A commentary by Adam Hart, MD, and Rafael J. Sierra, MD, is linked to the online version of this article at jbjs.org.

Computer-Assisted Compared with Conventional Total Knee Replacement

A Multicenter Parallel-Group Randomized Controlled Trial

Gunnar Petursson, MD, Anne Marie Fenstad, Øystein Gøthesen, PhD, Gro Sævik Dyrhovden, Geir Hallan, PhD, Stephan M. Röhrl, PhD, Arild Aamodt, PhD, and Ove Furnes, PhD

Investigation performed at Lovisenberg Diaconal Hospital, Oslo; Haukeland University Hospital, Bergen; Haugesund Sanitetsforenings Hospital for Rheumatic Diseases, Haugesund; and Haugesund Hospital, Haugesund, Norway

Background: We previously reported the short-term radiographic and functional results of a randomized controlled trial (RCT) comparing computer-assisted and conventionally performed total knee replacement. We currently report the 2-year clinical results from this trial.

Methods: One hundred and ninety patients were randomly allocated to undergo either computer-assisted or conventional total knee replacement. One hundred and seventy-two patients were available for clinical evaluation at 2 years, and 167 (97%) of those answered all patient-reported outcome measures (PROMs), including the Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Society Score (KSS), visual analog scale (VAS), and EuroQol-5 Dimensions (EQ-5D). Patients and clinical evaluators were blinded to the method of surgery. Surgical outcome was assessed using the Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) criteria to calculate responder rates, divided into high responders, moderate responders, and nonresponders.

Results: The computer-assisted group had significantly more improvement than the conventional group in the mean scores for 2 subscales of the KOOS (7.4 for symptoms [$p = 0.02$] and 16.2 for sport and recreation [$p < 0.01$]) and in 1 subscale of the WOMAC (8.8 for stiffness [$p = 0.03$]).The computer-assisted group also had significantly more high responders (82.8%) than the conventional group (68.8%; $p = 0.03$) at 2 years, with the number needed to treat determined to be 8.

Conclusions: In this study, the use of computer navigation provided better pain relief and restored better function than the use of the conventional surgical technique at 2 years after total knee replacement.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

The benefits of total knee replacement (TKR) in patients with advanced osteoarthritis of the knee are well documented[1,2]. Nonetheless, up to 20% of patients continue to have pain or other knee symptoms after TKR[2-4]. These symptoms can be related to postoperative malalignment of the knee[2]. Computer navigation in TKR has been used for over a decade to improve the alignment of the extremity and the positioning of the implant[5-13]. One meta-analysis of randomized controlled trials (RCTs) concluded that computer navigation significantly improved the mechanical axis of the leg and component positioning in TKR[14]. Another meta-analysis found fewer outliers in the mechanical axis of the leg with computer navigation compared with conventionally aligned TKR, but the difference was not significant[15].

Despite these prior findings, the role of computer navigation in TKR continues to be debated. It remains controversial

Disclosure: The Research Council of Norway and the Southern and Eastern Norway Regional Health Authority supported this study. None of the funding sources influenced the content or conclusion of the study. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/E838).

whether improved alignment leads to better clinical results or implant longevity[7-9,13,16]. The current consensus is that improved placement of the implants does lead to better clinical results and survival of the implants[17-19]. Most surgeons agree that postoperative limb alignment should be corrected to within 3° of neutral alignment (0°) of the mechanical axis of the leg[16,20]. However, this viewpoint has recently been challenged by Bellemans[21]. Nonetheless, Choong et al. concluded in their study that there is a correlation between neutral alignment and good function[22]. They viewed this result as supporting the use of computer navigation. However, their comparison was between well-aligned and malaligned knees, not between computer navigation and conventional TKR.

Most RCTs that we are aware of found no significant differences in functional outcomes or patient-reported outcome measures (PROMs) between computer-assisted and conventional TKR, but many of those had a small sample size and did not evaluate individual responses, only the mean change in the scores[10,12,23-25]. One RCT showed significant differences in functional scores in favor of computer navigation[26], but the differences were small and most likely of no clinical interest. Some studies have compared differences in PROMs by evaluating group changes in mean values, without employing the more appropriate methods of investigating the attainment of the minimal clinically important difference (MCID) in individual patients or studying responders and nonresponders, as recently recommended[27,28].

The MCID can be used to determine treatment efficacy or to compare the efficacy of 2 active treatments in clinical trials. To do so, an investigator first must calculate the proportion of patients in each treatment group who meet the MCID criteria for responders[28]. Escobar et al. concluded in their study that the Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) criteria can be used to define TKR responders[27]. One common error when determining treatment efficacy in clinical trials is to calculate mean differences (pretreatment compared with post-treatment) for the treatment groups and then compare mean differences between the groups with the MCID. The MCID is a metric that is based on longitudinal differences in individual patients and should be used in the same context[28]. Moreover, recovery after TKR is time-dependent, as Knee Injury and Osteoarthritis Outcome Score (KOOS) scores typically improve until 2 years postoperatively, after which there is often a slight decline in function, so the timing of evaluation should be carefully considered[29].

This RCT was designed to compare computer-assisted and conventionally performed TKR, with the null hypothesis that there would be no group differences in pain or function 2 years postoperatively. Early results have previously been reported for 54 patients analyzed with radiostereometric analysis (RSA) up to 24 months after the operation[30]. One-year results and radiographic findings were also previously reported, with the conclusion that computer-assisted TKR was more predictable, with fewer outliers, than conventional TKR with regard to mechanical alignment and positioning of the prosthesis[13]. At the 1-year follow-up, clinical results were marginally in favor of computer navigation using mean values of change. The present analysis describes the clinical outcomes at the 2-year follow-up using OMERACT-OARSI criteria for responders and nonresponders and assesses whether differences in alignment are associated with differences in PROMs.

Materials and Methods

Study design and implementation follow the Consolidated Standards of Reporting Trials (CONSORT) statement guidelines for reporting parallel-group randomized trials[31]. The regional committee for medical and health research ethics in Bergen, Norway, approved the trial in September 2007. The trial was registered with ClinicalTrials.gov (NCT00782444) in October 2008.

