No difference in clinical outcome between patient-matched positioning guides and conventional instrumented total knee arthroplasty two years post-operatively

A MULTICENTRE, DOUBLE-BLIND, RANDOMISED CONTROLLED TRIAL

Aims

We wished to compare the clinical outcome, as assessed by questionnaires and the rate of complications, in total knee arthroplasty (TKA) undertaken with patient-matched positioning guides (PMPGs) or conventional instruments.

Patients and Methods

A total of 180 patients (74 men, 106 women; mean age 67 years) were included in a multicentre, adequately powered, double-blind, randomised controlled trial. The mean follow-up was 44 months (24 to 57).

Results

There were no significant or clinically relevant differences between the two groups for all outcome measures (Knee Society Score, p = 0.807; Oxford Knee Score, p = 0.304; Western Ontario and McMaster osteoarthritis index, p = 0.753; visual analogue scale for pain, p = 0.227; EuroQol-5D-3L index score, p = 0.610; EuroQol-5D-3L VAS health, p = 0.968.) There was no difference in the rate of complications (p = 0.291).

Conclusion

PMPGs are already in relatively common use and their short-term clinical results are equal to conventional instrumented TKA.

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Patient-matched positioning guides (PMPGs) have been available for use in total knee arthroplasty (TKA) for several years. The technique uses MRI or CT scans to calculate the ideal position of the components from pre-determined reference axes and planes. The purpose of PMPG is, based on these scans, to create jigs that have only one appropriate position on the anatomy of the individual patient. The jigs can also be used to guide the placement of pins, onto which standard resection guides can be placed. Research has focused primarily on the alignment obtained with this relatively new technique. Most papers have shown comparable alignment obtained with PMPG and with conventional instruments.1-6

It is generally accepted that pain relief and improved function are the principal aims of arthroplasty. However, despite its current relatively widespread use, few authors have described the clinical outcomes and possible adverse events related to PMPGs. Studies that have addressed this issue have reported short-term results7,8 or suffered from a lack of adequate randomisation.9,10 To our knowledge, there are no appropriately powered randomised controlled trials (RCT) reporting the clinical outcome.

This double-blind, multicentre RCT comparing PMPG with conventional instrumentation, was designed to address the following research questions. First, is there a difference in clinical outcome between conventional instruments and PMPG as assessed with both examiner based outcome measures and patient reported outcome measures (PROMS)? Secondly, is there a difference in the rate of complications between the two techniques?

It was hypothesised that there would be no difference in clinical outcome and rate of adverse effects and complications between conventional TKA and PMPG TKA.

Patients and Methods

The Consolidated Standards of Reporting Trials (CONSORT) statement was strictly
followed in this trial. Between September 2010 and March 2013, 180 patients consented to take part in this prospective RCT. Two hospitals participated and enrolled 90 patients each. Patients with disabling osteoarthritis of the knee who were candidates for primary unilateral TKA, after extensive conservative treatment, were eligible for inclusion. Exclusion criteria were the presence of metal near the knee, ankle or hip joint, patients with contraindications to MRI scans, those who had previously undergone knee surgery (except for arthroscopic meniscectomy), those with indications for TKA other than osteoarthritis, those with active infection near the knee or with active systemic infection and those who were unable to comply with the post-operative rehabilitation protocol, or were unwilling to participate (Fig. 1).

Randomisation involved an online random number generator and was stratified per hospital. The 90 patients from each hospital were divided into two groups of 45 patients – a group in which TKA was undertaken using PMPG and a control group in which conventional instrumentation was used. The surgeon enrolling patients in the trial was unaware of the type of treatment that patients would receive. The patients were also blinded to the method of alignment of the components that would be used. The characteristics of the patients at the time of enrolment are shown in Table I. Despite randomisation, the patients in the conventional group were significantly younger than those in the PMPG group.

**Surgical procedure and post-operative protocol.** In the PMPG group, MRI scans of the hip, knee and ankle were performed six weeks prior to surgery according to the standard Signa scanning protocol. Software (Materialise NV, Leuven, Belgium) was used to create virtual 3D models of the femur and tibia. The programme was used to determine the appropriate size and optimal positioning of the components (Vanguard Complete Knee System, Biomet Inc., Warsaw, Indiana) for each individual patient. The position was calculated to obtain a neutral mechanical (hip-knee-ankle angle of 180°) axis and a neutral position of the femoral and tibial components to the mechanical axis in the frontal plane. In the sagittal plane, the posterior slope of the tibial component and flexion of the femoral component were set at 3°. A digital, virtual plan of the proposed positioning was sent to the surgeon, who could adjust the digital plan if desired. After approving the plan, guides (Signature, Biomet Inc.) for per-operative use were manufactured using a rapid prototype engineering technique.

