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DE DOCTEUR EN MÉDECINE

**Les fractures périprothétiques de hanche sont-elles des fractures
ostéoporotiques ?**

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AVERTISSEMENT

La faculté n'entend donner aucune approbation aux opinions émises dans les thèses : celles-ci sont propres à leurs auteurs.

REMERCIEMENTS

ABRÉVIATIONS

AOM	Anti-Osteoporotic Medication
BMD	Bone Mineral Density
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CIM-10	Classification Internationale des Maladies
COPD	Chronic Obstructive Pulmonary disease
DEXA	Dual-Energy X-ray Absorptiometry
DIM	Département d'Information Médicale
DMO	Densitométrie Minérale Osseuse
DT2	Diabète de Type 2
EN	English
FESF	Fracture de l'Extrémité Supérieure du Fémur
FLS	Fracture Liaison Service
FR	Français
ICD-10	International Statistical Classification of Diseases and Related Health Problems
MID	Medical Information Department
MOF	Major Osteoporotic Fracture
PFF	Periprosthetic Femoral Fracture/ Fracture périprothétique fémorale
PPF	Periprosthetic Fracture/ Fracture périprothétique
PTH	Prothèse Totale de Hanche
PTG	Prothèse Totale de Genou
SD	Standard Deviation
SEM	Standard Error of the Mean

T2DM	Type 2 Diabetes Mellitus
TAO	Traitement Anti-Ostéoporotique
THA	Total Hip Arthroplasty
TJA	Total Joint Arthroplasty
TKA	Total Knee Arthroplasty
UCPF	Unified Classification System for Periprosthetic Fractures

SOMMAIRE

Avertissements.....	2
Remerciements.....	3
Abréviations.....	4
Sommaire.....	6
Introduction (FR).....	7
Introduction (EN).....	9
Patients & Methods.....	10
Results.....	14
Discussion (EN).....	27
Discussion (FR).....	31
Liste des tables.....	35
Liste des figures.....	35
Références.....	36
Annexe.....	38

Introduction (FR)

L'allongement de l'espérance de vie et la demande croissante des patients pour une amélioration de leur qualité de vie et une meilleure mobilité ont entraîné une augmentation du nombre d'arthroplasties dans une population vieillissante. Le nombre d'arthroplasties totales de hanche (PTH) et du genou (PTG) devrait augmenter respectivement de 300 à 400 % d'ici 2040, pour atteindre environ 4 millions d'opérations par an en 2030 **(1,2)**.

Malgré la prévalence de ces interventions, des complications persistent, notamment des événements liés aux pertes sanguines, thrombo-emboliques ou infectieux ainsi que des fractures périprothétiques (PPF). Ces dernières représentent la deuxième cause de révision après une PTH **(3,4)**. Les PPF sont définies comme des fractures survenant autour d'un implant orthopédique, qu'il s'agisse d'une prothèse totale ou de tout autre dispositif de fixation interne. Ce type de fracture touche 0,5 à 5,5 %, voire jusqu'à 18 %, des patients ayant subi une arthroplastie, avec un risque annuel accru de 13 % au Royaume-Uni au cours des dernières années **(1,2,5,6)**.

La mortalité est globalement similaire à celle des fractures ostéoporotiques, avec un taux à un an compris entre 9,7 et 36,4 % pour les fractures périprothétiques fémorales (PFF) **(2,7–10)**. Les PPF représentent également un enjeu économique important en santé publique, la prise en charge d'une PFF coûtant environ 40 000 dollars aux États-Unis **(2)**. Les chirurgiens orthopédistes sont attentifs à cette complication et ont mené plusieurs études pour identifier les facteurs de risque potentiels de PPF. Certains facteurs sont spécifiques aux techniques chirurgicales, comme la mise en place d'une tige non cimentée **(3,11)**, mais la plupart sont similaires à ceux associés à l'ostéoporose, notamment le sexe féminin, les antécédents de fracture à faible cinétique et la polyarthrite rhumatoïde **(1,3,11)**. En outre, les PPF sont principalement la conséquence de traumatismes à basse cinétique **(12,13)** et les patients bénéficiant d'une arthroplastie totale ont généralement plus de 60 ans, et sont donc plus exposés au risque d'ostéoporose **(1)**.

Peu d'études ont analysé les valeurs densitométriques de patients présentant une PPF. Elles ont généralement mis en évidence une densité minérale osseuse (DMO) basse, témoignant d'une ostéopénie ou d'une ostéoporose sous-jacente **(2,14)**. Dans les récentes études, il était retrouvé une ostéoporose, définie par un T-score $\leq$

-2,5DS, chez 78% des patients avant l'apparition d'une PPF **(2,14)** et une ostéoporose/ostéopénie, définie par un T-score ≤ -1 DS, chez 50 à 86 % des patients avant une arthroplastie totale **(15–18)**. En outre, certaines études ont également démontré une diminution de la densité minérale osseuse dans les suites précoces d'une arthroplastie **(19,20)**.

Les études sur les PPF sont généralement basées sur des échantillons limités et les données de DMO sont encore rares. A notre connaissance, aucune étude n'a comparé les caractéristiques des patients ayant présenté une PPF à celles de patients présentant une fracture de l'extrémité supérieure du fémur (FESF), en particulier concernant les valeurs densitométriques. Nous avons comparé ces deux types de populations, afin de mieux caractériser les patients atteints de PPF et de renforcer l'hypothèse selon laquelle les PPF sont des fractures ostéoporotiques.

Introduction (EN)

The increase in life expectancy and the growing demand from patients for enhanced joint mobility and an improved quality of life have resulted in a rising number of total joint arthroplasties (TJA) performed daily in an ageing population. It is expected that the number of total hip arthroplasty (THA) and total knee arthroplasty (TKA) surgeries will increase by 300-400%, respectively, by 2040 reaching approximately 4 million interventions per year by 2030 **(1,2)**.

Despite the prevalence of these procedures, complications remain, including among others, blood loss, thrombo-embolic events, sepsis and periprosthetic fractures (PPF). The latter represents the second cause for revision following THA **(3,4)**. PPF are defined as fractures occurring around an orthopaedic implant, either a TJA or any other internal fixation device. This outcome affects 0.5-5.5%, and up to 18%, of patients following a primary TJA with an annual increased risk of 13% in the UK over the last few years **(1,2,5,6)**.

The mortality is broadly similar to osteoporotic fractures, with a one-year mortality rate of 9.7-36.4% for periprosthetic femoral fracture (PPF) **(2,7–10)**. It also represents a major public health burden, a PPF costing approximately \$40 000 in the United States **(2)**. Orthopedists are thus well aware of this complication and have conducted several studies to identify potential risk factors for PPF. Some of these are specific to the surgical procedure itself, such as an uncemented stem **(3,11)**, but most of them are actually similar to those associated with osteoporosis, including female gender, a history of low-energy fracture and rheumatoid arthritis **(1,3,11)**. Moreover, PPF are predominantly a consequence of low-energy trauma **(12,13)** and patients undergoing TJA are typically over 60 years of age, therefore more at risk of osteoporosis **(1)**.

Few studies have analyzed the bone mineral density (BMD) of patients presenting with PPF. They mostly found low bone density, indicative of an underlying osteopenia or osteoporosis **(2,14)**. In recent studies, osteoporosis, defined by a T-score ≤ -2.5 , was present in up to 78% before a PPF **(2,14)** and osteoporosis/osteopenia, defined by a T-score ≤ -1 , was present in 50 to 86% of patients prior to TJA **(15–18)**. Moreover, some studies have also demonstrated bone loss within a few months following TJA **(19,20)**.

