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Editorial

It is with great pleasure that I present to our readership the second issue of Volume 49 of the Journal of Southeast Asian Orthopaedics. This edition continues our commitment to fostering scholarly excellence and clinical relevance across the diverse and rapidly evolving field of orthopaedics in Southeast Asia and beyond.

In this issue, our featured original articles reflect the growing depth of regional research capacity and the clinical complexities our orthopaedic colleagues face daily. Notably, the lead article offers a rare comparative study on femoral geometry in bisphosphonate-related versus bisphosphonate-naïve atypical femoral fractures. This work contributes meaningful insight into pathophysiological distinctions that may influence clinical management, particularly in elderly women undergoing long-term osteoporosis treatment.

Another highlight includes the robust study on varus-valgus constrained implants in revision total knee arthroplasty, which provides a valuable survival analysis and identifies key risk factors for failure in an Asian population. The data presented will aid surgeons in surgical planning and implant selection for complex knee revision procedures.

Our additional original works span critical domains including hip fracture epidemiology, osteoporosis diagnostics using FRAX with or without BMD, biologic injections for knee osteoarthritis, and long-term outcomes of short-stem hip arthroplasty in young patients. These studies collectively underscore the breadth of conditions our regional population encounters, as well as the innovative strategies being employed in diagnosis, treatment, and follow-up.

Moreover, this issue features a review article addressing metastatic bone disease—an area of increasing clinical importance as life expectancy rises and systemic cancer care improves. Our single case report highlights the challenge of total hip arthroplasty in patients with compromised femoral bone quality, providing both technical insight and real-world applicability.

As we publish this issue, we also recognize the continued growth and strengthening of RCOST and our editorial board, whose tireless work ensures that this journal remains a credible academic resource and a regional platform for orthopaedic discourse. Our gratitude extends to all authors, reviewers, and contributors who continue to elevate the standards of our publication.

Lastly, I invite our readers to engage actively with this journal—whether as readers, authors, or reviewers—and to contribute toward the shared mission of advancing orthopaedic knowledge and improving patient care across Southeast Asia.

With best regards,

Professor. Thanainit Chotanaphuti, MD
Editor-in-Chief, Journal of Southeast Asian Orthopaedics
Past President, Royal College of Orthopaedic Surgeons of Thailand

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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 BPnAFF 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.

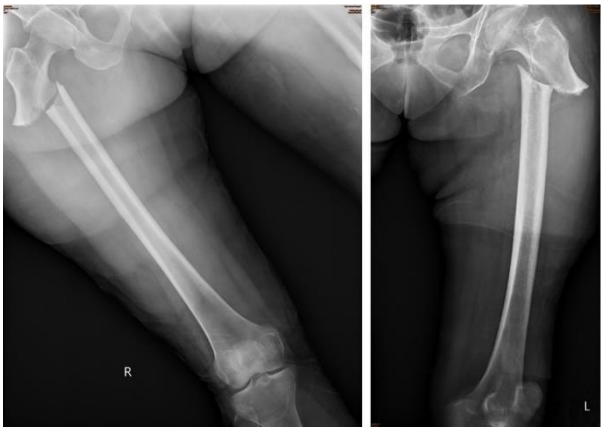

Fig. 1 Example of bisphosphonate-related atypical femoral fracture (BPAFF) radiographs.

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.

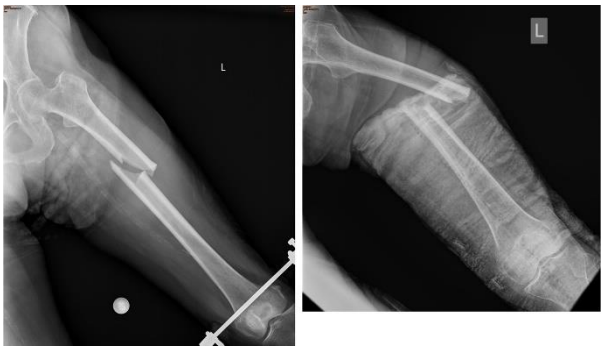

Fig. 2 Example of bisphosphonate-naïve atypical femoral fracture (BPnAFF) radiographs.

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.

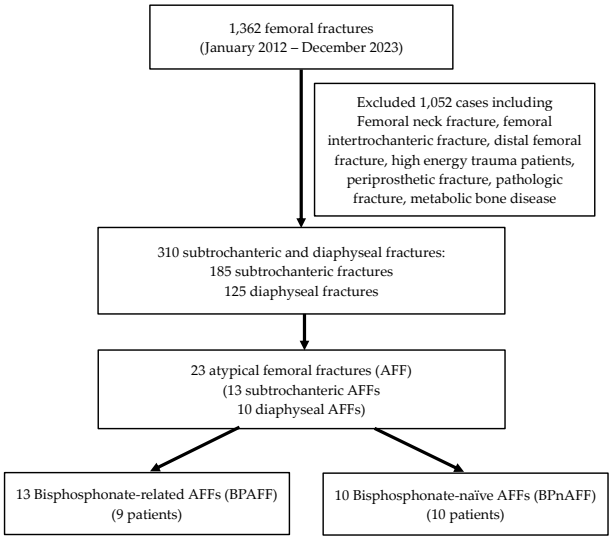

Fig. 3 Study flow chart.

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.

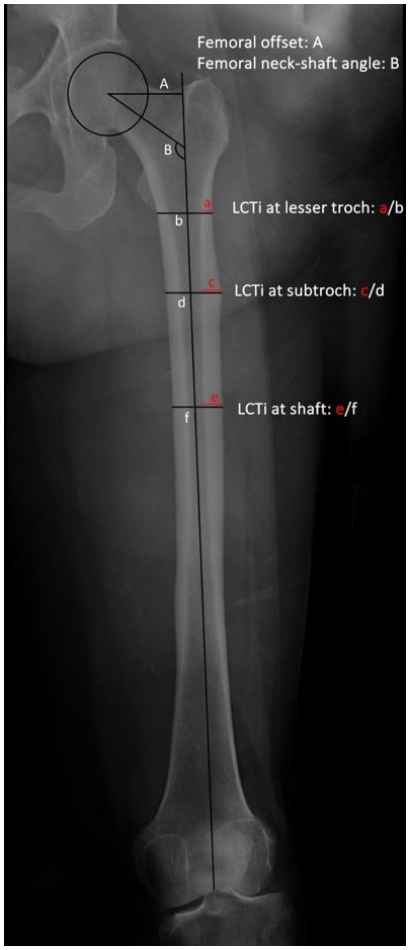

Fig. 4 Femoral geometry measurement.

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 ± 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 ± SD	N (%) or mean ± SD	
Age (years)	74 ± 7.14	82.6 ± 3.71	0.004
Sex			
Female	9 (100)	10 (100)	
Body mass index (kg/m^2)	22.7 ± 2.27	23.08 ± 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 ± SD		p-value
	BPAFF	BPnAFF	
Femoral offset	3.193 ± 0.82	3.252 ± 0.66	0.429
Femoral neck-shaft angle	139.138 ± 9.38	141.472 ± 7.56	0.264
LCTi (lesser trochanter)	0.1635 ± 0.029	0.1513 ± 0.028	0.165
LCTi (subtrochanter)	0.2581 ± 0.050	0.2118 ± 0.067	0.037*
LCTi (femoral shaft)	0.3579 ± 0.056	0.2887 ± 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 BPAFFand 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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Survivorship and Modes of Failure of Varus-Valgus Constrained Implants in Revision Knee Arthroplasty: A Study with a Median Follow-Up of 2.9 Years in an Asian Population

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Purpose: This study aims to evaluate the survival rate, primary causes of failure, and complications associated with varus-valgus-constrained (VVC) implants in revision total knee arthroplasty (TKA) at a large Asian medical institution.
Methods: We retrospectively reviewed 161 patients who underwent revision TKA with VVC implants at our institution between January 2013 and December 2021. Data on patient demographics, initial diagnosis, revision dates, causes of failure, and subsequent re-revisions were collected and analyzed. The Kaplan-Meier method was used to estimate implant survival rates.
Results: This study included 161 patients who received VVC implant revisions, with a mean age of 73 years at the time of surgery. The mean follow-up period was 2.9 years, extending up to 10.0 years. The primary reasons for revision were infection (47.8%), aseptic loosening (36%), and instability (8.1%). The overall survival rate of VVC implants was 86.3%, with aseptic revisions at 84.5% and septic revisions at 88.3%, based on a median follow-up of 2.9 years. The 2-year survival rates were 92.5% overall, 88.1% for aseptic revisions, and 97.4% for septic revisions. The re-revision rate was 13.7% (22 VVC implants), primarily due to infections (86.4%).
Conclusions: VVC implants demonstrated a high 2-year survival rate of 92.5% in revision TKA at a large Asian medical institution. The most common indications for VVC implant use in revisions were infection and aseptic loosening, with infection being the leading cause of subsequent re-revisions.

Keywords: Varus-valgus constrained, Revision knee arthroplasty, Survival rate

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A varus-valgus constrained (VVC) insert is an unlinked constrained device that utilizes a cam-and-post mechanism featuring a taller and thicker post. This design improves stability by resisting posterior translation and varus-valgus stress[1] and is indicated in both complex primary[2] and revision total knee arthroplasty (TKA). It is particularly indicated in cases involving medial collateral ligament insufficiency[3], flexion-extension gap mismatch[4], severe flexion contracture[5], and inade-

quate bone stock following prosthesis removal[6]. Notably, implant loosening is the most common reason for revision to a VVC implant[7]. Several studies[8 - 10] have reported that second-generation nonlinked semi-constraint implants, such as the CCK [Zimmer], TC-3 [Johnson & Johnson], and Endolink [Link], offer favorable survival rates with fewer complications.

Literature has identified instability, loosening, dislocation, arthrofibrosis, and fracture as potential failure modes for VVC implants. Additionally, aseptic revisions have been found to carry a 2.1 times higher risk of failure compared to primary VVC implants, while septic revisions have a 4.3 times higher risk of failure[7].

Notably, the majority of TKA prostheses have been designed primarily for the Caucasian population. Consequently, reports[11] suggest that anatomical and functional differences in Asian populations, such as a higher degree of tibial torsion and a mismatched femoral aspect ratio, may influence the suitability and performance of VVC implants originally designed for Caucasian populations[12].

This study aims to evaluate the survivorship of these implants, identify factors contributing to failures that necessitate revision TKA using a VVC insert, and assess the incidence of complications within a large Asian medical institution.

METHODS

We retrospectively reviewed our institution's database from January 1, 2013, to December 5, 2023, following approval from our institutional review board (COA No. Si 363/2023). The study included all patients who underwent revision knee replacement with VVC implants, performed by fellowship-trained orthopedic surgeons between January 2013 and December 2021. Patients who received VVC implants as their primary procedure or had incomplete data were excluded from the study. Data collection encompassed patient demographics, diagnosis at the time of revision, the revision date, and the cause of VVC implant failure. Failure causes were categorized into infection, aseptic loosening, periprosthetic fracture, polyethylene wear, instability, recurrent dislocation, and malalignment. The majority of VVC implants used at our institution were CCK [Zimmer] and TC-3 [Johnson & Johnson]. Implant survival was calculated from the date of surgery, with re-revision surgery serving as the endpoint. Re-revision included the exchange of modular components or partial or complete removal of implants. In the implant survivorship analysis, death was considered a competing risk to provide a comprehensive outcome evaluation. The reasons for re-revision were recorded and categorized similarly to the initial causes of failure. Prosthetic joint infection (PJI) was analyzed separately under 'Septic Revision' to account for revisions caused by infection-related complications. Additionally, re-revisions due to infection were classified as PJI-related, ensuring that the impact of infection on implant survival was independently assessed.

Statistical Analysis

Continuous data were presented as mean ± standard deviation or median (interquartile range), depending on data distribution. A comprehensive data collection process was conducted, including patient demographics, clinical characteristics, and follow-up information. To ensure accuracy and reliability, data validation processes were implemented, including double-checking entries by our author team. Categorical data were expressed as numbers and percentages. Comparisons of continuous variables across various failure causes were performed using a one-way analysis of variance or the Kruskal-Wallis test, depending on data distribution. Implant survivorship was assessed utilizing the Kaplan-Meier analysis, with hazard ratios calculated to estimate survival rates. Additionally, Cox regression analysis was used to adjust multiple variables. Statistical significance was defined as a p-value less than 0.05.

RESULTS

Our study included 161 patients who underwent revision surgery using a VVC insert. The patient group consisted of 28 (17.4%) males and 133 (82.6%) females. The mean age of participants at the time of surgery was 73 years, with a 95% confidence interval (CI) of 67–81 years. The mean

body mass index of participants was 25 kg/m² (95% CI: 23.7–27.4). Based on the World Health Organization classification[15], 7.5% of the participants were categorized as obese, 43.75% as pre-obese (overweight), and 48.75% as having a normal weight. The most prevalent underlying medical conditions were diabetes mellitus (72.7%), hypertension (54%), and dyslipidemia (26.7%). The average follow-up period was 2.9 years. A detailed summary of patient characteristics is presented in Table 1. The primary indications for revisions were PJI in 77 (47.8%) cases, aseptic loosening in 58 (36%) cases, and instability in 13 (8.1%) patients, as shown in Figure 1.

Table 1 Demographic data.

Variables	Data
Age	73 years (67–81)
Height	152.7 cm (149.1–157.7)
Weight	60.7 kg (54.2–64.8)
Body mass index	25 kg/m² (23.7–27.35)
Sex	
Female	133 (82.6%)
Male	28 (17.4%)
Side	
Right	96 (59.6%)
Left	65 (40.4%)
Underlying disease	
Diabetes mellitus	117 (72.7%)
Hypertension	87 (54%)
Dyslipidemia	43 (26.7%)
None	32 (19.9%)
Cause of Failure	
Aseptic loosening	58 (36%)
Dislocation	2 (1.2%)
Instability	13 (8.1%)
Loosening	2 (1.2%)
Malalignment	0 (0%)
Periprosthetic fracture	9 (5.6%)
Prosthetic joint infection	77 (47.8%)
Re-revision	22 (13.7%)
Cause of failure	
Dislocation	1 (4.55%)
Infection	19 (86.36%)
Instability	2 (9.09%)
Implant	
Exchange modular part	14 (63.63%)
Rotating Hinge Knee	4 (18.18%)
Debridement with prosthesis removal	2 (9.09%)
Revision Stem	1 (4.55%)

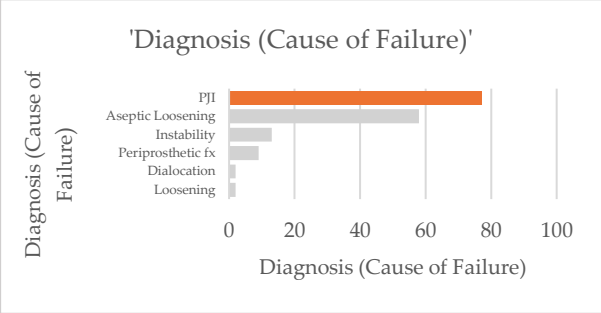

Fig. 1 Causes of failure.

This figure illustrates the distribution of various causes of failure in revision knee arthroplasty with varus-valgus-constrained inserts. The bar lengths represent the number of cases for each cause, highlighting PJI as the predominant cause of failure in the study cohort.

Survival Rate

The Kaplan-Meier analysis revealed that the average implant survival time in our study was 8.88 ± 0.21 years. The overall survival rate was 86.3%, with 84.5% for aseptic revisions and 88.3% for septic revisions, as depicted in Figure 2. Furthermore, the 2-year survival rate was 92.5% across all revisions, 88.1% for aseptic revisions, and 97.4% for septic revisions.

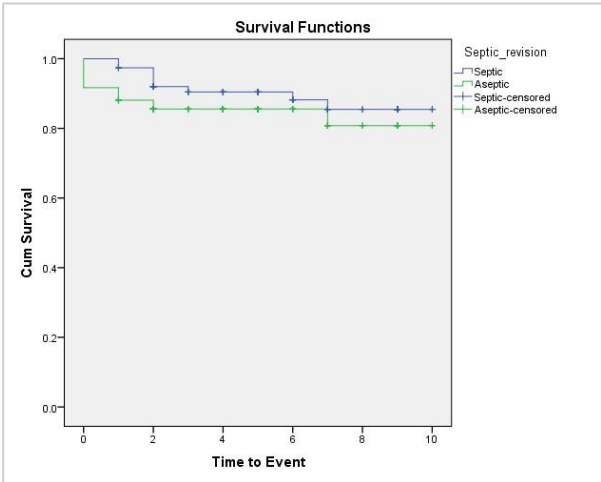

Fig. 2 Survival analysis.

This figure presents the Kaplan-Meier survival curves comparing the cumulative survival rates of septic and aseptic revisions in knee arthroplasty with varus-valgus-constrained inserts.

Complications

The overall re-revision rate was 13.7%, affecting 22 VVC implants. The predominant cause of these re-revisions was infections, which accounted for 86.4% (19 out of 22 cases). Instability was responsible for two (9.1%) cases, while dislocation occurred in one (4.6%) case. The most commonly performed procedure for re-revision was debridement, antibiotics, and implant retention, conducted in 14 (63.6%) knees, followed by a revision with a rotating hinge knee performed on four (18.2%) knees.

DISCUSSION

The consensus among surgeons is to use the least-constrained prosthesis possible in revision surgeries to minimize the risk of mechanical loosening and failure[4, 13, 14]. The VVC insert is widely used in both primary and revision procedures. Comparative studies have highlighted differences in the age at which revisions are performed. Hernandez et al.[15] reported a mean age of 63.9 years, while Siqueira et al.[7] found an average of 66.0 years. In contrast, our study demonstrated a higher average age of 73.0 years, reflecting differences in healthcare systems and the timing of specialist consultations between Asian and other regions. Furthermore, this study supports existing evidence that primary TKA is performed at an older age in Asian populations[16, 17].

The primary indications for revision TKA with VVC, as reported in previous studies[7, 15, 18], include aseptic loosening (29.9–48.8%), infections (28.1–32.1%), and instability (7.7–23.5%). These findings are consistent with our study, which identified PJI, aseptic loosening, and instability as the primary causes for revision procedures.

To the best of our knowledge, this study reports the largest VVC revisions in Asia currently available, demonstrating a strong survival rate of 86.3% overall, 88.3% for septic revisions, and 84.5% for aseptic revisions. As shown in Table 2, the survival rate in this study is slightly lower than that reported in other Asian studies[3, 19-21]. This difference may be attributed to the significantly higher proportion of septic revision cases in our study, which stands at 11.8%, a figure greater than those reported in any other Asian study. Notably, Mancino et al.[2] reported an overall reoperation rate of 11.1%. This finding aligns with those reported by Hernandez et al.[15], who additionally

Table 2 Revision total knee arthroplasty with varus-valgus-constrained implants in Asia.

Author (year of publication)	No. of Knees	Duration of follow-up (years)	Overall Reoperations	Overall Re-revisions	Re-revisions for Aseptic Loosening	Re-revisions for Infection	Reoperations for Other Reasons	Complications	All-Cause Survivorship
Nakano (2016)	41	4.1	7.30%	7.30%	0.00%	7.30%	0.00%	7.30%	92.68%
Lee JK (2012)	79	5.3	7.59%	7.59%	1.27%	5.06%	3.80% (1 Periprosthetic fracture and 2 stem tip pain)	10.10%	93% at 8 years
Kim YH (2009)	114	7.2	8.75%	7.00%	3.51%	1.75%	3.51% (Quadricep tendon rupture and fracture)	8.75%	96 % at 10 years
Hwang SC (2010)	15	2.4	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%
Current study	161	2.9	13.66%	13.66%	0.00%	11.80%	1.86% (Instability and dislocation)	13.66%	86.3%

reported survival rates of 81% at 3 years and 74% at 6 years. Moreover, Siqueira et al.[7] conducted a comprehensive analysis of 685 consecutive VVC cases, with an average follow-up period of 8.2 years, revealing a 10-year survival rate of 75.8% for aseptic revision and 54.6% for septic revisions.

Several studies[22-24] have highlighted the primary causes of failure in revision TKA to include infection (43%), stiffness (13%), and aseptic loosening (11%). Infection is often the leading cause of re-revision, likely due to the complexity of the procedure, prolonged operative times, and compromised soft tissue conditions[17, 25]. Specifically, in the context of revision TKA with VVC, a review by Siqueira et al.[7] supports our finding, showing that infection was the most frequent cause of re-revision, accounting for 42% of cases.

However, this study has some limitations, including the relatively short follow-up period and the limited sample size. We recommend that future research include longer-term follow-up periods and the implementation of prospective randomized controlled trials to provide more robust evidence.

CONCLUSIONS

At our large Asian medical institution, we recorded an impressive 2-year survival rate of 92.5% for revision TKA using a VVC insert. The primary reasons for VVC implant revisions were infection and aseptic loosening. Additionally, infection emerged as the most prevalent complication, which necessitated further revisions.

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The Impact of Postoperative CT Parameters on Functional Outcomes in Joint Depression-Type Calcaneal Fractures Fixed with Sinus Tarsi Locking Plate: A Retrospective Analysis

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Purpose: To examine the correlation between postoperative computed tomography (CT) parameters and functional outcomes in patients treated with sinus tarsi locking plates for joint depression-type calcaneal fractures.

Methods: This study retrospectively analyzed patients who underwent sinus tarsi locking plate fixation for joint depression-type calcaneal fractures at a tertiary hospital between 2019 and 2021. The patients were followed up for an average of 16 months. Collected data included demographic information and postoperative CT parameters, including Böhler's angle and posterior facet congruity. Functional outcomes were evaluated using the Foot and Ankle Ability Measure (FAAM) score.

Results: Postoperative CT scans were used to evaluate the quality of fracture reduction in 55 patients with calcaneal fractures treated with sinus tarsi locking plates. The mean FAAM score was 79.4 (range: 42–100). Among the patients, 45 (82%) achieved good functional outcomes, while 10 (18%) had poor outcomes, with no significant demographic differences between groups. Anatomical, near-anatomical, and poor reduction of the posterior facet were observed in 49%, 31%, and 20% of cases, respectively. Böhler's angle was >20º and <20º in 76% and 24% of cases, respectively. Anatomical reduction of the posterior facet showed a significant correlation (P=0.025) with favorable outcomes, whereas Böhler's angle showed no significant association (P=0.685).

Conclusions: Sinus tarsi locking plate fixation is effective in achieving satisfactory posterior facet reduction and functional outcomes for joint depression-type calcaneal fractures. Postoperative CT scans can help predict functional recovery by evaluating posterior facet reduction. Achieving posterior facet anatomical reduction is essential for favorable functional recovery.

Keywords: Calcaneus fracture, Postoperative CT, Sinus tarsi locking plate

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Calcaneal fractures are relatively common injuries, with their complex anatomy making effective treatment challenging[1,2]. Joint depression-type calcaneal fractures, in particular, pose significant management difficulties when using percutaneous techniques[3], often necessitating open reduction. Although the lateral extensile approach typically achieves better fracture reduction, the sinus tarsi

approach has shown promise in terms of functional outcomes and lower complication rates[4–6].

Sinus tarsi locking plate fixation has been demonstrated to offer reliable stability, low complication rates, and favorable functional outcomes in treating calcaneal fractures[7–10]. Additionally, postoperative computed tomography (CT) has emerged as a valuable tool for assessing the quality of reduction, particularly in examining posterior facet congruity, which can be challenging to evaluate with plain radiographs[11–13].

This study aims to examine the correlation between postoperative CT parameters and functional outcomes in patients with joint depression-type calcaneal fractures treated with sinus tarsi locking plates. By analyzing the postoperative CT images and patient-reported functional outcomes, we aim to identify significant correlations between these parameters.

MATERIALS AND METHODS

This retrospective study analyzed data from 55 patients who underwent sinus tarsi locking plate fixation for joint depression-type calcaneal fractures (Fig. 1) at a tertiary hospital between 2019 and 2021. The study was approved by the institutional review board, and informed consent was obtained from all patients.

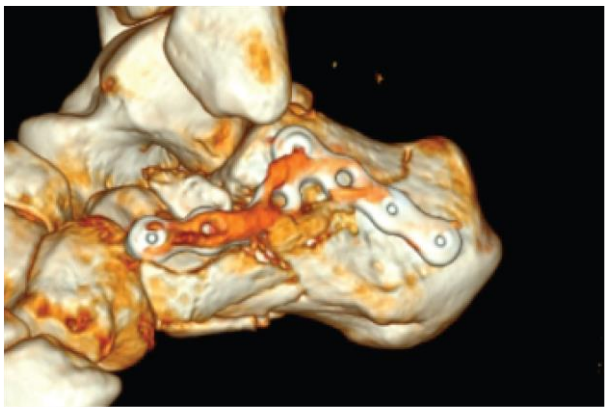

Fig. 1 Postoperative computed tomography scan of Sinus tarsi locking plate fixation.

Patients were followed up for a mean of 16 months, during which demographic data and postoperative CT parameters, including Böhler's angle and posterior facet congruity (Fig.2), were analyzed to assess the quality of reduction. Böhler's angle and posterior facet congruity were evaluated using postoperative CT reference points based on previously published studies[12]. The quality of reduction was classified as anatomical reduction (stepping <1 mm), near-anatomical reduction (stepping 1–3mm), and poor reduction (stepping >3mm)[14]. The Foot and Ankle Ability Measure (FAAM) score was used to evaluate clinical outcomes[15,16], with functional outcomes stratified as poor (score <90) or good (score ≥90)[17].

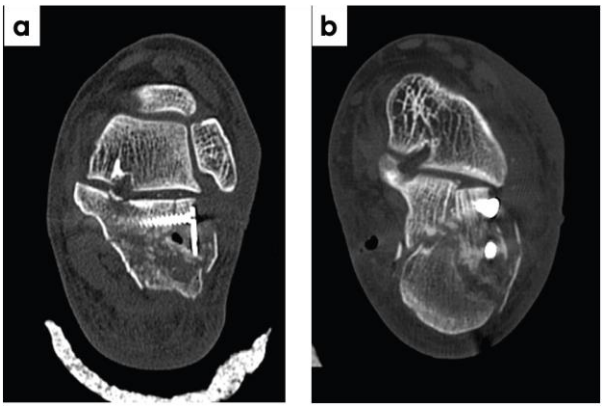

Fig. 2 Postoperative computed tomography scan of posterior facet reduction. **a.** anatomical reduction of posterior facet, **b.** poor reduction of the posterior facet.

Appropriate statistical methods, including multivariable logistic regression analysis, were used to analyze all data and examine the correlation between postoperative CT parameters and functional outcomes in patients with joint depression-type calcaneal fractures treated with sinus tarsi locking plates.

RESULTS

Postoperative CT scans were utilized to assess the quality of reduction achieved in 55 patients with joint depression-type calcaneal fractures treated with sinus tarsi locking plate fixation. Clinical outcomes were evaluated using the FAAM score, which revealed a mean value of 79.4 (range: 42–100) across all patients. Among these patients, 45 (82%) achieved good functional

outcomes, while 10 (18%) exhibited poor functional outcomes. No statistically significant differences in patient demographics were observed between the good and poor outcome groups (Table 1).

The results indicated that anatomical reduction with posterior facet congruity was achieved in 27 (49%) cases, near-anatomical reduction in 17 (31%) cases, and poor reduction in 11 (20%) cases. Multivariate analysis revealed a significant correlation between anatomical reduction and favorable functional outcomes (P=0.025). Additionally, Böhler's angle was restored to greater than 20º in 42 (76%) patients but remained less than 20º in 13 (24%) patients. However, no significant correlation was identified between Böhler's angle and the FAAM score (P=0.685) (Table 2).

Table 1 Patient demographics.

