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Utility of fragility fracture prediction tools in a group of postmenopausal women

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Abstract

Objectives: Fractures are a common complication of osteoporosis. The main aim of our study was to assess the relation between fractures identified as low energy fractures (fragility), bone mineral density (BMD), trabecular bone score (TBS), and handgrip in a group of postmenopausal women. An additional aim was to determine the relation between fragility fractures and age, height loss, and falls (reported in the last 12 months and 5 years).

Material and methods: The study was conducted in a group of 120 (mean age 69 years; 59–81, SD 5.3) postmenopausal patients who were referred to the Medical Centre for an osteoporosis screening appointment by their general practitioner. All patients were interviewed (with a questionnaire containing questions on fracture risk factors and highest height), had their anthropometric measures taken (current height and weight) as well as TBS analysis following their DXA (dual-energy X-ray absorptiometry) scan and handgrip measure.

Results: Sixty patients from the study group had a history of fractures (with a total of 92 fractures), of whom 39 women (76 fractures) were identified as those with a low-energy fracture. Fragility fractures were more likely to be reported in older patients (Me 71 vs. 68 years, $p < 0.05$). Differences observed between TBS, handgrip and BMD in reference to fragility fractures were not statistically significant. Analysis showed significant correlations between BMD (neck and L1–L4) and TBS fracture risk categories. Falls reported in the last 5 years and height loss were factors which correlated with fragility fractures ($p < 0.05$).

Conclusions: Risk of fragility fractures increases with age. Bone mineral density is insufficient as a fracture risk assessment tool. Information on falls and height loss may provide additional data on fracture risk assessment.

Key words: fragility fracture, trabecular bone score, bone mineral density, handgrip, height.

Introduction

Low-energy fractures are a frequent complication of osteoporosis. According to the statistics up to 8.9 million fragility fractures (resulting from a minimal trauma) occur annually – 1 fracture every 3 seconds [1]. Typical fragility fracture locations include the spine (vertebrae), proximal femur (hip), distal forearm (Colles' fracture) and proximal humerus (arm).

Studies report that approximately 80% of fragility fractures are not followed by appropriate pharmacological treatment, which puts the patients at risk of secondary fractures [2]. Depending on the location of the initial fracture, the risk of a subsequent fracture increases 5- to 11-fold [3–5].

Vertebral fractures are extremely difficult to diagnose as 60% of them are asymptomatic. They occur as a result of gravity or basic activities of daily living [6].

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Studies prove that a loss of at least 4 cm in height may imply the occurrence of a vertebral fracture [7].

Falls are reported to be a leading cause of fragility fractures. They are believed to be responsible for almost 100% of distal forearm fractures, 90% of proximal femur fractures and 25% of vertebral fractures [8].

Falls occur as a result of several risk factors which can be divided into environmental (external) and biological (internal). Approximately 60% of falls are accompanied by at least 2 risk factors. A total of 400 fall risk factors have been identified to date and some are believed to have more importance than others, i.e. decreased muscle strength, impaired vision and gait disturbance [9].

Dual X-ray absorptiometry scan (DXA) remains a gold standard in the diagnosis of osteoporosis (*t*-score ≤ –2.5). Nonetheless, studies have reported that bone mineral density (BMD) within the normal range does not preclude fracture risk. Furthermore, epidemiological data show that 50 to 70% of fractures occur in non-osteoporotic patients. In fact, the majority of fractures have been demonstrated to occur in patients with osteopenia (*t*-score between –1 and –2.4) [10].

The lumbar spine (L1–L4) and proximal femur (hip) are the typical locations of BMD measurement. Due to the limited effectiveness of DXA in fracture risk prediction it is necessary to explore tools which have a potential to improve fracture risk assessment such as FRAX, TBS and handgrip.

The fracture risk assessment algorithm allows one to calculate the 10-year probability of a relative risk of hip fracture as well as of a major osteoporotic fracture (such as distal forearm, proximal humerus or vertebral fracture). The algorithm takes into account the following risk factors:

- age,
- gender,
- body mass index (BMI),
- previous fractures,
- parental hip fractures,
- tobacco use,
- glucocorticoid intake,
- rheumatoid arthritis
- and alcohol consumption [11].

The trabecular bone score (TBS) is a trabecular structure index calculated on the basis of analysis of a lumbar DXA scan (L1–L4). The measured value portrays a mapping of pixels projected onto a plane which is then summed up. Dense trabecular bone presents a substantial number of pixels with low amplitude variation [12].

