, leisure, sport, exercise or part of their activities at home or in the garden were considered.[9]

Goniometry assessed range of motion (ROM). For DF, the individual was positioned sitting, with the knees flexed at around 25º or 30º so as not to interfere with the action of the muscles in the posterior region of the thigh and ankle in a neutral position. The fixed arm of the goniometer was placed parallel to the lateral surface of the fibula and the movable arm parallel to the lateral surface of the fifth metatarsal, with the axis of the goniometer positioned next to the lateral malleolus. For analysis of PF ROM, the positioning was the same. In the assessment of INV and EVE, the individual's positioning was like the previous ones, but with an axis between the talus and calcaneus, the arm fixed towards the anterior surface of the tibia and the mobile arm towards the third finger.[10]

To measure muscular strength, individuals were instructed about appropriate clothing, leaving their lower limbs free and barefoot. The patients underwent a 5-minute cardiocirculatory and musculoskeletal warm-up on a stationary bike (60-70 rpm) and were instructed on the procedures to be performed.

Isometric strength, with a unit of measurement in kilogram-force (kgf), was tested using the Lafayette Model 01165A isometric dynamometer (Lafayette Instrument, United States of America), size: 3.16" x 5.11" x 1.6" (8.03cm x 12.98 cm x 4.1cm), range: 0-300 lbs (136.1kg) (1335 N), accuracy: ± 1% of full scale or ± 0.2 lbs, resolution: 0.1lbs/0.1kg/0.1N(0-999.9N) /1N(1000N-1335N)).[11]

The patient was positioned in the supine position, with hip and knee flexion of approximately 30º and a neutral ankle position (90º),[12] which was stabilized by Velcro straps. The dynamometer was positioned on the ventral surface of the metatarsal head to collect plantar flexion data, on the dorsal surface of the metatarsal head to collect DF data, just below the head of the medial surface of the 1st metatarsal for inversion, just below the head of the lateral surface of the 5th metatarsal for eversion. The device recorded peak force for a period of six seconds, providing a reliable, accurate and stable isometric muscle strength reading.[13]

Isokinetic strength was measured using a Humac Norm® brand isokinetic dynamometer (Computer Sports Medicine, inc; United States of America). To perform the maximum torque exercises, the dynamometer was positioned in the same way as the isometric dynamometer, in the supine position, with Velcro straps located on the distal third of the thigh and abdomen. The thigh stabilizing cushion was placed close to the knee joint and the hip and knee joints were positioned at 30° flexion. The ankle remained in a neutral position (90º).[11]

To avoid detection bias, the subjects underwent familiarization with the isokinetic test, that is, four warm-up repetitions at 90% of maximum strength. Then, the real test was done with a belt, repetitions at 100% of maximum force and both at a speed of 30°/s.

Statistical Analisys

Exploratory data analysis was carried out using summary measures (mean, standard deviation, minimum, median, maximum, frequency and percentage). The correlation between numerical variables was assessed using the Spearman coefficient. Comparison between genders was performed using the Mann-Whitney test. The significance level adopted was 5%.

RESULTS

The 25 volunteers, with an average age of 28.8 (± 9.1) years, were 11 women and 14 men, with an average weight of 73.6 (± 12.9) kilograms, height 173.2 (± 11 .2) centimeters and body mass index of 24.4 (± 3.1) kg/m2.

Table 1 presents the mean values and standard deviations of goniometry in dorsiflexion, plantar flexion, inversion and eversion movements of the volunteers' dominant limbs.

Table 2 presents the mean values and standard deviations of goniometry in dorsiflexion, plantar flexion, inversion and eversion movements of the volunteers' non-dominant limbs.

Table 1. Mean values and standard deviations of goniometry of the volunteers' dominant limbs.

Variables	Healthy Subjects n = 25	Female n = 11	Male n = 14
DF (degree)	8.0 ± 4.1	9.1 ± 4.1	7.1 ± 3.9
PF (degree)	21.0 ± 7.6	20.0 ± 5.1	21.8 ± 9.2
INV (degree)	27.2 ± 5.4	26.5 ± 4.2	27.8 ± 6.3
EVE (degree)	13.9 ± 5.1	12.6 ± 4.6	15.0 ± 5.4

DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion.

<< SUMÁRIO

Table 3 presents the mean values and standard deviations of the isometric strength of the dorsiflexion, plantar flexion, inversion and eversion movements of the volunteers' dominant and non-dominant limbs.
Table 4 presents the mean values and standard deviations of the isokinetic strength of the dorsiflexion, plantar flexion, inversion and eversion movements of the volunteers' dominant and non-dominant limbs.
Table 5 presents the average deficit values, in percentage, for dorsiflexion, plantar flexion, inversion and eversion movements.
Table 6 presents the mean values and standard deviations of the isokinetic strength of the dorsiflexion, plantar flexion, inversion and eversion movements of the volunteers' dominant and non-dominant limbs, associated with the IPAQ.
Figure 1 shows the isokinetic strength of DF comparing first the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.
Figure 2 shows the isokinetic strength of PF comparing first the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.
Figure 3 shows the isokinetic strength of INV, first comparing the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.
Figure 4 shows the isokinetic strength of EVE comparing first the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.

Table 2. Mean values and standard deviations of goniometry of the volunteers' non-dominant limbs.

Variables	Healthy Subjects n = 25	Female n = 11	Male n = 14
DF (degree)	6.4 ± 3.9	7.6 ± 4.4	5.43 ± 3.2
PF (degree)	24.0 ± 7.1	23.0 ± 5.8	24.8 ± 8.1
INV (degree)	23.8 ± 7.0	25.8 ± 4.6	22.2 ± 8.6
EVE (degree)	16.6 ± 7.9	17.5 ± 7.5	15.8 ± 8.4

DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion.

Table 3. Mean values and standard deviations of the volunteers' isometric strength.

Variables	Male (D) n = 14	Female (D) n = 11	p-values	Male (ND) n = 14	Female (ND) n = 11	p-value
DF (kgf)	18.6 ± 4.0	17.2 ± 7.0	0.1627	16.7 ± 3.3	14.4 ± 4.0	0.1469
PF (kgf)	21.8 ± 7.0	17.2 ± 5.0	0.0752	22.1 ± 8.6	16.5 ± 5.2	0.072
INV (kgf)	10.6 ± 4.3	10.1 ± 4.2	0.7843	12.2 ± 5.5	11.1 ± 4.2	0.8911
EVE (kgf)	13.1 ± 4.0	13.3 ± 6.2	0.5470	12.5 ± 3.9	12.1 ± 6.3	0.3380

D = dominant; ND = non dominant; DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion; kgf= kilogram-force.

Table 4. Mean values and standard deviations of the volunteers' isokinetic strength.

Variables	Male (D) n = 14	Female (D) n = 11	p-value	Male (ND) n = 14	Female (ND) n = 11	p-value
DF (Nm)	52.9 ± 23.9	30.1 ± 8.7	0.0018*	48.9 ± 18.9	33.1 ± 12.1	0.0229*
PF (Nm)	130.2 ± 36.4	55.9 ± 23.5	0.0002*	123.5 ± 30.6	56.2 ± 17.6	<0.0001*
INV (Nm)	41.3 ± 7.8	25.1 ± 6.8	0.0002*	49.2 ± 11.3	30.1 ± 8.2	0.0006*
EVE (Nm)	27.7 ± 6.6	18.7 ± 5.9	0.0037*	26.8 ± 5.0	18.0 ± 3.9	0.0004*

D = dominant; ND = non dominant; DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion; Nm= Newton-meter; * = significance p <0,05.

Table 5. Average values of isometric and isokinetic deficits.

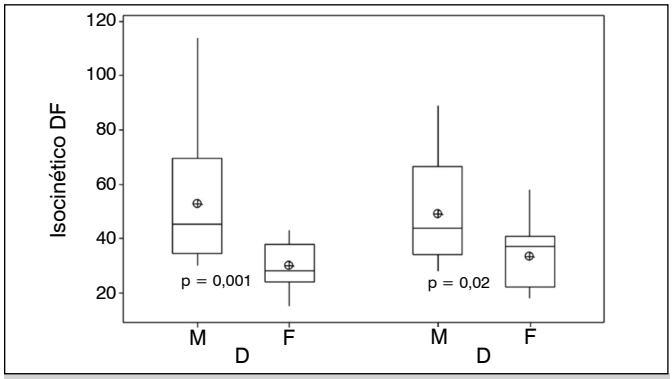
Variables	Male n = 14		Female n = 11	
	Isometric	Isokinetic	Isometric	Isokinetic
DF	14.1 ± 0.0	11.2 ± 10.1	21.4 ± 0.1	19.0 ± 20.9
PF	15.1 ± 0.1	16.5 ± 11.3	19.0 ± 0.1	13.3 ± 14.4
INV	13.9 ± 0.0	19.0 ± 11.5	15.1 ± 0.1	22.9 ± 10.6
EVE	11.3 ± 0.0	13.4 ± 10.5	16.3 ± 0.0	8.9 ± 8.3

DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion.

Table 6. Mean values and standard deviations of isokinetic strength and physical activity level of volunteers.

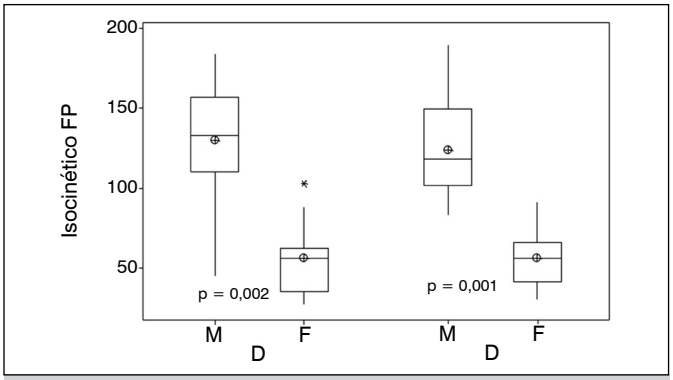
		IPAQ		
	Isokinetic Strength	Very Active	Irregularly Actives e Sedentaries	P-value
Dominant	DF	51.7 ± 23.8	42.2 ± 30.4	0.43
	FP	136.7 ± 27.1	65.8 ± 27.4	0.01*
	INV	41.7 ± 7.1	31.0 ± 11.1	0.10
	EVE	28.7 ± 7.5	19.5 ± 6.8	0.14
Non Dominant	DF	52.8 ± 23.0	42.0 ± 18.3	0.24
	FP	123.2 ± 23.1	69.1 ± 20.8	0.02*
	INV	50.5 ± 10.0	30.7 ± 9.5	0.01*
	EVE	25.4 ± 4.7	20.1 ± 6.2	0.20

IPAQ = questionnaire of level of activity; DF = dorsiflexion; PF = plantar flexion; INV = inversion; EVE = eversion; * = significance p <0,05.



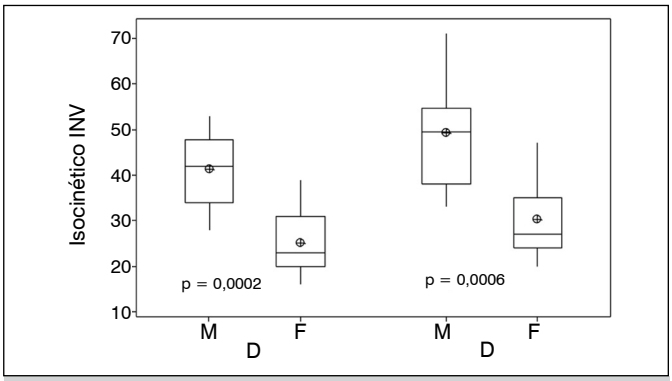
Legend: ⊕ = mean.

Figure 1. Comparison of the isokinetic DF strength of dominant (D) male (M) x female (F) and non-dominant (ND) male x female limbs.



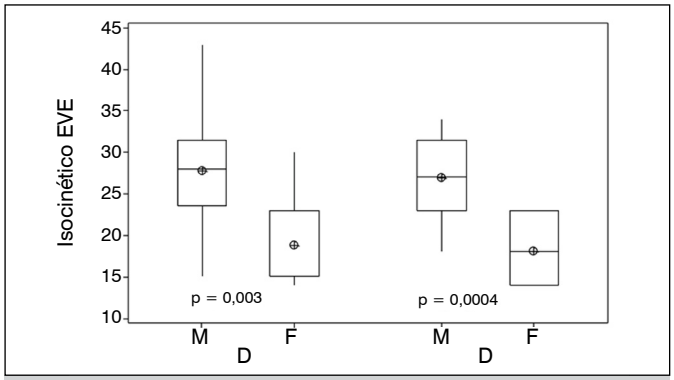
Legend: *: highest observed values; ⊕ = mean.

Figure 2. shows the isokinetic strength of PF comparing first the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.



Legend: ⊕ = mean.

Figure 3. Shows the isokinetic strength of INV, first comparing the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.



Legend: ⊕ = mean.

Figure 4. Shows the isokinetic strength of EVE comparing first the dominant limb between the male and female groups and then the non-dominant limb also between the male and female groups. It presents a significant difference between the variables studied.

After analyzing the data, a significant difference in isokinetic strength was observed in which men had greater strength than women and very active individuals were stronger than irregularly active and sedentary individuals. Furthermore, the strength of the dominant side was greater than the non-dominant side.

On the other hand, analyzes related to isometric strength did not show significant differences between sex, dominance and level of physical activity.

DISCUSSION

The present study was considered a pilot of large research that intends to associate variables of isometric and isokinetic strength in the ankle. We evaluated 25 healthy individuals of both genders and different levels of physical activity. With the preliminary results, significant differences were found between genders for dominant and non-dominant limbs in all isokinetic strength movements. In terms of isometric strength, no significant differences were found, possibly due to the current sample size.

There was a relevant difference between strength and physical activity levels. In the isokinetic strength of dominant and non-dominant plantar flexion, and isometric strength of non-dominant inversion, it was observed that individuals classified as very active presented a higher peak torque in relation to individuals classified as irregularly active and sedentary. This corroborates the results reported by Keles et. Al,[14] who analyzed 24 healthy male recreational athletes divided into two groups. The control group did not practice exercises, and the exercise group practiced evertor and dorsiflexor activities. After six weeks, the exercise group demonstrated a significantly higher peak eccentric torque than the control group in dorsiflexion and eversion movements.[14]

The differences in strength between genders found in the present study is in agreement with the study by Preininger et. al, who analyzed 93 computed tomography scans of the pelvis of 45 men and 48 women. They observed greater muscle strength in men due to the greater absolute total volume of the hip muscular system ($p<0.0001$).[15]

Spink et al. investigated the isometric strength of inversion and eversion in individuals aged between 23.2 ± 4.3 years of both sexes, comparing the right and left sides, without taking into account limb dominance. For inversion force they demonstrated values of 18.8 ± 4.5 and for eversion force 18.2 ± 3.7.[16]

The sample of the present study was composed of subjects between 18 and 60 years old, subdivided by gender and dominance, in the analysis of the same variable. The isometric strength values of male subjects on the dominant side were 10.6 ± 4.3 and 13.1 ± 4.0 for inversion and eversion respectively, while the non-dominant side were 12.2 ± 5.5 and 12 .5 ± 3.9 of inversion and eversion respectively. Female individuals on the dominant side had 10.1 ± 4.2 and 13.3 ± 6.2 of inversion and eversion respectively, while the non-dominant side had 11.1 ± 4.2 and 12.1 ± 6 .3 of inversion and eversion respectively.

In the present study, the mean values of maximum isometric strength of the inversor and evertor muscles of the ankle were lower than the mean values found by Spink et al,[16] who positioned the tested limb in hip and knee extension, which is a likely explanation for the difference between the results of both studies.

In this study, we found significant differences in isokinetic and isometric strength between men and women, as well as dominant and non-dominant side. Corroborating these data, Pellicer-Chenoll et al. compared the ratio between hamstrings and quadriceps, at different knee angles, to determine differences between gender and dominance. The ratio in the dominant limb demonstrated an average of 9% higher than that of the non-dominant limb. Another contribution of this study was in relation to limb positioning. The ratios were on average 53.4% lower in positions close to flexion than in positions close to extension.[17] This piece of information supports the concern in maintaining the appropriate positioning of the two strength measurements, ensuring that both are like each other.

Kim et al. analyzed muscle strength in flexion and extension of the hip, knee and ankle using an isometric dynamometer in 55 students, 19 men and 36 women. The intra-examiner reliability found was above 0.9 for hip, knee and ankle flexion and extension strengths. Likewise, inter-rater reliability was found to be above 0.8 for the same measures. Therefore, the objective of the present study is viable and of high interest to the scientific community. Although there is a difference in the positioning of the volunteers, the strength values found are like previous studies.[18]

This study has limitations. Association, comparison and agreement calculations for the values were not performed, as the sample size was not considered sufficient to carry out these statistical tests. There are still few consistent studies, with robust methodology, that demonstrate normative data on foot and ankle strength, as well as other joints. [19] These data are essential for further investigation of the same variables in pathological conditions. Therefore, in the present study, the search for these results began in a group of healthy individuals. Future studies are needed to verify the correlation between ankle strength assessment methods.

CONCLUSION

The results of the present pilot study demonstrated greater isokinetic strength in men than in women, as well as in active individuals compared to sedentary ones. However, it was not possible to establish an association between isometric and isokinetic ankle measurements.

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IMPACT AND HEALTHCARE UTILIZATION PATTERNS OF AN ORTHOPEDIC TELEMEDICINE PROGRAM IN BRAZIL

IMPACTO E PADRÕES DE UTILIZAÇÃO EM UM PROGRAMA DE TELEMEDICINA ORTOPÉDICA NO BRASIL

Fabio Seiji Mazzi Yamaguchi[1], *Vitor Matheus Silva*[2], *Hector Fugihara Kroes*[2], *Jorge dos Santos Silva*[1], *Raphael Martus Marcon*[1], *Henrique Melo de Campos Gurgel*[1]

1. Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas, Instituto de Ortopedia e Traumatologia (HCFMUSP), Sao Paulo, SP, Brazil.
2. Universidade de Sao Paulo, Faculdade de Medicina (FMUSP), Sao Paulo, SP, Brazil.

ABSTRACT

Objective: To examine the relationship between place of residence, social vulnerability, and telemedicine access among orthopedic patients at a tertiary hospital in São Paulo, Brazil. Methods: A cross-sectional, comparative study analyzing sociodemographic, economic, and geographic characteristics of 475 patients who attended telemedicine consultations between August 2022 and August 2023. Patients were grouped by their Social Vulnerability Index (IVS) to assess differences in travel distances, costs, and accessibility challenges. The analysis included comparisons of demographic factors, financial burdens, and telemedicine's impact on reducing travel constraints. Results: Telemedicine consultations avoided an average travel distance of 211 km and saved approximately 44 USD per consultation. Patients from higher IVS regions had significantly greater travel distances, longer travel times, lower formal education levels, and were more likely to be younger, male, and of non-White race. Additionally, these patients more frequently reported missing work for in-person visits. Telemedicine access disparities reflect broader socioeconomic and geographic inequalities. Conclusions: This study highlights how spatial and socioeconomic vulnerabilities shape telemedicine access in Brazil. Travel burdens and job insecurity disproportionately affect vulnerable groups, while social support mitigates barriers for older adults. ***Level of Evidence III; Cross-Sectional Study.***

Keywords: Telemedicine; Social Vulnerability; Orthopedics.

RESUMO

Objetivo: Examinar a relação entre local de residência, vulnerabilidade social e acesso à telemedicina entre pacientes ortopédicos de um hospital terciário em São Paulo, Brasil. Métodos: Estudo transversal e comparativo que analisou características sociodemográficas, econômicas e geográficas de 475 pacientes que participaram de consultas por telemedicina entre agosto de 2022 e agosto de 2023. Os pacientes foram agrupados conforme seu Índice de Vulnerabilidade Social (IVS) para avaliar diferenças em distâncias percorridas, custos e desafios de acessibilidade. A análise incluiu comparações de fatores demográficos, encargos financeiros e o impacto da telemedicina na redução de restrições ao deslocamento. Resultados: As consultas por telemedicina evitaram, em média, deslocamento de 211 km e economizaram aproximadamente 44 dólares por consulta. Pacientes de regiões com maior IVS apresentaram distâncias significativamente maiores, tempos de viagem mais longos, menor escolaridade e eram, com mais frequência, mais jovens, do sexo masculino e de raça não branca. Além disso, relataram mais frequentemente faltar ao trabalho para consultas presenciais. Conclusões: Este estudo destaca como vulnerabilidades espaciais e socioeconômicas moldam o acesso à telemedicina no Brasil. O ônus do deslocamento e a insegurança no trabalho afetam desproporcionalmente os grupos vulneráveis, enquanto o apoio social contribui para mitigar barreiras entre os idosos. ***Nível de Evidência III; Estudo Transversal.***

Descritores: *Telemedicina; Vulnerabilidade Social; Ortopedia.*

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INTRODUCTION

Brazil's vast geography and regional disparities create significant barriers to equitable healthcare access.[1] Even in urban centers like São Paulo, socioeconomic inequalities lead to uneven healthcare distribution, with low-income communities experiencing greater challenges in accessing specialized care.[2]

Telemedicine has emerged as a promising solution to bridge gaps by reducing geographic and economic barriers to care, a process that was significantly accelerated by the COVID-19 pandemic. Telemedicine minimizes the need for costly and time-consuming trips to healthcare facilities, improves access for isolated communities, and ensures continuity of care by allowing patients to receive medical

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The study was conducted at Instituto de Ortopedia e Traumatologia do Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Rua Dr. Ovidio Pires de Campos, 333, Cerqueira Cesar, Sao Paulo, SP, Brazil. 05403-010.
Correspondence: Fabio Seiji Mazzi Yamaguchi. 333, Rua Dr. Ovidio Pires de Campos, Cerqueira Cesar, Sao Paulo, SP, Brazil. 05403-010. fabio.mazzi@hc.fm.usp.br

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consultations remotely.[3] For patients living in remote regions or underserved urban areas, telemedicine can represent not only a lifeline for timely medical care but also significant economic relief by reducing travel-related expenses and the opportunity costs associated with missing work or other responsibilities.[4-5] The widespread use of mobile devices, such as smartphones, enhances the feasibility of expanding this modality, even among vulnerable populations.[6-9]

Among orthopedic patients, these benefits are especially significant, as their conditions often involve mobility limitations, chronic pain, or the need for frequent post-surgical follow-ups that require long-term management.[10] For individuals with physical disabilities or those recovering from procedures, traveling to healthcare facilities can be particularly burdensome, increasing the risk of delays or interruptions in care.[10]

By evaluating the economic and social impacts of telemedicine and their relationship to socioeconomic conditions, this study seeks to highlight its role as a tool for reducing healthcare disparities in Brazil. The findings will provide a better understanding of how geographic distance, financial burdens, and social inequities influence patients' access to care, helping to guide policies aimed at improving healthcare delivery for the most vulnerable populations. In a country as geographically and socially diverse as Brazil, such knowledge is essential for addressing regional inequities and ensuring that telemedicine fulfills its promise of expanding access to quality healthcare for all.

METHODS

This single-center, cross-sectional observational study assessed the perceptions of telemedicine patients between August 2022 and August 2023 using questionnaires. Ethical approval was obtained from the Research Ethics Committee of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo (approval number 5.022.929; CAAE: 51877521.0.0000.0068). Patients provided consent through a digital informed consent form (ICF) and answered a questionnaire providing information on their demographic characteristics, orthopedic care at our facility, and travel plans for a hypothetical in-person consultation at our hospital. Social vulnerability was indirectly measured.

Population

The study included patients who attended at least one telemedicine outpatient consultation, provided by various orthopedic subspecialties, between August 2022 and August 2023 at a single, orthopaedics specialized, quaternary care hospital in Brazil. Exclusion criteria included individuals who did not sign the informed consent form or who withdrew from the study at any stage.

Social Vulnerability

Social vulnerability was indirectly assessed through patients' place of residence. Addresses obtained from hospital records were matched with a publicly available IVS, developed by the governmental research institute IPEA.[11] The IVS is a composite measure that evaluates social and economic vulnerability in a given region, incorporating indicators such as income, education, housing conditions, employment rates, and access to essential services like healthcare and sanitation. To ensure greater specificity, we prioritized IVS data based on Human Development Units (UDHs), the most detailed geographic level available. When UDH-level data were unavailable, IVS values at the municipal (city) level were used.

Distance and Travel Time

The coordinates of the hospital and patients' residences were manually obtained via Google Maps using 'Clipcoords v0.1.0' software for assistance.[12] Travel distances were calculated using a custom Python-based algorithm that employed Google's geocoding API via Google Cloud.[13] Travel times were manually determined by inputting the coordinates into the "Google Maps" website, selecting 8 a.m. on a Monday as the arrival time and following the first suggested route. The "car" option was chosen for individuals traveling by private cars or publicly funded vans/ambulances, while the "public transport" option was selected for those using mass transit public transportation.

Travel Cost

To assess potential transport cost savings from telemedicine consultations, we used a hybrid method combining self-reported and indirect cost measures based on the mode of transport. This approach accounted for the complexity of estimating public transportation costs in São Paulo, which can vary significantly depending on patient access to government-subsidized discounts and integrated fare systems that lower expenses for users relying on multiple transport lines. In contrast, private transportation costs could be estimated more directly using an indirect measure of fuel expenses.

For individuals using a private car, travel costs were based on fuel consumption, which was estimated considering twice the travel distance previously obtained, the fuel efficiency of ten kilometers per liter, and BRL 6.12 (six Brazilian reais and 12 cents) per liter as the price of gasoline.[14,15] For public transportation, costs were informed by patients through the questionnaire. A rate of 2.3 BRL (two Brazilian reais and 30 cents) per USD was used to convert costs to international standards and facilitate comparison as per the "CCEMG–EPPI Centre Cost Converter".[16]

Statistical Analysis

The Wilcoxon rank-sum test with continuity correction was applied to compare continuous variables between two independent groups. When comparing continuous variables across more than two independent groups, the Kruskal-Wallis test was employed. Correlations between continuous variables were assessed using Spearman's rank correlation coefficient. Categorical variables were analyzed using Pearson's chi-squared test. To account for potential confounding effects, partial correlations were performed. Statistical significance was set at $p < 0.05$, and all analyses were conducted using R version 4.3.1. (RStudio v2023.09.1).

RESULTS

We collected data from 475 eligible participants, comprising 206 men (43%) and 269 women (57%). The participants had an average age of 53 years (SD = 16 years) and were categorized into three groups: 18 young adults, 296 adults, and 161 elderly individuals (>60 years). Regarding education, 22% had completed higher education, 7.8% had incomplete higher education, 29% had completed high school, 6.1% had incomplete high school, 9.7% had completed elementary school, 24% had incomplete elementary school, and 2.5% had no formal education. Most participants identified as white (49%) or mixed race (38%), while 11% identified as Black, 1.1% as Asian, and 0.6% as Indigenous (Table 1).

Most patients resided in the hospital's city or nearby areas, with 231 from the city of São Paulo, 221 from other cities in the state, and 23 from outside the state (Figures 1 and 2). The median travel distance avoided through telemedicine was 54 km (IQR 34-96 km), averaging a distance of 211 km. The median travel time to an in-person appointment was 170 minutes (IQR 130-222 min), resulting in an average travel time avoided of 286 minutes. Travel distance and time avoided were much more relevant in groups from outside the city of São Paulo (Table 2). Among the participants,

Table 1. Cohort's sociodemographic data.

Characteristic	N = 475
Age (years)	
Mean (SD)	53 (16)
Median (IQR)	54 (43, 65)
Range	4, 91
Age groups	
Children	18 (3.8%)
Adults	296 (62%)
Elderly	161 (34%)
Sex	
Men	206 (43%)
Women	269 (57%)
Race	
White	235 (49%)
Mixed race	179 (38%)
Black	53 (11%)
Asian	5 (1.1%)
Indigenous	3 (0.6%)
Education	
No formal education	12 (2.5%)
Incomplete elementary school	112 (24%)
Completed elementary school	46 (9.7%)
Incomplete high school	29 (6.1%)
Completed high school	136 (29%)
Incomplete higher education	37 (7.8%)
Completed higher education	103 (22%)

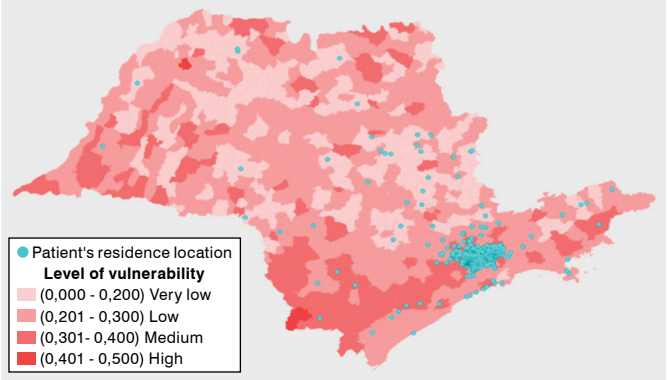

Figure 1. Map of the State of São Paulo highlighting cities, their respective vulnerability levels, and the place of residence of each patient.

