

# Serum intact-parathyroid hormone level following total knee arthroplasty

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## ABSTRACT

**Purpose.** To evaluate short-term parathyroid hormone (PTH) secretion following total knee arthroplasty (TKA).

**Methods.** 119 Caucasian postmenopausal women aged 49 to 81 (mean, 69.8) years who underwent TKA for end-stage knee osteoarthritis were included. Serum levels of intact-PTH, calcium, phosphorus, and creatinine were evaluated pre- and post-operatively (on days -1 and 7). Creatinine clearance was also calculated.

**Results.** In 67 of the patients, serum intact-PTH levels decreased after TKA; this sample proportion was not significant ( $p=0.82$ ). In 16 of the patients, such levels elevated abnormally (above normal range). In the remaining 36 patients, such levels elevated within the normal range. Therefore, the mean serum intact-PTH level of all patients increased slightly after TKA (45.4 vs. 45.3,  $p=0.162$ ). The serum intact-PTH level did not correlate to body weight ( $r=-0.045$ ,  $p=0.624$ ), patient age ( $r=-0.061$ ,  $p=0.508$ ), serum creatinine level

( $r=0.084$ ,  $p=0.366$ ), and clearance of creatinine ( $r=-0.037$ ,  $p=0.692$ ).

**Conclusion.** In most postmenopausal women, the serum intact-PTH level decreased moderately following TKA, but in some, the level was abnormally elevated. This may interfere the prosthesis incorporation process.

**Key words:** arthroplasty, replacement, knee; osteoarthritis, knee; osteoporosis, postmenopausal; parathyroid hormone

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## INTRODUCTION

Parathyroid hormone (PTH) is a major regulator of bone metabolism and calcium homeostasis.<sup>1</sup> Continuously elevated PTH levels activate osteoclasts; intermittent administration of PTH induces osteoblastic activity and may enhance early fixation of both cemented and non-cemented implants.<sup>2,3</sup> Fixation of an implant depends partly on bone growth at its surface, and may be the end result of fracture healing.<sup>3</sup> The actual effects (if any) on

the implant incorporation process by continuously elevated serum PTH levels remain unknown. We evaluated short-term PTH secretion following total knee arthroplasty (TKA).

## MATERIALS AND METHODS

This prospective, observational study was approved by the scientific research board of our institution and conducted in accordance with the World Medical Association Declaration of Helsinki. Informed consent of each patient was obtained.

Between November 2004 and March 2007, 119 Caucasian postmenopausal women aged 49 to 81 (mean, 69.8) years who underwent TKA for end-stage knee osteoarthritis were included (Table). The mean postmenopausal period was 20.6 (range, 3–32) years. Patients were excluded if they had endocrine disorder, rheumatoid arthritis, secondary arthritis, osteoporosis (a t score of  $\leq -2.5$  in the hip and lumbar spine as measured by a bone density scan), or diseases that could interfere with bone homeostasis. Those receiving medication affecting bone metabolism were also excluded. Blood samples were collected after fasting for at least 12 hours, and the serum levels of intact-PTH, calcium, phosphorus, and creatinine were determined pre- and post-operatively (on days -1 and 7). The clearance of creatinine was also calculated. Patients with any abnormal value preoperatively were also excluded. No patient had had any fracture or had undergone any orthopaedic operation during the previous 36 months.

All patients underwent primary unilateral TKA by 3 different surgeons (under spinal or epidural anaesthesia), with the use of a pneumatic tourniquet. Two types of prostheses with a cemented tibial and a non-cemented femoral component (chromium-cobalt, metal on polyethylene) were used. The standard drain tubes were removed on postoperative day 2.

A difference of  $\geq 5$  pg/ml in mean intact-PTH levels before and after TKA was considered

important.<sup>4-6</sup> Based on the preoperative intact-PTH levels, the standard deviation was estimated as 12 pg/ml. Using Lehr's formula, the optimal sample size was  $\geq 94$  in order to have an 80% chance of detecting a difference of 5 pg/ml in the mean intact-PTH level at a 5% level of significance.