The result of the analysis known as the 'score' is therefore understood as a trabecular bone quality measure. Studies have confirmed that women with prior fractures have lower TBS as compared to those without fractures. The TBS has been found to be a value independent from BMD and is an indirect bone structure analysis which can be applied in fracture prediction [13].

Muscle strength measurement (handgrip) has been found useful as a custom method for the identification of frail patients at risk of fragility fracture [14].

The potential correlation between BMD and handgrip has hitherto been examined by authors who have emphasised the relation between the handgrip and fragility fractures [15, 16].

The aim of the present study was to demonstrate the correlation between low-energy fractures (fragility) and BMD, TBS, handgrip and, which is especially important, with falls in a group of postmenopausal women.

An additional objective was to determine a possible relationship between fragility fractures and age, height difference (current vs. peak height), falls in the preceding 12 months and finally the occurrence of falls in the last 5 years.

Material and methods

The study was conducted in a group of 126 postmenopausal patients who were referred to the Medical Centre (MC) for osteoporosis screening by their general practitioner (GP). A total of 120 (mean age 69 years; 59–81, SD 5.3) patients were enrolled in the study while 6 did not meet the inclusion criteria (BMI outside the range of 15–37 kg/m^2, residency outside Malopolska voivodeship, premenopause).

All patients were interviewed (completing a questionnaire on fracture risk factors and peak height), had their anthropometric measures taken (current height and weight) along with TBS analysis following the DXA scan and handgrip measure.

Dual X-ray absorptiometry scans (Hologic, Horizon W, Bedford, USA) were performed by the same trained technician (20 years of experience) at the lumbar spine (BMD spine) and hip (BMD neck). Handgrip muscle strength was measured by means of a handheld hydraulic dynamometer (Baseline, 12-0240, NY, USA).

Measurements were taken in a sitting position with the dominant arm bent at 90° – two measurements were taken (with one 1-minute rest in between), of which the superior one was selected for further analysis.

The cut-off point for an appropriate handgrip result was taken from the guidelines of the European Working Group on Sarcopenia in Older People from 2010 (EWGSOP1, > 20 kg for women) and 2018 (EWGSOP2, > 16 kg for women) [17, 18]. The following TBS thresholds introduced by the metanalysis of McCloskey et al. were applied: low (TBS > 1.31), medium (TBS 1.23–1.31) and high risk of fracture (TBS < 1.23) [19].

Table I. Characteristics of study group – 120 postmenopausal women

Variable	Study group		With fragility fracture		Without fragility fracture	*p*-value
	n	Average (min–max), SD	*n*	Average (min–max), SD	*n*	Average (min–max), SD	
Age [years]	120	69.3 (59–81), SD 5.3	39	71 (59–81), SD 6.06	79	68.5 (60–81), SD 4.8	< 0.05[a]
BMI [kg/m^2]	120	27.6 (17–37), SD 4.9	39	27.6 (19.1–36.7), SD 5	79	27.6 (17.2–36.3), SD 4.8	> 0.05[b]
Height loss [cm]	80	–3.72 (–15.5–2.6), SD 3.05	26	–4.9 (–15.5 to –1.4), SD 3.03	52	–3.21 (–10.5–2.6) SD 2.96	< 0.05[a]
BMD spine [g/cm^2]	120	0.832 (0.526–1.214), SD 0.14	39	0.82 (0.559–1.141), SD 0.146	79	0.834 (0.526–1.214) SD 0.14	> 0.05[b]
BMD neck [g/cm^2]	118	0.653 (0.469–1.095), SD 0.1	38	0.63 (0.495–0.976), SD 0.092	79	0.666 (0.469–1.095) SD 0.105	> 0.05[a]
TBS	120	1.166 (0.874–1.403), SD 0.1	39	1.175 (0.874–1.356), SD 0.09	79	1.16 (0.889–1.403), SD 0.106	> 0.05[b]
Handgrip [kg]	120	22.3 (3–38), SD 6.04	39	22.3 (3–36), SD 6.6	79	22.2 (10–38) SD 5.9	> 0.05[b]
Falls – last year [number]	115	0.37 (0–4), SD 0.74	36	0.47 (0–4), SD 0.97	77	0.29 (0–3), SD 0.58	> 0.05[a]
Falls – last 5 years [number]	97	1.02 (0–15), SD 2.2	27	2.04 (0–15), SD 3.4	68	0.59 (0–6), SD 1.29	< 0.05[a]

n – number of available subjects, [a] – Mann-Whitney U test, [b] – Student's t-test. BMI – body mass index, BMD – bone mineral density, TBS – trabecular bone score.