	Good	Poor	P-value
Age (years)	46.6 (±11.27)	49.3 (±12.55)	0.505
Sex			
Male	32 (71.1%)	9 (90%)	0.423
Female	13 (28.9%)	1 (10%)	
Mechanism of injury			
Fall from height	40 (88.9%)	9 (90.0%)	1.000
Traffic accident	5 (11.1%)	1 (10.0%)	
Initial Böhler's angle (º)	-0.62 (±10.28)	-1.5 (±7.63)	0.800
Smoking	17 (37.8%)	3 (30%)	0.731
Body mass index (kg/m²)	23.60 (±3.46)	21.88 (±3.49)	0.161
Time to surgery (h)	157.56 (±132.90)	209.5 (±130.32)	0.267

Table 2 Correlation between postoperative computed tomography parameters and functional outcome (Multivariate analysis).

Postoperative CT parameters	Odd ratio	95% CI	P-value
Böhler's angle (º)			
0–20	1		
>20	1.41	0.09–14.16	0.687
Posterior articular facet reduction			
Poor	1		
Near	6.55	0.90–47.56	0.063
Anatomical	7.52	1.23–43.95	0.025*

DISCUSSION

The optimal surgical approach for displaced intra-articular fractures is influenced by multiple factors, including the surgeon's experience with different methods, patients' comorbidities, and characteristics of the fracture and soft tissues. Over the past few decades, novel surgical approaches and techniques have been developed to minimize soft tissue complications and achieve a more precise restoration of the posterior facet[1]. The sinus tarsi approach involves making an incision from the tip of the lateral malleolus towards the base of the fourth metatarsal bone, providing excellent visualization of the subtalar joint. A comprehensive meta-analysis has supported this approach, highlighting its multiple advantages over the extensile lateral approach. The study demonstrated statistically significant reductions in operative time, complication rates, reoperations, and postoperative articular displacement[18,19].

Fixation options for the sinus tarsi approach include screw fixation, plate fixation, and anatomic plate fixation. Although no significant differences have been observed in wound complications and functional outcomes, both biomechanical and clinical studies have consistently shown that plate fixation offers superior performance in terms of stability, preservation of Böhler's angle, and the rate of implant removal compared to screw fixation[7,9,10,20]. In this study, all the patients were treated using an anatomical locking plate for the sinus tarsi approach, with no reported wound complications or hardware removal.

The posterior facet of the calcaneus is essential for weight-bearing and the biomechanics of subtalar motion. Cadaveric studies have demonstrated that articular incongruity leads to a major shift in load. Incongruent reduction of this joint can also impair foot and ankle function and may lead to osteoarthritis over time. Posterior facet congruity has been linked to better functional outcomes. The postoperative CT evaluation in this study revealed that 80% of cases achieved anatomical or near-anatomical alignment, which was associated with favorable functional outcomes.

The normal range for Böhler's angle is 20–40º. A reduction in this angle indicates a collapse of the posterior facet of the calcaneus, resulting in increased pressure on the subtalar joint. Several studies have reported a correlation between Böhler's angle and functional outcomes. However, in this study, no significant association was found between the angle and functional outcomes. Notably, the majority of patients who underwent sinus tarsi locking plate fixation achieved a restoration of Böhler's angle to greater than 20º.

CONCLUSIONS

In conclusion, sinus tarsi locking plate fixation for joint depression-type calcaneal fractures offers effective posterior facet reduction and favorable functional outcomes. Postoperative CT assessments can help predict functional outcomes by evaluating the posterior facet alignment. Anatomical reduction of the posterior facet is essential for achieving optimal functional recovery.

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Combined Vertebral Fracture Assessment and FRAX Tool Thailand With or Without Bone Mineral Density for Diagnosis of Osteoporosis in Elderly

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Purpose: To evaluate the reliability of using vertebral fracture assessment by radiography (VFA) in combination with FRAX tool Thailand to diagnose osteoporosis in elderly patients, without the need for bone mineral density (BMD) measurement.
Methods: All elderly individuals who fulfill the criteria for osteoporosis assessment according to the 2021 CPG for osteoporosis care by the Thailand osteoporosis foundation were assessed BMD, VFA, and FRAX tool Thailand with and without BMD. Fracture risk was first evaluated using only FRAX without BMD and the presence of asymptomatic vertebral fractures (AVF). The second assessment used FRAX with BMD, the results of BMD measurements, and the presence of AVF. The results of these two assessments were compared to evaluate the reliability of the osteoporotic diagnosis.
Results: The prevalence of osteoporosis in the study was found to be 67% (95% CI: 60%–72.9%). The test exhibited high sensitivity (90.6%, 95% CI: 84.5%–94.9%) and specificity (92.9%, 95% CI: 84.1%–97.6%), indicating its strong ability to accurately identify both individuals with and without osteoporosis. The Receiver Operating Characteristic (ROC) area of 0.918 (95% CI: 0.879–0.956)**.** For subgroup analysis, in males (n=44), the test demonstrated excellent performance with a sensitivity of 95.2%, specificity of 100%, and a sensitivity of 89.8% and specificity of 89.4% in females (n=165). In the age-based subgroup analysis, the results in those aged >80 years (n=35) had highest sensitivity at 96.8% but lower specificity at 75.0%. For participants aged 70-80 years (n=84), sensitivity was 94.7%, and specificity was 88.9%. The youngest group, aged <70 years (n=90), had the lowest sensitivity of 82.4% but a high specificity of 97.4%. The ROC area ranged from 0.85 in those >80 years, 0.89 in those <70 years, and 0.91 in the aged 70-80 years group.
Conclusions: The combined use of VFA and FRAX without BMD offers a simple, highly effective method for diagnosing osteoporosis in elderly patients, especially in all men and women aged 70-80 years at minimal cost.

Keywords: osteoporosis diagnosis, vertebral fracture assessment, FRAX, Bone mineral density

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Osteoporosis is a skeletal disorder characterized by diminished bone strength, resulting in an increased susceptibility to fractures[1]. According to definition by the National Institutes of Health (NIH), bone strength is determined by two principal factors: bone mineral density (BMD) and bone quality[2]. The World Health Organization (WHO) further defines osteoporosis as a systemic skeletal condition marked by reduced bone mass and micro-architectural deterioration of bone tissue, which contributes to bone fragility and an elevated risk of fractures[3].

Osteoporosis is a growing public health concern globally, including in Thailand, where it notably increases the risk of fragility fractures. A national health survey of the elderly population in Thailand found that osteoporosis is among the most prevalent health problems. This condition is becoming increasingly common due to the aging population, with the prevalence of osteoporosis being approximately 23% in women and 12% in men worldwide[4]. Furthermore, osteoporotic fractures, especially those involving the hip, are strongly associated with increased mortality. A study conducted in Chiang Mai between 1987 and 1988 demonstrated that 2.1% of patients died during hospitalization following a hip fracture. Long-term follow-up over a 5-year period revealed an overall mortality rate of 29%[5].

The main aim of diagnosing and treating osteoporosis is prevention of osteoporotic fractures. Low bone mineral density (BMD) is one of the most predictive factors for osteoporotic fracture[6,7]. The presence of a vertebral fracture is also a strong predictor of new fractures, and this risk is independent of BMD. Therefore, even with only modestly decreased or even normal BMD vertebral fractures can be present. When both of these risk factors, low BMD and prevalent of vertebral fracture are present, the risk of a new fracture may be increased by a factor of 25[8]. The gold standard evaluation of fracture risk is based on the results of BMD test and there are many study suggested using vertebral fracture assessment and FRAX to improved osteoporosis diagnosis[9-11]. Following risk stratification, treatment is then guided by the severity of fracture risk.

In clinical practice, diagnosing osteoporosis by BMD testing is challenging, especially for elderly patients who may have difficulty traveling to other medical centers where the necessary diagnostic equipment is available. Moreover, the cost of BMD testing is often prohibitive, and in some cases, patients are unable to access reimbursement for these tests, resulting in a significant number of individuals not receiving proper diagnosis or treatment.

The purpose of this study is to evaluate the reliability of using vertebral fracture assessment by radiography (VFA) in combination with FRAX Thailand to diagnose osteoporosis in elderly patients, without the need for bone mineral density (BMD). By this alternative diagnostic criteria, there could be significantly increase the rate of diagnosis and ensure that more patients receive appropriate management, particularly in community hospitals that lack the resources for BMD testing.

METHODS

The study population consisted of all elderly individuals who fulfill the criteria for osteoporosis assessment according to the 2021 clinical practice guidelines for osteoporosis care by the Thailand osteoporosis foundation[12] which are 1) Women aged 65 years and older and men aged 70 years and older. 2) Women who experienced menopause before age 45, including those who have had both ovaries removed (bilateral oophorectomy). 3) Women with persistent low estrogen levels for more than 1 year prior to menopause. 4) Postmenopausal women younger than 65 years or men younger than 70 years with at least one of the following risk factors. (Currently using glucocorticoid medication at an equivalent dose of prednisolone 5 mg/day or higher for more than 3 months, Their parents had a hip fracture from a minor accident (low-impact trauma), A body mass index (BMI) of less than 20 kg/m^2, A height reduction of 4 cm or more compared to the patient's highest recorded height, or a reduction of 2 cm or more from two separate height measurements, Women receiving aromatase inhibitor therapy or men undergoing androgen deprivation therapy,

Radiographic evidence showing osteopenia or vertebral deformity due to vertebral fractures, A history of fragility fractures)

Exclusion Criteria are Elderly individuals who are unable to do bone mineral density testing at either hip or have a history of hip fracture from low-energy trauma (fragility fracture), and who are unable to provide the necessary information for the FRAX Thailand assessment

The study was approved by the Provincial Public Health Office of Sakaeo ethics review board and was considered to be evaluation of modern patient care.

BMD Measurement

BMD was measured by using dual-energy X-ray absorptiometry (DXA) over the lumbar spine and proximal femur. The results were expressed as T-scores[13]. The reference standard of a T-score is the peak bone density, as reached in men or women age 30 years. The T-score is then defined as the number of standard deviations from this value. According to the commonly used World Health Organization definition, ''osteoporosis'' is defined as a T-score lower than -2.5; ''osteopenia'' as a T-score between -2.5 and -1.0; and when the T-score is greater than -1.0, the BMD is ''normal.''

Vertebral Fracture Assessment

Vertebral fracture was assessed by radiograph of thoracolumbar spine in the lateral position. The range of vertebral visualization is from the level of T4 through L4[14,15]. The radiographic images were sent to the radiologist for evaluation of vertebral collapse according to the Genant's classification[16]. In this classification, a relative height reduction between 20%-25% was designated a ''mild'' fracture, 25%-40% was a ''moderate'' fracture, and >40% was a ''severe'' fracture. (Figure 1)

Patient was interviewed by orthopedic surgeon to collect various data for the assessment of FRAX Thailand[17,18], which includes personal information such as age, gender, weight, height, and specific clinical factors. The collected data of each patient was entered into the FRAX Thailand tool twice, once with BMD inserted and once without BMD. 10-year risk of hip fracture of 3% was determined as high risk group.

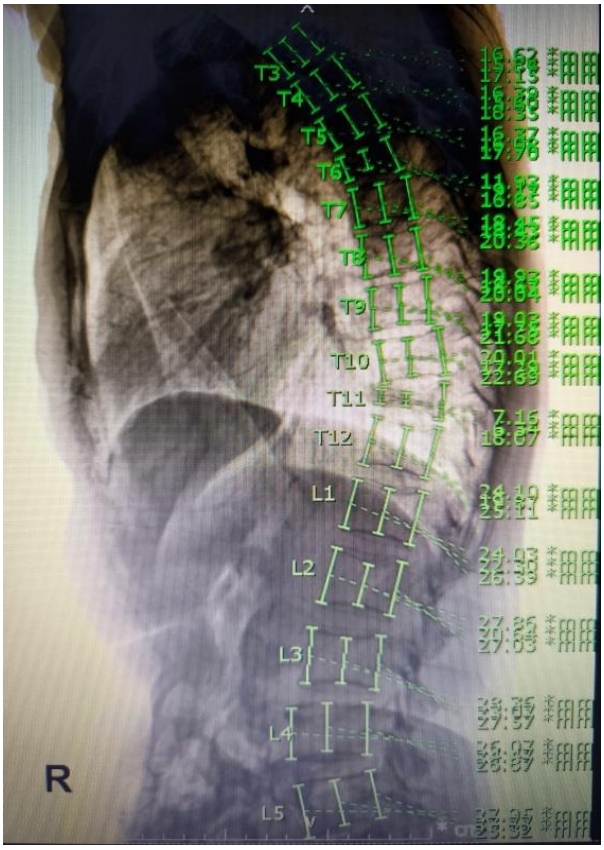

Fig. 1 Vertebral fracture was assessed by radiograph of thoracolumbar spine in the lateral position FRAX.

Interpretation

Fracture risk assessment was performed by two orthopedic surgeons to ensure accuracy of the diagnosis according to the guidelines of the Osteoporosis Foundation of Thailand (2021) which are 1) History of vertebral compression fractures or hip fractures due to osteoporosis, 2) T-score ≤ -2.5, 3) 10-year risk of hip fracture, assessed by the FRAX tool for Thailand, is ≥ 3%,and 4) T-score between -1.0 and -2.5, combined with a history of fragility fractures at sites other than the spine or hip, such as fractures at the proximal humerus, pelvis, or forearm.

First assessment use only FRAX without BMD and the presence of asymptomatic vertebral fractures (AVF), and second assessment use FRAX

with BMD, the results of BMD measurements, and the presence of asymptomatic vertebral fractures. The results of these two assessments were compared to evaluate the reliability in osteoporotic diagnosis. A contingency table was used to calculate the following diagnostic performance metrics including sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

RESULTS

Patients

This study focuses on elderly individuals who fulfill the criteria for osteoporosis assessment created by Osteoporosis Foundation of Thailand. Most women aged 65 years and men aged 70 years and over were enrolled from out-patient department of Aranyaprathet Hospital in July 2022-December 2023. Of 235 patients, 26 patients were excluded due to previous history of hip fracture from low-energy trauma.

A total of 209 participants were included in the study. The mean age of participants was 71.48 years. The majority of participants were female (78.95%), with a mean Body Mass Index (BMI) of 24.85 ± 4.84 kg/m². Fracture history was reported in 18.18% of the participants, with vertebral compression fractures (VCF) accounting for 35%, distal radius fractures 24%, proximal humerus fractures and distal femoral fractures each 13%, and other fractures 15%. Bone mineral density (BMD) measurements were obtained from several sites. The mean BMD at the neck of the femur was -1.68 g/cm², at the total hip was -1.44 g/cm², and at the L1-L4 vertebral level was -2.21 g/cm². Asymptomatic vertebral fracture was found in 49% of patients.

In terms of specific clinical factors, 14.83% of participants had a previous fragility fracture. 2.87% had a parent with a history of fractured hip. 1.91% was current smokers. 2.39% were using glucocorticoids at the time of the study. 1.43% had a diagnosis of rheumatoid arthritis. 3.34% had secondary osteoporosis. 1.43% reported consuming ≥ 3 alcohol units/day. More patient data are presented in Table 1.

Risk assessments using the FRAX without BMD indicated a mean fracture risk of 3.75 ± 2.79%, while including BMD in the FRAX calculation led to a mean risk of 2.71 ± 3.04%. When categorized according to risk levels, 37.32% of participants were classified as having low to moderate risk of fracture without BMD data, while 62.68% were classified as high to very high risk. When BMD was included in the FRAX calculation, the proportion of participants in low to moderate risk category decreased to 33.49%, while those in the high to very high risk group increased to 66.15%

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Table 1 Baseline Characteristics, Bone mineral density (BMD), Vertebral fracture (VF), Fracture risk assessment tool (FRAX), Risk of fracture.

Variable	Overall (n=209)
Age (years), mean ± SD	71.48±6.80
Sex (Female, %)	165 (78.95)
BMI (kg/m²), mean ± SD	24.85±4.84
Fracture history (%)	38 (18.180)
BMD neck (g/cm²), mean ± SD	-1.68±1.00
BMD total hip (g/cm²), mean ± SD	-1.44±0.97
BMD L1-L4 (g/cm²), mean ± SD	-2.21±1.36
Asymptomatic VF, N (%)	103 (49.28)
Previous fragility fracture, N (%)	31 (14.83)
Parent fractured hip, N (%)	6 (2.87)
Current smokers, N (%)	4 (1.91)
Current glucocorticoid use, N (%)	5 (2.39)
Rheumatoid arthritis, N (%)	3 (1.43)
Secondary osteoporosis, N (%)	7 (3.34)
Alcohol ≥ 3 units/day, N (%)	3 (1.43)
FRAX w/o BMD (%), mean ± SD	3.75±2.79
FRAX with BMD (%), mean ± SD	2.71±3.04
Risk without BMD (%)	
Low - moderate	78 (37.32)
High – very high	131 (62.68)
Risk with BMD (%)	
Low - moderate	70 (33.49)
High – very high	139 (66.15)

Diagnostic Performance

The diagnostic performance of the screening test, combining VFA and FRAX without BMD was evaluated in comparison to VFA, BMD and FRAX with BMD which served as the gold standard

for osteoporosis diagnosis. The prevalence of osteoporosis in the study cohort was found to be 67% (95% CI: 60%–72.9%). The test exhibited high sensitivity (90.6%, 95% CI: 84.5%–94.9%) and specificity (92.9%, 95% CI: 84.1%–97.6%), indicating its strong ability to accurately identify both individuals with and without osteoporosis. The Receiver Operating Characteristic (ROC) area of 0.918 (95% CI: 0.879–0.956) further support the excellent discriminatory power of the test in distinguishing between those with and without the condition.

In terms of predictive accuracy, the positive predictive value (PPV) was 96.2% (95% CI: 91.3%–98.7%), meaning a positive result had a very high likelihood of indicating osteoporosis, while the negative predictive value (NPV) was 83.3% (95% CI: 73.2%–90.8%), suggesting a moderately high ability to rule out the condition. Collectively, these results highlight the robust diagnostic capabilities of the combined VFA and FRAX test without BMD, demonstrating it as an effective and reliable tool for osteoporosis screening in clinical settings. As shown in Table 2 and Figure 2.

Table 2 Diagnostic Performance of VFA and FRAX (Without BMD) Compared to VFA, BMD, and FRAX (With BMD) as the Gold Standard.

Metric	Value	95%CI
Prevalence	67%	60% - 72.9%
Sensitivity	90.6%	84.5% - 94.9%
Specificity	92.9%	84.1% - 97.6%
ROC area	0.918	0.879 - 0.956
PPV	96.2%	91.3% - 98.7%
NPV	83.3%	73.2% - 90.8%

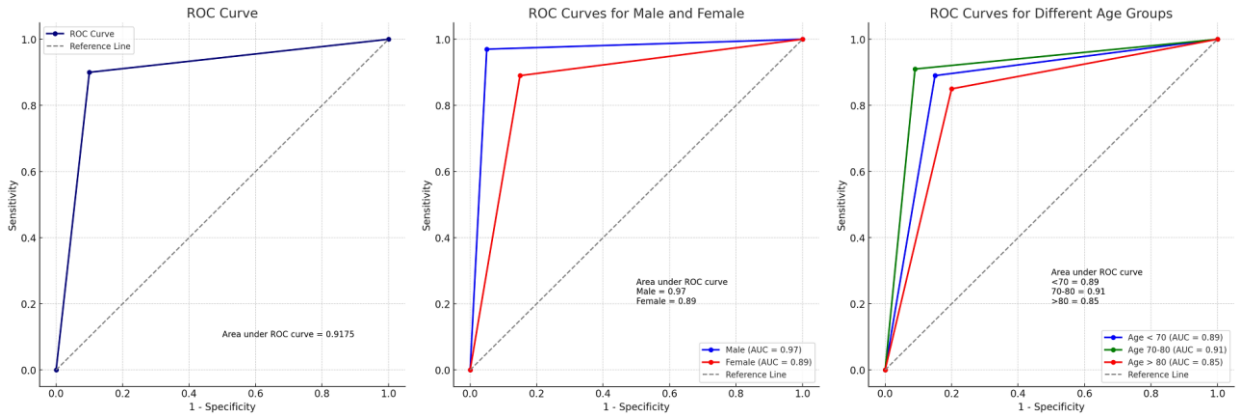

Fig. 2 Receiver Operating Characteristic (ROC) curves for Diagnostic performance, sex subgroups, and age subgroups.

Subgroup Analysis

In a subgroup analysis by sex, the diagnostic performance of the combined VFA and FRAX without BMD revealed notable differences between males and females. In males (n=44), the test demonstrated excellent performance with a sensitivity of 95.2%, specificity of 100%, and a positive predictive value (PPV) of 100%, highlighting its high accuracy in identifying osteoporosis. In contrast, females (n=165) exhibited a sensitivity of 89.8% and specificity of 89.4%, both slightly lower than in males. The PPV for females was 95.5%, and the NPV was 77.8%, indicating a slightly lower ability to rule out the condition compared to males. The ROC area for males was 0.97, indicating excellent discriminatory ability, while for females it was 0.89.

In the age-based subgroup analysis, the results in those aged >80 years (n=35), had the highest sensitivity at 96.8% but lower specificity at

75.0%. The PPV was 96.8%, and the NPV was 75%. For participants aged 70-80 years (n=84), sensitivity was 94.7%, and specificity was 88.9%, with a PPV of 94.7% and an NPV of 88.9%. The youngest group, aged <70 years (n=90), had the lowest sensitivity (82.4%) but a high specificity of 97.4% and a PPV of 97.7%. The ROC area ranged from 0.85 in those >80 years to 0.91 in the overall group, suggesting strong performance across all age groups, with slightly reduced specificity in older adults. (Figure 2)

DISCUSSION

The aim of this study was to evaluate the reliability of using Vertebral Fracture Assessment (VFA) in combination with FRAX without BMD to diagnose osteoporosis in elderly patients, without the need for bone mineral density (BMD). The results show that the prevalence of osteoporosis in the study population is quite high (67%) compared to a recently published study in Thailand, which reported a prevalence of 30% among elderly individuals over 60 years of age, diagnosed based solely on BMD measurements[19]. This suggests that osteoporosis is common in the elderly population and reinforces the need for effective and user friendly diagnostic tools. A sensitivity of 90.6% and a specificity of 92.9% are excellent, indicating that the combined use of VFA and FRAX without BMD is very effective at detecting patients who have osteoporosis and also good at ruling out individuals who do not have the disease. ROC Area of 0.918 (95% CI: 0.879 - 0.956) indicates excellent discrimination between those with and without osteoporosis. The high ROC area supports the validity of the VFA and FRAX without BMD combination as a reliable tool for osteoporosis diagnosis in elderly patients.

All patients were assessed for vertebral compression fractures using lateral thoracolumbar radiographs. If a patient had a compression fracture at only one level, they were diagnosed with osteoporosis. Many studies have now demonstrated good agreement between densitometry and radiography in vertebral fracture assessment, with very good sensitivities and specificities when using radiographs as the gold standard, especially for moderate and severe fractures[20]. This served as the first part of screening for osteoporosis without the need for BMD testing. In this study, asymptomatic vertebral compression fracture was found in 49% of patients, similar to a study in postmenopausal Chinese women, which reported the prevalence of vertebral fractures ranged from 13.4% in those aged 50 to 59 years to 58.1% in those aged 80 years or older[21].

When using the FRAX assessment, in the FRAX without BMD group, the mean score was 3.75 ± 2.79, compared to 2.71 ± 3.04 in the group with BMD. The FRAX score without BMD was higher than the FRAX score with BMD. Since a FRAX score of ≥3 is used to predict the 10-year risk of hip fracture and serves as a criterion for diagnosing osteoporosis, the combination of these factors improves the reliability and accuracy of the diagnosis. Gadam and colleagues compared FRAX calculations with and without BMD to predict the 10-year risk of fracture. Their study found that 84% of patients had an identical fracture risk prediction whether or not BMD was included[22]. In a more recent study in 2872 postmenopausal Thai women, using the receiver operating characteristic (ROC) curve to determine the optimal intervention threshold of the Thai-specific FRAX model, the optimal FRAX thresholds for hip fracture with and without BMD were 4% and 4.9% respectively[23]. The thresholds for FRAX with and without BMD are still controversial.

In the gold standard for osteoporosis diagnosis, the use of bone mineral density (BMD) in combination with Vertebral Fracture Assessment (VFA) and FRAX with BMD increases the likelihood of accurate diagnosis[24]. According to established diagnostic criteria, osteoporosis can also be diagnosed based on a BMD T-score of ≤ -2.5, or a T-score of ≤ -1.0 in the presence of a non-vertebral fragility fracture, such as fracture of proximal humerus, pelvis, or forearm. Our results demonstrate that a higher proportion of individuals were classified as high to very high risk in the group assessed with BMD (66.15%) compared to those assessed without BMD (62.68%). These findings suggest that the inclusion of BMD in the risk assessment slightly increases the proportion of patients classified as high risk for osteoporosis.

However, the use of VFA and FRAX without BMD remains a valuable screening tool, particularly in settings where BMD testing is unavailable or impractical.

The results of the subgroup analysis by sex and age range reveal significant insights into the diagnostic performance of the screening tool across different groups. In terms of sex, males demonstrated slightly better performance, with higher sensitivity, specificity, PPV, and ROC values. Males had an outstanding ROC area of 0.97, suggesting near-perfect diagnostic ability compared to females which had an ROC area of 0.89, although both sexes showed high diagnostic accuracy. Regarding age, the tool's sensitivity increased with age, and specificity decreased with age reflecting its effectiveness in detecting osteoporosis but with higher likelihood of false positives in older individuals. ROC values were highest in the 70-80 age groups (0.91) with the overall ROC was 0.91. This suggests that the test performs best in the 70-80 age groups with a slightly reduced diagnostic performance in the younger and older individuals.

The hypothesized are individuals aged less than 70 years had lower prevalence of asymptomatic vertebral fractures results in a reduced sensitivity of the screening tool, as the absence of fractures diminishes the tool's ability to identify osteoporosis as reported by Zeynep that postmenopausal women in the 50-87 age range, the ratio of vertebral fractures was 21.4% and 46.3% for women over 75 years of age[25]. Conversely, in individuals aged over 80 years, the increased prevalence of low BMD associated with age-related bone loss leads to a higher rate of osteoporosis diagnoses based on BMD alone. A study of BMD in 2,702 Chinese females aged 5 to 96 years showed that the prevalence of osteoporosis at least one site in these women 23.9 ± 13.3% in those aged 50–59, 56.3 ± 20.3% in those aged 60–69, 71.8 ± 16.7% in those aged 70–79, and 83.2 ± 12.1% in those aged over 80 years[26]. This, in turn, results in a reduction in the specificity of the test in this age group, as more individuals are classified as positive for osteoporosis. In contrast, the age group between 70-80 years exhibited the most balanced diagnostic performance, with optimal sensitivity and specificity.

The cost-effectiveness of combining VFA and FRAX without BMD can be evaluated by considering several factors. This diagnostic approach has a high yield with minimal patient burden, as it can be performed in any hospital in Thailand equipped with plain radiographs and an orthopedic specialist, requiring only a few additional minutes for patient interviews and data entry. The cost is approximately less than 500 baht. The diagnosis of osteoporosis often leads to treatment for many patients who otherwise would not have received it. Several studies have shown that early treatment reduces future fracture risk and hospitalizations[27-29]. One report specifically highlights the cost-effectiveness of VFA in postmenopausal women with osteopenia[30]. While formal evidence is still limited, the balance between low costs and significant clinical benefits suggests that this diagnostic strategy is likely cost-effective. Thus, using VFA in combination with FRAX without BMD offers a valuable and potentially cost-effective method for osteoporosis diagnosis.

A limitation of the current study is that the sample was not fully representative of the general population. The sample size may also have been insufficient for robust subgroup analyses, particularly in certain age groups, which could potentially lead to misinterpretations of the data. However, the study does reflect the population typically encountered in routine clinical practice, without any selective bias, and provides valuable insights into the management of osteoporosis in this context.

CONCLUSIONS

The combined use of Vertebral fracture assessment and FRAX without BMD offers a simple, highly effective method for diagnosing osteoporosis in elderly patients, especially in all men and women aged 70-80 years at minimal cost. Given its ease of implementation and low resource requirements, we suggest that this approach could serve as a valuable screening tool, particularly in settings where BMD testing is unavailable or impractical.

