



Femoral Geometry in Bisphosphonate-related Atypical Femoral Fracture and Bisphosphonate-naïve Atypical Femoral Fracture

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Purpose: To compare the radiographic characteristics of femoral geometry between bisphosphonate-related atypical femoral fracture (BPAFF) and bisphosphonate-naïve atypical femoral fracture (BPnAFF).

Methods: A case-control study was conducted at the Police General hospital in Bangkok, Thailand, from January 2012 to December 2023; medical records and all available radiographs of hip and femoral fractures were reviewed. Atypical femoral fractures (AFF) were defined using the American Society for Bone and Mineral Research (ASBMR) 2013 criteria. BPAFF was identified in patients with a documented history of bisphosphonate prescription. The analysis encompassed a comparative assessment of femoral geometry parameters, including femoral offset, neck shaft angle, and lateral cortical thickness index (LCTi), between individuals with BPAFF and BPnAFF.

Results: A total of 13 BPAFFs and 10 BPnAFFs were identified in 19 patients. The prevalence rate in our hospital was 1.69%. Patients with BPAFF were comparatively younger (73.46 ± 6.30 vs. 82.6 ± 3.71 years, $p < 0.001$). Fractures were more prevalent in the subtrochanteric region in the BPAFF group (10 [76.92%] vs. 3 [30%], $p = 0.04$). BPAFF group had significantly higher LCTi at both subtrochanteric region (0.258 ± 0.050 vs 0.211 ± 0.067 , $p = 0.037$), and the femoral shaft level (0.357 ± 0.056 vs 0.288 ± 0.059 , $p = 0.005$). However, no statistically significant differences were observed in other femoral geometry parameters between both groups.

Conclusions: BPAFF exhibited a higher LCTi at the subtrochanteric and femoral shaft levels than BPnAFFs. On average, patients with BPAFF were younger than those with BPnAFF. Most BPAFF cases occurred in the subtrochanteric region, whereas BPnAFF cases were more commonly located in the diaphysis.

Keywords: Postmenopausal osteoporosis, atypical femoral fracture, femoral geometry, Bisphosphonate-related AFF, Bisphosphonate-naïve AFF

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Bisphosphonates (BP) are widely used as the first-line treatment for osteoporosis. While BP effectively reduce the risk of future fractures, long-term use can lead to a rare yet devastating condition, bisphosphonate-related atypical femoral fracture (BPAFF) (Fig 1A, 1B) ⁽¹⁾. According to the American Society for Bone and Mineral Research (ASBMR) 2013 criteria, atypical femoral fractures (AFF) can also occur in individuals who have not

been exposed to BP; these are termed BP-naïve AFF (BPnAFF) (Fig 2A, 2B) ⁽²⁾. However, the true incidence of BPnAFF remains unclear, with one Swedish study reporting an incidence of approximately 0.8 per 100,000 person-years ^(3,4). Growing evidence suggests that factors such as the prolonged use of medications, such as glucocorticoids or proton pump inhibitors, contribute to the development of BPnAFF ^(5,6). However, the mechanism underlying BPnAFF remains unclear.

Femoral geometry, which imposes an excessive load on the lateral femoral cortex, is believed to be associated with the development of BPAFF ⁽⁴⁾. Femurs with increased anterolateral curvature (bowing) are expected to experience higher tensile stress than those with straighter femur configurations ⁽⁷⁾. Individuals with a BPAFF were found to exhibit a greater varus hip angle, greater femoral offset, and increased thickness of the lateral cortex at the lesser trochanter ⁽⁸⁾. These anatomical characteristics may affect the distribution of forces during weight-bearing activities in patients with BPAFF. Unfortunately, studies on the femoral geometry in BPnAFF and the differences in femoral geometry between BPAFF and BPnAFFs are scarce. In this study, we conducted a comparative analysis of the radiographic characteristics of the femoral geometry between BPAFF and BPnAFFs. We also explored the prevalence and demographic characteristics of patients with BPAFF and BPnAFF.

