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Original article

Quadriceps muscle characteristics and subcutaneous fat assessed by ultrasound and relationship with function in patients with knee osteoarthritis awaiting knee arthroplasty

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Background: Patients with severe knee osteoarthritis are evaluated for total knee replacement (TKR), whose main indications are persistent pain and severe functional limitations substantially affecting mobility. However, evaluation of pain intensity and functional disability is difficult to standardize.
Objective: To evaluate the relationship between quadriceps muscle thickness (QMT) and quality; the QMT and subcutaneous fat thickness (SFT) and QMT and function in patients with knee OA on a waiting list for TKR.
Methods: Cross-sectional study in consecutively-enrolled patients. Variables: SFT, QMT and rectus femoris muscle quality, assessed by echointensity (EI). Function by the Timed Up & Go Test (TUG); sociodemographic and clinical variables and physical activity were determined. Karl Pearson correlations and multiple linear regression were used.
Results: 61 patients (45 female, mean age 69.7 years [SD 7.2], mean BMI 33.0 [SD 5.7], mean comorbidities 3.3 [SD 2.0], 52.5% regular physical activity) were studied. Mean TUG was 15.1 (SD 6.1). Variables retained in the regression model explained 36% of variability in the TUG. Greater muscle content (percentage) (r = −0,291) was associated with better TUG scores (p = 0.001). Greater muscle EI was negatively (r = −0,364) associated with function (p = 0.006). Older age was associated with worse TUG scores while regular physical activity was associated with better TUG scores (p = 0.001 and p = 0.008, respectively).
Conclusions: A higher percentage of quadriceps muscle and better muscle quality (lower EI) was associated with better function. Age and exercise levels influenced function. Ultrasound may provide

1. Introduction

Knee osteoarthritis (OA) is a high-prevalent chronic process that is enhanced by aging and increased bodyweight in developed countries.[1] It has been reported that 9.2% of people aged ≥ 60 years are diagnosed with symptomatic knee OA.[2] In the USA, 15% of the population had knee OA in 1995 and projections of an increasingly aging population show an estimate of 18.2% in 2020.[3] In Spain, the highest prevalence is 18.1% in males aged 60–70 years and 44.1% in females aged 70–80 years.[4] More than half of persons aged > 65 years are overweight or obese.[5] In the knee joint, increased loadbearing and the weakness of the muscle that stabilizes the joint are factors that accelerate destruction.[6] Pain, instability, and a greater risk of falls reduce physical capacity and limit functional performance in tasks such as walking and standing up from a chair.[3] When conservative treatment is ineffective, prosthetic replacement is often proposed.[7] The goal of total knee replacement (TKR) is to reduce pain and improve function and quality of life in

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order to preserve active and independent lifestyles. However, the indication and optimal time for TKR is not standardized or well-defined.[7] Some studies suggest that up to 14% of indications for TKR are not appropriate and that between 14 and 30% of patients undergoing TKR are not satisfied with the results.[1,8] TKR in patients with severe or morbid obesity is followed by a higher frequency of problems and worse TKR outcomes. Despite achieving similar changes in HRQL scores as non-obese patients, obese patients have more and more severe postoperative complications. We also found that various lower limb anthropometric features negatively influence postoperative outcomes.[1,8] Overweight and obesity compromise functional capacity and this may be related to a reduction in muscle mass and increased fat mass.[9] The decline in muscle mass and loss of quality due to increased intramuscular fat or fibrosis are known changes that occur with aging and affect function.[10,11] Ultrasound (US) of the musculoskeletal system is sufficiently accurate and reproducible to be used routinely in various clinical and research fields. It is simple, non-invasive, and cost-effective compared with other imaging techniques. In OA, US is a supplementary method that may complement the physical and radiological examination. [6,12–14] As pain and disability are difficult to standardize, the search for more accurate and objective measures to determine the suitability of therapeutic options in knee OA patients led us to evaluate quadriceps muscle thickness and quality and subcutaneous fat thickness using ultrasound and their relationship with performance-based tests. [15] In the context of a longer-term prospective study of TKR outcomes, we hypothesized that quantification of these structures could provide useful objective information to complement the clinical evaluation. Thus, the objectives of this pilot study were to evaluate the relationships between quadriceps muscle thickness and quality and subcutaneous fat thickness and function in older patients with knee OA on a waiting list for TKR.