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Risk Factors for Fragility Hip Fracture in the Older in Northern Thailand: A Community-Based Retrospective Cohort Study

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Purpose: This community-based retrospective cohort study aimed to identify risk factors for fragility hip fractures among older individuals in three districts of Nan Province, Thailand. The study addresses a knowledge gap regarding hip fracture risk factors specific to northern Thai communities.
Methods: Health data from the Nan Provincial Health Office database, covering the period January 1, 2019 to December 31, 2023, were analyzed for 36,521 older individuals aged ≥ 60 years. Participants had no prior history of hip fracture. Data on demographics, chronic diseases, use of walking aids, history of non-hip fragility fractures, and FRAX hip scores were collected. Multivariate Cox regression analysis was performed to identify significant risk factors for hip fractures.
Results: Key risk factors for hip fractures included female sex, age ≥ 70 years, body mass index (BMI) < 20 kg/m², use of walking aids, history of non-hip fragility fractures, hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease, cerebrovascular accident, and Parkinson's disease. In males, significant risk factors included a BMI < 20 kg/m² and COPD, whereas in females, risk factors included hypertension, use of walking aids, and a FRAX hip score > 3.3%. Diabetes mellitus, dementia, heart disease, and lack of a caregiver were not found to be significant risk factors.
Conclusions: This study identified key risk factors for fragility hip fractures among community-dwelling older individuals in Northern Thailand, highlighting sex-specific risk profiles. The findings emphasize the need for targeted prevention strategies. Additionally, certain risk factors may be influenced by regional characteristics, geographical factors, and cultural aspects, limiting their generalizability.

Keywords: risk factor, fragility hip fracture, osteoporosis, community-based

The global population is aging, a trend particularly evident in developed countries. By 2050, an estimated 21% of the world's population will be 65 years or older [1]. Thailand is also experiencing rapid demographic aging, with projections indicating that over 14.2% of its population will be 65 or older by 2024 [2].

As life expectancy increases, age-related declines in physical function heighten the risk of falls, including hip fractures, which are becoming increasingly common [3]. Hip fractures not only pose serious health risks but also place a significant financial burden on healthcare systems. In Thailand, the average cost of hip fracture treatment is $5,013.25 (equivalent to 168,896.39 baht) [4]. In 2017, the incidence of hip fractures was 238.5 per

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100,000 population, resulting in annual treatment costs of approximately 1.76 billion baht [5]. Despite treatment, hip fractures are associated with severe complications and long-term consequences, underscoring the critical need for effective preventive strategies [6].

Several studies have examined risk factors for hip fractures in the older, identifying risk factors such as female sex, osteoporosis, hypertension, Parkinson's disease, diabetes, lung disease, and dementia [7,8]. However, findings across studies remain inconsistent. For instance, a study in Finland found that rheumatoid arthritis, diabetes, and a history of CVAs were not significant risk factors for hip fractures [9].

Cultural and lifestyle differences across populations, along with limited research on hip fracture risk factors in Thai communities, pose challenges for effective risk management. Additionally, tools such as dual-energy X-ray absorptiometry (DEXA) scans, commonly used to identify individuals at risk of fractures, may not be widely accessible in developing countries. As an alternative, the World Health Organization developed the Fracture Risk Assessment Tool (FRAX) to estimate the 10-year probability of hip fracture, using a threshold FRAX hip score of ≥ 3% [10]. However, Thai studies suggest sex-specific variations in the optimal FRAX cut-off values, with thresholds of 1.1% for men and 3.3% for women [11]. Given the multifactorial nature of hip fracture risk, a combination of risk factors and FRAX hip score should be used to improve screening accuracy for high-risk older individuals. This study aimed to identify important risk factors for hip fractures among high-risk older individuals in Northern Thailand to enhance early detection and prevention strategies in this population.

METERIALS AND METHODS

This retrospective cohort study included all older individuals aged ≥ 60 years residing in three districts of Nan Province (Mueang Nan, Phu Piang, Wiang Sa) who had no prior history of hip fracture. Older individuals with hip fractures because of severe trauma or pathological fracture were excluded. The study was conducted from January 1, 2019, to December 31, 2023. Health and mortality data were extracted from the Nan Provincial Health Office database. Collected variables included age, sex, weight, height, body mass index (BMI), caregiver presence, and history of non-hip fragility fractures. Data on chronic diseases such as type II diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD, defined as glomerular filtration rate < 60 ml/min/1.73 m^2), cerebrovascular accidents (CVAs), Alzheimer's disease, dementia, and Parkinson's disease were also collected. The Thai version of the FRAX hip score, excluding bone mineral density (BMD), was calculated using the online tool (https://frax.shef.ac.uk/FRAX/tool.aspx?lang=th).

For each participant, follow-up duration was calculated from the study's initiation to the occurrence of a hip fracture, death, or the study's end. Hip fractures were identified using International Classification of Diseases, 10th revision (ICD-10) codes S72.0, S72.1, and S72.2, retrieved from the Nan hospital database.

Clinical characteristics were summarized using descriptive statistics (frequencies, percentages, and means). Multivariate Cox regression analysis was employed to identify risk factors for hip fracture, reporting adjusted hazard ratios (HR) and 95% confidence intervals (CI). Statistical analyses were conducted using SPSS version 26 (IBM Corporation, Armonk, New York), with a statistical significance set at $p < 0.05$. This study was approved by the Research Ethics Committee of Nan Hospital (Nan Hos. REC No 014/2024).

RESULTS

This study included 36,521 older individuals residing in three districts of Nan Province (Mueang Nan, Phu Piang, Wiang Sa). Of these, 17,138 (46.9%) were male, and 19,383 (53.1%) were female. The mean age was 69.7 ± 7.8 years, ranging from 60 to 115 years, with the highest proportion of individuals in the 60-64 age group (31.6%). The average BMI was 22.4 ± 3.8 kg/m^2, with 9,526 individuals (26.1%) classified as underweight (BMI < 20 kg/m^2). Additionally, 5,926 (16.2%) had a FRAX hip score ≥ 3%.

Among the older study population, 4,034 individuals (11.0%) lived without caregivers or co-resided with other older individuals. A total of 2,768 (7.6%) required walking aids, and 610 (1.7%) had a history of non-hip fragility fractures. The prevalence of chronic diseases included DM in 4,178 individuals (11.4%), HT in 13,259 (36.3%), COPD in 797 (2.2%), CKD in 553 (1.5%), CVAs in 319 (0.9%), dementia in 188 (0.5%), and Parkinson's disease in 68 (0.2%) (Table 1).

During the follow-up period, 2,909 individuals died (Fig. 1). A total of 580 olderindividuals sustained hip fractures, comprising 171 males (1.0%) and 409 females (2.1%). The mean age at the time of fracture was 80.2 ± 8.3 years. The incidence rate of new hip fractures was 327.3 cases per 100,000 person-years, with a total follow-up duration of 9,214,421 weeks.

Multivariate Cox regression analysis identified several significant risk factors associated with hip fractures in the community (Table 2). Female sex was a significant predictor (adjusted HR = 1.64, $p < 0.001$), with the highest risk observed in individuals aged 90 years and older (adjusted HR = 15.05, $p < 0.001$). Other significant factors included BMI < 20 kg/m² (adjusted HR = 1.36, $p = 0.001$), use of a walking aid (adjusted HR = 1.83, $p < 0.001$), history of non-hip fragility fractures (adjusted HR = 1.65, $p = 0.004$), HT (adjusted HR = 1.27, $p = 0.006$), COPD (adjusted HR = 1.81, $p = 0.001$), CKD (adjusted HR = 1.69, $p = 0.020$), CVA (adjusted HR = 2.78, $p < 0.001$), and Parkinson's disease (adjusted HR = 4.16, $p = 0.002$).

Risk factor analysis was stratified by sex using FRAX score cut-off values of 1.1% for males and 3.3% for females. Among males, significant predictors of hip fracture included BMI < 20 kg/m² (adjusted HR = 1.64, $p = 0.004$), COPD (adjusted HR = 2.47, $p < 0.001$), CVAs (adjusted HR = 3.03, $p = 0.008$), Parkinson's disease (adjusted HR = 4.77, $p = 0.032$), and history of non-hip fragility fractures (adjusted HR = 3.64, $p = 0.002$) (Table 3).

For females, risk factors included FRAX hip score > 3.3% (adjusted HR = 1.88, $p = 0.045$), HT (adjusted HR = 1.27, $p = 0.023$), CVAs (adjusted HR = 2.91, $p < 0.001$), Parkinson's disease (adjusted HR = 3.87, $p = 0.020$), and use of a walking aid (adjusted HR = 2.03, $p < 0.001$), history of non-hip fragility fractures (adjusted HR = 1.52, $p = 0.031$) (Table 4).

In summary, specific risk factors for hip fractures in males included low BMI (< 20 kg/m²) and COPD, whereas in females, significant risk factors included HT, use of a walking aid, and FRAX hip score ≥ 3.3%.

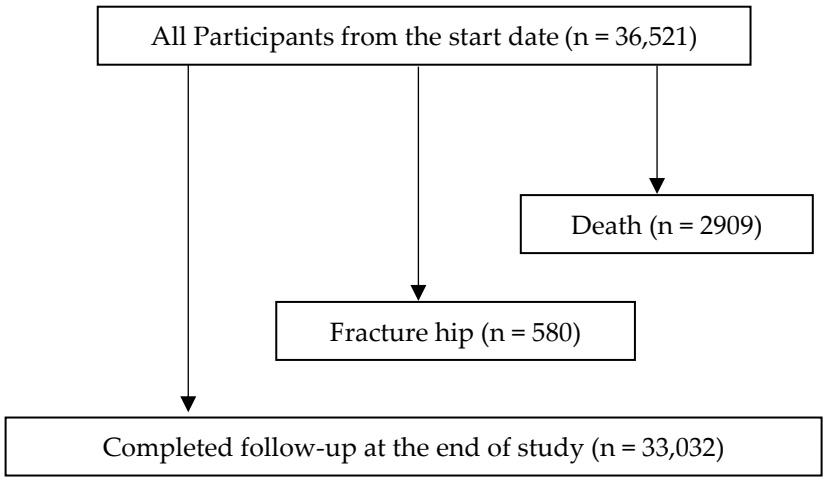

Fig. 1 Flow chart of the follow-up period.

Table 1 Clinical parameters. (N=36,521)

Characteristic	n (%)
Sex, female	19,383 (53.1)
Age group (year)	
60-64	11,529 (31.6)
65-69	9,817 (26.9)
70-74	6,298 (17.2)
75-79	4,036 (11.1)
80-84	2,647 (7.2)
85-89	1,539 (4.2)
90 up	655 (1.8)
BMI < 20 kg/m^2	9,526 (26.1)
FRAX hip score ≥ 3%	5,926 (16.2)
No Caregiver	4,034 (11.0)
DM	4,178 (11.4)
HT	13,259 (36.3)
COPD	797 (2.2)
Heart disease	1,088 (3.0)
CKD	553 (1.5)
CVA	319 (0.9)
Dementia	188 (0.5)
Parkinson disease	68 (0.2)
History of non-hip fragility fracture	610 (1.7)
Ambulate with gait aid	2,768 (7.6)

Table 2 Multivariate analyses of factors for predict fracture hip all sexes by FRAX hip score ≥ 3%.

Characteristic	Fracture hip	Adjusted HR	95% CI	*p*-value
Sex, female	409 (2.1)	1.64	1.285-2.028	<0.001
Age group (year)				
60-64	42 (0.4)	reference		
65-69	44 (0.4)	1.17	0.764-1.781	0.476
70-74	78 (1.2)	2.85	1.947-4.183	<0.001
75-79	106 (2.6)	5.40	3.628-8.027	<0.001
80-84	118 (4.5)	7.53	4.988-11.366	<0.001
85-89	132 (8.6)	13.87	9.018-21.341	<0.001
90 up	60 (9.2)	15.05	9.352-24.205	<0.001
BMI < 20 kg/m^2	267 (46.0)	1.36	1.124-1.634	0.001
FRAX hip score ≥3%	338 (58.3)	1.16	0.856-1.573	0.338
No Caregiver	50 (1.2)	1.20	0.897-1.607	0.219
DM	77 (1.8)	1.19	0.923-1.524	0.183
HT	310 (2.3)	1.27	1.073-1.512	0.006
COPD	35 (4.4)	1.81	1.280-2.561	0.001
Heart disease	31 (2.8)	1.21	0.841-1.742	0.305
CKD	21 (3.8)	1.69	1.085-2.659	0.020

Table 2 Multivariate analyses of factors for predict fracture hip all sexes by FRAX hip score ≥ 3%. (Cont.)

Characteristic	Fracture hip	Adjusted HR	95% CI	*p*-value
CVA	19 (6.0)	2.78	1.756-4.415	<0.001
Dementia	11 (1.9)	1.72	0.942-3.151	0.077
Parkinson's disease	5 (7.4)	4.16	1.718-10.078	0.002
History of non-hip fragility fracture	35 (5.7)	1.65	1.169-2.336	0.004
Ambulate with gait aid	192 (6.9)	1.83	1.507-2.222	<0.001

Table 3 Multivariate analyses of factors for predict fracture hip in male by FRAX hip score ≥ 1.1%.

Characteristic	Fracture hip n (%)	Adjusted HR	95% CI	*p*-value
Age group (year)				
60-64	8 (0.1)	reference		
65-69	11 (0.2)	1.49	0.599-3.708	0.391
70-74	29 (1.0)	4.31	1.801-10.313	0.001
75-79	27 (1.4)	4.04	1.346-12.102	0.013
80-84	41 (3.5)	9.03	3.071-26.550	<0.001
85-89	34 (5.5)	14.45	4.871-42.863	<0.001
90 up	21 (7.9)	20.32	6.556-62.980	<0.001
BMI < 20 kg/m^2	81 (1.9)	1.64	1.169-2.311	0.004
FRAX hip score ≥ 1.1%	138 (2.9)	2.00	0.915-4.369	0.082
No Caregiver	19 (0.9)	1.06	0.657-1.723	0.801
DM	23 (1.3)	1.50	0.943-2.388	0.087
HT	82 (1.5)	1.30	0.949-1.783	0.102
COPD	21 (4.5)	2.47	1.547-3.945	<0.001
Heart disease	9 (1.7)	1.08	0.548-2.143	0.816
CKD	11 (2.9)	1.88	0.995-3.560	0.052
CVA	6 (3.2)	3.03	1.329-6.901	0.008
Dementia	4 (4.7)	2.48	0.907-6.805	0.077
Parkinson's disease	2 (4.3)	4.77	1.14719.833	0.032
History of non-hip fragility fracture	6 (5.8)	3.64	1.604-8.261	0.002
Ambulate with gait aid	44 (4.4)	1.40	0.955-2.054	0.084

Table 4 Multivariate analyses of factors for predict fracture hip in female by FRAX hip score ≥ 3.3%.

Characteristic	Fracture hip n (%)	Adjusted HR	95% CI	*p*-value
Age group (year)				
60-64	34 (0.6)	reference		
65-69	33 (0.6)	1.09	0.677-1.767	0.713
70-74	49 (1.5)	2.22	1.428-3.457	<0.001
75-79	79 (3.7)	3.07	1.5356.144	0.002
80-84	77 (5.2)	3.34	1.6006.989	0.001
85-89	98 (10.7)	6.83	3.28014.240	<0.001
90 up	39 (10.0)	6.87	3.196-14.785	<0.001

Table 4 Multivariate analyses of factors for predict fracture hip in female by FRAX hip score ≥ 3.3%. (Cont.)

Characteristic	Fracture hip n (%)	Adjusted HR	95% CI	*p*-value
BMI < 20 kg/m²	186 (3.6)	1.22	0.984-1.500	0.070
FRAX hip score ≥ 3.3%	286 (6.3)	1.88	1.013-3.500	0.045
No Caregiver	31 (1.5)	1.27	0.876-1.830	0.209
DM	54 (2.3)	1.10	0.819-1.486	0.518
HT	228 (3.0)	1.27	1.033-1.554	0.023
COPD	14 (4.3)	1.25	0.7322.144	0.411
Heart disease	22 (3.9)	1.27	0.8241.954	0.280
CKD	10 (5.6)	1.51	0.7952.871	0.207
CVA	13 (9.7)	2.91	1.6665.088	<0.001
Dementia	7 (6.9)	1.51	0.7063.212	0.289
Parkinson's disease	3 (13.6)	3.87	1.238-12.111	0.020
History of non-hip fragility fracture	29 (5.7)	1.52	1.039-2.225	0.031
Ambulate with gait aid	148 (8.4)	2.03	1.613-2.541	<0.001

DISCUSSION

Hip fractures represent a significant public health concern, particularly among the older population. Identifying and understanding the associated risk factors are crucial for developing effective prevention and management strategies. This community-based retrospective cohort study highlights key risk factors contributing to hip fracture incidence.

Age and sex emerged as primary risk factors. Individuals ≥ 70 years faced a substantially higher risk, with the risk doubling approximately every five years. Notably, those aged ≥ 90 years exhibited a 15-fold higher risk compared to individuals aged 60-64 (95% CI: 9.352-24.205; p < 0.001). Aging negatively affects the musculoskeletal system, leading to both functional decline and muscle mass loss [12]. Additionally, disturbances in calcium homeostasis contribute to decreased bone mass [13], whereas age-related impairments in postural control, including visual and vestibular decline, further increase fall risk [14,15].

Females had a 1.6-fold higher risk of hip fracture than males (95% CI: 1.285-2.028; p < 0.001), which can be attributed to longer life expectancy (79.9 years for females vs. 71.9 years for males in Thailand in 2024) and estrogen loss on menopause[2,16].

Patients with HT exhibited a similar risk to that reported by Xu B et al. (adjusted rate ratio 1.34; 95% CI: 1.29–1.40; p < 0.001) [7]. Additionally, CKD was associated with a 2- to 4-fold increased risk of hip fracture compared to the general population of the same age group [17,18]. Both HT and CKD contribute to osteoporosis through abnormalities in the renin-angiotensin system, where increased angiotensin II levels stimulate osteoclast activity, inhibit osteoblasts, and disrupt calcium homeostasis [19-21].

Balance impairments and gait dysfunction in patients with stroke, Parkinson's disease, and those using gait aids were identified as significant risk factors for hip fracture [22-24]. Patients with Parkinson's disease had a 4.16-fold higher risk (95% CI: 1.718-10.078; p = 0.002), compared to the general population, exceeding the 2.6-fold increased risk reported in a Swiss study (95% CI: 1.4–4.6). This discrepancy may be attributed to limited access to disability support systems in developing countries.

Patients with COPD, a BMI < 20 kg/m², and a history of fragility fractures also exhibited significantly higher risks of hip fractures, with HRs of 1.81, 1.36, and 1.65, respectively. Graumam RQ et al. reported that up to 40% of COPD patients are underweight, exhibit osteoporosis, and have vitamin D deficiency [25]. Additionally, a meta-analysis by Morin SN et al. confirmed that

individuals with a history of fragility fractures have an increased risk of hip fractures (95% CI: 1.05–1.53; $p < 0.05$), which aligns with our findings [26]. This increased risk is primarily because of the early loss of trabecular bone in these individuals [27].

Interestingly, this study did not identify a significant association between DM or dementia and hip fracture risk. In contrast, Vilaca T et al. reported that type I DM increased hip fracture risk (relative risk = 4.93; 95% CI: 3.06-7.95), whereas type II DM was associated with a lower relative risk of 1.33 (95% CI: 1.19-1.49) [28]. The variability in findings across studies may stem from the heterogeneity of DM, including differences in disease type, duration, and severity. Additionally, strong social support systems in Thai families may provide protection against hip fractures in individuals with dementia, as suggested by Pothiban L. et al [29]. Furthermore, Yamaguchi T. et al found that individuals with DM had a higher femoral neck BMD than controls, which could explain the lack of association in this study [30].

When analyzed by sex, men with COPD (95% CI: 1.547-3.945; $p < 0.001$) and a BMI < 20 kg/m^2 (95% CI: 1.169-2.311; $p = 0.004$) exhibited a significantly increased risk of hip fracture. This disparity may be attributed to the high prevalence of COPD among Thai men, with smoking being the primary cause in 90% of cases [31].

Among females, significant factors included HT (95% CI: 1.033-1.554; $p = 0.023$) and the use of gait aids (95% CI: 1.613-2.541; $p < 0.001$). The protective role of estrogen against HT through its modulation of the renin-angiotensin system suggests that estrogen abnormalities in hypertensive women may contribute to increased fracture risk [32]. Furthermore, Patcharawan S. reported that gait aid users in Thailand are predominantly individuals older than 75 years and often have chronic conditions, aligning with the longer life expectancy of females, which may explain their increased fracture risk [33].

A study in Thailand determined that FRAX hip score cut-off values vary by sex (1.1% for men and 3.3% for women) [11]. Notably, when using a universal 3% cut-off for both sexes, the FRAX hip score was not identified as a significant risk factor predictor. However, when analyzed separately by sex using respective cut-offs, FRAX hip score was a significant predictor in females (95% CI: 1.013-3.500; $p = 0.045$) but not in males. These findings are consistent with Hamdy RC et al., who reported limited sensitivity and specificity of FRAX hip score in men [34].

This study benefits from a five-year longitudinal follow-up of a large community-based older population. However, limitations include its retrospective design and focus on the Northern Thai population, which may limit generalizability to other ethnic groups. Additionally, reliance on database-derived data precluded comprehensive assessment of disease severity.

Key risk factors for hip fracture were identified as age, sex, history of fragility fractures, and underlying conditions such as CVAs and Parkinson's disease. In men, COPD and a BMI < 20 kg/m^2 were significant risk factors for men, whereas in women, HT, FRAX hip score, and gait aid use were associated with increased risk. Future research should focus on developing screening and surveillance systems using these identified risk factors to proactively identify high-risk individuals and implement preventive measures to reduce hip fracture incidence.

CONCLUSIONS

Significant risk factors for hip fracture in community-dwelling older individuals in Northern Thailand include age ≥ 70 years, female sex, BMI < 20 kg/m^2, History of non-hip fragility fractures, use of a gait aid, HT, COPD, CKD, CVAs, and Parkinson's disease. Although DM, dementia, and lack of a caregiver were not identified as significant risk factors, implementing appropriate screening and surveillance systems and targeted fall prevention strategies for high-risk older individuals could potentially reduce hip fracture incidence in the older community.

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Single Intra-Articular Platelet-Rich Growth Factor Injection for Knee Osteoarthritis: Is It Effective in Severe Patients?

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Purpose: This study evaluated the clinical outcomes of intra-articular (IA) platelet-rich growth factor (PRGF) in patients with varying severities of knee osteoarthritis (KOA) using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. It also examined whether IA PRGF could delay or prevent surgical intervention in patients with severe KOA.

Methods: In this analytical observational cohort study, 120 patients with KOA, without systemic inflammatory disease or other intra-articular lesions, were classified using the Kellgren-Lawrence (KL) grading system. PRGF, a combination of leukocyte-rich platelet-rich plasma (LR-PRP) and injectable platelet-rich fibrin (iPRF), was prepared using the PP, GF, and ALPAS systems. A single 7 mL IA PRGF injection was administered. WOMAC scores were assessed at baseline, 1 week, and 1, 3, 6, and 12 months post-injection.

Results: Ninety-six female and 21 male patients (mean age: 64.9±8.3 years) were included. Based on KL grading, 38 patients were classified as mild (grade I-II), 44 as moderate (grade III), and 35 as severe (grade IV). All groups showed a decline in WOMAC scores after PRGF injection. Although baseline scores were highest in the severe group, the pattern of score reduction was similar across all severities. WOMAC scores at 3 months were lower in the mild and moderate groups than in the severe group. At 12 months, all groups maintained significantly reduced scores compared to baseline.

Conclusions: A single IA PRGF injection effectively improves pain, stiffness, and function in patients with severe KOA, with outcomes comparable to those in mild and moderate cases over 12 months of follow-up.

Keywords: PRGF, single intra-articular injection, severe, knee osteoarthritis

Osteoarthritis (OA) is a degenerative condition in humans. The prevalence in individuals aged > 18 and 70 years is approximately 22.7% and 40%, respectively. Knee OA (KOA) is one of the most common symptomatic forms of OA requiring treatment. Thailand is among the countries with the fastest aging populations worldwide. As the population ages more rapidly, increasing health and economic resources are required for the treatment of KOA. Late-stage KOA is often characterized by both demonstrable structural damage and patient-reported joint pain, stiffness and disability[1].

Conservative treatment modalities for KOA include physical therapy, weight loss, oral and topical non-steroidal anti-inflammatory drugs

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(NSAIDs), and IA injections. Corticosteroids, hyaluronic acid, ozone, collagen, and normal saline solutions are widely used for the IA treatment of KOA[2,3]. In recent years, regenerative treatment modalities, including stem cells, growth factors (GFs), and platelet-rich plasma (PRP) applications, have emerged as new treatment options for OA. An analysis of 30 published articles on PubMed indicated that PRP treatment was effective in patients with KL grade I-II KOA but had minimal effects in those with KL grade IV (severe) KOA, without serious adverse effects. PRP was found to be effective and safe, comparable with traditional conservative treatments such as hyaluronic acid injection[4].

PRP, first introduced in the 1970s in hematology, is now used for many conditions, including cosmetic, dental, and tissue healing in orthopedics. Its advantages include personalization, biological effects, safety, and minimal religious limitations. PRP is an autologous blood product containing a high concentration of multiple GFs, such as fibroblast GF, epidermal GF, vascular endothelial GF, transforming GF-beta, platelet-derived GF, and insulin-like GF[4]. These GFs have been proposed to possess regenerative capabilities and can inhibit chondrocyte inflammation by modulating nuclear factor-kappa B, interleukin-1 (IL-1) , and nitric oxide[5]. Various proteins also contribute to tissue repair. PRGF, combination of LR-PRP and iPRF, is classified as a subtype of LR-PRP under the MARSPILL classification. PRGF, prepared according to the specified protocol [6], has been reported to delay the need for knee surgery for up to 36 months, even in patients with KL grade IV KOA[7], while requiring fewer sessions of injection.

Some studies have demonstrated the significant effectiveness of IA PRP in the treatment of mild-to-moderate KOA; however, the results for severe KOA remain controversial. In many cases of severe OA, treatment is limited by factors such as an inability to maintain weight control, limited bracing or physical therapy options, and prolonged medication use. Moreover, these patients often face higher surgical risks due to comorbidities and advanced age. This study aimed to evaluate the clinical outcomes of single IA PRGF injections in patients with severe KOA, offering a potential alternative treatment option for this patient population.

METERIAL AND METHODS

This observational, analytical cohort study was conducted at the outpatient clinic of the orthopedic department of our institution between November 2022 and March 2023, following approval from the Internal Review Board and Hospital Ethics Committee. A total of 138 patients diagnosed with KOA and interested in IA PRGF treatment were recruited and screened for inclusion and exclusion criteria by a single orthopedist. Bilateral knee severity was assessed using plain radiographs taken in either the anteroposterior standing position or the Rosenberg view, and graded according to the KL classification. Patients with KL grades I (KL1) and II (KL2) were categorized as the mild KOA group, those with KL grade III (KL3) as the moderate group, and those with KL grade IV (KL4) as the severe group. All patients received information about KOA and PRGF from their orthopedists.

Inclusion criteria were as follows: patients aged > 18 years, diagnosed with KOA, able to communicate in the Thai language, who consented to treatment with PRGF following the study protocol, and agreed to attend scheduled follow-up interviews. Exclusion criteria included systemic inflammatory diseases, uncontrolled bleeding disorders, thrombocytopenia, malignancies, pregnancy, active infections, meniscal or knee ligament injuries, inflammatory arthritis (determined by history and physical examination), other IA lesions such as fractures, calcific loose bodies, osteolytic lesions (diagnosed via plain radiography), and the use of disease-modifying osteoarthritis drugs (e.g. diacerein, tocilizumab, infliximab, etanercept, anakinra, and adalimumab) during the follow-up period.

A total of 120 participants met the inclusion criteria. All were informed of the study protocol and provided written informed consent to participate in this study. Three participants dropped out of the study: two underwent knee

replacement surgery, and one died due to an underlying condition.

