




Wild goose chase – no predictable patient subgroups benefit from meniscal surgery: patient-reported outcomes of 641 patients 1 year after surgery

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ABSTRACT

Background Despite absence of evidence of a clinical benefit of arthroscopic partial meniscectomy (APM), many surgeons claim that subgroups of patients benefit from APM.

Objective We developed a prognostic model predicting change in patient-reported outcome 1 year following arthroscopic meniscal surgery to identify such subgroups.

Methods We included 641 patients (age 48.7 years (SD 13), 56% men) undergoing arthroscopic meniscal surgery from the Knee Arthroscopy Cohort Southern Denmark.

18 preoperative factors identified from literature and/or orthopaedic surgeons (patient demographics, medical history, symptom onset and duration, knee-related symptoms, etc) were combined in a multivariable linear regression model. The outcome was change in Knee Injury and Osteoarthritis Outcome Score (KOOS₄) (average score of 4 of 5 KOOS subscales excluding the activities of daily living subscale) from presurgery to 52 weeks after surgery. A positive KOOS₄ change score constitutes improvement. Prognostic performance was assessed using R² statistics and calibration plots and was internally validated by adjusting for optimism using 1000 bootstrap samples.

Results Patients improved on average 18.6 (SD 19.7, range –38.0 to 87.8) in KOOS₄. The strongest prognostic factors for improvement were (1) no previous meniscal surgery on index knee and (2) more severe preoperative knee-related symptoms. The model's overall predictive performance was low (apparent R²=0.162, optimism adjusted R²=0.080) and it showed poor calibration (calibration-in-the-large=0.205, calibration slope=0.772).

Conclusion Despite combining a large number of preoperative factors presumed clinically relevant, change in patient-reported outcome 1 year following meniscal surgery was not predictable. This essentially quashes the existence of 'subgroups' with certain characteristics having a particularly favourable outcome after meniscal surgery.

Trial registration number NCT01871272.

INTRODUCTION

Arthroscopic partial meniscectomy (APM) for patient-reported knee pain or functional impairment shows no clinically relevant benefit over sham surgery or in addition to exercise therapy for middle-aged and older patients.^{1–4} APM is also associated with a risk of adverse events^{5,6} and

the procedure has been reported to carry with it increased risk of worsening of cartilage damage and knee replacement surgery as compared with knees with meniscal tears left in situ.⁷

Critics of the studies that underpin these conclusions—that APM is largely unhelpful for degenerative meniscal tears and potentially harmful for patients with knee pain—argue that randomised trials often include narrowly selected patients and therefore may not entirely reflect daily clinical practice. If subgroups of patients that have a particular benefit from APM really do exist, what might these subgroups be?

Surgeons often argue that younger patients with traumatic meniscal tears and/or a locked knee benefit the most from meniscal surgery,^{8,9} but these patients were not included in previous randomised trials.^{1,10–15} Furthermore, trials often lack power for detecting differences in treatment effects among subgroups of patients.¹⁶ A recent systematic review aimed to summarise the existing evidence on patient-specific factors' association with patient-reported outcomes after arthroscopic meniscal surgery.¹⁷ Findings were inconclusive, and the combined ability of factors to predict outcome was not evaluated.¹⁷

Therefore, to identify those who might improve after APM, we combined the most logical prognostic factors to develop and validate a prognostic model to predict patients' change in their self-reported outcome 1 year following arthroscopic meniscal surgery.

METHODS

The Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis guideline¹⁸ was followed to report this study.

Data source and patients

For the development and validation of the prognostic model, we used all patients included in the Knee Arthroscopy Cohort Southern Denmark (KACS).¹⁹ KACS is a prospective cohort following patients undergoing knee arthroscopy for a meniscal tear. Patients were consecutively recruited at four public hospitals in the Region of Southern Denmark between 1 February 2013 to 31 January 2014, and at one of the original four hospitals from 1 February 2014 to 31 January 2015. Inclusion criteria in KACS were age 18 years and above, assigned for knee arthroscopy by an orthopaedic

surgeon on suspicion of a meniscal tear (based on clinical examination, injury history and MRI if considered necessary), able to read and understand Danish and having an email address. Patients were excluded if not having a meniscal tear at surgery, having previous or planned reconstruction of the anterior or posterior cruciate ligament in either knee, fracture(s) to the lower extremities within the last 6 months, or not being able to reply to questionnaires because of mental impairment.¹⁹

Outcome

The outcome measure was the Knee injury and Osteoarthritis Outcome Score (KOOS).²⁰ KOOS is a validated and often used knee-specific patient-reported outcome in studies concerning meniscal surgery.^{10 12 15 20 21} The score consists of five subscales covering pain, symptoms, activities of daily living (ADL), sports and recreational activities (Sport/Rec) and knee-related quality of life (QoL). Each subscale ranges from 0 to 100 with 0 representing extreme knee problems and 100 representing no knee problems.²⁰ KOOS was completed using online questionnaires emailed to patients within 2 weeks prior to surgery (median 7 days, IQR 3 to –10 days) and at 12 and 52 weeks after surgery.

