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COMPARATIVE ANALYSIS OF KNEE INJURY AND OSTEOARTHRITIS OUTCOME SCORE (KOOS) IN PRE AND POST-OPERATIVE TOTAL KNEE ARTHROPLASTY PATIENTS

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List of acronyms

ATJ – Artroplastia total do joelho

BMI – Body Mass Index

DEFI – Departamento de Ensino, Formação e Investigação

ICC – Intra-class correlation Coefficient

ICD-9-CM - International Classification of Diseases, Ninth Revision, Clinical Modification

IMC – Índice de Massa Corporal

KOOS – Knee Injury and Osteoarthritis Outcome Score

KOOS ADL – Knee Injury and Osteoarthritis Outcome Score Function in Daily Living

KOOS QoL – Knee Injury and Osteoarthritis Outcome Score Quality of Life

KOOS Spo/Rec – Knee Injury and Osteoarthritis Outcome Score Function in Sports and Recreation

MPCI – Minimal Perceptible Clinical Improvement

OA – Osteoarthritis

PROMS – Patient-reported Outcome Measures

TKA – Total Knee Arthroplasty

WOMAC – Western Ontario and McMaster Universities Osteoarthritis Index

Resumo

Introdução: A artroplastia total do joelho (ATJ) é um dos tratamentos mais bem sucedidos e rentáveis para a osteoartrite (OA) do joelho em estadios tardios, por isso o seu uso na prática clínica está a aumentar. Portanto, é importante que estudos sejam desenvolvidos com o objectivo de encontrar a melhor maneira de avaliar os resultados da ATJ e quais são os factores do paciente que afetam esses resultados. Existe também uma procura por métodos que consigam avaliar os resultados da ATJ com precisão o que leva também a uma importância cada vez maior de desenvolvimento de instrumentos que avaliem com precisão os resultados. Instrumentos que meçam resultados relatados pelo paciente (PROM), em particular, são instrumentos que permitem ao clínico perceber qual o impacto de uma condição clínica específica sobre o paciente e a sua utilização tem vindo a aumentar, não só para medir a eficácia dos cuidados como também os seus resultados na saúde dos doentes. O Knee Injury and Osteoarthritis Outcome Score (KOOS), uma extensão do Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) é um instrumento que proporciona resultados clínicos relatados pelo paciente com precisão.

Objectivos: Avaliar os resultados dos pacientes que foram submetidos a ATJ usando o KOOS eo WOMAC; para avaliar se o KOOS é um PROM confiável para avaliar uma população específica de pacientes com OA do joelho e para identificar factores do paciente que potencial ou definitivamente afetam o resultado.

Métodos: Os dados foram colhidos de 200 questionários KOOS (199 pacientes) que foram preenchidos no pré-operatório. Factores do paciente foram avaliados através da pesquisa do processo clínico de cada paciente. Os pacientes foram contactados, por telefone, 6 a 24 meses após a cirurgia e os questionários KOOS foram enviados pelo correio a cada paciente que foi contactado com sucesso. Os questionários KOOS também foram reenviados e recebidos pelo correio. A média das pontuações de cada sub-escala do KOOS e a média das pontuações transformadas do WOMAC foram comparados no pré e pós-operatório utilizando o teste de Wilcoxon-signed rank. A consistência interna e a reprodutibilidade do KOOS foram avaliadas calculando os coeficientes alfa de Cronbach e coeficientes de correlação intra-classe para cada uma das cinco sub-escalas do KOOS. Efeitos dos factores do paciente sobre os resultados foram avaliados, correlacionando as pontuações das subescalas do KOOS e as pontuações transformadas do WOMAC com os factores do paciente utilizando correlação de Spearman.

Resultados: Houve um aumento geral no pós-operatório da pontuação de todas as sub-escalas do KOOS e das pontuação transformadas do WOMAC. Todas as diferenças foram estatisticamente significativas. A consistência interna e reprodutibilidade foram aceitáveis para todos as sub-escalas do KOOS, exceto KOOS Symptoms, com coeficientes alfa de Cronbach entre 0,85 e 0,96 (0,47 para a sub-escala KOOS Symptoms) e coeficientes de correlação intra-classe (ICC) entre 0, 82 e 0,97 ([0,47-0,56], IC de 95% para a sub-escala KOOS Symptoms). Correlações significativas, mas fracas (coeficiente de correlação r <0,35 para todas as correlações significativas) foram encontradas entre o índice de massa corporal (IMC) e sub-escala KOOS Symptoms e pontuação transformada do WOMAC Stiffness no pós-operatório; entre a idade e a sub-escala KOOS Spo/Rec no pós-operatório; entre o sexo feminino e todas as subescalas KOOS e pontuações transformadas do WOMAC excepto a pontuação transformada do WOMAC Stiffness no pré-operatório (p <0,01 para todas as correlações) e com as sub-escala KOOS Pain e pontuação transformada do WOMAC Pain no pós-operatório; entre altura e sub-escala KOOS Pain no pós-operatório e pontuação transformada WOMAC dor no pré-operatório; entre o diagnóstico de depressão e as sub-escalas KOOS Pain, KOOS Symptoms e pontuação transformada do WOMAC Pain no pré-operatório e sub-escalas KOOS Pain, KOOS Symptoms, KOOS ADL, KOOS QoL e pontuações transformadas do WOMAC Pain e WOMAC Stifness no pós-operatório; entre o diagnóstico de doença cardíaca isquémica e sub-escalas KOOS Symptoms, KOOS ADL e pontuações transformadas do WOMAC Pain no pós-operatório; e entre o diagnóstico de ansiedade e a sub-escala KOOS ADL e pontuações transformadas do WOMAC Pain no pós-operatório (p <0,05).

Conclusão: ATJ provoca uma melhoria significativa quando avaliada pelo KOOS eo WOMAC. O MPCI é alcançado numa percentagem de pacientes que é menor em comparação com outros estudos. O KOOS provou ser um PROM fiável e com consistência interna globalmente, mas pode haver alguma redundância em algumas sub-escalas do questionário. Idade, sexo feminino, IMC e diagnóstico depressão, ansiedade e doença cardíaca isquémica podem afetar os resultados da ATJ.

