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ORIGINAL ARTICLE

Bone, cognitive, and anthropometric profiles and their relation to fracture sites in fallers: a cross-sectional study

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Abstract

Summary Risk factors involved in the different osteoporotic fracture locations are not well-known. The results of this study suggest that there is not one typical profile characterising a particular fracture site but that the occurrence of a fracture may result from the combination of different bone, cognitive, and anthropometrics characteristics.

Purpose Risk factors involved in the different osteoporotic fracture locations are not well-known. The aim of this study was to identify the differences in bone, cognitive, and anthropometric characteristics between different fracture sites, and to determine whether the site of a fall-related fracture is related to a specific profile.

Methods One hundred six women aged 55 years and older with a recent fall-related fracture of the hip ($n=30$), humerus ($n=28$), wrist ($n=32$), or ankle ($n=16$) were included. Bone, cognitive, and anthropometric characteristics were first compared among the four fracture site groups. Then, a principal component analysis (PCA) was performed and a comparison was made between the four profiles identified by the first two PCA components.

Results The four fracture site groups differed significantly in their education level, bone mineral density (BMD), body mass index (BMI), fear of falling, and number of errors in the Trail Making Test B, an executive function test. Each of the four fracture sites was found in each four PCA profiles, albeit with a different distribution. The profiles differed mainly by bone, cognitive, and anthropometric characteristics, but also by fear of falling.

Conclusions The fall-related fracture sites differ significantly in anthropometric and bone parameters, in fear of falling and in cognitive abilities. There is not one typical bone, cognitive, and anthropometric profile characterising a particular fall-related site, but rather several possible profiles for a given site. This suggests that the fracture site depends on a combination of several characteristics of the patient.

Keywords Bone-brain-nervous system interactions · DXA · Fracture risk assessment · Osteoporosis

Introduction

Osteoporotic fractures are extremely common, with an estimated 3.5 million new fractures in men and women aged 50 years or more in 2010 in the European Union [1]. The consequences of these fractures in terms of quality of life and economic impact are major, and the incidence of osteoporotic fractures and their socioeconomic consequences are likely to increase with an aging population. Osteoporotic fractures, with the exception of vertebral fractures, are mostly secondary to low-intensity trauma such as a fall from standing height [2, 3]. Their onset is of multifactorial origins linked to risk factors for bone fragility, but also falls [4, 5]. For example, age, vitamin D deficiency, muscle weakness, alcohol consumption, and Parkinson's disease are risk factors for both falls and osteoporosis.

Some authors suggest that age, bone mineral density (BMD), and body mass index (BMI) have a different impact on fracture risk depending on the fracture site. In the "Million Women Study" cohort, the role of age, body mass index (BMI), and physical activity on the risk of fracture at several

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sites were explored in 1,154,821 postmenopausal British women with a mean age of 56 years and a mean follow-up of 11 years. A high BMI increased the risk of humerus and ankle fractures, while a low BMI increased the risk of wrist and hip fractures [6]. In the same cohort, the relationship between the incidence rate of fractures and age was significantly more pronounced for hip than for ankle fractures [6]. In the EPIDOS French cohort, the relationship between BMD and fracture risk was assessed in women aged 75 years or older. The risk of hip fracture was assessed in 7575 women with an average of 1.9 years of follow-up, and the risk of humerus fracture was assessed in 6901 women with an average of 3.6 years of follow-up. A low BMD appeared to be more strongly associated with hip than humerus fracture risk [RR (95% CI) for a 1 SD decrease in femoral neck BMD: 1.8 (1.5–2.2) vs. 1.4 (1.1–1.7)] [4, 5]. Although some studies did not find any association between age, BMD, and ankle fracture risk, a recent meta-analysis that included seven observational cross-sectional studies found that older adults with a mean age of 65 years with ankle fractures have lower BMD than healthy controls (effect size 0.34; 95% CI 0.09–0.58; $I^2 = 98.39\%$) [7].

Several studies have investigated the factors playing a role in the site of a fall-related fracture. Some of them suggest that slow walking would increase the risk of falls [8, 9], especially the risk of lateral falls [10], and that lateral falls would preferentially increase the risk of hip [11] and humerus [12] fractures. Slow walking is known to be associated with many risk factors for falls, such as impaired cognitive functions, especially executive functions [13, 14], fear of falling [15], low handgrip strength [16], polypharmacy [17], and use of psychotropic drugs [18]. Cognitive functions, particularly the executive functions such as planning, cognitive flexibility, and decision making [19], seem to play a central role. Indeed, an alteration in planning ability, which is one of the key executive functions, could influence the orientation of the fall (forward, sideways, backward) and could also decrease an individual's ability to protect themself during a fall, in particular with the hands. Individuals with impaired executive functions may therefore be more likely to fracture their hip or humerus and less likely to fracture their wrist than those with better cognitive functions.

A multinational observational study examined the health-related quality of life impact of major fragility fractures in 4126 adults aged ≥ 50 years. At a 12-month follow-up, the proportion of patients who had recovered the health-related quality of life they had before their fracture varied across fracture sites (from 37.3% for hip to 49.5% for humerus) [20]. In the Australian arm of the cohort that included 524 older adults with a mean age of 70 years, the 5-year mortality rate was the highest in hip fracture participants (24.7%), followed by vertebral (16.4%), humeral (13.5%), and distal forearm fracture participants (6.1%) [21].

Therefore, as it can be hypothesised that fall victims with fractures at different sites have different profiles, the aim of this study was, first, to identify the differences in bone, cognitive, and anthropometric characteristics between different fracture sites in middle-aged and older adults who experienced a fall-related fracture. We, then, aimed to determine whether there are specific bone, cognitive, and anthropometric profiles related to the fracture sites.