2. Methods

2.1. Study design and setting

We carried out a cross-sectional observational pilot study in the rheumatology and orthopedic surgery service knee unit of an urban tertiary hospital. The study meets current standards of confidentiality and was approved by the hospital Ethics Committee.

2.2. Participants

Sixty-two patients diagnosed with knee OA (according to the Kellegren and Lawrence criteria) on a waiting list for TKR were initially enrolled.[16] Exclusion criteria were revision surgery, inflammatory musculoskeletal disease (such as rheumatoid arthritis, lupus), metabolic disease, psychopathology or severe comorbidity in the medical record that could impede patient participation in some or all of the study procedures, and functional illiteracy. All patients gave written, informed consent to participate. 1 patient was excluded.

2.3. Variables

The following variables were collected using a questionnaire, interview, and medical records:- Sociodemographic (age, sex); physical activity (defined as regular exercise $>$4 times weekly for $\geq$ 40 min per session [yes/no]); clinical (weight, height, body mass index [BMI], degree of radiographic knee OA (front and lateral radiographs with full-bearing and 30° of flexion); comorbidities (number and type: hypertension, cardiovascular disease, diabetes, renal disease, respiratory disease, emotional disorders (depression and anxiety) and other musculoskeletal disorders).[1]

2.4. Echographic assessment

US images were used to assess: subcutaneous fat thickness (distance from the skin to the fascia, in mm);quadriceps femoris thickness (summed rectus femoris and vastus intermedius thickness [distance between the outer fascia and the femur, in mm]); and the muscular quality of the rectus femoris, assessed by echointensity (EI). Measurements of the muscle layer of the quadriceps femoris were made from specific points, as previously described.[6] EI was evaluated using computer-assisted grayscale analysis according to the method described by Maurits et al.[17] EI quantifies muscle aspect on US and reflects the relative amounts ofmuscle and non-contractile tissue.[17,18] To standardize the measurements, which were made by a single evaluator, the following points were determined: midpoint between the iliac spine and the superior pole of the patella (vastus intermedius and rectus anterior).Transverse real-time US images were obtained by a single operator using the ALOKA F 31 ultrasound scanner (Hitachi Medical Systems SLU), with a high frequency linear 9 MHz probe. Patients were placed in the supine position with the legs extended and relaxed. Sufficient gel was used to ensure adequate transducer pressure, provide appropriate acoustic contact, and avoid compression of the skin and tissues. The ultrasound probe was placed at the standardized measurement locations and oriented perpendicular to the femur (maximum bone echo). All machine settings were kept constant and the image was focused at the muscle center for EI estimation. The images were stored as DICOM files. Image analysis was performed by another researcher. To estimate EI, a representative rectangle was selected using Matlab R2105b software (The MathWorks, Inc., Natick, Massachusetts, U.S.A) in the muscle image after calibration, which consisted of forcing 1% of the image pixels to be saturated at maximum and minimum grayscale values, so as to increase the contrast of the image. Fascia and muscle-tendon transitions were excluded from the image as much as possible. To estimate EI, the average pixel value in the selection was calculated using Matlab R2105b software.[17] A fully-black selection would result in an EI of 0, while a fully-white selection would result in an EI of 255.

2.5. Function

unction was measured using the Timed Up & Go Test (TUG), a simple and efficient performance-based test of the functional mobility (FM), balance and gait required for daily activities such as lying down, rising from a chair, getting out of a car, and walking. The TUG test requires participants to rise from a seated position in a chair with the back supported and arms resting on armrests, walk out 3 m, turn around, and return to a sitting position as quickly and safely as possible. Time is recorded to the nearest 0.01 s from the time the person's buttocks leave the chair until return contact with the chair.[15,19]

2.6. Data analysis

Descriptive statistics were expressed as frequencies and percentages for categorical variables and means and standard deviation (SD) for continuous variables. The percentage of muscle was calculated by dividing the quadriceps femoris thickness (rectus femoris and vastus intermedius thickness) by the total thickness of the subcutaneous fat thickness + quadriceps femoris thickness and multiplying it by 100. This percentage was used as it was less influenced by weight and height. Measurements were made in the knee awaiting surgery.The correlation between the quadriceps muscle thickness and quality and subcutaneous fat thickness and the TUG was determined using Karl Pearson's correlation analysis. A multiple linear regression model was constructed to determine the association between independent variables (percentage of muscle and echointensity) on the TUG scores (dependent variable). The model also included age, gender, and regular physical activity to determine whether these had any influence on the dependent variable. Forward-stepwise criteria with an entry criterion of $p < 0.05$ and an exit criterion of $p > 0.10$ were used to construct the regression model. Normality of the residuals was assessed.The statistical analysis was made using the Statistical Package for Social Science (SPSS) version 16.0 for Windows.