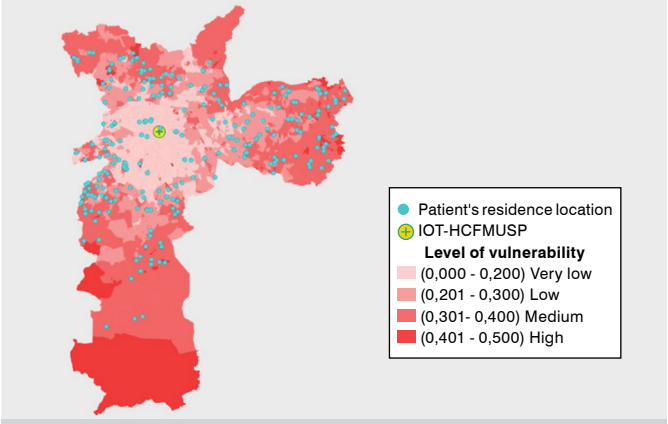

Figure 2. Map of the City of São Paulo highlighting Human Development Units, their respective vulnerability levels, and the place of residence of each patient.

Table 2. Telemedicine program socioeconomic impact and utilization patterns according to origin.

Characteristic	City of São Paulo N = 231	Another City in the State N = 221	Out of State N = 23	Total N = 475
Round-trip distance saved (km)				
Mean (SD)	39 (17)	185 (224)	2,184 (1,972)	211 (639)
Median (IQR)	36 (26, 50)	84 (54, 222)	1,274 (852, 2,867)	54 (34, 96)
Range	2, 92	22, 1,250	318, 7,758	2, 7,758
Sum	9,016	40,838	50,240	100,094
Round-trip time saved (min)				
Mean (SD)	138 (47)	292 (261)	1,716 (1,620)	286 (514)
Median (IQR)	140 (109, 170)	200 (160, 320)	1,000 (610, 2,360)	170 (130, 222)
Range	0, 274	12, 2,320	360, 6,600	0, 6,600
Sum	31,956	64,546	39,460	135,962
Travel Expenses avoided (USD)				
Mean (SD)	9 (11)	31 (52)	528 (512)	44 (160)
Median (IQR)	8 (0, 15)	17 (0, 28)	304 (200, 891)	11 (0, 19)
Range	0, 122	0, 277	0, 2,064	0, 2,064
Sum	2,166	6,822	12,135	21,122
Utilized device				
Only cellphone	194 (84%)	198 (90%)	18 (78%)	410 (86%)
Only computer	26 (11%)	20 (9.0%)	4 (17%)	50 (11%)
Cellphone or computer	11 (4.8%)	3 (1.4%)	1 (4.3%)	15 (3.2%)
Public transportation usage	169 (73%)	161 (73%)	13 (57%)	343 (72%)
Transportation gratuity	71 (31%)	67 (30%)	2 (8.7%)	140 (29%)
Accompanying person	117 (51%)	104 (47%)	8 (35%)	229 (48%)
Patient work absence	61 (26%)	70 (32%)	9 (39%)	140 (29%)
Accompanying person work absence	64 (28%)	78 (35%)	10 (43%)	152 (32%)

343 (72%) would have relied on public transportation, of whom 140 (28%) had access to free fare. Additionally, 229 (49%) of patients would have been accompanied to the appointment. Regarding teleconsultations, 86% used a mobile phone, 11% used a computer, and 3.2% reported using both devices. Telemedicine resulted in an average cost saving of 44 USD per patient.

Most patients had low or medium IVS levels (Figure 3), which were significantly correlated with various variables (Table 3). Data analysis showed a negative correlation between IVS and age, but a positive association with the necessity to skip work, travel distance and time (Figure 4). Among patients without transportation fare exemptions, those who avoided higher travel costs had a higher vulnerability index. IVS values decreased with higher education levels, with individuals who completed higher education showing a mean IVS of 0.256, compared to 0.310 among those without formal education. Race also significantly impacted IVS: Asian and White individuals had the lowest mean IVS (0.261 and 0.275), while Indigenous, Black, and Mixed-Race individuals had higher means (0.331, 0.316, and 0.299, respectively). Male patients had a significantly higher mean IVS (0.302) than female patients (0.279), even after adjusting for age. No significant relationship was observed between IVS and public transportation use, transport gratuity, presence of an accompanying person, or device utilization.

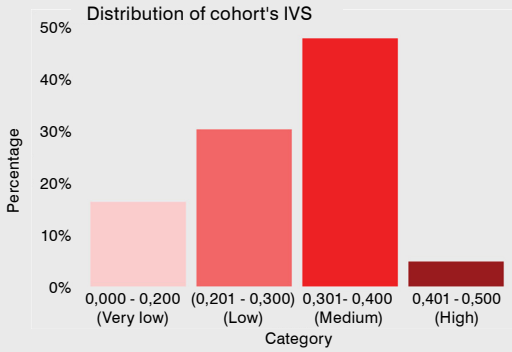

Figure 3. Vertical bar chart illustrating the distribution of the cohort's Social Vulnerability Index (IVS) categories. The graph shows the proportion of patients in each vulnerability range, with the majority falling within the Medium (0.301-0.400) and Low (0.201-0.300) categories, while fewer individuals are in the Very Low (0.000-0.200) and High (0.401-0.500) categories.

Table 3. Correlation between IVS and various cohort variables.

Variable	Test	P-Value	Significance
Age	Spearman	<0.0001	****
Travel distance avoided	Spearman	0.0420	*
Travel time avoided	Spearman	0.0033	**
Expenses avoided	Spearman	0.8768	
Sex	Wilcoxon	0.0128	*
Public transport	Wilcoxon	0.1603	
Transport gratuity	Wilcoxon	0.1830	
Accompanying person	Wilcoxon	0.5822	
Own work absence	Wilcoxon	0.0420	*
Accompanying person work absence	Wilcoxon	0.9170	
Computer usage	Wilcoxon	0.3106	
Education	Kruskal-Wallis	0.0087	**
Race	Kruskal-Wallis	0.0061	**

DISCUSSION

The results of this study provide insights into how patients' residence location influences healthcare utilization in Brazil. The significant correlations found between IVS and both potential travel distance and time avoided highlight how social vulnerability impacts access to specialized care (Figure 3). Notably, time presented a much stronger correlation than distance, likely because it captures additional barriers beyond physical proximity, such as transportation inefficiencies, traffic conditions, and accessibility issues, which disproportionately affect socially vulnerable populations.[17]

In further sub analyses, we found that, when analyzing based on mode of transport (public versus private), correlation between IVS with both distance and time only maintained significance in the public transport group. This reflects the unique challenges they face, including limited transit routes, longer travel times due to multiple transfers, and rigid public transport schedules.[18,19] In contrast, individuals using private transportation have greater flexibility and shorter travel times, mitigating some of the geographic barriers to care.[18,19] This finding underscores how reliance on public transportation exacerbates the relationship between distance and social vulnerability.

Although the interquartile range for round-trip travel distances was 34–96 km, some patients needed to travel up to 7,758 km. Many require frequent follow-ups after surgical interventions but struggle to maintain appointments due to relocation or distance barriers. These findings emphasize the crucial role of telemedicine in ensuring continuity of care where in-person visits would otherwise be unfeasible. An analysis of mean travel times in São Paulo revealed that a 39 km round-trip takes approximately 138 minutes, highlighting the inefficiencies of a transportation system reliant on buses. While not directly measured in our study, during data analysis, we observed that buses were the most accessible and widely used mode of transportation in many regions. Although the city has a railway network, its coverage remains insufficient, further reinforcing the

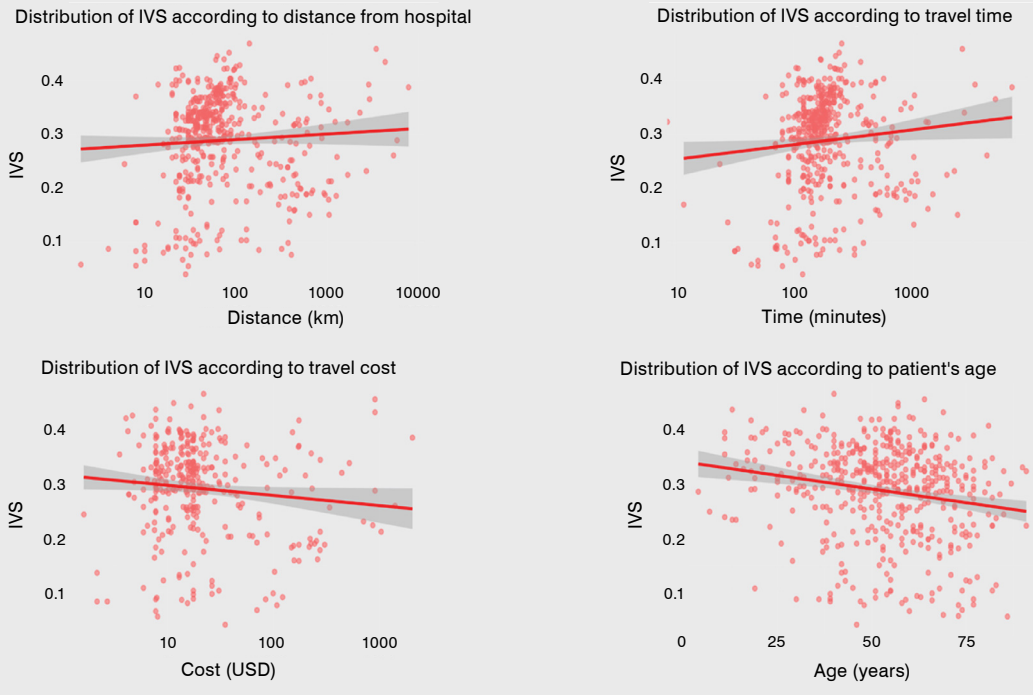

Figure 4. Scatter plots with regression lines illustrating the relationship between the Social Vulnerability Index (IVS) and four different variables: distance from the hospital (km), travel time (minutes), travel cost (USD), and patient's age (years). The plots show the distribution of data points and trends, with shaded confidence intervals around the regression lines.

need for expanding railway infrastructure to improve mobility and healthcare access.[20]

Regarding transportation costs, patients living outside São Paulo state faced significantly higher expenses. Even those from other cities within the state incurred an average round-trip cost of USD 31— a substantial amount in a country where the federal minimum wage is around USD 250. These findings align with studies in other Latin American countries, illustrating the widespread economic burden of travel for healthcare.[21,22]

A notable contribution of this study is the quantification of transportation fare exemptions, which benefited approximately 30% of patients. However, no significant correlation was found between fare exemptions and IVS, likely because these benefits were granted primarily based on age rather than socioeconomic status.

A significant association between IVS and the need to miss work for in-person visits was identified, indicating that socially vulnerable individuals face employment-related barriers to healthcare. Job insecurity, lack of labor protections, and inflexible workplaces may prevent timely medical visits, potentially leading to delayed diagnoses, suboptimal treatment, and worsened health outcomes.[23] A large proportion of the Brazilian workforce is engaged in informal employment, often lacking paid medical leave.[24] These structural issues may further increase the demand for telemedicine as an alternative to in-person care.

Interestingly, elderly telemedicine patients at our hospital were more likely to reside in areas with lower IVS. This may be explained by several factors, including greater financial stability accumulated over time, pension support, and infrastructure improvements in long-standing neighborhoods. However, selection bias may also play a role, as individuals from more advantaged areas might have better access to healthcare resources, leading to their overrepresentation in the study.[1,25]

Previous studies suggest that distance and social support influence healthcare access among older adults.[26] When comparing patients aged ≥60 years and <60 years, we found that IVS remained significantly associated with distance and travel time only in the elderly group. This suggests that older adults are disproportionately affected by geographic barriers due to mobility limitations and comorbidities.[26] Telemedicine serves as a valuable solution by addressing these challenges and facilitating access to care.

To further examine the role of social support, we stratified elderly patients into those with and without an accompanying person. Among those without a companion, IVS remained significantly correlated with travel distance, but this correlation was lost in those with a companion. This suggests that social support helps mitigate transportation barriers and may influence healthcare-seeking behavior.

Our study also found that 86% of patients opted to use smartphones for telemedicine consultations. Given their widespread affordability, smartphones can play a crucial role in enabling telemedicine, especially in populations with limited access to computers or broadband internet.[27,28] However, other studies have shown that, despite high mobile penetration, digital literacy remains a barrier in vulnerable regions, emphasizing the need for inclusive policies that ensure telemedicine benefits all socioeconomic groups.[29,30]

We also identified a significant association between IVS and sex, with women exhibiting lower social vulnerability than men. This aligns with previous research showing that women seek healthcare more frequently, participate in preventive care programs, and benefit from protective social factors.[1] These factors contribute to improved health outcomes and lower overall vulnerability. In contrast, men are more likely to underutilize healthcare services, potentially leading to delayed diagnoses and poorer health indicators.

Additionally, IVS was significantly correlated with race and education. Indigenous, Black, and mixed-race patients had higher IVS scores than White and Asian patients, likely reflecting systemic barriers such as economic inequality and limited access to resources.[1] Similarly, lower formal education levels were associated with higher IVS, underscoring the complex interplay between education, socioeconomic status, and healthcare access. While these disparities are well-documented in Brazilian healthcare, our study highlights that they persist in the telemedicine landscape, reinforcing the need for equity-driven policies.[1]

Our study has several limitations. Transportation cost data were self-reported, which may introduce bias. Social vulnerability was estimated based on residential location, which may not fully reflect individual circumstances. Additionally, the IVS used was developed in 2010 and may not represent current socioeconomic conditions. Questionnaire responses are subject to recall and self-report biases. As a single-center study conducted in a tertiary care hospital, findings may not be generalizable to other settings or regions in Brazil. By focusing on orthopedic patients, the study does not account for the needs of other medical specialties. Selection bias is also a concern, as patients who participated in telemedicine may already have better access to technology, potentially underrepresenting the most vulnerable groups. Lastly, patients who declined participation or withdrew from the study may have different barriers to telemedicine that remain unexplored.

CONCLUSION

This study highlights the role of telemedicine in addressing geographic and socioeconomic barriers to healthcare access among orthopedic patients in São Paulo, Brazil. By reducing travel distances, time, and costs, telemedicine improves accessibility, particularly for socially vulnerable populations who face significant mobility and financial constraints. It also demonstrates how, in Brazil, disparities in access to healthcare persist, influenced by factors such as public transportation dependency, employment-related barriers, age, sex, race and education. These findings emphasize the need for targeted policies to ensure telehealth provides equitable access to specialized care.

AUTHOR'S CONTRIBUTION: Each author contributed individually and significantly to the development of this article and approved the final version of the manuscript. FSMY: conception and design of the work, data analysis, and manuscript drafting. VMS: conception and design of the work, data acquisition and interpretation, manuscript drafting. HFK: statistical data analysis, interpretation of results, and manuscript drafting. JSS and RMM: data acquisition and analysis, and critical revision of its intellectual content. HMCG: conception of the work, data acquisition and analysis, and critical revision of its intellectual content.

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SPONTANEOUS RUPTURE OF BAKER'S CYST - CASE SERIES

RUPTURA ESPONTÂNEA DE CISTO DE BAKER – SÉRIE DE CASOS

GILBERTO LUIS CAMANHO[1], *RICCARDO GOMES GOBBI*[1], *MÁRCIA UCHÔA DE REZENDE*[1], *GUILHERME PEREIRA OCAMPOS*[1]

1. Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas (HC-FMUSP), Instituto de Ortopedia e Traumatologia, Sao Paulo, SP, Brazil.

ABSTRACT

Objective: The presence of popliteal cysts is common, although often unkown to the patient. When spontaneous rupture occurs, the clinical presentation is typically dramatic, frequently prompting the patient to seek emergency care. Eventually the condition can be mistaken for other pathologies, more commonly deep vein thrombosis, leading to inappropriate treatment. The objective of this study is to describe a case series of spontaneous Baker's cyst ruptures, with a 2-year follow-up. Methods: Sixteen consecutive patients with symptomatic ruptured popliteal cyst were treated acutely with anti-inflammatory measures and physical therapy. Results: All patients had a good resolution of their cases with conservative treatment over an average period of one week, and there was no recurrence of cyst rupture. Conclusion: Spontaneous rupture of Baker's cyst in adult patients can be very symptomatic and disabling; however, once diagnosed, it responds well to conservative treatment and rarely recurs. ***Level of Evidence IV; Case Series.***

Keywords: Popliteal Cyst; Acute Pain; Joint Capsule; Synovial Membrane; Synovial Fluid; Osteoarthritis.

RESUMO

Objetivo: A presença de cistos poplíteos é comum, embora nem sempre seja de conhecimento do paciente. Quando ocorre a ruptura espontânea do cisto, o paciente apresenta um quadro exuberante, geralmente buscando assistência no pronto-socorro. Eventualmente, a condição pode ser confundida com outras patologias, mais frequentemente com a trombose venosa profunda, o que leva a um tratamento inadequado. O objetivo é descrever uma série de casos de ruptura espontânea de cistos de Baker, com acompanhamento de 2 anos. Métodos: Dezesseis pacientes consecutivos com ruptura sintomática de cisto poplíteo foram tratados agudamente com medidas anti-inflamatórias e fisioterapia. Resultados: Todos os pacientes apresentaram uma boa resolução de seus quadros com tratamento conservador por um período médio de uma semana, e não houve recorrência da ruptura do cisto. Conclusão: A ruptura espontânea do cisto de Baker em pacientes adultos pode ser muito sintomática e incapacitante, mas uma vez diagnosticada, evolui bem com tratamento conservador e raramente recorre. ***Nível de Evidência IV; Série de Casos.***

Descritores: *Cisto Popliteal; Dor Aguda; Cápsula Articular; Membrana Sinovial; Líquido Sinovial; Osteoartrite.*

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INTRODUCTION

The presence of cysts in the posterior region of the knee is a common finding in the evaluation of patients with problems in this joint.[1] Asymptomatic cysts in adult patients result from some irritative process of traumatic or inflammatory origin in the synovial tissue resulting in an increased production of synovial fluid.[2,3] Through a communication in the posteromedial region of the joint capsule, the liquid leaks into the bursa between the medial and semimembranous gastrocnemius tendons, and through a valve mechanism a cyst is formed, called Baker's cyst,[4,5] described by William Baker in 1877.[6] Acute rupture of Baker's cyst (RABC) causes a very symptomatic condition, which occurs in patients who, in general, are unaware that they have the cysts. The intensity of the symptoms, which appear acutely, frightens patients and medical colleagues who are not familiar with the condition, a fact that often leads to inappropriate behavior. Despite its clinical importance, it is a topic that is little reported and studied. The objective of this work is to describe the symptoms, treatment and follow-up of RABC.

METHODS

Retrospective case series with 16 patients who presented with RABC. Casuistry originating from the project approved by the ethics committee 66509923.5.0000.0068.
Included were:

- Adult patients diagnosed with RABC, confirmed by clinical examination and ultrasound or MRI;
- Minimum of two years of follow-up;
- Absence of history of trauma at the time of symptom onset;
- Intensity of the condition sufficient to seek medical help within seven days at the onset of the condition.

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

The study was conducted at Universidade de São Paulo, Faculdade de Medicina, Hospital das Clinicas (HC-FMUSP), Instituto de Ortopedia e Traumatologia, Dr. Ovidio Pires de Campos, 333, Cerqueira Cesar, Sao Paulo, SP, Brazil. 05402-000.
Correspondence: Guilherme Pereira Ocampos. 333, Rua Dr. Ovídio Pires de Campos, Sao Paulo, SP, Brazil. drguilhermeocampos@gmail.com

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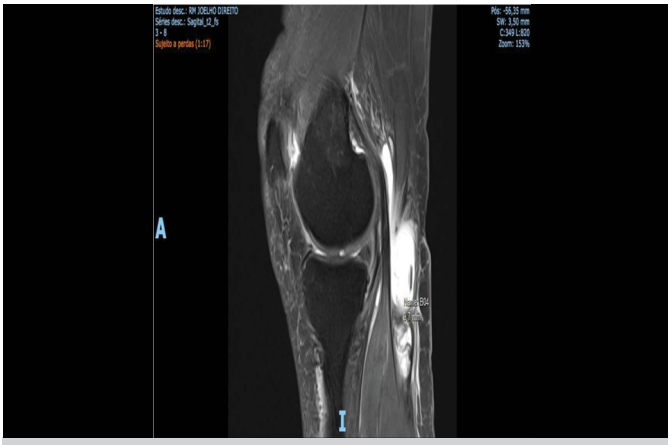
The medical records were searched to obtain: age, sex, laterality, previous pathology in the knee, symptoms, initial diagnosis given in the first medical evaluation, diagnosis of joint pathology related to the origin of the cyst, treatment instituted, and results after two years of follow-up.

RESULTS

Among the 16 patients included with RABC, 10 were male (62.5%). The right side was affected nine times (56.2%). The average age was 59.4 years (±7.08), varying between 46 years and 71 years.
All patients reported sudden and disabling pain in the posterior region of the knee, with worsening on palpation of the posterior region of the knee and calf, limitation of ankle dorsiflexion due to pain and lameness. The pain was progressive in the first few hours and was not sensitive to common analgesics, leading patients to emergency care. Its onset was not related to any traumatic event. In three cases with more than five days of evolution, distal hematomas were found on the posterior aspect of the leg or on the medial aspect of the ankle (Figure 1).
RABC was initially characterized in 11 cases by ultrasound, and in five by MRI (Figure 2). The differential diagnosis was deep vein thrombosis in most cases.
No patient related the symptom to previous pathology in their knee, although 12 were aware of some pathology in the affected knee. The diagnoses of related joint pathologies are detailed in Table 1.

Source: Author's personal fie.

Figure 1. Hematoma on the medial aspect of the ankle in a patient with spontaneous rupture of a Baker's cyst.



Source: Author's personal fie.

Figure 2. Sagittal magnetic resonance image demonstrating a partially ruptured Baker's cyst in its distal part.

Table 1. Distribution of Previous Joint Pathologies in Patients with RABC.

	Number of Cases	Percentage
Knee Osteoarthritis	6	37.5%
Meniscal Injury	4	25%
Previous Arthroplasty	2	12.5%
Previous Ligament Surgery	2	12.5%
Synovial Pathology	2	12.5%

RABC: acute rupture of Baker's cyst.

Among the four patients who were unaware of having any knee problems, two were diagnosed with osteoarthritis and two with meniscal injuries.
Treatment was always initially non-surgical with rest, ice and NSAIDs for five to seven days. After the acute phase, everyone underwent physiotherapy for analgesia and muscle rehabilitation until symptoms resolved.
The evaluation of patients after two years showed that all patients had a good evolution with conservative treatment for a period of up to three weeks, and there was no recurrence in any case.
Only one of those with a meniscal injury underwent partial medial meniscectomy before two years of follow-up due to persistence of joint and posterior knee symptoms.

DISCUSSION

The presence of popliteal cysts depends on the population studied and the technique used for diagnosis. In studies of asymptomatic knees in adults, popliteal cysts have been identified in 4.7% to 37% of cases.[2,3]
The integrity of the joint capsule decreases with age, and one theory is that the opening that forms the cyst results from an injury to the joint capsule degenerate.[4,5] Rauschning[7] noted that when no opening was found, capsular thinning allows herniation of synovial tissue.
When intact, it is visible in some cases, but most of the time the diagnosis results from an imaging exam, with ultrasound and resonance being the most common.[8]
In most cases it is asymptomatic and goes unnoticed by the patient. The treatment is based on the basic pathology that led to the cyst, surgical approach to the cyst is only necessary in cases of compression of important structures in the posterior region of the knee, a very rare occurrence.
The surgical approach to cyst resection leads to a high rate of recurrence and is not recommended.[7] A recent meta-analysis[9] on Baker's cyst treatment techniques compared the increase in communication between the cyst and the joint cavity and the closure of this communication. The success rates were 96.7% and 84.6% in the communication expansion group and the communication closure group, respectively. Resection of the cyst wall or non-resection of the wall has success rates of 98.2% and 94.7%, respectively.
RABC is uncommon and treated with some disregard in the literature, most of the time as case reports,[10] but it must be remembered due to the importance of the intensity of the initial symptoms, which when treated without knowledge lead to dramatic situations.[11] We have already followed a case of a patient whose RABC was diagnosed as compartment syndrome and underwent fasciotomy, causing unnecessary suffering to the patient.
We believe that asymptomatic cyst ruptures occur, as it is not uncommon to notice images on MRI described as ruptured cysts by the radiologist, without clinical correspondence.
Conservative initial treatment brings good results. Assessment of the cause of the cyst should guide the follow-up sequence. We had four patients with knee osteoarthritis without synovitis. Everyone had already taken some medication due to knee discomfort. Two of them needed of total arthroplasty in the evolution of symptoms. Four patients had degenerative medial meniscal injuries with involvement

of the articular cartilage. One patient underwent meniscectomy shortly after RABC. It progressed well, without recurrence.
Some patients had previous knee surgery. Two patients had total arthroplasty for knee arthrosis, carried out three and five years ago. They had no complaints about the affected knee despite having RABC. Two patients had undergone successful anterior cruciate ligament reconstruction and had no other apparent cause for the cyst. Everyone progressed well after treatment.

Two patients were being treated for inflammatory synovial disease. RABC treatment was conservative, as described, in all cases and resulted in a good evolution without recurrence.

CONCLUSION

Spontaneous rupture of a Baker's cyst in adult patients can be very symptomatic and disabling, but once diagnosed, it progresses well with conservative treatment and rarely recurs.

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APPLICATION OF ANTERIOR MINI-INCISION VERTEBROPLASTY IN CERVICAL METASTASES

APLICAÇÃO DE VERTEBROPLASTIA POR MINI-INCISÃO ANTERIOR EM METÁSTASES CERVICAIS

Guan Shi[1], *Hao Chen*[1], *Pu Jia*[1], *Li Bao*[1], *Fei Feng*[1]

1. Capital Medical University, Beijing Friendship Hospital, Department of Orthopaedics, Beijing, China.

ABSTRACT

Objective: To investigate the efficacy and safety of anterior cervical mini-incision vertebroplasty in the treatment of vertebral metastases. Methods: From July 2009 to March 2013, seven cases of vertebral metastases were treated by using vertebroplasty through an anterior cervical paratracheal mini-incision guided by C-arm X-ray in Beijing friendship hospital, Capital medical university. Among them, three were male and four were female, aged 51 to 74 years with an average age of 61.7 years. Preoperative and postoperative Visual Analog Scale (VAS) scores and analgesic medication usage were evaluated, and postoperative pain relief was assessed using the World Health Organization (WHO) criteria. Results: All seven surgeries were successful without any occurrences of complications such as nerve or vascular injury, pulmonary embolism, or hematoma. The average cement injection volume was 1.8ml, and postoperative X-rays and CT scans indicated satisfactory cement filling, with two cases showing paravertebral cement leakage, but without clinical symptoms. One week postoperatively, the VAS score decreased from a preoperative average of 8.86 to 2.14, with complete pain relief in three cases, leading to the cessation of analgesic drugs, and partial pain relief in four cases, resulting in a reduction or downgrade of analgesic medications. Follow-ups ranged from 3 to 28 months, with one patient dying at 3 months postoperatively, one at 4 months, two at 6 months, one at 8 months, and one at 17 months, while one patient survived 28 months postoperatively. Postoperatively, all patients showed no worsening of local pain symptoms, and the surgical efficacy remained stable. Conclusion: Anterior cervical mini-incision vertebroplasty is a precise and effective method for pain relief in the treatment of vertebral metastases, providing a safe approach that reduces the risk of damaging critical cervical tissues during the puncture procedure and postoperative hematoma formation. ***Level of Evidence III; Retrospective Study.***

Keywords: Neoplasm Metastasis; Vertebroplasty; Cervical Vertebrae.