Abstract

Introduction: Total knee arthroplasty (TKA) is one of the most successful and cost-efficient treatments for end stage knee osteoarthritis (OA), and its use in clinical practice is increasing. Therefore, it is important that studies are developed with the objective to find the best way to assess TKA outcomes and patient factors that affect said outcomes. There is also an increasing demand on accurate ways to assess outcomes; therefore there is also an increasing importance in developing instruments that accurately assess outcomes. Patient-reported outcomes (PROMS), in particular, are instruments that are more accurate in reflecting the perceived impact of a specific clinical condition on individuals and are being increasingly used to measure effectiveness of care and/or health outcomes. The Knee Injury and Osteoarthritis Outcome Score (KOOS), an extension of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is one instrument that provides accurate, patient-reported, clinical outcomes.

Objectives: Assess outcomes of patients that went through TKA using the KOOS and the WOMAC; to assess if the KOOS is a reliable PROM to assess a particular population of knee OA patients and to identify potential or definitive patient factors that affect outcome.

Methods: Data was collected from 200 KOOS questionnaires (199 patients) that were filled out pre-operatively. Patient factors were assessed by checking each patient's medical record. Patients were contacted by telephone 6 to 24 months after their surgery and the KOOS questionnaires were sent by mail to each patient that was successfully contacted. The KOOS questionnaires were also retrieved by mail. Each KOOS subscale score mean and transformed WOMAC score mean were compared pre and post-operatively using Wilcoxon signed-rank test. Internal consistency and test-retest reliability of the KOOS was assessed by calculating Cronbach's alpha coefficients and intra-class correlation coefficients for each of the five KOOS subscales. Patient factors effects on the outcome were assessed by correlating the KOOS subscale score means and transformed WOMAC score means with patient factors using Spearman's rank correlation.

Results: There was an overall increase in post-operative in the score means for all KOOS subscales and transformed WOMAC scores. All differences were statistically significant. Internal consistency and test-retest reliability was acceptable for all KOOS subscales except KOOS Symptoms, with Cronbach's alpha coefficients between 0,85 and 0,96 (0,47 for KOOS Symptoms subscale) and intra-class correlation coefficients (ICC)

between 0,82 and 0,97 (0,47-0,56; IC 95% for KOOS Symptoms subscale). Significant but weak correlations (correlation coefficient r<0,35 for all significant correlations) were found between IMC and post-operative KOOS Symptoms subscale scores and post-operative transformed WOMAC Stiffness scores; between age and post-operative KOOS Spo/Rec subscale scores; between female gender with all pre-operative KOOS subscales and transformed WOMAC scores except transformed WOMAC Stiffness (p<0,01 for all correlations) and with post-operative KOOS Pain subscale scores and transformed WOMAC Pain scores; between height and pre-operative transformed WOMAC Pain scores and post-operative KOOS Pain subscale scores; between diagnosis of depression with pre-operative KOOS Pain, KOOS Symptoms subscale scores, transformed WOMAC Pain scores, post-operative KOOS Pain, KOOS Symptoms, KOOS ADL and KOOS QoL subscale scores and transformed WOMAC Pain and Symptoms scores; between diagnosis of ischemic heart disease and post-operative KOOS Symptoms, KOOS ADL subscale scores and transformed WOMAC Pain scores; and between diagnosis of anxiety and post-operative KOOS ADL subscale scores and transformed WOMAC Pain scores (p<0,05).

Conclusion: TKA significantly improves outcomes when assessed by the KOOS and the WOMAC. MPCI is achieved in a percentage of patients that is subpar compared to other studies. KOOS proved to be an overall reliable and internally consistent PROM, but there might be some redundancy on the test. Age, female gender, BMI, depression, anxiety and ischemic heart disease, might affect TKA outcomes.

Introduction

Knee osteoarthritis (OA) is a disease that is associated with an important decrease in lower limb function and overall quality of life. End-stage knee OA treatments have improved over time, and today, total knee arthroplasty (TKA) has proven in many studies to be one of the most successful and cost-effective treatments for this disease. (Tan et al. 2014; Koh et al. 2014; Kahn and Schwarzkopf 2015; Xie et al. 2014; Vissers et al. 2012) Because of this, its use has increased worldwide, and its incidence is projected to increase from 500,000 procedures in 2005 to 3.48 million in 2030 on the US alone. (Nichols and Vose 2016) TKA is associated with significant improvement of pain, function and quality of life. (Vissers et al. 2012; Kahn and Schwarzkopf 2015) Given the increasing importance of TKA as form of treatment of knee OA, there is also an increasing importance for methods to accurately assess outcomes following this intervention. There is also a concern in identifying patient factors that can negatively affect TKA outcomes, therefore, there is a growing body of literature examining outcomes after TKA for different indications and in patients with various co-morbidities to identify and stratify high-risk patients (Bala et al. 2015). Evidence suggests that patient factors can influence response to surgical treatment, however which factors can be associated to orthopedic surgery, in particular, are unclear. (Haanstra et al. 2012) While there are many studies that have found that patient factors such as gender, age and body mass index (BMI) are significant outcome modifiers (Roos and Lohmander 2003; Goncalves et al. 2010; Singh 2011; Tamm et al. 2011; Haanstra et al. 2012; Vissers et al. 2012; Roth et al. 2013; Jacobs, Christensen, and Karthikeyan 2014; Koh et al. 2014; Tan et al. 2014; Young et al. 2014; Bala et al. 2015; Best et al. 2015; Lewis et al. 2015; Houdek et al. 2016; Keswani et al. 2016; Nichols and Vose 2016), other factors such as mental health, namely diagnosis of depression or anxiety disorders, ischemic heart disease and previous knee surgery are less consensual as whether they affect TKA outcomes (Roos and Lohmander 2003; Roth et al. 2013; Jacobs, Christensen, and Karthikeyan 2014; Singh and Lewallen 2014; Tan et al. 2014; Bala et al. 2015; Best et al. 2015; Khatib et al. 2015; Lewis et al. 2015; Lungu, Vendittoli, and Desmeules 2015) (Keswani et al. 2016).