In the control group, standard intramedullary instrumentation was used. These patients also underwent MRI scanning according to the same protocol as those in the PMPG group to maintain blinding of the patients to the type of alignment that was to be used. Again, the goal was...
to obtain a neutral mechanical axis in all patients. Flexion of the femoral component and the posterior slope of the tibia were set at 0°.

A standard medial parapatellar approach was used in both groups. All procedures were performed by one of three surgeons (one at Zuyderland Medical Centre (NK) and two at St Anna Hospital (RD and HH). All had extensive experience with conventional TKA and had undertaken at least 100 TKAs using the PMPG technology.

In the PMPG group, the guides were placed on the articular surface after removal of any soft tissues at this site. Pins were placed using these guides that determined the position of the standard cutting blocks. The femur was prepared first. A cemented Vanguard TKA (Vanguard Complete Knee System) was used. Patellar resurfacing was performed where necessary (i.e., in patients with rheumatoid arthritis). Soft-tissue balancing was also undertaken where necessary. In the control group, the same procedure was undertaken, except that standard intramedullary instruments were used to guide the position of the cutting blocks.

The post-operative protocol has previously been described.13 Arixtra 5mg/mL, 0.5 mL (GlaxoSmithKline) (Zuyderland hospital) or Xarelto 10 mg (Bayer) (St. Anna hospital) were used as thrombo-embolic prophylaxis for five weeks post-operatively. Patellar resurfacing was performed where necessary (i.e., in patients with rheumatoid arthritis). Soft-tissue balancing was also undertaken where necessary. In the control group, the same procedure was undertaken, except that standard intramedullary instruments were used to guide the position of the cutting blocks.

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The mean follow-up was 44 months (24 to 57). A total of 163 patients were analysed. All patients received the treatment that they were allocated to. No PMPG procedures had to be converted to a traditional instrumented TKA either pre- or post-operatively.

**Outcome measurements.** Pre-operatively, all patients completed the following questionnaires: the Knee Society Score (KSS),14 the Dutch translated and validated version of the Oxford Knee Score (OKS),15 the Western Ontario and McMaster osteoarthritis index (WOMAC),16 a visual analogue scale (VAS)17 for pain and EuroQol (EQ-5D, 3L version).18 The same set of questionnaires was completed at three months and one and two years post-operatively, by an independent physician (MS at the Zuyderland MC and WW at the St. Anna hospital), who was blinded to the type of instrumentation which had been used.

The KSS and WOMAC were scored from 0 to 100, 0 being the worst outcome and 100 being the best possible outcome.14,15 The OKS was scored from 12 to 60, with 12 being the best possible outcome and 60 being the worst.15 VAS pain was scored from 0 to 100, 0 representing no pain and 100 representing the worst possible pain.20 For the EQ-5D, a single summary index was calculated, using the value set for The Netherlands.18,21,22 An index of 1 represents perfect health and no disabilities.

Scores on the questionnaires were compared between both groups at the different follow-up visits.

All complications were recorded during the minimal two-year follow-up.

This study had ethical approval from both hospitals (File nr. 10-T-21).

**Statistical analysis.** This study was powered on the difference in KSS at two years post-operatively. (Probability of Type I error: 0.05, Probability of Type II error: 0.10, maximal clinically not relevant difference in KSS: 10, estimate of standard deviation of KSS at two years post-operatively: 19.657.) Based on this calculation, 158 patients would have to be included. In order to account for possible loss to follow-up, 180 patients were included.

A generalised linear mixed model (GLMM) approach was used to take into account the repeated-measures design of the study in order to cope with any missing data collected before and at three months and one and two years follow-up and to cope with the wide range of variation in relation to the time frame the data was collected.23 Student’s t-tests were performed on significant interactions. Fisher’s exact test was used to test differences of proportions.

A p-value of < 0.05 was considered significant.

SPSS-software was used for all statistical analyses (SPSS 14 Inc., Chicago, Illinois).

**Results**

The mean follow-up was 44 months (24 to 57). A total of 17 patients were lost to follow-up. Two in the PMPG group and one in the conventional group died of unrelated causes. Six in the PMPG group and eight in the conventional group withdrew two years post-operatively. Thus, at this time, a total of 163 patients were analysed. All patients received the treatment that they were allocated to. No PMPG procedures had to be converted to a traditional instrumented TKA either pre- or post-operatively.

The mean outcome scores at two years improved significantly within each group compared with the pre-operative values and there were no statistically significant differences in the outcome in the two groups (Table II). GLMM was adjusted for age and baseline of each outcome.