RESUMO

Objetivo: Investigar a eficácia e a segurança da vertebroplastia por mini-incisão anterior cervical no tratamento de metástases vertebrais. Métodos: Entre julho de 2009 e março de 2013, sete casos de metástases vertebrais foram tratados com vertebroplastia utilizando uma mini-incisão paratraqueal anterior cervical guiada por fluoroscopia (raios X com intensificador de imagem – C-arm) no Hospital da Amizade de Pequim, Universidade Médica Capital. Dentre os pacientes, três eram do sexo masculino e quatro do sexo feminino, com idades entre 51 e 74 anos (média de 61,7 anos). Avaliaram-se os escores da Escala Visual Analógica (EVA) e o uso de analgésicos no pré e pós-operatório, sendo o alívio da dor classificado de acordo com os critérios da Organização Mundial da Saúde (OMS). Resultados: Todas as sete cirurgias foram realizadas com sucesso, sem ocorrência de complicações como lesões nervosas ou vasculares, embolia pulmonar ou hematoma. O volume médio de cimento injetado foi de 1,8 ml. Radiografias e tomografias pós-operatórias mostraram preenchimento satisfatório do cimento, com extravasamento paravertebral em dois casos, porém sem sintomas clínicos. Após uma semana, o escore EVA médio caiu de 8,86 (pré-operatório) para 2,14, com alívio completo da dor em três pacientes (cessação do uso de analgésicos) e alívio parcial em quatro pacientes (redução ou substituição da medicação analgésica). O tempo de seguimento variou de 3 a 28 meses: um paciente faleceu com 3 meses de pós-operatório, um com 4 meses, dois com 6 meses, um com 8 meses e um com 17 meses; um paciente sobreviveu por 28 meses. Nenhum paciente apresentou agravamento dos sintomas locais de dor, e a eficácia cirúrgica manteve-se estável ao longo do tempo. Conclusão: A vertebroplastia por mini-incisão anterior cervical é um método preciso e eficaz para o alívio da dor no tratamento de metástases vertebrais, oferecendo uma abordagem segura que reduz o risco de lesão aos tecidos cervicais críticos durante o procedimento de punção e a formação de hematomas no pós-operatório. ***Nível de Evidência III; Estudo retrospectivo.***

Descritores: *Metástase Neoplásica; Vertebroplastia; Vértebras Cervicais.*

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The study was conducted at Beijing Friendship Hospital, Capital Medical Unversity, 36 Yongan Rd, Xicheng District, Beijing, China, 100052.
Correspondence: Fei Feng. No. 95, Yong An Rd, XiCheng District, Beijing, China. 100050. fengfei3456@sina.com

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INTRODUCTION

Vertebroplasty, as a minimally invasive technique for rapidly stabilizing pathological vertebrae and treating refractory pain caused by vertebral lesions, has been widely used in the treatment of vertebral hemangioma, malignant tumors, osteoporotic vertebral compression fractures, and multiple myeloma.[1,2] Although the first reported literature on vertebroplasty was for the treatment of vertebral lesions,[3] the low incidence rate, surgical difficulty, and high risk of vertebral lesions have limited the development of vertebroplasty for the treatment of vertebral lesions. Currently, there are relatively few domestic and international literature reports on vertebroplasty for the treatment of vertebral lesions, and most of them are presented as individual case reports.[4,5] In this study, the author employed an anterior cervical paratracheal mini-incision, guided by a C-arm X-ray machine, to perform vertebroplasty in seven cases of vertebral metastases, aiming to explore the feasibility and clinical efficacy of anterior cervical mini-incision vertebroplasty for the treatment of vertebral metastases.

MATERIALS AND METHODS

Patient data

From July 2009 to March 2013, a total of seven cases of vertebral metastases were treated using anterior cervical mini-incision vertebroplasty in Beijing friendship hospital, Capital medical university, including three males and four females, with ages ranging from 51 to 74 years and an average age of 61.7 years. All patients had a confirmed primary malignant tumor, with two cases of lung cancer, two cases of breast cancer, one case of renal cancer, one case of liver cancer, and one case of colon cancer (Table 1).

Clinical assessment

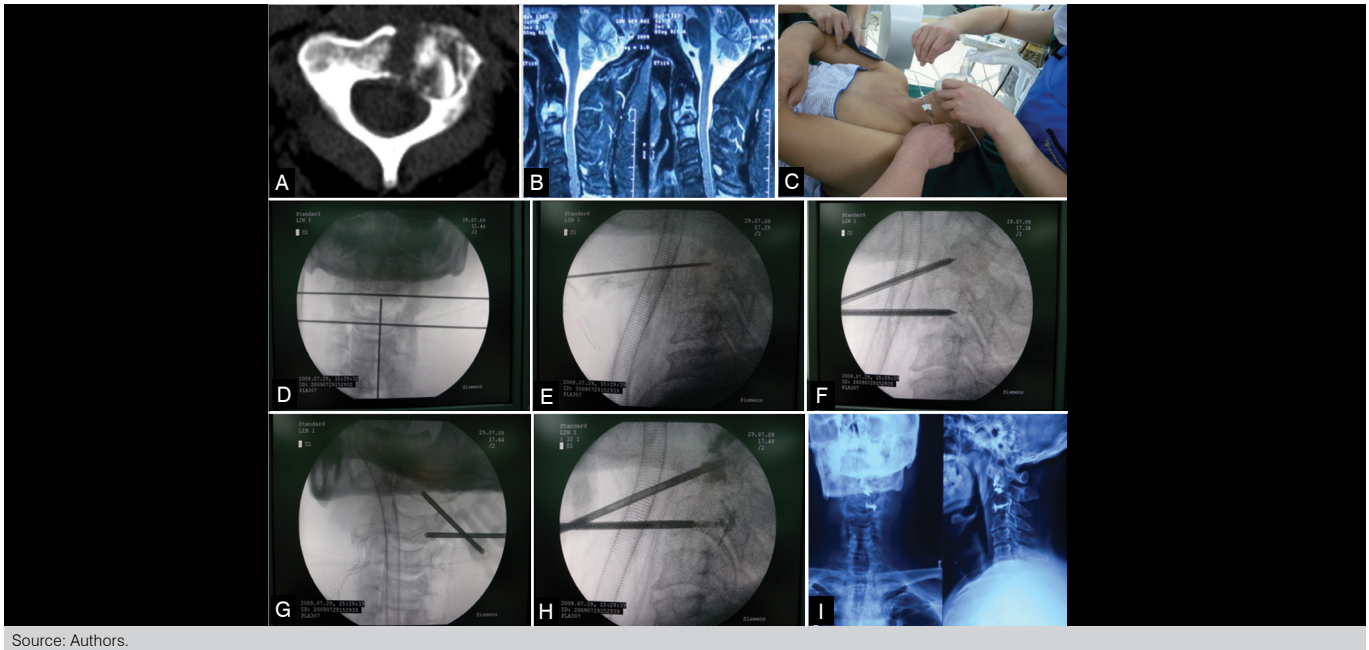
All seven patients had significantly restricted neck movements and experienced severe pain with slight neck movements. Neck rotation (left and right) was limited to within 20°, backward movement was 0°, and forward bending was approximately 15°-20°. Six patients required a neck brace preoperatively to control pain. Pain severity was graded using the Visual Analog Scale (VAS):[6] Grade 0 (0 points, no pain), Grade 1 (less than 3 points, mild pain), Grade 2 (4-6 points, moderate pain), Grade 3 (7-10 points, severe pain). All seven patients experienced severe pain (Grade 3) in the cervical vertebral region and required narcotic analgesics.

Preoperative preparation

Routine preoperative examinations were conducted, including blood, urine, and stool tests, biochemical tests, blood gas analysis, coagulation function tests, and electrocardiograms. Cervical X-rays, CT, and MRI scans were performed to assess the extent of vertebral destruction. CT revealed osteolytic destruction of the vertebrae (Figure 1a), and MRI showed vertebral erosion and signal changes due to the tumor invasion (Figure 1b).

Table 1. Baseline and follow-up of the cases.

Case	Age (years)	Primary tumor	Preoperative VAS	Postoperative VAS at 1 week	Postoperative VAS at 1 month	Postoperative VAS at 3 months	Follow-up
1	51	Lung	10	3	3	3	Died in April
2	74	Colon	8	1	1	1	Died in June
3	63	Liver	8	2	2	2	Died in September
4	56	Lung	9	1	1	0	Died in July
5	56	Breast	9	1	0	0	Alive
6	64	Breast	9	4	4	4	Died in the 17th month
7	68	Kidney	9	3	4	Died	



Source: Authors.

Figure 1. Preoperative CT showing lytic destruction of the vertebral body. B: Preoperative MRI demonstrating tumor invasion and signal changes in C2 and C3 vertebral bodies. C and D: Surface localization of the pedicle awl, determining the incision site. E-H: Fluoroscopic-guided simultaneous positioning, puncture, and bone cement infusion of the pedicle awl at C2 and C3. I: Postoperative X-ray showing satisfactory distribution of bone cement.

Surgical procedure

The specific surgical steps were as follows. The incision site was determined on the left or right side of the trachea at the level of the mandibular angle (Figure 1c and 1d). After endotracheal intubation under general anesthesia, the patient was placed in a supine position with a cushion under the shoulders. Routine disinfection and draping were performed, and a horizontal incision of approximately 2 cm was made through the skin. The surgeon palpated the anterior cervical fascia and the anterior edge of the vertebra. The Jamshidi needle was fixed approximately one-third of its length to the anterior edge of the vertebra, and its position was confirmed under X-ray fluoroscopy (Figure 1e). The position was confirmed again under X-ray fluoroscopy in both anterior-posterior and lateral views (Figure 1f and 1g). Once the position was deemed satisfactory, bone cement was prepared. The bone cement was injected into the vertebral body under fluoroscopic guidance during the dough phase (transitioning from a stringy to a toothpaste-like consistency, Figure 1h). The puncture site was compressed manually for 3-5 minutes after the needle was removed to prevent bleeding and the formation of hematomas. The incision was closed layer by layer, completing the surgery.

Treatment evaluation

On the second day after surgery, X-ray and CT examinations were performed to observe the distribution of the cement.VAS was reassessed one week after surgery, at one month and three months after the procedure. The postoperative pain relief was evaluated using the WHO standard[7] at one week after surgery, as follows: complete relief, partial relief, mild relief, ineffective. The effective treatment included complete relief + partial relief, while ineffective treatment included mild relief + no improvement.

Declarations

The requirement of ethical approval for this was waived by the ethic committee of Beijing Friendship Hospital, Capital Medical University. The need for written informed consent was waived by the ethic committee of Beijing Friendship Hospital, Capital Medical University due to retrospective nature of the study.

RESULTS

All seven cases in this group had successful surgeries, with an average operation time of 53 minutes and an average cement injection volume of 1.8ml. All wounds healed as Class I/A, and no complications such as nerve or vascular injury, pulmonary embolism, or hematoma occurred. Follow-up X-rays and CT scans on the second day after surgery showed satisfactory cement filling in all patients (Figure 1i), with two cases showing cement leakage into the paravertebral soft tissue, but without clinical symptoms.

Treatment efficacy

All seven patients experienced varying degrees of soft tissue swelling around the neck incision postoperatively, with no bleeding or hematoma formation along the puncture route. Swallowing movements caused discomfort, but with the use of anti-inflammatory and analgesic drugs, all patients could tolerate the symptoms, and they largely disappeared one week after surgery. The average VAS score one week after surgery decreased to 2.14, and according to the WHO standard, three cases achieved complete relief, and four cases achieved partial relief, resulting in an overall effective rate of 100%. After one week of orthopedic discharge, patients continued with systemic tumor treatment in other departments. All seven patients were followed up, with one patient dying at three months after surgery, one at four months, two at six months, one at eight months, one at seventeen months, and one patient surviving 28 months after surgery. During the follow-up period, there was no aggravation of local pain symptoms, and the surgical efficacy remained stable. VAS scores at different time points (preoperative, one week, one month, and three months after surgery) are shown in Table 1.

DISCUSSION

For patients with advanced tumors and bone metastases, the primary goal of orthopedic surgeons is to improve the quality of life and alleviate the pain. The traditional surgical treatment for cervical spine metastases involves tumor resection, decompression, and vertebral body reconstruction. However, this procedure is associated with significant trauma, high bleeding risk, and high cost. Conservative treatments include local immobilization, wearing a cervical collar, and oral analgesics, but the efficacy is often unsatisfactory. Radiation therapy can relieve pain to some extent,[8] but it cannot enhance the stability of the affected vertebrae. In cases of pathological fractures, instability of the atlantoaxial structure can lead to damage to the upper cervical cord, nerve roots, or blood vessels, resulting in high cervical myelopathy.

For the treatment of spinal bone metastases, vertebroplasty has advantages such as minimal invasiveness, low risk, rapid pain relief, and fast patient recovery. It can stabilize the vertebral body. However, due to the complex distribution of nerves, blood vessels, trachea, and esophagus, vertebroplasty for cervical spine lesions is more challenging. In this study, vertebroplasty for cervical spine were successfully operated to all seven patients.

Surgical method of vertebroplasty for cervical spine metastases

The transoral puncture approach requires complex preoperative preparation, including consultation with the oral and maxillofacial department to assist with oral cleaning. Intraoperatively, general anesthesia and tracheal intubation are needed, along with the use of a joint retractor, and cooperation among multiple departments, including oral and maxillofacial surgery. This approach carries a relatively higher risk of postoperative bleeding and infection, with an infection rate as high as 6.5%.[9,10] Patients may experience discomfort in the throat postoperatively, leading to limited oral intake, necessitating symptomatic treatment such as humidifying and inhaling sputum-dissolving agents.

The anterolateral approach is a classic approach for vertebroplasty in the treatment of cervical spine lesions, and its safety and efficacy have been recognized.[11] However, due to the high position of the atlantoaxial joint, the anterolateral approach requires the patient's head to be excessively tilted backward, lifting the mandible as much as possible to avoid interference with the puncture. This positioning often leads to increased pain, making it difficult for patients to cooperate, sometimes requiring surgery under general anesthesia. The atlantoaxial joint is surrounded by many vital structures, such as the accessory nerve, hypoglossal nerve, vagus nerve, carotid artery, and thyroid artery and vein.[12] The percutaneous puncture approach minimizes damage but is difficult to perform in obese patients. Therefore, to reduce the risk of injury to nerves and blood vessels during the puncture process, a modified anterolateral approach was used in this study. After general anesthesia, a transverse incision was made near the esophagus, and the subcutaneous tissue, fascia, and muscle layers were cut open. The sternocleidomastoid muscle was accessed along its inner edge, and the esophageal and vascular sheaths were bluntly separated to protect and pull the trachea and esophagus, minimizing traction on the carotid sheath to prevent cardiovascular reactions caused by vagus nerve or carotid sinus traction. The surgeon's fingers directly touched the anterior edge of the atlantoaxial joint, and then the puncture was performed, avoiding important anterior structures. The blood supply to the

surface of the atlantoaxial joint is abundant, and after the injection of bone cement, the puncture site was compressed with fingers for 3-5 minutes to prevent bone surface and muscle bleeding.

Preventive measures for bone cement leakage

Bone cement leakage is the most common complication of vertebroplasty, accounting for more than 50% of all clinical complications.[13] Bone cement leakage can occur in various locations, such as extradural leakage, foraminal leakage, disc leakage, paraspinal soft tissue leakage, paravertebral venous leakage, and puncture needle tract leakage. The vast majority of bone cement leakages do not cause clinical symptoms. A meta-analysis by Eck et al.[14] including 3,034 patients who underwent bone cement surgery, found that the overall incidence of bone cement leakage was 7%, while the incidence of symptomatic leakage was 0.3%. The vertebrae with metastases often have rich venous plexuses. During bone cement injection, the anesthesiologist should be vigilant and monitor the patient's vital signs to guard against the occurrence of pulmonary embolism. While a small amount of PMMA entering the vertebral canal and pulmonary artery does not cause clinical symptoms, once a certain amount is reached, it can lead to serious consequences. Patients may experience symptoms such as dyspnea, tachycardia, decreased blood oxygen levels, coughing, and sputum production, and even death.[15]

Leakage of bone cement into the spinal canal or intervertebral foramen at the level of the atlantoaxial joint can cause compression of the spinal cord or nerve roots, leading to radicular symptoms or high cervical myelopathy, resulting in catastrophic consequences. The author suggests that patients with this condition should undergo comprehensive X-ray, CT, and MRI examinations before surgery. During the puncture procedure, the needle tip should be positioned as far away from the endplates as possible. The instrument nurse should strictly follow the proportion to prepare the bone cement. When it reaches a slurry-like consistency, it is placed into the spiral pressurization device for approximately 1 minute. A small amount of bone cement is then extruded to observe its transition from a stringy state to a toothpaste-like state. Subsequently, the injection is performed under fluoroscopic guidance. The injection process should be slow to reduce the injection pressure. Alternatively, 0.5 ml can be injected first, and after waiting for about 15-20 seconds for the cement to disperse and stabilize within the vertebra, the distribution of bone cement is observed before continuing the injection. As soon as bone cement reaches the posterior wall of the vertebra or the paravertebral venous plexus is visualized, the injection should be immediately stopped. It has been reported[16] that the filling volume of bone cement in the lesion area is not directly proportional to the analgesic effect. Therefore, one should not intentionally pursue excessive bone cement filling, which could increase the risk of cement leakage.

The clinical efficacy of vertebroplasty in treating atlantoaxial metastases has been validated. In our opinion, patients without indications for resection of atlantoaxial metastases can undergo vertebroplasty to reinforce the stability of the affected atlantoaxial joint. We have successfully improved the classic anterolateral approach and achieved favorable clinical results, effectively reducing the risk of injury to vital structures in the anterior neck, with a high success rate and practical clinical value.

AUTHOR'S CONTRIBUTION: Each author made significant individual contributions to the development of this manuscript. FF and HT: designed the study; GS: wrote the manuscript; HC and PJ: collected, analyzed, and interpreted the data; LB and MC: critically reviewed, edited, and approved the manuscript.

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SURGICAL PROCEDURES PROLONG AMBULATION IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

PROCEDIMENTOS CIRÚRGICOS PROLONGAM A MARCHA PARA PACIENTES COM DISTROFIA MUSCULAR DE DUCHENNE

David Gonçalves Nordon[1], *Felipe Cruz Caetano dos Reis*[1], *Carlos Alberto dos Santos*[1], *Adilson de Paula*[1], *Maria Bernadete Dutra de Resende*[1], *Patricia Moreno Grangeiro*[1]

1. Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas (HCFMUSP), Instituto de Ortopedia e Traumatologia, Centro Integrado de Neuro-ortopedia, Sao Paulo, SP, Brazil.

ABSTRACT

Objective: The aim of this study was to evaluate the effect of surgical procedures on maintaining ambulation for Duchenne patients. Methods: This retrospective cohort study evaluated 35 patients for whom surgery was recommended at our institution from 2012 to 2020. Results: Twenty-seven patients were operated on before gait loss, and eight after. In this study, surgical treatment allowed recovery and prolongation of gait for 38.6 months, on average. The sooner the surgery was performed, the better the results were; logistic regression analysis showed that each day of delay after gait loss decreased the chances of success by 0.2%. The optimal interval for intervention was up to 12 months after gait loss. Conclusion: Our results thus corroborate the evidence that surgical interventions are beneficial for these patients and suggest a not previously described time window for achieving better outcomes. ***Level of Evidence III; Retrospective, Comparative Study of Surgical Interventions.***

Keywords: Duchenne Muscular Dystrophy; Treatment; Tenotomies.

RESUMO

Objetivo: O objetivo deste estudo foi avaliar o efeito de procedimentos cirúrgicos para manutenção da marcha em pacientes com Duchenne. Métodos: esta coorte retrospectiva avaliou 35 pacientes para os quais cirurgia foi recomendada na nossa instituição entre 2012 e 2020. Resultados: vinte e sete pacientes foram operados antes da perda de marcha, e oito pacientes, depois. Neste estudo, o tratamento cirúrgico permitiu recuperação ou manutenção da marcha por 38,6 meses, em média. Quanto mais cedo foi realizada a cirurgia, melhores os resultados. Análise de regressão logística mostrou que cada dia de atraso após perda da marcha diminuiu as chances de sucesso por 0,2%. O intervalo ótimo para intervenção foi de 12 meses após o paciente perder a marcha. Conclusão: nossos resultados assim corroboram para a evidência de que intervenções cirúrgicas são benéficas para estes pacientes e apresentam uma janela de tempo até então não definida para melhores resultados. ***Nível de Evidência III; Estudo Retrospectivo, Comparativo de Intervenções Cirúrgicas.***

Descritores: *Distrofia Muscular de Duchenne; Tratamento; Tenotomia.*

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is a genetic disease related to the X chromosome, that affects approximately 1 in every 20,000 boys.[1,2] The genetic mutation for DMD compromises the production of dystrophin, what leads to progressive muscular weakness, loss of developmental motor milestones, and loss of gait at around 13 years of age.[3]

The current main pharmacological treatment consists of glucocorticoids (GC), to be prescribed as soon as patients reach their motor developmental plateau, at around 5 years of age.[4,5] Physical therapy is directed towards the maintenance of strength and prevention of muscular and tendinous contractures, which are common as the disease progresses. Gait loss is directly related to disease progression, as wheelchair-bound patients present a faster decline in the course of the disease.[3] Orthopedic surgical interventions intended to release contractures may be used for preventative, rehabilitative, or palliative purpose.[6] The hip flexors and abductors, knee flexors, and the Achilles tendon may be addressed during treatment, all of which, when contracted, promote characteristic deformities, and impair gait.

There are some controversies regarding the effectiveness of surgical procedures for the treatment of contractures and gait maintenance: while several studies present good results for multilevel surgeries,[7-13] a specialists' consensus does not recommend multilevel procedures, restricting indications to Achilles tendon lengthening.[14]

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

The study was conducted at Instituto de Ortopedia e Traumatologia, Faculdade de Medicina, Universidade de São Paulo (USP).
Correspondence: Patricia Moreno Grangeiro. 333, Rua Dr. Ovidio Pires de Campos, Sao Paulo, SP, Brazil. 05403-010. patricia.moreno@hc.fm.usp.br

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To date, there is a lack of studies that have evaluated the effectiveness and prognostic impact of surgical treatment for patients with DMD in Brazil. Therefore, the objective of this study was to evaluate the direct effects of surgical procedures (maintenance, recovery, or deterioration) on the gait of patients with DMD that were operated on at our institution.

MATERIAL AND METHODS

Charts of patients with DMD followed by our neuro-orthopedics outpatients' clinics were retrospectively reviewed. This study was approved by the Hospital's Ethics Committee (CAAE 29523920.0.0000.0068).

Population

The study was conducted at the Orthopedics Department of a tertiary hospital. All patients submitted to surgery or on a waiting list for surgery during the period from January, 2012 to December, 2020 were analyzed for inclusion, thus defining a convenience sample. Inclusion criteria were: confirmed diagnosis of DMD (either by genome or muscle biopsy); minimum 24 months of post-operative follow-up; complete chart, containing data concerning the time of gait interruption, date of surgery, description of the performed surgical procedure, retainment or not of gait ability after surgery, and occurrence of postoperative complication. In cases where the chart was incomplete, the patient's family or caregiver was interviewed.

Exclusion criteria consisted of: muscular dystrophies other than Duchenne's; incomplete chart or unreliable information; post-operative follow-up shorter than 24 months. Age was not a criterion for inclusion or exclusion.

Included patients were divided into two groups: patients in group 1 had stopped walking before surgery, and patients in group 2 were still walking before surgery. If present, information on medication in use was included.

At our institution, surgery is recommended for all DMD patients who present tendon contractures, regardless of the patient's ambulatory status. Surgery might be indicated even for wheelchair bound patients, for comfort and/or hygienical purposes, according to parents' or legal guardians' desire.

The Covid-19 pandemic had an important impact in our services, and elective surgical procedures were interrupted for over 15 months, from March, 2020 on.

This generated an unexpected group: patients with tendon contractures who could not be operated on. For these patients, we collected data on their ambulatory status.

Statistical Analysis

In this study, a good outcome after surgery was considered when the patient retained or recovered the ability to walk. Three clinical questions were addressed:

1. Is it necessary to intervene before losing gait?
2. Is there a relationship between age and a good surgical outcome?
3. Is it more effective to perform the orthopedic procedure less than 12 months before the patient stopped walking?

Based on our limited sample size, we approached the first question using the Monte Carlo Sampling Algorithm,[15] then we applied a Fisher Exact Test.[16]

To answer the second question, we applied a T-Test[17] and performed a logistic regression analysis.[18]

For the third question, we applied a Hypothesis Test, a T-Test, and a Logistic Regression.

RESULTS

A total of 49 patients were identified. Their outcomes and distribution are presented in Figure 1 and Tables 1 and 2.

Single-level surgeries consisted of either uni- or bilateral Achilles' tendon lengthening. Multi-level surgeries consisted of unilateral or bilateral tenotomies at the hips (iliopsoas, fascia lata, gluteus), knees (ischiotibial muscles, femoral biceps), and ankles (Achilles' tendon), and were performed as required for adequate contracture release.

Timing of surgery in relation to gait loss and its effects

Groups 1 and 2 were compared for this analysis. There was a statistically significant difference concerning surgical results (gait maintenance/recovery) between both groups, in favor of the group that was still walking at the moment of surgery (29.6% recovered gait in Group 1, and 75% maintained gait in Group 2, $p = 0.04$).

Age at the procedure and gait recovery after the procedure

Within group 1, patients who recovered gait after the procedures were significantly younger than those who did not (average 10 years vs 12.9 years, $p = 0.$), as shown in Figure 2. Logistic regression suggested that the younger the patient was, the higher his chance of recovering gait, increasing by 5% per year younger (considering the sample age interval of 5 to 23 years old).

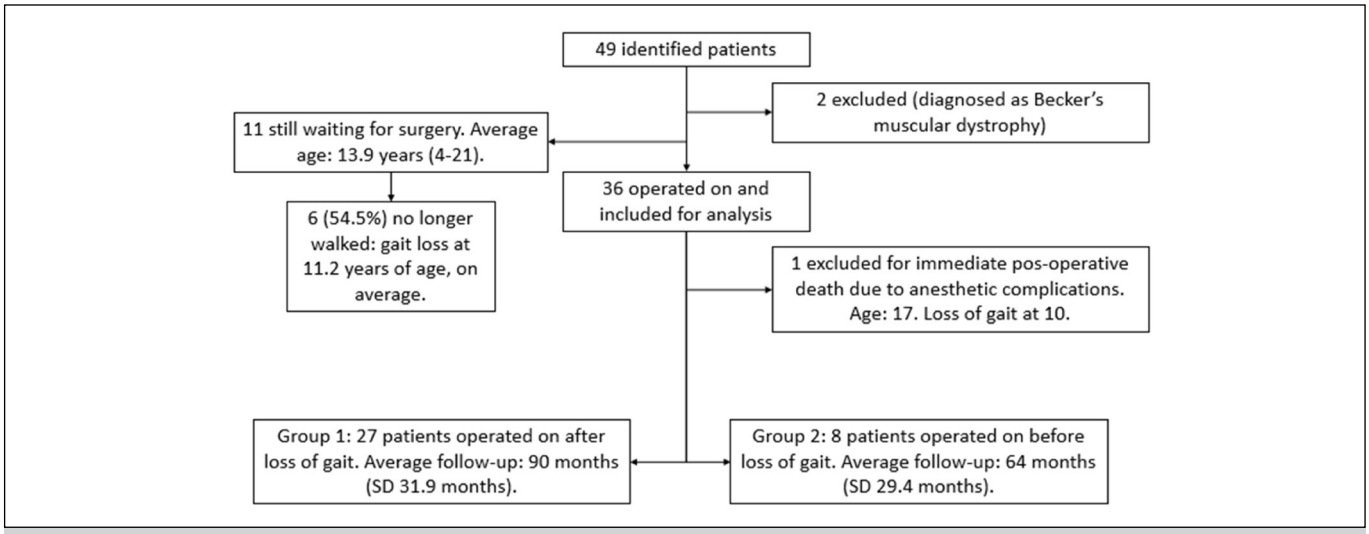

Figure 1. Distribution of the 49 identified patients.

<< SUMÁRIO

Table 1. Information on operated DMD patients (G1).

Patient number	Age when ceased walking (in years)	Interval between gait loss and procedure (in months)	Age at surgery (in years)	Single (S) or Multi (M) level surgery	Gait recovery after procedure (Yes/No)	Interval until new disability (in months)	Glucocorticoids use (Yes/No/NA = Not available)
1	10	120	19	M	No	NA	Yes
2	10	11	11	M	No	NA	Yes
3	8	36	10	M	No	NA	NA
4	7	36	10	M	No	NA	NA
5	9	120	9	M	No	NA	Yes
6	12	5	12	S	No	NA	Yes
7	11	12	12	M	No	NA	Yes
8	12	12	13	M	No	NA	NA
9	11	24	13	M	No	NA	NA
10	10	7	11	M	No	NA	Yes
11	17	24	19	M	No	NA	NA
12	11	9	12	M	No	NA	NA
13	10	24	11	M	No	NA	Yes
14	8	12	9	M	Yes	3	Yes
15	10	12	11	M	No	NA	NA
16	13	7	13	S	No	NA	NA
17	11	7	11	M	No	NA	NA
18	12	108	21	M	No	NA	Yes
19	10	17	11	M	No	NA	Yes
20	12	60	17	M	No	NA	Yes
21	10	24	12	M	Yes	120	Yes
22	13	12	14	M	Yes	30	Yes
23	8	2	8	M	Yes	30	NA
24	10	8	11	M	Yes	42	Yes
25	7	6	8	M	Yes	7	NA
26	8	9	9	M	Yes	Retains gait	NA
27	9	7	9	S	Yes	Retains gait	Yes

Table 2. DMD patients operated on before gait loss (G2).

Patient number	Age at surgery (in years)	Single (S) or Multi (M) level surgery	Gait maintained after procedure? (Yes/No)	Interval until new disability (in months)	Glucocorticoids use (Yes/No/NA = Not available)
1	7	M	Yes	Retains gait	Yes
2	11	S	Yes	Retains gait	NA
3	12	S	Yes	Retains gait	Yes
4	23	M	Yes	Retains gait	Yes
5	10	M	No	NA	NA
6	12	M	Yes	11	Yes
7	9	M	Yes	3,5	Yes
8	14	S	No	NA	Yes

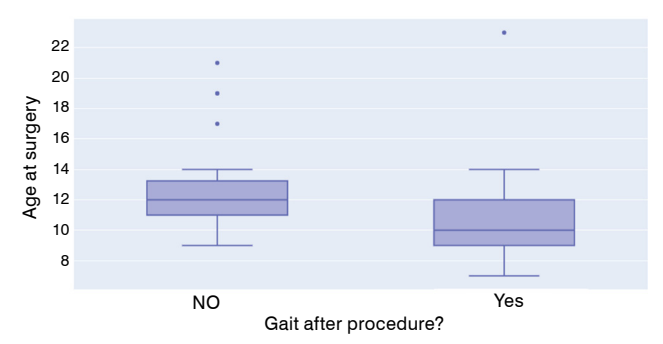

Figure 2. Age distribution of patients in Group 1 at the time of procedure and occurrence of gait recovery.