While in orthopedics there has been a focus on assessing outcomes by evaluating objective clinical factors or radiologic findings, patient-reported outcomes are more accurate in reflecting the perceived impact of a specific clinical condition on individuals and are being increasingly used to measure effectiveness of care and/or health outcomes.(Goncalves et al. 2009; van Kempen et al. 2013) In fact, patients are generally more concerned with symptoms such as pain and function of the injured limb. Therefore, it is important that there is a constant development of ways to assess patient-reported

outcomes, as well as validation of these instruments for any kind of patient in order to have an accurate assessment of outcome. For knee OA and TKA outcomes, there are currently several patient-reported outcome measurements (PROMS) which can be used, namely the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Knee Injury and Osteoarthritis Outcome Score (KOOS), which provide accurate patient-reported, clinical outcomes.

The Knee injury and Osteoarthritis Outcome Score (KOOS), in particular, is a joint-specific PROM which was developed to assess a large spectrum of patients with knee injuries and OA.(Goncalves et al. 2009) The KOOS is a valid, reliable, responsive, self-administered instrument which can be used for short-term and long-term follow-up of several types of knee injury including osteoarthritis.(Si et al. 2015) Its psychometric properties have been favourably evaluated by systematic reviews.(Waheeb et al. 2015) The KOOS holds 42 items within five separately scored subscales: Pain (9 items); other Symptoms (7 items); Function in daily living (ADL) (17 items); Function in Sport and Recreation (Sport/Rec) (5 items); and knee-related Quality of Life (QoL) (4 items). (Si et al. 2015) All items are scored from 0 to 4, and each of the five scores is calculated as the sum of the items included. Scores are then transformed to a 0-100 scale, with 0 representing extreme knee problems and 100 representing no knee problems. (Roos et al. 1998) The KOOS takes approximately 10 minutes to complete. It is a feasible instrument when administered by mail, since valid subscale scores can be calculated as long as less than half of the items, rounded down, are missing for each subscale. The KOOS was developed as an extension of the WOMAC, and it is possible to calculate WOMAC scores from the KOOS, as the WOMAC questions were included in their full and original form in the KOOS questionnaire. (Si et al. 2015) However, among PROMS used in orthopedics, the KOOS uniquely accounts for daily life activities related to sports and recreation, as well as quality of life. The KOOS is unique in asking about high-demand activities and global quality of life, which recognises the patient's desire to perform the high-demand activities that fully restore quality of life through regained confidence in the function of the knee following TKA. (Ramkumar, Harris, and Noble 2015) The KOOS has been validated, culturally adapted and translated to Portuguese. High Cronbach's alpha coefficients for the five subscales and acceptable corrected item-total coefficients for the 42 items confirmed that the Portuguese KOOS subscales are internally consistent, with the correspondent items properly correlated with each other. (Goncalves et al. 2009)

The goals of this study are three-fold: (1) to assess outcomes of patients that went through TKA by comparing their KOOS subscale score before and up to 2 years after the procedure; (2) to assess if KOOS is a reliable PROM to assess this particular knee OA population; (3) to identify potential or definitive patient factors that affect outcome, namely

age, gender, BMI, weight, height, previous knee surgery and diagnosis of obesity, anxiety, depression or ischemic heart disease.

Keywords: "Knee Injury and Osteoarthritis Outcome Score"; "Total Knee Arthroplasty"; "Outcomes"; "Patient factors"

Methods

The study was analysed and accepted by the Gabinete Coordenador de Investigação do Departamento de Ensino, Formação e Investigação (DEFI), the hospital's ethics committee, the hospital's board of administration and the hospital's clinical board.

Population and Measurements

Data was collected from 200 KOOS questionnaires (199 patients) that were filled out pre-operatively from June 2014 to December 2015: KOOS subscale scores and transformed WOMAC scores were calculated for each questionnaire.

Patient factors, namely age, gender, BMI, weight, height, previous knee surgery and diagnosis of obesity, anxiety, depression or ischemic heart disease were assessed by checking each patient's medical record. BMI was calculated using the formula Weight/(Height^2) if it was not available in the system. Every past knee surgery, regardless of side, was assessed and accounted for by checking each patient medical record for past surgery history. Diagnosis of obesity was obtained by either BMI > 25 kg/m^2 or by diagnosis on the medical record, identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codification. Diagnosis of anxiety, depression or ischemic heart disease was given by diagnosis on the medical record, identified using ICD-9-CM codification. Table I shows the ICD-9-CM codes that were used to assess the mentioned diagnostics.

After the patient data was gathered, patients were contacted by telephone 6 to 24 months after their surgery, depending on when the patient underwent surgery. This contact was made in order to get informed consent to participate on the study and to improve response rate. Then, KOOS questionnaires were sent by mail to each patient that was successfully contacted. KOOS were also retrieved by mail.

Out of 200 KOOS questionnaires, 110 were successfully retrieved. 38 KOOS questionnaires (37 patients) were not sent, 1 questionnaire because the patient was deceased, 36 questionnaires because the patients didn't answer or reply any telephone

contact made. 52 patients were contacted and the KOOS sent by mail, but the questionnaire wasn't successfully retrieved.

Obesity	Depression		Anxiety	Ischemic Heart Disease		
278	2962	29631	29384	413	4106	41091
2780	29620	29632	300	4139	41060	41092
27800	29621	29633	3000	410	41061	411
27801	29622	29634	30000	4100	41062	4110
27802	29623	29635	30002	41000	4107	4111
	29624	29636	30009	41001	41070	4118
	29625	29682	30924	41002	41071	41181
	29626	2980	30928	4101	41072	41189
	2963	30112		41010	4108	412
	29630	311		41011	41080	414
				41012	41081	4140
				4102	41082	4148
				41020	4109	4149
				41021	4104	41090
				41022	41040	41051
				4103	41041	41052
				41030	41042	
				41031	4105	
				41032	41050	

Table I – List of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used to assess diagnosis of obesity, depression, anxiety and ischemic heart disease. Any patient with any of these codes was assumed as having the corresponding disease

For each retrieved KOOS questionnaire, KOOS subscale scores and transformed WOMAC scores were calculated. Figure 1 shows a flow diagram of this process.

