

# Periprosthetic tibial bone mineral density changes after total knee arthroplasty

## A 7-year follow-up of 86 patients

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**Background and purpose** — Total knee arthroplasty (TKA) may cause postoperative periprosthetic bone loss due to stress shielding. Bone also adapts to mechanical alterations such as correction of malalignment. We investigated medium-term changes in bone mineral density (BMD) in tibial periprosthetic bone after TKA.

**Patients and methods** — 86 TKA patients were prospectively measured with dual-energy X-ray absorptiometry (DXA), the baseline measurement being within 1 week after TKA and the follow-up measurements being at 3 and 6 months, and at 1, 2, 4, and 7 years postoperatively. Long standing radiographs were taken and clinical evaluation was done with the American Knee Society (AKS) score.

**Results** — The baseline BMD of the medial tibial metaphyseal region of interest (ROI) was higher in the varus aligned knees (25%;  $p < 0.001$ ). Medial metaphyseal BMD decreased in subjects with preoperatively varus aligned knees (13%,  $p < 0.001$ ) and in those with preoperatively valgus aligned knees (12%,  $p = 0.02$ ) between the baseline and 7-year measurements. No statistically significant changes in BMD were detected in lateral metaphyseal ROIs. No implant failures or revision surgery due to tibial problems occurred.

**Interpretation** — Tibial metaphyseal periprosthetic bone is remodeled after TKA due to mechanical axis correction, resulting in more balanced bone stock below the tibial tray. The diaphyseal BMD remains unchanged after the initial drop, within 3–6 months. This remodeling process was related to good component survival, as there were no implant failures or revision operations due to tibial problems in this medium-term follow-up.

component in total knee arthroplasty (TKA) (Sundfeldt et al. 2006). One of them is the quality of the tibial metaphyseal bone, which is known to be able to adapt to mechanical alterations (Eckstein et al. 2009) such as malalignment caused by osteoarthritis (OA). After implantation of a knee prosthesis, these alterations in bone remodeling continue. Stress shielding means that the load is partially transferred through the cement and the prosthesis, which unloads periprosthetic bone (Au et al. 2007). The metaphyseal bone also adapts to the changed loading after correction of any preoperative malalignment. Intraoperative trauma and postoperative immobilization are other factors that affect bone quality in the postoperative recovery period.

Gait analysis has shown that in normally aligned knees, during walking, approximately 70% of the total load is transmitted through the medial compartment (Hurwitz et al. 1998) causing 2.5-fold load to the medial joint surface compared to the lateral one (Baliunas et al. 2002). The malalignment caused by knee OA affects this difference, either by enhancing it (varus) or diminishing it (valgus). Force-analysis calculations and dynamic analysis of forces around the knee during gait have also shown that the medial compartment bears the entire load in knees with varus malalignment, and that the lateral compartment bears load only in the case of more advanced valgus malalignment (Li and Nilsson 2001).

Dual-energy X-ray absorptiometry (DXA) is an accurate and reproducible method that can be used for measuring periprosthetic BMD; it has minimal precision error, a low coefficient of variation, and good reproducibility proven in a previous study (Soininvaara et al. 2000). The commercial software algorithms permit measurements of BMD adjacent to metal implants (Soininvaara et al. 2000).

Many factors influence the stability of the tibial prosthesis

**Table 1.** General patient characteristics at baseline (mean, range, and standard deviation as appropriate)

Baseline characteristics	Varus knees preoperatively	Valgus knees preoperatively
No. of patients	67	19
Male/Female	21/46	1/18
No. of knees operated	75	20
Age, years <sup>a</sup>	68 (48–83) (6.6)	67 (55–82) (7.4)
Body mass index <sup>a</sup>	30 (21–43) (4.5)	28 (19–39) (5.5)
Preoperative AKS score <sup>a</sup>	91 (15–179) (30)	99 (0–142) (39)

<sup>a</sup> mean (range) (SD)

Since poor bone quality—even though not convincingly proven—may contribute to early migration or even aseptic loosening (Tagil et al. 2003), it is important to gather more information on periprosthetic bone quality after TKA. In this prospective longitudinal follow-up study, we investigated the medium-term changes in BMD in tibial periprosthetic bone after TKA. We concentrated mainly on the lower limb alignment correction and the altered mechanical load generated by it. We hypothesized that mechanical axis correction has a decreasing effect on the periprosthetic BMD of preoperatively more loaded tibial condyle.