However, studies on PFF are usually based on a limited sample size and data on BMD are still scarce. To the best of our knowledge, no previous study has compared the characteristics of patients with PFF to those with native hip fractures, particularly with regard to BMD. We therefore aimed to compare both populations, in order to better characterize patients with PFF and reinforce the hypothesis that PFF are osteoporotic fractures.

PATIENTS AND METHODS

STUDY DESIGN

This is a retrospective, observational, single-center, descriptive and comparative study conducted at the Lille University Hospital between January 1st, 2016 and December 31st, 2022.

CRITERIA

The inclusion criteria were applied to patients with PFF identified by the Fracture Liaison Service (FLS) and/or the medical information department (MID) (via the ICD-10 M96.6 code). They required presenting with a PFF after (i) a low-energy trauma in patients (ii) aged ≥ 50 years, and with (iii) a recent available BMD assessment, conducted preferably in the year before or after the fracture but allowed up to three years.

A PFF was defined as a fracture around a surgically implanted femoral device (THA, hip resurfacing, gamma nail) at least 5 days prior to trauma. We included patients with Vancouver A, B, C PFF (*Figure 1*) and interprosthetic fractures (occurring between hip and knee arthroplasties). Acetabulum fractures were also considered as PFF.

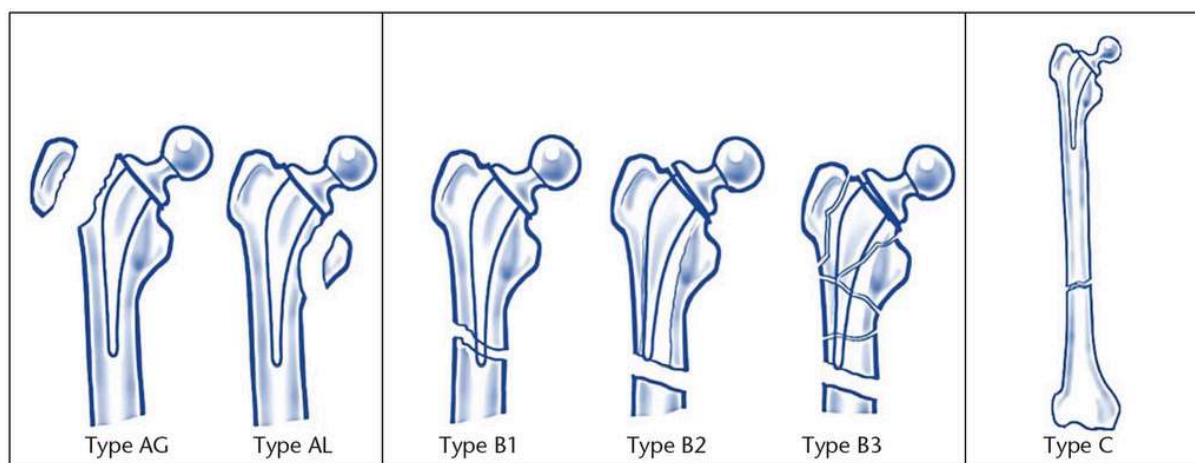


Figure 1: The Vancouver classification, a periprosthetic femoral fracture classification. (13)

Exclusion criteria included (i) high-energy trauma, (ii) pathological fractures, and (iii) specific prosthetic causes such as osteolysis, device wear and septic pseudarthrosis.

IDENTIFICATION OF PATIENTS

Patients with PPF and native hip fractures were identified through the FLS register. The Lille University Hospital FLS was implemented on January 1st, 2016 and has been previously described by Pflimlin (21) and Delbar (22).

Moreover, the MID of the Lille University Hospital identified all patients registered via the ICD-10 M96.6 code, corresponding to PPF, during this period of time (January 2016 to December 2022). The research yielded a total of 613 records, of which 115 were excluded. Of these, 60/115 were not PPF, while 55/115 had other causes than osteoporosis, such as sepsis, neoplasia, high-energy trauma and device wear. 149/613 were already identified via the FLS register and 349/613 were newly identified by the MID.

Added to the 19 PPF identified by the FLS alone, this resulted in 517 patients with a PPF. 71/517 patients had a PPF and a BMD assessment via Dual-energy X-ray absorptiometry (DEXA) in their files. Non-femoral PPF were classified according to whether they were related to a knee or shoulder implant. Other sites such as wrist, ankle and elbow were categorized as "Others". Flow-chart is displayed in Figure 2.

In case of a PPF identified by the MID prior to a fracture identified by the FLS for the same patient, we included the latter. On the contrary, if a PPF occurred after an episode of low-energy fracture registered by the FLS, we included the PPF.

In the event of simultaneous bilateral PPF, we only analyzed the patient once.

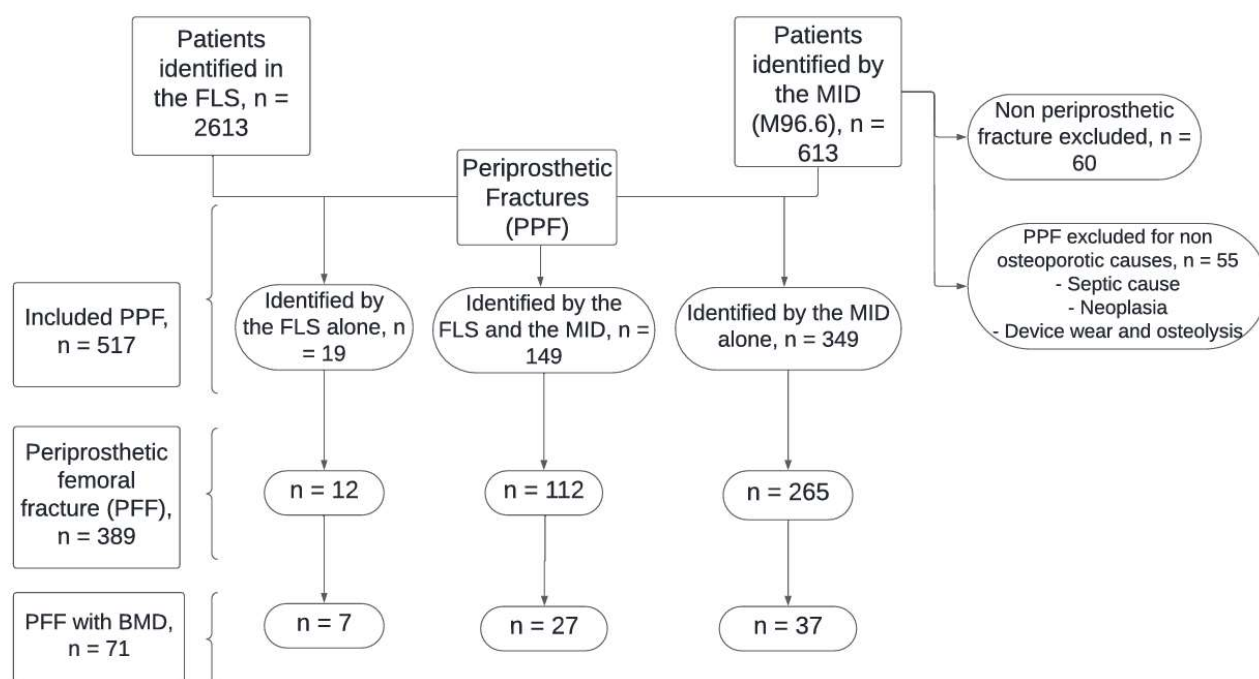


Figure 2: Flow-Chart

We compared this group of 71 patients with PFF to 117 patients with native hip fractures included by the FLS having a BMD available.

DATA RECORDING

Demographic, clinical, and biological data were collected, as well as BMD results, using our institution's medical software (*Sillage*).

Data were collected by reviewing the hospital software's medical records, from hospitalization reports to imaging and biological results, in order to obtain the most exhaustive database from Novembre 1st, 2023, to January 31st, 2024. Most DEXA examinations were performed at the Lille University Hospital. In other cases, the results were found in the patient's medical record.