Interval between gait loss and surgery

Patients from group 1 were evaluated concerning the interval, in months, between gait loss and surgical procedure, as well as the surgical outcome (Figure 3). Those who recovered gait after the procedure had a shorter interval than those who did not recover gait (10 vs 34.26 months, p= 0.001).

Time limit for intervention after the loss of gait

Different intervals were tested (3, 6, and 12 months) as the defining limit for the loss of gait. Procedures performed before 12 months of gait loss presented statistically significant better results than procedures performed after 12 months (p = 0.014). By logistic regression, it was possible to calculate that for each month of delay in surgery, chances of success (gait recovery) decreased by 6%

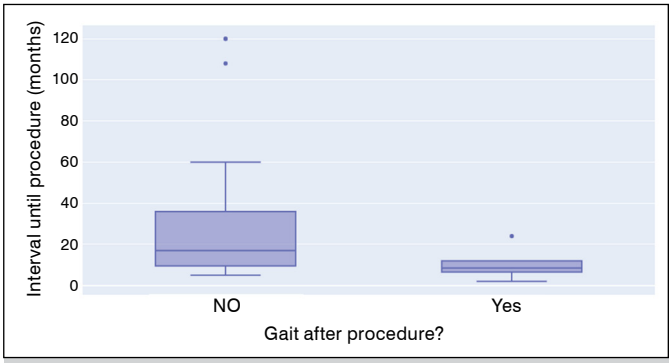

Figure 3. Distribution of the interval between loss of gait and surgery between in group 1 and the outcome (gait recovery).

in average; and each day of delay represented a 0.2% decrease in chances to recover gait.

When comparing different intervals (Figure 4), it was possible to observe that chances of success were higher in the first six months and each month of delay represented an 11% decrease in success rate. In the following six months, the decrease of chance of success was less intense (from 6 to less than 12 months, each month of delay represented a 7% decrease), and, finally, it was the smallest in the last interval (4% for each month of delay).

Gait recovery or maintenance depends on the patient's inherent chance of success, which is directly related to age and gait status. That is, chances of success are even slimmer for the older, non-ambulatory patients who wait longer for surgery.

Surgical procedure technique: single- or multi-level

Groups 1 and 2 were evaluated both separately and combined. In total, of those patients who underwent multi-level surgery, 10 recovered gait, and 18 did not (64,3%). Of those who underwent single-level surgery, four recovered gait, and two did not (33%) (p=0.34).

Glucocorticoid use

This information was missing in 14 patients' charts and remained unknown even after direct questioning, therefore it was impossible to analyze GC's influence on gait. However, all patients with available information (21 out of 35) used GC, what is in accordance with our institutional protocol.

Average extended time of gait after surgery

For those patients who recovered gait after surgery, the average extended time of gait was of 38.6 months before a new disability, which occurred at 14.9 years of age, on average. Of the eight patients operated on before losing gait, two ceased walking after surgery,

Figure 4. Monthly decrease in chances of success (gait recovery) after surgery, according to time frame after gait lost.

two retained gait for 3.5 and 11 months (average 7.2) before a new disability, and four retained gait until the end of follow-up (30 months on average). Gait maintenance could be even longer in the patients from both groups who were still walking at the end of follow-up.

DISCUSSION

Surgical recommendations for DMD are uncertain in the available literature. Our study demonstrated that orthopedic procedures may be of benefit for patients with DMD, even after gait loss (up to less than 12 months). This is the first study to suggest a window of opportunity for this type of intervention in DMD.

Several studies have highlighted the importance of orthopedic surgery for DMD, including classical studies from Rideau[19] and Forst.[9] Their procedures of choice were the severing of the tendons at the iliac spine (*tensor fasciae lata, sartorius*, and *rectus femoris*), resection of the gluteal fascia, excision of the iliotibial tract, tenotomy of the medial hamstrings, chevron fasciotomy of the lateral knee flexors, lengthening of the Achilles' tendon, and transfer of the posterior tibialis, if necessary.

These techniques were reproduced in following studies by Forst himself[10] and Weiss.[8] These classic procedures are, however, slightly different from the procedures used in our institution. Our choice of selectively treating muscle contractures was used to minimize strength loss. By using intraoperative evaluation, only muscles directly causing contraction were addressed, just enough to recover the range of movement. That is, not every muscle described by Forst was lengthened in our patients. Results were, nevertheless, positive, and the optimal surgical technique is yet to be defined.

Several studies have reported positive results of orthopaedic intervention on prolonging gait in DMD. In a retrospective study of 86 patients by Weiss'[8] they were divided into four groups: the first group, of 10 patients, was operated on and received no GC. They lost ambulation by the age of 11.1 years on average. A second group of 32 patients who received no treatment (neither surgery, nor GC), stopped walking at the average age of 9.6 years. A third group of 23 patients was treated only with GC, and lost ambulation at the average age of 11.2 years (what is the exact same age of our non-surgical group).

Finally, in this study,[8] a fourth group of 21 patients was treated with GC and operated on, and they preserved gait until the age of 14.9 years, the same average age that our patients ceased walking after the same treatment. Therefore, our study corroborates with the previous findings from Weiss, in 2020.[8]

Forst's study[10] was also positive concerning the importance of surgical procedures: early surgery (that is, before gait cessation) has prolonged gait ability for 15 months on average. There is a remarkable difference between the findings from Forst's study and ours, for in Forst's study patients did not use GC, since it was not the gold standard by then. Surgery (combined with GC) has prolonged gait for 38.6 months in our study.

Smith[12] has presented some positive results for the surgery on patients who did not use GC as well. Of the 29 patients included in the study, 14 were still walking before surgery, and 15 were not. All patients recovered their gait ability after the procedure, and gait was prolonged for another 3 years in the first group, and 2.5 years in the second group, thus presenting findings slightly better than the group from Weiss' study[8] that was not using GC. Smith's technique was different from the other studies, since it performed only percutaneous tenotomies. That might explain the difference in the results since smaller procedures are considered to generate less loss of strength.

Goertzen[20] also presented positive results after the orthopedic intervention. Procedures were performed at the average age of 6.1 years, what is considerably early in comparison to other studies, and

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patients were followed up until 9.7 years of age. A longer follow-up would have been more appropriate (since they usually stop walking at around 11 years of age).

In contrast, Griffet's study[7] was the first (and only) one to present "negative" results. It consisted of a retrospective analysis of cases operated between 1990 and 2009. Out of the 17 DMD cases operated on at an average age of 12.4 years, three were still walking before surgery and presented a gait prolonged for 8 more months (6-12 months), on average. The other 14 patients were unable to walk at the moment of surgery and presented no recovery afterwards, no matter if the loss was "a little before" or "much before" the surgery (the exact period of time was not described). Surgical technique and indication were very similar to ours. The authors conclude that procedures should be indicated when the patient is about to lose gait, with the intention to recover standing ability, more than recovering the ability to ambulate. Their results, as ours, once again highlight the role of age, when considering surgical treatment for DMD.

Despite so much evidence, the current consensus on the treatment of DMD[14] affirms that surgical treatment should only be indicated during the walking phase, and exclusively for Achilles' tendon lengthening, if it compromises gait. This consensus, however, is based on specialists' opinions and disregards several decades of evidence in favor of surgical treatment in DMD, as shown above.

Our findings, along with previous studies, indicate that patients with DMD may benefit from surgical procedures of multilevel lengthening or tenotomy for the preservation or recovery of gait, with further improved results if the patients are concomitantly using GC.[8] Our study also presents a time limit for this procedure – ideally, before 12 months of time after gait loss – and, by logistic regression, estimates how much each month of delay compromises surgical results.

Study limitations

This study was a retrospective cohort; therefore, there is a limitation in the data that can be obtained in group comparison. Even though the lack of data concerning GC does not compromise the results, it decreases the possibilities of analysis between different groups. The sample size was small, which limits the strength of conclusions that can be drawn, particularly in subgroup analyses. Nevertheless, the sample size was considerable when compared to similar studies. It is representative of the population that is treated in our outpatient clinic; however, more studies are necessary (ideally, clinical trials) to help in defining new guidelines to optimize outcomes for this patient cohort.

CONCLUSION

Surgical treatment for DMD extended gait for 38.6 months, on average in our patient cohort. The sooner it is performed, the better the results. The outcomes for single or multilevel surgeries did not show statistical differences. Surgery may be performed after the loss of gait and still have positive results, however, the time limit for intervention is less than 12 months. Each day of delay after gait loss decreases the chances of success by 0.2%.

AUTHOR'S CONTRIBUTION: Each author made significant individual contributions to the development of this manuscript. DN, PMG, AP, CS, MBDR: Study Design; DV, FR: Data collection; DN, PMG: Data interpretation; DN, PMG: Drafting Manuscript.

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PROFILE AND LEARNING CURVE OF BRAZILIAN SURGEONS REGARDING SHOULDER ARTHROSCOPY

PERFIL E CURVA DE APRENDIZADO DOS CIRURGIÕES BRASILEIROS COM RELAÇÃO À ARTROSCOPIA DE OMBRO

Guilherme Vieira Lima[1,2], Paulo Santoro Belangero[1,3], Renato Aroca Zan[1,4], Rafael Fuchs Lazarini[1,5], Bernardo Barcellos Terra[1,6], Marcelo Carvalho Krause Goncalves[1,7], Maria Isabel Pozzi Guerra[1], Lucas Braga Jacques Gonçalves[1,8], Marcio Diego Castro Teixeira[1], Sandro da Silva Reginaldo[1,9], Luis Alfredo Gomez-Vieira[1,10]

1. Sociedade Brasileira de Cirurgia de Ombro e Cotovelo (SBCOC), Sao Paulo, SP, Brazil.
2. Faculdade de Medicina do ABC, Disciplina de Ortopedia e Traumatologia, Grupo de Ombro e Cotovelo, Santo Andre, Sao Paulo, SP, Brazil.
3. Universidade Federal de Sao Paulo (UNIFESP), Escola Paulista de Medicina Disciplina de Medicina Esportiva, Departamento de Ortopedia e Traumatologia, Sao Paulo, SP, Brazil.
4. Universidade Federal de Sao Paulo (UNIFESP), Departamento de Cirurgia da Mao e Membro Superior, Sao Paulo, SP, Brazil.
5. Hospital Felicio Rocho Biocor, Rede D'Or, Belo Horizonte, Minas Gerais, MG, Brazil.
6. Santa Casa de Vitoria, Vitoria, Espirito Santo, ES, Brazil.
7. Instituto de Traumatologia e Ortopedia Romeu Krause, Recife, Pernambuco, PE, Brazil.
8. Hospital Madre Teresa, Servico de Ortopedia, Belo Horizonte, Minas Gerais, MG, Brazil.
9. Universidade Federal de Goias, Hospital das Clinicas/EBSERH, Unidade de Traumatologia e Ortopedia, Goiania, Goias, GO, Brazil.
10. Hospitais Portugues e MaterDei, Servico de Cirurgia de Ombro e Cotovelo, Salvador, Bahia, BA, Brazil.

ABSTRACT

Objective: The aim of this study is to investigate the number of surgeries necessary for an orthopedic surgeon specialized in shoulder surgery to become proficient in performing arthroscopy. This is an original article with level V evidence. Methods: A cross-sectional study was designed to examine the perspectives of surgeons at various stages of their careers, using an online questionnaire. Results: A total of 251 participants responded. The most prevalent training period was more than 15 years of experience. The proficient level was the most prevalent. In evaluating the number of arthroscopies by proficiency level, all agreed that for the specialist level, a total of over 500 arthroscopies is necessary. Most respondents judged 31 to 50 arthroscopies as necessary to perform safely. According to the methodologies, the best-rated were acting as the lead surgeon and training on cadavers. Conclusion: The study showed that 31 to 50 cases are necessary to perform shoulder arthroscopy safely, and over 500 cases to reach the specialist level. Participation as the lead surgeon and training on cadavers were rated as very important in specialist training. ***Evidence Level V; Expert Opinion.***

Keywords: Arthroscopy; Shoulder; Learning; Education.

RESUMO

Objetivo: investigar o número de cirurgias necessárias para que um ortopedista com especialização em cirurgia de ombro se torne seguro na realização de uma artroscopia. Trata-se de um artigo original com nível de evidência V. Métodos: Realizado um estudo transversal projetado para examinar as perspectivas dos cirurgiões em vários estágios de sua carreira, utilizando um questionário online. Resultados: Obtivemos 251 participantes. O tempo de formação mais prevalente foi mais 15 anos de experiência. O nível proficiente foi o mais prevalente e o número de artroscopias anuais mais prevalente foi a faixa de 51 a 99 cirurgias. Em relação ao nível de aptidão, para o nível especialista é necessário um número total de artroscopias superior a 500. Para realizar com segurança a maioria dos entrevistados julgam necessários de 31 a 50 artroscopias. De acordo com as metodologias as melhores avaliadas foram: atuação como cirurgião principal e treinamento em cadáver. Conclusão: O estudo mostrou que para realizar uma artroscopia de ombro com segurança são necessários 31 a 50 casos e mais de 500 casos para alcançar o nível de especialista. Participação como cirurgião principal e treinamento em cadáveres foram avaliados como muito importantes na formação do especialista. ***Nível de Evidência V; Opinião de Especialista.***

Descritores: *Artroscopia; Ombro; Aprendizado; Educação.*

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The study was conducted at members of the Teaching and Training Committee of the Brazilian Society of Shoulder and Elbow Surgery (CET SBCOC), located at Alameda Lorena, 427, 14th Floor, São Paulo, SP, Brazil. 01424-000.
Correspondence: Guilherme Vieira Lima. 855, Rua República do Iraque, apto 13, Campo Belo, Sao Paulo, SP, Brazil. 04611-001 guigavl@yahoo.com

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INTRODUCTION

Shoulder arthroscopy is a well-established procedure offering various advantages such as less trauma to soft tissues, better evaluation of the glenohumeral joint, subacromial space, and rotator cuff, lower infection rates, less postoperative pain, and earlier return to physical and work activities.[1,2] This surgical modality is widely used in the treatment of rotator cuff injuries, joint instability, certain types of fractures, among other pathologies.[3-5]

Although the surgical learning curve has been investigated for procedures such as hip and elbow arthroscopy,[6-8] there is a lack of literature on shoulder arthroscopy. How many surgeries are necessary for a surgeon to become a specialist in performing shoulder arthroscopy? Is there a difference in the perception of this number between more experienced surgeons and newly graduated ones? What are the best learning tools for shoulder arthroscopy? These questions remain unanswered.

The main objective of this study is to investigate the number of surgeries necessary for an orthopedic surgeon specializing in shoulder and elbow surgery in Brazil to become proficient and a specialist in performing shoulder arthroscopy. Additionally, we aim to compare the perceptions of more experienced surgeons and newly graduated ones. Secondly, we aim to evaluate the best training tools for shoulder arthroscopy.

The probable hypothesis is that there will be significant perspective differences between trainees and more experienced surgeons regarding the number of cases necessary to achieve each skill level, but the most valuable training tool will be similar regardless of the surgeon's level.

MATERIAL AND METHODS

This is a cross-sectional study designed to examine the current perspectives of orthopedic surgeons at various career stages using an online questionnaire for data collection.

We included orthopedic doctors with a specialty title in Orthopedics and Traumatology (TEOT) by the Brazilian Society of Orthopedics and Traumatology (SBOT) practicing in Brazil, who have specialized training in shoulder and elbow surgery and are registered in the Brazilian Society of Shoulder and Elbow Surgery database. Those who did not agree with the informed consent form or had incomplete or unfilled forms were excluded.

The questionnaire was emailed to all addresses registered in the SBCOC database in 2022. The document sent included a summary of the research and a link directing the participant to the questionnaire on the Google Forms platform as per Appendix 1.

Participants were subdivided into different groups for comparative analyses based on the following factors: years of training in shoulder surgery (≤5, 6-10, 11-14, and ≥15 years), whether they were a training program coordinator in shoulder surgery, the number of shoulder arthroscopies performed annually (≤10, 11-20, 21-30, 31-50, 51-99, and ≥100), self-assigned skill level (initial, safe, competent, proficient, or specialist).

We sought among Brazilian surgeons to (1) compare the perspectives of experienced surgeons and newly graduated trainees; (2) compare these recommended case volume requirements based on physician demographics, training, professional experience, and skill level; and (3) determine which training methodologies participants and trainees considered most valuable in acquiring shoulder arthroscopy skills.

The study was approved by the ethics committee CAAE: 61507822.5.00000.5125 according to the requirements of the Declaration of Helsinki. Opinion Number: 5.624.585.

Statistical Analysis

Participants' demographic data were used descriptively, including means with standard deviation, percentages, and variance, where appropriate. After evaluating the data for any parametric or non-parametric assumptions, all continuous variables were compared between the previously mentioned groups using the chi-square test. When comparing means between groups, the mean difference and 95% confidence interval (CI) were determined. P-values <0.05 were considered significant. Statistical analysis was performed using SPSS V20, Minitab 16, and Excel Office 2010 software.

RESULTS

The questionnaire was emailed to 934 individuals according to the SBCOC database. Forty-four email addresses were incorrectly registered, and 639 individuals did not respond to the questionnaire. We included 251 participants with a mean age of 43.2 ± 1.2 years (Table 1), ranging from 25 to 72 years, with 96.8% being male.

The most prevalent training period was ≥15 years, with 35.1%, but this is not statistically different from the 27.9% with ≤5 years (p= 0.084).

The proficient level in shoulder arthroscopy was the most prevalent with 55.8% of doctors, and the most prevalent number of annual arthroscopies was in the range of 51 to 99 surgeries at 29.5%.

The southeast region was the most prevalent geographical area of practice at 53.4% (Table 2).

Regarding training time and mean age of doctors, there was statistical significance; the mean age for professionals with ≤5 years of specialization was 34.2 ± 0.9 years and 53.0 ± 1.7 years for those with ≥15 years of specialization (Table 3).

When comparing training time with demographic factors, there was significance between group coordination and the number of annual arthroscopies performed. Both had a higher number of annual arthroscopies and greater participation in training group coordination for those with ≥15 years of training (Table 4).

According to the training method, the study did not present a statistically significant relationship with training time. There was consensus that the best (extremely valid) training methods are surgery performed as the lead surgeon, at 93.1%, followed by cadaver training at 81.4%. Courses, real simulators, and virtual simulators had the lowest frequency of "extremely valid" (Table 5).

In evaluating the number of arthroscopies by skill level, all agreed that for the SPECIALIST level, a total of over 500 arthroscopies is necessary, but for other levels, there was a difference between groups (Table 6).

DISCUSSION

Our study demonstrated a number of 31 to 50 arthroscopies to perform a procedure SAFELY. Similar studies conducted in hip arthroscopies showed that the first significant reduction in both surgical time and complications can be observed after 30 cases of arthroscopy. Moreover, it was reported that patient outcomes and

Table 1. Full Descriptive Analysis of Age.

	Age
Mean	43.2
Median	42
Standard Deviation	9.7
CV	22%
Q1	36
Q3	47.5
Min	25
Max	72
N	251
CI	1.2

Table 2. Distribution of Qualitative Factors.

		N	%	P-value
Leads a training group	No	157	62.5%	<0.001
	Yes	94	37.5%	
Skill level in shoulder arthroscopy	Proficient	140	55.8%	Ref.
	Specialist	53	21.1%	<0.001
	Competent	46	18.3%	<0.001
	Secure	9	3.6%	<0.001
	Beginner	3	1.2%	<0.001
Number of shoulder arthroscopies performed per year	≤10	15	6.0%	<0.001
	11-20	26	10.4%	<0.001
	20-30	1	0.4%	<0.001
	21-30	28	11.2%	<0.001
	31-50	35	13.9%	<0.001
	51-99	74	29.5%	Ref.
	≥100	72	28.7%	0.844
Holds SBCOC certification	No	16	6.4%	<0.001
	Yes	235	93.6%	
Region	Southeast	134	53.4%	Ref.
	Northeast	43	17.1%	<0.001
	South	36	14.3%	<0.001
	Central-West	29	11.6%	<0.001
	North	9	3.6%	<0.001
Sex	Female	8	3.2%	<0.001
	Male	243	96.8%	
Years of experience	Residency (2022)	4	1.6%	<0.001
	≤5 years	70	27.9%	0.084
	6- 10 years	49	19.5%	<0.001
	11-14 years	40	15.9%	<0.001
	≥15 years	88	35.1%	Ref.

Table 3. Comparison Between Years of Experience and Age.

Years of Experience	Mean	Median	Standard Deviation	CV	Min	Max	N	CI	P-value
≤5 years	34.2	33	4.0	12%	25	46	70	0.9	<0.001
6- 10 years	39.4	39	4.8	12%	33	65	49	1.4	
11-years	42.7	42	3.3	8%	38	53	40	1.0	
≥15 years	53.0	51	8.1	15%	42	72	88	1.7	

lower complication rates continued to improve at approximately 100 cases.[8-10]

Guttman et al.[11] evaluated the learning curve among shoulder surgeons in blocks of 10 rotator cuff repair surgeries and noted significant progress after the first block. Lim et al.[12] demonstrated a significant decrease in rotator cuff re-tear rates according to the surgeon's experience. Garstmans et al.[13] also affirmed that the learning curve is a determining factor in surgical outcomes. In our study, we did not evaluate operative outcomes such as re-tear rates or clinical assessment of patients, but we did note an increase in surgery volume according to the surgeon's experience, and once the surgeon has a higher total volume of procedures, they become more skilled with lower complication rates and better outcomes.

The complexity of an arthroscopic procedure varies according to the degree of injury and pathology involved. The surgical time required to repair extensive and chronic rotator cuff injuries is generally longer than for small to medium[14,15] injuries, and as surgical experience is acquired, learning can be demonstrated by a quantitative decrease in operative time.[16] Many authors use the time spent on the procedure as an evaluation element, but shorter surgical time is not necessarily related to better outcomes.[13] In our study, we did not include surgical time or address any specific pathology to avoid many biases that similar studies have shown.[16-20]

McColl et al.[21] showed that technological advancements had an impact on time and management during shoulder arthroscopy procedures; thus, we can consider that critical thinking regarding shoulder surgery may differ among surgeons of different generations. In our study, we did not observe significant differences in teaching tools among different generations of surgeons.

When evaluating participants' viewpoints on the most valuable educational tools, respondents rated the lead surgeon role and cadaver training as the best techniques for acquiring skills. Similar findings have also been reported in several studies involving orthopedic surgeons and other arthroscopic procedures.[15-18] Surprisingly, virtual simulators were rated as low-value tools for learning shoulder arthroscopy by respondents. Although these simulators have shown to improve overall arthroscopic performance in orthopedic residents, there are some technical limitations for certain real and virtual shoulder simulators. This is certainly an area that needs further exploration and study.

Technology can also produce simulators increasingly similar to the real procedure; however, we do not yet have any that reproduce the arthroscopic procedure attractively among orthopedic surgeons.

Table 4. Comparison Between Years of Experience and Distribution of Demographic Factors.

N		≤5 years		6- 10 years		11-14years		≥15 years		Total		P-value
		%	N	%	N	%	N	%	N	%	N	
Leads a training group	No	52	74.3%	31	63.3%	26	65.0%	45	51.1%	154	62.3%	0.028
	Yes	18	25.7%	18	36.7%	14	35.0%	43	48.9%	93	37.7%	
Holds TEOT – SBOT certification	No	0	0.0%	0	0.0%	0	0.0%	1	1.1%	1	0.4%	0.886
	Yes	70	100%	49	100%	40	100%	87	98.9%	246	99.6%	
Holds SBCOC certification	No	6	8.6%	2	4.1%	2	5.0%	4	4.5%	14	5.7%	0.713
	Yes	64	91.4%	47	95.9%	38	95.0%	84	95.5%	233	94.3%	
Sex	Female	1	1.4%	4	8.2%	2	5.0%	0	0.0%	7	2.8%	0.101
	Male	69	98.6%	45	91.8%	38	95.0%	88	100%	240	97.2%	
Number of shoulder arthroscopies performed per year	≤10	7	10.0%	3	6.1%	0	0.0%	2	2.3%	12	4.9%	<0.001
	11-20	14	20.0%	3	6.1%	4	10.0%	4	4.5%	25	10.1%	
	21-30	14	20.0%	10	20.4%	3	7.5%	2	2.3%	29	11.7%	
	31-50	13	18.6%	7	14.3%	6	15.0%	9	10.2%	35	14.2%	
	51-99	16	22.9%	15	30.6%	11	27.5%	32	36.4%	74	30.0%	
	≥100	6	8.6%	11	22.4%	16	40.0%	39	44.3%	72	29.1%	

Table 5. Comparison Between Years of Experience and Training Distribution.

N		≤5 years		6- 10 years		11-14years		≥15 years		Total		P-value
		%	N	%	N	%	N	%	N	%	N	
Surgery Performed as primary Surgeon	Neutral	0	0.0%	0	0.0%	0	0.0%	1	1.1%	1	0.4%	0.276
	Valid	2	2.9%	2	4.1%	2	5.0%	10	11.4%	16	6.5%	
	Extremely Valid	68	97.1%	47	95.9%	38	95.0%	77	87.5%	230	93.1%	
Cadaver surgery	Slightly Valid	0	0.0%	0	0.0%	0	0.0%	1	1.1%	1	0.4%	0.489
	Neutral	2	2.9%	0	0.0%	1	2.5%	4	4.5%	7	2.8%	
	Valid	13	18.6%	9	18.4%	2	5.0%	14	15.9%	38	15.4%	
	Extremely Valid	55	78.6%	40	81.6%	37	92.5%	69	78.4%	201	81.4%	
Observed surgery As Assistant	Not Valid	0	0.0%	0	0.0%	0	0.0%	1	1.1%	1	0.4%	0.121
	Slightly Valid	2	2.9%	0	0.0%	0	0.0%	1	1.1%	3	1.2%	
	Neutral	13	18.6%	2	4.1%	1	2.5%	7	8.0%	23	9.3%	
	Valid	24	34.3%	22	44.9%	13	32.5%	32	36.4%	91	36.8%	
	Extremely Valid	31	44.3%	25	51.0%	26	65.0%	47	53.4%	129	52.2%	
Courses	Not Valid	1	1.4%	0	0.0%	0	0.0%	2	2.3%	3	1.2%	0.792
	Slightly Valid	6	8.6%	2	4.1%	2	5.0%	6	6.8%	16	6.5%	
	Neutral	13	18.6%	6	12.2%	5	12.5%	18	20.5%	42	17.0%	
	Valid	29	41.4%	22	44.9%	22	55.0%	33	37.5%	106	42.9%	
	Extremely Valid	21	30.0%	19	38.8%	11	27.5%	29	33.0%	80	32.4%	
Literature	Not Valid	1	1.4%	1	2.0%	0	0.0%	5	5.7%	7	2.8%	0.594
	Slightly Valid	6	8.6%	4	8.2%	5	12.5%	4	4.5%	19	7.7%	
	Neutral	10	14.3%	9	18.4%	7	17.5%	10	11.4%	36	14.6%	
	Valid	22	31.4%	19	38.8%	15	37.5%	35	39.8%	91	36.8%	
	Extremely Valid	31	44.3%	16	32.7%	13	32.5%	34	38.6%	94	38.1%	
Physical simulators	Not Valid	0	0.0%	0	0.0%	0	0.0%	2	2.3%	2	0.8%	0.513
	Slightly Valid	3	4.3%	3	6.1%	4	10.0%	5	5.7%	15	6.1%	
	Neutral	8	11.4%	4	8.2%	1	2.5%	11	12.5%	24	9.7%	
	Valid	37	52.9%	21	42.9%	17	42.5%	36	40.9%	111	44.9%	
	Extremely Valid	22	31.4%	21	42.9%	18	45.0%	34	38.6%	95	38.5%	
Virtual simulators	Not Valid	0	0.0%	0	0.0%	0	0.0%	1	1.1%	1	0.4%	0.792
	Slightly Valid	6	8.6%	4	8.2%	3	7.5%	7	8.0%	20	8.1%	
	Neutral	16	22.9%	9	18.4%	5	12.5%	14	15.9%	44	17.8%	
	Valid	33	47.1%	20	40.8%	20	50.0%	35	39.8%	108	43.7%	
	Extremely Valid	14	20.0%	16	32.7%	12	30.0%	31	35.2%	73	29.6%	
Videos	Not Valid	1	1.4%	0	0.0%	0	0.0%	1	1.1%	2	0.8%	0.649
	Slightly Valid	1	1.4%	2	4.1%	4	10.0%	4	4.5%	11	4.5%	
	Neutral	8	11.4%	4	8.2%	1	2.5%	6	6.8%	19	7.7%	
	Valid	29	41.4%	21	42.9%	15	37.5%	42	47.7%	107	43.3%	
	Extremely Valid	31	44.3%	22	44.9%	20	50.0%	35	39.8%	108	43.7%	

Perhaps in the coming years, with technological advances, the perception of this type of tool may change.