The distribution of the data among different groups was not normal according to the Kolmogorov-Smirnov test. The Wilcoxon signed rank test was therefore used to evaluate the impact of TKA on serum intact-PTH levels. All statistical tests were 2-tailed. The alpha level for all analyses was set at 0.05. The Spearman correlation coefficient was used to assess the relationship between serum intact-PTH levels and body weight, patient age, serum creatinine level, or clearance of creatinine.

## RESULTS

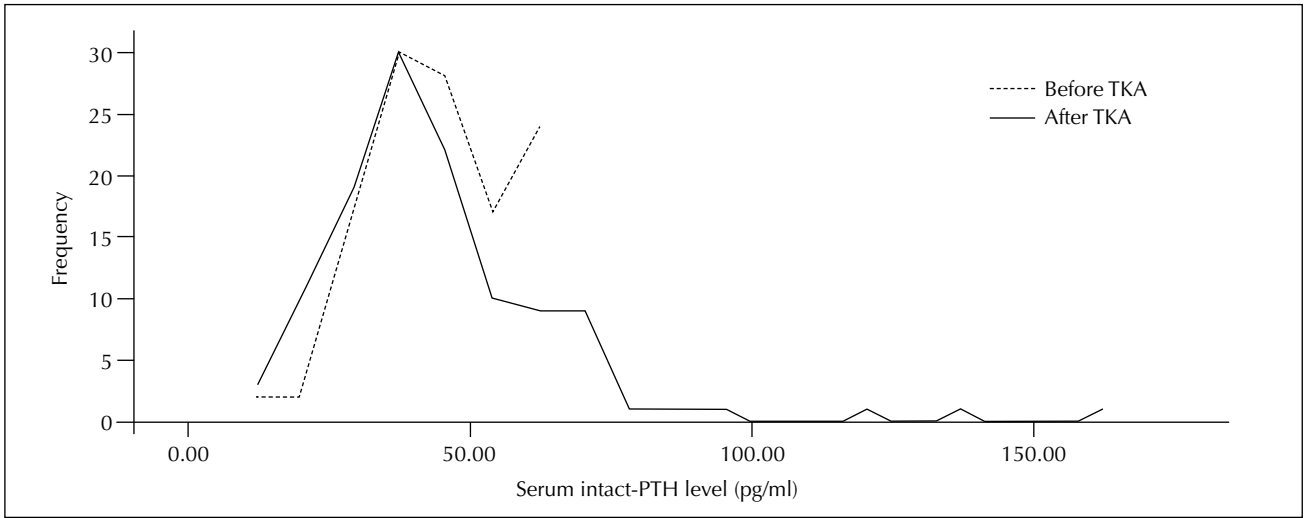
In 67 of the patients, serum intact-PTH levels decreased after TKA; this sample proportion was not significant ( $p=0.82$ ). In 16 of the patients, such levels elevated abnormally (above normal range). In the remaining 36 patients, such levels elevated within the normal range. Therefore, the mean serum intact-PTH level of all patients increased slightly after TKA ( $45.4 \pm 22.5$  vs.  $45.3 \pm 12.1$ ,  $p=0.162$ ) [Figs 1 and 2]. The serum intact-PTH level did not correlate to body weight ( $r=-0.045$ ,  $p=0.624$ ), patient age ( $r=-0.061$ ,  $p=0.508$ ), serum creatinine level ( $r=0.084$ ,  $p=0.366$ ), and clearance of creatinine ( $r=-0.037$ ,  $p=0.692$ ). The postoperative serum calcium and phosphorus levels remained within the normal range and thus not subjected to further analysis.