## Patients and methods

86 patients were recruited from the waiting list of the orthopedic department at Kuopio University Hospital between May 1997 and February 2001. The study material consisted of 91 knees with primary OA and 3 knees with posttraumatic OA (previous meniscectomy or anterior cruciate ligament rupture). Furthermore, in 1 knee there was an aseptic bone necrosis of the lateral femoral condyle. Knees that had previously had fractures were excluded. TKA with all 3 components cemented using standard techniques included the following prostheses: Duracon modular (Howmedica Inc. Rutherford, NJ/International Division of Pfizer, n = 50), NexGen (Zimmer, Warsaw, IN, n = 30), AMK (DePuy, Warsaw, IN, n = 14), and AGC (Biomet Merck Limited, Bridgend, South Wales, UK, n = 1).

All patients were operated on by experienced orthopedic surgeons. Full weight bearing was allowed immediately after the operation. The American Knee Society score (AKS) was used to clinically evaluate the knee status and function during daily activities preoperatively and at each follow-up visit—3 months and 1, 2, 4, and 7 years postoperatively.

The patients were free of any diseases and medications known to influence bone mineral metabolism, which was also confirmed at every follow-up visit and appointment for BMD measurement throughout the follow-up period.

A long standing radiograph was taken both preoperatively and at each follow-up visit, to measure the tibiofemoral angle.

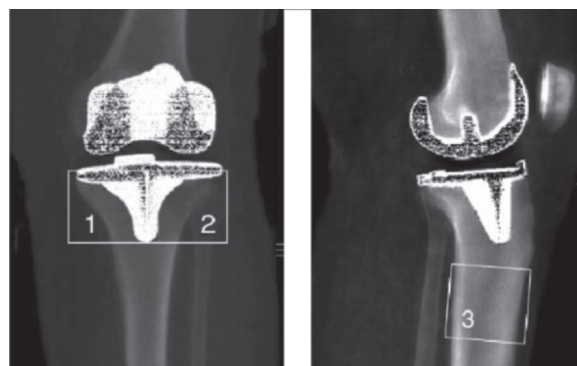


Figure 1. Periprosthetic regions of interest (ROIs) of the tibia: medial metaphyseal (1), lateral metaphyseal (2), and diaphyseal (3).

67 patients had a varus aligned knee and 19 of them had a valgus aligned knee. 9 subjects had both knees operated, 8 of them with both knees varus aligned and 1 with both knees valgus aligned. The preoperative long standing radiographs revealed mean malalignment of the lower limb mechanical axis of 11° (1–30) of varus in the preoperative varus group and 7.6° (0–24) of valgus in the preoperative valgus group. In preoperatively varus aligned knees, the mean postoperative mechanical axis was straight (0.0°) and remained virtually unchanged throughout the follow-up. In preoperatively valgus aligned knees, the mean correction was to 0.6° of valgus (range: 4° varus to 9° valgus) at 3 months postoperatively, but a slight transition towards residual valgus occurred during the follow-up (1.6° in 7 years). Postoperative mechanical axis malalignment (deviation of more than ± 3° of straight lower limb mechanical axis) was found in 19 preoperatively varus aligned knees (12 residual varus and 7 valgus), and in 4 preoperatively valgus aligned knees (1 varus and 3 residual valgus).

The proportion of women was higher in the valgus group than in the varus group (95% and 69% of operated knees). Age, body mass index, and preoperative AKS score were similar between the groups (Table 1).

BMD of the proximal tibia was measured by fan-beam dual-energy X-ray absorptiometry (DXA) (Lunar Expert). 7 measurements were taken, the first within 1 week after the operation and the others 3, 6 months, and 1, 2, 4, and 7 years postoperatively. Bone in the diaphyseal ROI (Figure 1) was expected to be minimally affected by the operation, as we used the extramedullar guiding systems; thus, it was expected to show the normal age-related decrease in BMD during the follow-up. The precision, expressed as the coefficient of variation for repeatedly measured BMD in these ROIs, is 2.9% (2.3–3.3) (Soininvaara et al. 2000). In order to minimize operator-related inaccuracies, no attempt was made to exclude a cement mantle from the analysis.