Moreover, a data storage facility (INCLUDE) was asked to retrieve missing data including demographic characteristics such as BMI ≥ 40 kg/m², DEXA and blood test results.

STATISTICAL ANALYSIS

We conducted a comparative study and analyzed patients in two groups. Statistical analyses were conducted by our Biostatistic Team. Categorical variables are expressed as numbers (percentage) while continuous variables are expressed as means (standard deviation, SD) in the case of normal distribution or medians (interquartile range) otherwise. Normality of distribution was assessed using histograms and the Shapiro-Wilk test.

Comparisons between patients presenting with PFF to patients presenting with native hip fracture have been achieved using Chi-square tests (or Fisher's exact tests when expected cell frequency was <5) for categorical variables and Mann-Whitney U or Student t tests (regarding the normality of distributions) for continuous variables.

For the comparison of densitometric data, we used a linear mixed model considering a predefined adjustment on sex, age and body mass index (BMI). Validity of linear mixed models was assessed by examining the residuals. Adjusted means (standard error of the mean, SEM) are derived from the mixed model.

Statistical testing was done at the two-tailed α level of 0.05. Data was analyzed using SAS software package, release 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

A total of 517 PPF were identified at the Lille University Hospital between January 2016 and December 2022. The distribution of PPF per year according to the source is presented in figure 3.

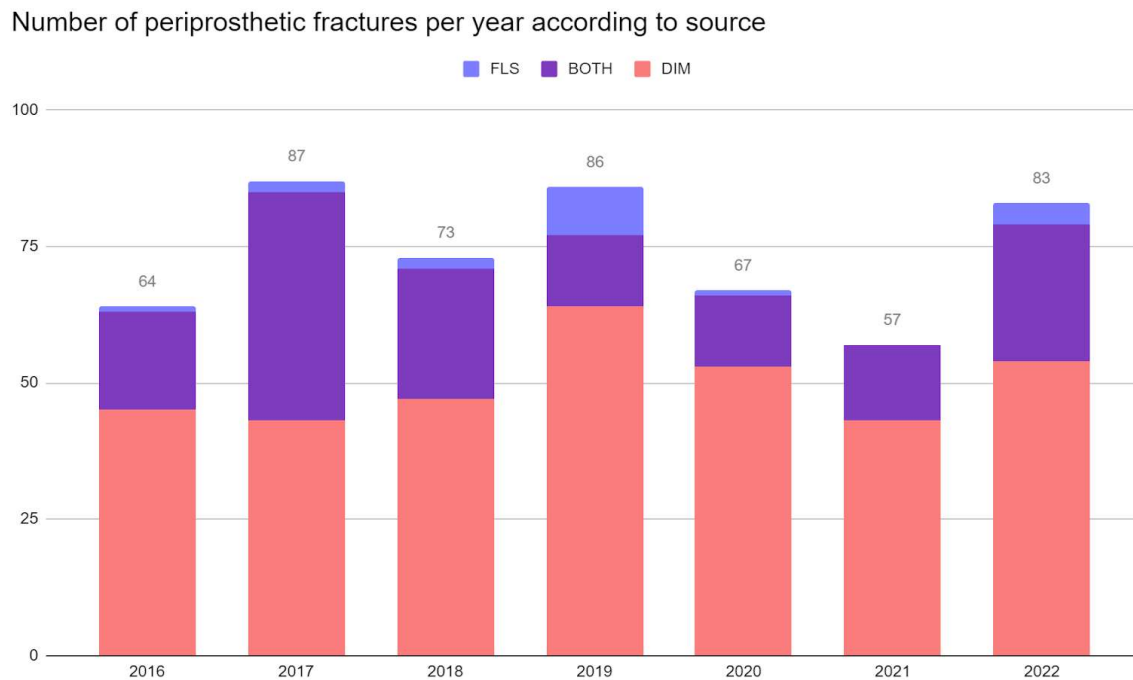


Figure 3: Number of fractures per year according to source.

The data revealed that in three-quarters of cases ($n=389$, 75.2%), PPF were PFF. Among PFF, 14/389 (3.6%) were acetabulum fractures. Examples of PFF are pictured in figures 4, 5, 6 and 7.

Figure 4: Vancouver A PFF





Figure 5: Vancouver B
PFF

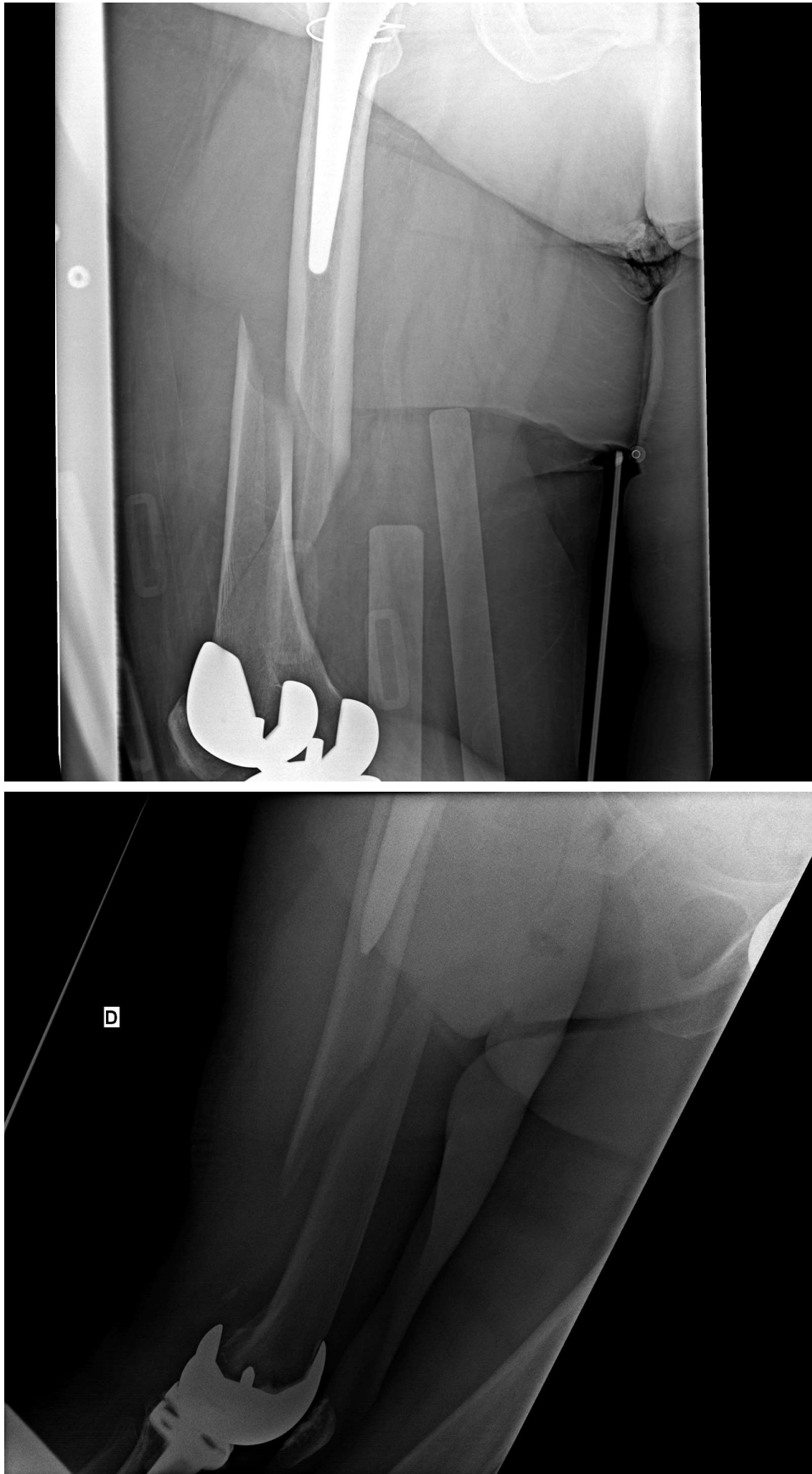




Figure 6: Vancouver C PFF



Figure 7: Interprosthetic Femoral Fractures



DEMOGRAPHIC AND DEXA CHARACTERISTICS

The demographic characteristics of patients presenting with PPF are shown in **Table 1**. Of the 517 patients with a PPF, 381 were women (73.6%) with a mean age of 79.6 ± 11.6 years. The mean BMI was 26.6 ± 6.1 kg/m². The median CCI was 4 (3; 5) and the two most prevalent comorbidities according to the CCI were cardiovascular diseases (19.1%) and type 2 diabetes mellitus (T2DM) (16.2%).