From May 2009 to August 2011, 190 patients were prospectively enrolled in the study and were randomly allocated at a ratio of 1:1 to either computer-assisted TKR (n = 96) or conventional TKR (n = 94). Inclusion criteria were men and women between 50 and 85 years old with inflammatory arthritis and primary or secondary osteoarthritis of the knee who needed a TKR. Exclusion criteria included an American Society of Anesthesiologists (ASA) category of >3, which indicates severe systemic disease[32]. Patients with severe neurological disease, dementia, previous cancer, a body mass index (BMI) of >35 kg/m^2, a previous tibial or femoral shaft fracture, severe preoperative valgus alignment of the knee (>15° from the mechanical leg axis), previous tibial or femoral osteotomy, recent knee injury (<1 year preoperatively), severe ipsilateral hip stiffness, ipsilateral hip replacement, or metal allergies were also excluded. For patients who had 2 knee replacements during the study period, only the first 1 was included in the trial.

Eight experienced surgeons (defined as those who had done >100 conventional TKRs) performed the TKRs in 4 orthopaedic clinics in Norway. Each surgeon had also performed ≥10 computer-assisted TKRs before recruiting patients into the trial.

A detailed description of the intervention has been previously published[13]. As the computer-assisted procedure required a stab incision in the midpart of the tibia, a similar sham incision was used in patients managed with the conventional technique, in order to be able to blind patients and observers (physiotherapists and radiologists).

The primary outcome of the study was the clinical results analyzed with RSA, which were previously reported by Petursson et al.[30]. The present study describes the secondary outcome, which was the function of the knee. The primary outcome for this part of the study was the KOOS pain score[33]. The follow-up period was 2 years, with scheduled follow-up visits at 3, 12, and 24 months. KOOS is a 42-item self-administered questionnaire with 5 subscales: pain (9 items), other symptoms (7 items), activities of daily living (17 items), sport and recreational function (5 items), and knee-related quality of life (QoL) (4 items). The MCID for KOOS used on knee replacement patients has not been determined; however, a

change in the KOOS pain score of 8 to 10 has been used earlier as a suggested MCID[33].

Secondary outcomes were the Knee Society Score (KSS)[34], EuroQol-5 Dimensions (EQ-5D)[35], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[36], and visual analog scale (VAS) together with alignment and rotational positioning of the implant. Radiographic findings were published previously[13]. KSS functional scores were assessed preoperatively, after 1 week (only range of motion), and after 3, 12, and 24 months by 8 physiotherapists. The WOMAC is a widely used, disease-specific measure for knee osteoarthritis with a multidimensional scale consisting of 24 items grouped into 3 dimensions: pain (5 items), stiffness (2 items), and physical function (17 items). WOMAC scores can be derived from the KOOS questionnaire[37].

OMERACT-OARSI criteria were applied to calculate responder rates at 2 years using WOMAC scores[27]. By definition, a high responder was considered to be a patient who had an improvement in pain or function of ≥50% and an absolute change of ≥20 points. If the patient did not meet these criteria, improvement in 2 of the following 3 subscales was considered to indicate a moderate responder: (1) improvement of ≥20% in the

