Meaningful Change Scores in the Knee Injury and Osteoarthritis Outcome Score in Patients Undergoing Anterior Cruciate Ligament Reconstruction

Lina Holm Ingelsrud,*†‡ PT, MSc, Caroline B. Terwee,§ PhD, Berend Terluin,‖ MD, PhD, Lars-Petter Granan,¶ MD, PhD, Lars Engebretsen,#** MD, Prof., Kathryn A.G. Mills,†† PT, PhD, and Ewa M. Roos,† PT, Prof.
Investigation performed at the Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark

Background: Meaningful change scores in the Knee injury and Osteoarthritis Outcome Score (KOOS) in patients undergoing anterior cruciate ligament (ACL) reconstruction have not yet been established.

Purpose: To define the minimal important change (MIC) for the KOOS after ACL reconstruction.

Study Design: Cohort study (diagnosis); Level of evidence, 2.

Methods: KOOS and anchor questions with 7-point scales ranging from ''better, an important improvement'' to ''worse, an important worsening'' were completed postoperatively by randomly chosen participants from the Norwegian Knee Ligament Registry. Presurgery KOOS scores were retrieved from the registry. The MIC for improvement was calculated with anchor-based approaches using the predictive modeling method adjusted for the proportion of improved patients, the mean change method, and the receiver operating characteristic (ROC) method.

Results: Complete data for at least one of the KOOS subscales were obtained from 542 (45.3%) participants. Predictive modeling MIC values were 12.1 for the KOOS subscales of Sport and Recreational Function and 18.3 for Knee-Related Quality of Life. These values aid in interpreting within-group improvement over time and can be used as responder criteria when comparing groups. The corresponding and much lower values for the subscales of Pain (2.5), Symptoms (–1.2), and Activities of Daily Living (2.4) are the results from patients reporting, on average, only mild problems with these domains preoperatively. Although 4% to 10% of patients reported subscale-specific worsening, MIC deterioration calculations were not possible. The ROC MIC values were associated with high degrees of misclassification. Values obtained by the mean change method were considered less reliable because these estimates are derived from subgroups of patients. Average KOOS change scores were approximately similar for patients reporting acceptable symptoms postoperatively and patients reporting important improvements on the anchor items after surgery.

Conclusion: KOOS users should apply subscale-specific cutoffs for meaningful improvement. Our results confirm using the subscales of Sport and Recreational Function and Knee-Related Quality of Life as primary patient-reported outcomes after ACL reconstruction. The predictive modeling approach gave the most robust estimates of MIC values. Our data suggest that reporting acceptable symptoms postoperatively corresponds to reporting an important improvement after ACL reconstruction.

Keywords: minimal important change; Knee injury and Osteoarthritis Outcome Score; anterior cruciate ligament reconstruction

The Knee injury and Osteoarthritis Outcome Score (KOOS) is a frequently used disease-specific patient-reported outcome measure (PROM) for measuring knee symptoms, function, and quality of life in patients with anterior cruciate ligament (ACL) injury undergoing ACL reconstruction. The KOOS is available in about 50 languages, and KOOS scores are monitored in national registries and international databases, as well as used in research and clinical practice.[7,14,21] The 37 studies (until January 2014) that evaluated KOOS psychometric properties were summarized in a systematic review, which found adequate content validity, internal consistency, test-retest reliability, construct validity, and responsiveness for age- and condition-relevant subscales.[1] However, the best way to interpret KOOS scores is not straightforward because a statistically significant change score is not necessarily clinically relevant or

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meaningful to patients.[3] The concept of minimal important change (MIC), also known as minimal (clinically) important difference, has been termed and defined in a variety of ways in the scientific literature. In recent years, emphasis has been placed on MICs being the smallest change in PROM score that is considered important by patients.[4]

There is limited knowledge regarding meaningful change scores for the KOOS. In 2003, Roos and Lohmander[21] suggested that a change exceeding 8 to 10 points represented a clinically important improvement. However, interpretability characteristics of a PROM are considered to be context specific.[10,13] For the KOOS, MIC values have been investigated for patients receiving rehabilitation after a total knee replacement[17] and nonoperative treatment for knee osteoarthritis.[16,24] No previous studies have investigated meaningful change scores for the KOOS in patients undergoing an ACL reconstruction.

The purpose of this study, therefore, was to define MIC values for the KOOS for those who have undergone an ACL reconstruction, intended to be used for interpreting longitudinal change in KOOS subscale scores within one group of patients or between groups with responder analysis.