Methods

Study design and population

We conducted an exploratory cross-sectional study.

The participants were 106 women, aged 55 years or older who had experienced a fall-related fracture. They were divided into four groups according to the fracture site: hip, ankle, humerus, or wrist. These women were part of the "Fall, Fracture and Cognition" cohort which was part of a hospital clinical research program that aimed at studying the role of cognitive impairment in fall-related fractures. The fracture had to be the result of a low-energy fall, e.g. the result of falling from standing height or less, while standing or walking, that occurred within 6 months prior to inclusion. Participants were recruited in the fracture liaison department of the University Hospital of Caen between November 2011 and May 2017. As the aim of the study was to analyse the relationship between the occurrence of a fall and the occurrence of a fracture, women with an osteoporotic vertebral fracture were not included.

Exclusion criteria were conditions affecting balance (for example, Parkinson's disease, stroke sequelae, or neuromuscular diseases), heavy alcohol consumption (more than 14 units of alcohol per week), visual impairment (corrected acuity < 6/10), and severe depression (score below 30 on the Montgomery-Asberg Depression Rating Scale) [22]. Fractures secondary to localised bone fragility, for example bone metastasis, were excluded. In addition, to meet one of the criteria of the "Fall, Fracture and Cognition" cohort, there were as many participants under as over 75 years of age in each fracture site group.

Free and informed consent was obtained for all participants. The study was approved by the Lower Normandy Ethics Committee (No. 2011A00556-35; Clinical Trial Registration: NCT02292316).

Data collected

The following data were collected during the medical examination: age, BMI, number of comorbidities as determined by the 12 classes included in the Kaplan-Feinstein index [23], and number of active molecules in the drugs consumed (two

molecules were counted in the case of a combination of two molecules in a single tablet) while distinguishing between polypharmacy (at least 5 molecules) [24], and number of psychotropic drugs. Participants were also asked about their attempt to protect themselves during the fall that caused their fracture.

A thorough cognitive assessment was conducted by a neuropsychologist. After collecting the education level (in number of years of schooling), global cognition was assessed by both the Mini Mental State Examination (MMSE) [25] and Montreal Cognitive Assessment (MoCA), [26] the latter being more sensitive than the MMSE in detecting mild cognitive impairment. Deficit thresholds were identified using French norms stratified by age, socio-cultural level, and gender for MMSE, [27] and by a score below 26 for the MoCA [28]. Several cognitive sub-domains were also assessed: processing speed using Zazzo's cancellation test [28] and the Trail Making Test (TMT) A [29], visuo-spatial attention using the Zazzo test [28], memory with the Rey Figure Test [30] and the Digit Span (forward and backward) [31], and executive functions with the TMT B [29], the TMT B-A score [32, 33], and copy of the Rey Figure [30].

In addition, autonomy was assessed by the Instrumental Activities of Daily Living (IADL) scale, which covers eight activities [34]. A score of 8 and 32 reflects perfect autonomy and total dependence for these activities, respectively. Fear of falling was assessed using the French version of the Activities-specific Balance Confidence Scale (ABC-s), which covers 16 situations with a greater or lesser risk of falling [35]. Rated from 0 to 160, a score of 160 reflects perfect confidence in one's balance. Handgrip was measured with a dynamometer. Each participant performed 2 trials per hand, then the best performance was recorded.

Finally, a total hip BMD was measured using osteodensitometry by biphotonic X-ray absorptiometry. A T-score below − 2.5 is considered the definition of osteoporosis.

Statistical analysis

Due to the small size of the groups, non-parametric analyses were conducted for quantitative variables. Intergroup comparisons were performed using the Kruskal–Wallis test followed by the Nemenyi post hoc test. Percentages were compared by chi-square tests if the theoretical numbers were greater than or equal to 5 and Fisher's exact tests otherwise. Multinomial logistic regressions were performed for cognitive tests having a p-value of less than 0.10 in univariate analysis adjusting for age and education level.

A principal component analysis (PCA) was performed to identify the groups and find the axes and attributes that contributed significantly to the variance. Two-dimensional scatterplots, thus forming 4 quadrants (from which 4 groups will be constituted), were created using the first two principal components, which represented the most variance (eigenvalue > 1.0). A Varimax rotation was performed to maximize the variance shared between items and thus obtain a simple structure that is easier to interpret. The variables included in the PCA were selected for their relevance and ability to be obtained during routine consultations. These were age, BMI, BMD, handgrip, MMSE score, number of omissions in the Zazzo test, and TMT B-A score.

Participants were then divided into groups named "profiles" according to the quadrants formed by the components highlighted by the PCA. Distribution of the fracture site groups according to the profiles and inter-profile comparisons were then done using the same statistical tests as those used for the above intergroup comparisons. However, no adjustments were made since the objective was to prioritise the interactions between the variables.

Results were considered significant if the two-tailed p-value was less than 0.05, and as a trend if it was between 0.05 and 0.10. The software used was IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Cor.

