

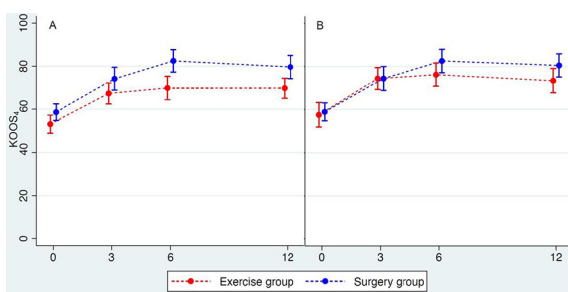
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Purpose: Knee injury, including meniscal tear, is a major risk factor for developing osteoarthritis. Although surgery is a common treatment of meniscal tears, no randomized controlled trials (RCTs) have compared surgery with non-surgical alternatives in young adults with a meniscal tear. We aimed to determine whether a strategy of early meniscal surgery was superior to a strategy of exercise and education with the option of surgery later in young adults with a meniscal tear in terms of pain, function, and quality of life.

Methods: This was a pragmatic, parallel-group, multicenter, RCT recruiting young adults (18–40 years) with MRI-verified meniscal tears eligible for meniscal surgery from seven Danish hospitals between January 26, 2017 through to December 4, 2019 (ClinicalTrials.gov NCT02995551). Primary endpoint was at 12 months with additional follow-ups at 3 and 6 months. Patients were randomized (1:1, by central study coordinator, stratified by hospital and sex) to surgery (partial meniscectomy or meniscal repair) or a strategy of 12-weeks supervised exercise therapy (two 60–90-minute sessions weekly) and 30–45min of patient education with the option of surgery later if needed. The primary outcome was difference in change from baseline to 12 months in the mean score of four Knee Injury and Osteoarthritis Outcome Score subscales, covering pain, symptoms, function in sport and recreation, and quality of life (KOOS₄ scale: 0 (worst) to 100 (best)). Intention-to-treat and per-protocol analysis were conducted. Per-protocol analysis excluded patients randomized to exercise therapy but participating in <18 of 24 exercise sessions or crossing over to surgery, and patients not having surgery in the surgery group.

Results: Out of the 121 young adults enrolled (mean age 29.7 years, 28% women, 60 allocated to surgery group), 107 patients (88%) completed the 12-month follow-up, 16 (26%) from the exercise group had meniscal surgery, while 8 (13%) from the surgery group did not have surgery. In total, 36 (59%) patients attended 18 or more of 24 exercise sessions. Both treatment groups experienced clinically relevant improvements (10 points or more on KOOS₄). The intention-to-treat analysis did not demonstrate a statistically significant difference in change between groups from baseline to 12 months in KOOS₄ (19.2 vs. 16.4 in surgery vs. exercise group; adjusted mean difference, 5.4 [95% CI, -0.7 to 11.4]; Figure 1A), with similar results in the per-protocol analysis (Figure 1B). No difference in serious adverse events was observed (4 in surgery vs. 7 in exercise group, $p=0.40$).

Conclusions: In a group of young, active adults with meniscal tears, our results suggest that a strategy of early meniscal surgery was not superior to a strategy of exercise and education with the option of later surgery. Both groups experienced clinically relevant improvements and one in four patients from the exercise group underwent surgery, suggesting that both treatment strategies could be viable and effective options in clinical practice. Our study therefore highlights that decisions on treatment of meniscal tears in young adults should include patient preferences and values.



V-16

SPONTANEOUS HEALING OF THE RUPTURED ANTERIOR CRUCIATE LIGAMENT: OBSERVATIONS FROM THE KANON TRIAL

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Purpose: Anterior cruciate ligament (ACL) rupture is a strong risk factor for the development of knee osteoarthritis, irrespective of management with ACL reconstruction (ACLR) or rehabilitation alone. Poor long-term physical and psychological outcomes are common. It is often assumed that a ruptured ACL cannot heal without surgery, despite a paucity of studies investigating the potential for a ruptured ACL to heal. It is not known if ACL healing on MRI is associated with restoration of knee function or favorable outcomes. The objectives were to: 1) Report the proportion of participants with 'ACL healing' as visualized on MRI in the first 5 years following acute ACL rupture 2) Describe 2- and 5-year outcomes stratified by ACL healing status and treatment 3) Investigate the relationship between ACL healing, patient-reported sport/recreational function and knee-related quality of life (QOL) at 2 and 5 years following acute ACL injury