Table 1: Demographic data and relevant characteristics of periprosthetic fractures

Characteristics	N total	Periprosthetic fractures (PPF) N = 517
Female gender, n (%)	517	381 (73.6)
Age [years], mean $\pm$ SD	517	79.6 ± 11.6
Height [m], mean $\pm$ SD	99	$1.61 \pm 0,1$
Weight [kg], mean $\pm$ SD	100	71.5 ± 13.2
Body mass index [kg/m ²], mean $\pm$ SD	99	26.6 ± 6.1
- 40-50 kg/m ² , n (%)	517	13 (2.6)
- > 50 kg/m ² , n (%)	517	3 (0.6)
CCI, median (Q1; Q3)	517	4.0 (3; 5)
Major comorbidities according to the CCI		
Cardiovascular diseases, n (%)	517	99 (19.1)
- Peripheral vascular disease, n (%)	517	26 (5.0)
- Congestive heart failure, n (%)	517	59 (11.4)
- Myocardial infarction, n (%)	517	14 (2.7)
Neurological diseases, n (%)	517	45 (8.7)
- Cerebrovascular disease, n (%)	517	27 (5.2)
- Hemiplegia or paraplegia, n (%)	517	18 (3.5)
Diabetes, n (%)	517	84 (16.2)

- Uncomplicated, n (%)	517	77 (14.9)
- With complication, n (%)	517	7 (1.3)
Chronic kidney disease, n (%)	517	38 (7.4)
Gastrointestinal diseases, n (%)	517	18 (3.5)
- Mild liver disease, n (%)	517	14 (2.7)
- Peptic ulcer disease, n (%)	517	4 (0.8)
Chronic pulmonary disease, n (%)	517	56 (10.8)
Connective Tissue disease, n (%)	517	21 (4.1)
Any malignancy, n (%)	517	27 (5.2)
Dementia, n (%)	517	45 (8.7)
Periprosthetic fracture localisation		
- Hip implant, n (%)	517	389 (75.2)
- THA, n (%)	389	369 (94.9)
- Gamma nail, n (%)	389	12 (3.1)
- Resurfacing, n (%)	389	8 (2.0)
- Knee implant, n (%)	517	86 (16.6)
- Shoulder implant, n (%)	517	31 (6.0)
- Others, n (%)	517	11 (2.2)

CCI: Charlson Comorbidity Index

The distribution of PPF per year was relatively consistent, with figures ranging from 11.4% of the 517 fractures in 2021 to 16.8% in 2017, as shown in figure 8.

Number of periprosthetic fractures per year and localisation

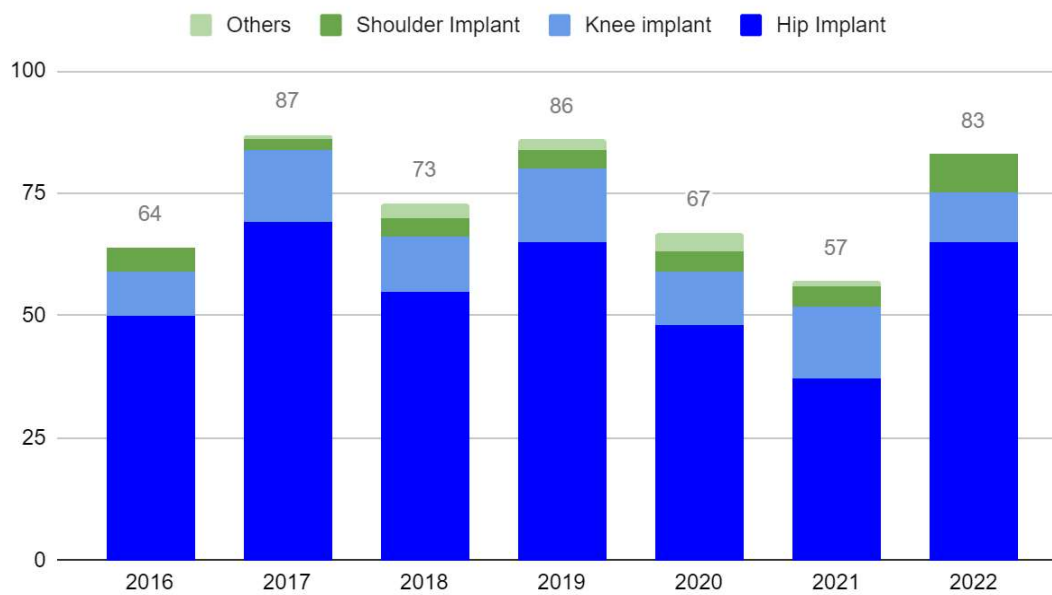


Figure 8: Number of periprosthetic fractures per year and localisation.

FOCUSING ON PFF

Table 2 presents a comparison of the demographic characteristics of 71 patients with PFF and available BMD data to 117 patients with native hip fractures from the FLS. Of the 71 patients with PFF, 68 (95.8%) underwent THA, while two patients (2.8%) were treated with a gamma nail and one patient (1.4%) benefited from resurfacing surgery. The primary indication for hip surgery in the PFF group was hip osteoarthritis in 41/71 (57.8%) patients or a fracture of the upper end of the femur in 25/71 (35.2%) patients. For the remaining 5/71 (7%) patients, the underlying reason was unknown. Patients had an acetabulum fracture in 11.3% (8/71).

The majority of patients with PFF were women (78.9%) with no significant difference between the two groups. Patients in the PFF group were significantly older (mean age 79.3 ± 10.6 versus 74.5 ± 10.7 years, $p=0.002$) and had a significantly greater BMI (26.2 ± 5.7 versus 24.6 ± 4.4 kg/m², $p=0.043$).

Among osteoporosis clinical risk factors, patients presenting with PFF had more corticosteroids exposure (18.3% versus 7.0%, $p=0.017$), less history of family hip fracture (4.3% versus 13.6%, $p=0.041$) and were more at risk of multiple falls (54.3% versus 26.1%, $p<0.001$). A significantly higher number of patients in the PFF group

had a prior history of fragility fracture (69.0% versus 44.0%, $p<0.001$), main sites being hip (35.2%) and vertebrae (33.8%). A history of anti-osteoporosis medication (AOM) was significantly more frequent in patients presenting with PFF (26.8% versus 11.1%, $p=0.006$).

