Total knee replacement or non-surgical therapy for osteoarthritis of the knee?

Skou ST, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, Rasamussen S. (Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense; Clinical Nursing Research Unit and Orthopedic Surgery Research Unit, Aalborg University Hospital, and Center for Sensory–Motor Interaction, Department of Health Science and Technology, Faculty of Medicine, and Department of Clinical Medicine, Aalborg University, Aalborg, Denmark.) A randomized, controlled trial of total knee replacement. *N Engl J Med* 2015;**373:**1597–605.

SUMMARY

Skou *et al*. screened 1475 patients and randomized 100 patients with 'moderate to severe' osteoarthritis who were 'eligible' for unilateral knee replacement to undergo total knee replacement (TKR) followed by 12 weeks of non-surgical treatment (TKR group) or to receive only 12 weeks of non-surgical treatment (non-surgical treatment group). Non-surgical treatment was administered in a manner similar to both groups by physiotherapists and dieticians. It essentially consisted of education, exercise, dietary advice, use of insoles and pain medication. Participants were eligible if they had radiologically confirmed knee osteoarthritis (i.e. a score $\geq$2 on the Kellgren–Lawrence [KL] scale) and were judged to need TKR by 1 of the 9 experienced orthopaedic surgeons at one of the two public outpatient clinics. They were excluded if they had previously undergone TKR or if they had 'a higher than 60 mm' (on a 100 mm visual analogue scale) knee pain during the previous week.

The authors primarily looked at the between-group difference in change from baseline to 12 months in the mean score on the four Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales, evaluating pain, symptoms, activities of daily living, and quality of life (KOOS4). Five secondary outcomes included change from baseline to 12 months in (i) scores on all five KOOS subscales (KOOS4 plus subscale covering function in sports and recreation); (ii) the timed up and go test; (iii) general health assessment with three-level version of the EurQol Group 5-Dimension Self-Reported Questionnaire (EQ-5D); (iv) weight (in kg); and (v) type, dose and quantity of pain medication taken during the previous week. Adverse events and serious adverse events during the 12 months of follow-up were identified as those involving the index knee, or sites other than the index knee, and recorded.

Twenty-six per cent of patients in the non-surgical treatment group underwent TKR before the 12 months of follow-up while 2% (1 patient) in the TKR group received only non-surgical treatment. In the intention-to-treat analysis, the TKR group showed greater pain relief and functional improvement evident in better KOOS scores compared to the non-surgical group. The TKR group had significantly greater improvements measured on all the five secondary outcomes. The results were similar for per-protocol analysis in terms of primary as well as most secondary outcomes. The efficiency of TKR was further reinforced by the analysis that showed that the number needed-to-treat with TKR for a 15% improvement from baseline to 12 months in KOOS was 5.7. TKR had a higher number of serious adverse events related as well as unrelated to the index knee.

COMMENT

TKR has evolved as a successful and cost-effective intervention for end-stage osteoarthritis of the knee joint. With increased life expectancy and a burgeoning elderly population, the prevalence of knee arthritis and the demand for TKR is on the rise. Over 670 000 TKRs are performed annually in the USA alone where the numbers of knee replacement have risen dramatically; over 7-fold in nearly 35 years.

In spite of the huge popularity of TKR, there is paucity of level 1 studies comparing the effectiveness of TKR vis-a-vis non-surgical interventions for osteoarthritis of the knee.

This unique trial underscores several important points. That non-surgical interventions are effective in the management of osteoarthritis of the knee has been amply shown previously although the effectiveness may vary in different populations depending on the stage of the disease. This study cautions that greater relief in pain and better improvement of function comes with an increased risk of adverse events. It is likely that this study had a fast-track review, which missed some of the finer details, or their absence.