PRGF Preparation

PRGF, a combination of LR-PRP and iPRF, was prepared according to the established protocol[6]. A 30 mL peripheral blood sample was collected from each participant for a single knee injection and subsequently cryoprecipitated. All procedures were performed under sterile conditions in a clean and well-controlled environment (Fig. 1).

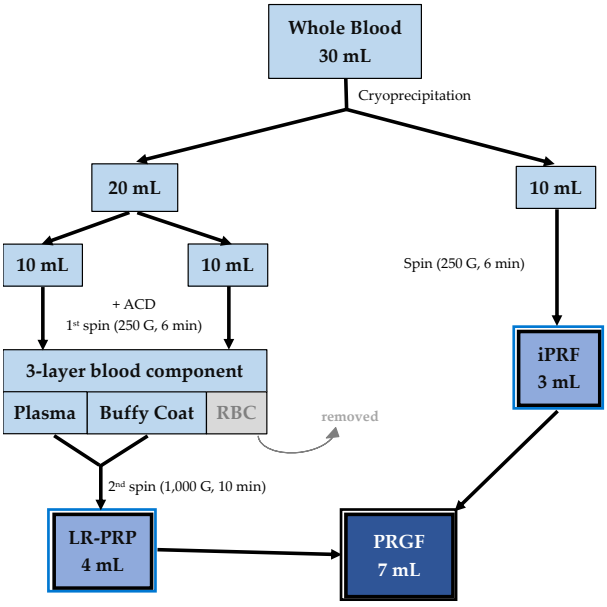

Fig. 1 Preparation of PRGF for single knee injection.

Injection Protocol

All IA knee injections were administered by a single orthopedist. Using the inferomedial patellar approach with the knee flexed to 30°, an 18G needle was used to administer PRGF via the single needle, two syringes technique: 4 mL of LR-PRP followed by 3 mL of iPRF. No synovial fluid aspiration was performed prior to injection. The knee was extended immediately after the administration of PRGF. All participants were permitted full weight-bearing after the injection. Cold compression was applied around the injection site for 10 min, and clinical observations were conducted immediately thereafter. At 30 min post-injection, the local appearance, active range of motion, ability to stand on the injected limb, and performance of a 10-meter walk were assessed. Participants were then allowed to resume activities of daily living. Acetaminophen was prescribed every 8 h for pain control. In cases of persistent pain, patients were instructed to contact their orthopedist via the provided contact channels before taking other analgesics with antiplatelet effects, such as NSAIDs and steroids. Full activity was permitted two days after injection.

Rehabilitation Protocol

All participants were instructed to begin exercise therapy 2 days after the injection. The exercise therapy was explained to all participants by an experienced nurse prior to injection. The rehabilitation regimen included fixed-arc quadriceps exercises, such as sitting on a chair with one leg extended forward for 100 s on each side. Multi-angle isometric exercises were performed to target the knee muscles, quadriceps femoris, thigh abductors, and adductors. In addition, hamstring stretching exercises were prescribed: three sets of 10 repetitions of 10 s stretches per day. After one month, participants were encouraged to gradually transition to closed-chain isotonic exercises.

Follow-up Assessment

Five follow-up visits were scheduled for each participant: at baseline, one week, one month, three months, six months, and 12 months after the injection. At each visit, the WOMAC scores and medication use were evaluated.

Statistical Analysis

To assess the WOMAC score and baseline characteristics, all patients with KOA were categorized into three groups: severe (KL4), moderate (KL3), and mild (KL1-2). Differences between the groups were tested using Fisher's exact test and analysis of variance (ANOVA). Statistical significance was set at $P \leq 0.05$.

The sample size was calculated using a computer program. The mean number of injected osteoarthritic knees for mild to moderate KOA (KL1-3) and severe KOA (KL4) were 2.47 ± 0.73 and 2.87 ± 0.22, respectively, based on the study by Cheeva-akrapan and Turajane, 2023[7]. The alpha

error was 0.05, power was 90%, and the group ratio was 2.5:1. The total calculated sample size was 76 (54 in the KL1-3 group and 22 in the KL4 group). Continuous data are expressed as means and standard deviations. Ordinary data are presented as percentages and proportions. Two-tailed tests were conducted.

For the evaluation of PRGF treatment outcomes, ANOVA, regression analysis of repeated responses, paired t-test, and Wilcoxon signed-rank test were used to determine statistical significance.

RESULTS

Among the 117 patients included in this study, 38 were in the KL grade I-II (mild KOA) group, 44 were in the KL grade III (moderate KOA) group, and 35 were in the KL grade IV (severe KOA) group. The demographic characteristics of the participants are presented in Table 1. Most participants were female, had right knee involvement, and had underlying diseases. A total of 81.2% of participants were aged between 56 and 74 years. The mean age was 64.9 ± 8.3 years (range, 45-90 years), and the mean body mass index (BMI) was 26.0 ± 3.7 kg/m² (range, 17-38 kg/m²). Both age and BMI were significantly higher in the severe group (KL4) than in the mild (KL1 and KL2) and moderate (KL3) groups. According to sex preference, the male-to-female ratio also increased in the severe group.

Table 1 Baseline demographics of all participants.

Character	KL1- 2	KL3	KL4	p-value
Number (cases)	38	44	35	
Sex (male : female)	7 : 31	5 : 39	9 : 26	0.264
Age (years)	62.0 (±8.09)	63.57 (±7.02)	69.86 (±8.06)	0.001
BMI (kg/m^2)	25.37 (±3.66)	25.35 (±2.92)	27.51 (±4.29)	0.015

Fisher's exact test and ANOVA were used for statistical analysis.

Table 2 WOMAC scores in the severe (KL4), moderate (KL3), and mild (KL1-2) KOA groups.

Timing	WOMAC Scores			p-value
	Severe KOA (KL4)	Moderate KOA (KL3)	Mild KOA (KL1-2)	
	Mean ± SD P_{50} (P_{25}, P_{75})	Mean ± SD P_{50} (P_{25}, P_{75})	Mean ± SD P_{50} (P_{25}, P_{75})	
Baseline	112.7 ± 48.2 121 (80, 140)	78.2 ± 38.7 73 (48.5, 108.5)	88.7 ± 42.8 91 (64, 118)	0.002
After 1 week	60.3 ± 43.4 59 (22, 98)	37.8 ± 38.7 19.5 (5, 71.5)	39.6 ± 39.5 31 (10, 71)	0.026
After 1 month	41.3 ± 36.3 27 (8, 70)	22.2 ± 27.1 12 (2.5, 31.5)	33.2 ± 28.4 26 (10, 56)	0.013
After 3 months	40.6 ± 47.3 16 (0, 82)	18.8 ± 26.8 8.5 (0, 25)	18.7 ± 29.1 8 (2, 22)	0.213
After 6 months	38.5 ± 46.9 15 (0, 77)	24.1 ± 35.4 5 (0, 35.5)	13.5 ± 20.1 5 (0, 16)	0.221
After 12 months	43.0 ± 42.6 41 (1, 66)	30.8 ± 43.1 4 (0, 72.5)	19.9 ± 27.2 8 (0, 43)	0.093

Statistical analyses were performed using ANOVA and ANOVA by rank (Kruskal–Wallis test).
SD, standard deviation

Table 3 Percent change in WOMAC scores at each time point after PRGF injection.

Time	KL1-2 (Mild)		KL3 (Moderate)		KL4 (Severe)		p-value
	mean	(±SD)	mean	(±SD)	mean	(±SD)	
Week 0-1	59.44	(±29.84)	56.80	(±41.56)	47.12	(±31.15)	0.133
Month 0-1	63.44	(±28.25)	71.38	(±35.32)	50.60	(±86.22)	0.081
Month 0-3	82.32	(±24.36)	74.55	(±33.86)	66.94	(±34.14)	0.342
Month 0-6	83.62	(±28.47)	74.62	(±30.71)	69.91	(±35.20)	0.269
Year 0-1	76.53	(±33.46)	66.33	(±44.57)	63.25	(±39.21)	0.258

Statistical analyses were performed using ANOVA by rank (Kruskal–Wallis test).

The highest baseline WOMAC score was observed in the severe group (KL4), which was statistically significant. After PRGF injection, WOMAC scores in the severe KOA group remained significantly higher than those in the mild and moderate KOA groups at all follow-up periods. However, the WOMAC scores in the mild (KL1, KL2) KOA group were higher than those in the moderate (KL3) KOA group at 1 week and 1 month after PRGF treatment (Table 2).

All groups demonstrated a similar pattern of improved clinical outcomes after PRGF injection. At 1 week post-injection, the WOMAC scores decreased in all groups, with continued decline observed up to 6 months post-injection. At 12 months post-injection, WOMAC scores showed a slight increase compared to the 6 months scores but remained lower than baseline levels (Table 2). One week after the single treatment, the percentage reduction in WOMAC scores from baseline was statistically significant in all groups: 47.12%, 56.8%, and 59.44% in the severe, moderate, and mild KOA groups, respectively. The highest percentage reduction in scores was observed at 6 months post-injection in all groups: 69.9% in the severe group, 74.6% in the moderate group, and 83.6% in the mild group (Table 3).

After calculating age and BMI, statistically significant differences in WOMAC scores were observed at 1 week, 1 month, 3 months, 6 months, and 12 months after treatment compared with baseline in all KOA groups, following a similar trend. WOMAC scores decreased from baseline across all KOA groups throughout the study period. The lowest WOMAC score in the mild and moderate KOA groups was observed at 3 months post-injection, whereas in the severe KOA group, it was observed at 6 months post-injection (Fig. 2).

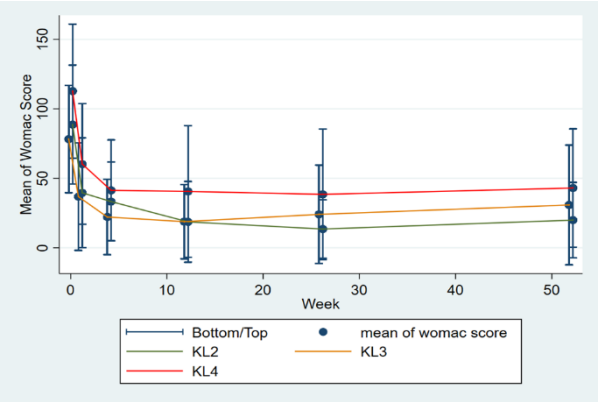

Fig. 2 Mean WOMAC scores in the mild (KL1, KL2), moderate (KL3) and severe (KL4) KOA groups at baseline and at follow-up after PRGF injection. Regression analysis of repeated responses.

At 6 months after PRGF injection, WOMAC scores significantly decreased in all three categories: pain, stiffness, and function (Table 4). Scores in each category remained lower than baseline in all KOA groups at 6 months after PRGF injection. Functional category scores in the severe KOA group were higher than those in the mild and moderate KOA groups at both baseline and 6 months after PRGF injection.

During the 12-month follow-up period, two participants in the severe KOA group underwent knee replacement surgery, resulting in a dropout rate of 5.71% (2 of 35 patients). These patients were unable to postpone surgical

treatment for the full 12 months. In contrast, 94.29% of participants with severe KOA were able to delay surgery for up to 12 months following the PRGF injection.

Table 4 WOMAC scores at 6 months after PRGF injection.

Detail	After 6 months	Baseline	p-value
	Mean ± SD	Mean ± SD	
Pain			
Mild KOA (KL1-2)	3.0 ± 4.9	20.1 ± 11.5	< 0.001
Moderate KOA (KL3)	5.7 ± 8.7	18.4 ± 9.2	< 0.001
Severe KOA (KL4)	8.4 ± 10.5	24.5 ± 11.1	< 0.001
Stiffness			
Mild KOA (KL1-2)	0.9 ± 2.1	6.8 ± 4.3	< 0.001
Moderate KOA (KL3)	2.4 ± 3.5	6.4 ± 4.3	< 0.001
Severe KOA (KL4)	3.2 ± 4.3	9.3 ± 4.9	< 0.001
Function			
Mild KOA (KL1-2)	9.6 ± 15.6	61.7 ± 4.8	< 0.001
Moderate KOA	16.0 ± 23.9	53.3 ± 27.7	< 0.001
Severe KOA (KL4)	26.9 ± 5.6	78.9 ± 34.3	< 0.001

Statistical analyses were performed using paired t-test and Wilcoxon signed-rank test.

DISCUSSION

KOA has emerged as one of the most common degenerative diseases in recent years, with its incidence rising due to the increasing elderly population in rapidly-aging society. PRP has gained traction as a regenerative treatment of KOA. However, recent standard guidelines from the American Academy of Orthopaedic Surgeons, American College of Rheumatology, and Osteoarthritis Research Society International classify PRP as a treatment of KOA with limited recommendations, primarily due to inconclusive results. This variability is attributed to different preparation techniques, which result in different PRP components. However, positive outcomes have been reported for LR-PRP compared to leukocyte-poor PRP (LP-PRP) or hyaluronic acid in the treatment of KOA[8,9]. Most studies highlight the benefits of PRP in the mild-to-moderate stages of KOA.

Theoretically, numerous components within PRP may influence the progression of KOA. Platelets, which are cytoplasmic fragments derived from megakaryocytes, contain over 30 bioactive proteins. These factors target mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells, contributing to cellular proliferation, matrix formation, osteoid production, and collagen synthesis. During tissue repair and regeneration, platelets actively secrete growth factors from their alpha granules, beginning within 10 min of activation. Over 95% of these pre-synthesized growth factors are secreted within 1 h, causing antinociceptive effects and reducing the secretion of proinflammatory mediators[10]. Furthermore, some studies have suggested a chondroprotective effect of PRP [11]. The timing of PRP preparation is one of the major critical factors.

The buffy coat technique produces LR-PRP, whereas the plasma-based technique yields LP-PRP. Although leukocytes in PRP stimulate an immunological response, the reaction is typically mild and does not result in clinical inflammation. Moreover, leukocytes exhibit antibacterial effects. A disadvantage of high leukocytes concentration in PRP is the potential upregulation of catabolic cascades and inflammatory markers, such as IL-1 and tumor necrosis factor-α. However, LR-PRP is hypothesized to contain the IL-1 receptor antagonist protein, which blocks IL-1 activity and supports the healing cascade. M1 macrophages

function primarily as proinflammatory cells in the early phase of healing, whereas M2 macrophages, which mainly act as anti-inflammatory cells, usually function in the late phase of healing[6]. Jonathan et al. reported that adverse reactions to PRP may not be directly related to leukocyte concentration. LP-PRP injection resulted in significantly lower WOMAC scores and a higher incidence of adverse events than hyaluronic acid injection. In the present study, a single-dose technique was employed[12], as limited studies have concluded that multiple doses offer superior outcomes only in the early-stage KOA group[13,14]. A recent study also revealed that high lymphocyte count was common in the responder group.

Platelet count and platelet aggregation are two factors that may affect the efficacy of PRP. Kao et al. reviewed 1,711 studies and found that acetaminophen, a nonselective NSAID, significantly decreased platelet aggregation but had no effect on platelet count, whereas COX-2 NSAID and statins showed no significant difference in platelet count and aggregation. Based on these findings, there is no evidence to support that discontinuing COX-2 NSAIDs and statins prior to PRP injection improves clinical outcomes[15].

Large-bore needles (22G or larger) are recommended for blood collection. During centrifugation, a temperature range of 12°C-16°C has been reported in many studies to yield optimal platelet recovery[16]. Recommended preservatives and activators include A-form of acid-citrate-dextrose (ACD-A)[17]. In this study, PRGF was prepared using the buffy coat technique with controlled temperature, time, and specific centrifugal force in a sterile environment, following a previously described protocol[6,18] due to its safety[19] and effectiveness[7,20,21]. A single large-dose injection was administered without discontinuation of routine medications. No major adverse events were reported.

The characteristics of the participants in this study were consistent with those of the general population, with a higher prevalence of severe KOA observed among females, overweight individuals, and elderly individuals. After IA PRGF injection, WOMAC scores decreased in all the KOA groups at 1 week, 1 month, 3 months, 6 months, 12 months follow-ups. A consistent decline in the WOMAC scores was observed in all groups. However, the WOMAC score in the severe KOA group was significantly higher than those in the mild and moderate KOA groups at each time point.

A decline in WOMAC scores was observed at 1 week after PRGF injection, with a gradual deceleration noted at 1, 3, and 6 months, followed by a slight increase at the 12-month follow up. Some participants reported variations in WOMAC score pattern. The pattern of the WOMAC scores in the severe KOA group was similar to that in the mild and moderate KOA groups. At the 3-month follow-up, the WOMAC score in the moderate KOA group was lower than that observed at 6 months after injection. A few participants reported no change in their WOMAC scores, which may have been due to increased activity at the time of follow-up. Although the WOMAC score started to accelerate at 6 and 12 months of follow-up, most participants still had lower WOMAC scores than at baseline. All participants reported satisfaction with the PRGF injection. According to this finding, a single IA PRGF injection appears to be a beneficial treatment option for patients with mild, moderate, and severe KOA to reduce patient symptoms, minimize medications, and postpone joint replacement arthroplasty.

Therefore, further studies on PRGF preparation techniques are warranted. The combination of LR-PRP and iPRF in PRGF may help preserve osteoarthritic knees from surgical intervention by up to 80.18% at the 36th month follow-up [7], likely due to enhanced release of active molecules at each time point. LR-PRP releases growth factors immediately after injection, whereas iPRF function as a natural mesh for PRP and progressively releases growth factors. The findings of the present study support the notion that patients with KOA KL4 can also benefit from biological treatment. However, the survival rate was still lower than that in the less severe group.

Hamza et al. reported that three serial IA injections of LP-PRP resulted in a meaningful improvement in chronic knee pain in patients with KOA throughout a 12-week period. However, this

improvement remained stable between the 6th and 12th week. Moreover, the reduction in pain was less pronounced in patients with KL3 and KL4 KOA compared to those with KL2[22], although PRP treatment may help delay total knee arthroplasty[23]. The optimal timing for PRP reinjection in patients with severe KOA remains inconclusive. Some accessible objective investigations, such as knee MRI[24], may provide additional information for evaluating responses to PRGF. This information is helpful in determining subsequent treatment strategies, including repeat PRGF injections, minimal surgery, or knee arthroplasty. In this study, two patients dropped out before the end of the follow-up period because they underwent total knee replacement surgery. A longer follow-up period and separation of the severe KOA group into operable and inoperable subgroups may yield more accurate information regarding the ability of a single IA PRGF injection to postpone or avoid joint replacement surgery, which was the secondary outcome of this study.

A single PRGF injection is more beneficial than multiple injections in terms of cost-effectiveness and patient comfort, particularly in high-risk patients. Vilchez-Cavazos et al. reported that a single injection was as effective as multiple PRP injections for pain improvement[12]. Yurtbay et al. [13] reported that multiple LR-PRP injections had better efficacy than a single injection at 6 and 12 months, although no difference was observed at 24 months; both techniques were better than normal saline injections. Ngarmukos et al.[25] demonstrated no difference in the levels of synovial cytokines and growth factors between two or four sessions of IA PRP injection. However, both injection protocols significantly improved knee scores from 6 weeks to 1 year of follow-up. Subramanyam et al. suggested that a treatment regimen of three PRP injections should be repeated to maintain the results for up to one year [14].

This study has some limitations. First, the WOMAC score is clinically subjective; therefore, a decrease in the WOMAC score may not necessarily indicate cartilage restoration in all treated osteoarthritic knees[11]. Second, patients with severe KOA should be divided into operable and inoperable subgroups to determine whether a single IA PRGF injection can postpone or potentially prevent surgical intervention. Finally, further studies with longer follow-up periods are warranted to identify factors contributing to the rapid improvement or worsening of WOMAC scores compared to the group average.

CONCLUSIONS

A single IA injection of PRGF, comprising a combination of LR-PRP and iPRF, can improve clinical outcomes, as assessed by the WOMAC score, in patients with severe KOA for up to 12 months after injection. The degree of improvement in patients with severe KOA was lower than that in patients with mild or moderate KOA. A single injection without discontinuation of NSAID or other underlying medications is practical and beneficial for such patients in terms of cost and risk management. This treatment may help delay joint replacement surgery in patients with severe KOA for up to 1 year after injection.

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Comparative Effectiveness of Different Osteoporosis Medications in Enhancing Bone Mass

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Purpose: To compare the spine and non-dominant hip bone mineral density before and after treatment with different categories of osteoporosis medications.
Methods: In this retrospective cohort study, we analyzed the medical records of patients with osteoporosis who were prescribed anti-resorptive agents (bisphosphonates, alendronate, risedronate, intravenous ibandronate, and denosumab) or bone-forming agents (teriparatide). Patients were selected using purposive sampling. Descriptive statistical analysis was performed, including calculations of percentages, means, and standard deviations, along with hypothesis testing using Wilcoxon signed-rank and t-tests.
Results: Among the 80 participants treated with these medications and monitored over 3–5 years, with at least 2 years of continuous treatment, none had hip or spine fractures. In the bisphosphonate group (n = 59), both the spine and non-dominant hip bone mineral density showed significant improvements. The denosumab group (n = 17) demonstrated a significant increase in spine bone mineral density, whereas the increase in nondominant hip bone mineral density was not significant. The teriparatide group (n = 4) showed improvements in both the spine and non-dominant hip bone mineral density, although not significant, possibly because of the small sample size.
Conclusions: All medication categories had positive effects on bone mineral density. Antiresorptive agents, particularly bisphosphonates, showed significant improvements in both spine and hip bone mineral density, whereas denosumab showed significant improvement, specifically in spine bone mineral density. The bone-forming agent teriparatide showed a positive trend, although not significant, likely because of the limited sample size.

Keywords: Osteoporosis, anti-resorptive agents, bone-forming agents, bone mineral density, bisphosphonates, denosumab, teriparatide

Osteoporosis is a condition in which the bone strength decreases, making individuals more susceptible to fractures. It is a widely accepted fact that bone strength depends on both bone density and bone quality. Usually, after peak bone mass, the bone density declines by 0.3%–0.5% annually, and then rapid bone loss occurs during the menopausal period, with bone density loss of 3%–5%. Involutional bone loss in the elderly is another factor[3]. During this period, bone formation slows, leading to a gradual decline in bone mineral density (BMD). This decline is particularly obvious in

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women, as bone resorption rates increase rapidly after menopause. Non-modifiable risk factors for osteoporosis include age ≥ 65 years, Caucasian and Asian ethnicity, early menopause (< 45 years) , bilateral oophorectomy, small body frame, and a family history of osteoporosis. Modifiable risk factors include inadequate calcium intake, lack of physical activity, smoking, excessive alcohol and caffeine consumption, body mass index (BMI) < 19 kg /m^2, and estrogen deficiency before menopause. Epidemiological statistics estimate that osteoporotic fractures affect approximately 40% of women and 13% of men worldwide. Statistical predictions indicate that the number of hip fractures will increase from 1.7 million in 1990 to 6.3 million in 2050, with the majority occurring in Asia[2]. Indeed, by 2050, Asia is projected to account for more than 50% of all osteoporosis-related hip fractures.

In Thailand, the prevalence rate of female osteoporosis in the menopausal clinic at Chulalongkorn Hospital is 15.7%[3], whereas that of male osteoporosis (Pongchaikul Chatlert and team[4]) is 12.6% from small subjects. Thailand has become an aging society and the number of osteoporosis patients is expected to increase. Most osteoporosis treatments are original drugs, and studies on the efficacy of drug regimens are limited. Our Province has one of Thailand's highest proportions of elderly residents, with 24.24%[5] of the older population. Osteoporosis is a significant musculoskeletal disorder that is becoming increasingly prevalent in this population, making it crucial to implement preventive measures and establish a comprehensive care system. Our hospital founded the Osteoporosis Clinic, to investigate diseases and use osteoporosis drugs with standard protocol under Nation Osteoporosis Foundation[2] policy for specific patients with osteoporosis. In this study, we aimed to assess the effectiveness of different groups of osteoporosis medications and compare the mean BMD of patients at the osteoporosis clinic before and after treatment with these medications.

METHODS

This was a retrospective cohort study that analyzed data from medical records. The study utilized a sample group from the osteoporosis clinic consisting of individuals who underwent treatment between January 1, 2015, and May 31, 2021. The study received IRB approval from the Ethic Committee of our hospital in 012/2565 coding. Our hospital established a dedicated osteoporosis clinic in October 2014, which continues to operate to the present day. The clinic's service model relies on a multidisciplinary team approach, emphasizing screening activities to identify individuals at risk for osteoporosis (Appendix 1).

First, the hospital's multidisciplinary team developed a screening protocol specifically for individuals aged > 50 years. The screening protocol was as follows:

1. General risk factors include weight, height, BMI, dietary habits, physical activity, and underlying health conditions.

2. Specific risk factors include menstrual history[6], history of oophorectomy, history of minor trauma, and history of steroid use.

3. OSTA screening (Osteoporosis Self-assessment Tool Asian) check list for at risk patients.

4. Quantitative Ultrasound (QUS) Screening[7]: A QUS score < –2.5 is required for 1 risk point. However, the QUS is only a screening tool. For confirmation, the DXA, which is the main diagnostic tool according to WHO standards, is still required. After screening, if the patient is identified to be at risk (Two points out of four.), the patient underwent osteoporosis diagnostic testing using DXA scan as a standard diagnostic test, which measures the BMD as a representative of bone mass. A BMD score between + 1 and –1 is considered normal; a score below –1 but not lower than –2.5 indicates osteopenia (low bone mass); and a score below –2.5 is classified as osteoporosis[8,9]. The BMD T-score is essential for assessing the risk of fractures, with studies showing that the risk of fractures increases by 1.4 to 2.6 times for each standard deviation change in the T- Score[10]. Treatment decisions are not solely based on a BMD T-Score of ≤ –2.5 but also consider clinical factors when deciding whether to admit a patient to the clinic for further treatment.

Finally, the patients in the Osteoporosis Clinic at our hospital were treated with three categories of medications along with the National Osteoporosis Foundation regulation[2]. Bisphosphonate is the first-line drug used for treatment. A follow-up DXA scan will be considered after 2 years. If the results remain the same or do not improve, the treatment will need to be changed from bisphosphonate to Denosumab. Teriparatide was another drug considered in patients with hip or spine osteoporosis with a T-score < –3.5. The three categories of medications were as follows:

1. Bisphosphonates, which reduce the activity of the osteoclasts involved in bone resorption. The medications administered in the hospital include Actonel®, Fosamax®, and Ostex®.

2. Denosumab, a monoclonal antibody (mAb) and biologic agent that targets the cytokine RANKL to prevent bone loss and reduce bone resorption by inhibiting its activity. Our hospital uses Prolia®, but patients with hypocalcemia should not receive it.

3. Teriparatide is an analog of parathyroid hormone that stimulates the cyclic adenosine monophosphate/ protein kinase A (cAMP/ PKA) pathway to promote bone formation. Our hospital uses Forteo®.

Currently, this clinic has a total of 300 patients, including 195 patients with normal bone density and osteopenia. Only patients who were diagnosed with osteoporosis (n = 105) received osteoporosis medication, all of whom were provided with a guide for self-care, exercise instructions, and calcium and vitamin D supplementation. The patients received a DXA scan once a year for monitoring from the National Osteoporosis Foundation, as recommended[1,2].

Population and Sample Size

The study included 300 patients treated at the osteoporosis clinic of our hospital between January 1, 2015, and May 31, 2021. The medical records from this period were reviewed to analyze and categorize the population based on treatment. The inclusion criteria were as follows: diagnosed with osteoporosis; BMD ≤ –2.5 SD, as determined by DXA scan once a year[1,2]; and received continuous treatment with the same osteoporosis medication for at least 2 years without any missed doses. Initially, the study included 105 osteoporotic patients who met the criteria; however, Twenty-five patients were excluded from the study due to treatment discontinuation, medication use for less than 2 years, or fewer than two DXA scans (at least one per year) performed consecutively.

Therefore, 80 patients who qualified for the study were divided into three groups according to the medications available at the Osteoporosis Clinic (Table 1).