Results

Comparisons between fracture site groups

Demographic, clinical, and cognitive data of the study population are given in Table 1. Among the 106 participants, there were 30 (28.3%), 16 (15.1%), 28 (26.4%), and 32 (30.2%) participants in the hip, ankle, humerus, and wrist groups, respectively. Comparisons of demographic and clinical parameters by fracture site groups are shown in Table 1. There were a few missing data because some participants could not perform some examinations as specified in the legend of Table 1. The 4 groups differed significantly in education level ($p = 0.029$), BMI ($p = 0.001$), BMD ($p = 0.026$), fear of falling ($p = 0.017$), and fall protection ($p = 0.001$). For the cognitive parameters, the only significant difference between groups was for the number of errors in the TMT B ($n = 1$ (0.00–2.00), 0 (0.00–0.00), 0.50 (0.00–1.25), and 0 (0.00–0.75) for the hip, ankle, humerus, and wrist group, respectively; $p = 0.021$). Post hoc tests indicated that the hip group was the only group that differed from the others. Compared to the humerus group, the hip group had lower BMI ($p < 0.001$) and a tendency to have a lower BMD ($p = 0.052$) and lower ABC-s score (and therefore more fear of falling) ($p = 0.087$). Compared to the ankle group, the hip group had a significantly lower ABC-s score ($p = 0.033$), as well as a tendency to make more errors in the TMT B ($p = 0.071$). Finally, compared to the wrist group, the hip group had a higher education level ($p = 0.034$). Of note, 21/30 participants (75.0%) in the wrist group tried to protect themselves

Table 1 Demographic, clinical, and cognitive data of the study population ($n=106$) and by fracture site, and comparison of medians and percentages by fracture site

	Study population ($n=106$)	Hip ($n=30$)	Ankle ($n=16$)	Humerus ($n=28$)	Wrist ($n=32$)	p-value[a]	Post hoc: p-value[b]
Age (years)	70.5 (63.0–79.0)	74.0 (66.0–80.3)	64.5 (61.5–73.3)	70.0 (62.3–77.8)	72.5 (62.3–81.0)	0.177	-
Education (number of years of study)	11.0 (9.0–12.3)	11.5 (9.8–14.3)	11.5 (9.3–14.8)	11.0 (9.0–12.0)	10.0 (8.0–11.0)	0.029	W < Hi: 0.034
BMI (kg/m^2)	25.4 (22.8–30.0)	23.7 (20.5–28.4)	25.3 (23.3–32.6)	29.2 (25.5–32.1)	25.3 (22.2–30.1)	0.001	Hi < Hu: < 0.001, W < Hu: 0.085
Polypharmacy, *n* (%)	58 (54.7%)	18 (60.0%)	6 (37.5%)	16 (57.1%)	18 (56.3%)	0.523	-
Psychotropic drugs (number)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	0.371	-
Comorbidities (number)	1.0 (1.0–2.3)	1.0 (0.0–2.3)	2.0 (1.0–2.8)	1.5 (1.0–2.0)	2.0 (0.0–3.0)	0.752	-
IADL (score)	8.0 (8.0–8.0)	8.0 (8.0–9.0)	8.0 (8.0–8.0)	8.0 (8.0–8.0)	8.0 (8.0–8.8)	0.072	-
ABC-s (score)	119.3 (90.3–139.5)	101.3 (78.2–119.6)	128.0 (109.1–144.3)	124.8 (106.6–138.0)	120.7 (87.6–141.0)	0.017	Hi < A: 0.033, Hi < Hu: 0.087
Handgrip (kg)[c]	17.6 (14.2–21.4)	18.4 (15.6–21.9)	21.3 (15.4–24.2)	17.1 (14.1–19.9)	16.9 (13.2–21.1)	0.059	-
Fall protection, yes, *n* (%)	42 (42.9%)	7 (25.0%)	4 (28.6%)	10 (35.7%)	21 (75.0%)	0.001	-
BMD (T-score)[d]	− 1.4 (− 2.0 to − 0.7)	− 1.7 (− 2.9 to − 1.5)	− 1.2 (− 1.8 to − 0.2)	− 1.2 (− 1.7 to − 0.3)	− 1.2 (− 2.1 to − 0.6)	0.026	Hi < Hu: 0.052
Osteoporosis, *n* (%)[d]	16 (15.8%)	8 (30.8%)	1 (6.3%)	2 (7.4%)	5 (15.6%)	0.100	-
Global cognition							
MMSE (score)	28.0 (26.0–29.0)	28.0 (25.0–29.0)	29.0 (28.0–29.0)	29.0 (28.0–29.0)	27.0 (25.3–29.0)	0.085	-
MMSE impaired, *n* (%)	11 (10.4%)	4 (13.3%)	0 (0.0%)	2 (7.1%)	5 (15.6%)	0.371	-
MoCA (score)	27.0 (24.0–29.0)	27.0 (22.8–29.0)	28.0 (26.3–29.8)	27.5 (25.0–29.0)	26.5 (21.5–29.0)	0.148	-
MoCA, impairment, *n* (%)	36 (34.0%)	13 (43.3%)	2 (12.5%)	9 (32.1%)	12 (37.5%)	0.201	-
Processing speed							
Zazzo Test, completion time (sec)[e]	129.0 (103.5–156.0)	137.5 (99.8–166.5)	117.5 (87.8–153.5)	128.0 (106.0–153.0)	137.0 (106.5–161.5)	0.410	-
TMT A, completion time (sec)[f]	37.2 (29.0–50.0)	42.7 (32.6–50.6)	36.0 (26.5–43.8)	33.5 (28.3–52.5)	35.9 (31.5–51.1)	0.281	-
TMT A, impaired completion time, *n* (%)[f]	23 (22.1)	9 (30.0%)	2 (12.5%)	6 (21.4%)	6 (20.0%)	0.618	-
Visuo-spatial attention							
Zazzo Test, omissions (number)[e]	2.0 (1.0–4.0)	1.5 (1.0–3.0)	3.0 (2.0–4.0)	2.0 (1.0–4.0)	1.0 (0.0–3.5)	0.341	-
Zazzo Test, correct responses (number)[e]	38.0 (36.0–39.0)	38.5 (37.0–39.0)	37.0 (36.0–38.0)	38.0 (36.0–39.0)	39.0 (36.5–40.0)	0.349	-
Memory							
Digit Span (Forward) (number)	7.0 (6.0–9.0)	7.0 (6.0–8.3)	7.0 (7.0–8.0)	7.0 (6.0–9.0)	8.0 (6.0–9.0)	0.650	-
Digit Span (Backward) (number)	5.0 (4.0–6.0)	4.0 (3.0–5.8)	5.5 (5.0–6.0)	5.0 (4.0–6.0)	5.0 (3.3–6.0)	0.092	-
Rey Figure Test, recall (score)	13.0 (10.5–18.0)	13.5 (11.8–18.3)	11.5 (8.8–19.3)	11.5 (8.5–17.5)	13.8 (11.4–18.3)	0.444	-
Executive funtions							
TMT B, errors (number)[g]	0.0 (0.0–1.0)	1.0 (0.0–2.0)	0.0 (0.0–0.0)	0.50 (0.0–1.25)	0.0 (0.0–0.75)	0.021	A < Hi: 0.071