Methods: This secondary analysis used KANON Trial (ISRCTN84752559) data from participants randomized to rehabilitation and optional delayed ACLR (n=54), or early ACLR (n=62). The Anterior Cruciate Ligament OsteoArthritis Score (ACLOAS) was used to grade ACL healing status (a healed ACL was defined as a normal (grade 0), thickened/high signal but continuous (grade 1) or thinned/elongated but continuous (grade 2) appearance on MRI). Two- and five-year outcomes included the Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales (score range 0 to 100 (best)), Tegner Activity Scale, mechanical knee stability (pivot-shift test) and radiographic osteoarthritis (graded according to the Osteoarthritis Research International atlas, equivalent to Grade 2 on the Kellgren Lawrence Scale). The proportion of participants meeting KOOS criteria for patient acceptable symptomatic state (PASS) and treatment failure at 2 years were reported. The relationship between healing status, KOOS-Sports/Rec and KOOS-QOL was explored using mixed linear regression models adjusted for age, sex, smoking, baseline KOOS values, and unmeasured person-specific time-invariant confounding.

Results: Using our definition of ACL healing (ACLOAS grade 0–2), 76%, 56% and 58% of participants managed with rehabilitation alone had a healed ACL at 1-, 2- and 5-year follow-ups, respectively. In participants who were managed with rehabilitation alone at 5-year follow-up (n=24), 38% had a normal ACL appearance (ACLOAS grade 0) on MRI at 1 year, 30% at 2 years and 33% at 5 years. One in twenty-three (4%) participants who crossed over to delayed ACLR had a normal ACL appearance at any timepoint. Participants with a healed ACL reported high KOOS subscale scores at 2- and 5-year follow-up (Table 1). The proportion of participants with a healed ACL meeting the PASS threshold within a given KOOS subscale ranged from 67 to 93%, and no individuals met the criteria for treatment failure (Table 1). In the other groups, 31 to 61% met the PASS criteria and 0 to 17% met the criteria for treatment failure (Table 1). Tegner Activity Scores were similar between groups at 2 and 5 years. At 2 years, 73% (n=11) of the healed ACL group had a mechanically stable knee, compared to 50% (n=6) in the non-healed group, 92% (n=22) following delayed ACLR and 100% (n=60) after early ACLR (Table 1). Two (14%) participants in the healed ACL group had tibiofemoral OA at 5 years, compared to 1 (10%) in the non-healed, 1 (3%) in the delayed ACLR and 9 (15%) in the early ACLR group. One (7%) participant in the healed ACL and 1 (10%) in the non-healed ACL group had patellofemoral OA, compared to 6 (21%) participants in the delayed ACLR and 14 (24%) in the early ACLR group. The estimated between group differences in KOOS subscales suggest better outcomes in the healed group for both subscales at 2 years (mean difference (95% CI) in KOOS Sport/Rec in non-healed: -21.9 (-38.8, -5.0), delayed ACLR: -25.0 (-39.8, -10.1), early ACLR: -18.0 (-31.5, -4.5); mean difference (95% CI) in KOOS QOL in non-healed: -26.9 (-41.7 to -12.1), delayed ACLR: -19.4 (-32.3, -6.4), early ACLR: -13.9 (-25.6, -2.1)). At 5-year follow-up, the 95% CIs exclude the possibility that non-healed, delayed ACLR or early ACLR groups had better KOOS Sport/Rec or QOL scores compared to the

healed ACL group, and do not rule out clinically relevant differences in favour of the healed ACL group.

Conclusions: Spontaneous healing of a ruptured ACL was common amongst participants managed with rehabilitation alone. Participants with a healed ACL at 2 years, reported better KOOS Sport/Rec and KOOS QOL scores compared to the non-healed, delayed ACLR and early ACLR groups consistent with small to very large effects. To determine the relationship between ACL healing and osteoarthritis development, larger studies and longer follow-up are needed. The spontaneous healing potential of an acutely injured ACL should be considered in the choice of treatment strategy after acute ACL injury.

Table 1. Two- and five-year outcomes stratified by ACL healing status as visualized on MRI and ACL management strategy. The table shows mean ± SD and n (%) for various KOOS subscales across different ACL healing and management groups at 2 and 5 years.

Table 1. Two- and five-year outcomes stratified by ACL healing status as visualized on MRI and ACL management strategy. Data represent mean ± standard deviation or count (n). Mechanically stable = a mechanically stable knee defined as a pivot-shift grade 0 (normal mechanical stability (normal)) or grade 1 (nearly normal mechanical stability (+, glide)).

Table 2. Adjusted mean differences in KOOS Sport/Rec and KOOS QOL between ACL-healed and the other three groups, at 2- and 5-year follow-up. The table shows mean differences and 95% confidence intervals for KOOS Sport/Rec and KOOS QOL at 2 and 5 years.