METHODS

Study Design and Setting

We designed a prospective cohort study using registry data and an additional survey mailed to patients included in the Norwegian Knee Ligament Registry (NKLR). The NKLR gathers nationwide data on patients undergoing ACL reconstruction. All public and private hospitals performing ACL reconstructions participated in the registry, and voluntary compliance has been >85% since 2006.[8] The NKLR received approval from the Norwegian data inspectorate as an expansion of the Norwegian Arthroplasty Register concession.[7] Postoperative results on the patients' perceptions of treatment outcome have been published previously.[11]

Participants

Data were collected in 2012. A questionnaire was sent to 1197 randomly selected patients who were at 3 different follow-up time points after surgery: 397 at 6 months (range, 5-7 months), 400 at 12 months (range, 10-14 months), and 400 at 24 months (range, 20-28 months) postoperatively. Patients who had undergone bilateral or revision ACL reconstruction were excluded. Individual patients' preoperative data were retrieved from the NKLR database.

Variables/Questionnaires

An explanatory letter, paper-based questionnaires, and a prepaid envelope were mailed to the patients. Reminders were sent after 2 months. Questionnaires included the KOOS and a set of anchor questions.

The KOOS includes 5 subscales: Pain, Symptoms, Activities of Daily Living (ADL), Sport and Recreational Function (Sport/Rec), and Knee-Related Quality of Life (QOL). Each KOOS item is scored from 0 to 4, and the total score for each subscale is transformed into 0 (worst) to 100 (best) scales. The 2012 rule for handling missing items was used, allowing calculation of subscale scores when >50% of these subscale items were answered.[20]

When determining meaningful change values, self-reported anchor questions are considered optimal for capturing patient perspectives on important changes in health status.[2,12,13] Domain-specific questions asking for the importance of the change experienced within separate domains, such as pain, symptoms, function, and quality of life, are suggested to improve the anchor's validity.[27] Thus, we used 5 anchor questions, one for each KOOS subscale. Patients rated their perceived importance of the experienced change on 7-point scales ranging from "worse, an important worsening" to "better, an important improvement." Two additional anchor questions were asked: (1) whether or not patients had achieved acceptable symptoms and, if not, (2) whether they considered the treatment to have failed.[11] Both questions were answered "yes" or "no" (see Appendix, Section 1, available in the online version of this article).

Statistics

Patient demographics are presented as means with 95% CIs around the mean for continuous variables and n (%) for categorical variables.

All analyses were performed on separate KOOS subscales. Patients were excluded from MIC analyses if a subscale score was missing preoperatively or postoperatively or if the corresponding anchor question was missing.

The anchors' validity was evaluated with Spearman's correlation coefficients between the KOOS change scores and the respective subscale-specific anchors. Due to inconsistency in the literature and several MIC methods

*Address correspondence to Lina Holm Ingelsrud, PT, MSc, Department of Orthopaedic Surgery, Hvidovre Hospital, Kettegaard Alle 30, 2650 Hvidovre, Denmark (email: lina.holm.ingelsrud@regionh.dk).
†Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark.
‡Department of Orthopaedic Surgery, Copenhagen University Hospital Hvidovre, Copenhagen, Denmark.
§Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam Public Health Research Institute, Amsterdam, the Netherlands.
‖Department of General Practice and Elderly Care Medicine, VU University Medical Center, Amsterdam, the Netherlands.
¶Department of Pain Management and Research, Division of Emergencies and Critical Care, Oslo University Hospital, Oslo, Norway.
#Oslo Sports Trauma Research Center, Norwegian School of Sport Sciences, Oslo, Norway.
**Department of Orthopaedic Surgery, Oslo University Hospital and Faculty of Medicine, University of Oslo, Norway.
††Department of Health Professions, Macquarie University, Sydney, Australia.
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applied,[5,19] no predefined correlation level was set prior to performing the analyses.

Statistical analyses were performed with R (version 3.2.1; R-project.org).