Table 1 (continued)

	Study population ($n=106$)	Hip ($n=30$)	Ankle ($n=16$)	Humerus ($n=28$)	Wrist ($n=32$)	p-value[a]	Post hoc: p-value[b]
TMT B, completion time (sec)[h]	88.0 (67.1–118.5)	89.3 (74.0–149.0)	91.5 (61.5–105.0)	87.8 (61.8–122.5)	85.0 (66.8–116.9)	0.611	-
TMT B, impaired completion time, n (%)[h]	19 (19.8)	10 (37.0%)	1 (6.3%)	5 (19.2%)	3 (11.1%)	0.061	-
TMT B-A, impaired difference, n (%)[h]	15 (15.6)	7 (25.9%)	1 (6.3%)	4 (15.4%)	3 (11.1%)	0.361	-
Rey Figure Test, copying strategy (score)	2.0 (1.0–4.0)	2.0 (1.0–3.3)	2.0 (1.0–4.0)	4.0 (2.0–4.0)	2.5 (1.0–4.0)	0.167	-

Quantitative variables are expressed as median (1st quartile–3rd quartile) and qualitative variables as percentage

[a]Kruskal-Wallis, Fisher, or chi 2 depending on the variable

[b]Nemenyi test (only $p<0.10$ are presented)

[c]$n=103$ (hip = 29, ankle = 14, humerus = 28, wrist = 32)

[d]$n=101$ (hip = 26, ankle = 16, humerus = 27, wrist = 32)

[e]$n=102$

[f]$n=104$

[g]$n=97$

[h]$n=95$

Missing data for BMD and handgrip resulted from examinations not performed due to technical problems for BMD, hand osteoarthritis and pain for handgrip, and fatigue or inability to perform for some cognitive tests. *NS*, not significant; *Hi*, hip; *A*, ankle; *Hu*, humerus; *W*, wrist; *IADL*, Instrumental Activities of Daily Living; *BMI*, body mass index; *BMD*, bone mineral density; *TMT*, trail making test; *ABC-s*, Activities-specific Balance Confidence Scale; *MMSE*, Mini Mental State Examination; *MoCA*, Montreal Cognitive Assessment

during the fall, while only 7/30 (25.0%), 4/16 (28.6%), and 10/28 (35.7%) in the hip, ankle, and humerus groups did so, respectively (see Table 1). Besides these significant intergroup differences, a trend towards significance was found for the MMSE ($p=0.085$), Digit Span (Backward) ($p=0.092$), and percentage of impaired TMT B completion times ($p=0.061$).

In the multivariate analysis performed on cognitive scores after adjustment for age and education level, the TMT B remained significantly different between groups ($p=0.014$), whereas the trend disappeared for MMSE ($p=0.111$) and Digit Span (Backward) ($p=0.269$). The analysis was not carried out for the percentage of impaired TMT B completion times because this score was already standardised for age and education level.

Principal component analysis

Some participants ($n=19$) had to be excluded from the PCA due to missing data. Results of the PCA are shown in Table 2 for the matrix with the three components obtained after rotation, and in Fig. 1 for the plot of the components in space after rotation. In the first component, i.e. "cognitive", the higher the number of omissions on the Zazzo test, the greater the difference in completion time between TMT B and TMT A and the lower the MMSE. This component explained 32.64% of the total variance. In the second component, "bone and anthropometric", that explained 22.40% of the total variance, the higher the BMI, the higher the BMD. In the third component, "age", that explained 16.65% of the total variance, the higher the age, the lower the handgrip.

The PCA identified 8 different profiles based on combinations of the 3 components. However, because there were so few participants in each profile ($n=5$ to 17), we decided to keep only the first two. This allowed us to obtain 4 profiles with more participants ($n=12$ to 31).

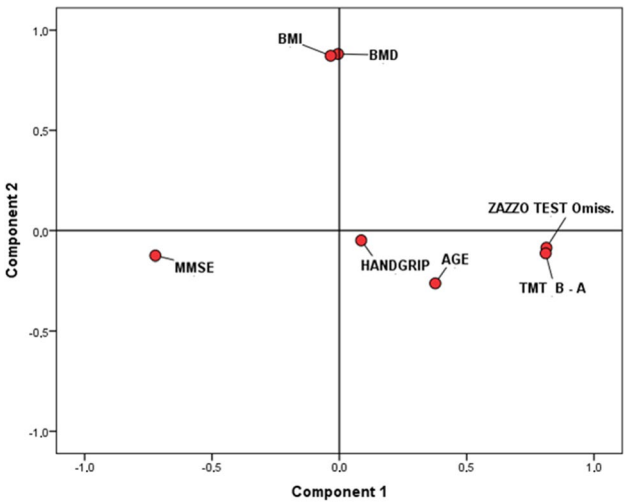

Fig. 1 Cognitive scores load highly on the first component, positively for the Zazzo Test and TMTB-A, and negatively for MMSE. Handgrip and age load moderately on this first component. BMI and BMD have a load near zero on the first component, but load highly on the second

Distribution of the fracture site groups by profile (n = 87)

The 4 profiles highlighted by the first two components were named P1 to P4. Among the 19 participants excluded from the PCA, 4 (21.1%), 3 (15.8%), 3 (15.8%), and 9 (47.4%) belonged to the hip, ankle, humerus, and wrist groups, respectively. Distribution of the fracture sites by profile is shown in Fig. 2 for the individual distribution of participants.