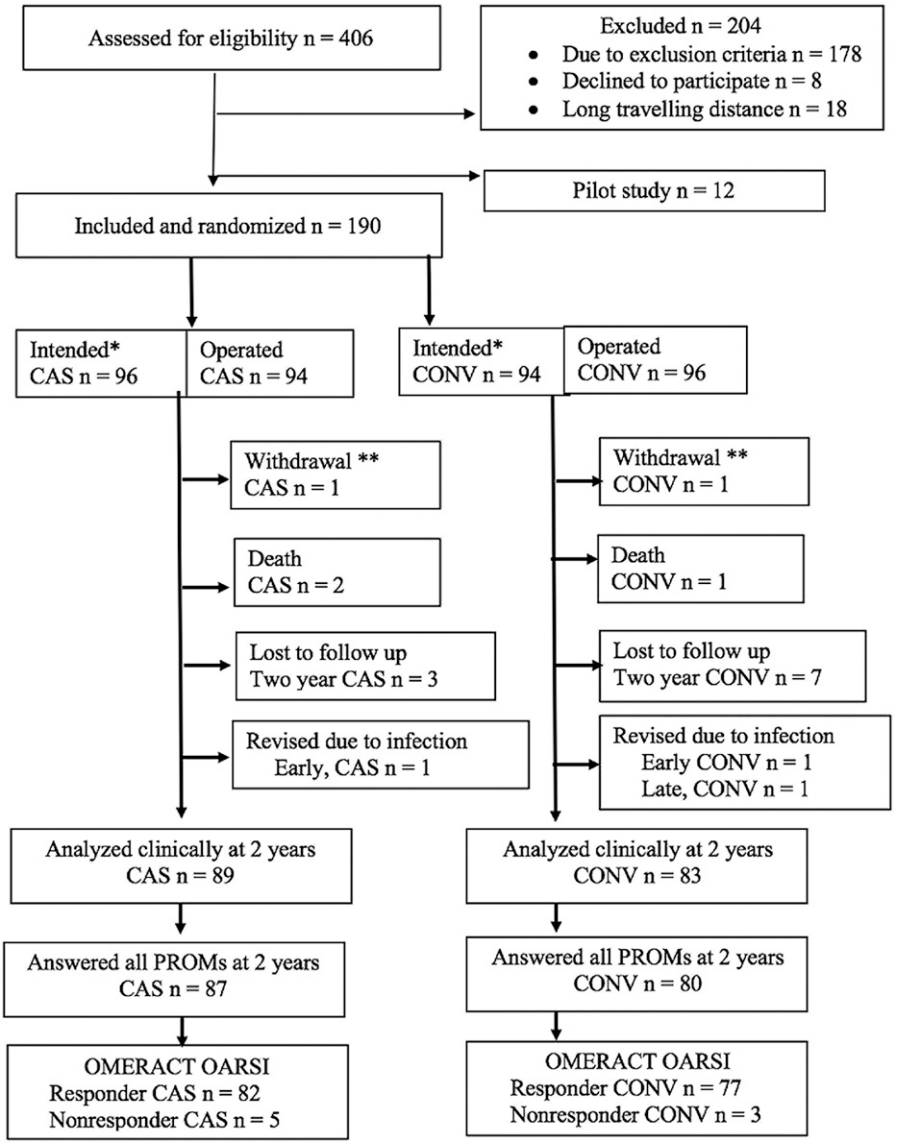

Fig. 1

Flowchart illustrating patient selection for the trial. *Two patients were converted from computer-assisted surgery (CAS) to the conventional (CONV) method because of technical problems with computer-assisted surgery (analyzed as intention to treat). **One patient in the computer-assisted group did not want to continue his participation in the trial owing to the long traveling distance from his home to the hospital. One patient in the conventional group changed his mind after inclusion and declined participation. PROMs = patient-reported outcome measures, and OMERACT OARSI = Outcome Measures in Rheumatology-Osteoarthritis Research Society International.

pain score and an absolute change of 10 points, (2) functional improvement of ≥20% and an absolute change of 10 points, and (3) KOOS QoL improvement of ≥20% and an absolute change of 10 points. According to these criteria, patients were categorized at the 2-year follow-up evaluation as high responders, moderate responders, or nonresponders[38].

The Charnley classification system was used to categorize patients according to the level of comorbidity and to adjust for potential group differences[39].

Statistical Analysis

We used the intention-to-treat principle for all analyses. The KOOS developers suggested that the minimum important change (MIC) is a difference of 8 to 10 points on an aggregated and averaged KOOS subscale[40]. A power analysis indicated that we needed 64 patients in each group to detect this MIC with 80% power, a 5% significance level, and a standard deviation of 20.

A clinical research unit handled the randomization procedure using SPSS Statistics software (version 19.0; IBM). We used a separate randomization list for each surgeon so that group assignment was balanced across surgeons[13].

TABLE I Demographic Data and Preoperative Findings

	Computer-Assisted TKR (N = 87)	Conventional TKR (N = 80)
Men *(no. [%])*	36 (41.4)	29 (36.3)
Age* *(yr)*	67.9 (6.8)	67.6 (6.6)
Right side *(no. [%])*	51 (58.6)	49 (61.3)
Charnley category *(no. [%])*		
1	27 (31.0)	24 (30.0)
2	59 (67.8)	50 (62.5)
3	1 (1.1)	6 (7.5)
Diagnosis *(no. [%])*		
Osteoarthritis	75 (86.2)	67 (83.8)
Other	12 (13.8)	13 (16.3)
Body mass index* *(kg/m^2)*	27.7 (3.5)	28.5 (3.8)
Preoperative motion* *(deg)*		
Mean lack of extension	4.6 (5.4)	4.6 (5.7)
Mean flexion	110 (15.2)	111 (18.3)
Preoperative anteroposterior stability *(no. [%])*		
<5 mm	80 (92.0)	68 (85.0)
5 to 10 mm	7 (8.0)	11 (13.8)
>10 mm	0	1 (1.3)
Missing	0	0
Preoperative mediolateral stability *(no. [%])*		
<5 mm	36 (41.4)	38 (47.5)
5 to 10 mm	40 (46.0)	33 (41.3)
>10 mm	11 (12.6)	7 (8.8)
Missing	0	2 (2.5)

*The values are given as the mean, with the standard deviation in parentheses.

TABLE II The Number of Responders in Each Study Group According to the OMERACT-OARSI Criteria

	Computer-Assisted TKR (N = 87)	Conventional TKR (N = 80)	P Value*
Pain *(no. [%])*			
High responders	68 (78.2)	51 (63.8)	0.04†
Function *(no. [%])*			
High responders	61 (70.1)	43 (53.8)	0.04†
Overall *(no. [%])*			
High responders	72 (82.8)	55 (68.8)	0.03‡
Moderate responders	10 (11.5)	22 (27.5)	
Nonresponders	5 (5.7)	3 (3.8)	
Overall, dichotomized *(no. [%])*			
Responders	82 (94.3)	77 (96.3)	0.72§
Nonresponders	5 (5.7)	3 (3.8)	

*Pearson chi-square test. †The proportion of patients classified as high responders, based on either pain or function, was higher in the computer-assisted group than in the conventional group. ‡Compared with the conventional group, the computer-assisted group had a higher proportion of high responders and a lower proportion of moderate responders, based on either pain or function, or both. §The proportion of responders (high and moderate combined) versus nonresponders did not differ by treatment group.

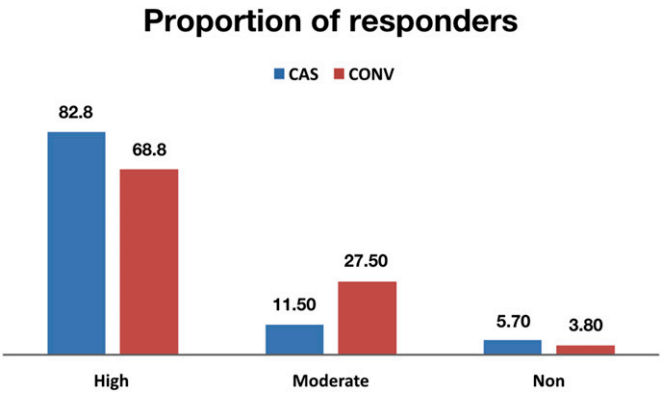

Fig. 2

The response to surgery determined using the OMERACT-OARSI criteria to calculate responder rates. CAS = computer-assisted TKR, and CONV = conventional TKR.