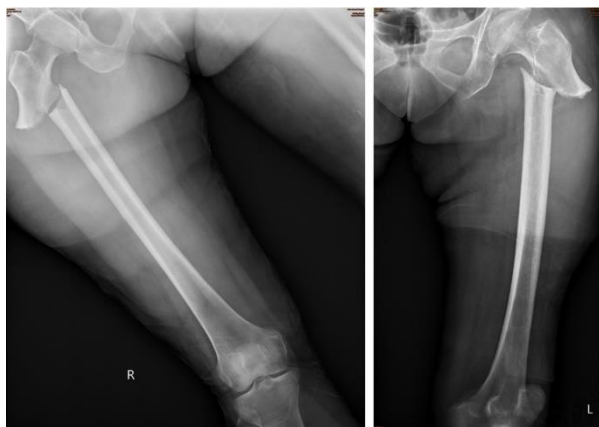


Fig. 1 Example of bisphosphonate-related atypical femoral fracture (BPAFF) radiographs.

Fig. 1A (Left): Radiograph from a 67-year-old woman experiencing a BPAFF at the right subtrochanteric region. The patient was diagnosed with osteoporosis and had a history of continuous alendronate usage for 10 years. She had no other underlying disease.

Fig. 1B (Right): Radiograph of a 73-year-old woman with type 2 diabetes mellitus with a history of continuous alendronate usage for 4 years, experiencing a BPAFF at the left subtrochanteric region.



Fig. 2 Example of bisphosphonate-naïve atypical femoral fracture (BPnAFF) radiographs.

Fig 2A (Left): Radiograph of a 72-year-old woman with type 2 diabetes mellitus who experienced a BPnAFF at the left femoral diaphysis. The patient was never diagnosed with osteoporosis, and had received no anti-osteoporosis treatment.

Fig 2B (Right): Radiograph of an 85-year-old woman without underlying disease who experienced a BPnAFF at the left femoral diaphysis.

MATERIALS AND METHODS

Study Design

This case-control study was conducted using the electronic database of a Police General hospital in Bangkok, Thailand. Ethical approval was obtained from the Institutional Ethics Committee. The initial search was performed utilizing diagnosis codes based on the 10th revision of the International Classification of Diseases (ICD-10) to identify hip and femoral fractures (ICD-10 codes S72.0-S72.9) from January 2012 to December 2023. The search strategy is illustrated in Fig 3.

Patient Inclusion and Exclusion Criteria

After the initial identification of hip and femoral fractures using the ICD-10, patient records and radiographic images were screened by two independent authors against the inclusion and exclusion criteria. Any discrepancies were resolved through discussions with a third author. The included patients had AFF as defined using the ASBMR task force 2013 criteria ⁽²⁾. The exclusion criteria were periprosthetic fractures, pathological fractures, metabolic bone diseases i.e., Paget's disease of the bone, and patients receiving radiation therapy.

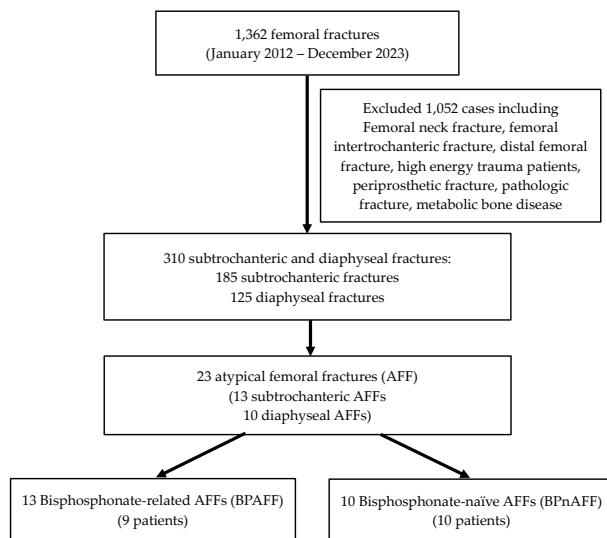


Fig. 3 Study flow chart.

Data Collection

The medical records of all patients with AFF were thoroughly reviewed to gather demographic data, including age, sex, body mass index (BMI), and underlying diseases (i.e., hypertension, dyslipidemia, diabetes mellitus type I or II, cardiovascular disease, rheumatoid arthritis, and knee osteoarthritis). Data regarding the diagnosis and pharmacological treatment of osteoporosis, including type and duration of BP use or prescription of denosumab, teriparatide, or selective estrogen receptor modulators (SERMs). Other risk factors for AFF have also been identified, such as smoking, alcohol consumption, history of fragility fractures, glucocorticoid use, and prolonged use of

proton pump inhibitors (PPI). In cases with missing data or concerns regarding the accuracy of medical records, patients were contacted via telephone for clarification. Finally, patients with AFFs were classified into two groups: BPAFF and BPnAFF.