Table 1 Number of patients with osteoporosis in the study group, categorized by medication received.

Patient Group	Medication Group	Number of Patients (Sample Size)
1	Anti-resorptive (osteoclast) (bisphosphonate) including: - Actonel® (150 mg), taken orally once monthly - Fosamax® (70 mg), taken orally once weekly - Ostex® (3 mg), taken intravenously every 3 months	59
2	Anti-resorptive (RANKL) (denosumab), (60 mg), taken subcutaneously every six months.	17
3	Bone forming agent (teriparatide), (20 micrograms), taken subcutaneously once daily.	4
	Total	**80**

Data Analysis

The SPSS statistical software package was used to analyze the data using descriptive statistics (percentage, mean, and standard deviation), paired sample t-tests, and Wilcoxon signed-rank tests. Analyses were conducted separately for the spine and hip to compare the effectiveness of the four types of medications.

RESULTS

Characteristics of the Sample Group

The sample group consisted of 80 individuals, including five males (6.67%) and 75 females (93.33%). The majority of the participants (42; 52.50%) had been attending the clinic for 5–6 years, followed by 30 people (37.50%) for 3–4 years and 80 people (10%) for 7 years. In terms of BMI[12], most participants were within the normal range (55; 68.75%), followed by 17 people (16.25%) above the normal range and eight people (10%) below the normal range. Among the female participants, the majority experienced menopause after the age of 45 (76; 88.37%), while 10 persons (11.63%) experienced menopause before the age of 45. On average, menopause occurs at a young age in these patients, and the earlier it occurs, the greater is the risk[3]. Most female participants (67, 89.33 %) had no history of oophorectomy, while eight (10.67%) had undergone the procedure. None of the participants (100 %) had a history of alcohol or tobacco use. The majority of the participants (52; 65%) had a history of regular exercise, while 28 (35%) reported no exercise routine. The majority of participants had no family history of hip fractures (75 people, 93.75%), while five people (6.25%) reported a family history of fractures. The majority of participants (73, 91.25 %) had no history of hip, spine, or wrist fractures, whereas seven (8.75%) had a history of minor fractures. Most participants had no history of steroid use (71; 88.75%), followed by six people (7.50%) with a history of steroid use and three people (3.75%) who did not specify their steroid use history.

Comparison of BMD Before and After Treatment

The paired sample t- test with a 95% confidence level revealed a significant improvement in the BMD of the spine and hip following bisphosphonate treatment compared to that before treatment ($p < 0.05$; Tables 3 and 4).

The Wilcoxon signed-rank test was used to evaluate spine and non-dominant hip BMD in the groups treated with denosumab and teriparatide, with a 95% confidence level. The results revealed a statistically significant difference in spine BMD before and after treatment with denosumab ($p < 0.05$), whereas the non-dominant hip BMD did not show a significant difference, as shown in Table 5.

There were no significant differences in spine and non-dominant hip BMD before and after teriparatide treatment, as shown in Table 6.

Table 2 Characteristics of the sample group.

Category	Number (n)	Percentage (%)	Category	Number (n)	Percentage (%)
Sex			**Oophorectomy (female only)**		
Male	5	6.67	Yes	6	8.00
Female	75	93.33	No	69	92.00
Duration of Clinic Attendance			**Alcohol/tobacco use**		
3–4 years	30	37.50	Yes	0	0
5–6 years	429	52.50	No	80	100
7 years	8	10.00	**Exercise**		
Age (years)			Yes	52	65.00
< 70	26	32.50	No	28	35.00

Table 2 Characteristics of the sample group. (Cont.)

Category	Number (n)	Percentage (%)	Category	Number (n)	Percentage (%)
≥ 70	54	67.50	**Family history of hip fractures**		
BMI			Yes	5	6.25
Below normal (< 18.5)	8	10	No	75	93.75
Normal (18.5–22.9)	55	68.75	**History of hip, spine and wrist fractures**		
Above normal (23.0)	13	16.25	Yes	7	8.75
Menopause before 45 years (female only)			No	73	91.25
Yes	8	10.67	**Steroid use history**		
No	67	89.33	Yes	6	7.50
			No	71	88.75
			Not Specified	3	3.75

Table 3 Mean and standard deviation of bone mineral density before and after treatment with bisphosphonates paired samples statistics.

		Mean (gm/cm²)	N	Percent change (%)
Spine bone mineral density	Before	−2.38	59	↑ 61.34
	After	−1.46	59	
Hip bone mineral density	Before	−1.94	59	↑ 76.80
	After	−1.49	59	

Table 4 Comparison of bone mineral density before and after treatment with bisphosphonates in the sample group paired samples test.

		Paired Differences					t	df	Sig. (2-tailed)
		Mean Difference	SD	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Spine bone mineral density	Before - After	−0.92	1.07	0.139	−1.20	−0.65	−6.633	58	0.000*
Hip bone mineral density	Before - After	0.45	1.23	0.160	−0.77	−0.13	−2.786	58	0.007*

*p < 0.05

Table 5 Comparison of bone mineral density before and after treatment with denosumab using Wilcoxon signed ranks test.

Denosumab (n = 17)		**Mean**	**Std. Deviation**	**Mean Rank**	**Asym.Sig (2-tailed)**
Spine bone mineral density	Before Min -4.40, Max -0.90	-2.72	1.03	6.50	0.002*
	After Min -2.30, Max 0.00	-1.01	0.74		
Non-dominant hip bone mineral density	Before Min -4.10, Max 0.60	-2.31	1.33	6.30	0.060
	After Min -3.10, Max 1.00	-1.59	1.22		

*p < 0.05

Table 6 Comparison of bone mineral density before and after treatment with teriparatide using Wilcoxon signed ranks test.

Teriparatide (n = 4)		**Mean**	**Std. Deviation**	**Mean Rank**	**Asym.Sig (2-tailed)**
Spine bone mineral density	Before Min -5.70, Max 1.30	-2.95	3.00	2.50	0.068
	After Min -3.00, Max 2.60	-0.33	2.42		
Non-dominant hip bone mineral density	Before Min -3.60, Max -1.70	-2.68	0.84	3.50	0.465
	After Min -3.90, Max 0.00	-2.20	1.62		

*p < 0.05

DISCUSSION

Until now, there have been no comparative studies on the effectiveness of different osteoporosis medications in Thailand. In this study, we evaluated the effectiveness of these medications for different types of patients, focusing on the spine and hip, at our osteoporosis clinic. Ultimately, the goal is to ensure that patients receive the most appropriate medication based on their symptoms and affected bone area. However, the response to bone density changes may differ among different patient profiles, such as that identified between male and female patients, as well as those who were treatment naïve and those who had received other treatments. This study adds to the existing evidence on the comparative effects of various osteoporosis medications on non-dominant hip and spine BMD. Empirical evidence supports the effectiveness of osteoporosis medications in reducing fracture rates, increasing BMD, and decreasing bone turnover[12-21]. The included patients were diagnosed and treated with osteoporosis medications, and the BMD increased across all groups; however, some osteoporosis medications did not significantly increase BMD. Most patients in the osteoporosis clinic at our hospital were women aged between 70 and 79 years. This is due to the significant hormonal changes that postmenopausal women experience, leading to physical changes during this period, including concerns about decreasing BMD[22,23]. Almost all of the participants (68.75%) had a BMI[24] between 18.5 and 23, which is within the normal

range. While BMI is a recognized risk factor for fractures[25], it did not appear to influence changes in BMD in this study, as the average BMI across different groups was similar. The desired outcomes of osteoporosis medications include reducing the rate of bone fracture[26], increasing bone mineral density, and decreasing bone turnover.

A comparison of the mean spine and nondominant hip BMD in the sample group treated with bisphosphonates before and after treatment showed a significant difference ($p < 0.05$). As shown in Table 1, bisphosphonates used in this study were obtained from three manufacturers. Although the methods of administration differed to ensure better patient compliance, the antiresorptive mechanism of action was consistent across all three medications[27-30], leading to similar effects on both the spine and non-dominant hip BMD[31-36].

For patients treated with denosumab, we found a statistically significant increase in spine BMD ($p < 0.05$), whereas the increase in nondominant hip BMD was not statistically significant. Several studies have demonstrated that denosumab can increase BMD in both the spine and hips . However, it has a more significant impact on increasing BMD in the spine, often resulting in a 2–3 times greater benefit compared to its impact on the hip, as reported by McClung MR[37], Cumming SR[38], and McCloskey EV[39]. However, the relatively small sample size of patients treated with denosumab may have limited the statistical power of the findings. Nonetheless, there was still an increase in hip bone mass compared to pre-treatment levels.

Before and after teriparatide treatment, there were no significant differences in the spine and non-dominant hip BMD. The primary indication for teriparatide is combination[40,41] or switch therapy, particularly for severe osteoporosis (BMD < –3.5). The small number of patients treated with teriparatide in this study, together with the high cost of the medication and restrictive guidelines, likely contributed to the lack of statistically significant results. However, there is a trend suggesting that teriparatide may have a better outcome on spine BMD, as indicated by the greater reduction in BMD.

A limitation of this study was the small sample size of each group, which resulted in low statistical power. This may lead to findings where certain medications show an increase in BMD but do not reach statistical significance, making it difficult to conclude that these medications are ineffective. Another limitation was the National Osteoporosis Foundation regulations. Furthermore, most of the treatments were bisphosphonates as a first-line drug, and patient drug compliance and transportation that cause incorrect drug doses and might lead to loss of patient follow-up at the osteoporosis clinic, respectively. The follow- up period of patients also varied owing to the realities of service delivery; therefore, comparisons of the effectiveness of different medications must be made with caution. Additionally, because this study was conducted at a single hospital, the results cannot be generalized to broader patient populations in other settings.

CONCLUSIONS

Since 2015, our hospital has been offering services at its osteoporosis clinic with efforts to promote BMD screening and provide treatment for patients with abnormal BMD. We conclude that all medication groups at the osteoporosis clinic of our hospital demonstrated an increase in BMD following treatment. Specifically, the groups treated with the bisphosphonate or denosumab showed a statistically significant increase in spine BMD. In addition, bone mineral density of the non-dominant hip increased significantly in the group treated with bisphosphonates but did not increase in the group treated with denosumab. However, due to limitations in the study population size, this outcome is inconsistent with previous studies.

However, another the limitations of this study include the National Osteoporosis Foundation regulations, and most of the treatments were bisphosphonates as a first-line drug, which resulted in different treatment outcomes. As Thailand transitions into an aging society, osteoporosis poses a significant economic threat with the potential for substantial costs associated with an increase in osteoporotic fractures. Therefore, it is crucial to promote health literacy among the older

population, emphasizing the importance of the early detection and treatment of osteoporosis to prevent fractures. For individuals diagnosed with osteoporosis, insurance coverage should not restrict access to services, such as bone mass screening and medication. It is essential to develop a system that supports the financial needs of this vulnerable population, ensuring that all older individuals have equitable access to the necessary osteoporosis care.

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Appendix 1 Osteoporosis clinic screening.

1. General History

Name _____ Surname _____ HN. _____

Birth Date _____ Age _____ year. Weight _____ kg. Height _____ cm. BMI. _____ (Below than 19 is not ok.)

Consumer Behavior ☐ cigarettes, ☐ alcohol, Coffee, Soft drink

Exercise Behavior ☐ more than 3 time/week.

Underlying disease _____

2. History of risk.

2.1 Menopause before 45 yrs or amenorrhea more than 1 yr. ☐

2.2 oophorectomy both side or on Hormonal drug irregularly ☐

2.3 Fracture around the hip in parent ☐

2.4 Fracture on minor trauma ☐

2.5 On steroid drug more than 3 month. ☐

3. Osteoporosis Self Assessment Tool for Asian (OSTA)

Age	Weight (kg.)										
(year)	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94
40-44											
45-49											
50-54											
55-59								Low risk			
60-64											
65-69				Moderate risk							
70-74											
75-9											
80-84		High risk									
85-86											
90-94											
95-99											

4. Quantitative Ultrasound (QUS) ☐ **Screening T-score ..... (<-1.0)**

Processing (2 in 4) ☐ Risk ☐ Not risk

- Go to DEXA scan, Date of appointment

_____ (Doctor Sign) Date _____

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Long-term Outcomes of Short-Stem Total Hip Arthroplasty in Patients Aged Forty Years or Younger with Osteonecrosis of the Femoral Head

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Purpose: This study aimed to analyze the clinical and radiographic results with a minimum 10-year follow-up of short-stem total hip arthroplasty (THA) in patients aged 40 years or younger with osteonecrosis of the femoral head (ONFH).

Methods: A retrospective analysis was conducted on 45 of 55 eligible patients with ONFH who underwent Metha® short-stem THA, with a minimum 10-year follow-up (82% follow-up rate). The clinical outcomes were measured using the Harris Hip Score (HHS) and Forgotten Joint Score (FJS). Radiography was used to assess osteointegration, stem subsidence, and stress shielding. Patient satisfaction was recorded.

Results: The mean HHS significantly improved from 43.2 preoperatively to 97.4 at the final follow-up (p<0.0001), and the mean FJS score was 93.4. Radiography revealed osteointegration mainly in zones 1 (95.6%), 2 (88.9%), 6 (100%), and 7 (91.1%). The patient satisfaction was 'very satisfied' in 43 (95.6%) and 'satisfied' in 2 (4.4%) patients. The Kaplan-Meier survivorship for the overall implant system was 93.3% at 10 years, with revisions required in 3 cases (acetabular component or liner only). At 10 years, stem survivorship was 100% for any reason and 100% for aseptic loosening.

Conclusions: Short-stem THA provides promising long-term clinical outcomes for patients aged 40 years or younger with ONFH. Radiographic results demonstrated physiological proximal load transfer with minimal stress shielding.

Keywords: short-stem, total hip arthroplasty, hip replacement, survival, osteonecrosis

Osteonecrosis of the femoral head (ONFH) is a condition in which the blood supply to the femoral head is disrupted, leading to bone tissue death. This lack of blood flow can result in collapse of the femoral head and subsequent arthritis of the hip joint. Treatment options vary depending on the stage of osteonecrosis [1,2]. Total hip arthroplasty (THA) is an effective treatment for advanced-stage ONFH. THA is highly successful in relieving pain and improving function and quality of life in patients with advanced stage [3-6].

Short-stem and conventional-stem THA aim to replace damaged hip joints with artificial components to improve pain and joint function. However, there are some clinical problems associated with conventional-stem THA such as

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metaphyseal-diaphyseal mismatch, stress shielding, thigh pain, periprosthetic fracture, greater loss of bone stock, and difficulty during removal when revision is necessary [7]. Short-stem THA was developed to reduce these problems because the short-stem is a metaphyseal anchorage without diaphyseal invasion, more anatomical reconstruction, elimination of disruption to the greater trochanter, and maintenance of bone in the femoral canal, allowing for an improved potential revision situation where a standard implant can be used instead of a long revision stem. Several authors have reported excellent outcomes and survivorship of short-stem THA in patients with ONFH, but studies on the long-term outcomes in young patients with ONFH were lacking [8-11].

The purpose of this study was to evaluate clinical and radiographic long-term outcomes of short-stem THA in patients aged 40 years or younger with ONFH. We hypothesized that short-stem THA would have promising outcomes in young patients.

METERIAL AND METHODS

This study was approved by the institutional review board (081/2024). This retrospective study included all patients aged 40 years or younger who underwent short-stem THA for ONFH in our department between February 2011 and January 2014. The inclusion criteria were patients aged 40 years or younger with advanced-stage ONFH (Ficat and Arlet stage III or IV) and good bone quality (Dorr type A or B) [12,13]. The exclusion criteria were age > 40 years, poor bone quality, and follow-up less than ten years. During the study period, a total of 73 patients aged ≤40 years underwent THA for ONFH. Of these, 55 patients received short-stem THA based on good bone quality (Dorr type A or B) and the operating surgeon's preference, while 18 patients received conventional stems because of poor proximal femoral bone morphology (Dorr type C) or other intraoperative considerations. Consecutive patients who underwent short-stem THA were included in this study. Ten patients were excluded owing to a follow-up duration of less than ten years, resulting in 45 patients being included in the final analysis. This study represents a nonrandomized, selected cohort of short-stem recipients during the study period, rather than a consecutive series of all ONFH-related THAs.

Fifty-five patients were included in the study. Ten cases were excluded because of loss to follow-up before a minimum of ten years, leaving 45 cases (81.8%) for analysis. Thirty-four patients were men, and 11 were women. The mean age of the patients was 34 years (21-40, SD 5.7). The mean body mass index (BMI) was 23.8 kg/m^2 (16.9-32.3, SD 4). The mean follow-up was 128.2 months (120-152, SD 10.8). The etiologies of ONFH included alcohol-induced (25 hips, 55.6%), corticosteroid-induced (10 hips, 22.2%), systemic lupus erythematosus (SLE) (5 hips, 11.1%), and post-traumatic (5 hips, 11.1%) (Table 1).

All cases in this study were performed with Metha® short-stem THA (B. Braun Aesculap AG, Tuttlingen, Germany) by single surgeon (YS) with a manual technique in lateral decubitus position through a modified Hardinge approach. The Metha® short-stem is a cementless, collarless, and tapered short-stem prosthesis. For osteointegration, the Metha® short-stem is round coated with Plasmapore, Calcium-phosphate layer (Figure 1). This layer is supposed to have an osteoconductive effect and accelerate the contact between the bone and prosthesis. Both modular and monobloc stems were included in this study. The monobloc stem was available at neck angles of 120°, 130°, and 135°. The modular stem was available with neck angles of 130°, 135°, and 140°, and versions included neutral, 7.5° anteversion, and 7.5° retroversion. The choice of stem type was based on the surgeon's preference. The modular neck stem was used in 20 hips (44.4%) and the monobloc stem was used in 25 hips (55.6%) with a 32-mm or 36-mm metal head. Stem sizes 0, 1, 2, and 4 were used in in 17 18 (40%), (37.8%), 8 (17.8%), and 2 (4.4%) hips, respectively (Table 1). A cementless acetabular cup (Plasmafit; B. Braun Aesculap AG, Tuttlinggen, Germany) with an ultra-high-molecular-weight polyethylene liner (Plasmacup SC liner; B. Braun Aesculap AG, Tuttlinggen, Germany) was used for all hips.

Table 1 Demographic data of patients with Metha short stem prosthesis.

Parameters	Values
Number of patients (hips)	45
Gender (male/female)	34/11
Mean age (years) (range, SD)	34 (21-40, 5.7)
Mean BMI (range, SD)	23.8 (16.9-32.3, 4)
Mean follow-up (months) (range, SD)	128.2 (120-152, 10.8)
Etiology of ONFH (hips) (%)	
Alcoholic induced	25 (55.6%)
Corticosteroid induced	10 (22.2%)
SLE	5 (11.1%)
Post traumatic	5 (11.1%)
Stem type (hips) (%)	
Modular neck	20 (44.4%)
Monoblock	25 (55.6%)
Stem size (hips) (%)	
Size 0	18 (40%)
Size 1	17 (37.8%)
Size 2	8 (17.8%)
Size 3	0 (0%)
Size 4	2 (4.4%)

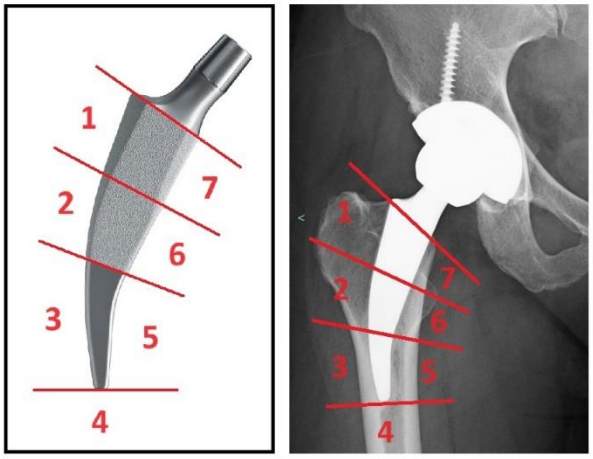

Fig. 1 Metha® short stem and definition of modified Gruen's periprosthetic zones [15].

Patients were allowed to walk using full-weight-bearing crutches on the second postoperative day. All patients were routinely contacted every three months during the first postoperative year and every six months thereafter. Anteroposterior (AP) radiographs of both hips with both legs at 15° internal rotation, lateral cross-table were taken. The Harris Hip Score (HHS) was recorded preoperatively, six months postoperatively, and annually to evaluate the clinical results. The Forgotten Joint Score (FJS) was recorded at ten-year follow-up. Patient satisfaction was indicated on a four-point scale as "very satisfied," "satisfied," "unsatisfied,"' or "very unsatisfied" [14]. The clinical results were recorded and analyzed by an independent author (BL) who was not involved in the surgery or patient care. Complications were analyzed.

The appearance of osteointegration and radiolucent lines was reviewed in all hips using modified Gruen zones, which are adapted regions of analysis specific to short femoral stems, based on the original Gruen classification[15] (Figure 1). Osteointegration is defined as the direct bone apposition to the implant, indicating stable biological fixation. Stress shielding was defined radiographically as proximal femoral bone loss or bone resorption according to the Engh's classification [16]. Stem subsidence >3 mm was defined as positive subsidence in comparison with

radiographs taken after surgery [17]. Radiographs were reviewed by two independent authors (BL, SK) who were not involved in the operation.

Statistical Analysis

A paired t-test was used to compare preoperative and postoperative HHS at the final follow-up. Cohen's kappa was used to measure the agreement between the two raters in the radiographic reviews. The inter-observer agreement ranged from 87.5% to 100%. The intra-observer agreement ranged from 81.25% to 100% for observers 1 and 2. Survivorship analysis was performed using the Kaplan-Meier estimator with endpoints of stem revision for any reason and stem revision for aseptic loosening. Ninety-five percent confidence intervals (CIs) were calculated. Statistical significance was set at *p-value* of < 0.05.

RESULTS

The mean HHS significantly improved from 43.2 (25.2-66, SD 8.4) points preoperatively to 97.4 (76-100, SD 5.2) points at the final follow-up (*p<0.0001*). The mean FJS was 93.4 (75-100, SD 8.3) points at the final follow-up. The patient satisfaction was "very satisfied" in 43 patients (95.6%), "satisfied" in two patients (4.4%), and "unsatisfied" in no patients (Table 2).

Table 2 Postoperative clinical outcomes.

Parameters	Preoperative	Final follow-up	*P*-value
Mean HHS (points) (range, SD)	43.2 (25.2-66, 8.4)	97.4 (76-100, 5.2)	*p<0.0001*
Mean FJS (points) (range, SD)	N/A	93.4 (75-100, 8.3)	N/A
Satisfaction (hips) (%)			
Very satisfied	N/A	43 (95.6%)	N/A
Satisfied	N/A	2 (4.4%)	N/A
Unsatisfied	N/A	0 (0%)	
Very unsatisfied	N/A	0 (0%)	

HHS, Harris Hip Score; FJS, Forgotten Joint Score; N/A, not applicable.

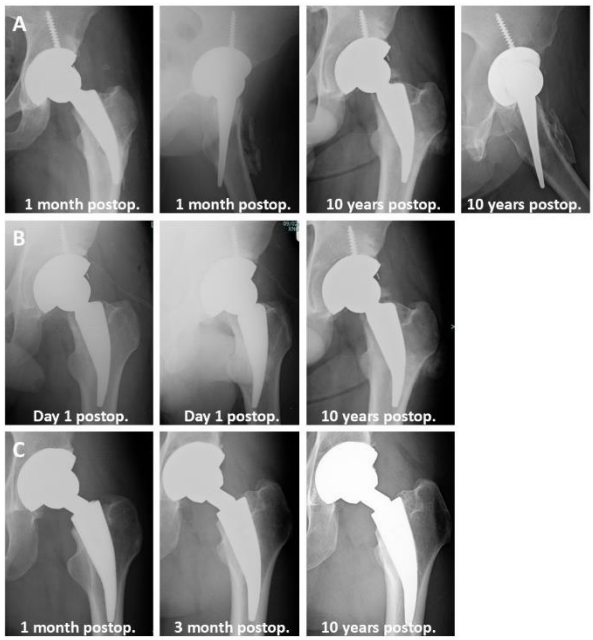

Fig. 2 Radiographs of complication cases.
(A) Distal stem perforation at 1 month and 10 years postoperatively, demonstrating stable bone ingrowth without need for revision.
(B) Distal stem perforation on postoperative day 1 and at 10 years, with maintained stability and no revision.
(C) Stem subsidence of 5 mm observed at 3 months; radiographs at 1 month, 3 months, and 10 years show subsequent stable fixation.

There were two hips (4.4%) with distal stem perforations, which had stable bone ingrowth and required no revision. There was one hip (2.2%) with a 5 mm subsidence, which was stable three months postoperatively (Figure 2).

The radiographic changes around the femoral stem, based on Gruen's classification,

revealed osteointegration in zone 1 (43 cases, 95.6%), zone 2 (40 cases, 88.9%), zone 3 (12 cases, 26.7%), zone 4 (3 cases, 6.7%), zone 5 (9 cases, 20%), zone 6 (45 cases, 100%), and zone 7 (41 cases, 91.1%) (Figure 3). No radiolucent lines were observed in any of these zones. Radiographic stress shielding around the femoral stem, based on Engh's classification, was observed as grade 1 in 38 cases (84.4%) and grade 2 in 5 cases (11.1%) (Table 3).

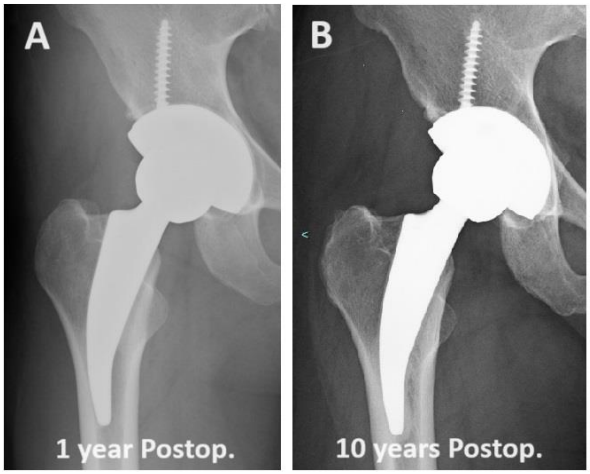

Fig. 3 Anteroposterior radiograph of Metha® short stem showed osteointegration at Gruen's zone 2, 3, 5, 6 and 7 at ten years (B) compared to one year (A) postoperatively.

Table 3 Radiographic change around stem.

Parameters	Values
Development of bone trabeculae (hips) (%)	
Zone 1	43 (95.6%)
Zone 2	40 (88.9%)
Zone 3	12 (26.7%)
Zone 4	3 (6.7%)
Zone 5	9 (20%)
Zone 6	45 (100%)
Zone 7	41 (91.1%)
Stress shielding of femur (hips) (%)	
Grade 1 (calcar round-off)	38 (84.4%)
Grade 2	5 (11.1%)

There were three cases of revision: one case of periprosthetic acetabular fracture with a loosening acetabular component at 126 months postoperatively, which was addressed by revising the acetabular component with a Burch-Schneider cage; one case of periprosthetic joint infection with acetabular component loosening at 117 months postoperatively, for which the patient underwent a two-stage revision with a Bursch-Schneider cage; and one case of polyethylene wear at 130 months postoperatively, which was managed by exchanging polyethylene. All three cases of short-stem revision remained stable, and no stem revision was performed in this study. The Kaplan-Meier survivorship for the overall implant system was 93.3% at 10 years, with revisions required in three cases (acetabular component or liner only) (Figure 4). At 10 years, stem survivorship was 100% for any reason and 100% for aseptic loosening.