Data were checked for normality using the Kolmogorov-Smirnov test. We used an independent samples t test with 95% confidence intervals (CIs) to compare mean angles, means, and mean improvements on the KSS, KOOS, EQ-5D, and WOMAC. The Mann-Whitney U test was used for skewed variables. The Pearson chi-square test was used for comparisons of OMERACT-OARSI responder rates[27] by sex, side, ASA status, and Charnley classification[39]. Multiple testing procedures on subgroups were analyzed with post hoc tests. Significance was defined as a p value of <0.05, and all tests were 2-sided. We used SPSS Statistics software (version 24.0; IBM) for all statistical analyses.

TABLE III Clinical Outcome: Mean Score at Preoperative and 2-Year Postoperative Evaluations, Change in Mean Score, and Number of Patients with Highest Possible Score

	Computer-Assisted TKR (N = 87)	Conventional TKR (N = 80)	P Value*
KOOS			
Pain			
Preop.†	44.0 (14.7)	46.0 (16.0)	0.41
2 yr†	88.2 (15.8)	85.6 (15.0)	0.27
Change†	44.2 (20.6)	39.6 (19.7)	0.14
Highest possible score *(no. [%])*	24 (27.6)	11 (13.8)	0.03‡
Symptoms			
Preop.†	52.4 (18.1)	55.7 (21.1)	0.28
2 yr†	86.3 (13.2)	82.2 (14.3)	0.05
Change†	33.9 (18.5)	26.5 (20.5)	0.02‡
Highest possible score *(no. [%])*	13 (14.9)	8 (10.0)	0.33
Activities of daily living			
Preop.†	48.4 (15.6)	50.0 (15.2)	0.50
2 yr†	87.4 (15.5)	83.4 (17.5)	0.12
Change†	38.9 (18.7)	33.4 (20.3)	0.07
Highest possible score *(no. [%])*	21 (24.1)	9 (11.3)	0.03‡
Sport/rec.			
Preop.†	12.1 (11.9)	15.3 (16.5)	0.16
2 yr†	57.0 (27.5)	44.7 (24.8)	<0.01‡
Change†	44.9 (26.6)	28.7 (28.9)	<0.01‡
Highest possible score *(no. [%])*	8 (9.2)	0	0.02‡
Quality of life			
Preop.†	24.5 (15.0)	25.5 (14.9)	0.67
2 yr†	79.1 (20.7)	74.0 (21.2)	0.12
Change†	54.6 (24.6)	48.5 (23.7)	0.11
Highest possible score *(no. [%])*	22 (25.3)	13 (16.3)	0.15
WOMAC			
Pain			
Preop.†	47.6 (15.7)	49.7 (16.8)	0.41
2 yr†	89.4 (15.4)	88.7 (14.2)	0.76
Change†	41.8 (21.4)	39.0 (19.2)	0.38
Highest possible score *(no. [%])*	32 (36.8)	25 (31.3)	0.45
Stiffness			
Preop.†	42.4 (21.4)	49.3 (21.5)	0.04‡
2 yr†	81.9 (17.8)	79.6 (19.5)	0.44
Change†	39.5 (24.1)	30.3 (25.4)	0.03‡
Highest possible score *(no. [%])*	30 (34.5)	23 (28.8)	0.26
Physical function			
Preop.†	48.4 (15.6)	50.0 (15.2)	0.50
2 yr†	87.4 (15.5)	83.4 (17.5)	0.12
Change†	38.9 (18.7)	33.4 (20.3)	0.07
Highest possible score *(no. [%])*	21 (24.1)	9 (11.3)	0.03‡
KSS			
Knee score			
Preop.†	37.9 (16.7)	41.5 (14.4)	0.14
2 yr†	69.7 (17.8)	69.2 (18.0)	0.86
Change†	31.8 (22.7)	27.7 (20.7)	0.23
Highest possible score *(no. [%])*	0	0	

continued

TABLE III (*continued*)

	Computer-Assisted TKR (N = 87)	Conventional TKR (N = 80)	P Value*
Function			
Preop.†	61.1 (15.0)	59.4 (15.8)	0.49
2 yr†	87.7 (17.6)	83.4 (18.4)	0.12
Change†	26.7 (18.0)	23.9 (18.6)	0.34
Highest possible score *(no. [%])*	48 (55.2)	33 (41.3)	0.07
EQ-5D			
Preop.†	55.9 (19.5)	57.6 (18.5)	0.58
2 yr†	88.0 (15.2)	85.9 (15.8)	0.39
Change†	32.0 (24.4)	28.7 (21.6)	0.37
Highest possible score *(no. [%])*	47 (54.0)	39 (48.8)	0.63

*Independent samples t-test. †The values are given as the mean, with the standard deviation in parentheses. ‡The difference was significant.

TABLE IV Mean Change in KOOS Scores (Pain and Symptoms) After 2 Years, by Degree of Radiographic Alignment

	<–3°	–3° to 3°	>3°	P Value*
Long axis alignment	<177° (valgus)	Near goal of 180°	>183° (varus)	
No. of knees	17	115	35	
Pain†	41.7 (19.6)	42.3 (21.3)	40.0 (17.1)	0.89
Symptoms†	37.7 (14.2)	28.7 (20.6)	31.8 (19.4)	0.16
Tibial flexion-extension	<83° (flexion)	Near goal of 86°	>89° (extension)	
No. of knees	3	97	67	
Pain†	38.0 (8.9)	42.2 (18.8)	41.0 (22.7)	0.90
Symptoms†	40.5 (24.3)	30.0 (18.3)	29.8 (21.6)	0.51
Tibial rotation	<77° (external)	Near goal of 80°	>83° (internal)	
No. of knees‡	62	65	34	
Pain†	43.0 (21.4)	42.5 (19.3)	38.8 (19.5)	0.55
Symptoms†	32.6 (21.0)	28.7 (18.2)	27.1 (20.2)	0.34
Tibial valgus/varus	<87° (valgus)	Near goal of 90°	>93° (varus)	
No. of knees‡	0	138	28	
Pain†		41.5 (20.0)	42.2 (21.5)	0.87
Symptoms†		29.0 (19.8)	35.6 (18.6)	0.10
Femoral flexion-extension	<87° (flexion)	Near goal of 90°	>93° (extension)	
No. of knees	72	83	12	
Pain†	41.3 (21.4)	41.5 (19.5)	44.7 (18.8)	0.83
Symptoms†	32.1 (21.1)	29.1 (18.2)	25.0 (21.5)	0.29
Femoral rotation	<87° (external)	Near goal of 90°	>93° (internal)	
No. of knees	11	112	44	
Pain†	46.8 (20.9)	41.1 (19.6)	42.6 (21.5)	0.61
Symptoms†	32.4 (20.9)	29.2 (20.1)	32.1 (19.0)	0.84
Femoral valgus-varus	<87° (valgus)	Near goal of 90°	>93° (varus)	
No. of knees	19	138	10	
Pain†	42.7 (16.6)	41.7 (21.0)	38.9 (16.8)	0.83
Symptoms†	33.3 (18.7)	30.2 (20.3)	22.0 (11.7)	0.18