According to the ASBMR 2013 criteria ⁽²⁾, AFF are defined as fractures that meet at least four of five major criteria. These criteria include fractures located anywhere along the femur from just distal to the lesser trochanter to just proximal to the supracondylar flare. The fractures are associated with minimal or no trauma, such as a fall from standing height or less. They typically originate in the lateral cortex and are substantially transverse in orientation, although they may become oblique as they progress medially. Complete fractures extend through both cortices and may be associated with a medial spike, whereas incomplete fractures involve only the lateral cortex. There was no evidence of comminution (fragmentation) at the fracture site. In the BPAFF group, BP use was defined as the use of any type of BP such as alendronate, ibandronate, or risedronate. The BPnAFF group also includes individuals who have not been exposed to BP ^(2,9). Alcohol consumption was defined as three or more units of alcohol consumed daily ⁽¹⁰⁾. Fracture history included any previous fractures resulting from high- or low-energy trauma or falls from standing height ⁽¹⁰⁾. Glucocorticoid use was determined as a cumulative dose of prednisolone equivalent exceeding 2 grams per year within one year before the occurrence of the fracture ⁽¹¹⁾. The presence of knee osteoarthritis (knee OA) was diagnosed based on the Kellgren-Lawrence classification stages 3 and 4 ⁽¹²⁾.

Radiographic Assessment

Radiographic assessments were performed using radiographs stored in a picture archiving and communication system (PACS). All radiographs were acquired in a uniform radiology unit using a standardized protocol. Anteroposterior (AP) radiographs of the femur were captured with the patient in the supine position, maintaining a source-to-film distance of 110 cm. The hips and knees were consistently extended and in neutral rotation with the patella oriented in an anterior direction. In each

instance, the X-ray beam was oriented perpendicular to the patient.

Radiographic parameters, including femoral offset, femoral neck-shaft angle, and lateral cortical thickness (LCT) index (LCTi) at the levels of the lesser trochanter, subtrochanteric region, and diaphysis, were measured on supine anteroposterior radiographs of the whole femur ⁽⁸⁾. In cases where obtaining a femoral radiograph was not feasible, supine anteroposterior radiographs of both hips were utilized ⁽¹³⁾. The specific measurements are shown in Figure 4. The measurements were conducted by a single investigator and subsequently verified by two co-authors with over five years of experience in orthopedics who were well acquainted with femur radiographs. The obtained results were compared between the two groups.

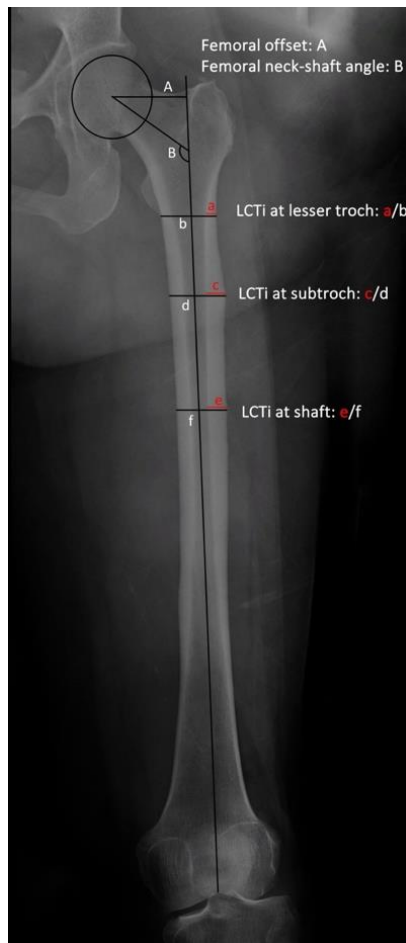


Fig. 4 Femoral geometry measurement.

Femoral offset: Mediolateral distance between the center of rotation of the femoral head and the long axis of the femur (A). Femoral neck-shaft angle: angle represented by the line bisecting the long axis of the femoral neck and femoral shaft (B). Lateral cortical thickness index (LCTi) at the lesser trochanter level: thickness of the lateral femoral cortex at the most distal point of the lesser trochanter divided by thickness of the entire width of the femur at the same level (a/b). Lateral cortical thickness index (LCTi) at the subtrochanteric level: thickness of the lateral femoral cortex at the subtrochanter divided by the thickness of the entire width of the femur at the same level (c/d). Lateral cortical thickness index (LCTi) at the femoral shaft: thickness of the lateral femoral cortex at the widest part of the femoral shaft divided by the thickness of the entire width of the femur at the same level (e/f).

