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Research Article

FRAX® in Hemodialysis with Osteoporosis- A Registry Study

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Abstract

Objectives: The best way to find out which hemodialysis patients are at high fracture risk is uncertain. The primary purpose of this study was to analyze the use of the Fracture Risk Assessment Tool (FRAX®) in hemodialysis subjects. **Methods:** Participants were recruited by the nephrology and family department. Each participant was to complete the structured questionnaire, which included the clinical risk factors specifically for the FRAX® calculation tool. **Results:** A total of 450 patients were enrolled. The age of the patients was 64 years (IQR, 58-70). Most of the patients were female (74.7%). The duration of hemodialysis was 3 years (IQR, 2-5).There was high correlation found between the 10-yr major osteoporotic fracture probabilities calculated with and without Bone Mineral Density (BMD) ($p < 0.001$). There was also correlation in terms of hip fractures risk. When we divided the patients into normal femoral neck BMD, osteopenia, and osteoporosis, there is still high correlation between those with and without BMD. 12.7% with BMD and 7.3% without BMD were above treatment threshold by major osteoporotic fracture risk, while 48.0% with BMD and 33.3% without BMD were above treatment threshold by hip fracture risk. **Conclusions:** FRAX is valuable in assess fracture risk in hemodialysis patients. FRAX® with and without BMD had high correlation with each other in hemodialysis patients. FRAX-based intervention thresholds are helpful for health economic assessment and to avoid unnecessary treatment.

Keywords: FRAX®; Hemodialysis; Osteoporosis; Bone mineral density

Introduction

Impaired bone strength will predispose patients to increased fracture risk [1-3]. The National Osteoporosis Foundation (NOF) defines the treatment threshold, that is, the risk of major osteoporotic fracture ≥20% and the risk of hip fracture ≥3% [4].

With the popular use of FRAX®, there is still a debate related to this tool without BMD information although the inclusion of BMD is optional [5,6]. However, another document found that including BMD in FRAX® may greatly underestimate the risk [7]. In countries with limited facilities equipped with Dual-energy X-ray Absorptiometry (DXA) machines, the evaluation of fracture risk without BMD may be the only choice. It has been emphasized that FRAX® without BMD is believed to be helpful for those who benefit from treatment [8,9].

Compared with the general population, patients with Chronic Kidney Disease (CKD) on dialysis have an increased risk of osteoporosis and fractures [10]. According to a previous study of the Taiwan Insurance Database, the cumulative survival rate after hip fracture was 74.6% in one year and only 29.6% in seven years [11]. FRAX® without BMD can well assess the risk of major bone fractures in these hemodialysis patients [12]. However, so far, there are no studies available to investigate the relationship between FRAX® with or without BMD in these patients and no available data on FRAX-based intervention threshold, so we developed this study to investigate the role of FRAX® in hemodialysis patients.

Research Methodology

This was a registry study of Hemodialysis-Osteoporosis. The interim analysis was conducted at CGMHK. The reporting of this study conforms to the STROBE statement [13]. The Ethics Committee approved the study (201801372B0). We obtained the informed consent of all study.

Inclusion criteria

- Those on maintenance hemodialysis were enrolled.
- Can read and willing to sign a written subject consent
- Can cooperate with outpatient consultation

Exclusion criteria

- Patients who refuse to sign the inform consent.

Clinical and biochemical Analysis

Clinical data is collected as daily practice routine, medications use include glucocorticoid and drugs for anti-osteoporotic medications.

Bone mineral density (DXA) evaluation

We collected BMD and T score data on the femoral neck and lumbar spine. These measurements were performed using Lunar DPX IQ equipment (GE Lunar Corporation, Madison, Wisconsin) and were calibrated daily. According to the classification a T score ≤ −2.5 are considered osteoporosis; people with a score of -1 to -2.5 are considered osteopenia; people with a score> -1 are considered normal [3].

Fracture Risk Assessment Tool

We calculated the 10-yr hip fracture and major osteoporotic fracture risk with FRAX® using the method developed by Kanis, et al. [14]. According to NOF criteria, patients with major osteoporotic fracture FRAX® score ≥20% or hip fracture ≥3% are defined as high-risk patients and must receive intervention [4].

Statistical Analysis

SPSS for Windows v.22 was used for all analysis of the research data. Pearson correlation test was used and Intra-class Correlation Coefficient (ICC) analysis was used to assess the deterministic agreement between FRAX® scores with and without BMD. We calculated the risk values of major osteoporotic fractures and hip fractures with and without BMD and ICC based on the Fleiss kappa index, and measured the mean values with 95% confidence intervals [15]. The co-efficient of variation was 0.1% for each reading.