Table 2: Comparison of demographic data and relevant characteristics of periprosthetic fractures

Characteristics	N total	Hip fractures N = 117	N total	Periprosthetic femoral fractures N = 71	P-value
Female gender, n (%)	117	87 (74.4)	71	56 (78.9)	0.48
Age [years], mean $\pm$ SD	117	74.5 $\pm$ 10.7	71	79.3 $\pm$ 10.6	0.002
Height [m], mean $\pm$ SD	116	1.6 $\pm$ 0.1	68	1.6 $\pm$ 0.1	0.26
Weight [kg], mean $\pm$ SD	116	65.4 $\pm$ 14.0	69	68.1 $\pm$ 16.5	0.30
BMI [kg/m²], mean $\pm$ SD	116	24.6 $\pm$ 4.4	68	26.2 $\pm$ 5.7	0.043
Osteoporosis risk factors					
Former or current smokers, n (%)	117	32 (28.1)	71	22 (31.0)	0.78
Alcohol abuse, n (%)	116	11 (9.5)	71	12 (16.9)	-
Premature menopause (<45 years), n (%)	75	18 (24.0)	46	13 (28.3)	0.39
Family history of hip fracture, n (%)	110	15 (13.6)	70	3 (4.3)	0.041
Corticosteroids exposure (current or prior use), n (%)	115	8 (7.0)	71	13 (18.3)	0.017
Multiple falls*, n (%)	115	30 (26.1)	70	38 (54.3)	<0.001
Previous anti-osteoporosis medication, n (%)	117	13 (11.1)	71	19 (26.8)	0.006
Previous fragility fracture, n (%)	116	51 (44.0)	71	49 (69.0)	<0.001
- Vertebra	116	11 (9.5)	71	24 (33.8)	<0.001
- Wrist	116	16 (13.8)	71	13 (18.3)	0.41

- Shoulder	116	9 (7.8)	71	17 (23.9)	0.002
- Hip	116	9 (7.8)	71	25 (35.2)	<0.001
- Ankle	116	7 (6.0)	71	5 (7.0)	0.77
- Pelvis	116	3 (2.6)	71	5 (7.0)	0.16

*at least two falls in the previous year

SD: standard deviation; BMI: Body mass index.

As seen in **Table 3**, patients in the PFF group exhibited a greater prevalence of comorbidities.

Table 3: Comparison of medical history data of periprosthetic femoral fractures

Comorbidities	Hip fractures N = 117	Periprosthetic femoral fractures N = 71	P-value
CCI, median (Q1; Q3)	4.0 (3.0; 5.5)	5.0 (4.0; 7.0)	<0.001
Digestive system diseases, n (%)	20 (17.2)	22 (31.0)	0.029
- Cirrhosis, n (%)	1 (0.9)	2 (2.8)	-
- Peptic ulcer disease, n (%)	2 (1.7)	6 (8.5)	0.055
- Gastritis	2 (1.7)	2 (2.8)	-
- Esophagitis	1 (0.9)	3 (4.2)	-
Cardiovascular diseases, n (%)	78 (67.2)	59 (83.1)	0.017
- HTA	64 (55.2)	47 (66.2)	0.14
- Peripheral vascular disease, n (%)	13 (11.2)	5 (7.0)	0.35
- Stroke, n (%)	15 (12.9)	14 (19.7)	0.21
- Coronary artery disease, n (%)	12 (10.3)	9 (12.7)	0.62
- Arrhythmia, n (%)	25 (21.6)	26 (36.6)	0.025

- Dyslipidemia, n (%)	41 (35.3)	28 (39.4)	0.57
Pneumological diseases, n (%)	20 (17.2)	23 (32.4)	0.017
- COPD, n (%)	8 (6.9)	13 (18.3)	0.016
- Asthma, n (%)	3 (2.6)	4 (5.6)	-
- Sleep apnea syndrome, n (%)	7 (6.0)	4 (5.6)	1.00
Endocrinological diseases, n (%)	34 (29.3)	18 (25.4)	0.56
- T2DM, n (%)	24 (20.7)	10 (14.1)	0.26
- Dysthyroidism, n (%)	19 (16.4)	6 (8.5)	0.12
Obesity, n (%)	10 (8.6)	21 (29.6)	< 0.001
Neurological diseases, n (%)	23 (19.8)	28 (39.4)	0.003
- Parkinson's disease, n (%)	2 (1.7)	1 (1.4)	-
- Epilepsy, n (%)	4 (3.4)	4 (5.7)	0.48
- Impaired cognitive function, n (%)	7 (6.0)	17 (23.9)	< 0.001
- Walking disorders**, n (%)	2 (1.7)	19 (26.8)	< 0.001
Depression, n (%)	10 (8.6)	18 (25.4)	0.002
Chronic kidney disease, n (%)	6 (5.2)	12 (16.9)	0.008
Rheumatologic diseases, n (%)	50 (43.1)	69 (97.2)	< 0.001
- Chronic Inflammatory Rheumatism, n (%)	2 (1.7)	11 (15.5)	< 0.001
- Scoliosis, n (%)	9 (7.8)	4 (5.6)	0.77
- Osteoarthritis, n (%)	24 (20.7)	55 (77.5)	< 0.001
Dermatological diseases, n (%)	11 (9.5)	7 (9.9)	0.93

Neoplasia, n (%)	23 (19.8)	18 (25.4)	0.38
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CCI: Charlson Comorbidity Index; T2DM: Type 2 diabetes mellitus; COPD: Chronic obstructive pulmonary disease

**·: Any chronic walking disability, including neurological disorders such as ataxia, polyneuropathy, orthopaedic and rheumatologic conditions including claudication, inducing a risk of fall.

Subsequently, patients in the PFF group exhibited a significantly greater CCI (5.0 (4.0; 7.0) versus 4.0 (3.0; 5.5), $p < 0.001$) as well as a higher number of drug prescriptions and risk of polypharmacy (number of treatments ≥ 5) (*Supplementary Table 1*).

DEXA RESULTS

When DEXA examinations were conducted at the Lille University Hospital, they were carried out either in the Rheumatology department in 35/71 (49.3%) patients or in the Nuclear Medicine Department in 28/71 (39.4%) patients. For eight of the 71 patients (11.3%), the examination was performed externally. Median time to BMD was 4 months (IQR: 1; 10). Almost half of the hip BMD measurements (femoral neck and total hip) were missing in the PFF group (33/71, 46.5%), due to bilateral THA in 25/71 (35.2%) patients. Hip DEXA measurements were unavailable at either femoral neck in 8/71 (11.3%) patients or total hip in 9/71 patients (12.7%) because examination was carried out in the Nuclear Medicine Department. Lumbar spine BMD measurements were missing in 5/71 (7.0%) due to multiple vertebral fractures ($n=2$, 2.8%), lack of documentation in the medical record ($n=2$, 2.8%) or thoracolumbar arthrodesis ($n=1$, 1.4%).

Osteoporosis (43.6% versus 29.6%) and osteopenia (47.9% versus 42.2%) were significantly more frequently found in the native hip fracture group ($p=0.001$). Distribution of osteoporosis among PFF and comparison of FRAX® score are presented in **Table 4**. **Table 5** illustrates the DEXA results adjusted for age, sex, and BMI.