There was no statistically significant difference in the total number of complications (p = 0.291, Fisher’s exact
A total of 14 patients in the PMPG group had a complication. Two had a haematoma and eight had a poor range of movement (< 90° of knee flexion); four underwent a manipulation under anaesthesia (MUA). Two had persistent pain and one had a persistent effusion, for which a cause could not be found. One patient had a pulmonary embolism.

A total of 11 patients in the conventional group had a complication. Eight had a poor range of movement; two underwent MUA. One patient had an early deep infection (within six weeks of TKA implantation) requiring debridement with retention of the components and antibiotics. Two patients had further surgery, a patellar button was introduced in one and a malaligned tibial component was revised in another.

**Discussion**

The most important finding of this study was that there was no difference in clinical outcome between PMPG and conventional instrumentation two years post-operatively, as was hypothesised. The second important finding was that there was no difference in the rate of adverse effects and complications, as was also hypothesised.

Our observations concerning the clinical outcome are in line with other authors. Yan et al and Abane et al found no difference in clinical outcome on short-term follow-up. Anderl et al and Chen et al also found no difference in clinical outcome two years post-operatively, however, these studies were not randomised. Expectations vary greatly between patients and the mismatch of experience versus expectation after TKA is a potent cause of dissatisfaction. PROMS are thought to represent the best objective measurement of clinical outcome. Currently, however, there is no single best outcome measure for TKA, and we therefore chose to use a number of scoring systems to obtain insight into the clinical function of the patients participating in this RCT.

Although we used various PROMS, there are some drawbacks associated with the use of these questionnaires. PROMS are subjective measures and suffer from a ceiling effect and the dominance of pain masks the functional changes. As the proportion of younger, more active and more demanding patients undergoing TKA is increasing, function after TKA is becoming more important. It has been suggested by Bolink, Grimm and Heyligers that in order to characterise the changes in physical function after TKA, PROMS could be supplemented by performance-based measures, assessing function during different activities and allowing kinematic characterisation with an ambulant inertial measurement unit. Concerning PROMS, The High Activity Arthroplasty Score (HAAS) could be of interest when assessing subtle variations in function in more demanding patients. This score allows for greater differentiation of the level of function between patients in assessing performance after TKA or total hip arthroplasty.
Given that most studies show comparable results for PMPG and conventional instruments for restoring a neutral mechanical axis and for percentages of outliers, and given our observation that there is no difference in clinical outcome or complications associated with PMPG, it seems reasonable to conclude that PMPGs are as reliable for aligning TKA as conventional instruments. However, no clear advantage seems to exist over conventional instruments. The cost effectiveness of the PMPG technique needs to be considered. Potential cost savings include a shortened operating time,13,30 reduction in the number of sets of instruments (and additional sterilisation costs in most cases), reduced processing time,31 and, purely theoretically, reduction in hospital shelf stock. Additional costs include the cost of an MRI or CT scans (hospital specific), costs of the PMPG (manufacturer and hospital specific), and time needed for logistical tasks, depending on the available personnel. These requirements include the scanning process, transfer of the images to the manufacturer, monitoring the delivery of PMPG to the hospital and approval of the digital plan by the surgeon prior to fabrication of the PMPGs. This last item is essential when using PMPG in order to avoid time-consuming intra-operative changes to the proposed size of the components and the levels of resection.32,33 It has been stated that PMPG would not be cost effective when looking only at reduction in operating time and the alignment obtained with this technique.34 Therefore, the hypothesised financial savings might only be realised when the pre-operative digital plan accurately predicts the size of the components.

The strengths of this study are the design and the large number of patients based on a power calculation. Furthermore, a mixed model approach was used to analyse the data. This is considered to be more appropriate for assessing repeated measurements in clinical trials.22,23 A limitation of the study was the relatively short follow-up. As a result, no reliable data could be provided on the survival of the TKA in both groups. Furthermore, the target flexion and posterior slope were not identical in both groups, which might have influenced clinical outcomes. It remains unclear from the presented data to what extent this variable has influenced outcomes.

Take home message:
Patient-matched positioning guides lead to equal clinical outcome in the short term with no difference in complication rate when compared with conventional instruments in TKA surgery.

Author contributions:
B. Boonen: Data collection, Writing manuscript. M. G. M. Schotanus: Data collection, Writing manuscript. B. Kerens: Data collection, Writing manuscript. W. Van der Weegen: Data collection, Data analysis, Writing manuscript. H. J. Hoekstra: Data collection, Correction of manuscript. N. P. Kort: Data collection, Correction of manuscript. N. P. Kort is a consultant for Zimmer Biomet. No funding was received for this study.

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References
16. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to anti-rheumatic drug therapy in patients with osteoarthri-
22. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valua-