Statistical analysis

The sample was tested for normality using Kolmogorov-Smirnov test. Since the sample didn't follow a normal distribution for most variables ($p<0,05$), non-parametric tests were used. Each KOOS subscale score means and transformed WOMAC score means were compared pre and post-operatively using Wilcoxon signed-rank test. Internal consistency and test-retest reliability of KOOS was assessed by calculating Cronbach's

alpha coefficients for each of the five KOOS subscales and intra-class correlation coefficients for each of the five KOOS subscales. An alpha value of 0,70 or more was regarded as acceptable internal consistency and a intra-class correlation coefficient of 0,70 or more was regarded as acceptable test-retest reliability. Patient factors effects on the outcome were assessed by correlating KOOS subscale score means and transformed WOMAC score means with patient factors using Spearman's rank correlation. As suggested by Roos et al. (2003), a 10 point difference of each KOOS subscale and each transformed WOMAC score was set as the minimal perceptible clinical improvement (MPCI). The percentage of patients that achieved the MPCI for each KOOS subscale score and each transformed WOMAC score was then calculated. A p value of 0,05 was used as reference for significance in all statistical tests used. Statistical tests were calculated using the software PASW Statistics 18.0 for Windows.

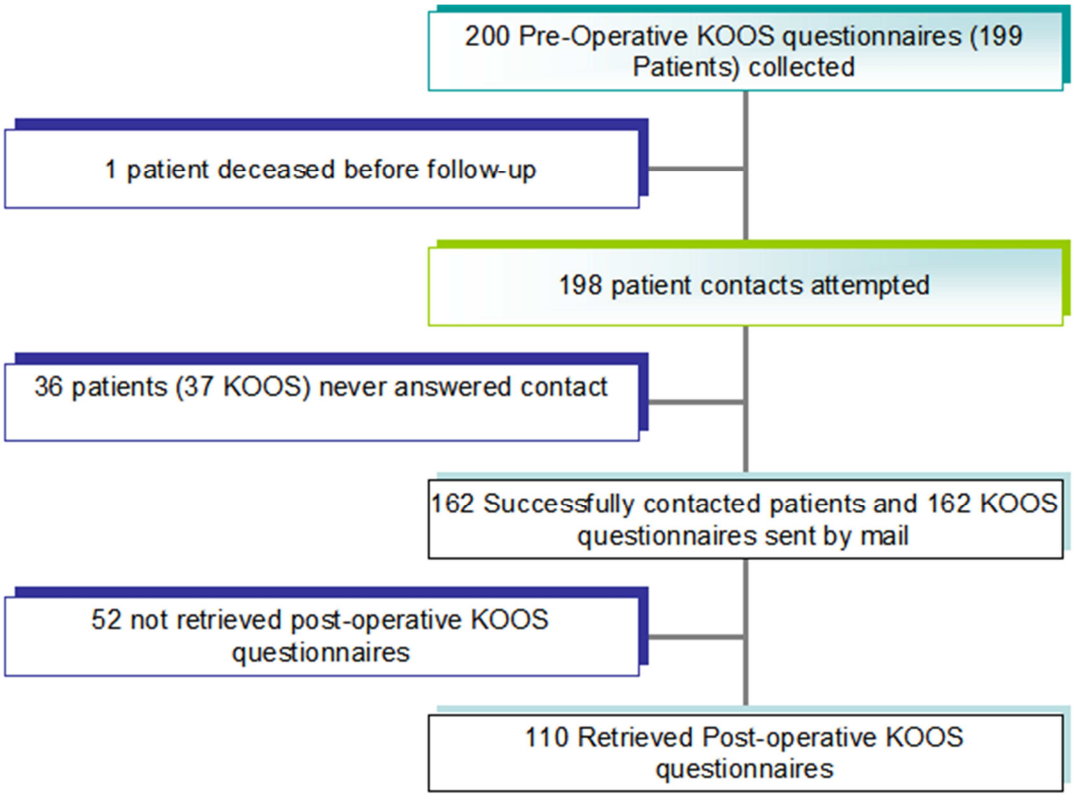

Figure 1 – Flow chart of patient's post-operative KOOS questionnaires retrieval process

Results

Demographic characteristics and other patient factors frequencies of the population are displayed on table II.

Patient Factors	Values (Total sample N=200)
Age (years)	68,94+-7,07
Female Gender	163 (0,815)
Height (m)	1,60+-0,85
Weight (kg)	78,27+-11,67
BMI (kg/m^2)	31,27+-5,04
Obesity	136 (0,68)
Depression	39 (0,20)
Anxiety	19 (0,10)
Knee Surgery	0,37+-0,60
Ischemic Heart Disease	18 (0,09)

Table II – Demographic characteristics and patient factors. Values for categorical variables are displayed in frequency (percentage); Values for quantitative variables are displayed in mean± standard deviation.

Regarding internal consistency and test-retest reliability of the KOOS, alpha values over 0,70 were achieved for every subscale except KOOS Symptoms. ICC values over 0,70 were achieved for every subscale except KOOS Symptoms. Individual subscale alpha values and ICC values, for each KOOS subscale, are shown in table III.

	Cronbach's alpha	Intra-class correlation coefficient (95% CI)
KOOS Pain	0,908	0,908 [0,890- 0,923]
KOOS Symptoms	0,467	0,467 [0,366- 0,558]
KOOS ADL	0,956	0,956 [0,948- 0,964]
KOOS Spo/Rec	0,956	0,956 [0,946- 0,963]
KOOS QoL	0,850	0,850 [0,820- 0,877]

Table III – Cronbach's alpha value and intraclass correlation coefficient (ICC) for each KOOS subscale. 95% confidence intervals are displayed for each ICC value

Regarding comparison of KOOS and WOMAC pre and post-operatively, there was an overall, statistically significant, improvement of score means in all KOOS subscales

and transformed WOMAC score means: KOOS subscale score means for Pain, Symptoms, ADL, Spo/Rec, QoL and transformed WOMAC Pain, Stiffness and Functionality score means pre-operatively were 38,3(±15,2); 42,1(±16,4); 34,4(±15,3); 13,9(±23,5); 19,6(±14,1); 41,5(±17,2); 40,2(±23,6) and 36,3(±17,5); respectively, whereas post-operative scores increased to 63,1(±22,0); 50,3(±15,0); 56,7(±23,4); 28,3(±32,9); 54,4(±28,2); 66,3(±22,3); 61,6(±25,4) and 59,1(±24,3), respectively. All differences were statistically significant, with $p<0,01$ for all scores. A KOOS profile for pre and post-operative score means is plotted in figure 2.