Assessment of Reliability of Radiographic Measurements

Reliability refers to the consistency of the measured values. Each observer was blinded to the measurements obtained by the other observers. The interobserver reliability of each radiographic measurement was assessed using an intraclass correlation coefficient (ICC).

Statistical Analysis

All continuous data are presented with means \pm SDs. Student's t-test was used to compare the differences between two groups. The chi-square test was used for discrete data. Statistical significance was set at $p < 0.05$, significant.

The interobserver reliability of continuous data between the two observers was analyzed using ICC with a 95% confidence interval (CI). The assessment employed a two-way random effects model. Perfect reliability was interpreted as an ICC of 1, whereas the opposite was indicated by an ICC value of 0. ICC values were categorized as follows: poor (<0.20), fair ($0.21-0.40$), moderate ($0.41-0.60$), good ($0.61-0.80$), and excellent ($0.81-1.00$) ⁽¹⁴⁾. All statistical analyses were performed using the IBM SPSS statistical software version 29.0.1.

RESULTS

Prevalence and Demographic Data

A total of 1,362 femoral fractures were identified and collected for this study (545 men, 817 women). After the initial screening of the radiographs, 1,052 patients with the following conditions were excluded: femoral neck fractures, intertrochanteric femoral fractures, distal femoral fractures, periprosthetic fractures, pathological fractures, and metabolic bone diseases. The remaining 310 patients had 185 subtrochanteric fractures and 125 diaphyseal fractures. A total of 23 AFF were identified in 19 patients, of which 56.5% had subtrochanteric fractures (n=13) and 43.5% had diaphyseal fractures (n=10). Bilateral AFF was observed in 21.05% of cases (n=4). Notably, patients with bilateral AFF were exclusively observed in the BPAFF group. The incidence of AFF in our Police General hospital was 1.69%. In cases involving fractures specifically located in the subtrochanteric and diaphyseal regions, the prevalence of AFF was 7.41%. The distribution of the fracture locations is presented in Table 1.

Within the study population, 9 patients were classified as having BPAFF, while 10 patients belonged to the BPnAFF group. Fractures in the BPAFF group were more frequently located in the subtrochanteric region than those in the BPnAFF group (76.92% vs. 30%, $p=0.04$). Conversely, fractures in the diaphyseal region were more common in the BPnAFF group than in the BPAFF group (70% vs. 23.08%, $p=0.04$).

The study population consisted entirely of female patients with a mean age of 77.4 years (range 61–88 years). Detailed demographic data are presented in Table 2. Notably, the BPAFF group was significantly younger than the BPnAFF group

(73.46±6.30 vs 82.6±3.71 years, $p<0.001$). When considering fracture risk factors, 11.1% (n=1) of the patients in the BPAFF group were smokers, whereas all patients in the BPnAFF group were non-smokers. There was no history of alcohol consumption in either group. A history of fracture was identified in four patients, with an equal distribution of 22.2% (n=2) in both groups. In the BPAFF group, one patient (11.1%) was diagnosed with rheumatoid arthritis. The patient had received glucocorticoid treatment at a dosage of 7.5 mg/day for > 10 years. Knee OA was found to be prevalent in our study population, with a frequency of 73.6% (n=14). Specifically, Knee OA was present in 66.67% (n=6) of the patients in the BPAFF group and in 80% (n=8) of the patients in the BPnAFF group, although the difference was not statistically significant ($p=0.628$). PPI use was reported in 57.9% (n=11) of the patients in both groups, with a distribution of 55.6% (n=5) in the BPAFF group and 60% (n=6) in the BPnAFF group. There was no use of estrogen supplements, SERM, or antidepressants in the study population.

Among the 19 patients with AFF, 47.4% (n=9) received BP treatment. The mean duration of BP treatment was 77.33 months (range: 24-156 months). Specifically, alendronate was prescribed to 6 patients (66.7%), risedronate to 2 patients (22.2%), ibandronate to 2 patients (22.2%), and zoledronate to 1 patient (11.1%). Two patients consecutively received two types of BP; however, the exact reasons for this were unidentified. In the BPAFF group, one patient also received denosumab treatment. Three patients (33.3%) had a drug holiday before experiencing a fracture at 2, 8, or 24 months.