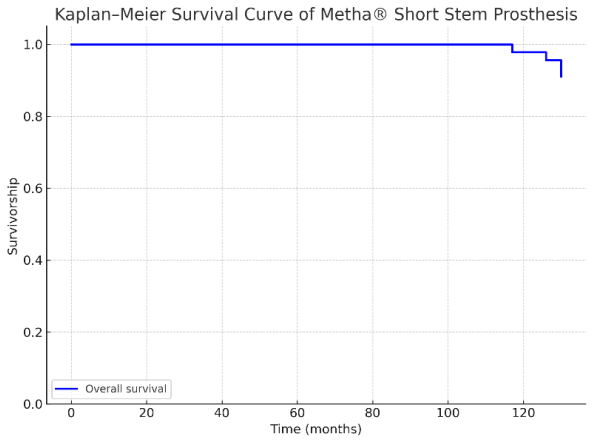

Fig. 4 The Kaplan-Meier survivorship for the overall implant system was 93.3% at 10 years, with revisions required in 3 cases (acetabular component or liner only).

DISCUSSION

Some studies reported poor bone quality and persistent defects in bone metabolism in patients with ONFH. This may lead to poor osteointegration, potentially resulting in stem loosening. Calder et al. [18] demonstrated that extensive osteonecrosis occurs in the proximal femur, extending up to four cm below the lesser trochanter. Additionally, there was a significant difference in the extent of osteocyte death distal to the femoral head.

Despite these concerns, many previous studies have reported that conventional cementless-stem THA yields good results in young patients with ONFH. Kim et al. [19] reported the outcomes of 93 hips in patients aged < 45 years with ONFH who underwent cementless THA with ceramic-on-ceramic (CoC) implants. At a follow-up of 11.1 years, these young patients demonstrated favorable clinical and radiographic performance. At 11.1 years, the survival rates were 99% (95% CI, 96–100) for the acetabular component and 100% (95% CI, 96–100) for the femoral component. Byun et al. [20] evaluated the functional and radiographic outcomes of cementless third-generation CoC-bearing THA in 56 hips of patients aged < 30 years with ONFH. Satisfactory clinical and radiological results were reported. Thirty-nine patients (95%) returned to their normal occupations, all patients (100%) could walk without support, and most were engaged in some form of sports activity. Johannson et al. [21] analyzed 67 studies encompassing 3,277 hips (2,593 patients) that underwent THA for ONFH. They found that patients with ONFH who underwent THA after the 1990s experienced clinical outcomes and implant longevity comparable to those reported in the national Joint Registries for all hip replacements. This systematic review provided evidence that ONFH is not associated with poor THA outcomes.

Few studies have examined the mid-to long-term outcomes of short-stem THA in young patients with ONFH. Capone et al. [22] focused on the NANOS® stem's performance in 37 hips of patients under 60 years with ONFH, with a follow-up period averaging 5.6 (3-10) years. They reported significant improvements in both clinical and functional outcomes. Additionally, all hips demonstrated successful bone ingrowth fixation in both the acetabular and femoral components, with no instances of osteolysis or need for surgical revision. Kim et al. [23] reported on the long-term outcomes of Proxima® ultra-short-stem THA in 335 hips of young patients with idiopathic or ethanol-induced ONFH. They observed excellent survivorship, no aseptic loosening, and good clinical outcomes at 14.7 (13–16) years. Computed tomography (CT) scan at the final follow-up revealed no signs of acetabular or femoral osteolysis in any hip. All acetabular components (100%) and 333 femoral stems (99.4%) exhibited solid fixation via osseointegration.

For the results of Metha® short-stem in patients with ONFH, Floerkemeier et al. [24] assessed the short to mid-term clinical and radiological outcomes of the Metha® short-stem THA in 73 hips (64 patients) with progressive ONFH. They observed a significant improvement in the pain scale, decreasing from 7.8 preoperatively to 1.7 postoperatively, and the HHS increased from 41.4 to 90.6 points at 34 months postoperatively. Radiological evaluation confirmed excellent bone ingrowth in all patients. These results demonstrate the Metha® short-stem's efficacy and its potential for good bone integration in patients with ONFH. Suksathien et al. [8] showed the mid-term results of Metha® short-stem THA in 83 hips of patients with ONFH at seven years. The HHS significantly improved from 44.7 preoperatively to 99.4 at 60 months and to 99.6 at 72 months postoperatively. Radiographic analysis revealed trabecular bone development primarily on the medial side of the stem, with 81 cases (97.6%) in zone 6 and 68 cases (81.9%) in zone 7. These findings suggest a concentrated load distribution in the calcar area, which is a crucial region for ensuring the long-term survival of the implant.

In this study, we also showed an excellent long-term outcome of the Metha® short-stem THA in patient aged 40 years or younger with ONFH. The mean HHS significantly improved from 43.2 (25.2-66, SD 8.4) points preoperatively to 97.4 (76-100, SD 5.2) points at the final follow-up ($p<0.0001$). The mean FJS was 93.4 (75-100, SD 8.3) points at the latest follow-up and all patients stated, “very satisfied” and “satisfied.” Consistent with our previous study, Tippimanchai et al. [25] evaluated the quality of life, patient satisfaction, patient expectations, and fulfillment of these expectations following Metha® short-stem THA at one year. The study found that 98% of the patients were satisfied and 96.4% felt that their expectations were met. There was a significant correlation among patient satisfaction, quality of life, and the extent to which expectations were fulfilled. We observed bone

trabecular development primarily on the medial side of the stem, with 45 cases (100%) in zone 6 and 41 cases (91.1%) in zone 7. This indicates concentrated load distribution in the calcar area, which is crucial for ensuring long-term implant survival.

In our study, there were two cases (4.4%) of distal stem perforations. We attributed this to technical errors during the initial learning period. Additionally, one of these patients underwent core decompression with a multiple drilling technique eight months prior to surgery, which may have compromised the integrity of the lateral femoral cortex. However, stable bone ingrowth and good clinical outcomes were observed, and revision surgery was not required. There was one case (2.2%) of 5 mm subsidence due to an undersized stem, which stabilized three months postoperatively.

In this study, we found stress shielding grade 1 (calcar round-off) in 38 hips (84.4%) and grade 2 in five hips (11.1%). Consistent with previous studies using short stems, Kim et al [26] studied in Proxima® stem and found only grade 1 stress shielding (100% in their long-term studies). Schader et al. [27] also demonstrated 86.2% of grade 1 and 3.8% of grade 2 stress shielding in their ten-year follow-up using Fitmore® stem. Similarly, Kim et al. [28] compared the Metha® short-stem with a conventional Excia® stem and found that all Metha® cases showed only grade 1 stress shielding, whereas the conventional group had significantly higher grades, supporting the bone-preserving nature of short stems. Kato et al. [29] conducted a five-year comparative study of standard and short fit-and-fill stems in Japanese patients. Although they found no statistically significant differences in the severity of stress shielding between the groups, the short-stem group demonstrated fewer contributing risk factors and more consistent remodeling, particularly in narrow femoral canals, suggesting clinical advantages in select anatomies. Additionally, finite element analysis by Batailler et al. [30] demonstrated that a shortened uncemented collared femoral stem exhibited a stress distribution pattern similar to that of a standard-length stem with the same design without increasing proximal stress shielding. This biomechanical evidence reinforces the concept that reduced stem length, when appropriately designed, does not compromise the physiological load transfer. These findings support that the use of metaphyseal-anchored short stems, such as the Metha® design, results in favorable stress shielding profiles and may reduce the long-term risk of proximal bone loss in young, active patients undergoing THA.

We revised only the acetabular cup and polyethylene liner with retained short stems in three hips, including one with acetabular fracture, one with periprosthetic joint infection, and one with polyethylene wear. These three hips exhibited polyethylene wear because only conventional ultra-high molecular weight polyethylene liners were available during the study period. Interestingly, the three short stems were stable. We believe that this was due to the preservation of the femoral bone stock, and that the proximal metaphyseal bone was not exposed due to the solid fixation of the proximal stem by osteointegration within the closed ring of the femoral neck. Thus, the diffusion of the intraosseous wear debris is extremely limited.

The long-term implant stability observed in this study suggests that short-stem THA may be a suitable option for selected young patients with ONFH, especially when preservation of the bone stock is a priority. This may also offer potential benefits in the event of future revision surgeries as the metaphyseal bone is preserved and the proximal fixation remains intact.

Our study has some limitations. First, this was a retrospective study with no randomization or control group, which may have introduced inherent biases in the outcome interpretation. Second, we did not use dual-energy X-ray absorptiometry (DEXA) prevent an objective evaluation of periprosthetic bone density changes over time. Additionally, all procedures were performed by a single experienced surgeon, which may limit the generalizability of the results to other settings, particularly those involving surgeons with less experience in short-stem THA. Furthermore, there is a possibility of selection bias. Although strict eligibility criteria were applied, the choice of short-stem prostheses was based on the preoperative

bone quality and intraoperative judgment. Patients with Dorr type C morphology or insufficient metaphyseal support may have been excluded in favor of conventional stems, potentially limiting the applicability of our findings to a broader ONFH population. Finally, 10 of the 55 eligible patients (18%) were lost to follow-up before reaching the 10-year minimum, which may have introduced attrition bias and affected the representativeness of the final cohort.

CONCLUSIONS

In conclusion, the Metha® short-stem THA provides promising long-term clinical outcomes in patients aged 40 years or younger with ONFH. The radiographic results demonstrated physiological proximal load transfer with minimal stress shielding, indicating successful integration of the implant and preservation of the bone stock, which are crucial for young and more active patients.

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Hip Fracture Surgery Between 24–48 Hours Is a Risk Factor for One-Year Mortality in Elderly Patients

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Purpose: This study compared one-year survival rates between elderly patients who underwent hip fracture surgery within 24 hours versus those between 24–48 hours, and assessed factors influencing survival.

Methods: This retrospective cohort study included elderly patients who underwent hip fracture surgery at Yasothon Hospital between June 1, 2019, and January 31, 2023. Patients were followed up until their final life status, as determined on January 31, 2024. In total, 212 patients were included, with 106 each undergoing surgery within 24 hours and between 24–48 hours. Statistical analyses were performed using the log-rank test and Cox regression.

Results: A total of 36 patients (16.98%) died during the one-year follow-up period, with most deaths occurring in the 24–48-hour surgery group (27 patients, 25.47%). The mortality rates at 3 months, 6 months, and 1 year were 5.19%, 3.30%, and 8.49%, respectively. Significant mortality predictors included: age (adjusted HR = 1.06, 95% CI = 1.01–1.12); ASA class 3 (adjusted HR = 8.17, 95% CI = 1.03–64.79); general anesthesia (adjusted HR = 3.10, 95% CI = 1.46–6.57); complications (adjusted HR = 2.16, 95% CI = 1.02–4.56); and surgery performed after 24 hours (adjusted HR = 3.88, 95% CI = 1.67–9.02).

Conclusions: Hip fracture surgery performed after 24 hours significantly increases the mortality risk in elderly patients. General anesthesia and postoperative complications are the key factors affecting survival. These findings emphasize the importance of surgery within 24 hours to reduce both mortality and complications in elderly patients.

Keywords: Hip fractures, Mortality, time to treatment

The hip bone is a vital component of the skeletal system; it supports body weight and enables movement. It also acts as a reservoir for essential minerals such as calcium [1]. Hip fractures are among the most common causes of emergency orthopedic surgery in the elderly and often require long-term care [2]. Despite advancements in medical treatment, mortality rates following hip fracture surgery remain high. Research shows that 10% of patients die within 30 days post-surgery, whereas 8–36% die within one year [3]. The global incidence of hip fractures is increasing, particularly among individuals aged ≥65 years. Many countries report 10–15 cases per 1,000 people annually, with women experiencing a 2–3 times higher prevalence because of their increased risk of osteoporosis [4].

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In the United States, approximately 280,000 hip fractures occur per year, with projections suggesting an increase to 500,000 cases annually by 2040 [5]. In Thailand, the number of hip fractures is expected to reach 34,246 cases by 2025 and 56,443 cases by 2050 [6]. Falls are the primary cause of hip fractures in the elderly; they are often associated with osteoporosis, sarcopenia, and impaired balance [7,8]. Patients with hip fractures typically experience intense pain and cannot bear weight, resulting in a loss of independence and an increased risk of complications such as pneumonia, pressure ulcers, and sepsis [9]. These increasing numbers underscore the urgent need for improved treatment and management strategies to reduce the burden of hip fractures and their associated complications in the elderly.

Surgical intervention is the gold standard treatment for hip fractures. For medically stable patients, surgery within 48 hours is recommended to reduce complications such as infections, venous thromboembolism, and prolonged immobility [10,11]. Postoperative rehabilitation, including physical therapy and structured exercise programs, is essential to restore muscle strength, flexibility, and overall quality of life [12,13]. Several studies state that early surgical intervention (within 24–48 hours) significantly improves survival rates. The National Institute for Health and Care Excellence (NICE) in the United Kingdom recommends surgery within 48 hours [14,15], although other studies state that surgery within 24 hours yields even better outcomes [16]. Earlier studies have demonstrated that surgery delayed beyond 48 hours increases the risk of mortality [10,11].

Although numerous international studies have demonstrated improved outcomes with early surgery, the applicability of these findings to the Thai population remains uncertain. Differences in healthcare systems, hospital resources, surgical access, and patient characteristics may influence the treatment outcomes. Therefore, local evidence is essential to validating international recommendations within the Thai context. Generating Thai-specific data will support evidence-based national clinical guidelines and help optimize the care of elderly patients with hip fractures.

In the context of clinical practice in Thailand, limited data exist regarding survival rates among elderly patients with hip fractures, highlighting the need for further research. This study aimed to compare one-year survival rates in elderly patients who underwent hip fracture surgery within 24 hours and those who underwent surgery between 24–48 hours at Yasothon hospital. Additionally, this study aimed to analyze the factors influencing survival, providing essential data for improving clinical guidelines and enhancing the standard of care for elderly patients with hip fractures in Thailand.

METHODS

Study Design

A retrospective cohort study was conducted using medical records at Yasothon Hospital.

Study Population

This study included elderly patients who underwent hip fracture surgery at Yasothon Hospital between June 1, 2019, and January 31, 2023. All patients were followed up until January 31, 2024, to assess their one-year survival status, and no data beyond one year were collected. Hip fractures were defined as low-energy fractures involving the proximal femur, specifically femoral neck, intertrochanteric, and subtrochanteric fractures, confirmed through radiography: x-rays or computed tomography (CT).

At Yasothon Hospital, Thailand, surgical techniques were selected based on fracture type. Non-displaced femoral neck fractures were primarily treated with multiple screws fixation. Displaced femoral neck fractures were typically managed using cementless bipolar hemiarthroplasty, Austin Moore hemiarthroplasty for limited activity levels, and total hip replacement for preexisting hip pathologies, such as osteonecrosis or severe osteoarthritis of the hip. Intertrochanteric fractures were typically managed using proximal femoral nailing (PFN) for unstable fractures or dynamic hip screw fixation for stable fractures. Subtrochanteric fractures were treated using long PFN. The attending orthopedic surgeon chose the

technique according to standard orthopedic management.

The timing of surgery (within 24 hours vs. 24–48 hours) was determined using a combination of clinical and logistical factors. Patients with stable vital signs who completed the preoperative assessments typically underwent surgery within 24 hours. Delays beyond 24 hours were usually due to comorbidities requiring further medical clearance, limited availability of operating rooms, or scheduling conflicts.

Sample Size Calculation

The sample size was calculated based on a previous study by Suttaphakti et al. [17], which reported a one-year survival rate of 95.5% for patients operated on within 72 hours and 83.8% for those operated on after 72 hours. The proportions in group 1 (p_1) and group 2 (p_2) were 0.950 and 0.830, respectively, with a ratio (r) of 1.00. The significance level (α) was set at 0.05, with Z (0.975) = 1.96, and the power (1-β) was 80%, corresponding to Z (0.800) = 0.84. The following equation was used to determine an approximate the sample size:

$$n_1 = \left[\frac{z_{1-\frac{\alpha}{2}} \sqrt{\bar{p}\bar{q}\left(1+\frac{1}{r}\right)} + z_{1-\beta}\sqrt{p_1 q_1 + \frac{p_2 q_2}{r}}}{\Delta} \right]^2$$

$$\Delta = p_1 - p_2, \quad \bar{p} = \frac{p_1 + p_2 r}{1+r}, \quad r = \frac{n_2}{n_1}$$

$$q_1 = 1 - p_1, \quad q_2 = 1 - p_2, \quad \bar{q} = 1 - \bar{p}$$

$$m_1 = \frac{n_1}{4}\left(1 + \sqrt{1 + \frac{2(r+1)}{n_1 r |p_2 - p_1|}}\right)^2$$

The estimated sample size was 212 patients, with 106 patients who underwent surgery within 24 hours and 106 patients who underwent surgery between 24–48 hours. At a total sample size of 212 patients (106 patients per group), the calculated power was 81.6% at a significance level of α = 0.05. This confirmed that the study had adequate power to detect a statistically significant intergroup differences. During the study period, more patients than the estimated sample size met the eligibility criteria. Therefore, we used simple random sampling based on medical records to select 212 patients, aligning with the calculated sample size for statistical power.

Inclusion and Exclusion Criteria

The inclusion criteria for the study were: patients aged ≥60 years, with radiographically confirmed hip fractures (via x-rays or CT scan), who underwent surgical treatment. The exclusion criteria were: a history of hip surgery (periprosthetic fracture), multiple fractures, head trauma, high-energy trauma, pathologic fractures, and surgery performed >48 hours after hospital admission. Pathologic fractures were defined as fractures caused by malignancy (primary or metastatic bone tumors) or metabolic bone diseases. Osteoporotic fragility fractures resulting from low-energy trauma (e.g., falls from standing height) were not considered pathological and were included in this study. Patients with high-energy trauma such as traffic accidents or falls from heights were excluded.

Definitions

Low-energy trauma refers to injuries resulting from minimal force, and is typically observed in elderly patients with osteoporosis. In this study, low-energy trauma was defined as a fall from standing height or less, such as tripping or slipping while walking.

High-energy trauma involves substantial external forces and is typically associated with traffic accidents, falls from significant heights, or direct impact injuries. These mechanisms often result in complex fractures and were therefore excluded from this study.

Pathological bone refers to bone that is structurally weakened due to underlying diseases, such as primary bone tumors, metastatic bone disease, or metabolic bone disorders. Fractures in these bones are considered pathological fractures. However, osteoporotic fractures from low-energy trauma were not considered pathological for exclusion purposes in this study.

Multiple fractures were defined as more than one fracture site occurring simultaneously during the same traumatic event (e.g., hip fracture

plus wrist fracture from the same fall). Patients with a history of fractures at different times were not excluded unless the prior fracture involved the hip and had undergone surgery.

Death from causes unrelated to hip fracture was defined as death clearly attributable to non-fracture-related causes such as advanced malignancy, cerebrovascular accident, myocardial infarction, or end-stage organ failure, based on medical records or the national death registry. These patients were censored for the survival analyses.

Patient Follow-up

The study subjects were followed up from the time of the hip fracture surgery until 365 days postoperatively. Patients who were lost to follow-up or died from causes unrelated to hip fractures were considered censored cases. Mortality status and the cause of death were verified using data obtained from the National Civil Registry database.

Material

Data were retrospectively collected from electronic medical records and inpatient department (IPD) charts at Yasothon Hospital from June 1, 2019, to January 31, 2023. The parameters collected included demographic data (age, sex, body mass index), fracture type, ASA classification, type of anesthesia, surgical technique, operative time, estimated blood loss, postoperative opioid use (oral morphine equivalents [OME]), complication types, and mortality status at 3, 6, and 12 months. Mortality data were cross-referenced and verified using the National Civil Registry Database as of January 31, 2024.

Research Ethics

This study was approved by the Human Research Ethics Committee of Yasothon Hospital under the approval document number YST-2024-20, issued on June 4, 2024.

Statistical Analysis

Descriptive statistics were used to present normally distributed data as mean ± standard deviation (SD), whereas non-normally distributed data were reported as median and interquartile range (IQR). For inferential statistics, the chi-square test or Fisher's exact test was used to compare categorical variables. The Kaplan-Meier method was used to analyze overall survival and disease-free survival, and the results are presented as a Kaplan-Meier survival curve. The log-rank test was used to compare survival distributions between groups. Cox regression analysis was performed to estimate both crude and adjusted hazard ratios (HR), along with 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$.

RESULTS

Of the 212 patients included in the study, 36 (16.98%) died by the one-year follow-up. Among the 36 patients who died during the one-year follow-up period, 27 deaths (25.47% of all participants) occurred in the group that underwent surgery between 24–48 hours, while 9 deaths (8.49%) occurred in the group that underwent surgery within 24 hours. In comparison, the group that underwent surgery within 24 hours had a significantly lower mortality rate (2.81%). Mortality rates were evaluated at three postoperative time points: 3 months (11 patients, 5.19%), 6 months (7 patients, 3.30%), and 1 year (18, 8.49%) (Table 1). The results of the log-rank test, which indicated a statistically significant difference in survival rates between the two groups ($p = 0.0011$), are shown in Figure 1.

Patients who underwent surgery within 24 hours were significantly older than those in the 24–48-hour group ($p = 0.011$) and had a higher proportion of intertrochanteric fractures ($p = 0.002$). The delayed surgery group had a significantly longer operation time and greater estimated blood loss ($p = 0.009$ and $p = 0.025$, respectively). Additionally, this group received higher opioid doses, as reflected by greater morphine consumption, cumulative postoperative OME, and average OME per hospital day (all $p < 0.05$). However, there were no statistically significant differences in postoperative complications, including anemia, urinary tract infection, pneumonia, or delirium, between the two groups (Table 2).

Table 1 Comparison of one-year survival rates following hip fracture surgery performed within 24 hours and between 24–48 hours (n = 212).

Mortality	Deaths (n, %)		p-value
	Surgery within 24 hours	Surgery between 24–48 hours	
3 months	3 (2.83)	8 (7.55)	0.122[a]
6 months	0 (0.97)	7 (6.60)	0.035[b]
1 year	6 (5.66)	12 (11.32)	0.139[a]

*p-values were calculated using the [a]chi-square test and [b]Fisher's exact test.

Table 2 General characteristics of the patients in the study, stratified according to time to surgery.

Variables	Surgery within 24 hours (n=106)	Surgery between 24–48 hours (n=106)	Total (n=212)	p-value
Sex (n, %)				1.000[a]
Male	33 (31.13)	33 (31.13)	66 (31.13)	
Female	73 (68.87)	73 (68.87)	146 (68.87)	
Age, years (Mean ± SD)	77.14 ± 7.72	74.44 ± 7.60	75.79 ± 7.76	0.011[b]
BMI, kg/m² (Mean ± SD)	22.45 ± 3.45	22.36 ± 3.48	22.41 ± 3.46	0.865[b]
Underweight (< 18.50) (n, %)	11 (10.38)	12 (11.32)	23 (10.85)	0.784[a]
Normal (18.50–22.99) (n, %)	49 (46.23)	53 (50.00)	102 (48.11)	
Overweight (≥ 23.00) (n, %)	46 (43.40)	41 (38.68)	87 (41.04)	
Fracture type (n, %)				0.002[a]
Neck of femur	26 (24.53)	47 (44.34)	73 (34.43)	
Intertrochanteric fracture	80 (75.47)	59 (55.66)	139 (65.57)	
ASA class (n, %)				0.563[c]
1	2 (1.89)	0 (0.00)	2 (0.94)	
2	24 (22.64)	26 (24.53)	50 (23.58)	
3	80 (75.47)	80 (75.47)	160 (75.47)	
Preoperative opioid use (n, %)				0.054[a]
No	57 (53.77)	43 (40.57)	100 (47.17)	
Yes	49 (46.23)	63 (59.43)	112 (52.83)	
Surgical fixation/treatment (n, %)				<0.001[c]
Multiple screws fixation	2 (1.89)	3 (2.83)	5 (2.36)	
Bipolar hemiarthroplasty	10 (9.43)	37 (34.91)	47 (22.17)	
Proximal femoral nailing	80 (75.47)	60 (56.60)	140 (66.04)	
Total hip replacement	0 (0.00)	1 (0.94)	1 (0.47)	
Austin Moore hemiarthroplasty	14 (13.21)	5 (4.72)	19 (8.96)	
Operative time, Min	48.76 ± 21.95	57.42 ± 26.39	53.09 ± 24.60	
(Mean ± SD) Median (Q1, Q3)	42.5	50.0	48.5	0.009[d]
	(32.0, 60.0)	(35.0, 70.0)	(35.0, 66.0)	
Estimate blood loss, ml	76.13 ± 44.56	103.21 ± 87.94	89.67 ± 70.86	
(Mean ± SD), Median (Q1, Q3)	50.0	100.0	100.0	0.025[d]
	(50.0, 100.0)	(50.0, 100.0)	(50.0, 100.0)	

Table 2 General characteristics of the patients in the study, stratified according to time to surgery. (Cont.)

Variables	Surgery within 24 hours (n=106)	Surgery between 24–48 hours (n=106)	Total (n=212)	p-value
Anesthesia type (n, %)				0.237[a]
Spinal Block	94 (88.68)	88 (83.02)	182 (85.85)	
General Anesthesia	12 (11.32)	18 (16.98)	30 (14.15)	
Morphine, mg (n=186)	15.84 ± 13.38	23.12 ± 17.65	19.36 ± 15.97	
(Mean ± SD) Median (Q1, Q3)	12.0 (8.0, 24.0)	18.0 (11.0, 30.0)	15.0 (8.0, 26.0)	0.001[d]
Tramadol, mg (n=28)	4.50 ± 1.41	6.33 ± 5.69	5.70 ± 4.69	
(Mean ± SD), Median (Q1, Q3)	5.0 (5.0, 5.0)	5.0 (1.0, 15.0)	5.0 (1.0, 5.0)	0.914[d]
Fentanyl, mcg (n=22)	11.82 ± 21.33	4.50 ± 3.24	8.33 ± 15.69	
(Mean ± SD), Median (Q1, Q3)	5.0 (3.0, 8.0)	5.0 (1.0, 8.0)	5.0 (1.0, 8.0)	0.495[d]
Total length of stay, hours	169.85 ± 86.39	194.51 ± 107.82	182.18 ± 98.24	
(Mean ± SD), Median (Q1, Q3)	146.5 (120.0, 190.0)	167.0 (142.0, 209.0)	163.0 (133.5, 197.0)	0.013[d]
Total oral morphine equivalents (n=194)	46.53 ± 39.99 36.0	72.66 ± 53.79 54.0	59.39 ± 48.95 45.0	<0.001[d]
(Mean ± SD), Median (Q1, Q3)	(18.0, 69.0)	(37.5, 94.5)	(27.0, 75.0)	
Cumulative post-operative OME (n=193)	40.61 ± 38.53 30.0	61.03 ± 47.51 45.0	50.60 ± 44.24 36.0	<0.001[d]
(Mean ± SD), Median (Q1, Q3)	(12.0, 48.0)	(30.0, 81.0)	(24.0, 69.0)	
Average OME per hospital day (n=194)	7.86 ± 5.49 6.63	10.08 ± 7.38 7.61	8.95 ± 6.57 7.29	0.049[d]
(Mean ± SD), Median (Q1, Q3)	(4.0, 11.25)	(4.8, 13.56)	(4.5, 12.0)	
Preoperative pain score	3.01 ± 1.01	2.91 ± 1.05	2.96 ± 1.03	
(Mean ± SD), Median (Q1, Q3)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.386[d]
Postoperative pain score	1.40 ± 0.95	1.34 ± 0.92	1.37 ± 0.94	
(Mean ± SD), Median (Q1, Q3)	2.0 (1.0, 2.0)	1.0 (1.0, 2.0)	2.0 (1.0, 2.0)	0.590[d]
Complication (n, %)				0.674[a]
No	65 (61.32)	62 (58.49)	127 (59.91)	
Yes	41 (38.68)	44 (41.51)	85 (40.09)	
Anemia	36 (33.96)	32 (30.19)	68 (32.08)	0.556[a]
Sepsis/Septic	1 (0.94)	2 (1.89)	3 (1.42)	0.561[c]
Pneumonia	4 (3.77)	2 (1.89)	6 (2.83)	0.407[c]
UTI	1 (0.94)	5 (4.72)	6 (2.83)	0.098[c]
Heart Failure	1 (0.94)	4 (3.77)	5 (2.36)	0.175[c]
Delirium	0 (0.00)	1 (0.94)	1 (0.47)	0.316[c]

*p-values were calculated using [a]chi-square test, [b]independent t-test, [c]Fisher's exact test, and [d]Mann–Whitney U test.
* OME= Oral Morphine Equivalent, ASA= American Society of Anesthesiologists

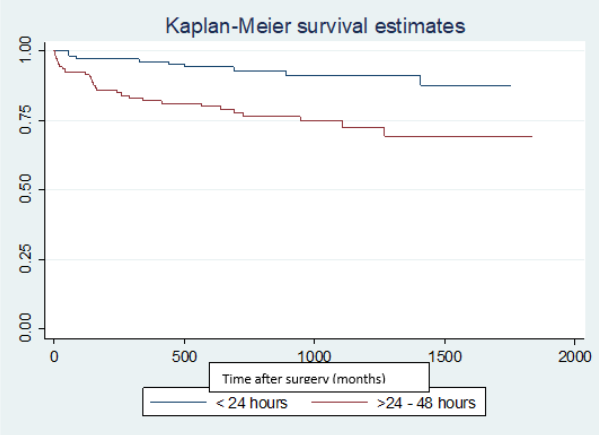

Fig. 1 Kaplan–Meier survival curves comparing cumulative survival between patients undergoing hip fracture surgery within 24 hours and those between 24–48 hours.