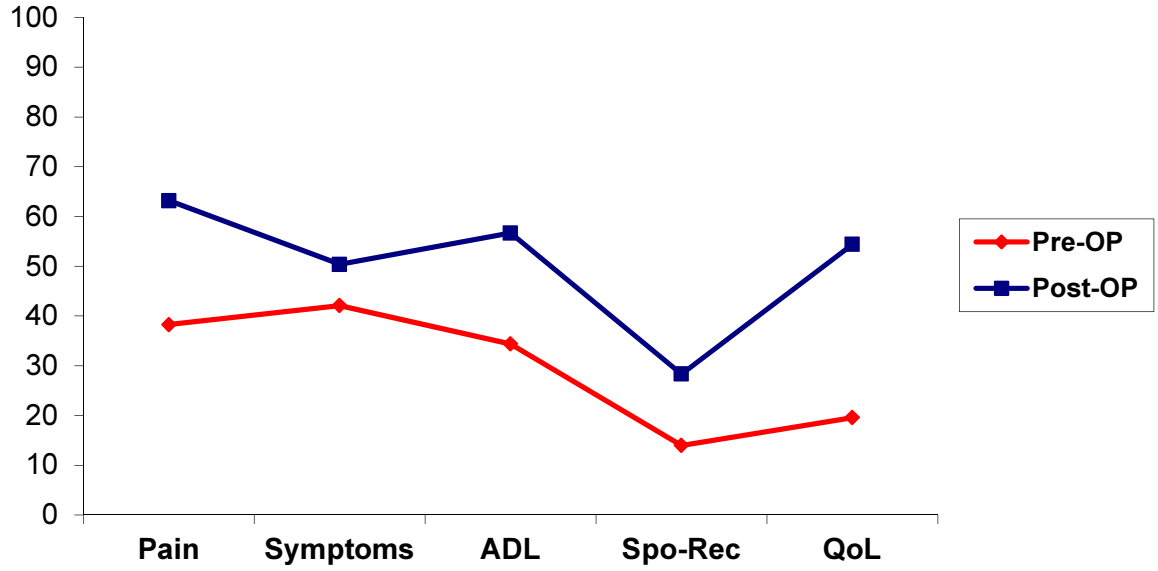

Figure 2 – KOOS Profile using pre and post-operative KOOS subscale score means. (KOOS score is 0-100 worst to best)

Regarding MPCI, increase of KOOS subscale scores and transformed WOMAC scores was 10 or higher in 71,7% of patients for KOOS Pain, 54,1% for KOOS Symptoms, 68,6% for KOOS ADL, 43,5% for Spo/Rec, 77,6% for KOOS QoL, 75,9% for transformed WOMAC Pain, 70,0% for transformed WOMAC Stiffness and 69,1% for transformed WOMAC Functionality score.

Regarding correlations with patient factors, a number of significant correlations were found:

BMI correlated negatively with post-operative KOOS Symptoms subscale scores ($p<0,05$) and correlated negatively with post-operative transformed WOMAC Stiffness scores ($p<0,05$).

Age correlated negatively with post-operative KOOS Spo/Rec subscale scores ($p<0,01$).

Correlated Pair	Correlation Coefficient (r)	Significance (α)
BMI / Post-op WOMAC Stiffness	-0,269	0,05
BMI / Post-op KOOS Symptoms	-0,407	0,01
Age / Post-op KOOS Spo/Rec	-0,311	0,01
Female gender / Pre-op WOMAC Pain	-0,203	0,01
Female gender / Pre-op WOMAC Function	-0,183	0,01
Female gender / Pre-op KOOS Pain	-0,214	0,01
Female gender / Pre-op KOOS Symptoms	-0,184	0,01
Female gender / Pre-op KOOS ADL	-0,219	0,01
Female gender / Pre-op KOOS Spo/Rec	-0,184	0,05
Female gender / Pre-op KOOS QoL	-0,171	0,05
Female gender / Post-op WOMAC Pain	-0,195	0,05
Female gender / Post-op KOOS Pain	-0,229	0,05
Height / Pre-op WOMAC Pain	0,180	0,05
Height / Post-op KOOS Pain	0,254	0,05
Depression / Pre-op KOOS Pain	-0,189	0,01
Depression / Pre-operative KOOS Symptoms	-0,186	0,01
Depression / Pre-op WOMAC Pain	-0,207	0,01
Depression / Post-op WOMAC Pain	-0,297	0,01
Depression / Post-op WOMAC Stiffness	-0,349	0,01
Depression / Post-op KOOS Pain	-0,324	0,01
Depression / Post-op KOOS Symptoms	-0,333	0,01
Depression / Post-op KOOS ADL	-0,208	0,05
Depression / Post-op KOOS QoL	-0,283	0,01
IHD / Post-op WOMAC Pain	-0,200	0,05
IHD / Post-op KOOS Symptoms	-0,244	0,05
IHD / Post-op KOOS ADL	-0,194	0,05
Anxiety / Post-op WOMAC Pain	-0,192	0,05
Anxiety / Post-op KOOS ADL	-0,200	0,05

Table IV – Correlation coefficient (r) and significance between patient factors and KOOS subscale scores and transformed WOMAC scores. Non-significant correlations are not displayed.

Female gender correlated negatively with all pre-operative KOOS subscale scores and transformed WOMAC scores except transformed WOMAC Stiffness ($p<0,01$ for all correlations). Female gender also correlated negatively with post-operative KOOS Pain subscale scores and transformed WOMAC Pain scores ($p<0,05$).

Positive correlation of height with pre-operative transformed WOMAC Pain scores and post-operative KOOS Pain subscale scores was also found. ($p<0,05$).