Anchor-Based MIC Methods

Anchor-based methods involve anchoring the PROM change score to an external measure of important change, such as a domain-specific anchor question. Several anchor-based MIC analyses have been proposed, using different statistical approaches to estimate the optimal cutoff for MIC.[2,13,19] In this study, the primary method was predictive modeling (MIC_{pred}) because it has been shown to be more precise compared with the frequently used receiver operating characteristic (ROC) method.[26] Simulations have shown that both the MIC based on ROC analysis and the MIC_{pred} identify the mean of the hypothesized latent individual MICs in a sample when the proportion of improved patients is 50% and the scores are normally distributed. Both MICs will be biased when the proportion of improved patients differs from 50%, which is the case after ACL reconstruction where a larger proportion commonly reports improvement. However, predictive modeling allows for the adjustment of proportions improved other than 50%.[25] To enable comparison with more traditional methods, we also applied the mean change method ($MIC_{Mean-Change}$)[12] and the ROC method (MIC_{ROC}).[6] Detailed descriptions of these MIC calculation methods are presented in the online Appendix. MIC analyses were performed on pooled data from the 6-, 12-, and 24-month postoperative time points.

KOOS Mean Change Scores for Patients Reporting Acceptable Symptoms or Treatment Failure

Mean KOOS change scores were calculated for patients responding "yes" to having "acceptable symptoms" and, if not, "yes" to considering the treatment to have failed. If patients answered "no" to having achieved "acceptable symptoms" and "no" to "treatment failure," they were categorized as an "undecided" intermediate group.

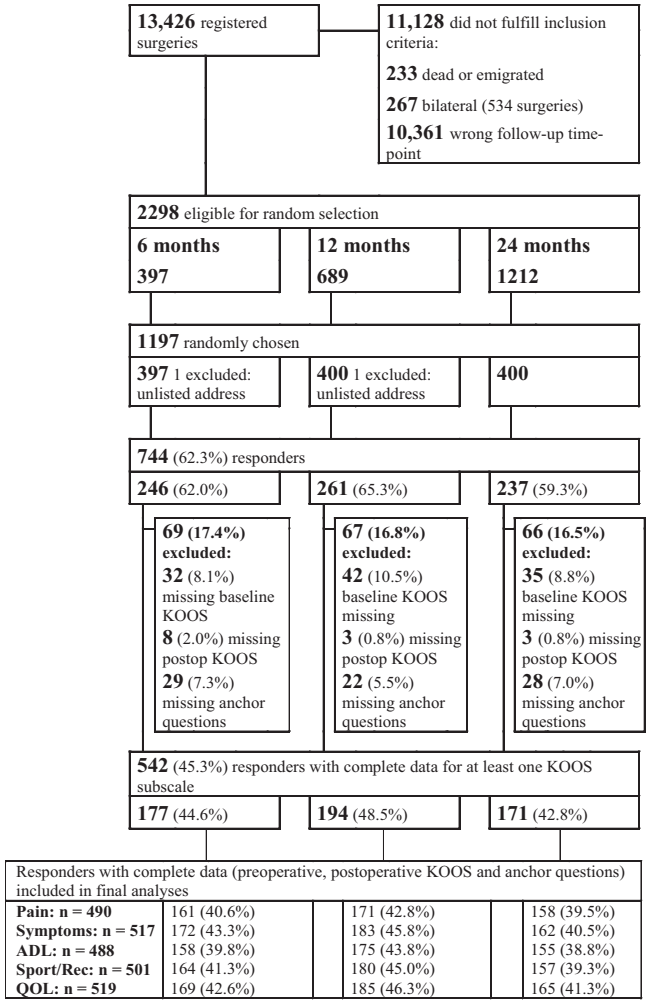
Sensitivity Analyses

To investigate the impact of time from surgery, adjusted MIC_{pred} analyses were stratified for the 6-, 12-, and 24-month follow-up subgroups. In addition, since previous studies have presented baseline-dependent MIC values,[5] we investigated the effect of preoperative severity. Preoperative KOOS scores were included as interaction terms in the MIC_{pred} analyses and considered to be effect modifiers if P values were $<.05$.

RESULTS

Participants

Of the total 1197 randomly selected patients, 744 (62.3%) replied. Of those who replied, 202 (27.2%) were excluded from further analyses due to lack of any preoperative KOOS subscale score or not answering any KOOS subscale or anchor questions postoperatively. As a result, the number of patients differed between subscales (Figure 1).