In the present study, the outcome was the change score from presurgery to 52 weeks after surgery in the mean score of KOOS₄ with a positive KOOS₄ change score constituting improvement. KOOS₄ is an aggregated mean score of four of the five KOOS subscales—pain, symptoms, Sport/Rec and QoL—but excludes the ADL subscale that is known to display ceiling effects in younger and more active populations.²¹ KOOS₄ has been used in previous trials assessing the effect of knee surgery.^{15 22}

Prognostic factors

Potential prognostic factors were gathered from patients prior to surgery as part of the same online questionnaire containing the preoperative KOOS. Among all available factors in KACS, we considered 26 factors for the prognostic model. These were identified from published literature suggesting an association with outcome after meniscal surgery^{17 23 24} and/or considered important by orthopaedic surgeons.^{8 9} Due to a desire to develop a parsimonious prognostic model that could be manageable in clinical practice, eight factors were omitted before model building. The omission of these was based on high correlations with other factors, and thus possible redundancy/overlap in prognostic information²⁵ or limited external validity (online supplementary table 1). As a result, 18 prognostic factors were included in the prognostic model (online supplementary table 2), with response categories shown in tables 1 and 2.

Statistical analysis method

Missing data

Under the assumption of data being missing at random,²⁶ we imputed the missing values using multiple imputation with chained equations.²⁷ The multiple imputation model included all 18 prognostic factors, the outcome, 3 interaction terms (ie, age and knee catching/locking, age and knee extension deficit, and age and symptom onset), and as auxiliary variables the presurgery and 12 weeks KOOS₄ scores. Multivariable fractional polynomials were used to explore whether nonlinear terms were appropriate for the continuous prognostic factors (ie, age, body mass index, presurgery and 12 weeks KOOS₄ scores).^{28 29} The ‘ice’-package³⁰ in Stata V.15.1 was used to generate a number of imputed data sets equal to the largest proportion of missing in any factor under consideration.²⁷

Model development

Multivariable linear regression was used to develop a prognostic model that included all 18 a priori-defined prognostic factors (model I), and a reduced model based on statistical significance (model II).

Before fitting the models and without knowledge of associations with outcome, categories in certain categorical prognostic factors were combined to eliminate sparse categories and retain a ratio of ≥ 20 patients per estimated model parameter.²⁵ Also, some ordinal categorical factors had categories combined if linearity with outcome could not be assumed (visually examined using scatter plots), otherwise they were handled as continuous in the models. Multivariable fractional polynomials were used to consider nonlinear associations between continuous factors and outcome,^{28 29} as opposed to categorisation, which has been shown to be suboptimal.^{31 32}

Models were fitted using the combined imputed data sets and model coefficients were estimated using Rubin’s rules.³³ Based on a previous study³⁴ and clinical reasoning, we included three interaction terms (ie, age and knee catching/locking,³⁴ age and knee extension deficit, and age and symptom onset) in the models. Their significance was tested as a group using multiple parameter Wald test and all terms were removed, and the models refitted, if group significance level was $p > 0.20$. For the reduced model (model II), backward stepwise elimination was performed in the combined imputed data sets to eliminate factors with $p > 0.20$ based on a likelihood-ratio test using the ‘mfpmi’-package³⁵ in Stata V.15.1.^{28 29}

As secondary models, using the same approach as above, we developed a full and reduced model for patients aged 40 years or younger (model I_{young} and model II_{young}) and patients aged 41 years or older (model I_{old} and model II_{old}), respectively. Furthermore, as sensitivity analyses, all models were also developed using only patients with complete data.

Prior to analyses, prognostic factors were investigated for collinearity by calculating variance inflation factors (VIFs). The level of collinearity was not considered problematic if mean VIF was ≤ 5 and individual VIFs were ≤ 10 .³⁶ For all models, the underlying assumptions of linearity, homoscedasticity and normality of residuals were assessed using scatter and Q-Q plots.

Performance measures

We evaluated the models’ overall predictive performance using the R^2 statistic, which is a measure of the proportion of variance explained by the models.³⁷ Calibration, that is, the models’ ability to give unbiased estimates of the predicted outcome, was assessed using three measures of calibration in a hierarchical order as defined by Van Calster *et al*³⁸: (1) Mean calibration (calibration-in-the-large), which is the difference between the mean observed outcome and the mean predicted outcome. Values less than or greater than 0 indicate average under or overestimation of the outcome, respectively. (2) Weak calibration (calibration slope), which reflects the average strength of the predictor effects and is the regression coefficients between predicted outcomes and observed outcomes. A value less than or greater than 1 indicates that the model systematically overestimates or underestimates predicted outcomes, respectively and (3) Moderate calibration, which is the agreement between observed outcomes and predicted outcomes and was assessed graphically using a calibration plot. If well calibrated, predictions should lie around the 45° line of the calibration plot.