Table 4: Comparison of osteoporosis distribution of periprosthetic femoral fractures

Characteristics		Hip fractures N = 117		Periprosthetic femoral fractures N = 71	P-value
BMD results, n (%) - Osteoporosis - Osteopenia - Normal	117	51 (43.6) 56 (47.9) 10 (8.5)	71	21 (29.6) 30 (42.2) 20 (28.2)	0.001
FRAX score, mean $\pm$ SD - Hip fracture - MOF	100	8.9 $\pm$ 10.2 18.3 $\pm$ 12.7	37	9.2 $\pm$ 8.6 18.7 $\pm$ 11.6	0.46 0.69
<i>Femoral neck:</i> Osteoporosis, n (%) Osteopenia, n (%) Normal, n (%)	99	45 (45.4) 48 (48.5) 6 (6.1)	38	13 (34.2) 20 (52.6) 5 (13.2)	0.27
<i>Total Hip:</i> Osteoporosis, n (%) Osteopenia, n (%) Normal, n (%)	100	29 (29.0) 56 (56.0) 15 (15.0)	37	9 (24.3) 19 (51.3) 9 (24.4)	0.44
<i>Lumbar Spine:</i> Osteoporosis, n (%) Osteopenia, n (%) Normal, n (%)	112	20 (17.8) 49 (43.8) 43 (38.4)	66	7 (10.6) 20 (30.3) 39 (59.1)	0.027

BMD: Bone mineral density; MOF: major osteoporotic fracture (hip, vertebra, proximal humerus and distal forearm/wrist); SD: Standard deviation

Table 5: Comparison of densitometric data of periprosthetic femoral fractures

Characteristics		Hip fractures N = 117		Periprosthetic femoral fractures N = 71	P-value
<i>Femoral neck:</i> - Adjusted T-score, mean (SEM) ^{***}	99	-2.3 (0.1)	38	-2.0 (0.1)	0.08
<i>Total Hip:</i> - Adjusted T-score, mean (SEM) ^{***}	100	-1.8 (0.1)	37	-1.7 (0.2)	0.49
<i>Lumbar Spine:</i> - Adjusted T-score, mean (SEM) ^{***}	112	-1.2 (0.2)	66	-0.5 (0.2)	0.008

^{***}: Adjusted for age, sex and BMI; SEM: Standard error of the mean

Discussion (EN)

MAIN FINDINGS

Upon comparing patients with PFF and those with native hip fractures, we observed that patients with PFF were of advanced age, had higher BMI, and exhibited a greater prevalence of comorbidities than those with native hip fractures. Osteoporosis risk factors include a greater frequency of previous fragility fractures, an elevated risk of falls, and an increased prescription of AOM in patients with PFF. BMD measurements at the total hip and femoral neck did not demonstrate statistically significant differences between the groups; however, significantly lower values were observed at the lumbar spine in the native hip fracture group. As a whole, patients with PFF had less frequent BMD osteoporosis/osteopenia compared to patients with native hip fracture.

COMPARISON WITH OTHER STUDIES

According to the literature (23), the majority of PPF cases were PFF. Demographic characteristics of patients in our cohort were broadly similar to previous studies (2,5,12,14). They were slightly older (mean age of 79.3 years) than that described by Toogood *et al.* (74.6 years) (5), or Whiting *et al.* (75.4 years) (2). The mean BMI was

26.2 ± 5.7 kg/m², comparable to what Ritter *et al.* **(14)** (26.4 ± 4.0 kg/m²) and Lindberg-Larsen *et al.* **(24)** (27.0 kg/m²) reported. Patients in the PFF group had more comorbidities, as evidenced by a significantly higher CCI. Interestingly, a higher CCI was found to be associated with a higher mortality rate in case of PFF by Moreta *et al.* **(9)**. The main comorbidity was cardiovascular disease (83.1%), as reported by Singh *et al.* **(25)**. Moreover, the prevalence of T2DM in patients with PFF was 14%, which was identical to that reported by Whiting *et al.* **(2)**.

Zhao *et al.* **(26)** and Agarwal *et al.* **(27)** showed that a history of fragility fractures was frequent in patients with PFF. Accordingly, we identified a significantly higher prevalence of fragility fractures in the PFF group. The prevalence of glucocorticoid exposure was similar to that reported by Whiting *et al.* (18.3% vs. 18%) **(2)**, whereas the incidence of a family history of hip fracture was lower in our study (4.3% vs. 6%) **(2)**. Osteoporosis has been repeatedly described as a predominant risk factor for PFF **(20,28)**. It was also part of the four non-modifiable risk factors for PFF described by Wyles *et al.*, as well as age, female gender and indication for THA other than osteoarthritis **(3)**. Osteoporosis was identified in 20% of patients prior to PFF by Seward *et al.* **(12)** and in 29.3% of patients by Whiting *et al.* **(2)**. These figures align with our own findings of 29.6%. However, some studies have reported higher prevalence of osteoporosis with the help of BMD measurements using computed tomography at the lumbar spine **(2,29)**. Notably, patients with PFF had a greater prevalence of prior AOM than those with native hip fractures (26.8% vs. 11.1%, $p=0.006$). Nevertheless, the proportion of patients who received AOM (26.8%) was comparable to that reported by Whiting *et al.* **(2)** (26.3%) and Ritter *et al.* **(14)** (22.5%). Regarding the prescription of AOM between these 2 groups, this discrepancy can be attributed to the fact that the initial exclusion criteria for the FLS comprised individuals already treated for osteoporosis, potentially introducing recruitment bias. It is also possible that, as the PFF group had a higher prevalence of previous fragility fractures, they were more likely to be treated.

As anticipated, more than half of the 71 patients in the PFF group exhibited osteopenia/osteoporosis ($n=51$, 71.8%), which was lower than that in the native hip fracture group (91.5%). BMD measurements at the total hip and femoral neck did not demonstrate statistically significant differences between the groups; however, higher

values were observed at the lumbar spine in the PFF group. This can be attributed to the fact that patients in the PFF group were older and more obese, therefore, possibly presenting with more osteoarthritis at the lumbar spine.

CLINICAL IMPLICATIONS

The results of this study demonstrate that patients presenting with PFF often exhibit osteoporosis, as defined clinically (history of fragility fracture) or through BMD measurements. They are also more fragile and comorbid patients. Based on the aforementioned findings, it can be reasonably proposed that low-energy PFF may be considered as osteoporotic fractures. Therefore, it is advisable to initiate AOM and subsequently arrange a follow-up consultation with a bone specialist. There is a need for the primary prevention of osteoporosis in patients undergoing THA, particularly in women and older patients. Despite the undeniable osteoporosis gap (30), osteoporosis can be diagnosed and prevented relatively easily. It is essential that patients aged ≥ 50 years undergo an evaluation of their risk factors for osteoporosis and a DEXA examination, ideally prior to surgery or a few months later. This approach would allow the identification of individuals who may benefit from anti-osteoporotic treatments.

STRENGTHS AND LIMITS

This study was based on a relatively large sample over a seven-year period. The use of the MID to create a register based on the ICD-10 M96.6 code allowed more systematic recruitment. Furthermore, the INCLUDE data facility storage enabled the recovery of a certain amount of data. Another strength of this study was the comparison group. To the best of our knowledge, no previous study has compared patients with PFF with patients who sustained a native hip fracture. Nevertheless, it represents the most appropriate comparison group for determining whether PFF can be defined as an osteoporotic fracture. There are only a few studies on PFF, especially regarding the demographic and DEXA characteristics. BMD assessment was an important variable in this study as it is known to be an objective criterion for osteoporosis.

This study has some limitations. This was a monocentric retrospective study, leading to potential biases. There were a number of missing data because most of the

patients in the PFF group did not undergo a dedicated consultation with a rheumatologist, unlike patients in the native hip fracture group, and data were retrieved through medical record screening. Moreover, the definition of PFF is somewhat vague, primarily due to the existence of different classifications (Vancouver **(13)**, UCPF **(31)**, Dorr **(32)**), the increasing number of distinct implants and localisation options for orthopaedic devices. The use of disparate criteria in the literature to identify patients with PFF also poses a significant challenge to the comparison of studies.

IN CONCLUSION:

Low-energy PFF should be considered as osteoporotic fractures and treated accordingly, even though BMD might be normal more often. Given the challenges associated with the management of PFF, it is imperative for bone specialists to collaborate with orthopaedic surgeons to improve the primary prevention of osteoporosis prior to surgery. In addition, research has indicated that antiresorptive therapy may reduce bone loss following TJA **(25,30)**, thereby contributing to the prevention of PFF. Moreover, further studies are required to investigate a recently proposed entity called atypical PFF (PAFF) **(33,34)**.