*One-way analysis of variance test. †The values are given as the mean, with the standard deviation in parentheses. ‡Some knees could not be measured because of artifacts.

TABLE V Mean Change in KOOS Scores After 2 Years Among Patients with Varus Alignment Preoperatively Who Had Either Normal or Varus Alignment Postoperatively

KOOS Subscale	Change in KOOS Score by Postoperative Alignment*		P Value
	Normal Alignment (N = 22)	Varus Alignment (N = 60)	
Pain	42.2 (20.2)	41.1 (17.8)	0.82
Symptoms	28.2 (20.0)	30.3 (17.0)	0.67
Activities of daily living	35.4 (19.8)	34.9 (18.4)	0.92
Sport and recreational function	42.2 (26.1)	29.4 (28.4)	0.06
Quality of life	51.9 (23.0)	50.7 (23.3)	0.83

*The values are given as the mean, with the standard deviation in parentheses.

Results

Of the 172 patients available for the 2-year follow-up, 167 (97%) completed all PROMs 2 years postoperatively and were included in this analysis (Fig. 1). We had a dropout rate of 12.1%, which included 2 patients who withdrew, 3 who died, 3 who had a revision, 10 who were lost to follow-up, and 5 with incomplete PROM data (Fig. 1). Radiographic analyses were performed 3 months postoperatively[13]. There were no differences between the 2 groups with respect to baseline characteristics (Table I).

At the 2-year follow-up, similar proportions of patients in the 2 groups were considered responders on the basis of the OMERACT-OARSI criteria: 94.3% of 87 patients in the computer-assisted group and 96.3% of 80 patients in the conventional group ($p = 0.72$) (Table II). However, 72 (82.8%) of patients in the computer-assisted group were high responders and 15 (17.2%) were moderate responders or nonresponders compared with 55 (68.8%) and 25 (31.3%), respectively, in the conventional group ($p = 0.03$) (Fig. 2 and Table II). The number needed to treat (NNT) was 8 in favor of computer navigation.

The computer-assisted group had better mean change in the results on all KOOS subscales compared with the conventional group, with 2 of the subscale results reaching significance. The group differences were 4.6 points for pain ($p = 0.14$), 7.4 points for symptoms ($p = 0.02$), 5.5 points for activities of daily living ($p = 0.07$), 16.2 points for sport and recreational function ($p < 0.01$), and 6.1 points for QoL ($p = 0.11$). In the computer-assisted group, significantly more patients had the highest possible score on 3 of the 5 KOOS subscales (Table III).

The computer-assisted group also reported significantly better results than the conventional group on the WOMAC stiffness subscale, with a difference of 8.8 points ($p = 0.03$). A

TABLE VI Preoperative PROM Values by Responder Type

	High Responder* (N = 127)	Moderate Responder* (N = 32)	Nonresponder* (N = 8)	P Value†
KOOS				
Pain	41.4 (13.1)	53.2 (16.6)	67.4 (12.6)	<0.01‡
Symptoms	51.1 (19.2)	62.3 (19.5)	68.3 (11.2)	<0.01§
Activities of daily living	45.6 (13.9)	58.5 (14.5)	68.0 (13.4)	<0.01§
Sport/rec.	12.5 (13.9)	14.8 (12.0)	26.9 (22.2)	0.02#
Quality of life	22.9 (13.5)	28.4 (14.9)	45.0 (21.2)	<0.01‡
WOMAC				
Pain	44.6 (13.5)	58.1 (18.0)	71.6 (17.4)	<0.01‡
Stiffness	43.1 (21.2)	50.0 (21.1)	70.3 (13.3)	<0.01‡
Physical function	45.7 (13.9)	57.7 (14.9)	68.0 (13.4)	<0.01‡
KSS				
Knee score	38.3 (15.0)	40.4 (15.9)	57.4 (16.4)	<0.01#
Function	58.8 (14.7)	64.8 (14.9)	66.2 (24.3)	0.07
EQ-5D	54.9 (19.0)	59.6 (18.2)	73.9 (13.1)	0.02#

*The values are given as the mean score, with the standard deviation in parentheses. †One-way analysis of variance test, ‡Tukey post hoc test shows significant difference between all groups. §Tukey post hoc test shows significant difference between high responders and moderate responders or nonresponders but not between moderate responders and nonresponders. #Tukey post hoc test shows only significant difference between high responders and nonresponders.

large number of patients had the highest possible score on the WOMAC pain and stiffness subscales in both groups and on the WOMAC physical function subscale in the computer-assisted group (Table III).

There were no significant group differences in terms of change in KSS or EQ-5D scores. As with the WOMAC, the KSS function subscale and EQ-5D had a high number of patients who had the highest possible score in both groups (Table III).

Most of the PROM data were not normally distributed. All data were therefore evaluated using both parametric (Table III) and nonparametric tests (see Appendix), and the results were comparable.

We compared patients achieving optimal alignment and those with malalignment (>3° of target), independent of the study groups. Early results (3 months) showed that internal malrotation of the femoral component (>3°) led to inferior results according to the KSS function score, KOOS subscale for sport and recreational function, and VAS at 3 months. However, these differences were no longer significant at 1 year[13]. Patients in whom the tibia had a posterior slope of <1°, or an anterior slope, were found to have worse KSS scores and KOOS QoL subscale scores at 3 months, and worse KSS function scores and VAS scores at 1 year[13]. At the 2-year follow-up, we did not find any significant differences in pain or function in a comparison of malaligned and well-aligned knees (Table IV); however, the number of patients was small and therefore the analyses were underpowered.