Robust methods (ie, the median) were used to combine R^2 statistics and calibration slopes across imputed data sets,³⁹ while

Table 1 Baseline patient characteristics

Variables	All (n=641)	Range	40 years or younger (n=150)	Range	41 years or older (n=491)	Range
Demographics						
Age, years (SD)	48.7 (13)	18–76	30.6 (7)	18–40	54.2 (9)	41–76
Sex, female, n (%)	280 (44)		50 (33)		230 (47)	
BMI, kg/m ² (SD)	27.3 (4.4)	18.9–47.2	26.4 (4.2)	18.9–44.1	27.5 (4.5)	18.9–47.2
Educational level, n (%)						
Elementary school	104 (16)		16 (11)		88 (18)	
High school	34 (5)		21 (14)		13 (3)	
Vocational education	227 (35)		49 (33)		178 (36)	
Short cycle education	63 (10)		13 (9)		50 (10)	
Medium cycle education	120 (19)		23 (15)		97 (20)	
Bachelor degree	43 (7)		17 (11)		26 (5)	
Master degree	31 (5)		8 (5)		23 (5)	
PhD	2 (0)		1 (1)		1 (0)	
Other	17 (3)		2 (1)		15 (3)	
Participation in physical activity prior to injury, n (%)						
Sport at competitive level	61 (9)		35 (23)		26 (5)	
Recreational sport	152 (24)		45 (30)		107 (22)	
Light sport	160 (25)		23 (15)		137 (28)	
Heavy household work	100 (15)		18 (12)		82 (17)	
Light household work	153 (24)		24 (16)		129 (26)	
Minimal household work	11 (2)		4 (3)		7 (1)	
No household work	4 (1)		1 (1)		3 (1)	
Physical activity at work, n (%)						
Very light (mainly desk work)	136 (21)		35 (23)		101 (20)	
Light (light industrial, salesman, office etc)	108 (17)		25 (17)		83 (17)	
Moderate (cleaning, kitchen, mail etc)	216 (34)		46 (31)		170 (35)	
Hard (heavy industrial, farmer etc)	100 (15)		30 (20)		70 (14)	
Unemployed	81 (13)		14 (9)		67 (14)	
Medical history						
Previous surgery on index knee, n (%) [*]	117 (18)		26 (17)		91 (19)	
Back problems, n (%)	189 (29)		28 (19)		161 (33)	
Feeling sad, n (%)						
All of the time	3 (1)		0 (0)		3 (1)	
Most of the time	9 (1)		6 (4)		3 (1)	
A good bit of the time	35 (5)		10 (7)		25 (5)	
Some of the time	92 (14)		22 (15)		70 (14)	
A little of the time	196 (31)		50 (33)		146 (30)	
None of the time	306 (48)		62 (41)		244 (50)	
Knee alignment, n (%)						
Pronounced varus	6 (1)		4 (3)		2 (1)	
Slightly varus	59 (9)		14 (9)		45 (9)	
Normal	528 (83)		121 (80)		407 (83)	
Slightly valgus	46 (7)		10 (7)		36 (7)	
Pronounced valgus	2 (0)		1 (1)		1 (0)	

^{*}Missing observation for one individual in the older age group.
BMI, body mass index; n, number.

Table 2 Baseline knee symptoms of included patients

Variables	All (n=641)	40 years or younger (n=150)		41 years or older (n=491)		
		Range	Range	Range	Range	
Meniscal tear characteristics						
Duration of symptoms, n (%)						
0–3 months	129 (20)		41 (27)		88 (18)	
4–6 months	181 (28)		24 (16)		157 (32)	
7–12 months	135 (21)		31 (21)		104 (21)	
13–24 months	94 (15)		20 (13)		74 (15)	
More than 24 months	102 (16)		34 (23)		68 (14)	
Symptom onset, n (%)						
Slowly evolved	208 (32)		29 (19)		179 (36)	
Semi traumatic	260 (41)		51 (34)		209 (43)	
Traumatic	173 (27)		70 (47)		103 (21)	
Knee-related symptoms						
Knee catching/locking, n (%)						
Never	301 (47)		61 (41)		240 (49)	
Rarely	102 (16)		18 (12)		84 (17)	
Sometimes	135 (21)		35 (23)		100 (20)	
Often	87 (14)		30 (20)		57 (12)	
Always	16 (2)		6 (4)		10 (2)	
Able to straighten knee fully, n (%)						
Always	349 (54)		68 (45)		281 (57)	
Often	133 (21)		41 (27)		92 (19)	
Sometimes	70 (11)		18 (12)		52 (11)	
Rarely	32 (5)		7 (5)		25 (5)	
Never	57 (9)		16 (11)		41 (8)	
Frequency of knee pain, n (%)						
None	10 (2)		3 (2)		7 (1)	
Monthly	31 (5)		12 (8)		19 (4)	
Weekly	71 (11)		29 (19)		42 (9)	
Daily	412 (64)		78 (52)		334 (68)	
Always	117 (18)		28 (19)		89 (18)	
Knee pain walking on stairs, n (%)						
None	51 (8)		19 (13)		32 (7)	
Mild	140 (22)		45 (30)		95 (19)	
Moderate	211 (33)		45 (30)		166 (34)	
Severe	186 (29)		27 (18)		159 (32)	
Extreme	53 (8)		14 (9)		39 (8)	
Difficulty twisting/pivoting knee, n (%)						
None	13 (2)		6 (4)		7 (1)	
Mild	48 (7)		15 (10)		33 (7)	
Moderate	89 (14)		25 (17)		64 (13)	
Severe	228 (36)		51 (34)		177 (36)	
Extreme	263 (41)		53 (35)		210 (43)	
Knee instability, n (%)						
Not unstable	107 (17)		22 (15)		85 (17)	
Unstable, but not affecting activities	64 (10)		14 (9)		50 (10)	
Unstable, slightly affecting activities	125 (19)		30 (20)		95 (19)	
Unstable, moderately affecting activities	127 (20)		22 (15)		105 (22)	
Unstable, highly affecting activities	199 (31)		57 (38)		142 (29)	
Unstable, preventing all activities	19 (3)		5 (3)		14 (3)	
KOOS, mean (SD)						
KOOS ₄	45.7 (15.3)	2.7 to 87.7	47.7 (16.8)	2.7 to 87.4	45.1 (14.8)	5.4 to 87.7
Pain	54.9 (18.5)	0.0 to 100.0	58.9 (20.2)	0.0 to 100.0	53.6 (17.8)	8.3 to 97.2
Symptoms	60.0 (18.6)	3.6 to 100.0	60.6 (19.2)	10.7 to 100.0	59.8 (18.4)	3.6 to 100.0
ADL	63.7 (19.5)	2.9 to 100.0	69.8 (19.6)	7.4 to 100.0	61.8 (19.0)	2.9 to 100.0