Statistical analysis was carried out with Statistica 13 (TIBCO Software, StatSoft, Palo Alto, CA) and Microsoft Excel (Microsoft Corporation, Redmond, WA). Statistical tests used in the study included: Student's *t*-test, the Mann-Whitney *U* test, ANOVA and the χ^2 test.

In order to assess possible correlations the Pearson correlation coefficient was used. Values of $p < 0.05$ were considered to be statistically significant.

The study design was positively reviewed by the Ethics Committee of the District Medical Chamber in Krakow (no. 113/KBL/OIL/2014 dated December 2014). All patients who participated in the study signed an informed consent form.

Results

Out of 120 participants, 62 (52%) were diagnosed with osteoporosis in accordance with the WHO definition (*t*-score ≤ –2.5). Osteopenia was reported in 53 patients (44%) and a normal BMD was reported in 5 women (4%). Nearly half of the patients with osteoporosis were undergoing antiresorptive, osteoporosis treatment ($n = 33$, 53% of those diagnosed). 50% ($n = 60$) of patients from the study group had a history of bone fractures (with a total of 92 fractures). Among them, women accounted for 65% ($n = 3$) with 76 fractures and were identified as having experienced a low-energy fracture.

The majority of cases included Colles' fractures (in total 36 incidents, 39% of all low-energy fractures); other parts of the skeleton such as vertebral (12 incidents), hip and proximal humerus (3 cases each). A detailed description of the study group with regard to the analysed data is provided in Table I.

In our study fragility fractures were more likely to be reported in older patients (Me 71 vs. 68 years, $p < 0.05$). Bone mineral density correlated with the age of the patients. Neck BMD decreased with age ($r = –0.29$, $p > 0.05$) and spine BMD was slightly higher in older patients ($r = 0.18$, $p < 0.05$). However, there was no correlation between BMD and the occurrence of fragility fractures.

Upon categorisation in accordance with the TBS fracture risk categories most of the patients fell into the high (84 subjects, 70% of the group) or intermediate (29, 24%) fracture risk group. Low risk was identified in 7 cases (6%) [19].

There were no significant differences between patients with or without low-energy fractures, either when TBS values or TBS fracture risk categories were taken into consideration. Additional analysis concerning TBS fracture risk categories and BMD (neck and spine) showed statistically significant differences in both DXA sites.

Muscle strength (handgrip assessed with a hydraulic dynamometer) was observed to decrease with age ($r = –0.22$, $p < 0.05$). The number of patients with abnor-

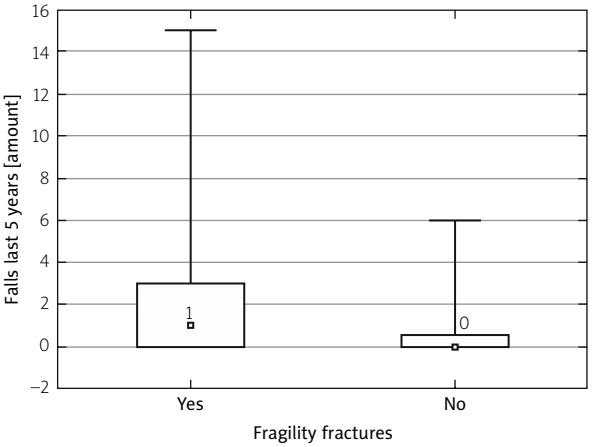

Fig. 1. Number of falls reported by patients in the last 5 years in groups with and without a history of fragility fractures.

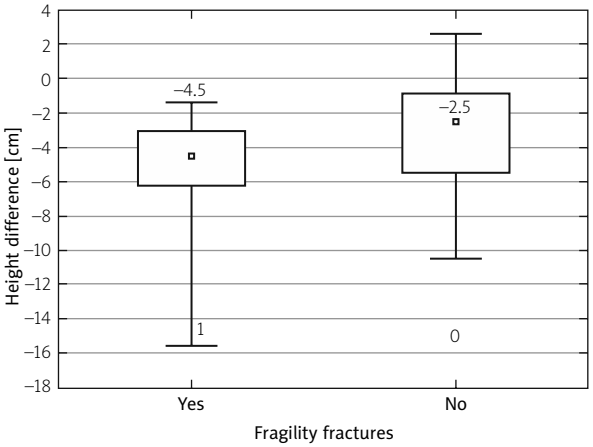

Fig. 2. Height difference (between the highest recollected by the patients and currently measured) in groups with and without a history of fragility fractures.

mally low muscle strength differed, depending on the cut-off point that was used – 13 (with EWGSOP2) and 39 (with EWGSOP1).