We also compared patients with varus alignment prior to surgery who ended up with varus alignment postoperatively, according to Bellemans' theory[21], and patients who had varus alignment prior to surgery but had normal alignment postoperatively. We found no difference between the groups (Table V); however, the number of patients was small and the analyses were underpowered.

When comparing the 3 responder groups, we found that high responders had significantly worse preoperative scores than moderate responders and nonresponders on most of the tests, and a similar pattern was evident when comparing moderate responders and nonresponders (Table VI).

Discussion

To our knowledge, the present investigation is the first randomized, double-blinded responder analysis comparing computer-assisted and conventional TKR. The main finding was that computer-assisted TKR had significantly better clinical results after 2 years evaluated with the KOOS and WOMAC scores. More patients were pain-free and had better function in the computer-assisted group at 2 years compared with the conventional group. In contrast, the KSS and EQ-5D scores did not show any significant differences. A similar result has been previously described, but it was thought to be attributable to ceiling effects[41]. We therefore rejected the null hypothesis that there would be no difference between the 2 groups at 2 years.

The higher proportion of pain-free knees in the computer-assisted group is important both at an individual patient level and from a health system perspective, considering a previous report on the economic expenses involved in investigating and treating painful TKRs[42] and the burden to the individual patients[43].

Whenever a new surgical method of alignment in TKR is introduced, there is a legitimate question about its impact on the survival of the prosthesis. Data from the New Zealand Joint Registry showed that patients with a higher Oxford Knee Score are unlikely to require early revision[44]. In a registry-based study from the Australian Orthopaedic Association National Joint Replacement Registry comparing the longevity of computer-assisted and conventional TKR, the main conclusion was that, at 10 years postoperatively, the use of computer navigation in TKR had reduced the overall rate of major revision in the entire study population and the rate of revision for loosening or lysis in patients who were <65 years old[45]. The same tendency was also evident in the 8-year follow-up from the Norwegian Arthroplasty Registry, although it did not reach significance[46]. It is possible that the better outcome scores in the computer-assisted group in our study may be predictive of a lower rate of revision. However, in another registry-based study from the Norwegian Arthroplasty Registry, the authors found that computer navigation was a risk factor for revision at the 2-year follow-up[47].

Previously published alignment data for the patients in the present study[13] showed that computer-assisted TKR provided more precision than conventional TKR and resulted in fewer outliers in the computer-assisted group. At 2 years, we did not find any differences in PROMs when comparing well-aligned and malaligned knees within all responder groups. However, there were few patients in the malaligned group, and thus this subgroup analysis was probably underpowered. In a recent overview of the literature on revision rates and functional outcome, Gromov et al. concluded that neutral overall coronal alignment is currently the gold standard[19]. In the present study, we were not able to prove a causal relationship between good alignment and good clinical outcome. Other explanations for better functional outcome in the knees that had computer-assisted TKR could be that computer navigation might allow the surgeon to achieve more accurate ligament balancing and more proper sizing of implant components. Furthermore, computer navigation might result in less extensive impact on the soft tissues, as improved alignment theoretically might need less surgical balancing of the ligaments and thus cause minimal tissue insult and less postoperative pain. We previously evaluated blood loss and found no differences between the 2 groups[13]. We did not register the extent of ligamentous release. However, we tested the stability of the knee preoperatively and postoperatively and found no group differences[13].

Earlier studies found no clinically important differences between computer-assisted and conventionally performed TKR[5,10,12,13,23-25]. All of those studies, as well as our earlier results, compared the groups by analyzing mean changes in PROM values and comparing them with the suggested MCID[33]. To our knowledge, there has been no evaluation of responders and nonresponders in earlier studies[13,27,28], even though this type of analysis is considered more clinically relevant[28].

In most studies on computer navigation and alignment, the definition of malalignment is based on the conclusion in the study by Jeffery et al., in 1991, that an alignment within 3° of a neutral mechanical axis is necessary for good implant survival[48]. Others have questioned this conclusion and suggested other acceptable alignment values[21]. We were not able to find any differences using Bellemans' criteria for constitutional varus in this trial.

Differences in the preoperative PROMs between responder groups are strong reminders of the importance of patient selection. These preoperative differences cannot explain the difference between computer-assisted and conventionally performed TKR in this trial, which suggests minimal selection bias; however, it is important to note that all of the nonresponders had high PROM values prior to surgery, indicating better function. If patients with higher preoperative function are more likely to become nonresponders, regardless of surgical method, this may have implications for the patient selection process for TKR.

The main strength of our study is a high follow-up rate of 88% at 2 years. This is one of the largest double-blinded RCTs of its kind, and the sham incision ensured blinding of patients, which we believe is important when a novel method is compared with an older method. This multicenter study involving a relatively large number of surgeons also had several limitations. Although we had a detailed surgical protocol, there may have been differences in surgical methods across hospitals and surgeons. There were unavoidable differences in physician experience, clinical skills, and patient selection for surgery, in addition to differences among clinical evaluators and rehabilitation programs. We tried to balance these differences through rigorous preparations prior to implementation of the study and balancing the randomized group assignment for each surgeon[13]. Further, other implants and other navigation systems may, of course, lead to different results.

In this study, use of computer navigation provided better pain relief and restored better function 2 years after TKR than the use of the conventional surgical technique. We believe that this difference is of clinical importance.

Appendix

eA A table showing the change in scores on the PROMs is available with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/E839). ■

NOTE: The authors thank the orthopaedic surgeons H. Luhr, T. Jervidalo, A. Skredderstuen, and C. Jacobsen for participating in this trial by recruiting and operatively treating patients. The authors also thank all patients for participating, all physiotherapists for their evaluation of the patients, the radiologists for radiographic evaluation, the clinical research ward for data entry, and Kjell G. Nilsson for helping us to plan this study.