Responders with complete data (preoperative, postoperative KOOS and anchor questions) included in final analyses			
Pain: n = 490	161 (40.6%)	171 (42.8%)	158 (39.5%)
Symptoms: n = 517	172 (43.3%)	183 (45.8%)	162 (40.5%)
ADL: n = 488	158 (39.8%)	175 (43.8%)	155 (38.8%)
Sport/Rec: n = 501	164 (41.3%)	180 (45.0%)	157 (39.3%)
QOL: n = 519	169 (42.6%)	185 (46.3%)	165 (41.3%)

Figure 1. Study flow diagram. ADL, Activities of Daily Living; KOOS, Knee injury and Osteoarthritis Outcome Score; QOL, Knee-Related Quality of Life; Sport/Rec, Sport and Recreational Function.

Baseline Characteristics and Descriptive Data

Included patients had a mean (SD) age of 29.9 years (11.6 years), and 52.6% were women. Responders with complete data were older and more were female than the responders without complete data and nonresponders combined. However, CIs around the mean presurgery KOOS scores overlapped widely (Table 1).

The percentages of patients reporting being importantly improved ranged from 71.3% to 78.7% and being unchanged ranged from 15.1% to 22.3% across the 5 KOOS subscales (Figure 2).

The percentages of deteriorated patients ranged from 3.9% to 10.4%. Due to the comparatively small number of deteriorated patients, MIC deterioration analyses were

TABLE 1
Preoperative Characteristics for Responders With Complete Data for at Least 1 KOOS Subscale, Responders Without Complete Data, and Nonresponders[a]

	Responders With Complete Data Set for at Least 1 KOOS Subscale (n = 542), Mean ± SD[n]	Responders Without Complete Data Set (n = 202), Mean ± SD[n]	Nonresponders (n = 453), Mean ± SD[n]
Female, n (%)	285 (52.6)	97 (48.0)	158 (34.9)
Age, y	29.9 (28.9-30.9)	28.5 (26.8-30.1)	27.4 (26.5-28.3)
KOOS Pain	72.4 (70.7-74.1)^{515}	74.4 (69.9-78.8)^{89}	71.6 (69.5-73.8)^{349}
KOOS Symptoms	71.1 (69.5-72.7)^{530}	74.0 (70.2-77.8)^{91}	71.4 (69.4-73.3)^{359}
KOOS ADL	81.7 (80.0-83.4)^{508}	81.4 (76.9-85.9)^{87}	80.2 (78.1-82.3)^{346}
KOOS Sport/Rec	40.2 (37.8-42.5)^{518}	46.4 (40.0-52.9)^{87}	42.6 (39.8-45.4)^{351}
KOOS QOL	33.9 (32.4-35.4)^{535}	35.3 (30.8-39.8)^{91}	35.2 (33.3-37.0)^{366}

[a]The number of patients included in each analysis varies due to degree of missing data. The actual numbers included in the Knee injury and Osteoarthritis Outcome Score (KOOS) analyses are presented as superscript n (^{n}) for each mean (95% CI) calculated. ADL, Activities of Daily Living; QOL, Knee-Related Quality of Life; Sport/Rec, Sport and Recreational Function.

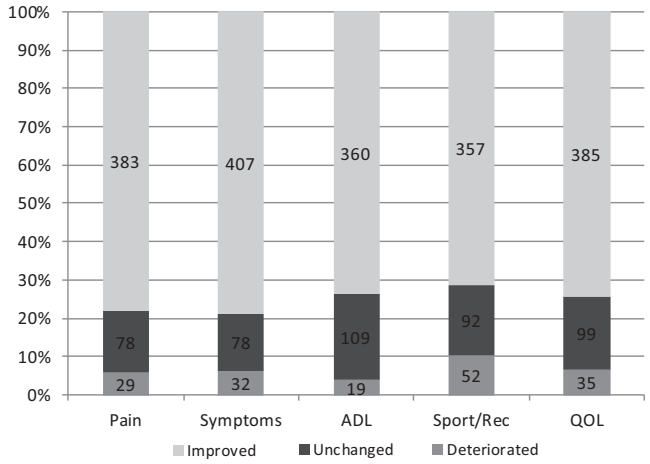


Figure 2. Percentages of improved, unchanged, or deteriorated patients for each Knee injury and Osteoarthritis Outcome Score subscale are given on the y-axis. Numbers given in each column represent the number of patients reporting to be improved, unchanged, or deteriorated. ADL, Activities of Daily Living; QOL, Knee-Related Quality of Life; Sport/Rec, Sport and Recreational Function.

not performed. KOOS mean change scores for each anchor response category ranging from better to worse are presented in Figure 3.

MIC Improvement Values

The correlations between anchor questions and KOOS change scores were 0.53 for QOL, 0.41 for Sport/Rec, 0.39 for Symptoms, and 0.32 for Pain and ADL.