Continued

Table 2 Continued

Variables	All (n=641)	40 years or younger (n=150)		41 years or older (n=491)		
		Range		Range	Range	
Sport/Rec	26.3 (21.9)	0.0 to 100.0	31.1 (23.3)	0.0 to 90.0	24.9 (21.3)	0.0 to 100.0
QoL	41.6 (15.4)	0.0 to 87.5	40.2 (16.1)	0.0 to 75.0	42.0 (15.2)	0.0 to 87.5

ADL, activities of daily living; KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, knee-related quality of life; Sport/Rec, sports and recreational activities; n, number.

the developed models' calibration-in-the-large and calibration plot were evaluated on patients with complete data.

Internal validation

We used the bootstrap resampling technique³⁷ to adjust the apparent R^2 for any optimism and estimate the optimism adjusted calibration slope. The latter was also used as a uniform shrinkage factor to adjust the effects of predictors (ie, regression coefficients) for potential over or underfitting, to make the models better calibrated for similar future patients.²⁵ In the bootstrap procedure, we repeated the entire modelling process, including variable selection in the reduced models, in 1000 bootstrap samples drawn with replacement from the original sample.⁴⁰ The models were fitted in each bootstrap replicate and tested on the original sample to estimate optimism in model performance. All analyses were performed in Stata V.15.1 (StataCorp).

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design or implementation of the study. No patients were consulted to advise interpretation or writing up results.

RESULTS

Patients

A total of 641 patients were included in the KACS cohort (table 1). With the exception of one participant having missing data for previous meniscal surgery, no patients had missing data in any of the prognostic factors. The outcome at 52 weeks was missing in 76 (12%) patients (figure 1). These patients were on

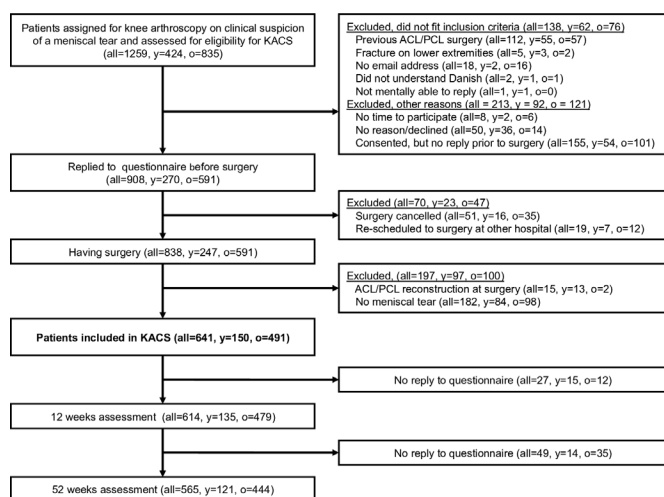


Figure 1 Study flow chart. 'y' denotes young patients (≤ 40 years) and 'o' denotes old patients (> 40 years). ACL/PCL, anterior or posterior cruciate ligament; KACS, Knee Arthroscopy Cohort Southern Denmark.

average a little younger than those with complete follow-up, but similar in all other characteristics (online supplementary table 3).

Most patients had resection of the meniscus ($n=600$), while 33 had it repaired and the rest received a combination of the two surgical procedures ($n=8$). Baseline knee symptoms and KOOS₄ scores are presented in table 2. The average improvement in KOOS₄ from before surgery to 52 weeks after surgery was 18.6 (SD 19.7) for the whole cohort, 16.2 (SD 20.1) and 19.2 (SD 19.5) for the young (≤ 40 years) and older (> 40 years) patients, respectively.