The duration of the shoulder surgery specialization program in Brazil in services registered by the SBCOC is on average 12 months. However, this period is often insufficient for adequate training in arthroscopy. We know that learning depends on personal skills, but the provided structure has a significant influence on the learning process.

Inadequate training will produce an insufficient surgeon with a higher risk of complications, unsatisfactory results, and low productivity.

The main limitation of the study was the number of participants included. Unfortunately, the adherence to the proposed questionnaire was very low, with only 39% of individuals who had correctly registered emails in the database responding to the questionnaire; the reason for non-adherence is unknown. No campaign was conducted through the website and social media to promote the research, which might have increased participation if the authors had used these tools. Additionally, the high number of incorrect email addresses also contributed to a lower number of participants.

The authors of this study have already communicated with the SBCOC coordination to rectify the addresses to improve the society's communication network.

Possibly the total number of orthopedic surgeons performing shoulder arthroscopy is underestimated when using the SBCOC database. Many surgeons perform this procedure and have never been registered with the society because they were trained in locations outside the society's registration network.

We hope this work serves as a framework for the clinical validation of the shoulder arthroscopy learning curve among Brazilian surgeons and allows for the optimization of training methodologies.

CONCLUSION

The study showed that most shoulder and elbow specialists in Brazil believe that 31 to 50 cases are necessary to perform the procedure safely, and over 500 cases to reach the specialist level. Participation as the lead surgeon and cadaver training were rated as very important in specialist training.

Table 6. Comparison Between Years of Experience and Distribution of Shoulder Arthroscopy Volume by Skill Level.

N		≤5 years		6- 10 years		11-14years		≥15 years		Total		P-value
		%	N	%	N	%	N	%	N	%		
Specialist	6-10	0	0.0%	1	2.0%	0	0.0%	0	0.0%	1	0.4%	0.575
	11-20	0	0.0%	1	2.0%	0	0.0%	0	0.0%	1	0.4%	
	21-30	1	1.4%	1	2.0%	0	0.0%	2	2.3%	4	1.6%	
	31-50	0	0.0%	1	2.0%	0	0.0%	2	2.3%	3	1.2%	
	51-100	4	5.7%	2	4.1%	1	2.5%	6	6.8%	13	5.3%	
	101-500	24	34.3%	14	28.6%	8	20.0%	26	29.5%	72	29.1%	
	>500	41	58.6%	29	59.2%	31	77.5%	52	59.1%	153	61.9%	
Proficient	6-10	0	0.0%	1	2.0%	0	0.0%	0	0.0%	1	0.4%	0.026
	11-20	2	2.9%	1	2.0%	1	2.5%	1	1.1%	5	2.0%	
	21-30	2	2.9%	1	2.0%	0	0.0%	1	1.1%	4	1.6%	
	31-50	3	4.3%	1	2.0%	1	2.5%	2	2.3%	7	2.8%	
	51-100	28	40.0%	14	28.6%	2	5.0%	21	23.9%	65	26.3%	
	101-500	28	40.0%	25	51.0%	23	57.5%	39	44.3%	115	46.6%	
	>500	7	10.0%	6	12.2%	13	32.5%	24	27.3%	50	20.2%	
Competent	6-10	3	4.3%	1	2.0%	1	2.5%	1	1.1%	6	2.4%	<0.001
	11-20	3	4.3%	0	0.0%	0	0.0%	3	3.4%	6	2.4%	
	20-30	1	1.4%	0	0.0%	0	0.0%	0	0.0%	1	0.4%	
	21-30	11	15.7%	5	10.2%	1	2.5%	1	1.1%	18	7.3%	
	31-50	26	37.1%	13	26.5%	9	22.5%	22	25.0%	70	28.3%	
	51-100	17	24.3%	20	40.8%	7	17.5%	32	36.4%	76	30.8%	
	101-500	8	11.4%	9	18.4%	18	45.0%	27	30.7%	62	25.1%	
	>500	1	1.4%	1	2.0%	4	10.0%	2	2.3%	8	3.2%	
Secure	≤ 5	5	7.1%	1	2.0%	1	2.5%	1	1.1%	8	3.2%	0.001
	6-10	6	8.6%	2	4.1%	1	2.5%	4	4.5%	13	5.3%	
	11-20	16	22.9%	7	14.3%	6	15.0%	7	8.0%	36	14.6%	
	21-30	23	32.9%	9	18.4%	4	10.0%	22	25.0%	58	23.5%	
	31-50	11	15.7%	20	40.8%	8	20.0%	21	23.9%	60	24.3%	
	51-100	7	10.0%	9	18.4%	14	35.0%	25	28.4%	55	22.3%	
	101-500	2	2.9%	1	2.0%	5	12.5%	8	9.1%	16	6.5%	
	>500	0	0.0%	0	0.0%	1	2.5%	0	0.0%	1	0.4%	

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Appendix 1.

I) Medical Registration

a) Email:
b) Sex: Male ( ) Female ( )
c) Age: _____ years
d) Region of practice in Brazil: South ( ) Southeast ( ) Central-West ( ) Northeast ( ) North( )
e) Do you coordinate or participate in any shoulder and elbow surgery training group (SBCOC)?
Yes ( ) No ( )
f) Years since completion of shoulder surgery training:
( ) Fellowship (2022)
( ) ≤5 years
( ) 6-10 years
( ) 11-14 years
( ) ≥15 years
g) Do you hold a TEOT certification?
Yes ( ) No ( )
h) What is the average number of shoulder arthroscopies you perform per year? (AS PRIMARY SURGEON)
( ) ≤10
( ) 11-20
( ) 21-30
( ) 31-50
( ) 51-99
( ) ≥100

II) Proficiency / Capability

a) What is YOUR level of skill in shoulder arthroscopy?
( ) Beginner: Very limited skill. Would have difficulty establishing portals
( ) Secure: oes not cause significant damage to cartilage, soft tissues or neurovascular structures. Would likely struggle to complete basic arthroscopic procedures.
( ) Competent: Able to reliably complete basic arthroscopic procedures, though may still exhibit inefficiencies in movement and execution.
( ) Proficient: Able to consistently and reliably complete both basic and more complex arthroscopic procedures.
( ) Expert: A distinguished leader in the field, recognized by peers for significant contributions to the advancement of surgical techniques.
b) How many shoulder arthroscopies do you believe must be PERFORMED to reach the SECURE level?
( ) ≤5
( ) 6-10
( ) 11-20
( ) 21-30
( ) 31-50
( ) 51-100
( ) 101-500
( ) >500
c) How many shoulder arthroscopies do you believe must be PERFORMED to reach the COMPETENT level?
( ) ≤5
( ) 6-10
( ) 11-20
( ) 21-30
( ) 31-50
( ) 51-100
( ) 101-500
( ) >500
d) How many shoulder arthroscopies do you believe must be PERFORMED to reach the PROFICIENT level?
( ) ≤5
( ) 6-10
( ) 11-20
( ) 21-30
( ) 31-50
( ) 51-100
( ) 101-500
( ) >500
e) How many shoulder arthroscopies do you believe must be PERFORMED to reach the EXPERT level?
( ) ≤5
( ) 6-10
( ) 11-20
( ) 21-30
( ) 31-50
( ) 51-100
( ) 101-500
( ) >500

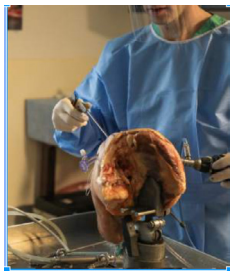
III) Regarding shoulder arthroscopy training methods, what is your opinion?

Please select one: 1- not valid 2- slightly valid 3- neutral 4-valid 5-extremely valid
Through LITERATURE (reading articles, books, journals)
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid
Through VIDEO / Online Video / Video Lecture / Live Surgery
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid
Through FORMAL COURSES / ONLINE COURSES / CONFERENCES
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid
Through REAL SURGICAL SIMULATORS
1- not valid
2- slightly valid
3- neutral
4-valid

5-extremely valid

Through VIRTUAL SURGICAL SIMULATORS
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely

Through CADAVER SURGERY
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid



Through SURGERY OBSERVED AS ASSISTANT
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid

Through SURGERY PERFORMED AS PRIMARY SURGEON
1- not valid
2- slightly valid
3- neutral
4-valid
5-extremely valid

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REINFORCEMENT WITH THE LONG HEAD OF THE BICEPS TENDON IN LARGE AND MASSIVE REPAIRABLE ROTATOR CUFF TEARS: A PROSPECTIVE CASE SERIES

REFORÇO COM O TENDÃO DA CABEÇA LONGA DO BÍCEPS EM LESÕES REPARÁVEIS GRANDES E EXTENSAS DO MANGUITO ROTADOR: SÉRIE PROSPECTIVA DE CASOS

Gustavo de Mello Ribeiro Pinto[1], *Cristiano Nabuco Dantas*[1], *Marcelo Costa de Oliveira Campos*[1], *Jorge Henrique Assunção*[2,3], *Mauro Emilio Conforto Gracitelli*[2], *Eduardo Angeli Malavolta*[2,4]

1. Universidade Estadual do Rio de Janeiro, Hospital Universitario Pedro Ernesto (HUPE), Rio de Janeiro, RJ, Brazil.
2. Universidade de Sao Paulo, Faculdade de Medicina Hospital das Clinicas (HCFMUSP), Sao Paulo, SP, Brazil.
3. DASA, Hospital 9 de Julho, Sao Paulo, SP, Brazil.
4. Hospital do Coração (Hcor), Sao Paulo, SP, Brazil.

ABSTRACT

Introduction: The treatment of large and massive rotator cuff tears remains challenging. This study evaluates the efficacy and safety of reinforcement with the long head of the biceps tendon (LHBT) in patients with large and massive repairable rotator cuff tears. Methods: This is a prospective case series involving 25 patients who underwent open repair of large and massive rotator cuff tears with LHBT reinforcement. All patients were operated by the same surgeon and followed up for one year. Results: Pain scores (VAS: 6.6 ± 2.30 vs. 2.68 ± 2.73; p<0.001) and function scores (ASES: 36.86 ± 19.27 vs. 73.96 ± 23.73; p<0.001; UCLA: 13.04 ± 3.83 vs. 26.04 ± 7.39; p<0.001) improved significantly postoperatively compared to preoperatively. The biceps healing rate was 84%, while the rotator cuff retear rate was 60%. No complications related to the biceps or surgical site infections were documented. Conclusion: Reinforcement with the long head of the biceps tendon in the repair of large and massive rotator cuff tears shows satisfactory clinical outcomes and a low complication rate. ***Level of Evidence: IV, Case Series.***

Keywords: Rotator Cuff; Shoulder; Tendon Transfer; Autografts.

RESUMO

Introdução: O tratamento das lesões grandes e extensas do manguito rotador continua desafiador. Este estudo avalia a eficácia e segurança do reforço com o tendão da cabeça longa do bíceps (TCLB) em pacientes com lesões reparáveis grandes e extensas do manguito rotador. Métodos: Esta é uma série de casos prospectivos com 25 pacientes submetidos ao reparo aberto das lesões grandes e extensas do manguito rotador com reforço do TCLB. Todos os pacientes foram operados pelo mesmo cirurgião com seguimento de um ano. Resultados: Os escores de dor (EVA: 6,6 ± 2,30 vs. 2,68 ± 2,73; p<0,001) e função (ASES: 36,86 ± 19,27 vs. 73,96 ± 23,73; p<0,001; UCLA: 13,04 ± 3,83 vs. 26,04 ± 7,39; p<0,001) melhoraram significativamente no pós-operatório em comparação com o pré-operatório. A taxa de cicatrização do bíceps foi de 84%, enquanto a taxa de re-rotura do manguito foi de 60%. Não documentamos nenhuma complicação relacionada ao bíceps ou infecção no sítio cirúrgico. Conclusão: O reforço com o tendão da cabeça longa do bíceps no reparo de lesões grandes e extensas do manguito rotador apresenta resultados clínicos satisfatórios e baixa taxa de complicações. ***Nível de Evidência: IV, Série de Casos.***

Descritores: *Lesões do Manguito Rotador; Ombro; Transferência Tendinosa; Autoenxerto.*

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INTRODUCTION

The treatment of large and massive rotator cuff tears remains challenging. In these injuries, after complete or partial tendon repair, the failure rates can reach up to 94% due to significant fatty degeneration, tendon retraction, reduced mobility, and muscle atrophy.[1,2]

Several procedures have been described to assist in the surgical repair of these lesions such as medialization of the footprint, anterior interval release, margin convergence and the use of synthetic or biological grafts in the repair.[3] Superior capsule reconstruction (SCR), initially described for irreparable supraspinatus tears using

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The study was conducted at Hospital Universitario Pedro Ernesto of the Universidade do Estado do Rio de Janeiro, Rua Blvd. 28 de setembro, 77, Vila Isabel, Rio de Janeiro, RJ, Brazil. 20551-030.
Correspondence: Gustavo de Mello Ribeiro Pinto. 176, Rua Oscar Valdetaro, apto 1604, Barra da Tijuca Rio de Janeiro, RJ Brazil. 22793-670. gusmrp@gmail.com

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autologous fascia lata graft, has been shown to reduce retear rates and improve tendon quality, as well as in SCR in repairable rotator cuff tears.[4]

An alternative to SCR is the use of the long head of the biceps tendon (LHBT) as an autologous graft. The transposition and incorporation of the biceps tendon into the rotator cuff repair adds native tissue rich in tenocytes and fibroblasts to the repair. Other advantages include reduced cost and decreased risk of disease transmission associated with allograft use; the lack of need for additional incisions preventing lower limb morbidity for fascia lata grafts; in addition to being technically more reproducible.[5]

The objective of this study is to evaluate the clinical and radiological outcomes of patients who underwent open repair of large and extensive rotator cuff tears with reinforcement using the long head of the biceps tendon.

METHODS

This is a prospective case series in which all patients were operated on between January 14, 2022, and April 14, 2023, by the same surgeon with six years of experience in shoulder and elbow surgery and approved by the Institutional Ethics and Research Committee (5.154.677). All patients signed the consent form.

Patients met the following inclusion criteria on magnetic resonance imaging: large (≥ 3 cm) or massive (> 5 cm) posterosuperior rotator cuff tears according to the DeOrio and Cofield classification,[6] intact LHBT, and fatty degeneration of the supraspinatus muscle ≤ 2 according to the Goutallier classification.[7]

Patients with a history of infection in the affected shoulder, inability to understand the preoperative questionnaires, patients who did not undergo at least one postoperative evaluation, tears where complete rotator cuff repair was not possible, and complete or partial tears > 25% of the LHBT diagnosed intraoperatively were excluded.

Clinical outcomes were assessed using the American Shoulder and Elbow Surgeons (ASES)[8] and the University of California Los Angeles (UCLA)[9] scores preoperatively and at 6 and 12 months postoperatively. The visual analog scale (VAS)[10] for pain was applied at the same intervals, and additionally on the 1st and 14th postoperative days. The scores were administered by the principal investigator.

Radiographic evaluation included the Hamada[11] classification and the measurement of the acromiohumeral distance (AHD) preoperatively and 6 months postoperatively, in an anteroposterior radiograph of the glenohumeral joint. The AHD was measured as the shortest distance from the inferior surface of the acromion to the superior face of the humerus.

Patients underwent preoperative and 6-month postoperative magnetic resonance imaging, evaluated by a musculoskeletal radiologist with 15 years of experience. Rotator cuff healing was classified according to Sugaya et al.[12] categorized as healed (stages I/II/III) or not healed (stages IV/V). LHBT reinforcement healing was also categorized as healed or not healed.

Surgical procedure

Patients were operated in a beach chair position using a surgical approach from the anterolateral border of the acromion, approximately 5 cm in length, followed by opening the interval between the anterior and middle portions of the deltoid with subsequent resection of the subdeltoid bursa. At this point, the integrity of the LHBT was assessed.

Next, the pattern of the rotator cuff tear and the mobility of the tendons were analyzed to achieve a complete repair. For this, braided polyethylene #2 sutures were placed in the tendon. The greater tuberosity of the humerus was debrided, and the footprint was medialized for tendon reinsertion (Figure 1).

The proximal insertion of the LHBT was kept intact, and the transverse ligament was excised in the bicipital groove to allow posteriorization of the biceps tendon. The LHBT was repositioned and fixed with a Super Revo® FT 5.0 mm metal anchor with two Hi-Fi® #2 sutures (Conmed, Largo, FL, USA) in the supraspinatus footprint, in a neo-groove with a depth of 3 mm and located 1 to 1.5 cm posterior to the lateral border of the bicipital groove, created with the aid of a curette, while maintaining the arm at 10° flexion and 30° abduction (Figure 2A-C). One suture from the anchor was used for anchoring and repositioning the LHBT in the footprint with a "lasso loop" stitch described by Lafosse et al.[13] and the other suture was tied around the tendon (Figure 3A-C).

The rotator cuff repair was performed using the transosseous suture technique.[14,15] The sutures were evenly distributed according to the size of the tear and tied with "Nicky's knot" sliding knots.[16] (Figure 4A-C).

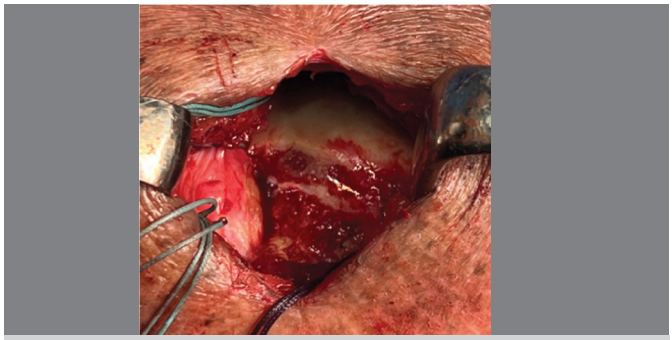

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Figure 1. Cruentation and medialization of the greater tuberosity *footprint*.

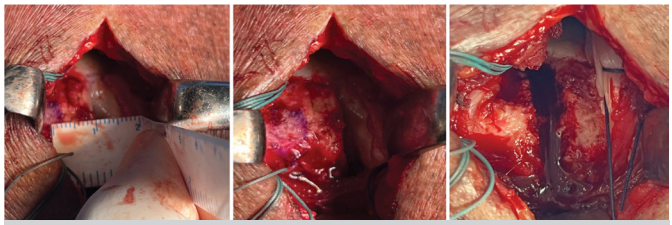

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Figure 2. A) Measurement of the neo-bicipital groove distance; B) Marking of the neo-groove 1 to 1.5 cm posterior to the native groove (blue pen); C) Neo-bicipital groove with a depth of 3 mm.

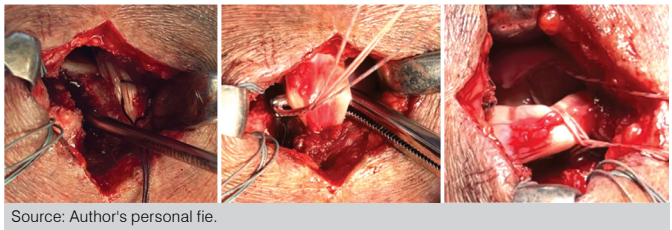

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Figure 3. A) Placement of the metal anchor in the neo-groove; B) Passage of the sutures through the biceps; C) "Lasso loop".

Postoperative follow-up

All patients used an abduction sling for 6 weeks but were encouraged to remove it during the day for personal care and to move the elbow, wrist, and fingers. After 6 weeks, patients were referred to physical therapy with guidance to perform assisted passive shoulder movement, and subsequently active movement. Sixteen weeks after surgery, patients began exercises to strengthen the rotator cuff and the scapular stabilizing muscles.

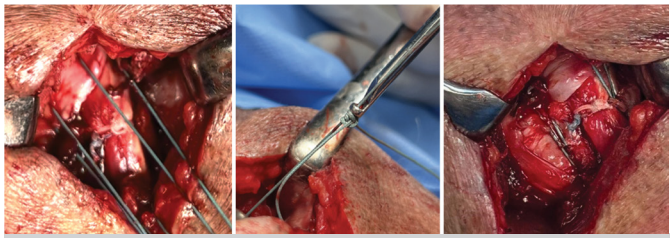

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Figure 4. A) Tensioning of the rotator cuff over the tenotomized long head of the biceps in the neo-groove; B) "Nicky's knot"; C) Final repair.

Statistical analysis

Intrinsic patient variables, factors related to the injury, and the intervention were evaluated between the groups.
Continuous variables were assessed for normality using the Kolmogorov-Smirnov test and for homogeneity using Levene's test.
Categorical data were presented in absolute and percentage values. Continuous data were presented as means and standard deviation and, when non-parametric also as median.
The results obtained by the assessment scales (UCLA, ASES, EVA and SF-12) at different follow-up times were compared by Analysis of Variance (ANOVA) and post-hoc analysis was performed with Bonferroni adjustment. The acromiohumeral distance preoperatively and at 6 months of follow-up were compared using the Wilcoxon test. The p value <0.05 was considered statistically significant. We used the SPSS version 20.0 program to analyze the data.

RESULTS

In total, 46 patients were operated on, of which 25 patients underwent complete repair of large and extensive rotator cuff tears with TCLB reinforcement, 13 men and 12 women with a mean age of 61 ± 7.7 years, followed for a year (Table 1). Twenty-one patients were excluded intra-operatively for the following reasons: irreparability of the injury (7); LHBT injury > 25% (6); partial repair (2); and rotator cuff injury < 3 cm (6).
The VAS scale decreased from 6.6 ± 2.3 to 2.7 ± 2.7 ($p < 0.001$) at 12 months. The ASES and UCLA scales evolved from 36.9 ± 19.3 and 13.0 ± 3.8 to 74.0 ± 23.7 and 26.0 ± 7.4, respectively ($p < 0.001$), at the end of the follow-up. Twenty-one (84%) patients surpassed the MCID in the 1-year postoperative evaluation using the ASES and UCLA scale.[16] Four patients did not reach the MCID, of which only one patient was dissatisfied after a 12-month follow-up evaluation. (EVA: 7; ASES: 27; UCLA: 17) and was converted to reverse arthroplasty (Table 2).
The comparison of SF-12 quality of life scores preoperatively and postoperatively showed a statistically significant improvement in the physical aspect ($p = 0.001$) but not in the mental aspect ($p = 0.391$).
Patients were divided according to the Hamada classification, with a predominance of type I (68%) compared to type II (32%) (Table 3).
The increase in acromiohumeral distance from preoperative to 6 months postoperative was from 6.28 mm to 6.92 mm, with no statistically significant difference ($p = 0.202$) (Table 4).
All patients underwent magnetic resonance imaging at 6 months post-surgery to evaluate rotator cuff and long head of the biceps

Table 1. Demographic Characteristics of the Patients.

Variables	n = 25
Sex, n(%)	
Male	13 (52)
Female	12 (48)
Age, years (mean SD)	61 ± 7.65
Affected side, n (%)	
Right	13 (52)
Left	12 (48)
Dominant side, n (%)	
Right	25 (100)
Left	0 (0)
Alcoholic, n (%)	13 (52)
Smoker, n (%)	2 (8)
Arterial hypertension, n (%)	13 (52)
Diabetes, n (%)	6 (24)
Hypothyroidism, n (%)	1 (4)
HIV, n (%)	3 (12)
Rheumatoid arthritis, n (%)	3 (12)

SD: standard deviation; n: number of patients.

Table 2. Preoperative and Postoperative Functional Outcomes.

	Mean	SD	p-value
VAS			**p<0.001***
Preoperative	6.6	2.3	
1º day	5.2	2.1	
14º day	4.3	3	
6 months	3.2	2.8	
12 months	2.6	2.7	
ASES			**p<0.001***
Preoperative	36.8	19.2	
6 months	66.7	24.2	
12 months	73.9	23.7	
UCLA			**p<0.001***
Preoperative	13	3.8	
6 months	23.1	7.8	
12 months	26	7.3	
SF-12 - Physical			**p=0.001**
Preoperative	32.7	8.5	
6 months	39.5	11.3	
12 months	41.2	13.1	
SF-12 - Mental			**p=0.391**
Preoperative	45.8	13.7	
6 months	42.3	14.2	
12 months	43	14.4	

VAS: Visual analogue scale; ASES: American society of shoulder and elbow score; UCLA: University of California Los Angeles score; SF-12: Short Form Health Survey; SD: Standard deviation. *Post-hoc analysis: The VAS score in the preoperative period differs from that obtained on the 1st day, 14th day, 6 months, and 12 months ($p<0.0001$). The comparison of the periods preop x 14th day, preop x 6 months, preop x 12 months, 1st day x 6 months, and 1st day x 12 months showed $p<0.0001$; however, it was not significant for the periods preop x 1st day ($p=0.1219$), 1st day x 14th day ($p=0.1486$), 14th day x 6 months ($p=0.1396$), 14th day x 12 months ($p=0.0306$), and 6 x 12 months ($p=0.1096$). The UCLA score in the preoperative period differs from that obtained at 6 and 12 months ($p<0.001$). The comparison of the periods preop x 6 months and preop x 12 months showed $p<0.0001$; however, it was not significant for the period 6 x 12 months ($p=0.005$). The ASES score in the preoperative period differs from that obtained at 6 and 12 months ($p<0.001$). The comparison of the periods preop x 6 months and preop x 12 months showed $p<0.0001$; however, it was not significant for the period 6 x 12 months ($p=0.016$). The SF-12/physical score in the preoperative period differs from that obtained at 6 and 12 months ($p<0.001$). The comparison of the periods preop x 6 months and preop x 12 months showed $p<0.001$; however, it was not significant for the period 6 x 12 months ($p=0.526$).

Table 3. Distribution of Patients by Radiological Classification.

Classification	n	%
Hamada		
I	17	68
II	8	32
Goutallier		
I	9	36
II	16	64

Table 4. Preoperative and postoperative acromiohumeral distance.

	Mean	SD	Median	p-value
Acromiohumeral distance (mm)				p=0.202
Preoperative	6.28	2.13	6.01	
6 months	6.92	2.73	6.66	

SD: Standard deviation.

tendon healing. We observed a 60% retear rate of the rotator cuff (Sugaya IV = 6; Sugaya V = 9) and 84% of patients showed signs of LHBT healing.

No postoperative complications such as infection, anterior shoulder pain, crackling, fatigue, or anatomical deformity of the biceps due to retear were reported.

DISCUSSION

The results of this prospective case series demonstrate that reinforcement of large and massive rotator cuff tears with the LHBT yields satisfactory outcomes with significant improvements in pain and UCLA and ASES scores.

The improvement in clinical scores is similar to that described by Rhee et al.[18] who reinforced the repair of large and extensive rotator cuff tears with TCLB, finding an increase in ASES and UCLA scores between the preoperative and postoperative periods of 56.4 to 73.7 and 19.7 to 25.6, respectively. Cho et al.[19] using the UCLA score, reported an increase in the score from 14.1 preoperatively to 32.6 points after surgery. In a similar way, but including lesions larger than 2 cm, Seo et al.[20] reported that the ASES score between the pre- and postoperative periods improved from 43.2 to 91.9.

We assessed the impact of the results obtained with this technique on patients' quality of life using the SF-12 questionnaire. We did not find similar studies in the literature that made this type of correlation. The physical component, which evaluates functional capacity, pain, and general health, showed significant improvement. However, the mental component, which relates to emotional and cognitive quality of life, did not show significant improvement. This component is influenced by sociodemographic aspects and patients' mental health, which can be affected by pain and functional deficits, contributing to a low score.

Our study also observed significant pain improvement on the VAS. This finding is similar to that of Cheppalli et al.[21] in a systematic review, which concluded that incorporating LHBT into the repair can improve VAS scores by up to 5 points.[21]

The rotator cuff retear rate in this study was 60%, which, although high, is considerably lower than that reported in the literature by other authors, ranging from 40 to 94%.[1,22] Using a methodology similar to ours, Rhee et al. found comparable results, with a retear rate of 54.2%. When considering patients with fatty degeneration > 2 by the Goutallier classification, this retear rate increases to 75%.[18] According to Malavolta et al.[23] low fatty degeneration is an important prognostic criterion for achieving better clinical outcomes after rotator cuff repair; therefore, we chose to include only patients classified as Goutallier 1 (36%) and 2 (54%) of the supraspinatus.

We attribute the significant improvement in functional scores to the high healing rate of TCLB that was assessed on the MRI scan performed 6 months after surgery. We found an 84% healing rate of TCLB in the new groove, as did Veen et al. who reported in a systematic review, a biceps healing rate of 82% after 2 years of surgery.[24] Restoration of the superior capsule in the treatment of large and extensive rotator cuff tears is essential to restore shoulder biomechanics, as demonstrated by Han el al.[25] in which RCS with TCLB restores glenohumeral stability by re-centering the humeral head on the glenoid, even in irreparable injuries

Regarding the radiographic evaluation, the AHD remained stable without reducing the interval during follow-up (6.92 ± 2.7 mm). Kim et al. suggested that rotator cuff repair with LHBT reinforcement can exert a depressive force on the humeral head, however no study has shown a significant increase in AHD with this technique.[5,18]

Some complications related to LHBT surgical procedures, such as anterior shoulder pain, the appearance of Popeye's sign, crackling, and fatigue have been described, although they rarely represent a functional problem for patients over time.[21] Nevertheless, we did not document any of these complications or surgical site infections.