MIC_{pred} improvement (95% CI) values were 12.1 (9.3 to 14.8) for Sport/Rec and 18.3 (16.0 to 20.6) for QOL (Figure 4 and Table 2), when calculated using pooled data from patients at 6, 12, and 24 months postoperatively and adjusted for the proportions of improved patients. The corresponding values for Pain, Symptoms, and ADL were 2.5 (0.4 to 4.5), –1.2 (–3.2 to 0.8), and 2.4 (0.7 to 4.1), respectively.

Sensitivity analyses performed separately on the 6-, 12-, and 24-month postoperative scores resulted in nonsignificant differences of less than 2.4 points in adjusted MIC_{pred} values (see the online Appendix, Section 3). Furthermore, preoperative KOOS scores interacted nonsignificantly with KOOS change in the predictive modeling analyses (data not shown), suggesting no baseline dependency of MIC_{pred} values.

$MIC_{MeanChange}$ values were higher than MIC_{pred} values for all subscales (Figure 4 and Table 2). Due to generally flattened ROC curves and low areas under the curves, selecting the best ROC cutoff point was highly affected by minor chance fluctuations in the sample (see the online Appendix, Section 4).

MIC Values in Comparison With KOOS Mean Change Scores for Patients With Acceptable Symptoms and Treatment Failure

To put MIC_{pred} values in context, we compared them with other longitudinal and cross-sectional determinants of outcome after ACL reconstruction. MIC_{pred} values were smaller than KOOS mean change scores for patients reporting important improvements and for those reporting acceptable symptoms after surgery. For Sport/Rec and QOL, MIC_{pred} values were similar to mean change scores for patients who were undecided about treatment outcome but larger than those for patients experiencing no important changes (Figure 4 and online Appendix, Section 5).

DISCUSSION

Summary of Findings

This study proposes estimates for the interpretation of meaningful improvement in KOOS scores after an ACL reconstruction. We found that these estimates are not