## Statistics

The statistical analysis was performed using SPSS software, version 19. The comparison between the series of the mea-

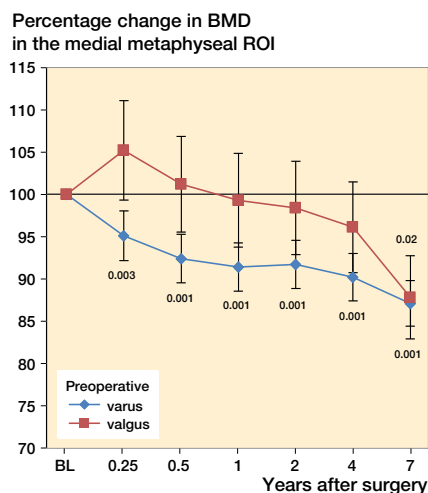


Figure 2. Percentage change in bone mineral density (BMD) of knees that were varus aligned and valgus aligned preoperatively. Medial tibial region of interest. 95% confidence intervals are shown. p-value shown are compared to baseline.

measurements against baseline and each follow-up point measured was tested with a linear mixed-effects model. The group differences in follow-up points were tested with the same model. The mixed model was used to assess the association between the AKS scores and BMD changes in ROIs measured at the 7 determined time points. In the model syntax, we used the patients as random effects. The effects of the background variables such as patient age, sex, BMI, and the model of prosthesis were also analyzed using the linear mixed effect model. All BMD data analyzed were confirmed to be normally distributed by mixed-model residuals histograms. The results are given as mean and 95% confidence interval (CI). Any p-values less than 0.05 were considered to be significant.

### Ethics

The study protocol was approved by the local ethics committee (decision number 71/97; May 13, 1997). All the patients gave written informed consent.

## Results

### Clinical evaluation

The AKS scores improved in both groups from baseline to 1 year ( $p < 0.001$ ). AKS score was significantly higher in the varus group from 3 months up to 7 years of follow-up (range of p-values: 0.03–0.001) (Table 2, see Supplementary data). Most of the patients attended all of the BMD measurements up to the 4-year control. However, for various reasons (patients unwilling, DXA equipment not functioning), some patients failed to attend the 7-year follow-up examination (Table 2, see Supplementary data). 2 patients suffered periprosthetic femoral fractures, 1 between the 2-year and 4-year measurements and the other between the 4-year and 7-year measurements, so

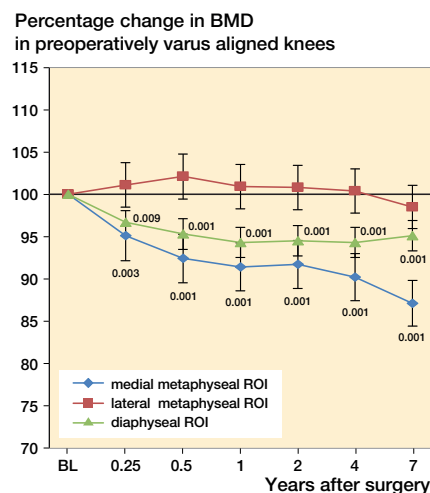


Figure 3. Percentage change in bone mineral density. Knees that were varus aligned preoperatively. 95% confidence intervals are shown. p-value shown are compared to baseline.

they were unable to continue in the study. No tibial component failures were found during the follow-up.

### Tibial BMD changes in knees that were varus and valgus aligned preoperatively

The mean baseline BMD of the medial metaphyseal ROI was higher in the (preoperatively) varus aligned group than in the valgus aligned group (25%,  $p < 0.001$ ). The difference remained statistically significant throughout the follow-up (13–18% ( $p = 0.04$ – $0.02$ ) from 3 months to 4 years; 23% ( $p < 0.002$ ) at 7 years) (Figure 2). However, the difference did not remain statistically significant when analyzed with the background variables of age, sex, prosthesis model, and body mass index. There were no statistically significant differences in the lateral metaphyseal or diaphyseal mean BMD values between the groups, either in baseline values or during the follow-up.