## DISCUSSION

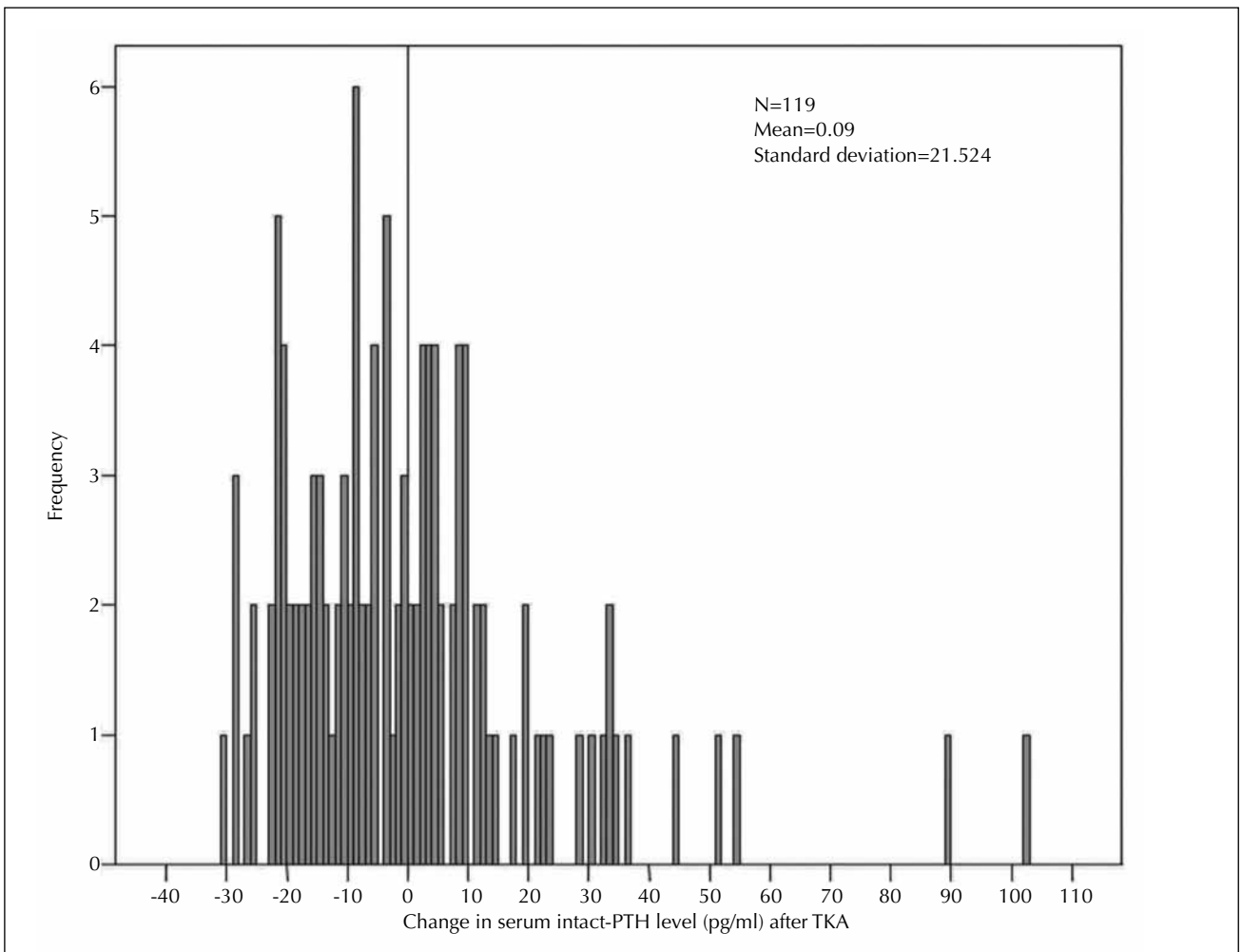
Serum PTH levels (and secretion) alter rapidly in response to calcium levels and other stimuli, as its main function is to maintain the calcium-ion concentration

Table  
Patient characteristics

Parameter	Mean $\pm$ SD
Age (years)	69.8 $\pm$ 6.0
Weight (kg)	75.8 $\pm$ 5.7
Serum creatinine level (mg/dl) [normal range, 0.6–1.2]	0.81 $\pm$ 0.12
Clearance of creatinine (ml/min) = $(140 - \text{age}) \times \text{weight} \times 0.85 \div 72 \times \text{creatinine level}$ (normal range, 75–115)	78.7 $\pm$ 15.5
Preoperative intact-parathyroid hormone level (pg/ml) [normal range, 12–65]	45.3 $\pm$ 12.1
Postoperative intact-parathyroid hormone level (pg/ml) [normal range, 12–65]	45.4 $\pm$ 22.5



**Figure 1** Distribution of serum intact-parathyroid hormone (PTH) levels before and after total knee arthroplasty (TKA) [normal range, 12–65 pg/ml].