Table 1 Fracture location of the atypical femoral fracture (AFF).

Fracture locations	BPAFF (13 fractures)	BPnAFF (10 fractures)	p-value
	N (%)	N (%)	
Subtrochanter	10 (76.92)	3 (30)	0.04*
Femoral shaft	3 (23.08)	7 (70)	0.04*

BPAFF, bisphosphonate-related atypical femoral fracture; BPnAFF, bisphosphonate-naïve atypical femoral fracture.

Table 2 Baseline characteristics of the included atypical femoral fracture (AFF) patients.

Demographic data	BPAFF (n=9 patients)	BPnAFF (n=10 patients)	p-value
	N (%) or mean \pm SD	N (%) or mean \pm SD	
Age (years)	74 \pm 7.14	82.6 \pm 3.71	0.004
Sex			
Female	9 (100)	10 (100)	
Body mass index (kg/m ²)	22.7 \pm 2.27	23.08 \pm 3.78	0.794
Smoking	1 (11.1%)	0 (0)	0.474
Fragility fracture history	2 (22.2%)	2 (22.2%)	1.000
Alcohol consumption	0 (0)	0 (0)	-
Proton pump inhibitor (PPI) use	5 (55.6%)	6 (60%)	0.587
Estrogen use	0 (0)	0 (0)	-
Selective Estrogen Receptor Modulators (SERMs)	0 (0)	0 (0)	-
Antidepressant	0 (0)	0 (0)	-
Bilateral AFF	4 (44.44)	0 (0)	0.102
Medical history			
Diabetes mellitus	2 (22.22)	0 (0)	0.211
Osteoarthritis of knee	6 (66.67)	8 (80)	0.628
Rheumatoid arthritis	1 (11.11)	0 (0)	0.474

BPAFF, bisphosphonate-related atypical femoral fracture; BPnAFF, bisphosphonate-naïve atypical femoral fracture.

Table 3 Femoral geometry measurement of bisphosphonate-related atypical femoral fracture (BPAFF) vs bisphosphonate-naïve atypical femoral fracture (BPnAFF).

Femoral measurements	Mean \pm SD		p-value
	BPAFF	BPnAFF	
Femoral offset	3.193 \pm 0.82	3.252 \pm 0.66	0.429
Femoral neck-shaft angle	139.138 \pm 9.38	141.472 \pm 7.56	0.264
LCTi (lesser trochanter)	0.1635 \pm 0.029	0.1513 \pm 0.028	0.165
LCTi (subtrochanter)	0.2581 \pm 0.050	0.2118 \pm 0.067	0.037*
LCTi (femoral shaft)	0.3579 \pm 0.056	0.2887 \pm 0.059	0.005*

LCTi = lateral cortical thickness index

Table 4 Interobserver reliability of radiographic measurements.

	Interobserver reliability	
	ICC	95% CI
Femoral offset	0.99	0.995-0.999
Femoral neck-shaft angle	0.90	0.745-0.962
LCTi (lesser trochanter)	0.94	0.770-0.978
LCTi (subtrochanter)	0.99	0.990-0.999
LCTi (femoral shaft)	0.82	0.623-0.919

ICC: intraclass correlation coefficient; CI: confidence interval

Comparison of Femoral Geometry

When comparing the BPAFF and BPnAFF groups, BPAFF group exhibited significantly higher LCTi at the subtrochanteric level (0.258 ± 0.050 vs. 0.211 ± 0.067 , $p=0.037$) and the femoral shaft level (0.357 ± 0.056 vs. 0.288 ± 0.059 , $p=0.005$). However, no statistically significant differences were observed between the two groups in terms of other femoral geometry parameters, including femoral offset, femoral neck-shaft angle, and LCTi at the level of the lesser trochanter (Table 3). The interobserver reliability exceeded 0.80 in five radiological measurements (Table 4).

DISCUSSION

The prevalence of AFF among the 1,362 radiographic findings of femoral fractures was 1.69%, which was not markedly different from that in other Asian populations. A retrospective cohort study in Japan reported a prevalence of 0.63% among 2,238 femoral fractures⁽¹⁵⁾. A recent large multicenter case-control study in Korea reported a prevalence of 2.95%⁽¹³⁾. Among Caucasian patients, the prevalence was 0.46% in Sweden⁽¹⁶⁾ and 0.77% in the UK⁽¹⁷⁾, which is considerably lower than that in Asians.