X-axis: Time after surgery (months); Y-axis: Cumulative survival probability.
Log-rank test: p = 0.0011

A total of 36 patients (16.98%) died within one year of surgery. The mean age of non-survivors was significantly higher than that of survivors (p = 0.004, and all non-survivors were classified as ASA Class 3 (p = 0.001). The non-survivor group also had a significantly higher proportion of patients receiving general anesthesia (p < 0.001), longer hospital stay (p = 0.001), and higher total oral morphine equivalent consumption (p = 0.047). Additionally, postoperative complications, particularly pneumonia (p = 0.013), heart failure (p = 0.003), and delirium (p < 0.001), were more frequent in this group. The results are summarized in Table 3.

Table 3 General characteristics of the patients in the study (n=212).

Variables	Survivors (n = 176)	Death (n=36)	Total (n=212)	p-value
Sex (n, %)				0.429[a]
Male	53 (30.11)	13 (36.11)	66 (31.13)	
Female	123 (69.89)	23 (63.89)	146 (68.87)	
Age, years (Mean ± SD)	75.11±7.75	79.14±6.99	75.79±7.76	0.004[b]
BMI, kg/m² (Mean ± SD)	22.40±3.30	22.45±4.19	22.41±3.46	0.903[b]
Underweight (< 18.50) (n, %)	19 (10.80)	4 (11.11)	23 (10.85)	0.955[a]
Normal (18.50–22.99) (n, %)	86 (48.86)	16 (44.44)	102 (48.11)	
Overweight (≥ 23.00) (n, %)	71 (40.34)	16 (44.44)	87 (41.04)	
Fracture type (n, %)				0.581[a]
Neck of femur	59 (33.52)	14 (38.89)	73 (34.43)	
Intertrochanteric fracture	117 (66.48)	22 (61.11)	139 (65.57)	
American Society of Anesthesiologists Physical Status Classification (ASA class) (n, %)				0.001[c]
1	2 (1.14)	0 (0.00)	2 (0.94)	
2	50 (28.41)	0 (0.00)	50 (23.58)	
3	124 (70.45)	36 (100.00)	160 (75.47)	
Preoperative opioid use (n, %)				0.922[a]
No	83 (47.16)	17 (47.22)	100 (47.17)	
Yes	93 (52.84)	19 (52.78)	112 (52.83)	
Surgical fixation/treatment (n, %)				0.586[c]
Multiple screws fixation	4 (2.27)	1 (2.78)	5 (2.36)	
Bipolar hemiarthroplasty	40 (22.73)	7 (19.44)	47 (22.17)	
Proximal femoral nailing	118 (67.05)	22 (61.11)	140 (66.04)	

Table 3 General characteristics of the patients in the study (n=212). (Cont.)

Variables	Survivors (n = 176)	Death (n=36)	Total (n=212)	p-value
Total hip replacement	1 (0.57)	0 (0.00)	1 (0.47)	
Austin Moore hemiarthroplasty	13 (7.39)	6 (16.67)	19 (8.96)	
Operative time, Min	53.47±24.33	51.22±26.14	53.09±24.60	0.474[d]
(Mean ± SD), Median (Q1, Q3)	50 (35, 65)	40 (33.5, 68.5)	48.5 (35, 66)	
Estimate blood loss, ml	87.24±70.58	101.53±72.00	89.67±70.86	0.200[d]
(Mean ± SD), Median (Q1, Q3)	90 (50, 100)	100 (50, 100)	100 (50, 100)	
Anesthesia type (n, %)				<0.001[a]
Spinal Block	157 (89.20)	25 (69.44)	182 (85.85)	
General Anesthesia	19 (10.80)	11 (30.56)	30 (14.15)	
Morphine, mg (n=186)	17.27±15.65	21.09±18.49	17.93±16.19	0.070[d]
(Mean ± SD) Median (Q1, Q3)	14 (8, 24)	20 (12, 33)	15 (8, 26)	
Tramadol, mg (n=28)	8.46±27.27	25.93±50.71	12.60±34.83	0.767[d]
(Mean ± SD) Median (Q1, Q3)	5 (5, 5)	1 (1, 15)	5 (1, 5)	
Fentanyl, mcg (n=22)	5.72±19.88	15.39±33.92	8.03±24.18	0.596[d]
(Mean ± SD), Median (Q1, Q3)	5 (3, 8)	4 (1, 8)	5 (1, 8)	
Total length of stay, hours	172.23±81.18	230.81±149.35	182.18±98.24	0.001[d]
(Mean ± SD), Median (Q1, Q3)	159.5 (133.5,191)	182 (134, 268)	163 (133.5, 197)	
Total oral morphine equivalents (n=194)	53.46±47.66	71.23±55.65	56.50±49.42	0.047[d]
(Mean ± SD), Median (Q1, Q3)	45 (24, 72)	60 (42, 87)	45 (27, 75)	
Cumulative post-operative OME (n=193)	43.86±41.97	59.23±54.28	46.55±44.60	0.057[d]
(Mean ± SD), Median (Q1, Q3)	36 (24, 63)	39 (30, 85.5)	36 (24, 69)	
Average Oral Morphine Equivalent (OME) per hospital day (n=194) (Mean ± SD), Median (Q1, Q3)	8.42±6.64 7.2 (4.5, 12.0)	8.97±7.01 8.0 (5.25, 10.8.0)	8.52±6.69 7.29 (4.5, 12.0)	0.613[d]
Preoperative pain score (Mean ± SD),	2.97±1.00	2.92±1.16	2.96±1.03	0.794[d]
Median (Q1, Q3)	3 (2, 3)	3 (2, 3)	3 (2, 3)	
Postoperative pain score (Mean ± SD)	1.38±0.91	1.31±1.06	1.37±0.94	0.662[d]
Median (Q1, Q3)	2 (1, 2)	1 (0, 2)	2 (1, 2)	
Complication (n, %)				0.025[a]
No	112 (63.64)	15 (41.67)	127 (59.91)	
Yes	64 (36.36)	21 (58.33)	85 (40.09)	
Anemia	54 (30.68)	14 (38.89)	68 (32.08)	0.467[a]
Sepsis/Septic	2 (1.14)	1 (2.78)	3 (1.42)	0.317[c]
Pneumonia	3 (1.70)	3 (8.33)	6 (2.83)	0.013[c]
Urinary Tract Infection (UTI)	6 (3.41)	0 (0.00)	6 (2.83)	0.297[c]
Heart Failure	2 (1.14)	3 (8.33)	5 (2.36)	0.003[c]
Delirium	0 (0.00)	1 (2.78)	1 (0.47)	<0.001[c]

*p-values were calculated using [a]chi-square test, [b]independent t-test, [c]Fisher's exact test, and [d]Mann–Whitney U test.

Multivariate Cox regression analysis was conducted to determine the risk factors of mortality in elderly patients undergoing hip fracture surgery with a one-year follow-up period. The analysis revealed that older age, ASA Class 3 classification, use of general anesthesia, postoperative complications, and surgery delayed beyond 24 hours were significantly associated with increased mortality risk (Table 4). The findings showed that for every one-year increase in age, the risk of mortality increased by 6% (adjusted HR = 1.06, 95% CI: 1.01–1.12, p = 0.027). Patients classified as ASA Class 3 had an 8.17 times higher risk of mortality (95% CI: 1.03–64.79, p = 0.047). The use of general anesthesia was associated with a 3.10-fold higher mortality risk (95% CI: 1.46–6.57, p = 0.003). Patients who developed postoperative complications had a 2.16-fold higher risk of mortality (95% CI: 1.02–4.56, p = 0.044). patients who underwent surgery after 24 hours had a 3.88-fold higher mortality risk (95% CI: 1.67–9.02, p = 0.002).

Table 4 Risk factors associated with mortality in the study.

Variables	Univariate Cox regression		Multivariate Cox regression	
	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age	1.07 (1.02–1.11)	0.004	1.06 (1.01–1.12)	0.027
ASA class (3)	13.59 (1.86–99.21)	0.010	8.17 (1.03–64.79)	0.047
General anesthesia	3.28 (1.61–6.67)	0.001	3.10 (1.46–6.57)	0.003
Total length of stay	1.00 (1.00–1.01)	0.001	1.00 (0.99–1.00)	0.347
Total oral morphine equivalents	1.01 (1.00–1.01)	0.047	1.01 (1.00–1.01)	0.092
Complication	2.11 (1.08–4.09)	0.028	2.16 (1.02–4.56)	0.044
Surgery after 24 hours	3.29 (1.55–6.99)	0.002	3.88 (1.67–9.02)	0.002

DISCUSSION

Hip fractures in the elderly significantly affect quality of life, functional independence, and survival [2]. Surgical intervention is essential, with early surgery (within 24 hours) linked to reduced mortality, faster mobilization, shorter hospital stays, and fewer complications [16, 18]. However, the survival outcomes between early and delayed surgeries are still debated. Our study shows that delayed surgery (24–48 hours) substantially increases mortality risk, with general anesthesia and postoperative complications as key factors.

The one-year mortality rate in our study was consistent with that of previous research: 16.6% and 19.9% [19, 20]. Klestil et al.'s meta-analysis of 46 studies also supports the benefit of early surgery, showing a significant reduction in 30-day (RR = 0.86, 95% CI: 0.82–0.91) and one-year mortality [16]. Seckel et al. demonstrated that surgery within 24 hours decreased mortality in patients older than 90 years from 15.2% to 4.2% [21], and Welford et al. found that it reduced 30-day mortality from 14% to 8.6% [22]. Our findings further confirm that timely surgical intervention enhances recovery and survival outcomes.

We found that delayed surgery increased mortality risk 3.88-fold (adjusted HR = 3.88; 95% CI: 1.67–9.02), consistent with Lieten et al.'s findings [23]. Delays also increased the risk of perioperative cardiac complications (p = 0.010), pneumonia (p < 0.001), and overall mortality (OR = 2.634, p < 0.001), highlighting the importance of early surgery. This supports the NICE and American Academy of Orthopaedic Surgeons guidelines advocating surgery within 24–48 hours [24]. Advanced age was an independent predictor of mortality, increasing death risk by 6% per year (adjusted HR = 1.06; 95% CI: 1.01–1.12), consistent with the outcomes reported by Morri et al. [19] and Luo et al. [25]. General anesthesia raised the mortality risk 3.10-fold (adjusted HR = 3.10; 95% CI: 1.46–6.57), similar to reports by Qiu et al. [26] and Desai et al. [27]. This is

likely due to hemodynamic instability, cognitive dysfunction, and other complications [28]. Although our findings showed a significantly increased mortality risk in patients who underwent surgery after 24 hours, this association should be interpreted with caution. In our study, the timing of surgery was influenced by both clinical and logistical factors. Patients who were medically stable typically underwent surgery within 24 hours, whereas delays beyond 24 hours were often due to comorbidities requiring further medical optimization or operating room constraints. These nonrandom factors could have introduced a selection bias. However, as shown in Table 4, we performed a multivariate Cox regression analysis after adjusting for key confounders, including age, ASA class, anesthesia type, length of stay, morphine use, complications, and surgical timing. This finding strengthens the validity of our conclusion that surgical delay beyond 24 hours is independently associated with increased mortality.

Patients classified as ASA Class 3 had an 8.17-fold increased mortality risk (adjusted HR = 8.17; 95% CI: 1.03–64.79), consistent with Luo et al. [25], reflecting the impact of severe comorbidities on perioperative stability and recovery. Our finding that postoperative complications doubled mortality risk (adjusted HR = 2.16; 95% CI: 1.02–4.56), is in line with the outcomes reported by Choi et al., who analyzed 1,363 hip fracture patients [29]. The most common complications contributing to increased mortality include hospital-acquired pneumonia, pulmonary embolism, deep vein thrombosis, and cardiovascular events [30]. These results underscore the critical role of careful perioperative management in mitigating the increased mortality risk associated with severe comorbidities and postoperative complications in elderly patients with hip fractures.

The findings of this study should be interpreted considering its retrospective design and reliance on electronic medical records from a single institution, which may limit the generalizability of the results to other settings with different treatment protocols, resources, and patient populations. Nevertheless, we recommend that future studies utilize a prospective cohort approach to improve data accuracy and explore long-term outcomes, such as mobility, pain, and quality of life post-surgery. Further research should investigate the role of nutritional status, frailty, and rehabilitation strategies in optimizing perioperative care and refining the guidelines for elderly patients with hip fractures.

CONCLUSIONS

In addition to its retrospective design and single-center setting, this study has several limitations. First, different fracture types were treated using different surgical techniques (e.g., multiple screws, hemiarthroplasty, and PFN), which may have introduced bias. We did not directly compare outcomes across fracture patterns or surgical methods. As a result, it is possible that differences in the surgical approach, rather than in surgical timing alone, contributed to the observed differences in mortality. Although we adjusted for several key confounders in the multivariate analysis, residual confounding factors related to fracture severity and surgical complexity may still exist.

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Metastatic Bone Disease: A Clinical Approach

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Background: Advances in oncological management have contributed to longer survival of patients, even in the presence of metastases. Consequently, more patients would be expected to present with symptomatic bony metastases. The major objectives of orthopaedic surgical interventions in bone metastases include stabilization of impending or actual pathological fractures, restoration of mobility and gait, with resultant reduction in the overall morbidity during the survival period of the cancer patient.
Purpose: This review was aimed at producing a synoptic material for ease of reference by students, trainees and young surgeons who come into contact with patients suffering from metastatic bone lesions.
Methods: A review of the literature on the subject of metastatic bone diseases was done. Information on epidemiology, pathophysiology and mechanisms of bone metastases, clinical problems and concept of skeletal related events (SREs), differential diagnoses, diagnostic approach, general principles and options of treatment, and prognosis was extracted and presented.
Conclusions: Metastatic lesions are the most common malignant tumours that affect the skeleton, and these malignant deposits in bones increase overall morbidity in cancer patients. Appendicular skeleton offers a large surface area for deposition of tumour cells from primary sites, including the breast, prostate, lung, kidney and thyroid, with the highest incidence coming from breast and prostate. The osseous lesions of primary malignant diseases predispose to pain, mechanical instability and fractures in the affected parts. These factors contribute to the overall morbidity and reduced survival in cancer patients.

Keywords: Clinical approach, metastases, bone, surgical guideline

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Metastatic lesions are the most common malignant tumours affecting the skeleton, but opinions are divided in literature as to whether or not the skeleton is the commonest site of metastatic disease, ahead of the lung and liver[1-4]. According to Utzschneider *et al.*,[2] and Coleman[1], the skeleton is the most common site of metastatic cancer. Teixeira *et al.*,[3] have documented that bone is the third most common site for metastatic disease, after the lung and the liver. Indeed, any malignancy can

metastasize to bone, but about 80% of these osseous metastases originate from primary diseases in the breast, prostate, lung, kidney and thyroid, with the highest incidence coming from breast and prostate according to a study by Riccio *et al*.,[5] in the United States. In Hong Kong, the lung was reported as the most common primary source for osseous metastasis[4].

Appendicular skeleton offers a large surface area for deposition of tumour cells from primary sites. These deposits, after establishing in the bones, predispose to pain, mechanical instability and fractures. These factors contribute to the overall morbidity and reduced survival in cancer patients. The risk of impending pathological fracture from lytic osseous metastases, especially in the extremity bones, is a concern to both the patient and the Surgeon and requires a decision for surgical intervention[4,5]. With recent advances in oncological management, patients are beginning to survive longer, even with metastases, and more patients would be expected to present with symptomatic bony metastases. The major objectives of orthopaedic surgical interventions in bone metastases include stabilization of impending or actual pathological fractures, restoration of mobility and gait, with resultant reduction in the overall morbidity during the survival period of the cancer patient[4,6,7].

Most metastatic bone lesions occur in adults older than 50 years. Metastatic lesions put significant economic burden on the healthcare systems of different nations. As at 2007, approximately 1.2 million new cancer cases were reportedly diagnosed each year in the United States, with the overall cancer prevalence estimated at over 4.5 million cases annually, and 5.3% of those patients had metastatic bone disease. The national cost burden for patients with metastatic bone disease in the United States at the time of that report was estimated at USD 12.6 billion, representing 17% of the USD 74 billion in total direct medical expenses allowed by the National Institutes of Health (NIH), thus leaving metastatic bone disease as a major influencer of overall oncology cost in the United States[7]. In 2007, the Hong Kong Cancer Registry showed that there were 24,000 new cases, out of which estimated 6,000 -12,000 developed metastases. In 2021, there were 38,462 new cases diagnosed with cancer in Hong Kong (https://www3.ha.org.hk/cancereg). As prolonged survival is recorded in more patients with primary malignancies following advances in oncological and surgical treatments, it is expected that the prevalence of metastatic bone diseases would also be on the increase[3,4,6]. This has been postulated to imply that the burden of the primary malignant diseases with the potentials of bone metastases would assume a chronic proportion[6].

Pathophysiology/Mechanisms of Bone Metastases

Bone metastases by a primary tumour greatly increases the morbidity and mortality of the primary disease, and the overall prognosis is considered as poor. Bone metastasis can be osteolytic or osteoblastic. The molecular mechanisms occurring between tumour cells and bone cells that promote tumour growth within the bone microenvironment, and leading to bone destruction or new bone matrix deposition have been studied by Yin *et al*.,[8] as depicted in Figure 1. The development of osteolytic and osteoblatic lesions depends on a functional interplay between tumour cells and osteoclasts or osteoblasts. Two modes of bone metastases have been suggested, namely, the Paget's fertile soil ('seed and soil') hypothesis and the Ewing circulation theory[8]. The fertile soil hypothesis conceptualizes the tumour cells as the 'seed' and the bone microenvironment as the 'soil', and tumour cells may reach the bone via the blood stream. Cellular motility is important for tumour cells to develop distant metastases, and is mediated by several factors such as growth factors, hyaluronians, matrix components, host factors, and tumour-secreted factors[9]. After tumour cells are deposited in the bone matrix, tumour-derived factors interact with the microenvironment of bone, causing either osteoclast or osteoblast stimulation. Therefore, bone metastasis can be osteoclastic, osteoblastic, or a mixture of both.

Osteolytic Bone Metastasis

This is caused by increased osteoclast stimulation, leading to increased osteoclast activity

and reduced osteoblast activity. Therefore, it is predominantly lytic and destructive, but occasional local bone formation response may be seen. It is not a result of direct effects of cancer cells on bone. Osteolytic metastasis is the most common form of bone metastasis in all cancer patients and occurs in such solid primary tumours as breast, thyroid, lung, renal and prostate cancers. The lung and renal cancers are reputed to produce a specific type of osteolytic metastasis known as cortical metastasis, in which the cortex of the bone is destroyed without any involvement of the medullary canal. The following molecular events are noted in osteolytic metastasis[8,10,11]:

a. Tumour cells produce chemokine receptors, cell adhesion molecules, and cell surface receptors that enable them to attach to the bone matrix and establish growth in the bone.
b. Tumour cells attach to the basement membrane of the vessel wall in distant sites using proteolytic enzymes such as integrins and cadherins. They disrupt the receptor site basement membrane, and then migrate into the substance of the distal host tissue. By means of chemotactic factors as well as receptor activator of nuclear factor kappa-B ligand (RANK ligand), the tumour cells stimulate osteoclast activity, causing bone resorption and leading to the formation of lytic areas in the bone in which the tumour cells grow. The RANK ligand is a soluble transmembrane protein required for the formation, function and survival of osteoclasts[4,8,10].
c. Tumour cells also produce factors that directly or indirectly stimulate osteolastic bone resorption. These include PTHrP, IL-1, IL-6, Prostaglandin E2, TNF, and CSF-1. PTHrP is particularly important in osteolytic bone metastasis of breast cancer and oat cell carcinoma[10,11]. IL-6 is important in the osteolytic bone metastasis of renal, bladder, prostate, cervical, breast and colon cancers. IL-6 stimulates osteoclast formation, and promotes the effects of PTHrP on osteoclasts.
d. The bone microenvironment is richly endowed with such growth factors as TGF-Beta, FGFs, IGFs and BMP-2. These factors are activated within the bone microenvironment by the process of bone resorption initiated by cancer cells, and they in turn promote the growth of metastatic cancer cells in the bone as well as the production and release of more bone resorbing factors (Cytokines) from tumour cells. This is a vicious cycle that promotes the process of bone metastasis[8,9].
e. Calcium is released from the bone matrix in the course of tumour induced osteoclastic bone resorption, leading to hypercalcaemia of malignancy[9].

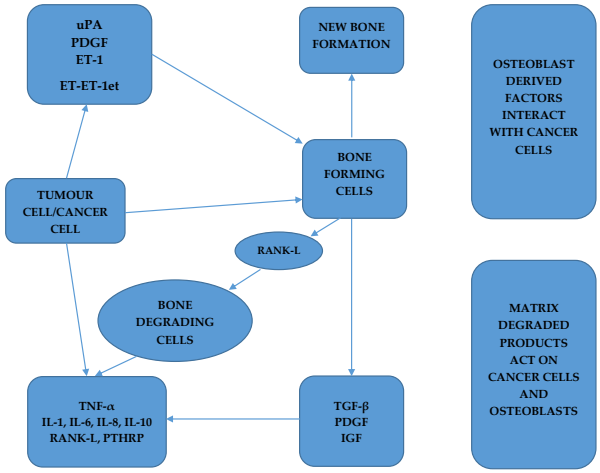

Fig. 1 Pathophysiology of Bone Metastases.

Osteoblastic Bone Metastasis

Unlike osteolytic metastasis, there is predominantly bone formation in osteoblastic metastasis. However, the quality of bone produced is poor and the patient is subject to bone pain and pathological fractures. Some mediators of osteoblastic metastasis have been identified to include Endothelin-1 (ET-1), which mediates bone formation through the Endothelin A (ET_A) receptor. ET-1 has been found to promote net bone formation by inhibiting osteoclast bone resorption and osteoclast motility. Other mediators of osteoblastic metastasis are BMP-4, 6 and 7, which have been proven to be elaborated by prostate cancer cells, and also exert paracrine effects on osteoblasts. Proteases such as urokinase-type plasminogen receptor (uPA) and Prostate Specific Antigen (PSA)

are known to activate TGF-Beta, which is also an osteoblast growth factor. PDGF is also involved in osteoblastic bone metastasis[8].

The pathophysiologic mechanisms described for metastatic dissemination of tumour cells have also been mentioned by other authors and summarized into key steps, namely, pre-metastatic niche formation by tumour cells; tumour cell dissemination through the circulation; chemotactic attraction and homing of tumour cells to the metastatic site of a target organ; and reciprocal interactions with local stromal cells and immune cells within the new microenvironment[12]. In line with this pathophysiologic pathway, researchers have documented the carcinoma of the prostate as an example of a solid tumour that follows this pathway. Prostate cancer metastasis to the bone follows at least four steps. The first step is colonization, in which circulating cancer cells enter the bone marrow niche. The next is the stage of metastatic dormancy, whereby cancer cells adapt to the bone microenvironment and remain dormant. This is followed by reactivation stage in which cancer cells switch from the dormant state to an actively proliferating state. The fourth step is reconstruction in which cancer cells disrupt the original bone structure and function[12-14].

Experimental studies show that up to 80% of tumour cells gain access into the circulation after release from the primary tumour. Out of this number, only about 2–4% initiate the growth of micro-metastases, and less than 0.01% survive in the new metastatic niche environment and give rise to macro-metastases[12,15,16]. Genetic studies of primary and metastatic tumours show that additional genetic events are required to enable metastases formation, and it has also been found that the time at which potentially metastatic cells are released from the primary tumour and arrive the secondary site may depend on the tumour type[12,17]. At the time of macro-metastases, the evolution of involved tumour cells ceases to be dependent on the primary tumour[12].

The unique vascular and cellular architecture of bone favour the entry of circulating tumour cells and eventual development of secondary deposits in the bone. The sinusoidshaped capillaries of bone, coupled with wide gaps between endothelial cells and a thin connective tissue envelope are easily permeable to tumour cells. The slow blood flow in the red bone marrow is believed to support the attachment of metastatic tumour cells to the endosteal bone surface[18]. The red bone marrow in the pelvis, sternum, cranium, ribs, vertebrae and scapulae, and to a variable extent, in the proximal ends of long bones such as the femur and humerus, constitute the major sites affected by bone metastases. Bone metastases, therefore, occur predominantly in the axial skeleton. Over 80% of patients with bone metastases show involvement of the axial skeleton, including the thoracic spine in 70%, the lumbosacral region in 20%, and the cervical vertebrae in 10%. Metastases to the pelvic bones, ribs and skull are found in 63%, 77% and 35% of cases, respectively. In the appendicular skeleton, the proximal humerus and femur are more frequently affected (53%) than the distal appendicular skeleton (1%)[12].

Common Patterns of Presentation of Metastatic Bone Disease

The common clinical presentations of bone metastasis include pain, pathological fracture, hypercalcaemia, and spinal instability with cord compression.

Pain

Bone metastases are the most common cause of cancer-related pain and the rate of pain from bone metastasis has been estimated at 35-45%. It is often insidious, poorly localised, becoming progressively more severe over a period of weeks or months. The character varies from deep, boring sensation, dull aching pain to occasional episodes of stabbing discomfort, often worse at night[9]. Pain may be spontaneous or related with activity such as weight bearing. The mechanisms of pain in patients with bone metastases are poorly understood, but a few explanations have been offered[1,9]. Pain from bone metastasis can be primary or secondary[9]. Primary bone pain is as a result of tumour-induced bone resorption, microfractures due to disruption of skeletal architecture, stretching of the periosteum by tumour expansion, nerve entrapment, and bone

collapse. Secondary bone pain occurs as a result of reactive muscle spasm, nerve root infiltration and compression by tumour, leading to neuropathic pain. There is also secondary pain from the release of chemical mediators. A variety of factors, such as bradykinin and substance P, that sensitize or directly excite primary afferent neurons to cause pain are elaborated by tumour cells[12]. The lower intracellular and extracellular pH of solid tumours is also known to activate sensory neurons, causing pain in cancer patients[9]. Tumour production of growth factors and cytokines, as well as local tissue production of endothelins, nerve growth factors and stimulation of ion channels have been documented[1,9].

Pathological Fracture

Sometimes, pathological fracture may be the first evidence of bone metastasis[19]. In a study[4], the rate of pathological fractures among Hong Kong Chinese with metastatic bone disease was found to be 34.3%. Pathological fracture occurs due to the destruction of cortical bone with attendant reduction in its load-bearing capabilities. Subsequently, there is trabecular disruption, microfractures, and complete loss of bone integrity. Pathologic fracture may occur spontaneously or following a trivial injury, especially in osteolytic metastasis. Frequent sites of election include the vertebral body, proximal ends of long bones, the pelvis, the ribs and skull. The occurrence of a fracture is a very serious event in the cancer patient. For this reason, increasing attention is advocated to predict these fractures, as well as to the use of prophylactic surgery, radiation and administration of Bisphosphonates in the management of the patients[9].