3. Results

Of the 62 patients originally enrolled, one was excluded due to rheumatoid arthritis. Therefore, 61 patients were included in the analysis. The mean age was 69.7 (SD 7.2) years and 45 (73.8%) were female. The sociodemographic, clinical and functional characteristics, and echographic measurements are shown in Table 1. Thirty-eight (62.3%) patients were awaiting right-knee TKR and 23 (37.7%) left-knee TKR. There was a significant negative correlation between quadriceps muscle thickness and percentage and the TUG scores ($r = -0.36$, $p = 0.004$ and $r = -0.29$, $p = 0.023$, respectively), and a significant positive correlation between EI and the TUG scores ($r = 0.27$, $p = 0.036$) (Table 2). Table 3 shows the variables associated with the TUG scores in the multiple linear regression analysis. The variables retained in the model explained 36% (R^2) of the variance in the TUG scores. Older age and greater muscle EI were associated with worse function ($p = 0.001$ and $p = 0.006$, respectively). A higher percentage of muscle and regular physical activity (≥ 4 times per week) were associated with better functional mobility in the TUG test ($p = 0.001$ and $p = 0.008$, respectively). No significant differences were found with respect to the BMI, the number of comorbidities, or gender, possibly due to the small number of males included.

Table 1
Patient characteristics.

	n = 61	
Age: mean (SD)	69.7 (7.2)	
Sex: n (%)		
Male	16	(26.2)
Female	45	(73.8)
Physical activity: n (%)		
Yes > 4 times weekly for ≥ 40 min per session))	32	(52.5)
BMI kg/m2: mean (SD)	33.0 (5.7)	
Degree of osteoarthritis: n (%)		
II	5	(8.2)
III	33	(54.1)
IV	23	(37.7)
No. of comorbidities: mean (SD)	3.3 (2.0)	
Comorbidity: n (%)		
Hypertension	37	(60.7)
Cardiovascular disease	11	(18.0)
Diabetes	8 (13.1)	
Renal disease	5	(8.2)
Respiratory disease	5	(8.2)
Anxiety/depression	17	(27.9)
Other musculoskeletal diseases	17	(27.9)
Function (Timed Up & Go Test)	15.1 (6.1)	
Echographic assessment		
Subcutaneous fat thickness (in mm)	22.4 (11.9)	
Quadriceps thickness (in mm)	34.7 (9.5)	
Rectus femoris echointensity	103.3 (11.4)	
Quadriceps muscle percentage	62.5 (11.9)	

N: number, SD: standard deviation; BMI: body mass index

Table 2
Correlations between function (TUG) and echographic assessment.

	Function (performance) TUG	
	Pearson Correlation r	p Value
Subcutaneous fat thickness	0.064	0.627
Quadriceps femoris thickness	−0.364	0.004
Rectus femoris echointensity	0.270	0.036
Quadriceps muscle percentage	−0.291	0.023

TUG: Timed Up & Go Test

Table 3
Variables independently associated with function (TUG) in the multiple linear regression model.

Independent variables	Dependent variable: Function (TUG)	
	(R^2: 0.356)	
	Coefficient (95% CI)	p Value
Rectus femoris echointensity	0.15 (0.30 to 0.26)	0.006
Quadriceps muscle percentage	−0.15 (−0.26 to −0.04)	0.001
Age (years)	0.32 (0.14 to 0.51)	0.001
Physical activity (regular exercise ≥4 times a week ≥ 40 min per session: yes = 1, no = 0)	−3.63 (−6.27 to −0.99)	0.008

TUG: Timed Up & Go Test.