**Figure 2** Distribution of changes in serum intact-parathyroid hormone (PTH) levels after total knee arthroplasty (TKA) [normal range, 12–65 pg/ml].

of extracellular fluids within physiological limits.<sup>1,7</sup> In 2 out of 32 patients with isolated tibial fractures, the serum PTH levels declined progressively over a period of 6 months.<sup>8</sup> In a study comparing several serum biochemical indices of bone and calcium metabolism of 20 elderly subjects with hip fracture versus 20 healthy age-matched controls,<sup>9</sup> the mean serum PTH concentrations were depressed one week after the fracture. In another study, serum PTH levels did not differ significantly between elderly women with hip fracture and controls 3 days after fracture, but increased significantly during the following year.<sup>10</sup>

Immediately after implantation, adjacent bone cells are likely to be dead due to necrosis or perhaps apoptosis.<sup>11</sup> The latter is a strong stimulus for bone resorption, which may lead to increased serum calcium concentrations and then decreased PTH secretion. Decreased PTH levels may also be due to temporary immobilisation. One week of immobilisation after a hip fracture<sup>9</sup> or a hemiplegic stroke<sup>12</sup> can lead to increased bone resorption, decreased bone formation, and elevated serum calcium levels; all inhibit PTH secretion.

Postoperative increase in intact-PTH levels may be partially attributed to increased secretion of catecholamines during the operation; catecholamines are known stimulants of PTH secretion.<sup>7,11,13</sup> In 21% of hip fracture patients, serum PTH levels increase above the reference range at postoperative week 2, owing to an adrenergic 'stress' response.<sup>15</sup> In patients undergoing orthopaedic operations, PTH secretion increases significantly from the day after surgery for more than a week.<sup>17</sup>

Intermittent administration of PTH enhances bone formation by increasing the number and activity of osteoblasts, by postponing their apoptosis, and by restricting their mineralisation.<sup>16</sup> On the contrary,

continuous administration of PTH decreases bone mass by activating osteoclasts.<sup>2</sup> Even though bone deposition occurs in both forms of administration, bone resorption offsets bone deposition during continuous administration.<sup>17</sup> Intermittent administration of PTH may improve the early fixation of both cemented and non-cemented implants, as it increases the density of regenerating bone in a dose- and time-dependent manner.<sup>18</sup> It also enhances the density of the bone surrounding the implant and increases the implant-to-bone contact.<sup>3</sup> In addition, it significantly increases the mechanical strength of cemented (polymethylmethacrylate) titanium implants,<sup>20</sup> and may facilitate bone formation and incorporation in non-cemented titanium implants.<sup>21</sup> It also stimulates implant anchorage in both normal and low-density trabecular bone.<sup>22</sup>

Continuous administration of PTH may have a negative impact on the synthesis of collagen type I and bone formation.<sup>16</sup> The risk of prosthetic loosening is determined during the first postoperative month.<sup>14,22</sup> Bone loss after TKA appears to be most obvious during the first 6 months and may be as high as 54 to 57%.<sup>23</sup>

A limitation of this study was that serum intact-PTH levels were not evaluated over a longer period. This may have generated different results. Not undertaking continuous blood samples was also a limitation, as initially elevated PTH levels in patients with hip fractures fell significantly at 2 weeks and remained significantly lower after 3 months.<sup>15</sup> In addition, TKAs were not standardised, as they were performed by 3 different surgeons and 2 different types of prostheses were used. There were no controls, as all patients had to have normal preoperative values and the strict inclusion criteria would have eliminated any exogenous or endogenous influences on the serum intact-PTH level.<sup>24</sup>

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