Model development

We generated 10 imputed data sets for the development of the main models (models I and II) and the models including patients aged 41 or older (model I_{old} and model II_{old}), respectively.²⁷ Due to a larger proportion of patients with incomplete follow-up among the younger patients (19%, figure 1), 20 imputed data sets were generated for the development of the models that included patients aged 40 or younger (model I_{young} and model II_{young}). Continuous factors were modelled as linear in all models (no non-linear trends identified), while the handling of specific ordinal categorical factors differed between models (tables 3 and 4).

Model specification

Of the 18 prognostic factors included in the full model (model I), only nine were retained in the reduced model (model II) (table 3). In both models, the strongest prognostic factors in terms of statistical significance were previous meniscal surgery, level of education and knee-related symptoms such as difficulty twisting/pivoting and inability to straighten the knee fully (table 3). A positive regression coefficient indicates improvement in KOOS₄, and a negative value indicates deterioration. The specification of the secondary models that included patients aged 41 or older (model I_{old} and model II_{old}) were similar to the main models', whereas the models that included patients aged 40 or younger (model I_{young} and model II_{young}) deviated somewhat with fewer factors retained in the reduced model (table 4). For the complete prognostic models including equations, see online supplementary tables 4 and 5.

Model performance

The apparent R^2 ranged from 0.13 to 0.42, but the internal validation revealed considerable optimism in all models. After adjusting for optimism, R^2 values ranged from 0.04 to 0.10 (figure 2). In all models calibration was poor with only mean calibration being satisfactory (ie, calibration-in-the-large close to 0), whereas weak and moderate calibration were low as all models systematically overestimated predicted outcomes (ie, calibration slope < 1) and had little agreement between observed and predicted KOOS₄ change scores (figure 2). Sensitivity analyses including only patients with complete data did not alter the

Table 3 Results from multivariable linear regression models including all patients

Variables	Multivariable model I (n=641)*		Multivariable model II (n=641)*	
	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value
<i>Model intercept</i>	-4.15		-7.44	
Age, years	0.13 (-0.01 to 0.26)	0.063		
Sex (female)	-0.01 (-3.42 to 3.40)	0.995		
BMI, kg/m ²	-0.32 (-0.69 to 0.06)	0.096		
Educational level (ref: elementary/high school)		0.023		0.025
Vocational/short education	5.47 (1.39 to 9.54)		5.32 (1.39 to 9.24)	
Medium duration/bachelor/master/PhD/other	2.41 (-1.91 to 6.72)		2.76 (-1.41 to 6.92)	
Participation in physical activity prior to injury (ref: light/minimal/no household work)		0.142		0.115
Light sport/heavy household work	2.78 (-0.97 to 6.54)		3.04 (-0.65 to 6.74)	
Competitive/recreational sport	4.29 (-0.04 to 8.61)		4.21 (0.14 to 8.29)	
Physical activity at work (ref: very light/light/unemployed)		0.518		
Moderate	-1.21 (-4.74 to 2.31)			
Hard	1.69 (-3.21 to 6.60)			
Previous surgery on index knee	-7.57 (-11.91 to -3.23)	0.001	-7.84 (-11.94 to -3.73)	<0.001
Back problems	-3.59 (-7.02 to -0.17)	0.040	-3.27 (-6.66 to 0.12)	0.059
Feeling sad (ref: none of the time)		0.820		
A little of the time	-1.07 (-4.67 to 2.53)			
All/most/a good bit/some of the time	0.08 (-4.15 to 4.31)			
Knee alignment (ref: normal)		0.662		
Slightly/pronounced varus	-2.41 (-8.04 to 3.23)			
Slightly/pronounced valgus	-1.10 (-7.22 to 5.01)			
Duration of symptoms (ref: 0–3 months)		0.433		
4–6 months	2.20 (-2.38 to 6.77)			
7–12 months	-1.24 (-6.27 to 3.78)			
More than 12 months	1.56 (-3.14 to 6.26)			
Symptom onset (ref: slowly evolved)		0.098		0.029
Semi traumatic	0.58 (-3.12 to 4.29)		0.16 (-3.45 to 3.77)	
Traumatic	-3.60 (-7.89 to 0.69)		-4.63 (-8.71 to -0.55)	
Knee catching/locking†	0.40 (-1.06 to 1.85)	0.593		
Able to straighten knee fully†	1.86 (0.51 to 3.22)	0.007	2.02 (0.70 to 3.35)	0.003
Frequency of knee pain†	2.44 (0.18 to 4.71)	0.035	2.39 (0.15 to 4.63)	0.036
Knee pain walking on stairs (ref: none/mild)		0.050		0.037
Moderate	3.14 (-1.03 to 7.30)		3.43 (-0.68 to 7.53)	
Severe/extreme	-1.44 (-6.13 to 3.26)		-1.15 (-5.57 to 3.27)	
Difficulty twisting/pivoting kneet	2.74 (0.92 to 4.56)	0.003	3.17 (1.39 to 4.96)	0.001
Knee instability (ref: not unstable/Unstable, but not affecting activities)		0.316		
Unstable, slightly/moderately affecting activities	-0.83 (-4.57 to 2.91)			
Unstable, highly affecting/preventing all activities	2.08 (-2.23 to 6.39)			

Interaction terms omitted from the models (p=0.590).