### Tibial changes in BMD in knees that were varus aligned preoperatively

The mean periprosthetic BMD decreased in medial metaphyseal and diaphyseal ROIs during the first 3 months postoperatively (4.9% and 4.3%;  $p = 0.003$  and  $p = 0.009$ , respectively). In the medial metaphyseal ROI, the decline continued up to the 7-year measurement (13% ( $p < 0.001$ ) between baseline and 7 years; 7.5% ( $p < 0.001$ ) between 3 months and 7 years), whereas in the diaphysis the BMD remained virtually unchanged from 3 months to 7 years (–0.9%). There were no statistically significant changes in mean BMD values in the lateral metaphyseal ROI during the follow-up (Table 3, see Supplementary data, and Figure 3).

### Subgroup analysis of preoperatively varus aligned knees, according to postoperative alignment

The preoperatively varus aligned knees were divided into 3

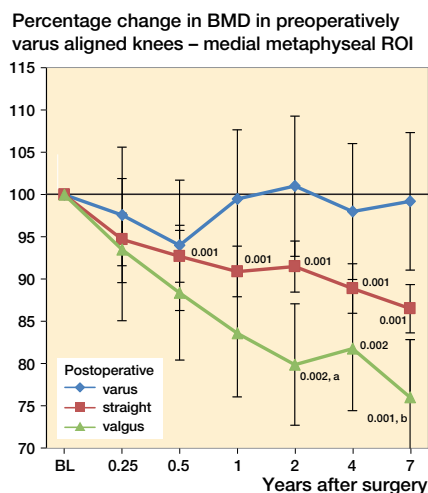


Figure 4. Subgroup analysis of the knees that were varus aligned preoperatively. Percentage change and the behavior of bone mineral density (BMD) in the medial tibial region of interest according to the postoperative alignment. 95% confidence intervals are shown. p-value shown are within the subgroup, compared to baseline BMD measurement. <sup>a</sup> p-value = 0.02 between the knees that were varus aligned and valgus aligned postoperatively, and between the knees that were straight and valgus aligned postoperatively. <sup>b</sup> p-value = 0.01 between the knees that were varus aligned and valgus aligned postoperatively, and p-value = 0.02 between the knees that were straight and valgus aligned postoperatively.

subgroups according to the postoperative lower limb mechanical axis. There were no statistically significant differences in the baseline mean periprosthetic BMD values between the postoperatively residual varus, straight, or valgus aligned subgroups. The BMD of the medial metaphyseal ROI decreased significantly in the subgroup where the mechanical alignment was adequately corrected, and especially in the subgroup where the postoperative mechanical alignment was in valgus. The decrease was significant from 1 to 7 years compared to the baseline value in the postoperatively valgus aligned subgroup (16% ( $p = 0.02$ ) in the 1-year measurement down to a 24% decrease ( $p < 0.001$ ) at 7 years). In the postoperatively straight aligned subgroup, the decrease was significant from 3 months (5.3%;  $p = 0.03$ ) to 7 years (14%;  $p < 0.001$ ) (Table 4, see Supplementary data, and Figure 4). The mean tibial diaphyseal BMD decreased in the postoperatively straight aligned subgroup from 3 months to 7 years compared to the baseline values (2.6% ( $p = 0.02$ ) at 3 months; 6.1% ( $p < 0.001$ ) at 7 years) (Table 4, see Supplementary data). In the postoperatively varus aligned subgroup, there were no significant differences measured during the follow-up in any of the ROIs measured (Table 4, see Supplementary data).

The mean medial metaphyseal periprosthetic BMD was lower in the postoperative valgus subgroup at the 2- and 7-year measurements compared to the postoperatively straight and varus aligned subgroups (range of p-values: 0.02–0.01) (Table 4, see Supplementary data, and Figure 4).

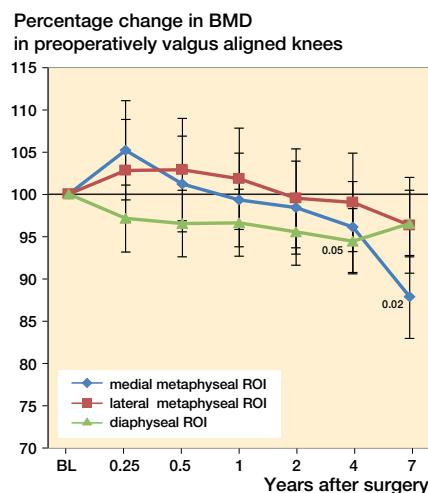


Figure 5. Percentage change in bone mineral density. Knees that were valgus aligned preoperatively. 95% confidence intervals are shown. p-value shown are compared to baseline.