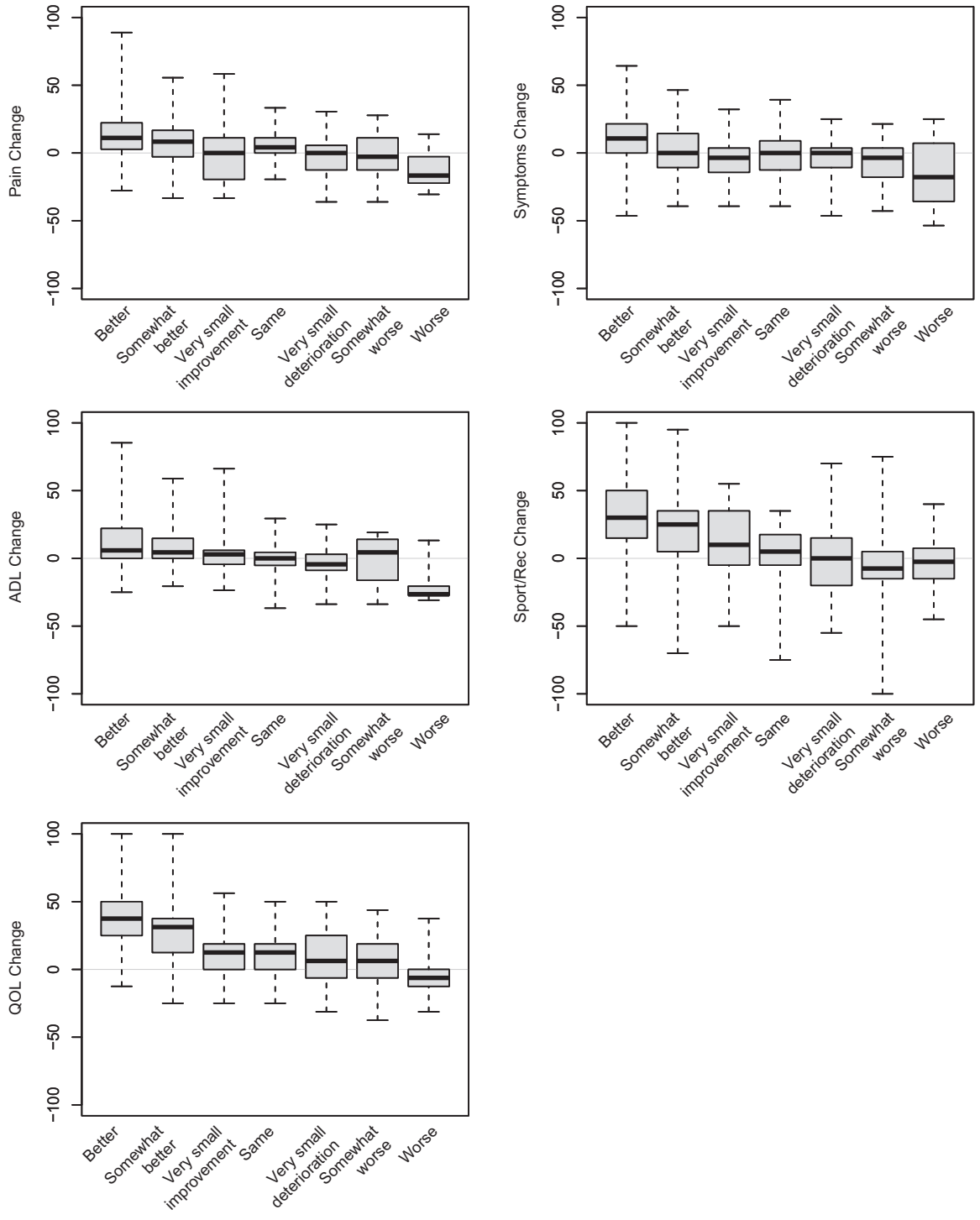


Figure 3. Knee injury and Osteoarthritis Outcome Score (KOOS) mean change scores by anchor question response category, ranging from better to worse. Horizontal bars represent the median, the box represents the interquartile range, and the whiskers represent the highest and lowest scores. ADL, Activities of Daily Living; QOL, Knee-Related Quality of Life; Sport/Rec, Sport and Recreational Function.

dependent on the time to follow-up and, therefore, can be applied 6 to 24 months after ACL reconstruction. The MIC values for the subscales Pain, Symptoms, and ADL were lower (–1.2 to 2.5) due to, on average, only mild problems preoperatively (mean subscale scores, 71-82), suggesting limited room for postoperative improvement

TABLE 2
MIC Improvement Values Obtained by Predictive Modeling Adjusted for Percentages of Improved Patients and by the Mean Change Method[a]

	Predictive Modeling MIC		Mean Change MIC	
KOOS	MIC_{pred}[b]	95% CI[c]	$MIC_{MeanChange}$	95% CI[d]
Pain	2.5	0.4 to 4.5	7.9	4.8 to 11.1
Symptoms	–1.2	–3.2 to 0.8	1.2	–1.7 to 4.1
ADL	2.4	0.7 to 4.1	8.1	4.9 to 11.2
Sport/Rec	12.1	9.3 to 14.8	21.7	17.3 to 26.2
QOL	18.3	16.0 to 20.6	27.3	24.3 to 30.3

[a]ADL, Activities of Daily Living; KOOS, Knee injury and Osteoarthritis Outcome Score; MIC, minimal important change; QOL, Knee-Related Quality of Life; Sport/Rec, Sport and Recreational Function.
[b]MIC_{pred} values are adjusted for the proportion of improved patients.
[c]95% CI calculated using 1000 bootstrap replications, reported as 0.025-0.975 quantiles.
[d]95% CI calculated as $Mean_{change} \pm 1.96\left(\frac{SD_{change}}{\sqrt{n}}\right)$.