Discussion (FR)

RÉSULTATS PRINCIPAUX

Les patients présentant des PFF sont plus âgés, ont un IMC plus élevé et un plus grand nombre de comorbidités que les patients nécessitant une arthroplastie à la suite d'une FESF. Parmi les facteurs de risque d'ostéoporose, il était retrouvé une plus grande prévalence d'antécédent de fractures de fragilité, un nombre plus élevé de chutes et une prescription accrue de traitement anti-ostéoporotique (TAO) chez les patients atteints de PFF. Les T-scores à la hanche totale et au col fémoral ne différaient pas de façon statistiquement significative, cependant, il était observé des valeurs significativement plus basses au rachis lombaire dans le groupe des FESF. Dans l'ensemble, les patients atteints de PFF avaient plus souvent une DMO normale que les patients présentant une FESF.

COMPARAISON AVEC LA LITTÉRATURE

En accord avec la littérature **(23)**, la majorité des cas de PFF étaient des PFF. Les caractéristiques démographiques des patients de notre cohorte étaient globalement similaires à celles des études précédentes **(2,5,12,14)**. Ils étaient légèrement plus âgés (âge moyen de 79,3 ans) que ceux décrits par Toogood *et al.* (74,6 ans) **(5)**, ou Whiting *et al.* (75,4 ans) **(2)**. L'IMC moyen était de $26,2 \pm 5,7$ kg/m², comparable à ce que Ritter *et al.* **(14)** ($26,4 \pm 4,0$ kg/m²) et Lindberg-Larsen *et al.* **(24)** ($27,0$ kg/m²) ont rapporté. Les patients du groupe PFF présentaient davantage de comorbidités, comme en témoigne un score de Charlson significativement plus élevé. Il est intéressant de noter que Moreta *et al.* **(9)** ont constaté qu'un score de Charlson plus élevé était associé à un taux de mortalité plus élevé en cas de PFF. La principale comorbidité était représentée par les maladies cardiovasculaires (83,1 %), comme l'ont rapporté Singh *et al.* **(25)**. En outre, la prévalence du DT2 chez nos patients atteints de PFF était de 14 %, identique à ce qui a été décrit par Whiting *et al.* **(2)**.

Zhao *et al.* **(26)** et Agarwal *et al.* **(27)** ont montré qu'un antécédent de fracture de fragilité était plus fréquent chez les patients atteints de PFF. De la même façon, nous avons identifié une prévalence plus importante d'antécédent de fractures de fragilité dans le groupe PFF. L'exposition aux glucocorticoïdes était similaire à celle rapportée par Whiting *et al.* (18,3 % vs. 18 %) **(2)** alors que la prévalence d'un

antécédent familial de fracture de la hanche était légèrement plus faible dans notre étude (4,3 % vs. 6 %) **(2)**. L'ostéoporose a été décrite à plusieurs reprises comme un facteur de risque majeur de PFF **(20,28)**. Il s'agit également d'un des quatre facteurs de risque non modifiables de PFF décrits par Wyles *et al.*, au même titre que l'âge, le sexe féminin et une indication d'arthroplastie initiale autre que l'arthrose **(3)**. Une ostéoporose a été identifiée chez 20 % des patients avant une PFF par Seward *et al.* **(12)** et chez 29,3 % des patients par Whiting *et al.* **(2)**. Ces chiffres sont en accord avec nos résultats (29,6 %). Cependant, certaines études ont rapporté un taux plus élevé d'ostéoporose avec l'utilisation de la tomодensitométrie pour réaliser des mesures densitométriques au rachis lombaire **(2,29)**. Les patients atteints de PFF bénéficiaient plus fréquemment de TAO (26,8 %) que ceux présentant des FESF (versus 11,1 %, $p=0,006$). La proportion de patients ayant reçu un TAO dans le groupe PFF était comparable à celle rapportée par Whiting *et al.* **(2)** (26,3 %) et Ritter *et al.* **(14)** (22,5 %). En ce qui concerne la différence de taux de prescription entre les deux groupes, celle-ci peut être attribuée au fait que les critères d'exclusion initiaux de la FLS excluaient les patients déjà traités pour l'ostéoporose, ce qui a potentiellement induit un biais de recrutement. Il est également possible que le groupe PFF, ayant une prévalence plus élevée d'antécédent de fracture de fragilité, était plus susceptible d'être traité.

Comme attendu, plus de la moitié des 71 patients du groupe PFF présentaient une ostéopénie ou une ostéoporose ($n=51$, 71,8 %), ce qui était inférieur au pourcentage du groupe de patients ayant subi une FESF (91,5 %). Les T-scores moyens ajustés sur l'âge, le sexe et l'IMC à la hanche totale et au col fémoral entre les groupes n'étaient pas statistiquement différents. Cependant, des valeurs significativement plus élevées ont été observées au rachis lombaire chez les patients présentant une PFF. Cela peut être dû au fait que les patients du groupe PFF étaient plus âgés et plus obèses et présentaient donc probablement plus d'arthrose au niveau du rachis lombaire.

IMPLICATIONS CLINIQUES

Les résultats de cette étude ont montré que les patients présentant une PFF sont souvent atteints d'ostéoporose, selon une définition clinique (antécédent de fracture de fragilité) ou selon des mesures densitométriques. Il s'agit également de patients

plus fragiles et présentant un nombre important de comorbidités. Sur la base des résultats mentionnés précédemment, il peut être raisonnable de considérer les PFF à faible cinétique comme des fractures ostéoporotiques. Par conséquent, il est conseillé d'initier un TAO et d'organiser une consultation de suivi avec un rhumatologue dans les suites d'un tel évènement. Il est également nécessaire de mettre en place une prévention primaire de l'ostéoporose chez les patients en attente d'arthroplastie, en particulier chez les femmes et les patients les plus âgés. Malgré un diagnostic facile et peu coûteux, ainsi qu'une prévention thérapeutique accessible, l'ostéoporose est encore insuffisamment diagnostiquée et traitée (30). Il est donc essentiel que les patients âgés de ≥ 50 ans fassent l'objet d'une évaluation de leurs facteurs de risque d'ostéoporose et d'une densitométrie avant, idéalement, ou quelques mois après une PTH. Cette approche permettrait d'identifier les personnes susceptibles de nécessiter un TAO.

FORCES ET LIMITES

Cette étude est basée sur un échantillon important au cours d'une période de sept ans. L'utilisation du DIM pour créer un registre basé sur le code de la CIM-10 M96.6 a permis un recrutement plus systématique. De plus, la sollicitation de l'entrepôt de données INCLUDE a permis de récupérer un certain nombre de données. Un autre point fort de cette étude est le groupe contrôle. À notre connaissance, aucune étude précédente n'a comparé des patients atteints de PFF à des patients ayant subi une FESF. Néanmoins, il s'agit du groupe de comparaison le plus approprié pour déterminer si les PFF peuvent être considérées comme des fractures ostéoporotiques. Il n'existe à ce jour que peu d'études sur les PFF, notamment concernant les caractéristiques démographiques et densitométriques. L'évaluation de la DMO était une variable importante dans cette étude car elle est reconnue comme critère objectif d'ostéoporose.

Cette étude présente certaines limites. Il s'agit d'une étude rétrospective monocentrique, à risque de biais. Un certain nombre de données manquaient car la plupart des patients du groupe PFF n'ont pas été reçus en consultation spécialisée de Rhumatologie, contrairement aux patients du groupe FESF. Les données étaient alors récupérées par l'analyse des dossiers médicaux. En outre, la définition des PFF est parfois vague, principalement en raison de l'existence de différentes

classifications (Vancouver **(13)**, UCPF **(31)**, Dorr **(32)**), de l'augmentation du nombre d'implants existants et des diverses localisations articulaires possibles pour implantation. L'utilisation de critères différents dans la littérature pour identifier les patients atteints de PFF constitue également un défi important pour la comparaison des études.