Results

A total of 450 patients were enrolled. The age of the patients was 64 years (IQR, 58-70). Most of the patients were female (74.7%) and the Body Mass Index (BMI) was [23.5 kg/m2 (IQR, 21.2-26.2)]. The duration of hemodialysis was [3 years (IQR, 2-5)]. The lumbar spine T score was [−1.8 , (IQR, -2.6~ -0.7), the femoral neck T score was [−2.2 (IQR, -2.8~ -1.6), and the mean total hip T score was [−1.4 , (IQR, -2.0~ -0.675). 102 (22.7%) patients had normal femoral neck T scores, 159 (35.3%) had femoral neck T scores between -1.5 and -2.5 (osteopenia or low bone mass), 189 (42%) had femoral neck T scores ≦-2.5 (osteoporosis). The 10-year major fracture risk with BMD was [11.0% , (IQR, 7.275-17.0), the 10-year major fracture risk without BMD was [8.5 % , (IQR, 5.6-14.0), the 10-year hip fracture risk with BMD was [2.85 %, (IQR, 1.2-6.15), while the mean 10-year hip fracture risk without BMD was [1.75%, (IQR, 0.9-4.25). Table 1 showed the characteristics of the study population.

Variables	Medium (IQR) (n=450)
Age (years), mean ± SD	64 (58-70)
Gender (female %)	336 (74.7)
Body mass index (kg/m^2), mean ± SD	23.5 (21.2-26.2)
Lumbar spine T score, mean ± SD	−1.8 (-2.6~ -0.7)
Femur neck T score, mean ± SD	−2.2 (-2.8~ -1.6)
Total hip T score, mean ± SD	−1.4 (-2.0~ -0.675)
10 year major fracture risk with BMD	11.0 (7.275-17.0)
10 year major fracture risk without BMD	8.5 (5.6-14.0)
10 year hip fracture risk with BMD	2.85 (1.2-6.15)
10 year hip fracture risk without BMD	1.75 (0.9-4.25)

Table 1: Characteristics of the patients enrolled in the study.

When we divided the patients into normal femoral neck BMD, osteopenia, and osteoporosis, there is still high correlation between those with and without BMD (Table 2).

Femoral neck BMD	Variables	Pearson correlation	P value
All	Major osteoporotic fracture risk	0.641	0.001
	Hip fracture risk	0.435	0.001
Normal	Major osteoporotic fracture risk	0.868	0.001
	Hip fracture risk	0.797	0.001
Osteopenia	Major osteoporotic fracture risk	0.831	0.001
	Hip fracture risk	0.92	0.001
Osteoporosis	Major osteoporotic fracture risk	0.746	0.001
	Hip fracture risk	0.459	0.001

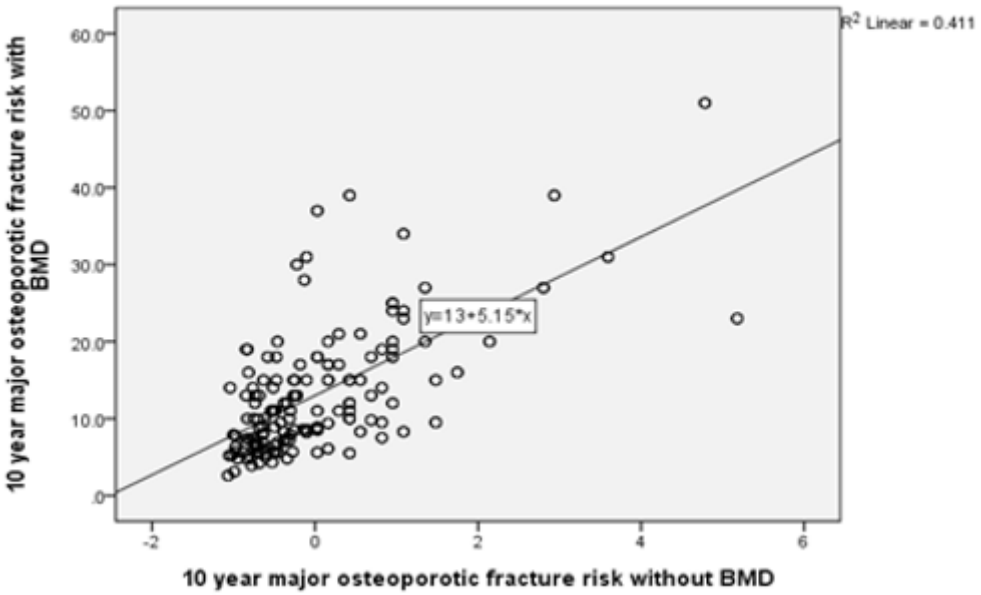

Table 2: Correlation of FRAX® with and without BMD.

When we checked according to the treatment thresholds, 57 of 450 patients (12.7%) had a risk of major osteoporotic fracture ≥20% when calculated with BMD. 33 of 450 patients (7.3%) had a risk of major osteoporotic fracture ≥20% when the BMD is not used to calculate the value. 216 of 450 patients (48.0%) had hip fracture risk ≥3% when calculated with BMD, and 150 of 450 patients (33.3%) had hip fracture risk ≥3% without BMD.