Each of the 4 fracture sites was found in each profile. However, P1 ($n=31$) mainly included wrist and hip fractures (38.7% and 35.5% respectively), P2 ($n=26$) mainly humerus fractures (50.0%), P3 ($n=18$) mainly hip fractures (50.0%), and P4 ($n=12$) mainly wrist and humerus fractures (50.0% and 33.3%, respectively).

Table 2 Component matrix after Varimax rotation

Variables	Cognitive component	Bone and anthropometric component	Age component
Zazzo Test, omissions	0.813*	−0.086	−0.012
TMT B-A	0.810*	−0.114	−0.168
MMSE	−0.722*	−0.125	0.001
BMD	−0.005	0.881*	0.177
BMI	−0.034	0.872*	−0.048
Handgrip	0.086	−0.049	0.909*
Age	0.377	−0.262	−0.703*

*Coefficient superior to ±0.5; *TMT B*, Trail Making Test B; *BMD*, bone mineral density; *BMI*, body mass index

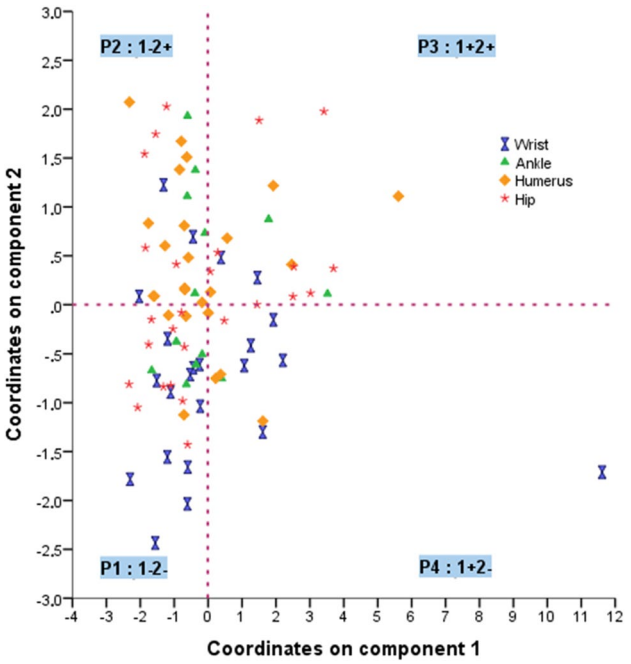

Fig. 2 The fracture sites (i.e. wrist, ankle, humerus, and hip) are distributed into four profiles according to their coordinates on the first two components. Profile 1 (P1) corresponds to fractures with negative coordinates on the axes of the two components (1–2 −). Profile 2 (P2) corresponds to fractures with negative coordinates on the axis of the first component and positive on the axis of the second component (1–2 +). Profile 3 (P3) corresponds to fractures with positive coordinates on the axes of both components (1 + 2 +). Profile 4 (P4) corresponds to fractures with positive coordinates on the axis of the first component and negative on the axis of the second component (1 + 2 −)

Profile comparisons based on the first two components

There were many significant differences between the different profiles, both in terms of demographic, clinical, and cognitive parameters (Table 3).

Significant differences between profiles were as follows: P2 was younger than P3 ($p = 0.023$) and P4 ($p = 0.020$), and the number of years of schooling was higher in P1 than in P3 ($p = 0.007$). On the other hand, P2 and P3 had a higher BMI and BMD than P1 and P4 ($p < 0.001$ for each comparison except for P4 vs P3: $p = 0.004$). In P2 and P3, no participants had densitometric osteoporosis, unlike P1 and P4 which included 9/31 (29.0%) and 2/12 (16.7%) patients with osteoporosis, respectively. P4 also had significantly less autonomy than P2 ($p = 0.045$) and less fear of falling than P1 ($p = 0.038$).

Regarding cognition, significant differences between profiles were found for all cognitive functions assessed, except processing speed. Thus, P1 and P2 had better global cognition than P3 and P4 ($p < 0.001$ for the 4 post hoc comparisons of the MMSE score; for the MoCA score: $p < 0.001$ for P3 vs P1, $p = 0.005$ for P3 vs P2, and $p = 0.012$ for P4 vs P1); only the P2 vs P4 comparison for the MoCA score was not significant. The percentage of impaired MMSE and MoCA scores also significantly differed between groups ($p < 0.001$ for each score), with again, lower percentage of impaired score in P1 and P2 than in P3 and P4 (for instance: none of the participants had an impaired MMSE score in P1 and P2 whereas there were 16.7 and 25% in P3 and P4, respectively). Furthermore, P3 had poorer visuo-spatial attention than P1 and P2 (number of correct responses on the Zazzo test: $p < 0.001$ for both), and worse memory than P1 (Backward Digit Span: $p = 0.025$, Rey Figure test: $p = 0.028$). P4 showed worse executive function performance on the TMT B (number of errors and completion time) than P1 ($p = 0.038$ and 0.006, respectively) and P2 ($p = 0.018$ and 0.015, respectively). P3 also performed worse on the TMT B completion time than P1 and P2 ($p = 0.005$ and $p = 0.014$, respectively) and made more errors than P2 ($p = 0.014$). In addition, the percentage of impaired TMT B completion time and impaired TMT B-A significantly differed between groups ($p = 0.027$ and < 0.001, respectively), with again, lower participants with impaired scores in P1 and P2 (less than 10%) than P3 and P4 (between 22 and 41%). Finally, P3 had less copying strategy (Rey Figure) than P1 and P2 ($p = 0.001$ and $p = 0.006$, respectively).