*Based on 10 imputed data sets.

†Handled as continuous using the original categories, assuming linearity. The coefficients are per category increase.

BMI, body mass index; n, number.

results much (online supplementary tables 6 and 7 and supplementary figure 1).

DISCUSSION

Recent randomised trials have strongly questioned the effectiveness of APM for degenerative meniscal tears. There is widespread debate about the use of APM and the existence of particular subgroups of patients benefiting from the procedure.^{41–44} Therefore, and to try identify any such subgroups who might benefit from APM, we developed a prognostic model.

We included a large number of factors considered important for the outcome after surgery and, importantly, factors often used as pivotal indications for knee arthroscopy. Yet, our

developed models failed to accurately predict change in patient-reported outcome after meniscal surgery and identify patients with certain characteristics having a particular outcome after meniscal surgery.

The majority of patients included in the development of the prognostic models were middle aged or older, reflecting current clinical practice.^{45–47} These patients typically have a degenerative meniscal tear,^{45–48} often in combination with other degenerative changes such as knee osteoarthritis (OA).^{48–49} Symptoms are, therefore, likely to result from the multiple and complex processes of OA rather than the meniscal tear per se.⁵⁰ This may in part explain why the main models and models that included only patients aged 41 or older failed to predict change

Table 4 Results from multivariable linear regression for models including young and older patients, respectively

Variables	40 years or younger (n=150)			41 years or older (n=491)		
	Multivariable model I*		Multivariable model II*		Multivariable model I†	
	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value
Model intercept	-0.29		-8.48		-0.14	
Age, years	0.52 (-0.14 to 1.18)	0.119	0.64 (0.13 to 1.16)	0.015	0.10 (-0.11 to 0.31)	0.343
Sex (female)	-1.67 (-9.98 to 6.63)	0.689			0.27 (-3.61 to 4.15)	0.891
BMI, kg/m ²	-0.28 (-1.15 to 0.58)	0.516			-0.34 (-0.74 to 0.06)	0.098
Educational level (ref: elementary/high school)‡	1.65 (-4.03 to 7.33)	0.565				0.073
Vocational/short education					4.40 (-0.47 to 9.27)	
Medium duration/bachelor/master/PhD/other					0.21 (-4.87 to 5.30)	
Participation in physical activity prior to injury (ref: light/minimal/no household work)§		0.777			2.41 (-0.08 to 4.90)	0.057
Light sport/heavy household work	0.27 (-10.31 to 10.85)					
Competitive/recreational sport	-2.48 (-11.91 to 6.96)					0.454
Physical activity at work (ref: very light/light/unemployed)		0.971				
Moderate	0.07 (-8.31 to 8.46)				-0.81 (-4.77 to 3.16)	
Hard	-1.13 (-11.79 to 9.52)				2.97 (-2.76 to 8.70)	
Previous surgery on index knee	-13.96 (-25.04 to -2.88)	0.015	-13.87 (-24.72 to -3.01)	0.014	-6.17 (-10.68 to -1.66)	0.007
Back problems	-9.62 (-19.52 to 0.28)	0.057	-8.97 (-17.53 to -0.42)	0.040	-2.83 (-6.47 to 0.81)	0.128
Feeling sad (ref: none of the time)§		0.833			0.17 (-2.15 to 2.48)	0.889
A little of the time	0.57 (-7.72 to 8.87)					
All/most/a good bit/some of the time	2.80 (-6.40 to 11.99)					
Knee alignment (ref: normal)		0.460		0.279		0.689
Slightly/pronounced varus	0.06 (-12.26 to 12.38)		0.22 (-10.79 to 11.22)		-2.34 (-8.57 to 3.90)	
Slightly/pronounced valgus	-9.20 (-23.49 to 5.09)		-10.78 (-23.71 to 2.15)		1.30 (-5.39 to 8.00)	
Duration of symptoms (ref: 0–3 months)		0.080		0.041		0.352
4–6 months	-0.60 (-11.85 to 10.65)		-1.66 (-11.76 to 8.45)		0.82 (-4.38 to 6.02)	
7–12 months	1.90 (-8.28 to 12.09)		-0.08 (-9.48 to 9.65)		-3.34 (-9.07 to 2.38)	
More than 12 months	10.16 (0.32 to 19.99)		9.67 (-0.15 to 19.49)		-2.02 (-7.62 to 3.59)	
Symptom onset (ref: slowly evolved)		0.895				0.119
Semitraumatic	0.09 (-10.31 to 10.51)				0.43 (-3.72 to 4.59)	
Traumatic	-1.71 (-11.71 to 8.30)				-4.30 (-9.30 to 0.70)	
Knee catching/locking (ref: never)§		0.441			-0.98 (-3.57 to 1.61)	0.456
Rarely/sometimes	5.67 (-3.10 to 14.45)					
Often/always	3.96 (-7.51 to 15.43)					
Able to straighten knee fully (ref: always)¶		0.054		0.018		0.005
Often/sometimes	-5.98 (-14.47 to 2.52)		-5.06 (-12.59 to 2.47)		2.15 (0.65 to 3.66)	
Never/rarely	7.18 (-4.43 to 18.79)		9.08 (-0.70 to 18.86)			
Frequency of knee pain**	1.68 (-3.36 to 6.72)	0.510			2.79 (0.14 to 5.44)	0.039
						0.042