In practice, pathological fracture from tumour invasion of bone should be regarded as a spectrum, comprising actual pathological fracture on one extreme and mechanically weakened bone with impending pathological fracture on the other extreme. The radiologic criteria for predicting pathological fractures or diagnosing impending pathological fractures have been enumciated in the Mirels' scoring system.

Hypercalcaemia

Malignant hypercalcaemia occurs particularly in patients with metastasis from the lung, breast, kidney, thyroid, and haematologic malignancies such as multiple myeloma and lymphoma. It is a result of osteoclastic bone destruction from osteolytic metastasis. The pathophysiology is believed to be due to the activity of Parathyroid hormone related peptide (PTHrP) secreted by tumour cells, and to increased renal tubular reabsorption of calcium. The clinical features of hypercalcaemia such as pain, fatigue, anorexia, nausea, vomiting, dehydration, constipation, polyuria, mental disturbances and confusion are non-specific, and a high level of suspicion is needed to diagnose it. Death may occur through renal failure and cardiac arrhythmias[1,9]. The rate of hypercalcaemia has been quoted as 4.3% in a study of surgically-treated metastatic extremity bone tumours[4].

Spinal Instability with Cord Compression

Spine is the most common site of bone metastasis. Spine metastasis with spinal cord compression is the basis for the neurological compromise that may be observed in metastatic bone disease. Spinal cord compression is a medical emergency, and most patients will have weakness or paralysis. Back pain is due to spinal instability in about 10% of cases; often localised over the tumour; and is aggravated by such activities as coughing, sneezing or straining that increase intradural pressure. There may or may not be a radicular component. Pain may also be exacerbated by recumbency, straight leg raising and local pressure. Early recognition and appropriate adjunctive measures are important for a successful rehabilitation[1,9].

The Concept of Skeletal Related Events (SREs)

Skeletal related events describe the presence of pathologic fractures, spinal cord compression, hypercalcaemia, and requirement for surgery or radiotherapy to treat bone pain or impending fracture. Patients may have at least one SRE at presentation. They are difficult to treat and also diminish patients' quality of life[20]. There

seems to be a common finding among researchers indicating that mortality in metastatic bone disease may be directly proportional to the number of skeletal related events in the patients, but this relationship was not found statistically significant in a series among Hong Kong Chinese patient population, and also, the number of skeletal related events did not have any consistent effect on the mean survival duration before death in the same patient population[4].

Differential Diagnoses

Paget sarcoma, primary bone sarcoma such as malignant fibrous histiocytoma (MFH) and chondrosarcoma, benign radiolucent bone lesions such as bone cysts, malignant lymphoma, multiple myeloma, chronic osteomyelitis, osseous tuberculosis, post-radiation sarcoma, etc, are some of the clinical conditions that may very closely mimic metastatic bone lesions. Therefore, the need to consider these entities in the differential diagnosis of musculoskeletal metastasis cannot be overemphasized. Clinical diagnostic difficulty in differentiating osseous tuberculosis from metastatic bone tumours has been documented, and multifocal skeletal tuberculosis can closely mimic the distribution of multiple metastatic diseases to the central skeleton, ribs, vertebrae and pelvis[21-23]. It has also been documented that modern radiological investigations, including Flourodeoxyglucose Positron Emission Tomography/Computerized Tomography (FDG PET/CT), may also not be able to conclusively distinguish between tuberculosis and metastasis or primary malignancy, because these diseases, as well as other types of infections and inflammatory conditions, can produce areas of abnormally increased FDG activity on PET/CT. Therefore, high index of clinical suspicion as well as judicious biopsy procedures for both histopathological and microbiological examinations remains the gold standard in distinguishing these conditions[23-24].

Diagnostic Approach

In patients with known primary tumours, skeletal lesions are regarded as bone secondary until proven otherwise. In such patients, laboratory workup towards diagnosis of the bone lesion may not usually be indicated. However, when no known primary tumour exists in a patient with bone lesion mimicking metastasis, diagnostic workup is indicated for unravelling the primary tumour. Instances may exist when diagnostic search fails to suggest any primary focus. In such instances, the bone lesion may be described as metastasis of unknown primary (MUP). Generally speaking, the investigation protocol for bone lesions suspected to be metastases would include imaging techniques, laboratory tests and tissue biopsy.

Imaging Techniques

Plain radiographs (anteroposterior and lateral views) of the bone involved, and showing the joints above and below may be obtained in the first instance. It should be noted that metastatic lesion may not be obvious on plain radiograph, if significant bone destruction has not occurred. Technetium bone scan is a fairly sensitive technique for detecting bone metastases, and can detect these lesions earlier than plain radiographs. It is low in specificity because it cannot conclusively distinguish between bone metastases and other hot spots generated by such lesions as benign tumours or tumour-like conditions, infection, fracture or degenerative diseases. Computed Tomography (CT) shows bone details, including the extent of cortical destruction, but does not delineate the extent of surrounding soft tissue infiltration and medullary canal involvement. Magnetic resonance imaging (MRI) defines the extent of surrounding soft tissue infiltration and medullary canal involvement by the tumour, as well as locates metastases prior to their appearance on radiographs and CT. Positron emission computerised tomography (PET/CT scan) is a prototype of advances in imaging techniques, which now make possible the early detection of osseous involvements by primary tumours. The use of dual- tracer positron emission computerised tomography (PET/CT scan), can detect lesions anywhere between the base of the skull and the sole of the feet.

Laboratory Investigations

Routine blood tests, including complete

blood count (CBC), erythrocyte sedimentation rate (ESR), renal function tests (Electrolytes, Urea and Creatinine), C- reactive protein (CRP), liver function tests and clotting profile are some of the baseline blood workup required in the initial care of patients with metastatic bone tumours. Tumour markers such as prostate specific antigen (PSA), carcinoembroynic antigen (CEA), faecal occult blood test (FOBT), and alpha fetoprotein (AFP) may give a clue to the primary lesion. Metabolic panel needs to be explored, including serum calcium, serum phosphate and serum alkaline phosphatase levels. Higher calcium levels are an indicator of osteolysis.

Tissue Biopsy

The principles guiding tissue biopsy for musculoskeletal malignancies need to be observed. In the diagnosis of metastatic bone lesions, tissue samples may be obtained by fine needle aspiration (FNAC), Core needle biopsy (CNB), image-guided biopsy or by open biopsy.

Treatment Options and Principles in Metastatic Bone Disease

The treatment for bone metastases is primarily palliative, aimed at alleviating pain and improving quality of life. Treatment decisions for bone metastases depend on tumour location, the patient's general condition and previous treatment received by the patient, and it is usually a combination of local and systemic treatments. The systemic treatment options include chemotherapy, hormonal therapy, bisphosphonate, denosumab and target therapy. Local treatment includes radiotherapy, surgery, and radiology-guided interventions such as cement augmentation and radiofrequency ablation. Based on response to non-surgical treatment, patients are classified into good responders and poor responders. In good responders, such as in multiple myeloma, regression of lytic bone lesion may occur, and pathological fracture may unite. For this category of patients, the tendency is towards non-operative treatment or more conservative surgery. In poor responders, such as in renal cell carcinoma, lytic bone lesion may progress, and healing of pathological fracture is not guaranteed. For this category of patients, the tendency is towards more aggressive surgery.

Surgical Consideration, The Role of Surgery and Surgical Treatment Guideline in Metastatic Bone Disease

The optimum surgical management for metastatic bone disease considers such indices as the indication for surgery, estimated life expectancy of the patient, expected clinical response of non-surgical treatment, surgical treatment options and associated risks, the general health status of the patient, and the anaesthetic risk. The question of whether or not surgery is indicated and the expected benefit of surgical intervention should be carefully considered. For instance, in the presence of a systemic involvement by the primary disease, survival or cure rates following surgery depends on the response to adjunctive systemic treatment. Local treatment alone usually does not improve survival, and it is mainly for palliation or local disease control. However, a few exceptions exist, such as the isolated bone metastasis of renal cell carcinoma, in which adequate surgical excision is associated with improved survival[4]. Therefore, whenever applicable, systemic treatment should always be considered along with local tumour excision.

Surgical intervention in metastatic bone disease is indicated for the purpose of fixation of pathological fractures, stabilization of impending pathological fractures, and improving survival in selected cases. Fixation of pathological fracture stabilizes the bone, restores mobility of limbs, achieves pain relief and improves quality of life (QoL). Stabilization of impending fracture augments bone to prevent a pathological fracture, achieves pain relief and maintains mobility of limbs. Surgery improves survival in selected cases, such as solitary bone metastasis in renal cell carcinoma, after wide resection of metastatic lesions. Resection surgeries with curative intents are often indicated for solitary metastases. There is lower incidence of recurrence, and evidence shows that survival rates after resections are higher than after other standard treatments[4,6]. The indications

for amputation due to cancer metastases are extremely rare[4,6].

Approach to Impending Pathological Fractures (The Mirels' Scoring System)

There are no universally accepted criteria for operative intervention in impending pathological fractures following metastatic disease in long bones. However, the Mirels' scoring system is the most popular guideline for assessment, diagnosis and surgical decision making. The original work by Mirels[25] assessing the risk of pathological fracture in metastatic disease of the long bones was published in 1989. The Mirels' system of classification is considered reproducible, valid, and more sensitive than clinical judgment across all experience levels[26]. The Mirels' scoring system takes four (4) variables into consideration, namely, site of the lesion, nature of the lesion, size of the lesion in relation to bone cortical thickness, and nature of pain. These variables are awarded risk scores ranging from a minimum of one (1) to a maximum of three (3), depending on observation of set parameters as shown in Table 1[26,26].

Table 1a Mirels' Scoring System.

Score	Site of lesion	Size of lesion	Nature of lesion	Nature of pain
1	Upper limb	Less than 1/3 of cortex	Blastic	Mild
2	Lower limb	1/3 to 2/3 of cortex	Mixed	Moderate
3	Trochanteric region	> 2/3 of cortex	Lytic	Functional

Table 1b Clinical recommendation based on Mirels' score.

Mirels' score	Clinical recommendation
< 7	Radiotherapy and observation
8	Use clinical judgement
$\geq$ 9	Prophylactic fixation

It is commonly believed that lesions in the peritrochanteric area are associated with high risk for fracture. Furthermore, it is believed that chances of pathologic fractures are greater for weight-bearing bones than for non-weight-bearing bones. However, in Mirels' original investigation, these commonly held beliefs were not confirmed and site of lesion did not independently predict a fracture[25,26]. The nature of the lesion is either blastic, mixed or lytic. In the original investigation by Mirels, the rates of fracture in the three categories were 0%, 32%, and 48%, respectively. Size of lesion is expressed as a fraction of the cortical thickness. In the original evaluation, the rate of pathologic fracture was 0% for lesions less than 1/3 the size of the cortex, 5% for lesions between 1/3 to 2/3 the size of the cortex, and 81% for lesions occupying more than 2/3 of the cortex[25,26]. Pain is the only subjective variable in this classification system. The rate of fracture was 10% among patients with mild to moderate pain. However, all the patients with functional pain progressed to a fracture. Mirels also reported an association between pain and the size of the lesion[25,26].

Based on an overall Mirels' score, a recommendation for or against prophylactic fixation of a lesion is offered. Prophylactic fixation is strongly recommended for lesions with overall scores of nine or more. A lesion with an overall score of seven or less can be managed using radiotherapy and drugs. An overall score of eight is considered a clinical dilemma. The probability of fracture is 15%, and Mirels recommended that the attending physician use clinical judgment in such cases and consider prophylactic fixation[25,26]. Elsewhere in the literature, it is recommended that surgery be done in all cases where metastases posing risks of fractures are diagnosed, and this

applies to lesions with Mirels' scores of > 7. Such prophylactic surgeries for impending pathological fractures are believed to positively impact the QoL, and perhaps the survival profile of patients with extremity metastasis[1]. According to Guzik[6], the overall treatment results are better in cases where pathological fractures have not occurred. In another series[4], the patients that had prophylactic fixations had significantly higher postoperative duration of survival than the ones operated for actual pathological fractures. This finding was statistically significant at $p < 0.05$ (Chi-square test = 13.6267; $p = 0.001$). The researchers believed that it was difficult to measure the lag in time between metastasis and fracture occurrence, and that much less complication was associated with prophylactic fixation[4]. However, the authors adduced no immediate proof for this supposition, and believed that, in the absence of such proofs, it may be argued that the higher postoperative duration of survival in those with prophylactic fixations as against those with fixation for actual pathological fractures may only be a reflection of the natural history of the disease process, rather than the effect of surgery[4].

Another method of predicting an impending pathological fracture is according to Harrington classification, which predates the Mirels' classification[26]. According to Harrington, an impending pathologic fracture is defined as a lytic bony lesion involving more than half the diameter of the bone, greater than 2.5cm in its greatest diameter, or associated with persistent pain or radiographic progression[26].

Life Expectancy as a Surgical Consideration in Patients with Metastatic Bone Disease

After major surgical intervention, recovery and rehabilitation may take up to two months. Major surgical intervention is considered worthwhile if life expectancy of the patient is more than three months. The estimated life expectancy of the patient will dictate whether surgery is worthwhile as well as the aggressiveness of such surgical intervention. Sometimes, life expectancy may be difficult to predict as patients may suddenly deteriorate. From surgical point of view, life expectancy represents the estimated survival period of the patient after surgical intervention. Current guidelines suggest that surgical treatment for bone metastases be considered, when indicated, in patients with life expectancy of more than three months[4,27]. The estimation of life expectancy is within the domains of the Oncologists using the instrument of the Kaplan-Meier survival curve, but the essence of the surgical intervention is to maximise the quality of remaining life[6,27].

Surgical Treatment Options

The treatment of bone metastases is palliative, and surgery is probably one of the most important aspects of multimodal therapies available to these patients to improve prognosis[2]. The surgical considerations take into account the fact that fracture healing is unpredictable, that patients in general are weak physically, and that local tumour may progress. Stability after surgery relies mainly on surgical construct. Surgical construct is intended to bear the physiological stress, allow simple rehabilitation, and be stable at least for the survival period of the patient. A range of surgical treatment options with varying risk, durability and stability profile are available for consideration in patients with metastatic bone disease. These options include radiological intervention such as radiofrequency ablation (RFA), cement augmentation, osteosynthesis (internal fixation), prosthetic replacement, re-enforced prosthetic replacement, and resection with skeletal reconstruction. The internal fixation for bone metastases can either be a simple internal fixation, or internal fixation with cement re-enforcement. Prosthetic replacement can be accomplished with standard prosthesis, long stem prosthesis, megaprosthesis or intercalary spacer. Re-enforced prosthetic replacement may be accomplished with cementation or the use of allograft-prosthesis composite. Wide resection is not to be embarked on, if there are no plans for reconstruction. The simpler procedures such as cement augmentation and osteosynthesis are less risky, less durable and less stable, but the more complex procedures such as wide resection and reconstruction with megaprosthesis are more risky, more durable and more stable. Such reconstruction is often strong enough

to allow immediate mobilization and simple rehabilitation of the patient.

Avoiding postoperative complications in the circumstance of bone metastasis may depend on proper patients' selection, adequacy of operative techniques and planning, and strict adherence to the surgical principles of asepsis as well as avoidance of tumour contamination of surgical fields. These surgical due diligence help to pave the way for successful rehabilitation of patients to ambulatory status. It might well be argued that any failure in rehabilitation is an indication of failure of the surgical effort[4]. It is important that the patients are followed-up in the physiotherapy and oncology clinics. The rehabilitation potentials of patients require consideration as a guide to predicting the outcome of rehabilitation measures in individual patients. With advances in oncological services and surgical techniques, it is anticipated that the overall prognosis of metastatic bone diseases will continue to improve[4].

Prognostic Factors in Metastatic Bone Disease

Bone metastasis often suggests that the disease has reached a late stage, with a poor prognosis[28], and some of the patients may not be considered fit for bony operative procedures targeted at the bone metastases[19]. Factors acting singly or in combination with others to impact on prognosis include age, the primary tumour (lung cancer carries poor prognosis compared to other solid tumours), presence of other metastasis, pathological fracture, adjuvant therapy, other complications such as the SREs, albumin level and overall nutritional status. The duration of post-operative survival in metastatic bone disease depends on a number of factors, such as age of the patient, site of primary malignancy, indication for surgery, and the option of surgery[19,23]. Apart from predicting the risk of bone metastasis from colorectal carcinoma (CRC), the tumour markers alkaline phosphatase (ALP) and carcinoembryonic antigen (CEA) are also important in its prognosis. Evidence exists in literature to suggest that elevated levels of ALP and CEA in colorectal carcinoma patients with bone metastasis are associated with poor prognosis[28,29].

CONCLUSIONS

Metastatic lesions are the most common malignant tumours that affect the skeleton, and these malignant deposits in bones increase overall morbidity in cancer patients. Appendicular skeleton offers a large surface area for deposition of tumour cells from primary sites, including the breast, prostate, lung, kidney and thyroid, with the highest incidence coming from breast and prostate. The osseous lesions of primary malignant diseases predispose to pain, mechanical instability and fractures in the affected parts. These factors contribute to the overall morbidity and reduced survival in cancer patients. The care of the patients suffering metastatic bone tumours is generally palliative. Palliative surgical intervention, when indicated, reduces associated morbidity, but should be guided by the expected life expectancy of the patient and the overall rehabilitation potential of the patient. The surgical management of bone metastasis is a key consideration in averting potentially crippling morbidity occasioned by mechanical instability arising from the deposition of cancer cells on skeleton.

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Short Metaphyseal Femoral Stem Total Hip Arthroplasty in Poor Quality Bone Cortex Without Neck Length Sparing: A Case Report

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Purpose: The principle of short metaphyseal femoral stem total hip arthroplasty (short stem THA) required the cortical ring of the femoral neck and lateral touch of the distal stem at the proximal femur, but this case had an improper cortical ring of the femoral neck and lateral touch.
Methods: A case report of a 39-year-old male who underwent short stem THA surgery owing to a failure of the femoral neck fixation and delayed union of the femoral shaft fracture.
Results: The patient reported successful 5-year clinical and radiographic outcomes for a short stem THA.
Conclusions: Short stem THA could be an alternative implant option, compared with conventional cementless stem, for young patients with good bone quality, despite lacking femoral neck anchoring, with superiority in terms of bone stock preservation and more natural loading.

Keywords: Short stem total hip arthroplasty, fixation failure in femoral neck fracture, ipsilateral neck-shaft fractures of femur, cortical femoral neck ring

Total hip arthroplasty (THA) was proposed by Smith-Petersen[1] and has become a frequent surgical procedure, providing excellent results in younger, more active patients with hip joint pathologies or traumatic femoral neck fractures. In recent years, short metaphyseal femoral stem total hip arthroplasty (short stem THA) has been an increasingly popular implant choice, providing better stress distribution and greater bone stock for subsequent conventional THA[2]. However, short stem THA has some limitations that surgeons should avoid using such devices. Specifically, it should not be used in cases where there is a bone defect along with the length of the cortical ring femoral neck, both medial and lateral sides, with less than 5 mm of bone remaining or bone defect on the lateral side of the proximal femur. Due to the strength of the femoral stem, the 3-point fixation principle must be applied in this area[3].

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CASE REPORT

A 39-year-old male who smoked half a pack per day had a severe traffic accident with ipsilateral neck-shaft fractures of the right femur. Status postoperative closed reduction and internal fixation with multiple screws fixation of the right femoral neck and open reduction and internal fixation with board plate of the right femoral shaft for nine months with loosening multiple screws fixation of the femoral neck. There was a crescent sign on the femoral head, indicating osteonecrosis

of the femoral head and delayed union of the femoral shaft (Figure 1). Because of the bone necrosis at the femoral head, the patient smoked heavily. Therefore, the surgeons considered it most appropriate to perform total hip arthroplasty (THA) surgery, which was the option of surgery rather than refixation or valgus osteotomy. Additionally, THA in this patient had another advantage. The bone graft obtained from the femoral head could be inserted into the femoral shaft fracture, which delays union. However, in this patient, if using conventional THA, there was a chance that the femoral stem would collide or affect the screw fixation at the shaft of the femur, which was still delayed union, and the screws could not be removed. Therefore, it was necessary to choose short stem THA even though the neck length could not be set to 5 mm, and the quality of the lateral cortex of the proximal femur was poor owing to a bone defect from multiple screws fixation.

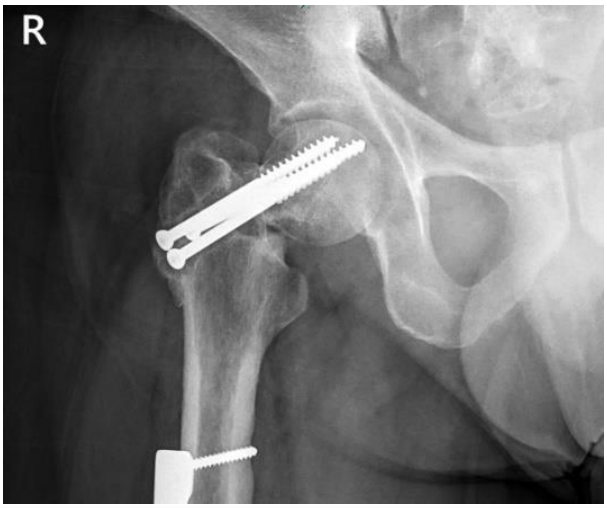

Fig. 1 Improper screws nearly protruding to the hip joint.

The short stem THA surgery was performed (Metha® features of B Braun (Thailand) co. ltd.), in which Melicki M et al.[4] and Thanut T et al.[5] have reported the effectiveness of this device as having good results of treatment. The operation was performed through the posterior approach, and the multiple screws were exposed and removed, as well as the femoral head, which was later prepared and used to promote femoral shaft fracture healing. The acetabulum cup was pressed-fit, one screw was inserted according to standard procedure, and the short cementless femoral stem was inserted, achieving the same level of the femoral head center as the tip of the greater trochanter. There was no postoperative complication. Standard routine care for the postoperative period included ankle pumping exercises, hip flexion/extension/abduction strengthening exercises, quadriceps strengthening exercises, and posterior hip precaution. Since there was also a non-united femoral shaft fracture, this patient was protected from weight bearing for three months before progressing to bear weight fully.

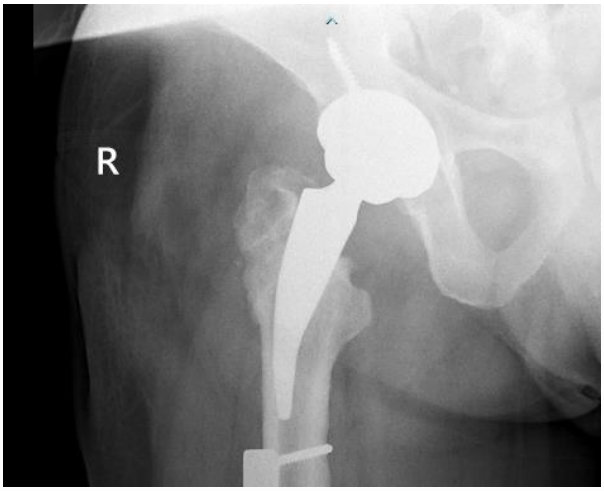

Fig. 2 The film one month after short stem THA showed no neck length sparing of a femoral stem with poor quality bone at the lateral cortex of proximal femur from multiple screws fixation.

One month after surgery, the femoral shaft began to form calluses on both AP and lateral sides, and short stem THA did not migrate or subside (Figure 2). The patient was allowed to bear full weight after three months of surgery. The X-ray was evaluated every three months in the first year after surgery, then every six months. Thereafter, complications were not detected, and the patient could resume his normal daily activities. Five years after short stem THA surgery, it was found that the femoral shaft had a complete union, and short stem

THA, especially the lateral cortex of the proximal femur, which had been eroded by the multiple screws, was healed with bone ingrowth. Although the film X-ray of both hip AP showed stable fibrous ingrowth at the lateral side of the stem; however, the medial side of the stem showed stable fixation by bone ingrowth. There was no sign of loosening, no limb length discrepancy, no subsidence, or migration of short stem THA (Figure 3). The patient had no clinical hip pain, was able to walk normally, and was very satisfied with the result of treatment, and the Harris hip score was 93.

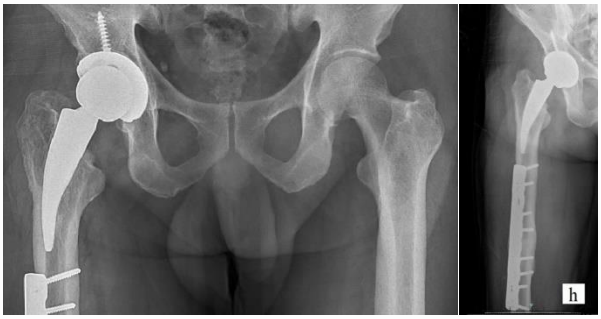

Fig. 3 The film five years after short stem THA.

DISCUSSION

Walker PS et al.[6] have described the principle of force distribution of short stem THA, which required neck length sparing of the medial and lateral side and good quality of the lateral side of the proximal femur. However, in some cases, it is not possible to preserve sparing bone to produce 3-point fixation, requiring the use of short stem THA.

However, this patient showed satisfactory results with short stem THA. One possible explanation might be that we found the cortical ring of the femoral neck in some patients that had a flat oval shape, with the result that the proximal stem had a stable fixation with the anterior and posterior neck instead of mediolateral. Three-point fixation in this patient might be at anterior and posterior neck and distal stem contact at the lateral part of the proximal femur, which is below the insertion point of the screws.

Literature Review of Short Stem THA

Short stem THA could be a useful tool for the total hip replacement procedure. Conventional stem requires stem length to ensure fixation; therefore, this complicates surgical plans in some conditions. Advantages of short stem THA include 1) the preservation of the femoral bone stock, which would be beneficial for a future revision, particularly in young patients, 2) a decrease in cortical stress and proximal stress shielding, which would also provide better biomechanics and long-term survival of the prosthesis, 3) the feasibility of the minimally invasive surgical technique, 4) viability of the alternative plan for femoral deformity/fracture requiring multiple types of implants[7-13]. Literature regarding the versatile uses of short stem THA was collected in the table below (Table 1).

CONCLUSIONS

Short stem THA might be a potential alternative for patients for whom conventional THA could not be used, such as in this patient. However, the intraoperative stability of the stem must be evaluated carefully, which is very essential in terms of stem survival.

Table 1 Literature review of short stem THA.

References	Cases	Condition	Implant	Follow-up period
Coutandin (2022)	6 patients (male, mean age 73 years)	failed conventional hip arthroplasty	Calcar-guided short stem optimys (Mathys. Bettlach, Switzerland)	3.32 ± 0.63 years
Thorate (2020)	55-year-old male	posterior hip dislocation along with aseptic loosening of the cemented acetabular component	Short stem high offset femoral component [SMF™ STIKTITE™, Smith & Nephew, Memphis (TN), USA]	2 years

Table 1 Literature review of short stem THA. (Cont.)

References	Cases	Condition	Implant	Follow-up period
Lee (2017)	65-year-old male	intraprosthetic fracture of the femoral stem	Proximal-filled short femoral stem	42 months
Moga (2014)	35-year-old male	Posttraumatic hip arthritis	Proxima prosthesis, with a short femoral stem	
Diamond (2013)	43 year-old female	Posttraumatic hip arthritis in below-knee amputated limb	Metha Short Hip Stem (B Braun®, Aesculap, AG, Tuttlingen, Germany)	2 years
Oh (2013)	43-year-old female, 52-year-old male	Postseptic hip sequele, Osteonecrosis with subtrochanteric fracture,	Modular short uncemented stem (Metha; B Braun®, Aesculap, Tuttlingen, Germany)	20 months
Kim (2010)	47-year-old male	Femoral neck-shaft fracture with osteonecrosis	Short cementless anatomical stem (PROXIMATM; DePuy, Leeds, UK)	5 years

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