It should also be noted that the percentage of participants who protected themselves during the fall was not significantly different between profiles.

Discussion

The results of this study, conducted in a group of women with a recent fall-related fracture, confirm that the different fracture sites differ significantly in anthropometric and bone parameters. Moreover, the study shows that they also differ in cognitive abilities. Interestingly, several clinical profiles based on bone, cognitive, and anthropometric characteristics and with a specific fracture site distribution could be identified.

The four fracture sites (hip, humerus, wrist, and ankle) differ significantly in education level, BMI, BMD, fear of falling, fall protection, and number of errors in the TMT B. However, only the participants with a hip fracture differ significantly from those with other fractures. This was found for anthropometric, bone, and cognitive characteristics. The lower BMI and BMD in the hip compared to the humerus fracture group are consistent with previous studies [3–5, 36]. Patients with a hip fracture are also known to be older than those with a wrist or ankle fracture [5, 36], which was not found in the present study since we purposely recruited participants with similar ages in each fracture group. Interestingly, this suggests that the above characteristics of the

Table 3 Comparison of medians and percentages of demographic, clinical, and cognitive data by profile based on the first two components

		P1 ($n=31$)	P2 ($n=26$)	P3 ($n=18$)	P4 ($n=12$)	p-value[a]	Post hoc: p-value[b]
Age (years)		69.0(63.0–76.0)	63.5 (58.8–68.2)	73.5 (67.5–83.5)	74.5 (66.3–83.5)	0.006	P2 vs P3: 0.023, P2 vs P4: 0.020
Education (number of years of schooling)		12.0 (10.0–16.0)	11.0 (9.0–12.5)	9.0 (8.8–11.0)	10.5 (8.3–12.0)	0.008	P3 vs P1: 0.007
BMI (kg/m^2)		22.7 (21.0–24.4)	31.2 (29.0–34.0)	28.5 (25.8–31.8)	23.3 (21.1–24.6)	< 0.001	P1 vs P3: < 0.001, P1 vs P2: < 0.001 P4 vs P3: 0.004, P4 vs P2: < 0.001
Handgrip (kg)		19.3 (14.9–21.9)	17.0 (14.2–20.8)	20.5 (13.7–23.4)	18.8 (16.2–23.2)	0.469	-
Comorbidities (number)		1.0 (0.0–2.0)	1.0 (0.0–2.0)	2.0 (1.0–3.0)	1.5 (1.0–3.0)	0.216	-
BMD (T-score)		− 1.9 (− 2.6 to − 1.5)	− 0.5 (− 1.2 to 0.0)	− 0.7 (− 1.2 to − 0.1)	− 1.6 (− 2.4 to − 1.5)	< 0.001	P1 vs P3: < 0.001, P1 vs P2: < 0.001 P4 vs P3: 0.001, P4 vs P2: < 0.001
Osteoporosis, n (%)		9 (29.0)	0 (0.0)	0 (0.0)	2 (16.7)	0.002	-
Polypharmacy, n (%)		11 (35.5)	13 (50.0)	13 (72.2)	8 (66.7)	0.060	-
Psychotropic drugs (number)		0.0 (0.0–1.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	0.118	-
ABC-s (score)		133.2 (106.4–147.0)	114.2 (82.7–139.3)	117.4 (81.2–132.7)	95.4 (63.9–131.8)	0.029	P4 vs P1: 0.038
IADL (score)		8.0 (8.0–8.0)	8.0 (8.0–8.0)	8.0 (8.0–8.0)	8.0 (8.0–10.0)	0.032	P2 vs P4: 0.045
Fall protection, yes, n (%)		14 (48.3)	9 (37.5)	8 (47.1)	5 (45.5)	0.873	-
Global cognition	MMSE (score)	29.0 (28.0–29.0)	29.0 (29.0–30.0)	26.0 (24.5–27.0)	26.5 (23.5–28.0)	< 0.001	P3 vs P1: < 0.001, P3 vs P2: < 0.001, P4 vs P1: < 0.001, P4 vs P2: < 0.001
	MMSE, impairment, n (%)	0 (0.0)	0 (0.0)	3 (16,7)	3 (25.0)	< 0.001	
	MoCA (score)	29.0 (27.0–30.0)	28.0 (26.0–29.5)	25.0 (21.5–27.5)	26.0 (22.3–27.8)	< 0.001	P3 vs P2: 0.005, P3 vs P1: < 0.001, P4 vs P1: 0.012
	MoCA, impairment, n (%)	3 (9.7)	4 (15.4)	11 (61.1)	5 (41.7)	< 0.001	
Processing speed	Zazzo Test, completion time (sec)	128.0 (95.0–155.0)	116.0 (102.5–151.5)	129.0 (122.5–161.0)	134.5 (97.5–151.5)	0.245	-
	TMT A, completion time (sec)	33.0 (29.0–42.0)	34.0 (28.0–46.0)	43.7 (31.4–51.8)	40.0 (24.9–56.5)	0.196	-
	TMT A, impaired completion time, n (%)	4 (12.9)	3 (11.5)	4 (22.2)	3 (25.0)	-	-

Table 3 (continued)