In our study, we reproduced the technique described by Kim et al.[5] with adaptations for open rotator cuff repair. We opted to perform LHBT transposition with tenodesis in the new groove because we believe that keeping the LHBT intact after transposition allows the biceps muscle-tendon unit to theoretically add static force, keeping the humeral head centered and consequently ensuring good shoulder function.

We can cite some disadvantages of the study, such as the short follow-up time, which may not be sufficient to evaluate all possible complications and the long-term durability of the results. Another weakness is the need for a good-quality LHBT, which is often not seen in cases of massive rotator cuff tears. Thirdly, the small sample size may limit the generalizability of the results. Another important point is that only open rotator cuff repairs were performed, although the literature demonstrates that the results between arthroscopic and open techniques are similar.[26] Finally, the absence of a control group prevents direct comparison with other repair techniques.

However, we used a methodology similar to other authors regarding functional assessment and repair healing.[18,27] Moreover, Cañete San Pastor et al.[28] believe that this technique would also have a therapeutic effect on patients with biceps pathology, thus eliminating the need for a good-quality LHBT.

The transposition and incorporation of the biceps tendon into the rotator cuff repair adds native tissue rich in tenocytes and fibroblasts for the repair. Other advantages include reduced procedure cost and disease transmission risk from allograft use, easy access to the LHBT during arthroscopy, and being technically more reproducible than other graft options for treating large and massive rotator cuff tears.[18] This technique has proven to be safe and cost-effective, with the potential to increase rotator cuff repair healing rates and improve functional outcomes. However, future studies with larger samples and control groups are needed to confirm these findings.

CONCLUSION

Reinforcement with the long head of the biceps tendon in the repair of large and massive rotator cuff tears offers satisfactory clinical outcomes. Patients showed significant improvements in pain scores, in the physical component of the Short Form Health Survey, and function after one year of follow-up, with a low complication rate.

AUTHOR'S CONTRIBUTION: Each author contributed individually and significantly to the development of this article. GMRP: manuscript writing, review, and performance of the surgeries; CND and MCOC: critical review of its intellectual content and translation; HA: statistical analysis and manuscript review; MECG: translation and manuscript review; EAM: intellectual concept of the article, manuscript review, and data analysis.

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TREATMENT OF LATERAL EPICONDYLITIS OF THE ELBOW WITH HYALURONIC ACID INJECTIONS

TRATAMENTO DA EPICONDILITE LATERAL DO COTOVELO COM INFILTRAÇÕES DE ÁCIDO HIALURÔNICO

Mauro Emilio Conforto Gracitelli[1], Luiza de Campos Moreira da Silva[1], Jorge Henrique Assunção[1,2], Fernando Brandão de Andrade e Silva[1], Arnaldo Amado Ferreira Neto[1], Eduardo Angeli Malavolta[1,3]

1. Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas (HCFMUSP), Sao Paulo, SP, Brazil.
2. DASA, Hospital 9 de Julho, São Paulo, SP, Brazil.
3. Hospital do Coracao (Hcor), São Paulo, Brazil.

ABSTRACT

Introduction: The primary objective was to evaluate the efficacy of hyaluronic acid injections for lateral epicondylitis. Secondary objectives included assessing pain and functional outcomes at various time points following the injection. Methods: This prospective cohort study included patients who received two hyaluronic acid injections one week apart after prior conservative treatment. Assessments were conducted at two and six weeks, and at three, six, and 12 months post-injection. Outcome measures were pain scores (Visual Analogue Scale), functional assessment (Single Assessment Numeric Evaluation), and injection site complications. Results: A total of 46 patients (52 elbows) were included. Significant improvements were observed in pain scores measured by VAS at rest, from 4.5±2.8 initially to 2.7±2.8 at 3 months and 2.3±3.0 at 12 months ($p<0.001$). Similar improvements were seen in VAS scores during maximum hand grip strength, from 5.8±3.1 initially to 2.8±3.4 at 12 months ($p<0.001$). SANE score also improved significantly. No complications were reported. Conclusions: Treatment of lateral epicondylitis with hyaluronic acid showed statistically significant improvement in VAS scores at rest and during maximum hand grip strength, as well as in SANE scores, with no reported complications. ***Level of Evidence IV; Case Series.***

Keywords: Tennis Elbow; Lateral Epicondylitis; Hyaluronic Acid; Viscosupplementation.

RESUMO

Introdução: O objetivo primário foi avaliar a eficácia das infiltrações com ácido hialurônico para epicondilite lateral. Os objetivos secundários incluíram avaliar a dor e os resultados funcionais em vários momentos após a infiltração. Métodos: Este estudo de coorte prospectivo incluiu pacientes que receberam duas injeções de ácido hialurônico com uma semana de intervalo após tratamento conservador prévio. As avaliações foram conduzidas em duas e seis semanas, e em três, seis e 12 meses após a infiltração. As medidas de desfecho foram escores de dor (Visual Analogue Scale), avaliação funcional (Single Assessment Numeric Evaluation) e complicações no local da infiltração. Resultados: Um total de 46 pacientes (52 cotovelos) foram incluídos. Melhoras significativas foram observadas nos escores de dor medidos pela EVA em repouso, de 4,5 ± 2,8 inicialmente para 2,7 ± 2,8 em 3 meses e 2,3 ± 3,0 em 12 meses ($p < 0,001$). Melhoras semelhantes foram observadas nos escores VAS durante a força máxima de preensão manual, de 5,8 ± 3,1 inicialmente para 2,8 ± 3,4 em 12 meses ($p < 0,001$). O escore SANE também melhorou significativamente. Não foram relatadas complicações. Conclusões: O tratamento da epicondilite lateral com ácido hialurônico apresentou melhora estatisticamente significativa nos escores VAS em repouso e durante a força máxima de preensão manual, bem como nos escores SANE, sem complicações relatadas. ***Nível de Evidência IV; Série de Casos.***

Descritores: *Cotovelo de Tenista; Epicondilite Lateral; Ácido Hialurônico; Viscossuplementação.*

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INTRODUCTION

Lateral epicondylitis is a common cause of elbow pain, affecting approximately 1 to 3% of the population annually.[1] Studies show that about 80% of cases experience symptomatic improvement within one year.[2,3] Conservative treatment is the cornerstone approach for managing lateral epicondylitis.[4] However, it can often be protracted and restrictive for both daily activities and sports participation.[5] Despite the widespread adoption of conservative measures such as rest, physiotherapy and nonsteroidal anti-inflammatory drugs, a significant proportion of patients experience persistent symptoms

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The study was conducted at Instituto de Ortopedia e Traumatologia do Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (FMUSP), Rua Dr. Ovidio Pires de Campos, 333, 3rd floor, Cerqueira Cesar, Sao Paulo, SP, Brazil. 05403-90.
Correspondence: Mauro Emilio Conforto Gracitelli. 333, Rua Dr. Ovidio Pires de Campos, 3rd floor, Cerqueira Cesar Sao Paulo, SP, Brazil. 05403-90. mgracitelli@gmail.com

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and functional limitations. Between 4 to 11% of patients develop chronic symptoms requiring surgical intervention.[2,6-8] This underscores the search for adjunctive therapeutic modalities to enhance conservative treatment outcomes.

Several types of injections have been explored in the management of lateral epicondylitis, including corticosteroid injections, hialuronic acid, platelet-rich plasma (PRP), and autologous blood injections. A meta-analysis by Krogh et al.[9] compared the efficacy of corticosteroid injections, PRP, and placebo for the treatment of lateral epicondylitis. The analysis revealed that corticosteroid injections provided short-term pain relief but were associated with a higher risk of symptom recurrence compared to PRP and placebo. PRP injections demonstrated superior long-term outcomes in terms of pain reduction and functional improvement compared to corticosteroid injections, albeit with a higher cost and increased risk of complications, such as local hematoma or infection.

In light of the limitations and potential adverse effects associated with corticosteroid injections and the higher cost of PRP, alternative approaches such as hyaluronic acid injections (HA) have gained attention. Petrella et al.[10] conducted a randomized trial evaluating the efficacy of HA in comparison to corticosteroid injections for lateral epicondylitis. The results demonstrated comparable short-term pain relief between HA and corticosteroid injections, with HA showing a lower recurrence rate and fewer adverse effects. Given these findings, our approach leans towards considering HA as a viable alternative to corticosteroid injections, particularly in patients who are refractory to conservative management or have concerns regarding the potential adverse effects associated with corticosteroid use.

Objectives

Primary objective: to analyze the functional results, according to the visual analogue scale (VAS) at rest of patients undergoing treatment with hyaluronic acid injections after 3 months.

Secondary objectives: evaluate the VAS scale at rest at 2 and 6 weeks, after 6 and 12 months, the VAS scale during maximum hand grip strength and the Single Assessment Numeric Evaluation (SANE) scale at 2 and 6 weeks, 3, 6 and 12 months.

METHODS

Study design

Patients with lateral epicondylitis were included in a prospective case series, after signing the informed consent. The patients were treated by doctors certified by the Brazilian Society of Shoulder and Elbow Surgery. The study was approved by the local ethical committee (CAAE 32016620.4.0000.0068).

Population

Patients older than 18 years and with clinical diagnosis of lateral epicondylitis, with pain on the lateral aspect of the elbow and in the lateral epicondyle, and positive clinical Cozen and Mills tests and imaging examination (ultrasound or magnetic resonance imaging) with signs of lateral epicondylitis were included in the study. Patients should have undergone conservative treatment for at least 2 months before enrollment.

Non-inclusion criteria were previous history of fracture or dislocation, osteoarthritis or focal cartilage lesion, neurological injury, previous surgery for epicondylitis, or any surgery on the upper limb, lack of mental capacity to understand the questionnaires, and active or previous infection in the affected elbow. Exclusion criteria comprised loss to follow-up before the first assessment, at 1 month.

Interventions

Included patients underwent two injections for lateral epicondylitis with hyaluronic acid, 1 week apart. Sportvis® hyaluronic acid was used (Biolab®) (12mg in 1.2ml of 1% sodium hyaluronate in a phosphate-buffered solution, biocompatible for periarticular infiltration in soft tissues).

Injection was performed 1 cm distal to the lateral epicondyle, at the point of greatest pain, using the technique described by Petrella et al.[10] The usual sterile preparation was performed and a local anesthetic injection was applied with 2% lidocaine without vasoconstrictor. The hyaluronic acid injection was performed next, with a 30x7 needle and distributed in at least 2 points around the initial insertion point. A second injection was administered in the same manner after 2 weeks.

In the following 2 weeks, the patient was instructed to use elbow, wrist and hand mobilization, but avoiding exertion with the affected limb. No type of immobilization was recommended.

The medication protocol was the same for all patients and consisted of Dypirone 1g 6/6h and Diclofenac sodium 8/8h for 3 days after the first and second infections. Patients were instructed to perform home stretches for the forearm extensor muscles for 2 weeks after the first injection.

Outcomes and Variables

The outcomes were evaluated before treatment and after inclusion in the study, after 2 and 6 weeks, 3, 6 and 12 months. The scores comprised the visual analogue scale (VAS) at rest, the VAS scale during maximum hand grip strength, and the Single Assessment Numeric Evaluation (SANE).

Additionally, assessments included an evaluation of complications at the injection site, such as infection, skin atrophy, or intense pain. The following patient-related variables were evaluated: age, gender and elbow side treated.

Minimal important differences for VAS at rest were defined for the 3 months follow-up evaluation as 1 point, as described by Challoumas et al.[11]

Sample size

The sample was defined by convenience, defined by the total number of patients who wish to participate during the study period. The recruitment period was 3 years.

Bias and loss of follow-up

The clinical assessment questionnaires used were applied in person, by telephone or email. Cases with missing data were treated by imputation with the last observation carried forward (when with a minimum of 3 months of follow-up) or by excluding the patient (when with no post-injection evaluation).

Statistical analysis

We subjected continuous variables to assessment of normality, using the Kolmogorov-Smirnov test, and homogeneity, using the Levene test. The continuous data were exposed by mean and standard deviation. Categorical variables were displayed in absolute value and percentage. Comparison between sequential evaluation times was performed using Analysis Of Variance (ANOVA) with Bonferroni post-hoc test for multiple comparisons. We used $p<0.05$ as the significance level. For data analysis, we used the SPSS version 24.0 program (SPSS Inc®, Chicago, IL, USA).

RESULTS

During the period evaluated, 55 patients with a confirmed diagnosis of lateral epicondylitis underwent two sequential injections of hyaluronic acid. After applying the inclusion and non-inclusion criteria, our series comprised 46 patients (52 elbows). Of these, 33 (63%) were male, 6 patients underwent to bilateral injections and 27 (52%) had only the right side treated. The mean age was 46 years ± 7.

According to the VAS at rest, the average score was 4.5 ± 2.8 in the initial assessment and 2.7 ± 2.8 at 3 months of follow-up, showing significant improvement ($p<0.001$). At 12 months of follow-up, the mean score was 2.3 ± 3.0, with statistically significant difference ($p<0.001$). In relation to the initial assessment, all periods showed statistically significant improvement (Figure 1). Regarding sequential evaluations after the initial assessment, we did not obtain a statistically significant difference. Clinical results are detailed in Table 1. According to the VAS during maximum hand grip strength, the average score was 5.8 ± 3.1 in the initial assessment and 3.0 ± 3.0 at 3 months of follow-up, showing significant improvement ($p<0.001$). At 12 months of follow-up, the mean score was 2.8 ± 3.4, with statistically significant difference ($p<0.001$). In relation to the initial assessment, all periods showed statistically significant improvement.

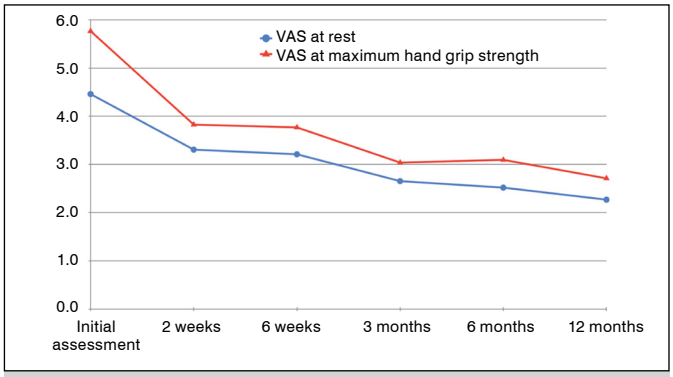

Figure 1. Visual analogue scale (VAS) at sequential follow-ups. VAS at rest (blue line) and VAS during maximum hand grip strength (red line).

Table 1. Funcional evaluation at initial assessment and at sequential follow-ups.

	Mean	SD	P-value
VAS at rest			
Initial assessment	4.5	2.8	p<0.001*
2 weeks	3.3	2.6	
6 weeks	3.2	2.9	
3 months	2.7	2.8	
6 months	2.5	3.0	
12 months	2.3	2.9	
VAS at maximum hand grip strength			
Initial assessment	5.8	3.1	p<0.001**
2 weeks	3.8	2.9	
6 weeks	3.8	2.7	
3 months	3.0	3.0	
6 months	3.1	3.4	
12 months	2.7	3.3	
SANE			
Initial assessment	57.1	23.2	p<0.001***
2 weeks	64.5	27.3	
6 weeks	69.3	23.1	
3 months	73.2	25.8	
6 months	78.2	23.0	
12 months	77.8	23.8	

* Post-hoc analysis: difference between the follow-up times - initial assessment to all follow-ups, 2 weeks to 12 months. ** Post-hoc analysis: difference between the follow-up times - initial assessment to all follow-ups. *** Post-hoc analysis: difference between the follow-up times - initial assessment to all follow-ups, except to 2 weeks; 2 weeks to 6 and 12 months.

SANE score also showed significant improvement after the procedure, from 57.1% ± 23.2 from the initial evaluation to 78.2% ± 23.5 ($p<0.001$) at final follow-up. In relation to the initial assessment, all periods showed statistically significant improvement, except for 2-week follow-up (Figure 2).

The results reached minimal important differences for VAS at rest in 67% of the elbows for the primary outcome. Nine elbows (17%) didn't achieve satisfactory results after the procedure, with persistence pain (VAS at rest > 5) at final follow-up (12 months).

No patient had complications related to the procedure, such as infection or skin complications. No patient underwent further surgery.

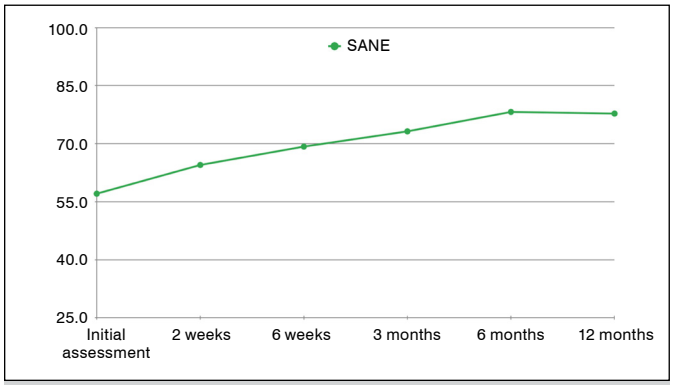

Figure 2. Single Assessment Numeric Evaluation (SANE) at sequential follow-ups.

DISCUSSION

The use of hyaluronic acid (HA) in sport-related tendinopathies has garnered considerable attention in recent years(12). Concurrently, various HA preparations and procedural approaches are currently under scrutiny to ascertain optimal therapeutic strategies. Encouraging outcomes have also been observed in the treatment of tendinopathies, predominantly attributed to HA's anti-inflammatory properties, augmented cellular proliferation, collagen deposition, and its lubricating effect on the tendon's gliding surface.[13,14] However, it is noteworthy that in the majority of studies, HA administration was not localized within the degenerated tendon itself but rather adjacent to it and/or within the articular space. This raises the possibility that alterations in synovial fluid dynamics facilitated by HA may exert a beneficial influence directly on the tendon[12]

While the literature demonstrates promising outcomes of HA therapy in the management of tendinopathies, including lateral epicondylitis, comprehensive comparative analyses evaluating the efficacy and safety profiles of various HA preparations are scarce.[15] Moreover, the optimal dosing regimens, frequency of administration, and long-term outcomes remain to be elucidated.[15]

Over the course of our study, we observed a notable decrease in pain levels, both at rest and during maximum hand grip strength, among the majority of participants. This reduction in pain was evident not only in the short term, but also persisted up to the 12-month. Additionally, patients reported improvements in their overall satisfaction with elbow function, as demonstrated by decreases in VAS and SANE scores. The results reached minimal important differences for VAS at rest in 67% of the elbows at 3 months follow-up and as defined by Challoumas et al.[11] However, it is important to acknowledge that not all patients experienced complete relief from their symptoms. Approximately 17% of elbows did not respond favorably to the HA injections, with some individuals still reporting significant pain even after the treatment period. Despite this, it is noteworthy that none of the patients experienced any adverse effects or complications related to the procedure, highlighting the safety profile of HA injections for lateral epicondylitis.

One study by Pellegrino et al.[16] explored the efficacy of a combined approach involving high-intensity laser therapy (HILT) and HA injections compared to therapeutic exercise (TE). They found that the HILT + HA group exhibited significant increases in muscle strength compared to the TE group, suggesting potential benefits of HA associated with HILT in the short to medium term. On the other hand, Yalcin and Kayaalp[17] conducted a prospective randomized controlled study comparing the efficacy of HA injections with triamcinolone injections in chronic lateral epicondylitis. They found that triamcinolone injections provided superior short-term pain relief and functional improvements compared to HA injections. Furthermore, Zinger et al.[18] conducted a randomized controlled trial comparing HA injections with a saline control group. They reported significant success in pain relief with HA injections, which persisted up to 12 months post-injection.

In comparison to the study by Stirma et al.[19] which also investigated the effectiveness of hyaluronic acid (HA) infiltration for lateral epicondylitis, our study had a larger sample size (12 vs 52 elbows) and a longer follow-up (3 vs 12-months). They reported a reduction in positivity rates for specific tests and improvements in the Mayo Elbow Performance Score, consistent with our observations of decreased pain levels and enhanced functional status. Moreover, both studies reported a high level of patient satisfaction with the treatment, with no complications or adverse effects observed.

Our study has some limitations. We lacked a comparative group, limiting our ability to assess HA treatment's relative efficacy against other modalities. While lateral epicondylitis typically allows for shorter follow-ups, longer-term studies could provide a more comprehensive understanding of outcomes. Moreover, HA treatment's higher cost may hinder accessibility for some patients. Lastly, not using a specific epicondylitis scoring system may have limited the depth of our assessment of treatment outcomes.

CONCLUSIONS

Treatment of lateral epicondylitis with hyaluronic acid led to a statistically and clinically significant improvement for the visual analogical pain score at rest and during maximum hand grip strength and for the Single Assessment Numeric Evaluation, with no reports of complications.

AUTHOR'S CONTRIBUTION: Each author contributed personally and significantly to the development of this article: MECG, LCMS, JHA, FBAS, AAFN, and EAM: Substantial contribution to the conception or design of the work, or acquisition, analysis, or interpretation of data for the work; MECG and JHA: Writing the manuscript or critical revision of its intellectual content; LCMS, FBAS, and EAM: Final approval of the version of the manuscript to be published.

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DOI: http://dx.doi.org/10.1590/1413-785220253302e290211

OUTCOMES OF EARLY SURGICAL REPAIR OF THE KNEE EXTENSOR MECHANISM INJURY, COMPARING THE QUADRICEPS AND PATELLAR TENDON INJURIES: A PROSPECTIVE OBSERVATIONAL STUDY

RESULTADOS DA REPARAÇÃO CIRÚRGICA PRECOCE DA LESÃO DO MECANISMO EXTENSOR DO JOELHO, COMPARANDO AS LESÕES DO QUADRÍCEPS E DO TENDÃO PATELAR: UM ESTUDO PROSPECTIVO OBSERVACIONAL

Vinícius Antônio Santos Aragão[1], *João Victor Lacerda Belfort*[1], *Flavio de Fava Sanches*[1], *Renan José Rigonato*[1], *Maria Adelaide de Miranda Gonçalves*[1], *Marcos de Camargo Leonhardt*[1], *Jorge dos Santos Silva*[1], *Kodi Edson Kojima*[1]

1. Universidade de Sao Paulo, Faculdade de Medicina, Hospital das Clinicas (HCFMUSP), Instituto de Ortopedia e Traumatologia, Grupo de Trauma, Sao Paulo, SP, Brazil.

ABSTRACT

Objectives: this study aimed to compare the radiographic, functional and isokinetic results of the early repair of quadriceps tendon rupture (QTR) and patellar tendon rupture (PTR). Methods: We conducted a prospective observational study at a level one urban university trauma center from January 2022 to March 2023. The study included patients aged 18 years and older who underwent surgery within three weeks of injury and had at least one year of follow-up. The evaluation used the patellar indices (Insall-Salvati, Blackburn Peel and Caton Deschamps), functional (Lysholm and PCS-12) and isokinetic assessment. Results: the study involved 20 patients, predominantly male, with a slight predominance of left-sided injuries. The mean age was 39.4 years. Surgical outcomes showed no significant radiographic differences post-repair. Functionally, the PTR group exhibited better recovery compared to the QTR group, particularly in returning to sports and work. Isokinetic testing revealed a substantial reduction in strength on the injured side compared to the uninjured side across both groups. Conclusion: early surgical intervention leads to favorable radiographic and functional outcomes. The PTR group showed better functional recovery, especially in return to work and sports. No significant differences were found in isokinetic strength recovery between the QTR and PTR groups. ***Level of Evidence III; Prospective Observational Study.***

Keywords: Knee Injuries, Patellar Ligament, Quadriceps Muscle, Muscle Strength, Lysholm Knee Score.

RESUMO

Objetivo: este estudo teve como objetivo comparar os resultados radiográficos, funcionais e isocinéticos da reparação precoce da rutura do tendão do quadríceps (RQT) e da rutura do tendão patelar (RTP). Métodos: Realizamos um estudo observacional prospetivo em um centro de trauma universitário urbano de nível um de janeiro de 2022 a março de 2023. O estudo incluiu pacientes com 18 anos ou mais que foram submetidos à cirurgia dentro de três semanas após a lesão e tiveram pelo menos um ano de acompanhamento. A avaliação utilizou os índices patelares (Insall-Salvati, Blackburn Peel e Caton Deschamps), funcional (Lysholm e PCS-12) e avaliação isocinética. Resultados: o estudo envolveu 20 pacientes, predominantemente do sexo masculino, com ligeiro predomínio de lesões do lado esquerdo. A idade média foi de 39,4 anos. Os resultados cirúrgicos não mostraram diferenças radiográficas significativas após a reparação. Funcionalmente, o grupo RTP apresentou melhor recuperação em relação ao grupo RQT, nomeadamente no regresso ao desporto e ao trabalho. Os testes isocinéticos revelaram uma redução substancial da força no lado lesionado em comparação com o lado não lesionado em ambos os grupos. Conclusão: a intervenção cirúrgica precoce conduz a resultados radiográficos e funcionais favoráveis. O grupo PTR apresentou melhor recuperação funcional, especialmente no retorno ao trabalho e ao desporto. Não foram encontradas diferenças significativas na recuperação da força isocinética entre os grupos RQT e PTR. ***Nível de Evidência III; Estudo Observacional Prospectivo.***

Descritores: *Traumatismos do Joelho; Ligamento Patelar; Músculo Quadríceps; Força Muscular; Escore de Lysholm para Joelho.*

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The study was conducted at Instituto de Ortopedia do Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, R. Dr. Ovidio Pires de Campos, 333, Cerqueira Cesar, Sao Paulo, SP, Brazil. 05402-000.
Correspondence: Vinícius Antônio Santos Aragão. 1504, Rua Oscar Freire, apto 124, Pinheiros, Sao Paulo, SP, Brazil. viniciusvasa@hotmail.com

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INTRODUCTION

Injuries to the knee extensor mechanism significantly impact orthopedic practice, often leading to substantial morbidity, pain, and functional impairment.[1] These injuries are categorized into three clinical types: quadriceps tendon rupture, patellar tendon rupture, and patellar fracture. Despite their differences, all types share a potential for knee extension deficit, often necessitating early surgical intervention.[2,3]

Quadriceps tendon ruptures (QTR) are approximately twice as common as patellar tendon ruptures (PTR), with incidences of 1.3% and 0.6%, respectively, among all soft tissue injuries in orthopedics.[4] QTRs are frequently associated with tendinopathy, comorbidities, anabolic steroid use, and advanced age, typically occurring in patients over 40 years. Conversely, PTRs are more prevalent in younger patients (under 40 years), often resulting from repetitive microtrauma. The injury mechanisms to the knee extensor tendons can be direct or indirect, with indirect mechanisms—often due to eccentric contraction of the quadriceps muscle with the knee in flexion—being two to three times more common.[3-6]

Non-surgical management is appropriate for cases of partial tendon rupture where full knee extension is maintained. However, early surgical intervention within the first three weeks post-injury is recommended to prevent worse functional outcomes, often necessitating autologous graft reinforcement or reconstruction.[7-9] Although postoperative outcomes are generally favorable, with a high rate of athletes returning to sports and high patient satisfaction, significant challenges remain. These include reductions in quadriceps muscle strength, loss of knee flexion, soft tissue shortening, and reports of residual pain.[8,10]

The primary aim of this study was to evaluate the functional and isokinetic outcomes of early surgical treatment for knee extensor mechanism tendon ruptures. The secondary outcome was to assess the radiographic outcomes of the tendon repairs.

PATIENTS AND METHODS

This prospective observational study was conducted at a level one urban university trauma center from January 2022 to March 2023. The study received approval from the Research and Ethics Committee (approval number 81967024.4.0000.0068), and written informed consent was obtained from all participants.

The inclusion criteria were individuals aged 18 years and older, literate, with quadriceps or patellar tendon injuries, operated on within 3 weeks, with a minimum follow-up of one year, and who attended radiographic, functional, and isokinetic evaluations. Participants were also required to have signed an informed consent form.

The exclusion criteria included associated multiligamentar knee injury, ipsilateral patella fracture, previous knee fractures, associated ipsilateral injury, femoral or tibial nail fixation with entry point in the knee, and dementia syndrome.

The primary surgical method for tendon repair was transosseous reattachment of the tendon. The tendon end was exposed, nonviable tissue was removed, and a Krakow-type locking stitch suture was performed using a number five braided polyester non-absorbable suture (Ethibond, Ethicon, Somerville, NJ, USA). Three parallel longitudinal drill holes were made in the patella, and the four suture ends were passed through them. The tendon was anatomically reduced to the patella surface, and all sutures were tied, ensuring the patella was returned to its anatomical position in the trochlea, avoiding patella alta or baja. In cases with tear extension to the retinaculum, the injury was closed with number one Vicryl (Ethicon). At the end of the tendon repair, before final wound closure, the knee was moved from total extension to at least 110 degrees of flexion to ensure the quality of the repair.[11]

To reinforce quadriceps tendon repair, the Scuderi technique was used, involving a wide-based inverted V tendon flap. The tendon used to augment the primary repair of the patellar tendon was the ipsilateral autologous semitendinosus tendon, which was kept attached distally and looped around the proximal pole of the patella and sutured back to the patellar tendon distally.[11]

All patients used a knee brace in extension for two weeks, allowing weight-bearing as tolerated. Physiotherapy commenced in the third week.