Diagnosis of depression had negative correlation with pre-operative KOOS Pain and KOOS Symptoms subscale scores as well as transformed WOMAC Pain scores ($p<0,01$). It also had a negative correlation with post-operative KOOS Pain, Symptoms, ADL and QoL subscale scores as well as transformed WOMAC Pain and Stiffness scores. All correlations had p values $<0,01$, except for the correlation with KOOS ADL ($p<0,05$).

Diagnosis of ischemic heart disease had negative correlation with post-operative KOOS Symptoms and ADL subscale scores and transformed WOMAC Pain scores ($p<0,05$).

Diagnosis of anxiety had a negative correlation with post-operative KOOS ADL subscale scores and transformed WOMAC Pain scores ($p<0,05$).

No statistically significant correlations were found between weight, obesity diagnosis or previous knee surgery with any pre or post-operative KOOS subscale score and/or transformed WOMAC score. Strength of all significant correlations, given by the correlation coefficient r, is shown in table IV.

Discussion

Regarding the population of this study, there are two factors that could lead to erroneous results: first, the studied population has an age mean that is very high. Other studies that used the KOOS for assessing outcome had lower age means (Roos et al. 1998; Roos and Lohmander 2003; Tamm et al. 2011; Sivachidambaram, Ateef, and Tahseen 2014; Oishi et al. 2016), and it is reported that higher age leads to overall lower scores in the KOOS. (Oishi et al. 2016) It can also explain many missing items, especially on the KOOS Spo/Rec subscale, as many elderly patients cannot perform any activity mentioned in the items of the subscale and therefore do not respond to them. Second, the sample has a very high percentage of female over male patients. This fact could also lead to overall lower KOOS subscale score means, as there are studies that report that female patients have lower KOOS subscale score means. (Oishi et al. 2016)

Response rate was acceptable at 55%. Patients who answered had various levels of willingness to cooperate, so the probability that there is a response or non-response bias is low.

Other limitations regarding the methodology of the study were considering a single moment of post-operative follow-up not taking into account the different surgery to post-operative KOOS questionnaire answering times. Since there are patients that have considerably more time between surgery and answering their post-operative KOOS, it could affect negatively KOOS subscale score means, since other longer-term studies have reported that there is a continuing decline in KOOS subscale scores post operatively after a period of improvement. (Brander et al. 2003; Brander et al. 2007) Multiple follow-up moments at 6, 12, 18 and 24 months could provide more accurate data and could allow to even profile and conclude over if there are patterns in the KOOS subscale score means over time. The other limitation was using Spearman's rank correlation to assess whether or not patient factors affected outcomes. The main issue with using Spearman correlation coefficient is, even though we could find many significant correlations, ignoring potential bias or confounding factors from the other patient factors. This could also explain the low correlation coefficients for each statistically significant correlation found. For example, anxiety diagnosis had a significant correlation with post-operative transformed WOMAC Pain and KOOS ADL subscale score. However, depression diagnosis had a more significant and stronger correlation with the same scores. Since there is a significant and moderate correlation found between depression diagnosis and anxiety diagnosis, we are unable to conclude whether anxiety actually affects those scores of if those correlations were a product of depression being a confounding factor. To avoid this in further studies, a multivariate regression analysis could've been used, given that a larger sample size would also be needed to achieve acceptable results and extrapolate conclusions.

In this study, we could confirm that the KOOS is an acceptable and reliable PROM. Regarding its internal consistency and test-retest reliability, we achieved Cronbach's alpha values that were similar with those of Gonçalves et al. 2009 and intra-class correlation coefficients similar with those of Gonçalves et al. 2009 and Roos et al. 2003 for every KOOS subscale except KOOS Symptoms. Extremely high Cronbach alpha scores for KOOS ADL and KOOS Spo/Rec subscales also caused some concern. Studies claim that Cronbach's alpha values of over 0,95 can be interpreted as presence of redundant items on the test. (Tavakol and Dennick 2011) More studies with different Portuguese populations should be made using KOOS, assessing its validity to conclude whether or not adaptations to the questionnaire should be made to more accurately assess the outcomes.

Regarding the comparative analysis of the KOOS per se, we achieved good results in all KOOS subscales and transformed WOMAC scores, with significant increases in all score means. As expected and documented by Roos et al 1998, Roos et al. 2003, (Roos and Lohmander 2003), given its standardized effect size on responsiveness studies, the highest difference between pre and post-operative score means were on the KOOS QoL subscale. Other studies (Christen, Aghayev, and Christen 2014) also had the highest increase on the same subscale. However, there were a percentage of patients that didn't achieve the MPCI or that reported worse post-operative scores. Also, the percentage of patients that achieved MPCI is subpar compared to other studies. (Christen, Aghayev, and Christen 2014) This shows that there are patients that either have post-operative complications or, most likely, unmet expectations regarding the results and goals of the surgery. More thorough explanation of the intents, goals and results of the surgery and exploration of expectations of each patient regarding TKA should be a priority for physicians.

Regarding patient factors and whether they affect outcomes, even though there were limitations in the analysis, relevant conclusions can still be extrapolated from the collected data. For clarity, it should be noted that negative correlations mean that the presence of the factor is associated with a lower KOOS subscale and/or transformed WOMAC score. KOOS and transformed WOMAC scores are scaled into a 0-100 scale, with 0 representing extreme knee problems and 100 representing no knee problems. (Roos and Lohmander 2003) So negative correlations mean the factor worsens outcomes and positive correlations mean the factor improves the outcome.

All factors that other studies already claimed to clearly affect outcome, namely BMI, gender and age (Roos and Lohmander 2003; Goncalves et al. 2010; Singh 2011; Tamm et al. 2011; Haanstra et al. 2012; Vissers et al. 2012; Roth et al. 2013; Jacobs, Christensen, and Karthikeyan 2014; Koh et al. 2014; Tan et al. 2014; Young et al. 2014; Bala et al. 2015; Best et al. 2015; Lewis et al. 2015; Houdek et al. 2016; Keswani et al. 2016; Nichols and Vose 2016) had at least one significant correlation with one of the KOOS subscale or transformed WOMAC scores, further cementing that assumption.