### Tibial BMD changes in knees that were valgus aligned preoperatively

In the medial metaphyseal ROI, there was a slight but statistically insignificant increase in mean BMD at the 3-month measurement (5.2%;  $p = 1.0$ ) compared to the baseline. After that, the BMD began to decrease and the decline reached statistical significance at 7 years compared to the baseline and 3-month measurements (12% ( $p = 0.02$ ) and 15% ( $p < 0.001$ ), respectively) (Figure 5). In diaphyseal ROI, the BMD decreased from baseline to the 4-year measurement (5.6%;  $p = 0.05$ ). There were no significant changes in BMD values in the lateral metaphyseal ROI during the follow-up (Table 5, see Supplementary data, and Figure 5).

## Discussion

The DXA measurements of periprosthetic bone at our institution have been shown to be precise, reproducible, and safe, with an average precision error of 2.9% in tibial ROIs after TKA (Soininvaara et al. 2000). Trevisan et al. (1998) reported the reproducibility of measurements of bone mineral content and density in the tibial regions, which ranged from 0.9% to 2.6% for the posteroanterior scans and from 2.3% to 4.7% for the lateral scans, depending on the region considered.

This medium-term follow-up study showed that the mean BMD in medial metaphyseal ROI was higher in (preoperatively) varus aligned knees than in valgus knees. It decreased during the first year of the follow-up, thus slightly leveling the difference between the groups. At the 7-year follow-up, the mean medial BMD of the valgus group also decreased compared to baseline, reaching an almost similar decline to that which occurred in the varus group (12% and 13%, respectively), although the decline configurations were quite differ-



ent during the early phase of follow-up (Figure 2). Our previously published 1-year follow-up study of 69 subjects from this same patient population described similar early-phase results (Soininvaara et al. 2004).

The subgroup analysis of the (preoperatively) varus aligned knee group revealed differences in mean BMD values between the correctly re-aligned knees and the inaccurately re-aligned knees. The mean medial BMD of the knees with residual varus postoperatively did not decrease, possibly because the alignment was not properly corrected. In the postoperatively optimally aligned straight knees, the decrease was clearly detected and in the postoperatively valgus aligned knees, the decrease was most prominent (up to 24% at 7 years).

The varus and valgus groups differed in terms of group sizes and sex distribution (Table 1); neither prospective matching nor blinding was performed between groups. A retrospective matching was carried out with background variables known to affect BMD. The mean baseline BMD values of tibial diaphyseal and lateral metaphyseal ROIs between the (preoperatively) varus and valgus aligned knees resembled each other quite closely. On the other hand, the mean baseline BMD values of the medial metaphyseal ROI differed in favor of the varus group with higher BMD values, even when the background variables were included in the analysis. These results are in accordance with findings in the literature (Li and Nilsson 2000).

The medial metaphyseal BMD remained different between the varus and valgus groups during the follow-up, when the background variables were not included in the analyses, but the difference between the groups was not statistically significant from the 3-month to the 7-year measurements when they were included. We therefore suggest that this leveling of the medial metaphyseal periprosthetic BMD between the groups after baseline measurements is an effect of mechanical axis correction. The subgroup analysis of the (preoperatively) varus aligned knee group also supports this hypothesis. Bone mineral distribution is affected directly by local mechanical stress and loading in patients with OA of the medial compartment of the knee. This was also the conclusion of Wada et al. (2001).

The decrease in BMD of the more loaded medial condyle could also be a desirable change concerning the survivorship of the prosthesis component. In a finite element analysis study, Taylor et al. (1998) suggested that an increase in bone stress to the medial cancellous bone is related to component migration, and it may contribute to a lower survival rate of the tibial component. This result highlights the importance of a straight postoperative mechanical axis and balanced bone stock after TKA.