Gunnar Petursson, MD[1,2]
Anne Marie Fenstad[2]
Øystein Gøthesen, PhD[2,3,4]
Gro Sævik Dyrhovden[2,3]
Geir Hallan, PhD[3]
Stephan M. Röhrl, PhD[5]
Arild Aamodt, PhD[1]
Ove Furnes, PhD[2,3]

[1]Lovisenberg Diaconal Hospital, Oslo, Norway

[2]The Norwegian Arthroplasty Register, Department of Orthopaedic Surgery, Haukeland University Hospital, Bergen, Norway

[3]Department of Clinical Medicine, Faculty of Medicine, University of Bergen, Bergen, Norway

[4]Haugesund Sanitetsforenings Hospital for Rheumatic Diseases, Haugesund, Norway

[5]Department of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway

E-mail address for G. Petursson: gunnar.petursson@lds.no

ORCID iD for G. Petursson: 0000-0001-5698-748X
ORCID iD for A.M. Fenstad: 0000-0002-6429-0153
ORCID iD for Ø. Gøthesen: 0000-0002-8254-9106
ORCID iD for G.S. Dyrhovden: 0000-0001-7208-0693
ORCID iD for G. Hallan: 0000-0002-8202-3462
ORCID iD for S.M. Röhrl: 0000-0001-5784-2055
ORCID iD for A. Aamodt: 0000-0002-2879-9382
ORCID iD for O. Furnes: 0000-0001-8223-2515

References

1. Robertsson O, Dunbar M, Pehrsson T, Knutson K, Lidgren L. Patient satisfaction after knee arthroplasty: a report on 27,372 knees operated on between 1981 and 1995 in Sweden. Acta Orthop Scand. 2000 Jun;71(3):262-7.

2. Carr AJ, Robertsson O, Graves S, Price AJ, Arden NK, Judge A, Beard DJ. Knee replacement. Lancet. 2012 Apr 7;379(9823):1331-40. Epub 2012 Mar 6.

3. Baker PN, van der Meulen JH, Lewsey J, Gregg PJ; National Joint Registry for England and Wales; Data from the National Joint Registry for England and Wales. The role of pain and function in determining patient satisfaction after total knee replacement. J Bone Joint Surg Br. 2007 Jul;89(7):893-900.

4. Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? Clin Orthop Relat Res. 2010 Jan;468(1):57-63.

5. Chauhan SK, Scott RG, Breidahl W, Beaver RJ. Computer-assisted knee arthroplasty versus a conventional jig-based technique. A randomised, prospective trial. J Bone Joint Surg Br. 2004 Apr;86(3):372-7.

6. Lüring C, Bäthis H, Tingart M, Perlick L, Grifka J. Computer assistance in total knee replacement - a critical assessment of current health care technology. Comput Aided Surg. 2006 Mar;11(2):77-80.

7. Bauwens K, Matthes G, Wich M, Gebhard F, Hanson B, Ekkernkamp A, Stengel D. Navigated total knee replacement. A meta-analysis. J Bone Joint Surg Am. 2007 Feb; 89(2):261-9.

8. Kim YH, Kim JS, Choi Y, Kwon OR. Computer-assisted surgical navigation does not improve the alignment and orientation of the components in total knee arthroplasty. J Bone Joint Surg Am. 2009 Jan;91(1):14-9.

9. Longstaff LM, Sloan K, Stamp N, Scaddan M, Beaver R. Good alignment after total knee arthroplasty leads to faster rehabilitation and better function. J Arthroplasty. 2009 Jun;24(4):570-8. Epub 2008 May 19.

10. Lad DG, Thilak J, Thadi M. Component alignment and functional outcome following computer assisted and jig based total knee arthroplasty. Indian J Orthop. 2013 Jan;47(1):77-82.

11. Dyrhovden GS, Gøthesen Ø, Lygre SHL, Fenstad AM, Søråas TE, Halvorsen S, Jellestad T, Furnes O. Is the use of computer navigation in total knee arthroplasty improving implant positioning and function? A comparative study of 198 knees operated at a Norwegian district hospital. BMC Musculoskelet Disord. 2013 Nov 14; 14:321.

12. Cip J, Widemschek M, Luegmair M, Sheinkop MB, Benesch T, Martin A. Conventional versus computer-assisted technique for total knee arthroplasty: a

minimum of 5-year follow-up of 200 patients in a prospective randomized comparative trial. J Arthroplasty. 2014 Sep;29(9):1795-802. Epub 2014 May 4.

13. Gøthesen O, Espehaug B, Havelin LI, Petursson G, Hallan G, Strøm E, Dyrhovden G, Furnes O. Functional outcome and alignment in computer-assisted and conventionally operated total knee replacements: a multicentre parallel-group randomised controlled trial. Bone Joint J. 2014 May;96-B(5):609-18.

14. Cheng T, Zhao S, Peng X, Zhang X. Does computer-assisted surgery improve postoperative leg alignment and implant positioning following total knee arthroplasty? A meta-analysis of randomized controlled trials? Knee Surg Sports Traumatol Arthrosc. 2012 Jul;20(7):1307-22. Epub 2011 Jul 6.

15. Shi J, Wei Y, Wang S, Chen F, Wu J, Huang G, Chen J, Wei L, Xia J. Computer navigation and total knee arthroplasty. Orthopedics. 2014 Jan;37(1):e39-43.

16. Parratte S, Pagnano MW, Trousdale RT, Berry DJ. Effect of postoperative mechanical axis alignment on the fifteen-year survival of modern, cemented total knee replacements. J Bone Joint Surg Am. 2010 Sep 15;92(12):2143-9.

17. Fehring TK, Odum S, Griffin WL, Mason JB, Nadaud M. Early failures in total knee arthroplasty. Clin Orthop Relat Res. 2001 Nov;392:315-8.

18. Ritter MA, Faris PM, Keating EM, Meding JB. Postoperative alignment of total knee replacement. Its effect on survival. Clin Orthop Relat Res. 1994 Feb;299:153-6.