BP have been identified as a risk factor for the development of AFF with estimated risk ratio of 1.7% (95% CI, 1.22-2.37)⁽⁴⁾. Prolonged duration of BP usage has been associated with an increased incidence of AFF, typically observed after using BP for more than five years⁽⁴⁾. However, Dell et al. reported that the incidence of AFF began to rise after three years of BP use⁽¹⁸⁾. In our study, the minimum duration of BP use was only two years. Notably, the timeframe for AFF development is comparatively faster than that reported in the literature⁽⁴⁾. Therefore, physicians must be vigilant against AFF during the early years of BP prescription. Alendronate was the most commonly prescribed medication in the BPAFF group. This may be attributable to the health coverage status of our study participants, in which alendronate was the only anti-osteoporotic medication that could be fully reimbursed for most patients. Owing to its superior affinity compared to other oral BP,

alendronate exhibited a more than seven-fold increase in the incidence of bone microdamage compared to the control group⁽¹⁹⁾. This escalation in microdamage was concomitant with a simultaneous 40% reduction in bone mineral density, ultimately leading to increased vulnerability to fractures⁽¹⁹⁾. Within our study population, three patients encountered fractures during a drug holiday program to mitigate the risk of AFF. The first patient received BP prescriptions for seven years and stopped usage for two months before suffering from the fracture. The second patient had 13 years of BP prescription with an months drug holiday protocol. The last patient experienced a fracture after 24 months of drug holidays, following six years of BP use. Based on the information provided above, it is apparent that even if we decide to discontinue medication or follow a drug holiday protocol, the risk of developing AFF persists. Consequently, in the context of patient care, it is advisable to schedule continuous follow-up appointments, such as those for prodromal thigh pain, to assess the risk factors for AFF.

All the patients in our study were postmenopausal women. The increased susceptibility of women to AFF compared to men can be associated with differences in femoral geometry and the resulting mechanical stress. Women typically have a narrower bone structure and wider pelvis, which result in greater stress on the lateral femoral cortex⁽³⁾. These variations in stress levels could potentially explain why women tend to accumulate more microcracks along the lateral femoral cortex with age, leading to greater vulnerability to fatigue fractures⁽²⁰⁾. Participants in the BPAFF group were younger, and the difference in mean age was statistically significant. These individuals may have started treatment at a younger age⁽²⁾, leading to the possibility of developing AFF at a younger age than the BPnAFF group.

AFF occurred more commonly in the subtrochanteric region (56.52%) than in the femoral shaft (43.48%). This result is consistent with that of a previous retrospective study in another hospital in Thailand⁽²¹⁾, which reported that 56% of AFF were in the subtrochanteric region. However,

several studies have reported that AFF are more common in the diaphyseal region^(13, 15-17). When comparing between 2 groups, subtrochanteric AFF were more common in the BPAFF group than in the control group. One possible explanation is that the subtrochanteric region has a higher LCT than the diaphyseal region, which increases the propensity for fracture⁽²²⁾. We also found that 21.05% of the patients had bilateral AFF. It is significant to emphasize that bilateral AFF was observed solely within the BPAFF group (44.44%). Our findings are consistent with those of a large Korean study⁽¹³⁾ that reported that 29% of the patients had bilateral lesions.

Although increased femoral curvature and varus alignment of the lower limbs are considered risk factors for AFF, the association between the LCT and AFF remains controversial⁽⁴⁾. A study by Koeppen et al.⁽²³⁾ found no statistically significant difference in LCT between the AFF and non-AFF groups. Meanwhile study by Lee et al.⁽²⁴⁾ reported a correlation between AFF and thicker lateral cortices at the level of the lesser trochanter. Furthermore, statistically significant differences in LCT were observed at the level of the lesser trochanter and 50 mm below it when compared to control groups⁽⁸⁾. In a recent multicenter case-control study conducted in Korea, the LCTi at the shaft level was greater in the AFF group than in the non-AFF group⁽¹³⁾. However, our research specifically focused on the AFF population, categorizing them into BPAFF and BPnAFF groups. Because BPnAFF is a very rare condition, no previous studies have compared this particular femoral geometry between BPAFF and BPnAFF. The results of our study revealed that the BPAFF group exhibited significantly higher LCTi at both the subtrochanteric ($p=0.037$) and femoral shaft levels ($p=0.005$) than the BPnAFF group. The inhibitory effect of BP on bone remodeling contributes to the impaired healing of stress fractures, leading to an increase in LCT in BPAFF⁽⁴⁾. Additionally, these fractures typically occur in the lateral cortex without precise localization. The likelihood of their occurrence depends on the individual's femoral geometry and area exposed to the greatest tensile stress.