Rates of TKA vary widely as there are no defined indications.[1] Inclusion criteria for the current study included KL grade 2 or more. KL grade 2 knee (5 patients in the non-surgical group and 7 in TKR—a total of 12% patients in the study) is confirmed to be osteoarthritic and does not merit a title 'moderate to severe'. Also, for the inclusion in the study, a patient should not have had a VAS

score of >60 mm during the previous week. While the rationale for selecting patients with mild-to-moderate pain only (?selection bias) is not clear, the table outlining baseline characteristics reveals that the VAS scores for both groups were well over 60 at the time of inclusion in the study. More than two-thirds of patients in the TKR group and more than half in the non-surgical group had not taken any pain medication in the past week before inclusion! Pain certainly did not figure as an important inclusion criterion, thus skewing the study towards greater acceptance of non-surgical treatment and possibly better results. Although lacking consensus, some authors have surmised that patients with more preoperative pain have greater improvement in pain and functional score than patients with less preoperative pain.[2] Cross *et al*.[3] studied indications for TKR among orthopaedic surgeons, rheumatologists and primary care providers and evaluated 27–42 different patient factors. 'Pain not responsive to drug therapy' was the only factor with consensus for TKR. Though pain relief was reportedly more in the TKR group, no data have been furnished about any difference in consumption of analgesics between the groups. Also, the literature is replete with reports about the association of preoperative comorbid conditions with worse outcome following TKR.[4] However, this paper fails to mention this confounding factor, indicating that either patients in the two groups were entirely fit or their comorbid conditions were equitably distributed among both groups.

Though the paper claims that similar non-surgical treatment was given to both the groups, it might have been difficult. (The authors admit it in the limitations!). For instance, one cannot imagine a patient with a successful TKR needing an insole for a knee moving over, or lateral to, fifth toe in a single limb mini-squat. Similarly, dietary advice seems to have made a dent only in the non-surgical group at 12 months. The same advice, when given to the TKR group made little overall difference. Maybe the non-surgical group was more motivated to lose weight in order to avoid surgery.

The authors have also used a special, previously described individualized goal-based NEMEX-TJR training programme aimed at functional alignment of the legs by building compensatory functional stability and improving sensorimotor control.[5] This programme is distinct from and possibly better than strengthening programme alone and later, while most commonly administered, may not produce comparable results.

A follow-up of one year is reasonable for this comparative study as most authors would agree that the results following TKR have stabilized at one year. However, the question whether this difference in scores would increase with time as the natural history of knee arthritis would lead to progression should encourage a longer follow-up of these patients.

I would be remiss if I did not point out that the abstract erroneously describes one of the secondary outcomes (without the fifth subscale) as the primary outcome in the methods section.

In conclusion, this randomized controlled trial, the first of its kind, has revealed that patients with radiologically confirmed osteoarthritis with 'mild to moderate' pain, eligible for unilateral TKR and motivated for multimodality intervention including exercises, diet and individualized neuromuscular training programme improved more following TKR in terms of pain relief and functional improvement compared to the non-surgical group at 12 months though with a higher number of serious adverse events.

The study raises more questions than provide answers about the indications for TKR; it is extremely difficult to define 'appropriate' indications for TKR.[6]

The Rand group uses clinical characteristics that affect the risks and benefits based on published literature and expert opinion to decide on the appropriateness of surgery by using a scale (1 most inappropriate; 9 most appropriate).[7] Using the Rand model, Escobar *et al*.[8] analysed that fewer than half (44%) TKRs done in the USA are appropriate. However, since their publication, indications for TKR have evolved.

Selection and prioritization criteria developed by professionals are often in conflict with the views of the patient. Appropriateness therefore cannot be decided without taking into consideration the prevailing values attached to functional deterioration and preservation by the patient as well as society.[6] The patient must always be a party to decision-making about TKR after being explained all the risk and benefits of the procedure.

Lastly, I would ask 'if we adhere to the basic tenet of offering surgery to a patient only after all the appropriate conservative measures have failed', will there ever be room for an investigation such as this one?

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