		P1 ($n=31$)	P2 ($n=26$)	P3 ($n=18$)	P4 ($n=12$)	p-value[a]	Post hoc: p-value[b]
Visuo-spatial attention	Zazzo Test, omissions (number)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	5.0 (3.0–7.5)	3.5 (1.0–4.8)	-	-
	Zazzo Test, correct responses (number)	39.0 (38.0–40.0)	39.0 (38.0–40.0)	34.0 (32.5–36.5)	36.5 (35.3–39.0)	< 0.001	P3 vs P2: < 0.001, P3 vs P1: < 0.001 P4 vs P1: 0.086
Memory	Digit Span (Forward) (number)	7.0 (6.0–9.0)	8.0 (7.0–9.0)	7.0 (6.0–9.0)	8.0 (6.0–9.0)	0.448	-
	Digit Span (Backward) (number)	5.0 (5.0–6.0)	4.0 (4.0–6.0)	4.0 (3.5–5.0)	4.0 (3.3–5.8)	0.014	P3 vs P1: 0.025
	Rey Figure Test, recall (score)	16.5 (11.0–21.0)	15.5 (11.5–19.3)	12.5 (9.5–13.3)	14.0 (10.0–17.6)	0.036	P3 vs P1: 0.028
Executive functions	TMT B, errors (number)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	1.0 (0.0–2.0)	1.5 (0.0–2.0)	0.004	P2 vs P4: 0.018, P1 vs P4: 0.038 P2 vs P3: 0.099
	TMT B, completion time (sec)	76.0 (62.0–98.0)	80.0 (59.5–94.2)	112.0 (86.3–142.1)	113.5 (111.4–160.0)	< 0.001	P1 vs P3: 0.005, P1 vs P4: 0.006, P2 vs P3: 0.014, P2 vs P4: 0.015
	TMT B, impaired completion time, *n* (%)	3 (9.7)	2 (7.7)	5 (27.8)	5 (41.7)	0.027	
	TMT B-A, impaired difference, *n* (%)	0 (0.0)	2 (7,7)	4 (22.2)	5 (41.7)	< 0.001	
	Rey Figure Test, copying strategy (score)	1.0 (1.0–4.0)	2.0 (1.0–4.0)	4.0 (4.0–4.0)	2.5 (1.3–4.0)	0.001	P1 vs P3: 0.001, P2 vs P3: 0.006

Quantitative variables are expressed as median (1st quartile–3rd quartile), and qualitative variables as percentage

[a]ANOVA, Kruskal–Wallis, Fisher, or chi2 depending on the variable

[b]Neminyitest, only $p < 0.10$ are presented

IADL, Instrumental Activities of Daily Living; *BMI*, body mass index; *BMD*, bone mineral density; *ABC-s*, Activities-specific Balance Confidence Scale; *TMT*, Trail Making Test; *MMSE*, Mini Mental State Examination; *MoCA*, Montreal Cognitive Assessment

Table 4 Summary of profile characteristics

	P1	P2	P3	P4
Fracture site	Wrist 38.7% Hip 35.5% Ankle 16.1% Humerus 9.7%	Humerus 50.0% Hip 19.2% Ankle 19.2% Wrist 11.5%	Hip 50.0% Humerus 27.8% Ankle 11.1% Wrist 11.1%	Wrist 50.0% Humerus 33.3% Hip 8.3% Ankle 8.3%
Age	69	63	73	74
Education level	+ +	+	-	+
Fear of falling	Very low	Low	Low	Medium
Autonomy	Very high	Very high	Very high	High
BMI[a]	Normal	Overweight-obesity	Overweight-obesity	Normal
BMD[b] (T-score)	Low (between − 1 and − 2.5)	Normal (> − 1)	Normal (> − 1)	Low (between − 1 and − 2.5)
Osteoporosis	29.9%	0%	0%	16.7%
Fall protection	48.3%	37.5%	47.1%	45.5%
Cognition				
Global cognition	High	High	Medium[c]	Medium[c]
Processing speed	High	High	High	High
Visuo-spatial attention	High	High	Medium	Medium
Memory	Very high	High	Medium	High
Executive functions	High	High	Medium	Low

−, +, and + +: relative difference in the education level

[a]Body mass index according to WHO standards[43]

[b]Average bone mineral density according to WHO standards[40]

[c]Still remains on average above the deficit score

hip group would not be limited to the elderly since they also apply to seniors as soon as they reach 55 years old. Furthermore, to our knowledge, no studies have investigated fear of falling and cognitive abilities related to fracture site. In the present study, patients with a hip fracture tended to have poorer executive functions than those with an ankle fracture, which is a new finding. This suggests that impaired executive functions can lead to lateral falls, which, in combination with a low BMI and BMD, may cause more hip fractures. Patients with a hip fracture also had a greater fear of falling. However, because fear of falling was assessed after the fracture occurrence, further studies are required to improve knowledge about the relationship between fear of falling and fracture sites.

The four distinct clinical profiles identified by PCA (named P1 to P4) show distinct characteristics which are summarised in Table 4. There is no clear relationship between a fracture site and a given profile. Each profile is defined by different interactions between anthropometric, bone, and cognitive characteristics. The higher the BMI, the higher the BMD, which is consistent with the literature [37]. In addition, a low education level is associated with a high number of errors in the TMT B and a high fear of falling, which is also consistent with the literature [38–41]. Fear of falling is considered either as a prodrome [42, 43] or a consequence of an alteration in cognitive functions [44]. It is therefore possible to define the different profiles by referring to the value of only two parameters: BMI and cognitive performance.