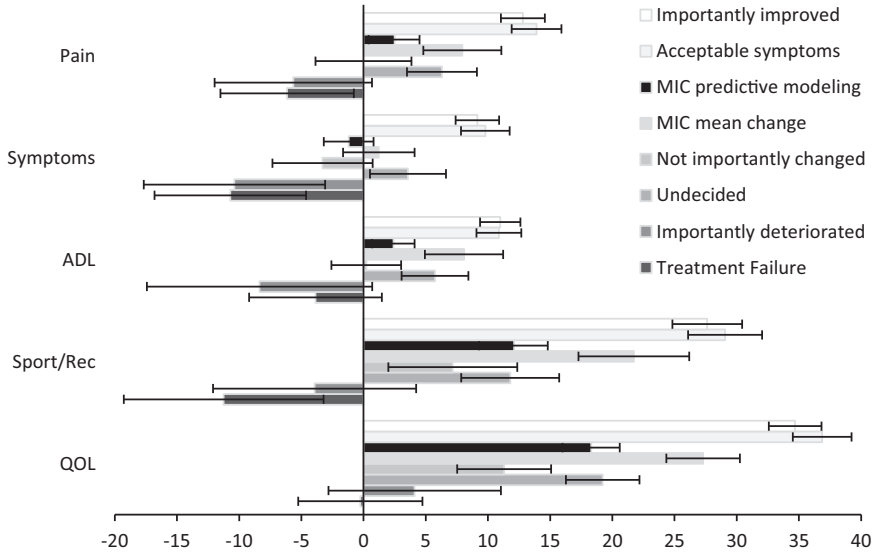


Figure 4. Minimal important change (MIC) values in comparison to other determinants of outcome after anterior cruciate ligament (ACL) reconstruction for the 5 Knee injury and Osteoarthritis Outcome Score (KOOS) subscales. Predictive modeling MIC values and mean change MIC values are compared with mean change scores for patients who report to be ''importantly improved,'' ''importantly deteriorated,'' or ''unchanged'' and mean change scores for patients reporting ''acceptable symptoms'' or being ''undecided'' regarding the outcome after ACL reconstruction. Error bars represent 95% CI.

compared with Sport/Rec and QOL with preoperative mean scores of 40 and 34, respectively (Table 1). However, the proportions of patients who consider themselves importantly improved on the subscales of Pain, Symptoms, and ADL are comparable with the subscales Sport/Rec and QOL, implying that the correspondingly smaller MIC values may still be a true reflection of what the average patient considers to be a minimal important improvement. While it is important to acknowledge that some ACL-injured patients actually report problems with pain, other symptoms, and ADL function, the overall limited room for improvement on the Pain, Symptoms, and ADL subscales with treatment confirms the previous recommendation to use the KOOS subscales Sport/Rec and QOL as primary outcomes after ACL reconstruction.[1]

Comparison of 3 Different MIC Methods

Different MIC analysis methods resulted in quite different MIC values. In line with previous simulation studies, predictive modeling was more precise than the ROC and mean change methods, giving smaller 95% CIs around the MIC values.[25,26] Other benefits of predictive modeling are the reduced sensitivity to low correlation with the anchor question and the capacity to adjust when the proportions of improved patients differ from 50%.[25]

Due to the low to moderate correlations, however, comparable with those observed in other studies,[16,27] we found that using the Youden principle for defining the "best" ROC cutoff point gave somewhat arbitrary MIC_{ROC} values because a large range of cutoff points was associated with approximately the same relatively large degrees of misclassification. MIC_{ROC} values are not recommended for further use but are presented in the online Appendix for those with a methodological interest.

We found larger $MIC_{MeanChange}$ than adjusted MIC_{pred} values for all subscales, which is to be expected because the adjusted MIC_{pred} reflects the mean of the individual MICs in a sample, whereas the $MIC_{MeanChange}$ represents the mean change score of a subgroup whose perceived change has exceeded its individual MICs.[26] $MIC_{MeanChange}$ values are considered less credible because the calculations are based on subgroups of patients, while the MIC_{pred} values are calculated using the whole patient sample.[26,27] In addition, the mean change method is dependent on a reasonable correlation between the change in score and the anchor item. Furthermore, since $MIC_{MeanChange}$ is the mean change in the subgroup of patients having minimal important improvement, assuming normally distributed data, only half of the patients who reported a minimal important improvement would actually be characterized as responders. Hence, $MIC_{MeanChange}$ is considered less suitable to define responders.[15]

Further investigation is needed to confirm whether the predictive modeling approach is capable of producing reliable MIC values in circumstances where the ROC and mean change methods are inappropriate due to the scores' distributional characteristics, low correlation between change in score and anchor question, and, especially after surgical treatment, the proportion of improved patients is greater than 50%.

Comparison With Previous Studies

Three previous studies have proposed MIC estimates for the KOOS in older populations with knee osteoarthritis undergoing rehabilitation, all of which have used the ROC and/or mean change methods.[16,17,24] These studies differ from our study with regard to patient group, intervention, and MIC methodology used. Since MIC values are context specific, it is less meaningful to compare the current MIC values determined in young adults with surgically reconstructed ACL-deficient knees with those obtained in studies of older and less physically active people having had their knee joints replaced.