BMI is the better factor over weight, height and obesity diagnosis for predicting outcomes: the strongest and most significant correlations were all between BMI and KOOS subscales and/or WOMAC scores. Height showed a positive correlation with pre-operative KOOS Pain subscale scores and post-operative transformed WOMAC Pain scores, but both correlations were weaker and less significant than those found by BMI. Mathematically, it makes sense that height, which is inversely correlated to BMI, is the only patient factor that has positive correlations with the scores. Weight and obesity

diagnosis showed no significant correlations, so in future studies BMI should be the anthropomorphic factor used in the analysis.

Age, expectedly, negatively correlated with the KOOS Spo/Rec. Given that elderly patients with end-stage knee OA have serious difficulties regarding mobility, it is to be expected that the subscale that measures the limitations in the most demanding activities of the lower extremity have significantly lower scores than younger patients.

Female gender had the highest number of significant correlations. However, as stated, given the fact that this sample is constituted of mostly female patients (81,5% of patients were females), results might be exaggerated. Like Oishi et al. 2016, female gender was significantly correlated with worse pre-operative scores in all KOOS subscales. However, there were no significant correlations with post-operative scores except for the KOOS Pain subscale and transformed WOMAC Pain scores, which rises an interesting hypothesis. This fact could mean that, given that the baseline for female patients is lower than male patients (as showed by the negative correlation), that females benefit more from surgery, with a greater increase in the KOOS subscale scores and transformed WOMAC scores than males. Comparison between the percentage of female and male patients that achieved MPCI and/or analysis of whether there is a difference between female and male patients regarding the increase in each KOOS subscale and/or transformed WOMAC score was not in the scope of this study, but could be an interesting follow-up for this study to more accurately assess the role of gender on TKA outcome.

Regarding the other patient factors that were less consensual on whether or not they affected outcome, only depression diagnosis had several significant correlations, most notably it had significant negative correlations with all post-operative scores except for KOOS Spo/Rec subscale scores and transformed WOMAC Functionality scores, showing that patients with depression benefit less from surgery if mental health is not assessed and measures are taken regarding improvement of pre-operative mental health. These findings are coherent other studies that state that mental health, namely depression, has an influence on TKA outcome and increases dissatisfaction rate. (Vissers et al. 2012; Singh and Lewallen 2014; Khatib et al. 2015)

A significant negative correlation between ischemic heart disease and KOOS ADL was also a finding that could lead to a doubt on whether knee function or cardiac function is the main factor that limits these particular set of patients. Even though KOOS is designed to specifically assess knee-related outcomes (Roos and Lohmander 2003), an in-depth analysis of which items in the subscale are reported with worse scores in ischemic heart disease patients and whether those items can be related to activities that are strenuous and demanding enough to cause cardiac symptoms could be made.

Conclusion

In summary, TKA significantly improves outcomes when assessed by the KOOS and the WOMAC. MPCI is achieved in a percentage of patients that is subpar compared to other studies in all subscales of the KOOS. KOOS proved to be an overall reliable and internally consistent PROM, but very high Cronbach's alpha values for KOOS ADL and KOOS Spo/Rec may mean there is some redundancy on the items in those subscales. Significant correlations were found between patient factors and KOOS and WOMAC subscales, namely age, female gender, BMI, depression, anxiety and ischemic heart disease, which could mean that these factors can affect TKA outcomes. However, correlation coefficients for all significant correlations were weak. Further studies with a more thorough follow-up and a more in-depth analysis of the data should help to assess more accurately which patient factors actually affect TKA outcomes.

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Bibliography

1. Bala, A., C. T. Penrose, T. M. Seyler, R. C. Mather, 3rd, S. S. Wellman, and M. P. Bolognesi. 2015. 'Outcomes after Total Knee Arthroplasty for post-traumatic arthritis', *Knee*, 22: 630-9.
2. Best, M. J., L. T. Buller, R. G. Gosthe, A. K. Klika, and W. K. Barsoum. 2015. 'Alcohol Misuse is an Independent Risk Factor for Poorer Postoperative Outcomes Following Primary Total Hip and Total Knee Arthroplasty', *J Arthroplasty*, 30: 1293-8.
3. Brander, V. A., S. D. Stulberg, A. D. Adams, R. N. Harden, S. Bruehl, S. P. Stanos, and T. Houle. 2003. 'Predicting total knee replacement pain: a prospective, observational study', *Clin Orthop Relat Res*: 27-36.
4. Brander, V., S. Gondek, E. Martin, and S. D. Stulberg. 2007. 'Pain and depression influence outcome 5 years after knee replacement surgery', *Clin Orthop Relat Res*, 464: 21-6.
5. Christen, M., E. Aghayev, and B. Christen. 2014. 'Short-term functional versus patient-reported outcome of the bicruciate stabilized total knee arthroplasty: prospective consecutive case series', *BMC Musculoskelet Disord*, 15: 435.
6. Goncalves, R. S., J. Cabri, J. P. Pinheiro, and P. L. Ferreira. 2009. 'Cross-cultural adaptation and validation of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score (KOOS)', *Osteoarthritis Cartilage*, 17: 1156-62.
7. Goncalves, R. S., J. Cabri, J. P. Pinheiro, P. L. Ferreira, and J. Gil. 2010. 'Reliability, validity and responsiveness of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score--Physical Function Short-form (KOOS-PS)', *Osteoarthritis Cartilage*, 18: 372-6.
8. Haanstra, T. M., T. van den Berg, R. W. Ostelo, R. W. Poolman, E. P. Jansma, P. Cuijpers, and H. C. de Vet. 2012. 'Systematic review: do patient expectations influence treatment outcomes in total knee and total hip arthroplasty?', *Health Qual Life Outcomes*, 10: 152.
9. Houdek, M. T., C. D. Watts, S. F. Shannon, E. R. Wagner, S. A. Sems, and R. J. Sierra. 2016. 'Posttraumatic Total Knee Arthroplasty Continues to Have Worse Outcome Than Total Knee Arthroplasty for Osteoarthritis', *J Arthroplasty*, 31: 118-23.
10. Jacobs, C. A., C. P. Christensen, and T. Karthikeyan. 2014. 'Patient and intraoperative factors influencing satisfaction two to five years after primary total knee arthroplasty', *J Arthroplasty*, 29: 1576-9.