Table 2. Adjusted mean differences in KOOS Sport/Rec and KOOS QOL between ACL-healed and the other three groups, at 2- and 5-year follow-up

The model includes the exposure (healing/treatment status), time point (1, 2 or 5 years), their interaction, baseline value of the KOOS subscale, and potential confounders (age, sex, smoking status)

V-17 PREDICTION MODELS TO ESTIMATE FUTURE INDIVIDUAL RISK OF OSTEOARTHRITIS IN THE GENERAL POPULATION: A SYSTEMATIC REVIEW

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Purpose: The need for health systems to shift from late, reactive care of osteoarthritis (OA) to earlier, preventative strategies is widely acknowledged. Rigorously derived and validated models capable of predicting future individual-level risk of OA incidence in the general population, based on affordable and easily accessible sources of data, could play an important role in this endeavour. Our objective was to critically synthesise published evidence on the performance of multi-variable prediction models for OA incidence and their applicability to large-scale use in the general population.

Methods: For this systematic review with narrative synthesis, we searched MEDLINE, EMBASE and Web of Science from inception to November 2020, and supplemented this with reference list screening, citation searches, and hand-searches. We included longitudinal studies conducted in a general population sample that reported the derivation, comparison, or validation of a multivariable prediction model to predict individual risk of future OA incidence, defined by recognised clinical or imaging criteria. We excluded studies reporting prognostic models in populations with prevalent OA at baseline and those with joint

arthroplasty as the sole outcome. Pairs of reviewers independently performed article selection, data extraction, and risk of bias assessment using PROBAST. We summarised evidence on model performance and calibration, as well as describing the types of predictors included in final models and how they were assessed. Our review was prospectively registered on PROSPERO (CRD42020220446).

Results: Of 6,462 records identified, 21 original research articles published between 2010–2020 were eligible and included (Table 1). From these we extracted data on 26 final multivariable prediction models for incident knee OA (18), hip OA (4), hand OA (3), and any-site OA (1). The most common outcome was incident OA defined by plain radiography. Other outcomes included first OA diagnosis in the electronic health record, symptomatic radiographic OA, frequent pain in the target joint, and American College of Rheumatology clinical classification criteria. The median prediction horizon was 8 years (range 2 to 41 years), median number of participants/joints with the outcome of interest was 99 (range 27 to 12,803), and the median number of predictors included in the final models was 5.5 (range 3 to 13). Models used multiple modes of assessment for predictors (self-report (25 models), physical examination (21), imaging (12), urinary/serum biomarkers (6), electronic health record (2)). Age, body mass index (BMI), previous injury, and (occupational) physical exposures were commonly included predictors but there was heterogeneous predictor measurement within most domains and the majority of predictor variables were included in only a single final model. Beyond age, sex, and occupational exposures, educational level was the only other social stratifier, which was included in 5 final models. No final models included race/ethnicity, indicators of individual socioeconomic position, or measures of area-level deprivation. All except 3 final models used either internal validation processes, e.g. cross-validation/bootstrapping (14), external validation in a separate cohort (7), or both (2). Model performance for 25 of the 26 models was presented by Area under the Curve (AUC). Median performance for knee, hip and hand OA was 0.72, 0.76, 0.62, respectively. The one model for any-site OA had an AUC of 0.84. All but one model was judged to have high overall risk of bias. Common reasons for this were the use of univariate analysis in predictor selection and lack of accounting for competing risks. Many models also lacked credibility for large-scale use in the general population, for instance by requiring imaging, or restricting model derivation to a specific subpopulation.

Conclusions: Of the 21 studies found and included in our review, 15 were published within the past 4 years, suggesting increasing interest among researchers in predicting individual-level risk for OA. The widespread use of internal and external validation is encouraging and in general the level of discrimination appears comparable to established risk prediction models for cardiovascular outcomes. However, models published to date remain heavily focussed on knee OA and have relied on a relatively small number of underlying cohort datasets. A relative lack of OA-relevant predictors and outcomes recorded in routine datasets may be one reason for this. Furthermore, our systematic review highlights common shortfalls in applicability, suggesting that many models are not designed (nor yet intended) for mass application. Future studies could be enhanced with the standard inclusion of key social stratifiers (e.g. race/ethnicity) to explicitly encourage an equity lens in this field, and by greater patient, public, and stakeholder involvement with a view to clarifying and strengthening intended 'real-world' application.

Table with 10 columns: First Author, Year, Study Type, Disease, Country, OA Site of Prediction, Prediction Horizon (Max), No. Predictors in Final Model, No. of Participants (n), Performance AUC (95% CI), Validated Internal (Y/N). Rows include studies like Zhang 2010, Kline 2012, Knapik 2014, etc.

* Certain studies had follow-up at interim intervals; † p < 0.05 level of interest; ‡ n represents 985 knees included, of which 189 knees developed outcome; § RF internal validation was performed; ¶ this knee was not presented