Understanding the MIC Concept Relative to Other Outcome Cutoff Points

To facilitate the understanding of how the MIC concept relates to other relevant cutoff points for interpreting outcomes from an intervention, we displayed MIC_{pred} and $MIC_{MeanChange}$ values together with mean KOOS change scores for those reporting different levels of change postoperatively and for those who reported acceptable postoperative symptoms, who considered the treatment a failure, or who were undecided about their treatment outcome (Figure 4). The finding that mean changes in KOOS scores were approximately similar for patients reporting acceptable symptoms postoperatively and for patients reporting important improvements on the anchor items after surgery implies that reporting acceptable symptoms corresponds to perceiving an important improvement after ACL reconstruction. We consider it important to acknowledge that these values do not represent an optimal postoperative outcome or readiness to return to sport.

Another explanation for the similarity in mean change scores in those having acceptable postoperative symptoms and those being importantly improved is that patients value their postoperative state more than the actual change when responding to the anchor questions. In line with previous research, the anchor questions in this study correlated more with the postoperative KOOS scores than with the KOOS change scores (see the online Appendix, Section 6), which could be caused by response shift and recall bias.[13,23] When responding to the anchor questions, patients are required to retrospectively consider to what degree their state has changed and make a judgment of importance. The response shift theory implies that patients may change their criteria for how they judge their own state, leading to paradoxical responses to the anchor response questions when compared with the degree of score change found in the PROM.[23] One such example could be if a patient presented with an unchanged KOOS Sport/Rec score but still reported to be importantly improved. Recall bias implies that patients may not remember their initial state and consequently base their judgment of important change on their postoperative state more than on the actual change.[13] To what degree recall bias and response shift affect the MIC estimations is unclear.[13,23]

Limitations

This study is limited by the low response rate, with less than half of the randomly selected patients included in the final analyses. The responders were older and more often female, which may limit the generalizability of our results to the younger, male ACL-reconstructed population. However, the mean age difference was only 2 years. In support of the preoperative differences being negligible, CIs around the mean preoperative KOOS scores overlapped widely (see Table 1), suggesting that responders and nonresponders did not differ with respect to their knee-specific functional states.

Another limitation is that even though 4% to 10% of patients reported worse outcomes for the 5 KOOS subscales after surgery, we were not able to estimate MIC values for deterioration. We have previously reported that when asked postoperatively, approximately 10% considered the ACL reconstruction to have failed, and their KOOS scores corresponded to moderate to severe problems on average.[11] A responder analysis from a randomized controlled trial should present both the proportion of importantly improved and the proportion of importantly deteriorated patients to help interpret treatment effects.[9] In theory, 2 treatments could result in the same rates of importantly improved patients, but 1 treatment presents a larger proportion of importantly deteriorated patients,

which is an important aspect to include in shared decision making.

Finally, even though our findings suggest no baseline dependency of MIC_{pred} values, further adjustment using more elaborate methods for proportions of patients who reported being improved may result in differences between severity subgroups in adjusted MIC_{pred} values. Nevertheless, the proposed MIC_{pred} estimates are considered applicable for interpreting group-level results for the ACL-reconstructed population.

Implications of Findings

The presented MIC values of 12.1 for Sport/Rec and 18.3 for QOL can aid in interpreting average within-group improvements and in defining responders (ie, individuals who experience an adequate treatment effect). A responder analysis facilitates the interpretation of results from clinical trials by presenting the proportion of responders in each group.[10,15,18] In a clinical context, the individual patient is capable of defining what is important to him or her,[13] although the MIC values may serve as references to what the "average patient" undergoing an ACL reconstruction would deem important. Due to the smaller room for improvement for the average patient after an ACL reconstruction on the subscales Pain, Symptoms, and ADL, the content validity for these subscales may be questioned, and we do not consider the estimates useful for interpreting within-group change over time, nor as responder criteria. Based on this study, we are not able to recommend estimates for future sample size calculations or interpretation of difference in mean change scores between groups of patients. Such minimal important difference values are much more complex to derive, involving not only perceived changes in pain and functional status but, more important, value judgments about the costs and risks involved in the comparison treatments.[22]

CONCLUSION

In conclusion, we found that meaningful score changes vary across KOOS subscales. MIC values calculated with predictive modeling were 12.1 for Sport/Rec and 18.3 for QOL. Predictive modeling yielded more robust MIC estimates than the ROC and the mean change methods. Our findings confirm the previous recommendation that after ACL reconstruction, the KOOS subscales Sport/Rec and QOL are preferred as primary outcomes.

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