11. Kahn, T. L., and R. Schwarzkopf. 2015. 'Does Total Knee Arthroplasty Affect Physical Activity Levels? Data from the Osteoarthritis Initiative', *J Arthroplasty*, 30: 1521-5.
12. Keswani, A., M. C. Tasi, A. Fields, A. J. Lovy, C. S. Moucha, and K. J. Bozic. 2016. 'Discharge Destination After Total Joint Arthroplasty: An Analysis of Postdischarge Outcomes, Placement Risk Factors, and Recent Trends', *J Arthroplasty*, 31: 1155-62.
13. Khatib, Y., A. Madan, J. M. Naylor, and I. A. Harris. 2015. 'Do Psychological Factors Predict Poor Outcome in Patients Undergoing TKA? A Systematic Review', *Clin Orthop Relat Res*, 473: 2630-8.
14. Koh, I. J., W. S. Cho, N. Y. Choi, and T. K. Kim. 2014. 'Causes, risk factors, and trends in failures after TKA in Korea over the past 5 years: a multicenter study', *Clin Orthop Relat Res*, 472: 316-26.
15. Lewis, G. N., D. A. Rice, P. J. McNair, and M. Kluger. 2015. 'Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis', *Br J Anaesth*, 114: 551-61.
16. Lungu, E., P. A. Vendittoli, and F. Desmeules. 2015. 'Preoperative determinants of early and medium term patient-reported pain and disability following total knee arthroplasty: A systematic review', *Osteoarthritis and Cartilage*, 23: A406-A07.
17. Nichols, C. I., and J. G. Vose. 2016. 'Clinical Outcomes and Costs Within 90 Days of Primary or Revision Total Joint Arthroplasty', *J Arthroplasty*.
18. Oishi, K., E. Tsuda, Y. Yamamoto, S. Maeda, E. Sasaki, D. Chiba, I. Takahashi, S. Nakaji, and Y. Ishibashi. 2016. 'The Knee injury and Osteoarthritis Outcome Score reflects the severity of knee osteoarthritis better than the revised Knee Society Score in a general Japanese population', *Knee*, 23: 35-42.
19. Ramkumar, P. N., J. D. Harris, and P. C. Noble. 2015. 'Patient-reported outcome measures after total knee arthroplasty: a systematic review', *Bone Joint Res*, 4: 120-7.
20. Roos, E. M., and L. S. Lohmander. 2003. 'The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis', *Health Qual Life Outcomes*, 1: 64.
21. Roos, E. M., H. P. Roos, L. S. Lohmander, C. Ekdahl, and B. D. Beynnon. 1998. 'Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure', *J Orthop Sports Phys Ther*, 28: 88-96.
22. Roth, J. S., K. C. Buehler, J. Shen, and M. Naughton. 2013. 'Patient factors predict functional outcomes after cruciate retaining TKA: a 2-year follow-up analysis', *J Arthroplasty*, 28: 1321-6.

23. Si, H. B., Y. Zeng, B. Shen, J. Yang, Z. K. Zhou, P. D. Kang, and F. X. Pei. 2015. 'The influence of body mass index on the outcomes of primary total knee arthroplasty', *Knee Surg Sports Traumatol Arthrosc*, 23: 1824-32.
24. Singh, J. A. 2011. 'Smoking and outcomes after knee and hip arthroplasty: a systematic review', *J Rheumatol*, 38: 1824-34.
25. Singh, J. A., and D. G. Lewallen. 2014. 'Depression in primary TKA and higher medical comorbidities in revision TKA are associated with suboptimal subjective improvement in knee function', *BMC Musculoskelet Disord*, 15: 127.
26. Sivachidambaram, K., M. Ateef, and S. Tahseen. 2014. 'Correlation of Self-Reported Questionnaire (KOOS) with Some Objective Measures in Primary OA Knee Patients', *ISRN Rheumatol*, 2014: 301485.
27. Tamm, A. E., M. Lintrop, Y. Hansen, J. Kumm, and A. O. Tamm. 2011. 'Associations between KOOS (knee injury and osteoarthritis outcome score) and bone–cartilage biomarkers', *Bone*, 48: S261.
28. Tan, S. C., Y. H. Chan, H. C. Chong, P. L. Chin, A. Yew, S. L. Chia, D. Tay, N. N. Lo, and S. J. Yeo. 2014. 'Association of surgeon factors with outcome scores after total knee arthroplasty', *J Orthop Surg (Hong Kong)*, 22: 378-82.
29. Tavakol, Mohsen, and Reg Dennick. 2011. 'Making sense of Cronbach's alpha', *International Journal of Medical Education*, 2: 53-55.
30. van Kempen, R. W., J. J. Schimmel, G. G. van Hellemondt, H. Vandenneucker, and A. B. Wymenga. 2013. 'Reason for revision TKA predicts clinical outcome: prospective evaluation of 150 consecutive patients with 2-years followup', *Clin Orthop Relat Res*, 471: 2296-302.
31. Vissers, M. M., J. B. Bussmann, J. A. Verhaar, J. J. Busschbach, S. M. Bierma-Zeinstra, and M. Reijman. 2012. 'Psychological factors affecting the outcome of total hip and knee arthroplasty: a systematic review', *Semin Arthritis Rheum*, 41: 576-88.
32. Waheeb, A., M. G. Zywiel, M. Palaganas, V. Venkataramanan, and A. M. Davis. 2015. 'The influence of patient factors on patient-reported outcomes of orthopedic surgery involving implantable devices: a systematic review', *Semin Arthritis Rheum*, 44: 461-71.
33. Xie, X., L. Lin, B. Zhu, Y. Lu, Z. Lin, and Q. Li. 2014. 'Will gender-specific total knee arthroplasty be a better choice for women? A systematic review and meta-analysis', *Eur J Orthop Surg Traumatol*, 24: 1341-9.
34. Young, S. W., J. Mutu-Grigg, C. M. Frampton, and J. Cullen. 2014. 'Does speed matter? Revision rates and functional outcomes in TKA in relation to duration of surgery', *J Arthroplasty*, 29: 1473-77.e1.