There were no significant differences in handgrip between patients with or without a fragility fracture regardless of whether a general handgrip result was analysed or whether the subgroups based on previously mentioned guidelines were used. The only correlation was associated with fractures resulting from an accident (high-energy trauma) with patients without such an incident having a higher handgrip strength (7 kg difference in median, $p < 0.05$).

No such correlation was found in reference to low-energy incidents. Handgrip also did not correlate with current fracture risk assessed with FRAX (for both major and hip fracture risk) including results following TBS inclusion in the algorithm.

There was no relation between handgrip and TBS (in general and in reference to the TBS fracture risk subgroups). Additionally, similar results were observed in reference to BMD (spine and neck) as well as falls (in the last year and the last 5 years).

Falls (recognized as one of the major causes of low-energy fractures) were reported by 33 (last year, 27.5% of the group) and 46 (last 5 years, 38%) patients depending on the timeline covered by the question. The average number of falls reported was 1 for those in the last year (42 falls) and 2 for the last 5 years (99 falls). Number of fallers increased with age.

A significant difference was observed in relation to patients with fragility fractures and falls reported in the last 5 years (but not for falls reported in the past year). The majority of patients who had experienced a fall in the last 5 years had a history of fragility fractures (55%).

In comparison the fracture rate was significantly lower (19%, $p < 0.05$) in the subjects who did not have a history of falls in the same time period. This leads to the conclusion that the greater the number of reported falls is, the higher is the fracture risk (Fig. 1).

The final analysed variable in the study was the height difference between the peak self-reported height and the current one. As mentioned above, the height difference of 4 cm is often listed in the literature as one of the crucial factors for vertebral fracture identification (in our group there were 12 women with a history of spinal fractures).

In the following study an overall difference in height was used (without a 4 cm cut-off point) in order to assess its potential use for fragility fracture risk assessment (regardless of the fracture site). The analysis showed that subjects with a greater height loss were more likely to have a history of fragility fractures (median loss of 4.5 cm vs. 2.5 cm, $p < 0.05$) (Fig. 2).

In order to evaluate the possible correlation between the difference in height (4 cm or more) and the condition of the spine, BMD was taken into consideration. The analysis showed that patients with a confirmed height loss had a significantly higher spinal BMD than those with an acceptable height on the day of the examination (0.91 vs. 0.78). A similar but less significant result was observed in reference to the neck BMD (0.65 vs. 0.63, $p < 0.05$).

Discussion

Aging is an integral part of human life. As it progresses gradual physiological changes such as decline of muscle and bone condition are observed, as well as higher occurrence of musculoskeletal diseases [20].

During the course of the present study we have confirmed a significant decrease of the BMD (neck) and muscle strength (handgrip) and an increase in the number of falls reported with advancing age.

A similar observation was made by Wearing et al. [21], where the authors emphasized that greater strength loss was noted in men than women. Regardless of that, men were characteristically observed to have a higher handgrip no matter the age group [21]. These results were also confirmed in a Danish study (subjects born in 1905, alive in 1998) by Oksuzyan et al. [22].

A significant age-associated decrease in BMD, measured in the proximal femur, was reported in the Rotterdam Study (most noticeably in the neck: 0.8%/year). A similar association was not observed in reference to the BMD in the lumbar spine [23].

Spine BMD and age correlations reported within the Rotterdam Study as well as in the present analysis are most likely associated with spinal osteoarthritis and may impact the percentage of patients diagnosed with osteoporosis. For this reason the WHO recommends two locations for BMD measurement: spine (L1–L4) and hip [24].

At the same time Alarkawi et al. [25] emphasize that the spine BMD should not be disregarded as a fracture risk factor, as it may potentially exceed the usefulness of hip BMD in fracture risk assessment.

Fragility fractures bear a substantial risk of subsequent secondary fractures. Worldwide respected secondary prevention models such as Fracture Liaison Services are based on the idea of intense screening in the groups with the highest fragility fracture risk (which includes BMD and more recently also vertebral fracture assessment – VFA) [26].

Despite the fact that a high percentage of fractures occur in subjects with a normal BMD (*t*-score > –2.5), DXA remains an important tool in fracture risk assessment, if it is systematically checked [27].

Our study showed lower BMD values (in both neck and spine) in patients with fragility fractures, but the differences were not statistically significant. The importance of BMD was emphasized in the past by a number of guidelines and national recommendations as a gold standard, i.e. by EFORT, EULAR, ESCEO and IOF [28, 29].

Kanis et al. [30] recommend the inclusion of BMD as a major fracture risk factor in FRAX (calibrated with the epidemiology from 67 countries covering 80% of the population).