The short-term decrease in BMD in our study population in the medial metaphyseal and diaphyseal ROIs is in accordance with many previous studies (Petersen et al. 1995, Li and Nilsson 2000, Lonner et al. 2001, Petersen et al. 2005, Abu-Rajab et al. 2006, Saari et al. 2007, Hernandez-Vaquero et al. 2008, Munro et al. 2010). The metabolic reaction of the bone to the operative trauma combined with the effect of postoperative

immobilization would explain this decline. Li and Nilsson (2000) found a recovery in BMD after 2 years of follow-up, but ongoing bone loss is a more common finding in follow-ups (Hvid et al. 1988, Petersen et al. 1995, 2005, Saari et al. 2007). Preoperative varus malalignment causes more load and high initial BMD in the medial tibial metaphysis. The postoperative loss of BMD in this preoperatively more loaded condyle that we found is in accordance with previous findings (Hvid et al. 1988, Petersen et al. 1995, Regner et al. 1999). However, there are still few long-term results concerning changes in BMD. Levitz et al. (1995) found a similar recovery in overall BMD at the 1-year measurement, as did Li and Nilsson (2000) after 2 years, but surprisingly they found a 36.4% decrease in overall periprosthetic tibial bone mineral density when 7 patients were followed up for 8 years after TKA. Saari et al. (2007) found an initial decline in periprosthetic BMD at the 1-year measurement, but BMD was similar between the measurements at 1 and 2 years, and at 2 and 5 years, in any of the ROIs measured. The decrease in BMD was notably deeper than that found in our study: 18–26% in medial metaphyseal ROIs, 12–21% in lateral metaphyseal ROIs, and 5–20% in diaphyseal ROIs. These results resemble the findings of Regner et al. (1999), who found a 26% decrease in the medial tibial condyle. Hernandez-Vaquero et al. (2008) found a decrease in periprosthetic bone below the tibial component of 5.1% at 7 years after the surgery. The decline in medial tibial metaphyseal periprosthetic bone was 9.1% with cylindrical-type components and 6.1% with cruciform-type components. These declines more closely resemble our findings.

During follow-up, we did not detect any changes in mean BMD values of the preoperatively more loaded lateral condyle in the preoperatively valgus aligned group. The minor, statistically not significant increase (5.2%) in the BMD of (preoperatively) more unloaded medial condyle leveled at 6 months to 2 years. A similar minor increase was also found by Petersen et al. (1995). However, the BMD of this ROI did not decrease statistically significantly compared to mean baseline BMD values before the 7-year measurement. The preoperative malalignment (7.6 degrees of valgus) and the number of subjects were probably too low, thus leading to the unpowered study design for this group. Even so, the pattern of change was different from that seen with varus aligned knees (Figure 2).

The diaphyseal BMD remained unchanged after the initial drop within 3–6 months. Even the normal annual decline of 1%—or 8–9% over a decade previously reported in the literature (Bohr and Schaadt 1987, Petersen et al. 1995)—could not be detected. This might be a result of improved functional capability, which is clearly shown as improved mean AKS scores. In the varus group, there were no changes in BMD of the lateral metaphyseal ROI. The preserved diaphyseal and lateral periprosthetic BMD probably increases the stability and therefore also the longevity of the prosthesis component.

The influence of tibial insert design and also the differences between cemented and uncemented implants have been stud-

ied in the past decade. Saari et al. (2007) did not detect any influence of tibial insert constraint on the postoperative bone remodeling over 5 years of follow-up. Munro et al. (2010) found no difference in changes in BMD between the rotating- and fixed-platform knees at 2-year follow-up. Li and Nilsson (2000) were unable to identify any differences in BMD between cemented and uncemented fixation with a 2-year follow-up. The study of Lonner et al. (2001) does, however, support the contention that use of a cemented stem reduces proximal stresses and may result in proximal bone resorption.

The strengths of the present study were the long follow-up and also the study method, which is considered to be precise and reproducible. The limitations of the study were the rather high number of dropouts in 7 years, which is rather common in this kind of study population of elderly patients, and the fact that there were some missing data in the BMD measurements.

In summary, tibial metaphyseal periprosthetic bone is remodeled after TKA due to mechanical axis correction, resulting in more balanced bone stock below the tibial tray. This remodeling process was related to good component survival, as there were no implant failures and there was no revision surgery due to tibial problems in this medium-term follow-up.

### Supplementary data.

Tables 2–5 are available on the Acta Orthopaedica website at [www.actaorthop.org](http://www.actaorthop.org), identification number 9469.

AJ: analysis and interpretation of data, and drafting of the manuscript. TS: collection and interpretation of data, design of the study, and revision of the manuscript. HK: collection and interpretation of data, design of the study, and revision of the manuscript.

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No competing interests declared.

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