Continued

Table 4 Continued

Variables	40 years or younger (n=150)			41 years or older (n=491)		
	Multivariable model I*		Multivariable model II*	Multivariable model I†		Multivariable model II†
	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value
Knee pain walking on stairs (ref: none/mild)‡	5.29 (-0.71 to 11.30)	0.083	6.23 (1.35 to 11.10)	0.013	0.98 (-3.91 to 5.86)	0.050
Moderate					1.27 (-3.49 to 6.03)	0.062
Severe/extreme					-4.38 (-9.79 to 1.02)	
Difficulty twisting/pivoting knee**	2.74 (-0.96 to 6.45)	0.145	2.89 (-0.33 to 6.11)	0.078	2.45 (0.31 to 4.59)	0.025
Knee instability (ref: not unstable/unstable, but not affecting activities)		0.728				0.207
Unstable, slightly/moderately affecting activities	-3.96 (-14.08 to 6.16)				0.69 (-3.53 to 4.90)	
Unstable, highly affecting/preventing all activities	-2.53 (-13.24 to 8.19)				3.99 (-0.78 to 8.77)	

Interaction terms omitted from all models (p=0.288 for the models including young patients, and p=0.810 for the models including older patients).

*Based on 20 imputed data sets.

†Based on 10 imputed data sets.

‡Handled as continuous in the models including young patients using the combined categories, assuming linearity. The coefficients are per category increase.

§Handled as continuous in the models including older patients using the combined categories, assuming linearity. The coefficients are per category increase.

¶Handled as continuous in the models including older patients using the original categories, assuming linearity. The coefficients are per category increase.

**Handled as continuous in all models using the original categories, assuming linearity. The coefficients are per category increase.

n, number; BMI, body mass index.

in patient-reported outcome after a procedure targeting the meniscus. On the other hand, younger patients more often have a traumatic meniscal tear (eg, sports-related trauma) in an otherwise normal joint^{48,51} making symptoms more likely to originate from the meniscal tear or be a consequence of loss of meniscus function. This might explain the better apparent predictive performance observed for the models that included only patients aged 40 or younger. However, due to the small sample size, these models were severely overfitted and should be regarded as exploratory, needing to be confirmed.

Some previous studies have investigated if APM was more effective in subgroups of patients with traumatic meniscal tears or mechanical symptoms, but failed to show any additional benefit of APM for these patients.^{14 52 53} Our results confirm this, but in addition to those studies, we included several other factors and used data from a large clinical cohort that included a heterogeneous population in which the average improvement after surgery is comparable to the average improvement observed in previous trials.²⁻⁴ Our results do not support the existence of specific subgroups of patients with certain preoperative characteristics having larger improvements in patient-reported outcomes after meniscal surgery. As a consequence, the observed variations in effect in this cohort and the surgical arm of previous randomised trials^{2 3} may be due to random variation rather than a sign of the existence of specific subgroups with a particular effect of meniscal surgery.

Limitations

This study has some limitations. Although we included a large number of factors considered to be important for the outcome after meniscal surgery,^{17 23} some important prognostic factors might have been missed. For instance, radiographic knee OA has been reported to be associated with worse outcome after meniscal surgery,^{17 23} but radiographs were not available in this study. Information from preoperative MRI of the knee was also not available, thus specific characteristics of the meniscal tear could not be included in the models. This may be a limitation for especially the models predicting the outcome in younger patients. For middle-aged and older patients, however, use of MRI to diagnose a meniscal tear is generally not recommended,^{54 55} as meniscal tears are frequent incidental findings on MRI in asymptomatic adults with uncertain clinical relevance.^{56 57} Other potential prognostic factors that are missing are workers' compensation and self-reported fitness level, which have been found to be associated with outcome after meniscal surgery in a few low-quality studies,^{17 23} but this information was not available in the KACS cohort.¹⁹ Importantly, however, prognostic factors not included in the present models need to be strongly associated with the outcome and only weakly associated with already included factors to substantially improve the predictive performance of any of the models.³⁷ This makes it less likely that the developed models' performance would improve considerably with the inclusion of potentially missing prognostic factors.

We cannot rule out the possibility of misclassifications of prognostic factors affecting the prognostic performance of models. However, the degree of misclassification is likely low as all prognostic factors were self-reported using online questionnaires.