4. Discussion

We evaluated the relationship between quadriceps muscle thickness and quality and subcutaneous fat thickness and function in older patients with knee OA on a waiting list for TKR. Patients with a higher percentage of muscle had a better function and those with greater EI had a worse function.We found, as did other studies, that older age had a negative influence on functional mobility, while moderate regular exercise had a positive influence.[20–22] However, neither BMI nor subcutaneous fat thickness were significantly associated with function. Aging produces anthropometric changes: muscle mass declines and fat mass increases. Obesity is reported to compromise functional capacity in the elderly, but it is unclear whether the increase in fat mass or the reduction in muscle mass is the most-significant predictor of functional limitations.[6,9]In addition to age, increased muscle EI was also associated with poorer function. Arts et al. [23] evaluated muscle thickness and EI in five muscle groups and found higher EI values in older age groups, showing the effect of age on the characteristics of muscle tissue. They also found that, with aging, sarcopenia-related changes appear, namely reductions in the thickness of the muscle mass and an increase in fat, which increases EI.[17,23] Therefore, enhanced EI is likely the result of an intramuscular increase in connective and adipose tissue.[11,17,23–25] Other studies have also used US to evaluate the morphology of compromised muscles involved in musculoskeletal dysfunction by evaluating muscle quality through computer assisted greyscale analysis,which allows differentiation of quantitative parameters, such as the thickness of subcutaneous tissue, muscle thickness, and echogenicity in combinations of muscle groups.[17,23,26] Maurits et al. [17] quantified structural changes in neuromuscular disorders and determined differences according to the disease (myopathy and neuropathy) and established population norms in the healthy population. Koca et al.[6] studied the relationship between clinical and radiological variables and quadriceps femoris thickness measured by US in patients with knee OA who were younger than and had different characteristics (mean age 57.9 ± 5.2 years, BMI 27.6 9 ± 2.2) from our sample. They also found negative correlations between the thickness of the quadriceps, age and function (quantified by the 50 m walking test and the stair walking test [10 steps]), and concluded that assessment of the quadriceps muscle by US is a convenient and inexpensive method for the diagnosis and monitoring of knee OA.Two Japanese and Brazilian studies in active populations that used US analyzed with computer-aided greyscale intensity also showed similar results to ours.[10,18]Watanabe et al. studied males (74.4 ± 5.9 years, height [cm] 163.2 ± 6, weight [kg] 62.3 ± 9.5) living independently with no history of trauma, surgery, neuromuscular disorders or acute comorbidity and who were not using assistive devices and found that rectus femoris EI correlated positively with age, thus demonstrating age-related changes in muscle aspect.[10] Rech et al. studied active older females (n = 50, 70.28 ± 6.2 years, BMI [kg/m2 27.89 ± 3.6]) in Brazil and found that quadriceps femoris EI significantly correlated with function/performance as evaluated by the 30-s sit-to-stand test and usual gait speed, and concluded that EI may be an important predictor of functional performance in active elderly women.[18]Our study has several limitations. The sample size is relatively small because the present study is the first report of a prospective study on the influence of anthropometric measures on TKR outcomes. For similar reasons, we did not evaluate other variables that may contribute to loss of function, such as the type of comorbidities. Our results suggest that, in patients with severe knee OA in whom conservative treatment has failed and TKR is indicated, quantification of function may reveal characteristics susceptible to modification. It is known that symptoms such as pain and disability are not the only symptoms associated with the indication for TKR. The rapidly-aging population of developed countries signals the need to identify factors that may help maintain mobility and autonomy, as reductions in mobility are often a precursor of functional decline,disability, and increased frailty.[27] Better understanding of the many characteristics that determine function in older patients with OA may aid better patient identification and the development of possible interventions [28]related to exercise, obesity and sedentarism. Our results suggest that US analysis may be a useful complementary procedure in the clinical evaluation.[12] In a future study we hope to analyze the outcomes of this group of patients after receiving TKR and determine whether the methodology reported here has predictive value. In conclusion, a greater percentage of quadriceps muscle and better muscle quality (lower echointensity) was associated with better function in patients with knee OA on a waiting list for TKR. Age and the level of exercise also influenced function. Ultrasound is useful in determining objective measures of function in these patients. Quantification of the echographic knee structure might provide complementary information in the clinical examination of this group of patients with knee OA awaiting for TKR.

Conflict of interest

The authors declare no competing interests.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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