19. Gromov K, Korchi M, Thomsen MG, Husted H, Troelsen A. What is the optimal alignment of the tibial and femoral components in knee arthroplasty? Acta Orthop. 2014;85(5):480-7.

20. Bonner TJ, Eardley WGP, Patterson P, Gregg PJ. The effect of post-operative mechanical axis alignment on the survival of primary total knee replacements after a follow-up of 15 years. J Bone Joint Surg Br. 2011 Sep;93(9):1217-22.

21. Bellemans J. Neutral mechanical alignment: a requirement for successful TKA: opposes. Orthopedics. 2011 Sep 9;34(9):e507-9.

22. Choong PF, Dowsey MM, Stoney JD. Does accurate anatomical alignment result in better function and quality of life? Comparing conventional and computer-assisted total knee arthroplasty. J Arthroplasty. 2009 Jun;24(4):560-9. Epub 2008 May 19.

23. Spencer JM, Chauhan SK, Sloan K, Taylor A, Beaver RJ. Computer navigation versus conventional total knee replacement: no difference in functional results at two years. J Bone Joint Surg Br. 2007 Apr;89(4):477-80.

24. Lützner J, Dexel J, Kirschner S. No difference between computer-assisted and conventional total knee arthroplasty: five-year results of a prospective randomised study. Knee Surg Sports Traumatol Arthrosc. 2013 Oct;21(10):2241-7. Epub 2013 Jul 14.

25. Blakeney WG, Khan RJ, Palmer JL. Functional outcomes following total knee arthroplasty: a randomised trial comparing computer-assisted surgery with conventional techniques. Knee. 2014 Mar;21(2):364-8.

26. Blakeney WG, Khan RJK, Wall SJ. Computer-assisted techniques versus conventional guides for component alignment in total knee arthroplasty: a randomized controlled trial. J Bone Joint Surg Am. 2011 Aug 3;93(15):1377-84.

27. Escobar A, Gonzalez M, Quintana JM, Vrotsou K, Bilbao A, Herrera-Espiñeira C, Garcia-Perez L, Aizpuru F, Sarasqueta C. Patient acceptable symptom state and OMERACT-OARSI set of responder criteria in joint replacement. Identification of cut-off values. Osteoarthritis Cartilage. 2012 Feb;20(2):87-92. Epub 2011 Nov 20.

28. Katz NP, Paillard FC, Ekman E. Determining the clinical importance of treatment benefits for interventions for painful orthopedic conditions. J Orthop Surg Res. 2015 Feb 3;10:24.

29. Nerhus TK, Heir S, Thornes E, Madsen JE, Ekeland A. Time-dependent improvement in functional outcome following LCS rotating platform knee replacement. Acta Orthop. 2010;81(6):727-32.

30. Petursson G, Fenstad AM, Gøthesen Ø, Haugan K, Dyrhovden GS, Hallan G, Röhrl SM, Aamodt A, Nilsson KG, Furnes O. Similar migration in computer-assisted and conventional total knee arthroplasty. Acta Orthop. 2017 Apr;88(2):166-72. Epub 2016 Dec 20.

31. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010 Mar 23;340:c332.

32. Dripps RD. New classification of physical status. Anesthesiol. 1963;24:111.

33. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and Osteoarthritis Outcome Score (KOOS)—development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998 Aug;28(2):88-96.

34. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. Clin Orthop Relat Res. 1989 Nov;248:13-4.

35. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. Health Policy. 1990 Dec;16(3):199-208.

36. 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 antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988 Dec;15(12):1833-40.

37. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. Health Qual Life Outcomes. 2003 May 25;1:17.

38. Pham T, van der Heijde D, Altman RD, Anderson JJ, Bellamy N, Hochberg M, Simon L, Strand V, Woodworth T, Dougados M. OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis Cartilage. 2004 May;12(5):389-99.

39. Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. J Bone Joint Surg Br. 1972 Feb;54(1):61-76.

40. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes. 2003 Nov 3;1:64.

41. Aunan E, Næss G, Clarke-Jenssen J, Sandvik L, Kibsgård TJ. Patellar resurfacing in total knee arthroplasty: functional outcome differs with different outcome scores: a randomized, double-blind study of 129 knees with 3 years of follow-up. Acta Orthop. 2016;87(2):158-64. Epub 2015 Nov 5.

42. Kassam AM, Dieppe P, Toms AD. An analysis of time and money spent on investigating painful total knee replacements. BJMP. 2012;5(3):a526.

43. Lindberg MF, Miaskowski C, Rustøen T, Rosseland LA, Cooper BA, Lerdal A. Factors that can predict pain with walking, 12 months after total knee arthroplasty. A trajectory analysis of 202 patients. Acta Orthop. 2016;87(6):600-6.

44. Rothwell AG, Hooper GJ, Hobbs A, Frampton CM. An analysis of the Oxford hip and knee scores and their relationship to early joint revision in the New Zealand Joint Registry. J Bone Joint Surg Br. 2010 Mar;92(3):413-8.

45. de Steiger RN, Liu YL, Graves SE. Computer navigation for total knee arthroplasty reduces revision rate for patients less than sixty-five years of age. J Bone Joint Surg Am. 2015 Apr 15;97(8):635-42.

46. Dyrhovden GS, Lygre SHL, Badawy M, Gøthesen Ø, Furnes O. Have the causes of revision for total and unicompartmental knee arthroplasties changed during the past two decades? Clin Orthop Relat Res. 2017 Jul;475(7):1874-86. Epub 2017 Mar 15.

47. Gøthesen Ø, Espehaug B, Havelin L, Petursson G, Furnes O. Short-term outcome of 1,465 computer-navigated primary total knee replacements 2005-2008. A report from the Norwegian Arthroplasty Register. Acta Orthop. 2011;82(3):293-300.

48. Jeffery RS, Morris RW, Denham RA. Coronal alignment after total knee replacement. J Bone Joint Surg Br. 1991 Sep;73(5):709-14.