Sample sizes were sufficient in most models to maintain a ratio of 15–20 participants per model parameter, as recommended.²⁵ Despite this, predictive performance diminished considerably after adjustment for optimism, reflecting that

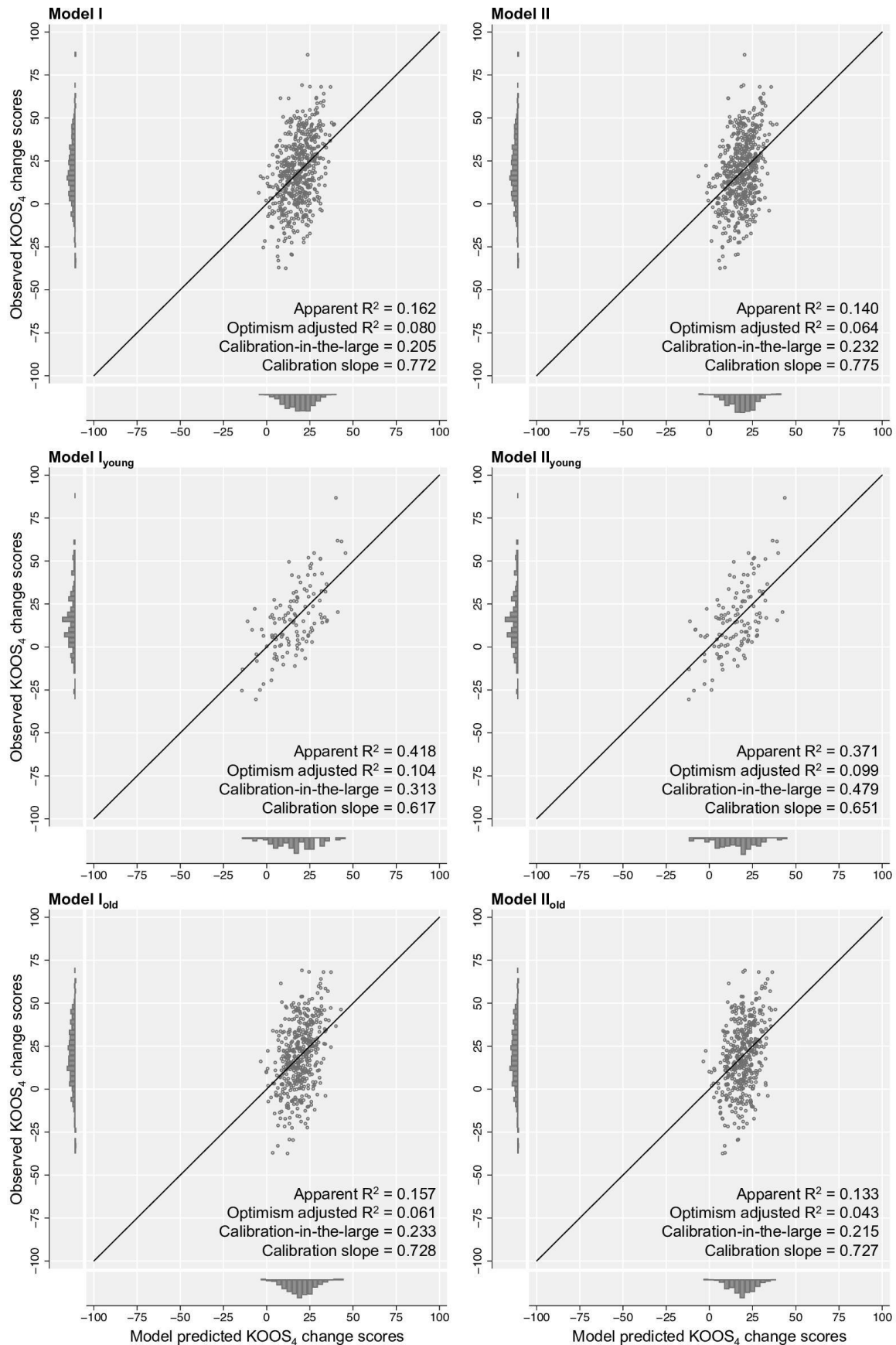


Figure 2 Calibration plots comparing the distribution of observed and model predicted KOOS₄ change scores, respectively, and performance measures for all models. A well-calibrated model would be indicated by all predicted values being close to the black identity line. KOOS, Knee injury and Osteoarthritis Outcome Score.

none of the included factors were strongly predictive of outcome.

Due to the poor performance of all models no external validation was indicated.⁵⁸ Nevertheless, we believe our findings have high external validity,⁵⁹ as distribution of age and sex of included patients are similar to the underlying population that had meniscal surgery in the same period in Denmark (The Danish National Patient Register, www.esundhed.dk) and to what has previously been reported for patients undergoing meniscal surgery in Denmark and the USA.^{45 60}

CONCLUSION

Despite considering a large number of clinically relevant factors collected preoperatively, change in patient-reported outcome 1 year following meniscal surgery was not possible to predict. Our results do not support the existence of subgroups with certain characteristics having a particularly favourable outcome after meniscal surgery.

What are the findings?

- ▶ A combination of the major preoperative clinical factors proposed to be important for outcome after meniscal surgery, including mechanical symptoms and traumatic meniscal tears, poorly predicts change in patient-reported outcome after meniscal surgery.

How might it impact on clinical practice in the future?

- ▶ Preoperative factors have limited utility in clinical practice to identify patients who may have favourable or unfavourable outcome after meniscal surgery.
- ▶ The results question the existence of presumed subgroups of patients with certain characteristics having a particular favourable outcome after meniscal surgery.

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