According to Compston et al. [31], BMD has a high specificity but a low sensitivity and therefore it is not suitable for consideration as a sole risk factor used for fracture risk assessment in the elderly.

Due to the insufficient role of BMD in fracture risk assessment, there is a great need of different, simple, inexpensive solutions such as the FRAX calculator. In search of those tools we have included TBS, handgrip, height difference and falls as potential variables.

The efficacy of TBS has been demonstrated in the meta-analysis by McCloskey et al. [19], composed of 14 cohorts with a total of 17,809 patients. The authors confirmed that TBS is useful as a single risk factor but also it increases the prognostic value of FRAX (accordingly GR 1.32 and 1.76) [19].

In our study there were no significant differences in TBS between patients with or without a fragility fracture. Also the grouping of patients into TBS fracture risk categories by McCloskey et al. [19] did not result in any significant differences between the groups. It is our belief that this result may be the effect of an insufficient study sample size as well as a general 'fracture burden' in the study group (50% of patients had a total of 92 fractures). It should be stressed that study subjects were referred to the medical centre in order to undergo osteoporosis and fracture risk assessment.

Studies have shown that TBS is a promising tool for fracture prediction as a single risk factor or a component of other methods [19, 32, 33]. Our study confirmed the previous observations [19] about the link between TBS fracture risk category and BMD value, measured at either the hip or the spine (the lower the BMD, the higher the risk). This finding is in line with the theory that BMD measured in major locations (spine and neck) may complement the TBS score and therefore improve the fracture risk prediction in postmenopausal women.

According to Kolta et al. [32] the superiority of TBS over BMD is that it is not dependent on the spinal osteoarthritis, which may affect the result of the density measurement, as was also observed in our study.

At the same time Pouillès et al. [33] emphasize that the utility of TBS may by compromised in women with severe osteoporosis observed in spine scans (*t*-score ≤ –3) and therefore it does not significantly contribute to the general fracture risk assessment in this group. The authors state that low bone mass is very likely to be associated with low bone peak mass (in this group of patients) rather than structural degeneration observed shortly after menopause.

Our pilot study in 2018 [6] showed possible potential for the use of handgrip as a vertebral fracture risk assessment tool (for screening purposes). The importance of handgrip was reported in the past in reference to sarcopenia, cognitive impairment, reduced activities of daily living (ADL) and increased mortality [34–36].

The study described in the present paper did not confirm the correlation between muscle strength (handgrip) and fragility fracture (regardless of its location) or any other analysed variables (BMD, TBS, FRAX, falls).

Correlation between handgrip and FRAX hip was confirmed previously by Catalano et al. [37] ($r = –0.39$, $p = 0.002$).

A similar observation was reported by Henriquez et al. [38] with low values of handgrip (< 20 kg for women and < 30 for men) and FRAX as well as osteoporosis, falls and nutrition. After the follow-up phase (42 weeks) the authors additionally confirmed the correlation between fracture risk (HR 4.25 [1.37–13.2], $p = 0.01$) and serious adverse events (SAE, HR 2.80 [1.35–5.81], $p = 0.006$) [38]. We believe that the potential use of handgrip in fracture risk assessment requires large randomized studies (including subjects with a diverse medical history).

For many years falls have been recognized as a major cause of fragility fractures – as studies show they may be responsible for approximately 87% of fractures in the elderly [38]. Our study confirms the relation between fragility fractures and falls reported in the past 5 years.

Despite the fact that the prognostic value of falls in fracture risk assessment has been confirmed multiple times in studies, falls remain neglected as a single risk factor or as a component of other methods such as FRAX (although they appear in less popular algorithms such as Garvan or QFracture) [39].

Height loss of at least 4 cm is recognized as a conventional risk factor for vertebral fractures [7]. Hillier et al. [40] reported in their study that it may also be associated with a higher risk of non-vertebral fractures including hip fracture (50% increase in risk). Our study confirms those results as patients with a history of fragility fractures had a greater average height loss than those without fracture incidents.

Our study had a few limitations, mostly associated with the clinical profile of the study group (patients referred for osteoporosis screening by their GP). Therefore it is fair to assume that the group was afflicted with a higher risk of fragility fractures than observed within the general population.

Despite the fact that the interviews were carried out with great accuracy, some data were missing (i.e. height loss, falls in the past 5 years) as some patients were unable to recollect their peak height or the exact number of falls in the past 5 years.

Conclusions

Risk of fragility fractures increases with age. Bone mineral density is insufficient as a fracture risk assessment tool. Data on height loss and falls may be useful in identifying patients at high risk of fragility fracture.

The authors declare no conflict of interest.

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