Demographic data collected included age, sex, side of injury, BMI (Body Mass Index), comorbidities, smoking habits, previous symptoms in the knee, and sports activity. Treatment-related data included whether augmentation with autologous tendon was performed. Outcome-related data collected included re-rupture, return to work, and return to sport activity.

Radiographic measurements of the patellar indices (Caton-Deschamps, Blackburn-Peel, and Insall-Salvati) were performed using lateral knee radiographs taken with 30 degrees of flexion. The Caton-Deschamps index calculates the ratio between the patellar articular surface and its distal distance to the anterosuperior margin of the tibia. The Blackburn-Peel index compares the patellar articular surface with its distal distance to a line projected from the superior articular surface of the tibia. The Insall-Salvati index measures the ratio between the total length of the patella and the length of the patellar tendon. Normal values range between 1 and 1.2, while a ratio of 1.3 or greater indicates a high-riding patella.[7]

Functional outcomes were assessed using the Lysholm Knee Score questionnaire, and quality of life was evaluated using the Short Form (SF)-12v2, which provides mental and physical component summary scores (MCS-12 and PCS-12).[12-14]

The isokinetic test was conducted to assess the functional performance of the knee muscles, focusing on peak torque, peak torque to body weight ratio (peak BW), total work, and the hamstring-to-quadriceps (H/Q) ratio at two different angular velocities: 60 degrees/second and 240 degrees/second. Testing was performed with a Biodex System 3 dynamometer (Biodex Medical System, Inc., Shirley, NY). The 60 degrees/sec velocity was used to assess maximal strength, and the 240 degrees/sec velocity to evaluate muscle endurance.[15]

Qualitative characteristics were described using absolute and relative frequencies, while quantitative characteristics were summarized using descriptive statistics (mean and standard deviation). Parametric data were compared with the Student t-test, and the association between categorical variables with the Chi-square test of independence. Isokinetic measurements and functional scales were compared using paired Wilcoxon tests, and the correlation of percentage differences between the injured and contralateral sides with quantitative characteristics was examined using Spearman's correlation. Differences in isokinetic measurements according to relevant qualitative characteristics were compared using Mann-Whitney tests. Data analysis was conducted using IBM-SPSS for Windows version 22.0, with tabulations in Microsoft Excel 2013, and a significance level set at 5%.[16]

RESULTS

The study included 20 participants with a mean age of 39.4 years (median: 37 years). There were 8 patients (40%) in the group with QTR with a mean age of 46.7 ± 13.1 years and 12 patients (60%) in the PTR group with a mean age of 34.3 ± 13.5 years ($p = 0.055$). The cohort was predominantly male (95%) and primarily injured on the left side (70%). The mean Body Mass Index (BMI) was 28.2, indicating a tendency towards being slightly overweight. Most participants (70%) had no comorbidities, while 15% had one comorbidity, and another 15% had two or more. A logistic regression

analysis was performed to examine the influence of comorbidities, diabetes, previous symptoms, smoking, and BMI on the variable local of injury to predict the value "0". Logistic regression analysis showed that the model as a whole was not significant (Chi2(6) = 7.07, p = 0.315, n = 20). Regarding lifestyle factors, 20% of participants were smokers, and 65% engaged in regular sports activities (Table 1). Additionally, 40% of patients underwent autograft tendon augmentation during surgery—three in the QTR (37.5%) and five in the PTR (41.6%) (Table 1). Post-surgical radiographic scores showed no significant differences between sides. The Insall-Salvati Score for the injured knee had a mean of 1.3, compared to 1.27 for the healthy knee (p = 0.926). The Blackburn-Peel score was slightly higher in the injured knee, with a mean of 1.3 compared to 1.2 on the contralateral side (p = 0.422). The Caton-Deschamps score similarly showed no significant difference, with a mean of 1.52 for the injured knee compared to 1.54 on the contralateral side (p = 0.255) (Table 2).

Re-rupture occurred in 2 cases (10%)—one in each group—and reoperation was required in one (5%). In terms of recovery, 85% of participants returned to their previous work, and 69.2% of those previously active in sports returned to sports activities post-recovery. The statistical analyses of the correlation between return to work and the location of the injury showed a non-significant difference (p = 0.097). For the return to sports, the statistical analyses showed a marginal association of more return to sports in the PTR group than the QTR group, but it did not reach the threshold for statistical significance (p = 0.054) (Table 3).

The Lysholm score for the PTR group (82.7 ± 15.8) was higher than the score for the QTR group (63.2 ± 28.5) (p = 0.114). The PCS-12 of the PTR group (0.6 ± 0.5) was significantly better than the QTR group (1.4 ± 0.9) (p = 0.045) (Table 3). In a 60° isokinetic evaluation, the injured knee exhibited a mean peak torque of 106.9 ± 58.4 Nm, while the uninjured knee showed a higher mean of 182.5 Nm (p < 0.001). The peak torque normalized to body weight (peak/BW) for the injured knee was 120.5 Nm/kg, compared to 203.2 Nm/kg for the uninjured knee (p < 0.001). Total work was also significantly higher on the uninjured knee, with a mean of 589.5 J compared to 345.1 J on the injured knee (p < 0.001). Similarly, the hamstring/quadriceps ratio (H/Q) at this level was higher on the injured knee, with a mean of 90.4, versus 56.7 on the uninjured knee (p < 0.001) (Table 4). At the 240° isokinetic evaluation, the injured knee showed a mean peak torque of 77.5 Nm, lower than the uninjured knee's mean of 108.6 Nm (p = 0.002). The peak/BW ratio for the injured knee was 87 Nm/kg, compared to 126.8 Nm/kg for the uninjured knee (p < 0.001). The total work at this level was also significantly lower on the injured knee, with an average of 917.1 J, compared to 1332.8 J on the uninjured side (p < 0.001). The agonist/antagonist ratio for the injured knee was 88.4, while the uninjured knee had a mean of 63.8 (p < 0.001) (Table 4). No statistical differences were observed between quadriceps tendon and patellar ligament injuries in functional, radiographic, or isokinetic assessments. Surgical techniques with tendon augmentation did not show statistical differences across all functional, clinical, and radiographic assessments. There was also no difference between those who returned to their previous work activities and those who did not. Among those who returned to previous sports activities, only the difference in peak/BW and total work at 240° was statistically greater in those who resumed sports (p = 0.020 for both). The other characteristics evaluated did not statistically influence the percentage difference in isokinetic exams in this population (p > 0.05).

Table 1. Demographic results.

Variable	Total (N = 20)	QTR (N = 8)	PTR (N = 12)	p
Age (years) Mean SD	39.4 ± 14.5	46.9 ± 13.3	34.3 ± 13.5	0.055
Sex, n (%)				
Female	1 (5)	1 (12.5)	0	
Male	19 (95)	7 (87.5)	12 (100)	
Laterality, n (%)				
Right	6 (30)	2 (25)	4 (33.3)	
Left	14 (70)	6 (75)	8 (66.7)	
BMI Mean SD	28.2 ± 4.0	29.3 ± 5.0	27.5 ± 3.1	0.910
Comorbidities, n (%)				
None	14 (70)	4 (50)	10 (83.4)	
One	3 (15)	2 (25)	1 (8.3)	
Two or more	3 (15)	2 (25)	1 (8.3)	
Smoking, n (%)				
No	16 (80)	6 (75)	10 (83.4)	
Yes	4 (20)	2 (25)	2 (16.6)	
Previous symptoms, n (%)				
No	13 (65)	6 (75)	7 (58.3)	
Yes	7 (35)	2 (35)	5 (41.7)	
Sport activity, n (%)				
No	7 (35)	5 (62.5)	2 (16.6)	
Yes	13 (65)	3 (37.5)	10 (83.4)	
Tendon augmentation n(%)				
No	12 (60)	5 (62.5)	7 (58.3)	
Yes	8 (40)	3 (37.5)	5 (41.7)	

Student t test

Table 2. Radiographic patellar indices results.

Variable	QTR			PTR			
	Injured	Normal	p	Injured	Normal	p	p (Q/P)
Insall-Salvati	1.1 ± 0.1	1.2 ± 0.2	0.926	1.4 ± 0.4	1.3 ± 0.2	0.520	0.055
Blackburn Peel	1.0 ± 0.1	1.1 ± 0.3	0.422	1.4 ± 0.3	1.2 ± 0,2	0.120	0.070
Caton Deschamps	1.3 ± 0.3	1.5± 0.5	0.255	1.7 ± 0.3	1.6 ± 0.3	0.650	0.423

Paired Wilcoxon test. QTR = quadriceps tendon rupture, PTR = patellar tendon rupture.

DISCUSSION

The present study aimed to compare the outcomes of acute repair of the knee extensor mechanism injury. Despite the limitation of a small sample size, the analysis focused on the differences between quadriceps tendon and patellar tendon injuries, comparing the demographics, clinical outcomes, radiographic, and functional assessments as described above.

Table 3. Functional results.

Variable	QTR (N = 8)	PTR (N = 12)	p
Re-rupture, n (%)			
No	7 (87.5)	11 (91.7)	0.805
Yes	1 (12.5)	1 (8.3)	
Return to work, n (%)			
No	3 (37.5)	0	0.097
Yes	5 (62.5)	12 (100)	
Return to sports, n (%)			
No	7 (87.5)	4 (33.3)	0.054
Yes	1 (12.5)	8 (66.7)	
Lysholm score Mean SD	63.5 28.5	82.4 15.8	0.114
PCS-12, n (%) Mean SD	1.4 0.9	0.6 0.5	0.045

Paired Wilcoxon test.

Table 4. Isokinetic assessment results.

Variable	QTR			PTR			
	Injury	Normal	p	Injury	Normal	p	p (Q/P)
60 peak torque	101.1 ± 50.3	168.9 ± 35.4	0.007	110.7 ± 65.1	191.5 ± 62.1	0.005	0.715
60 peak body weight	108.3 ± 55.6	181.7 ± 45.9	0.021	128.5 ± 76.7	217.5 ± 69.7	0.007	0.504
60 total work	320.4 ± 160.5	556 ± 118.1	0.004	361.5 ± 240.8	611.8 ± 211.8	0.013	0.652
60 H/Q	77.9 ± 26.0	53.4± 9.9	0.025	58.5 ± 14.4	98.8 ± 33.4	0.001	0.135
240 peak torque	64.5 ± 30	86 ± 34.5	0.205	86.1 ± 40.2	123.6 ± 32.7	0.020	0.187
240 peak body weight	69.4 ± 33.5	106.4 ± 23.9	0.023	98.7 ± 45.6	140.5 ± 37.4	0.022	0.116
240 total work	742.2 ± 419.6	1051 ± 307.6	0.115	1033.6 ± 524.8	1520.1 ± 442.5	0.022	0.187
240 H/Q	79.7 ± 23.4	64.1 ± 14.4	0.131	94.2 ± 48.7	63.5 ± 9.3	0.043	0.387

Paired Wilcoxon test. QTR = quadriceps tendon rupture, PTR = patellar tendon rupture.

Our results indicate a significant age difference between the two groups, with the mean age for patients with QTR being higher (46.9 years) compared to those with PTR (34.3 years, p = 0.017). Comparing to Garner et al.3 the mean age for PTR was similar (34.3 vs. 39.6 years), but for the QTR our patients showed a lower mean age (46.7 vs. 61.0 years). This may explain the absence of correlation of the QTR with comorbidities as described by Boudissa et al.[8] where older patients tend to have more comorbidities.

The injury to the left knee represented 70% of the total, with a higher incidence in both the QTR (75%) and PTR (66.7%). We could not find in the literature neither a similar number nor an explanation for this higher incidence on the left side. This may be related to lower leg muscle dominance and protective responses.

The higher incidence of previous symptoms in the PTR (41.7%) compared to the QTR (25%) is consistent with the literature and shows the presence of degenerative changes predisposition to injury.[1,3]

The need for augmentation of the repair was at the surgeon's discretion according to his impression of the amount of degeneration of the tendon and showed no difference in both groups (QTR 37.5% vs. PTR 41.6%). And the augmentation had no correlation with the radiographic and functional results (p > 0.05).

When the patient suffers a knee extensor mechanism injury, the position of the patella will depend on the rupture location; in the QTR, the patella tends to stay in its position or lower, whereas in the PTR the patella is usually in a higher position. This may lead to a repair with an altered patella position after the suture. But the radiographic measurements of the patellar indices (Caton-Deschamps, Blackburn-Peel, and Insall-Salvati) in our study showed that the repair reestablished the patellar height similar to the contralateral normal side in both the QTR and PTR, demonstrating the good reconstruction of the patellar height (Table 2).

In general, the patients with PTR had a better recovery compared to the patients with QTR, as assessed by return to previous work and sports activity. In the PTR group, all patients (100%) returned to their previous occupation, and 66.7% resumed sports activities. In contrast, only 37.5% of the patients with QTR returned to their previous work, and just 12.5% were able to return to sports. The differences could be explained by the greater mechanical demands placed on the quadriceps, as well as the older age and possibly lower baseline activity level of the QTR group.

The same happened in the objective assessment. The Lysholm score was higher in the PTR group (82.4 ± 28.5) compared to the QTR group (63.2 ± 12.5), indicating a better functional outcome. Similarly, the SF-12 physical component score was more favorable in the PTR group (0.6) versus the QTR group (1.4), with lower scores indicating better health. West et al.[17] have also found a high Lysholm score ranging from 70 to 100, but they did not make a separate analysis between QTR and PTR. In their comparative study, Hantes et al.[18] the Lysholm score had no difference between the groups (QTR 91 and PTR 85, p = 0.124). But they found better Kujala score and VAS in the QTR group.

The better functional result of the PTR group may be explained by the higher tensile strength and stiffness of the patellar tendon compared to the quadriceps tendon, which allows more effective force transmission during activities like jumping and running, and in contrast, the quadriceps tendon is more complex in its anatomy and its biomechanical function in the knee, leading to a less predictable healing.[19]

In the isokinetic evaluation, the peak torque and peak body weight ratio showed both groups with significant differences between the injured side and the normal side, with the injured side exhibiting 60% of the contralateral normal side, representing a substantial reduction of strength, affecting the knee's ability to generate force during extension.

The total work also showed an endurance reduction of 40% on average in both QTR and PTR groups, indicating that the knee can do less work overtime in contrast to the normal side. The H/Q ratio just confirms the imbalance due to the quadriceps weakness. The isokinetic results persisted at higher speed (240o), but less pronounced, suggesting that the deficit in muscle function in the injured knee is less detectable at higher speeds.

Comparing the isokinetic results of the injured knee between the QTR and PTR groups, the results showed similar levels of performance across all parameters (peak torque, peak BW ratio, total work, and H/Q ratio) and at different speeds (60o and 240o per second), with no statistically significant differences. This suggests functional equivalence between QTR and PTR groups in the injured knee, similar to the results of Yalcin et al.[20]

This study has some limitations. The study may have a small sample size, that can be explained by the low incidence of this injury, as shown by the number of patients included by Hantes et al. in their comparative study (n = 24) and Strother et al.[21] in a ten-year study included only 43 patients. The sample size limits the comparability and generalizability of the results. The functional result may be influenced by variability of the rehabilitation by the patient regardless of the orientation given. The heterogeneity of the study population may introduce confounding variables. The use of self-reported measures, such as the Lysholm score and SF-12 physical component score, introduces a level of subjectivity. Patients' perceptions of their recovery and function might be influenced by factors such as pain tolerance, psychological status, or expectations, which could lead to variability in the results.

We can conclude that the PTR occurs in younger patients, more on the left side, with more previous symptoms, have better Lysholm and SF-12-PS scores, and similar isokinetic assessment compared to the QTR group. In both groups, all three patellar indices showed similar results in comparison to the normal side.

CONCLUSIONS

The Lysholm and SF-12 PS scores were better in the PTR group. All isokinetic measurements showed similar results between the PTR and QTR groups, with an average 40% deficit of the operated knee. The radiographic indices showed similar ratios between the operated and normal knee.

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ROLE OF POLYMORPHISMS IN VEGF AND KDR GENES IN OSTEOSARCOMA SUSCEPTIBILITY: A SYSTEMATIC REVIEW

PAPEL DOS POLIMORFISMOS NOS GENES VEGF E KDR NA SUSCEPTIBILIDADE AO OSTEOSSARCOMA: UMA REVISÃO SISTEMÁTICA

Amanda dos Santos Cavalcanti[1], Jéssica Vilarinho Cardoso[2], Verônica Aran Ponte[3], Jade Pires Nascimento[2], Mariana Chantre-Justino[1], Ana Cristina de Sá Lopes[1], Walter Meohas[1], Jamila Alessandra Perini[2]

1. Instituto Nacional de Traumatologia e Ortopedia (INTO), Divisao de Pesquisa, Rio de Janeiro, RJ, Brazil.
2. Universiodade do Estado do Rio de Janeiro (UERJ), Laboratorio de Pesquisa em Ciencias Farmaceuticas (LAPESF), Rio de Janeiro, RJ, Brazil.
3. Instituto Estadual do Cerebro Paulo Niemeyer, Laboratorio de Biomedicina do Cerebro, Rio de Janeiro, RJ, Brazil.

ABSTRACT

Osteosarcoma is the most common aggressive primary bone tumor in children and adolescents. Angiogenesis, induced by vascular endothelial growth factor (VEGF) and its receptor (kinase insert domain receptor - KDR) is involved in tumor development. Both genes (VEGF and KDR) are polymorphic, and their association with osteosarcoma remains unclear. A systematic review of observational studies was performed to evaluate the association between polymorphisms in these genes and osteosarcoma development. Pubmed, Medline, Lilacs, and Scielo databases were searched for observational studies published up to April 2024. Eight publications of case-control studies were included, with quality ranging from 82% to 95%. All subjects were from the Chinese population: 1,681 cases and 2,049 controls. A total of six VEGF polymorphisms were analyzed. For osteosarcoma susceptibility, three studies found an increased risk with VEGF rs699947, four with VEGF rs2010963, two with VEGF rs3025039, one with VEGF rs833061, and no studies found an association with the VEGF rs1570360 and VEGF rs10434 SNPs. In addition, no studies evaluated SNPs in the KDR gene and osteosarcoma susceptibility. Further studies in diverse populations, particularly in Brazil, are necessary to clarify the role of VEGF and KDR polymorphisms in osteosarcoma development and prognosis. ***Level of evidence III; Systematic Review.***

Keywords: Osteosarcoma; Genetic Polymorphism; Angiogenesis; VEGF; Systematic Review.

RESUMO

O osteossarcoma é o tumor ósseo primário agressivo mais comum em crianças e adolescentes. A angiogênese, induzida pelo fator de crescimento endotelial vascular (VEGF) e seu receptor domínio quinase (KDR), está envolvida no desenvolvimento tumoral. Ambos os genes (VEGF e KDR) são polimórficos, e sua associação com o osteossarcoma permanece incerta. Uma revisão sistemática de estudos observacionais foi realizada para avaliar a associação de polimorfismos nesses genes com o desenvolvimento de osteossarcoma. As bases de dados Pubmed, Medline, Lilacs e Scielo foram consultadas em busca de estudos observacionais publicados até abril de 2024. Foram incluídas oito publicações de estudos de caso-controle, com qualidade variando de 82% a 95%. Todos os participantes eram da população chinesa: 1.681 casos e 2.049 controles. Foram analisados seis polimorfismos do VEGF. Três estudos encontraram um risco aumentado de desenvolvimento do osteossarcoma com VEGF rs699947, quatro com VEGF rs2010963, dois com VEGF rs3025039, um com VEGF rs833061, e nenhum estudo encontrou associação com os SNPs VEGF rs1570360 e VEGF rs10434. Nenhum estudo avaliou SNPs no gene KDR. Estudos adicionais em populações diversas, especialmente no Brasil, são necessários para esclarecer o papel dos polimorfismos nos genes VEGF e KDR no desenvolvimento e também no prognóstico do osteossarcoma. ***Nível de Evidência III; Revisão Sistemática.***

Descritores: *Osteossarcoma; Polimorfismo Genético; Angiogênese; Fator de Crescimento Endotelial Vascular; Revisão Sistemática.*

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INTRODUCTION

Osteosarcoma is a rare malignant primary bone tumor that usually affects long bones such as the distal femur, tibia, and proximal humerus.[1,2] Its age distribution is bimodal, with a higher peak between 10 and 20 years of age and a second peak between 70 and 80 years of age.[1] In childhood, the incidence is higher in females, but between 15 and 19 years of age, it becomes higher in males.[3] The most common symptoms of osteosarcoma are pain and local swelling. The bone becomes fragile due to the tumor presence,[4] and approximately 17% of patients present with

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The study was conducted at Instituto Nacional de Traumatologia e Ortopedia (INTO), Av. Brasil, 500, Caju, Rio de Janeiro, RJ, Brazil. 20940-070.
Correspondence: Jamila Alessandra Perini Machado. 1203, Av. Manuel Caldeira de Alvarenga, prédio II, 2° andar, sala 224, Campo Grande, Rio de Janeiro, RJ, Brazil. 23070-200. jamilaperini@yahoo.com.br

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pathologic fractures.[5] Imaging and laboratory tests aid in the diagnostic investigation; however, the definitive diagnosis is confirmed by histologic evaluation.[6] The standard treatment consists of neoadjuvant and adjuvant chemotherapy combined with surgery.[7] Survival rates for patients with localized disease range from 60-75%.[8-10] On average, 20% of patients have pulmonary metastases at diagnosis.[11] The presence of metastases significantly decreases overall survival in 10 years, approximately 12.5% in Brazil[11] and 25% in the United States and Europe.[12]

The mechanism of osteosarcoma development is complex, and its exact etiology is still unknown. However, environmental and genetic factors have been associated with the development of this type of tumor.[13] Additionally, angiogenesis is a crucial process in the development, and proliferation of tumor cells, cancer progression, and metastasis development.[14] Vascular endothelial growth factor (VEGF) is one of the main pro-angiogenic factors, and high expression of VEGF and its kinase insert domain receptor (KDR) has been observed in osteosarcoma tissue samples compared to adjacent tissues.[15,16] VEGF expression was significantly correlated with histological grade, tumor stage, distant metastasis, and lower survival.[17-19] Positive VEGF status in tumor samples from osteosarcoma patients negatively impacts overall survival and disease-free survival, suggesting this factor is an effective biological marker for prognosis.[20,21] In this regard, anti-angiogenic inhibitor drugs targeting VEGF/VEGFR successfully inhibited osteosarcoma angiogenesis and cell proliferation *in vivo* and *in vitro,*[22] supporting the relevance of VEGF and its receptor in osteosarcoma.

The *KDR* and *VEGF* genes are located on chromosomes 4q11-q12 and 6p21.1, respectively, and have several single nucleotide polymorphisms (SNPs) in the coding and regulatory regions that may affect enzyme activity or expression.[23-25] In addition, different populations show increased frequencies of these SNPs.[26-28] Additionally, *VEGF* SNPs have been associated with osteosarcoma risk in the Chinese population[29-34] although the literature reports show controversial results. Different isoforms of VEGF have been associated with osteosarcoma progression,[35] metastases development,[36] and poor response to chemotherapy.[37] Among these, the most important isoform involved in angiogenesis and vasculogenesis is VEGF-A,[38] which is the subject of the current study. In this context, the aim of this study was to perform a systematic review of observational studies evaluating *VEGF* and *KDR* SNPs and osteosarcoma susceptibility to discuss the causes of the previously described conflicting results.

METHODS

Systematic Review Search Strategy

A literature search was conducted in the Pubmed, Medline, Lilacs, and Scielo databases to identify all articles that evaluated SNPs in the VEGF and KDR genes associated with the risk of developing osteosarcoma. These last two databases were consulted with specific interest in studies involving Latin American populations. All studies published up to April 2024 were evaluated, considering the following combined descriptors in both English and Portuguese: osteosarcoma and ("polymorphism" or "SNP" or "genetic polymorphism") and ("VEGF" or "Vascular endothelial growth factor" or "VEGFR-2" or "Vascular endothelial growth factor-2" or "KDR" or "Kinase Insert Domain Receptor"). Additionally, the reference list of review/meta-analysis articles and of each selected article were reviewed to identify any other articles that might not have been included in the initial data search.

Inclusion and Exclusion Criteria

The articles selected for this review followed the following inclusion criteria: (i) observational studies that evaluated the association of SNPs in the VEGF and KDR genes with the development of osteosarcoma; (ii) studies published in English or Portuguese; (iii) studies published up to April 2024. The exclusion criteria were: (i) publications that did not include osteosarcoma patients, (ii) did not analyze VEGF and KDR SNPs; (iii) analyzed only disease progression; and (iv) publications without completely accessible texts.

Data Extraction

After selecting the studies according to the inclusion and exclusion criteria, the following information was extracted from each article by two reviewers (JVC and JPN): first author and year of publication; study population; the number of osteosarcoma cases and controls; the age of both groups; gender; type of control recruited; patient-reported family history of cancer; location of the osteosarcoma; presence or absence of metastasis; clinical staging of the osteosarcoma cases; identification of SNPs; genotyping technique for SNP identification; SNP allele frequency data; and Pearson's chi-square test and odds ratio (OR) values with their respective 95% confidence intervals (CI 95%).

Data management

The data extracted from the studies included in this review were organized and analyzed using Excel spreadsheets. Percentages were used as statistical measures to compare the frequency of each variable extracted from the studies, followed by a descriptive analysis of the data. To aid in data synthesis and visualization, Excel tools were employed for basic calculations such as sums and percentages, as well as for arranging the characteristics of each study. All data were reviewed by two researchers (JVC and JPN). When an article did not report the frequency of the alleles for the polymorphisms included, the frequencies were calculated based on genotype information. Since each individual has two alleles, the total number of alleles was determined by summing the set of genotypes.

Quality Assessment of Included Studies

All included studies were independently analyzed by two reviewers (JVC and JPN) according to the STROBE checklist used for observational studies. This quality assessment tool has twenty-two items related to: title and abstract (item 1), introduction (items 2 and 3), methodology (items 4 to 12), results (items 13 to 17), discussion (items 18 to 21), and funding of each study (item 22), assigning a score of 0 or 1 for each item. In the end, studies with a score greater than 50% were approved for evaluation in this review according to the guideline.[39]

RESULTS

The flowchart of the included articles is illustrated in Figure 1. Out of the 206 publications found, we excluded 189 duplicates and were left with 17 valid publications. One additional article[31] was identified after reviewing the reference list of the 17 selected articles, making a total of 18 articles for evaluation of eligibility criteria. Subsequently, 10 articles were excluded: 4 meta-analyses,[40-43] 3 studies that analyzed only disease progression,[16,44,45] 2 studies that did not analyze SNPs in the *VEGF* or *KDR* genes,[46,47] and one study that did not include osteosarcoma patients.[48] Consequently, eight publications[29-34,49,50] were selected for full-text evaluation and included in this review. All eight studies investigated SNPs in the VEGF gene only. No publication was found that described an association of SNPs in the KDR gene with osteosarcoma development (Figure 1).