54 had histories of falling and fractures. In these patients, 18 of the 54 (35.3%) patients had a major osteoporotic fracture risk of ≥20% when calculated with BMD and 18 of the 54 (35.3%) patients had a major osteoporotic fracture risk of ≥20% when calculated without BMD. 36 of the 54 (70.6%) patients had a hip fracture risk of ≥3% when calculated with BMD and 33 of the 54 (64.7%).

Discussion

The frequency of osteoporosis in CKD increases with advancing age. CKD patients had a marked increase in the risk of hip fracture [16]. It has been reported that CKD patients have a 4.4-fold higher risk of fractures than the general population [17]. A low BMD at the lumbar spine and femoral neck and the risk of bone fracture had been reported in hemodialysis patients [18].

In this study, there are correlation between those with and without BMD regarding major osteoporotic fracture risk and hip fracture risk in hemodialysis patients. In one study, FRAX® score data can be calculated with or without T-scores in normal and osteoporotic patients [7].

In current study, when we consider the patients who need

intervention, taking the risk of major osteoporotic fracture ≥20% as the threshold, the patients with or without BMD are 12.7% and 7.3%, respectively. When the risk of hip fracture was ≥3% as the threshold, the patients with or without BMD were 48% and 33.3%, respectively. It seems that when using the risk of hip fracture as the threshold, there will be more cases of hemodialysis patients that require treatment. Taking past fracture patients as the observation point, among patients with major osteoporotic fracture risk threshold, there were 35.3% and 35.3% in those with BMD or without BMD respectively. While using hip fracture risk threshold, there were 70.6% and 64.7% in those with BMD or without BMD respectively. So the adoption of FRAX-based intervention thresholds will be helpful for health economic assessment and to avoid unnecessary treatment [19].

Physicians may worry about whether FRAX® without BMD and FRAX® with BMD have considerable inconsistencies, especially in patients with a lower risk of fracture and a diagnosis of osteoporosis. However, in the study of Imerci et al., FRAX® without BMD may be useful even for patients with only osteopenia [20]. In current study, even in normal femoral neck BMD, FRAX with either major osteoporotic fracture risk or hip fracture risk had high correlation between those with or without BMD. So FRAX can be used to predict the fracture risk in normal BMD in hemodialysis patients.

Although the FRAX® [7], it is recommended that the DXA facilities [8] could be used in hemodialysis patients also. In some countries, the use of DXA for population screening does not seem feasible, mainly for economic reasons. With the aging of the population, the increased demand for DXA examinations must be adapted to the limited resources [21] which will represent a more valuable approach and can help select available resources, obtain the best results and make clinical decisions.

The advantage of FRAX is that it can indicate the possibility of fracture, which provides convenience for doctors and patients when understanding the severity of the disease and making a decision about the risk and benefit of starting treatment or when requesting DXA in case of doubt. This is the most useful way to express risk in clinical practice. Shared decision-making may increase compliance, which is necessary to reduce the risk of vertebral fractures (40-70%), non-vertebral fractures (20-25%), and hip fractures (20-40%) [22]. Therefore, in the case of rapid loss of bone density (cancer, long-term rest, medication, etc.), it may not be possible to estimate fractures. For these special situations, clinicians should consider using BMD for fracture reassessment based on clinical judgments to better assess the fracture situation of hemodialysis patients.

Conclusions

FRAX is valuable in assess fracture risk in hemodialysis patients. FRAX-based intervention thresholds are helpful for health economic assessment and to avoid unnecessary treatment. In areas where DXA is not available, the use of FRAX may be the only possible fracture assessment. Our data supports the idea that FRAX is an effective tool in hemodialysis patients.

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Author Contributions

Conceptualization: Wei-Cheng Huang, Yu-Wei Wang; Data curation: Wei-Cheng Huang, Yu-Wei Wang; Formal analysis: Wei-Cheng Huang, Yu-Wei Wang; Funding acquisition: Wei-Cheng Huang, Yu-Wei Wang; Investigation: Wei-Cheng Huang, Yu-Wei Wang; Project administration: Wei-Cheng Huang, Yu-Wei Wang; Software: Chao-Tung Chen, Ying-Chou Chen; Supervision: Chao-Tung Chen, Ying-Chou Chen; Validation: Chao-Tung Chen, Ying-Chou Chen; Visualization: Chao-Tung Chen, Ying-Chou Chen; Writing – original draft: Chao-Tung Chen, Ying-Chou Chen; Writing – review & editing: Chao-Tung Chen, Ying-Chou Chen

Ethics Approval

The Ethics Committee of Kaohsiung Chang Gung Memorial Hospital approved the study : IRB202000325B0.

Data Availability Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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