CONCLUSION :

Les PFF à faible cinétique doivent être considérées comme des fractures ostéoporotiques et traitées de la même façon, malgré une DMO plus souvent normale. Compte tenu des défis liés à la prise en charge des PFF, il est impératif que les rhumatologues collaborent avec les chirurgiens orthopédiques pour améliorer la prévention primaire de l'ostéoporose avant une arthroplastie. De plus, il a été évoqué dans la littérature qu'un traitement anti-ostéoporotique par inhibiteur de la résorption osseuse réduirait la perte osseuse induite après une PTH **(25,30)**, contribuant ainsi à la prévention des PFF. Par ailleurs, des études complémentaires sont nécessaires afin d'étudier une entité nouvellement proposée, correspondant aux PFF atypiques (PAFF) **(33,34)**.

Liste des tables

Table 1: Demographic data and relevant characteristics of periprosthetic fractures

Table 2: Comparison of demographic data and relevant characteristics of periprosthetic fractures

Table 3: Comparison of medical history data of PFF

Table 4: Comparison of osteoporosis distribution of periprosthetic femoral fractures

Table 5: Comparison of densitometric data of periprosthetic femoral fractures

Supplementary Table 1: Distribution of treatments taken by patients in the non-periprosthetic and periprosthetic fracture groups

Liste des figures

Figure 1: The Vancouver classification, a periprosthetic femoral fracture classification.

Figure 2: Flow-Chart

Figure 3: Number of fractures per year according to source.

Figure 4: Vancouver A PFF

Figure 5: Vancouver B PFF

Figure 6: Vancouver C PFF

Figure 7: Interprosthetic Femoral Fractures

Figure 8: Number of periprosthetic fractures per year and localisation.

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ANNEXE :

Supplementary Table 1: Distribution of treatments taken by patients in the non-periprosthetic and periprosthetic fracture groups

Treatments	Hip fractures N = 117	Periprosthetic hip fractures N = 71	P-value
Polypharmacy^o, n (%)	31 (26.5)	66 (54.9)	<0.001
Number of drugs prescribed (median (Q1; Q3))	3.0 (1.0; 5.0)	4.0 (2.0; 5.0)	<0.001
Antiepileptic medication, n (%)	10 (8.5)	15 (21.4)	0.012
Corticoids, n (%)	12 (10.3)	13 (18.6)	0.11
Chemotherapy, n (%)	6 (5.1)	3 (4.3)	1.00
Anti-hypertensive, n (%)	64 (54.7)	47 (67.1)	0.094
Blood thinner, n (%)	25 (21.4)	21 (30.0)	0.18
Alpha-blockers, n (%)	6 (5.1)	9 (13.2)	0.051
Beta-blockers, n (%)	32 (27.4)	25 (35.7)	0.23
Cholesterol-lowering agent, n (%)	46 (39.7)	28 (40.0)	0.96
Antiarrhythmics, n (%)	11 (9.4)	7 (10.3)	0.84
Thyroid hormones, n (%)	16 (13.7)	5 (7.1)	0.17
Hormone treatment, n (%)	4 (3.4)	11 (15.7)	0.003
Oral antidiabetic, n (%)	16 (13.7)	6 (8.6)	0.29
Insulin Therapy, n (%)	11 (9.6)	3 (4.3)	0.19
Anxiolytics, n (%)	14 (12.0)	13 (18.6)	0.21
Hypnotics, n (%)	14 (12.0)	15 (21.4)	0.084

Antidepressants, n (%)	9 (7.7)	19 (27.1)	<0.001
Anti-asthmatics, n (%)	8 (6.8)	12 (17.4)	0.025
Immunomodulators/Immunosuppressants, n (%)	5 (4.3)	6 (8.6)	0.34
Diuretics, n (%)	19 (16.2)	20 (28.6)	0.045

°: Number of treatments $\geq$ 5.

AUTEURE : Nom : HOUEL

Prénom : Victoria

Date de soutenance : 03/10/2024

Titre de la thèse : Les fractures périprothétiques de hanche sont-elles des fractures ostéoporotiques ?

Thèse - Médecine - Lille 2024

Cadre de classement : Rhumatologie

DES + FST/option : Rhumatologie

Mots-clés : Fracture, Périprothétique, Ostéoporose, Densitométrie, FLS, DMO

Résumé :

Introduction : Les fractures périprothétiques (PPF) sont de plus en plus fréquentes en raison d'une demande croissante d'arthroplasties dans une population vieillissante. Elles sont peu étudiées et la nature ostéoporotique de ces fractures est encore débattue. L'objectif principal de cette étude était de comparer des patients ayant une fracture périprothétique de hanche (PPF) à des patients nécessitant une arthroplastie totale de hanche suite à une fracture de l'extrémité supérieure du fémur (FESF).

Matériel et méthode : Il s'agit d'une étude rétrospective réalisée au CHU de Lille regroupant 517 PPF identifiées entre Janvier 2016 et Décembre 2022 chez des patients ≥ 50 ans via la filière fracture et/ou par le codage M96.6 (CIM 10). Parmi ces 517 PPF, il y avait 71 PPF avec une densitométrie osseuse (DMO) disponible. Ces patients ont été comparés à 117 patients identifiés par la filière fracture nécessitant une arthroplastie totale de hanche suite à une FESF et ayant eu une DMO.

Résultats : Parmi les 71 patients avec PPF et DMO, il s'agissait majoritairement de femmes (78,9%), d'un âge moyen de $79,3 \pm 10,6$ ans. Les patients du groupe PPF, comparativement au groupe FESF, étaient plus âgés ($79,3 \pm 10,6$ vs. $74,5 \pm 10,7$ ans, $p < 0,002$), plus souvent obèses ($\text{IMC} \geq 30 \text{ kg/m}^2$ 29,6% vs. 8,6%, $p < 0,001$) et comorbides (Score de Charlson avec une médiane de 5,0 (4,0-7,0) vs. 4,0 (3,0-5,5), $p < 0,001$). Les chutes (54,3% vs. 26,1%, $p < 0,001$) et les antécédents de fractures de fragilité (69,0% vs. 44,0%, $p < 0,001$) étaient également plus fréquents. La DMO était anormale (ostéopénie/ostéoporose) pour 71,8% d'entre eux (vs. 91,5%, $p < 0,001$). Les T-scores moyens ajustés (SEM) sur l'âge, le sexe et l'IMC différaient entre les 2 groupes au rachis lombaire (-0,5 (0,2) vs. -1,2 (0,2), $p = 0,008$) mais pas au col fémoral (-2,0 (0,1) vs. -2,3 (0,1), $p = 0,08$) ni à la hanche totale (-1,7 (0,2) vs. -1,8 (0,1), $p = 0,49$).

Discussion : La prévalence de l'ostéoporose/ostéopénie dans le groupe PPF, bien qu'élevée, est significativement inférieure à celle du groupe FESF. Pour autant, les caractéristiques démographiques (âge, IMC), cliniques (comorbidités, chutes) et les facteurs de risque d'ostéoporose (antécédents de fracture de fragilité) des patients avec PPF semblent indiquer une fragilité plus importante que chez les patients avec FESF. Au vue des résultats de cette étude, il y a un rationnel à traiter les PPF comme des fractures ostéoporotiques et à améliorer la prévention primaire des PPF avant toute arthroplastie, en partenariat avec les orthopédistes.

Composition du Jury :

Président : Professeur Christophe CHANTELOT

Assesseurs : Docteur Isabelle LEGROUX & Docteur Sophie PUTMAN

Directeur de thèse : Professeur Julien PACCOU