In P2 with higher than normal weight and normal BMD, humerus fractures are numerous and hip fractures are few compared to P1 with normal weight and lower BMD. These two fracture sites are related to lateral falls[9,10] that can be explained by postural instability in individuals with high weight [45, 46]. The presence of soft tissue padding facing the trochanter could reduce the risk of hip fracture [47] to the benefit of humerus fractures in high weight individuals. In addition, low BMD appears to be more strongly associated with hip than humerus fracture risk, which may explain the high percentage of hip fractures in individuals with normal weight but low BMD (P1) [4, 5].

The two profiles with a low BMD and normal BMI, P1 and P4, also show some differences. P4, with fewer participants with osteoporosis than P1, has a lower percentage of hip fractures. P4 has poorer cognitive performance than P1, mainly in terms of both global cognitive functions and executive functions. P4, which contains relatively more humerus and wrist fractures than P1, is therefore characterised by poorer cognitive performance and higher fear of falling, than P1. Handgrip, polypharmacy, and the number of psychotropic drugs do not seem to play a role, nor does autonomy since the IADL score is less than 9 in both groups, reflecting almost perfect autonomy

(score = 8). Factors that differentiate P1 from P4 (cognition and fear of falling) are known to be associated with slower gait [13–15] and risk of falling [48–50]. Poorer executive functions could prevent effective fall planning, which would favour the occurrence of a lateral fall and lead to more hip and humerus fractures. This seems to be particularly true for hip fracture since P3, who also has poor cognitive performance, is the profile with the highest proportion of hip fractures (50%). Moreover, while P2 and P3 are both characterised by high weight and normal BMD, P2 has a higher proportion of humerus fractures and a lower proportion of hip fractures than P3, in which cognitive performance is more impaired. This hypothesis should be confirmed by investigations focussing on the direction of the fall as a function of cognitive status. This would improve our understanding of the impact of cognitive ability on the fracture site.

According to data in the literature [12], people who try to protect themselves while falling fracture their wrist more often than any other bone. However, although the percentage of participants in our study who protected themselves while falling was not significantly different between profiles, the proportion of wrist fractures was markedly higher in P1 and P4 than in P2 and P3. This is probably because bone mass is lower and the percentage of osteoporosis is higher in P1 and P4. In P1, patients are relatively young, with a low fear of falling and good cognitive performance. Therefore, wrist fractures in P1 are probably the consequence of both high mobility and bone weakness.

P1 and P2 have a higher proportion of ankle fractures than P3 and P4. Interestingly, patients in P1 and P2 are younger than those in P3 and P4 and have a good education level, a low fear of falling, a high degree of autonomy, and high global and specific cognitive functions. All these characteristics suggest that ankle fractures in P1 and P2 were the consequence of a fall-related trauma. Moreover, P1 and P2 strongly differ in the proportion of patients with osteoporosis, with 29% and 0% of osteoporosis, respectively. Therefore, we can speculate that a number of ankle fractures in P1 and P2 were not osteoporotic fractures.

The present study has several strengths. It is, to our knowledge, the first to focus on fracture sites related to the profiles of the participants as determined by the interactions between various patient characteristics. In addition, besides bone and anthropometric characteristics, classically analysed when studying fracture sites, cognitive abilities were also considered. Taking into account global cognition as well as cognitive sub-domains is another strength of our study, as it allowed us to highlight that specific cognitive functions, especially executive functions, could play a role in the fracture site. This is a potentially fruitful avenue for future studies designed to deepen our knowledge of the role of cognitive function in fall-related fractures.

However, some limitations should be addressed. First, being cross-sectional, it does not allow to establish a causal link between the different parameters investigated. Second, our different groups are composed of a small number of participants, which may have reduced the statistical power of the study. However, it should be noted that our study meets the two existing rules regarding the sample size required for the validation of PCA, namely the rule of having at least 10 cases for each item in the instrument being used [51], and the rule of having 5 cases per variable present in the analysis model [52]. In addition, although the large number of outcome measures in the present study exposes the results to alpha risk inflation, most of our significant results are associated with very small p-values ($p < 0.001$), which reassures us of the validity of many of our results. Third, the age factor could not be fully investigated due to the procedure for recruiting the participants. No significant age difference was found between fracture sites, highlighting that the present findings apply to seniors as soon as they reach age 55. Nevertheless, comparison between adults aged under and over 65 years of age would be useful to improve knowledge and adapt the patient's management accordingly. Finally, these results can only apply to women since our population does not include any men.

Despite these limitations, our study confirms previously reported data on the relationship between BMI, BMD, and fracture site. In addition, it highlights innovative results regarding the existence of profiles related to the combination of a few key characteristics, in particular the cognitive ability of victims of fracture, which has never been studied to date. However, these results would need to be confirmed and refined by a prospective study with a larger number of subjects and greater population heterogeneity in terms of cognitive performance and age. There is also a need for in-depth studies on the type of fall (direction, mechanism, control) and walking speed in seniors who have experienced a fall-related fracture.

In conclusion, the results of this study confirm that anthropometric and bone parameters in seniors differ significantly depending on the fracture site. Moreover, the study shows that fear of falling after a fall-related fracture and cognitive abilities also differ depending on the fracture site. However, only the participants with a hip fracture differ significantly from those with other fractures. The present study also identified four distinct clinical profiles which are defined by different interactions between anthropometric, bone, and cognitive characteristics, together with the presence or absence of a fear of falling. This suggests that the occurrence of a fracture at one specific site may result from the combination of these different characteristics. Consequently, there does not appear to be one typical profile characterising a particular fall-related fracture site, but rather several profiles for each fracture site. This new knowledge

about fall-related fracture should allow clinicians to personalise a fracture prevention strategy to the patient's profile by taking into account the combination of these different characteristics.

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Declarations

Conflicts of interest None.

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