The varus and acute angles of the femoral neck shaft have been identified as potential risk factors. Studies by Mahjoub et al.⁽⁸⁾ and Taormina et al.⁽²⁵⁾ found that AFF had a mean neck shaft angle of approximately less than 128.3 degrees and 128.9 ± 7 degrees, respectively. However, we acknowledge that there may be variations among races and further investigation is required to determine an appropriate cutoff point. In our study, we did not observe a statistically significant difference in the femoral neck shaft angle between the BPAFF and BPnAFF groups (139.138 ± 9.38 vs. 141.472 ± 7.56 , $p=0.264$).

This study highlighted the differences in fracture causation between patients with BPAFF and those with BPnAFF. Patients with BPAFF, who are typically younger, show higher LCTi in the subtrochanteric and femoral shaft regions, with fractures predominantly in the subtrochanteric area. This suggests that prolonged BP use increases the cortical bone density and alters bone remodeling, thereby increasing the risk of stress fractures, particularly in the subtrochanteric region, which bears higher loads because of its location near the hip joint⁽²⁶⁾. In contrast, patients with BPnAFFs, who are older, experience fractures due to age-related bone fragility, and these fractures are more common in the femoral diaphysis. Variations in the femoral diaphysis curvature and mechanical axis across individuals complicate the load distribution, contributing to different fracture sites in both groups⁽²⁷⁾. This variability introduces a limitation in our study, making it difficult to consistently assess the fracture risk. The precise pathogenesis that differentiates BPAFF from BPnAFF remains unclear and warrants further investigation.

In this study, all reliability values surpassed 0.90, except for LCTi. LCTi exhibited the lowest ICC at 0.82 (95% CI: 0.623-0.919). This may be due to the difference in measurement of the widest part of the femoral shaft between the two observers. However, it is noteworthy that the reliability value still exceeded 0.8. Conversely, the higher reliability observed for the other four measurements can be attributed to the relatively accurate specification of the reference points for these measurements.

This study has several clinical implications. First, bisphosphonate therapy should be initiated only when there are clear indications, and its use in younger patients should be avoided unless necessary. Regular monitoring, including inquiries regarding prodromal thigh pain and imaging, is crucial for the early detection of fractures. A drug holiday should be implemented when appropriate. Second, in cases with at-risk femoral geometry, it may be advisable to use oral bisphosphonates with lower bone affinity, such as risedronate, for short durations (no more than five years), with close monitoring. Third, this study highlights that individuals who have never used BP may still develop AFF, although in a relatively small number. This observation underscores the need for vigilance regarding delayed union after fixation.

This is the inaugural study in Thailand that focuses on comparing the geometric morphology of the proximal femur between the BPAFF and BPnAFF groups. To our knowledge, this is the first comparative analysis of its kind, incorporating data spanning up to 12 years and involving 23 AFF cases, a relatively substantial sample compared to previous Thai studies⁽²¹⁾ that primarily examined prevalence without detailed geometric analysis. However, this study has several limitations, including its case-control study design and reliance on medical records for data collection. Nevertheless, we attempted to address this issue by calling and inquiring for additional information from patients to obtain the most comprehensive data possible. Furthermore, certain important parameters, such as lower limb alignment, require additional imaging modalities, such as scintigraphy, which were not available for some of our patients. Future studies could benefit from incorporating CT images for comparison and further research, such as finite element analysis, to better understand the femoral geometry and fracture mechanics.

CONCLUSIONS

AFF is rare but can still be observed in patients with both BPAFF and BPnAFF. Although the mechanism underlying BPnAFF remains inconclusive, femoral geometry may play a role in its development. On average, patients with BPAFFs

were younger than those with BPnAFFs. Most BPAFF were found in the subtrochanteric region, whereas BPnAFFs were more commonly found in the diaphysis. Comparatively, the BPAFF group exhibited higher LCTi in the subtrochanteric and shaft regions, which is consistent with the pathophysiology of delayed healing. Further studies are required to elucidate the precise underlying mechanisms.

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