Table 1 describes the characteristics of osteosarcoma cases from the studies included in this review. Regarding the STROBE rating of the included articles, the studies had a quality score of over 80%, with Wang et al.[50] having the highest score (21 out of 22 items) and

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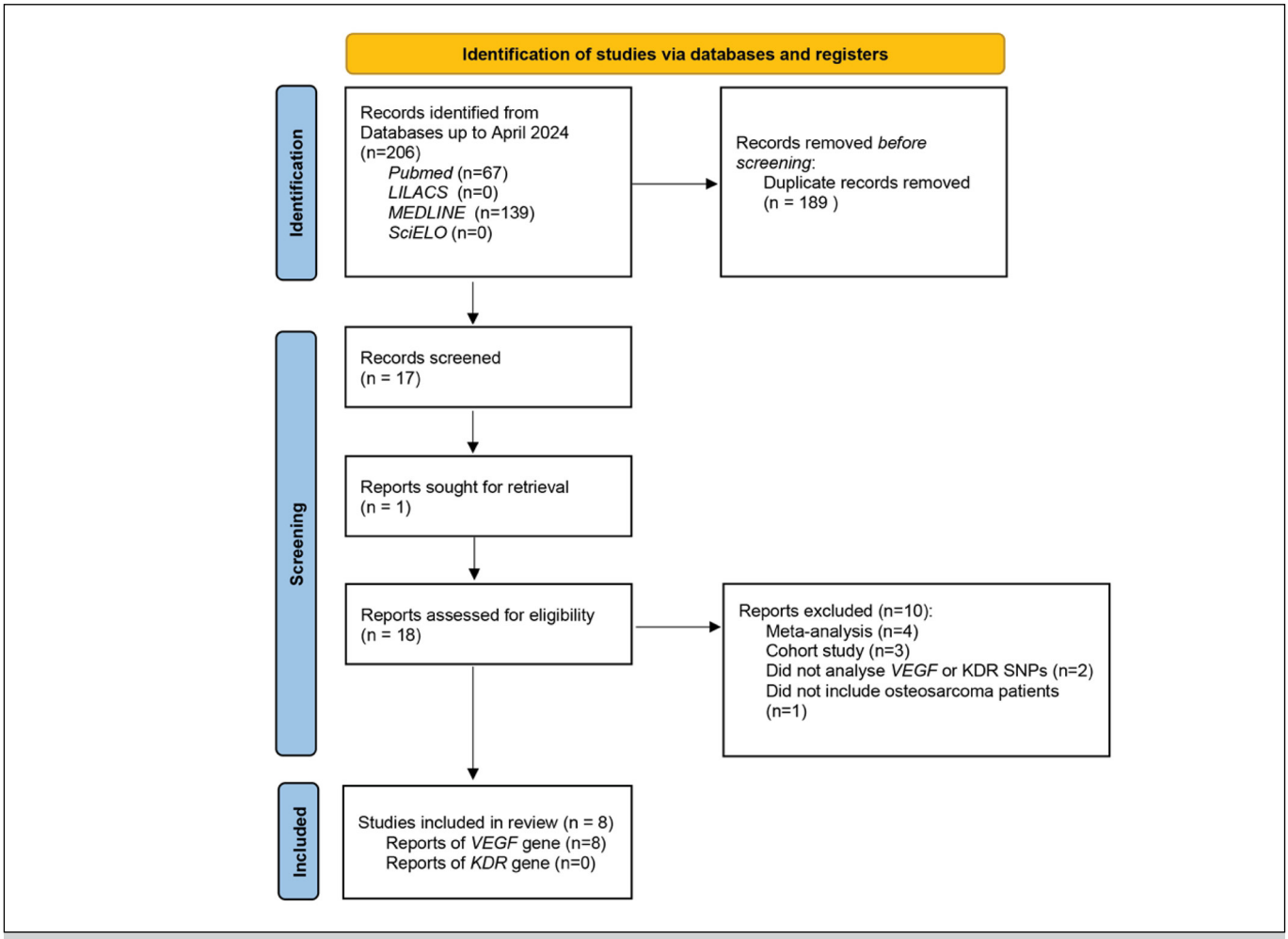
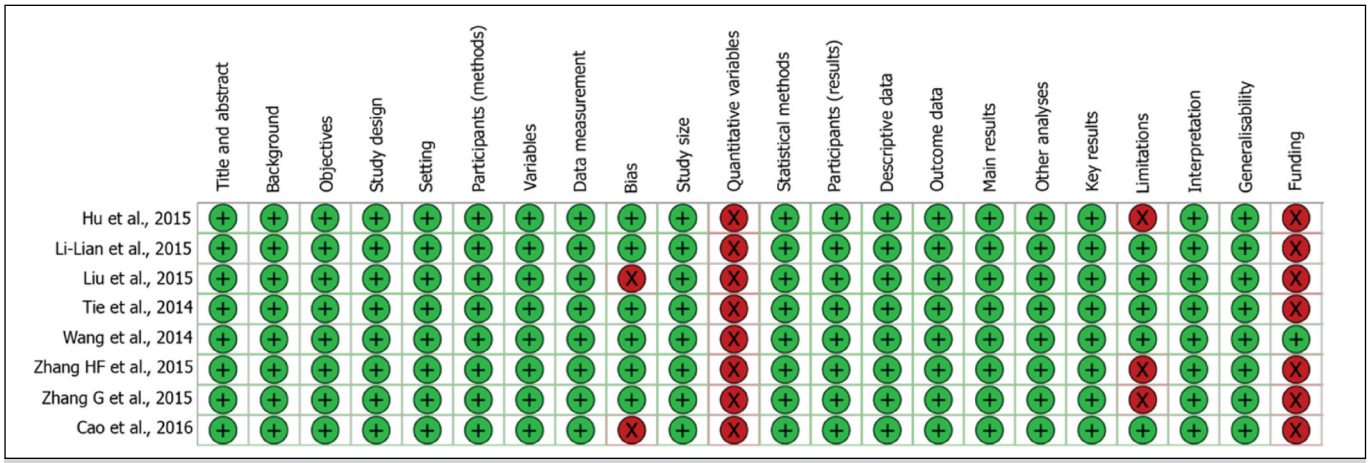


Figure 1. Study flowchart.



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Supplementary Figure 1. Quality assessment by the STROBE checklist.

the studies by Hu et al.[29] Zhang et al.[33] and Zhang et al.[34] having the lowest scores (18 out of 22 items).

The study population in all articles was Chinese, with a total of 1,681 osteosarcoma cases analyzed, with the majority (75%) of articles presenting more individuals under the age of 20 years,[29,31-33,49,50] and males being the most common sex in all articles (100%). Only the studies by Hu et al.[29] and Liu et al.[31] did not include information on family history of cancer (25%). Among the other studies, four (50%) observed a high frequency of cancer in the family[30,32-34] and two (25%) reported a low frequency of this characteristic.[49,50] In all articles, osteosarcoma was more frequently located in the long bones, and only in the article by Liu et al.[31] about 77% of patients had metastasis, while the other studies (n = 6; 75%) observed a much lower frequency (ranging from 19.4 to 34.6%).[29,32-34,40,50]

Table 1. Demographic and clinical data of osteosarcoma cases from eligible studies and quality assessment of included articles.

Reference	Population (n)*	Age (%)		Sex (%)	Family history of cancer (%)	Topography (%)		Metastasis (%)	Tumor Staging (%)		Strobe (%) #
		≤ 20	> 20	Men	Yes	Long bones	Axial skeleton	Yes	I-II	III-IV	
Tie et al.[32]	Chinese (165)	92 (55.6)	73 (44.4)	108 (65.3)	145 (87.6)	118 (71.3)	47 (28.7)	37 (22.3)	105 (63.4)	60 (36.6)	19 (86)
Wang et al.[50]	Chinese (330)	251 (76.1)	79 (23.9)	188 (57.0)	49 (14.8)	257 (78.9)**	73 (21.1)**	87 (26.4)	NI	NI	21 (95)
Hu et al.[29]	Chinese (130)	80 (61.5)	50 (38.5)	76 (58.5)	NI	94 (72.3)	36 (27.7)	28 (21.5)	89 (68.5)	41 (31.5)	18 (82)
Li-Lian et al.[30]	Chinese (176)	81 (46.0)	95 (54.0)	109 (61.9)	160 (90.9)	134 (76.1)	42 (23.9)	NI	101 (57.4)	75 (42.6)	19 (86)
Liu et al.[31]***	Chinese (186)	119 (64.0)	67 (36.0)	114 (61.3)	NI	135 (72.6)	51 (27.4)	143 (76.9)	NI	NI	20 (91)
Zhang G. et al.[33]	Chinese (180)	123 (68.3)	57 (31.7)	110 (61.1)	163 (90.6)	128 (71.1)	52 (28.9)	35 (19.4)	105 (58.3)	75 (41.7)	18 (82)
Zhang H. F. et al.[34]****	Chinese (182)	82 (45.1)	100 (54.9)	106 (58.2)	167 (91.8)	125 (68.7)	57 (31.3)	63 (34.6)	NI	NI	18 (82)
Cao et al.[49]	Chinese (322)	217 (67.4)	105 (32.6)	231 (71.7)	24 (7.5)	226 (70.2)	96 (29.8)	80 (24.8)	NI	NI	20 (91)

*Number of osteosarcoma cases in each article. **Tumor location categorized as extremities (long tubular bones) or other (axial skeleton).[50] ***Reported collecting information on tumor staging, family history of cancer, and histological type (osteoblastic, chondroblastic, fibroblastic, and mixed types); however, the sample size of each was not described.[31] ****Reported collecting information on tumor stage, but the sample size for each was not described.[34] #22 items related to the STROBE checklist. NI – not informed.

The study by Li-Lian et al.[30] did not include this information. In addition, four (50%) studies[29,30,32,33] reported stage I-II being the most common. Wang et al.[50] Liu et al.[31] Zhang et al.[34] and Cao et al.[49] did not report the tumor staging, although Liu et al.[31] reported collecting this information along with histologic subtype (osteoblastic, chondroblastic, fibroblastic, and mixed types). However, the frequency of both characteristics was not found in the text. The demographic characteristics and inclusion and exclusion criteria of the control participants from the selected studies (a total of 2,049 controls) are also described in this review (Table 2). The study period of the included articles ranged from 2008 to 2015, with seven being hospital-based (87.5%) and one being population-based.[50] For controls (healthy individuals), most studies (n = 7; 87.5%) reported a negative personal history of cancer and matched controls to cases by age and sex. In the article by Cao et al.[49] the authors only reported a negative personal history of cancer for healthy individuals. In the study by Wang et al.[50] controls were also matched by area of residence. Li-Lian et al.[30] and Zhang et al.[34] also reported a negative personal history of chronic diseases, while only Liu et al.[31] reported that the controls had no family history of cancer. In most articles (75%), the controls were under 20 years of age,[9,31-34,49,50] with a higher frequency of males observed in all studies. Four studies (50%) reported a high frequency of family history of cancer in the control group.[30,32-34] This characteristic was less frequent only in the studies of Wang et al.[50] and Cao et al.[49] Hu et al.[29] did not provide this information.

Figure 2 displays the frequencies of the variant alleles of each *VEGF* gene SNP found in the eligible studies of this systematic review. For the rs699947 *C>A* SNP, the variant allele frequency ranged from 37.4% to 42.6% in the case group and from 31.2% to 33.6% in the control group. Of the four published articles on this SNP,[30-32,34] three[30,32,34] found a positive association with the development of osteosarcoma (Figure 2A; Table 3). For the rs1570360 *A>G* SNP, the variant allele frequency ranged from 26.8% to 31.7% in cases and from 24.5% to 26.2% in controls, with no significant differences observed between groups observed in any study (Figure 2B; Table 3).[30-32] Regarding the rs833061 *T>C* SNP, the variant allele frequency ranged from 39.3% to 47.4% in cases and from 36.8% to 38.3% in controls, with only Li-Lian et al.[30] finding an increased risk of developing osteosarcoma with the CC genotype or the dominant model (TC+CC) (Figure 2C; Table 3). Seven articles evaluated the rs2010963 *G>C* SNP,[29-33,49,50] with four reporting a positive association with disease development in the presence of the G allele or GG genotype.[31-33,49] The variant allele frequency varied from 40.2% to 58.8% in the case group and from 39.1% to 61.8% in the control group across published studies (Figure 2D; Table 3). All articles in this review examined the rs3025039 C>T SNP, but only Wang et al.[50] and Hu et al.[29] observed an approximately twofold increased risk of developing osteosarcoma. The frequency of the rs3025039 T variant allele ranged from 20.1% to 37.8% in cases and from 15.4% to 34.6% in controls (Figure 2E; Table 3). Finally, six articles examined the rs10434 G>A SNP,[29-33,50] and none of

Table 2. Demographic characteristics and criteria used to select the controls from eligible studies.

Reference	Chinese-Region (n)*	Study Period	Study Design	Type of Control	Control matched by	Age (%)		Sex (%)	Family history of cancer (%)
						≤ 20	> 20	Men	Yes
Tie et al.[32]	Inner Mongolia (330)	2011 to 2013	HB	RE, NegCanP	Sex and age	170 (51.6)	160 (48.4)	215 (65.3)	303 (91.8)
Wang et al.[50]	Ningxia (342)	2009 to 2013	PB	RE, NegCanP	Sex, age, and residence	244 (71.3)	98 (28.7)	176 (51.5)	33 (9.6)
Hu et al.[29]	Wuhan (130)	2011 to 2013	HB	RE, NegCanP	Sex and age	77 (59.2)	53 (40.8)	76 (58.5)	NI
Li-Lian et al.[30]	Beijing (176)	2011 to 2013	HB	RE, NegCanP, NegChr	Sex and age	86 (48.9)	90 (51.1)	109 (61.9)	163 (92.6)
Liu et al.[31]	Jinan (186)	2008 to 2010	HB	RE, NegCanP, NegCanF	Sex and age	117 (62.9)	69 (37.1)	114 (61.3)	NA
Zhang G. et al.[33]	Chongqing, Inner Mongolia (360)	2011 to 2013	HB	RE, NegCanP	Sex and age	236 (65.6)	124 (34.4)	220 (61.1)	349 (96.9)
Zhang H. et al.[34]	Weifang (182)	2011 to 2013	HB	RE, NegCanP, NegChr	Sex and age	86 (47.2)	96 (52.8)	106 (58.2)	171 (94.0)
Cao et al.[49]	Shanghai (343)	2009 to 2015	HB	NegCanP	NI	217 (67.4)	130 (37.9)	242 (70.6)	27 (7.9)

*Number of controls in each article. HB = hospital-based. PB = population-based. RE = routine examination. NegCanP = negative personal history of cancer. NegCanF = negative family history of cancer. NegChr = negative history of chronic diseases. NA = not applicable once controls did not have a family history of cancer. NI = not informed by authors.

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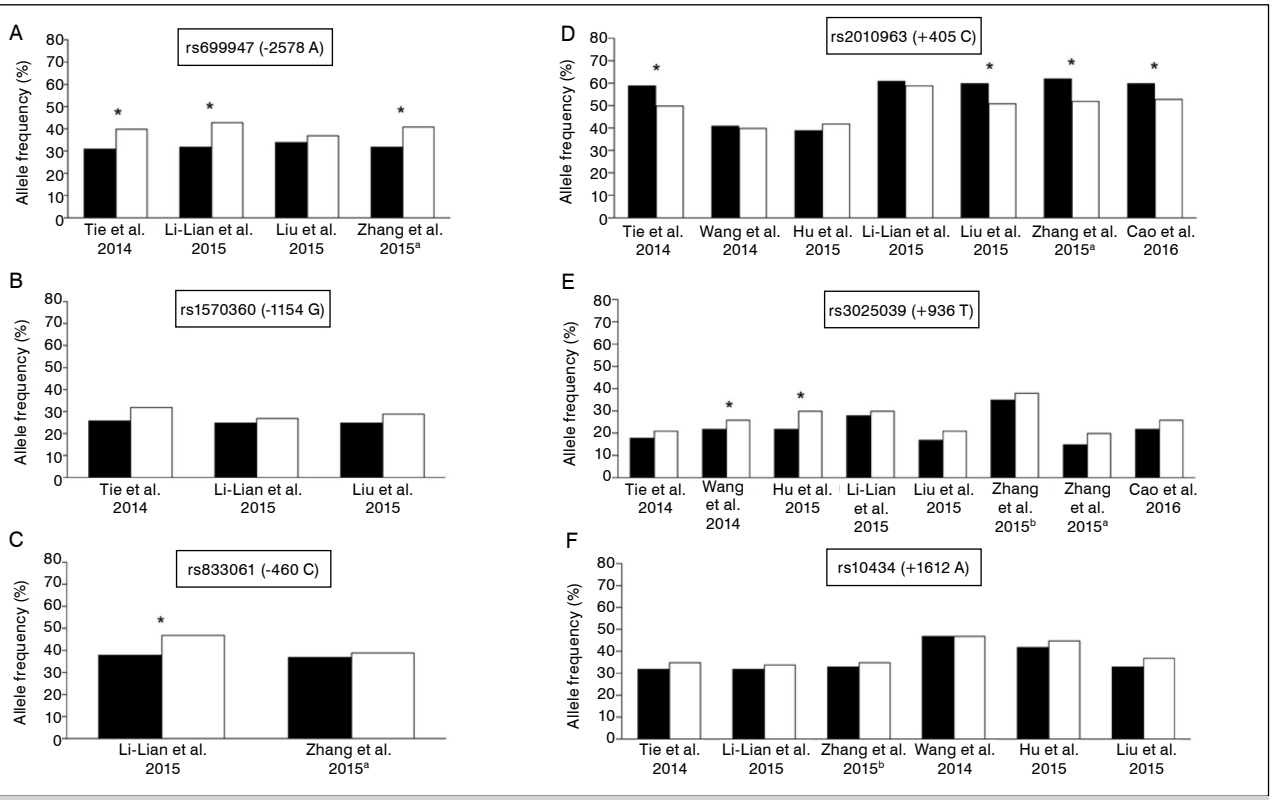

Zhang H. et al. 2015;[34] Zhang G. et al, 2015.[33] * P-value of Person's Chi-square test < 0.05.

Figure 2. Frequency of variant alleles of the SNPs *VEGF* rs699947 *A* (A), *VEGF* rs1570360 *G* (B), *VEGF* rs833061 *C* (C), *VEGF* rs2010963 *C* (D), *VEGF* rs3025039 *T* (E), and *VEGF* rs10434 *A* (F) found in the studies included in this review.

Table 3. Description of the results regarding the association of the studied polymorphisms in the *VEGF* gene with osteosarcoma.

SNP (rs)	Localization*	Genotypes	OR (CI 95%)	Reference
rs699947	-2578C>A (PR)	CA and AA	No association	Liu et al.[31]
		AA CA+AA	2.3 (1.2-4.6) 1.7 (1.1-2.6)	Li-Lian et al.[30]
		AA CA+AA	2.0 (1.02-3.8) 1.6 (1.01-2.4)	Zhang H. et al.[34]
		AA	2.06 (1.1-3.5)	Tie et al.[32]
rs1570360	-1156 (or -1154) A>G (PR)	AG and GG	No association	Liu et al.[31]
		AG, GG, and AG+GG	No association	Li-Lian et al.[30]
		AG and GG	No association	Tie et al.[32]
rs833061	-460T>C (PR)	CC TC+CC	2.2 (1.1-4.2) 1.6 (1.0-2.6)	Li-Lian et al.[30]
		TC, CC, and TC+CC	No association	Zhang H. et al.[34]
rs2010963	-634 (or +405) G>C (5'UTR)	GG	2.0 (1.1-3.8)	Liu et al.[31]
		GC, CC, and GC+CC	No association	Hu et al.[29]
		CG, GG, and CG+GG	No association	Li-Lian et al.[30]
		GG	2.1 (1.2-3.7)	Tie et al.[32]
		GC, CC, and GC+CC	No association	Wang et al.[50]
		GG	2.3 (1.3-4.0)	Zhang G. et al.[33]
		GG	1.5 (1.04-2.3)	Cao et al.[49]
rs3025039	+936C>T (3'UTR)	TT	2.7 (1.02-8.3)	Hu et al.[29]
		CT and TT	No association	Liu et al.[31]
		CT, TT, and CT+TT	No association	Li-Lian et al.[30]
		CT and TT	No association	Zhang G. et al.[33]
		CT, TT, and CT+TT	No association	Zhang H. et al.[34]
		CT and TT	No association	Tie et al.[32]
		TT	2.7 (1.3-5.5)	Wang et al.[50]
		TT and CT+TT	No association	Cao et al.[49]
rs10434	+1612G>A (3'UTR)	GA, AA, and GA+AA	No association	Hu et al.[29]
		GA and AA	No association	Liu et al.[31]
		CT, TT, and CT+TT	No association	Li-Lian et al.[30]
		CT and TT	No association	Zhang G. et al.[33]
		CT and TT	No association	Tie et al.[32]
		GA, AA, and GA+AA	No association	Wang et al.[50]

SNP = single nucleotide polymorphism; *Position and region of the polymorphism in the gene: PR = promoter region; UTR = untranslated region. OR = odds ratio. CI = confidence interval. (+) = dominant models.

them found a significant association with tumor development. The frequency of the variant allele ranged from 33.5% to 47.4% in cases and from 32.2% to 46.5% in controls (Figure 2F; Table 3). It is worth noting that, of the articles included in this review, only one evaluated both the impact of polymorphisms on the risk of developing osteosarcoma and their prognostic value. The authors[31] associated the polymorphism rs2010963 (-634GG) with a shorter overall survival (OS) time (HR, 3.10; 95% CI, 1.17-8.38).

Table 3 details the characteristics of the *VEGF* gene SNPs and the data from the association analyses of each study. The eight studies included in this review, identified six VEGF gene variants: rs699947 *C>A,* rs1570360 *A>G,* rs833061 *T>C,* rs2010963 *G>C,* rs3025039 *C>T,* and rs10434 *G>A*. The first three variants are located in the promoter region, one in the 5' UTR, and the remaining two in the 3' UTR, respectively. All studies used the same genotyping technique for these SNPs, polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Additionally, Li-Lian et al.[30] Tie et al.[32] and Zhang G. et al.[33] performed stratification analyses based on environmental characteristics for the SNPs in their respective studies. Li-Lian et al.[30] found no associations for any variables, whereas Tie et al.[32] reported that the rs699947 *AA* and rs2010963 *GG* genotypes were associated with an increased risk of osteosarcoma in individuals younger than 20 years and those with a family history of cancer. Furthermore, the rs699947 and rs2010963 genotypes were associated with an increased risk of developing osteosarcoma in males and females, respectively. Zhang et al.[33] also found that the rs2010963 GG genotype was associated with an increased risk in individuals younger than 20 years, in both sexes and with a family history of cancer. In addition, Liu et al.[31] evaluated the survival of osteosarcoma cases and found that the rs2010963 SNP could be considered as a prognostic factor for the disease, with the rs2010963 genotype being associated with a threefold higher risk of decreased survival (OR = 3.1; 95% CI = 1.17-8.38).

DISCUSSION

This study conducted a systematic review of observational studies investigating the potential relationship between SNPs in the *VEGF* and *KDR* genes and the risk of developing osteosarcoma. However, at the time of the literature review, none of the published studies had evaluated the association between SNPs in the KDR gene and osteosarcoma susceptibility. Eight studies examined the interaction of *VEGF* SNPs and osteosarcoma susceptibility,[29-34,49,50] and only four SNPs (rs699947, rs833061, rs2010963, and rs3025039) were associated with osteosarcoma risk.[29-34,49,50] Furthermore, one *VEGF* SNP (rs2010963) was associated with shorter survival.[31]

In most articles, osteosarcoma cases involved men under the age of 20, which is consistent with other studies conducted in different populations.[1,51] A study by our group of Brazilian patients with osteosarcoma recruited from a reference orthopedic hospital included samples from 37 histologically confirmed patients (24 males and 13 females) with a mean age of 18 years,[52] which is consistent with the current systematic review. A family history of cancer was highly prevalent (87.6-91.8% and 91.8-96.9%) among cases and controls, respectively, in four of the selected studies.[30,32-34] Various studies have found that a family history of cancer increases the likelihood of developing endometrial and prostate cancer by 3.1% and 59.7%, respectively, and that 15-20% of breast cancer cases are associated with a family history of cancer.[53,54] For osteosarcoma, a 3.6-fold risk was observed, associated with maternal endocrine gland cancer.[55]

In all reviewed articles, osteosarcoma was more commonly found in long bones, which is consistent with the literature.[1,51] The growth plate has a higher rate of cell proliferation, making cells more susceptible to mutations.[51] Similarly, our group's study showed that most tumors were located in the knee region (81%) and the most common histologic variant was high-grade central conventional osteosarcoma (83.8%), with 27% presenting metastases.[52] Most patients in this review did not have metastases and had stage I-II tumors, corroborating other studies.[56,57] Advanced age, axial skeletal location, lesion size, and residence in disadvantaged areas are risk factors associated with the presence of metastases at diagnosis.[56]

The angiogenic process involving VEGF and its receptors plays an important role in bone tissue regeneration and in the growth, progression, and metastasis of bone tumors.[58] Studies suggest an imbalance between angiogenic inducers and inhibitors, leading to an angiogenic tumor phenotype and tumor development.[15,59] In osteosarcoma, *VEGF* expression is associated with poor prognosis and metastasis development.[60] *In vitro*, VEGF silencing inhibits proliferation and promotes apoptosis in SaOS-2 cells, while in vivo, it suppresses tumor growth and angiogenesis.[61] Zheng et al.[62] showed higher expression of VEGF receptor (VEGFR2) in metastatic tumor samples (lung) compared to the primary tumor, and receptor inhibition reduces metastatic ability in vitro and significantly attenuates metastatic capacity *in vivo*.

In 2016, a meta-analysis of seven articles to provide a comprehensive assessment of the associations of SNPs in the *VEGF* gene with osteosarcoma susceptibility found that the *VEGF* rs3025039 *C>T* and rs2010963 *G>C* SNPs were associated with increased risk and protection, respectively, and that the rs10434 *G>A* SNP had no association with disease development.[40] Then, in 2017, another meta-analysis observed that the *VEGF* rs699947 C>A, rs1570360 A>G, rs833061 T>C, rs2010963 G>C, and rs3025039 C>T SNPs were associated with osteosarcoma risk in the Han Chinese population, while the *VEGF* rs10434 G>A SNP showed no significant association with the disease.[43] Recently, in 2022, another meta-analysis highlighted that the *VEGF* rs1570360 *A>G,* rs2010963 *G>C,* and rs3025039 *C>T* SNPs were associated with osteosarcoma risk, while the C allele of the *VEGF* rs699947 *C>A* SNP had a protective effect.[42] More recently, a meta-analysis that included the analysis of five SNPs, four of which were also evaluated in this review. The data from Hassanain et al.[63] support the risk analysis for the *VEGF* rs3025039 TT and rs2010963 GG SNPs. In contrast to our results, the leave-one-out analysis showed that the *VEGF* rs699947, rs10434, and rs1570360 SNPs were not significant. The *VEGF* rs833061 CC SNP was excluded from the meta-analysis because of the low quality of the articles. However, in our review, the association (2-fold risk) was based on the study by Li-Lian et al.[30] which was not cited in the meta-analysis by Hassanain et al. Similarly, contrary to our findings, the authors reported a risk associated with the *VEGF* rs157090360 based on Zhao's meta-analysis,[43] which was not included in this review once we excluded meta-analysis studies.

The *VEGF* rs699947 C>A, rs1570360 A>G, and rs833061 T>C SNPs may affect transcriptional activity and lead to increased protein levels because they are located in the promoter region of the gene.[64] The *VEGF* rs2010963 G>C SNP, located in the 5'UTR, is significantly positively correlated with VEGF protein synthesis by peripheral blood mononuclear cells (PBMCs).[24] Meanwhile, the *VEGF* rs3025039 C>T SNP, located in the 3'UTR, may influence plasma VEGF levels.[23] For *VEGF* rs10434 G>A SNP, also located in the 3'UTR, no studies have yet confirmed its influence on the gene; however, this type of SNP may affect mRNA stability and alter the ability of microRNAs to interact with their target due to its position in the gene.[65]

Although most of the studies included in this review reported similar frequencies of *VEGF* SNPs, they were all conducted in the Chinese population, which could lead to the inconsistencies in the association results. These inconsistencies may also be explained by (i) variability

in sample size, which may affect risk estimates, and (ii) the type of control used, which may also be associated with the variants studied. In case-control studies, the selection of the control group is critical, as these individuals should not have the chance of developing the outcome or have risk factors similar to the outcome, such as SNPs in the *VEGF* gene, which could bias risk estimates. Most articles in this review recruited healthy hospital-based controls matched to the case group by age and sex and with a negative personal history of cancer, which is a positive aspect as the ideal control group is directly determined by the definition and selection of the case group and recruited from the same source.[66] A limitation of the present review, common to other literature reviews, is the possibility that we did not include all the literature and missed some relevant studies. We included three databases, English-language articles only, and did not include grey literature.

Comparing the frequencies of *VEGF* rs699947 *A,* rs1570360 G*,* rs833061 C, and rs2010963 C SNPs in populations from different regions worldwide (according to data from the National Center for Biotechnology Information - NCBI), with the Chinese population (from this review) and the Brazilian population,[67] which has an extensive admixture of three major ancestral roots (indigenous, European and African) and is predominant in today's Brazilian population.[68] For *VEGF* rs699947 A SNP, the frequencies in Chinese (31.2-33.6%), Asian (28-34%) (NCBI), and Brazilian (31.9%) populations[67] were found to differ from those in African American (23%) and Sub-Saharan African (12-17%) populations (NCBI). For *VEGF* rs1570360 G SNP, the frequencies in European (67-69%), African (91-97%), American (78-80%), Latin American (75-80%) (NCBI), and Brazilian populations (83.8%)[67] differ from those in the Chinese population (24.5-26.2%). For the *VEGF* rs833061 C SNP, the frequencies in European (47%) (NCBI) and Brazilian (41.7%) populations[67] differ from those in Asian (27-34%), Chinese (38.3-36.8%), African American (33%), and Sub-Saharan African (30%) populations (NCBI). Finally, for the *VEGF* rs2010963 C and rs3025039 SNPs, the frequencies in European (27-42%; 10-23%, respectively), African American (24-36%; 5-12%, respectively) (NCBI), and Brazilian (38.6% and 12.5%, respectively) populations[67] differed from those in the Chinese population (39.1-61.8%; 15.4-34.6%, respectively).

The inconsistencies in SNP frequencies reinforce the idea that the variants studied in this review may exist at variable frequencies in both more homogeneous populations, such as the Chinese, and more heterogeneous populations, such as the Brazilians. This phenomenon may occur because of factors such as long-distance migration and the encounter of different populations during demographic expansion, resulting in genetic mixing or complete population replacement.[69,70] In addition, genetic interactions with environmental factors may influence these frequencies.[71] Therefore, extrapolation of data from Chinese SNP association studies to mixed populations is likely to lead to conclusions that are inconsistent with reality. In addition, the paucity of studies evaluating SNPs in the *KDR* gene identified in this review highlights the need for further investigation of this gene, given its importance in VEGF signaling and consequently in the angiogenic process.

CONCLUSIONS

For osteosarcoma susceptibility, three studies found an increased risk with *VEGF* rs699947, four with *VEGF* rs2010963, two with *VEGF* rs3025039, one with *VEGF* rs833061, and no studies found an association with the *VEGF* rs1570360 and *VEGF* rs10434 SNPs. In addition, no studies evaluated SNPs in the *KDR* gene and osteosarcoma susceptibility.

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