



The Characteristics of Women with Subsequent Distal Radius Fracture after Initial Distal Radius Fracture

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Background: The purpose of this study was to investigate the characteristics of women with subsequent distal radius fracture (DRF) and to compare bone fragility variables in women with initial and subsequent DRF. **Methods:** We enrolled 227 women who experienced DRF (203 women with initial DRF and 24 women with subsequent DRF) between September 2016 and April 2019. We compared demographic characteristics and bone fragility variables, including bone mineral density, trabecular bone score, hip geometry, bicortical thickness of the distal radius, and fracture risk assessment tool (FRAX) scores between the 2 groups. To reduce bias, patients with subsequent DRF were propensity score-matched in a 1:2 manner with patients affected by initial DRF, and additional comparisons were performed. **Results:** Patients in the subsequent DRF group were older than those in the initial DRF group, but this difference was not significant ($P=0.091$). The proportion of patients receiving treatment with osteoporosis medication was significantly higher in the subsequent DRF group (41.7% vs. 19.2%, $P=0.011$). Bone fragility variables did not differ significantly between the 2 groups. However, the ten-year probability of major osteoporotic fractures based on FRAX scores was significantly higher in patients with subsequent DRF (7.5% vs. 10.8%, $P<0.001$). Similar results were observed when comparing the propensity score-matched initial and subsequent DRF groups. **Conclusions:** These findings suggest that the occurrence of subsequent DRF after initial DRF can be attributed to multiple factors rather than bone fragility alone. Systematic and multidisciplinary management would be helpful in preventing the occurrence of subsequent DRF after the initial DRF.

Key Words: Bone density · Hip geometry · Osteoporosis · Radius fractures · Trabecular bone score

INTRODUCTION

The purpose of osteoporosis evaluation and management is to prevent the occurrence of osteoporotic fractures. This concept is most applicable to patients who have already experienced an osteoporotic fracture, as these patients are at higher risk of subsequent osteoporotic fracture.[1,2]

Distal radius fracture (DRF) is the most common upper extremity fracture in women aged ≥ 50 years,[3] and the occurrence of DRF is considered indicative of bone

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fragility.[2,4] The risk of future fractures at multiple sites, especially the hip and spine, has been reported to be higher in patients who have experienced wrist fractures than those who have not.[2,5-7] In addition, the wrist has been reported to be the most vulnerable site for subsequent fracture after initial wrist fracture, with the risk of subsequent wrist fracture being higher than the risk of hip fracture after an initial wrist fracture.[6] However, to date, the characteristics of patients with subsequent DRF after initial DRF have not been determined.

Bone mineral density (BMD) has been widely used for diagnosing bone fragility and is currently used as a parameter for diagnosing osteoporosis. However, because BMD does not always reflect fracture risk, other bone fragility parameters, such as trabecular bone score (TBS), hip geometry parameters, and cortical thickness of long bones, have been evaluated.[8-10] In addition, the fracture risk assessment tool (FRAX) was developed to reflect the clinical situation of the patients.[11] To our knowledge, these bone fragility parameters have not been evaluated in patients with subsequent DRF.

The present study was designed to investigate the characteristics of patients with subsequent DRF after initial DRF. In addition, bone fragility parameters were compared in patients with initial and subsequent distal radius fractures to identify the factors contributing to the occurrence of subsequent DRF.

METHODS

1. Study population

The protocol used for this cross-sectional, retrospective review of medical records was approved by the institutional review board of our institute. We enrolled women who experienced a DRF between September 2016 and April 2019 and met the following inclusion criteria: (1) acute DRF caused by minor trauma, such as a fall from standing height; and (2) performed a dual energy X-ray absorptiometry (DXA; Lunar Prodigy Advance; GE Lunar, Madison, WI, USA) within 2 weeks after diagnosis of the fracture. The exclusion criterion was DRF by major trauma such as traffic accidents. An osteoporosis examination is routinely recommended by a treating orthopedic surgeon for all patients with DRF on their first follow-up visit to the outpatient clinic or after admission for operation. Finally, 227 women who met the

criteria were enrolled. The mean age of the cohort was 65.1 ± 10.1 years, mean body mass index (BMI) was 23.4 ± 3.1 kg/m², and 163 patients (71.8% of 227 patients) were treated surgically.

Among the 227 patients with DRF, 203 experienced a first-time DRF (initial DRF group) and 24 had a previous history of DRF (subsequent DRF group). The demographic characteristics, osteoporosis treatment history, and bone fragility parameters, including BMD, TBS, hip geometry parameters, bicortical thickness (BCT) of the distal radius, and FRAX scores, were compared between the 2 groups. To reduce bias, patients in the subsequent DRF group were propensity score-matched at a 1:2 ratio with patients in the initial DRF group, and additional comparison was performed between these groups. The propensity score was calculated for each patient based on logistic regression analysis, using patient age and BMI for matching.

2. BMDs and TBS

At our institute, BMD (g/cm²) was measured in the lumbar spine, femoral neck, trochanter, Ward's triangle, and the total hip using Lunar Prodigy DXA scans (GE Lunar) and was analyzed using Encore Software ver.11.0. The lowest BMD T-score was derived from the BMDs of the lumbar spine, total hip, and femoral neck only, in accordance to the classification proposed by the World Health Organization (WHO).[12] Osteoporosis was defined as the lowest BMD T-score < -2.5 . The BMD precision errors (percentage of the coefficient of variation)—measured by assessing 30 individuals with 2 scans at our institution—were 1.9% for the lumbar spine, 2.5% for the femoral neck, and 1.8% for the total hip. The least significant changes in BMD, calculated as $2.77 \times$ precision error and at a 95% confidence level, were 0.053 g/cm² for the lumbar spine, 0.069 g/cm² for the femoral neck, and 0.050 g/cm² for the total hip. For the lumbar spine BMD, the L1–4 value was used for analysis. All TBS measurements were performed retrospectively using TBS iNsite Software, version 3.02 (Med-Imaps, Needham, MA, USA) based on spine DXA files from the database to ensure that the investigators are blinded to all clinical parameters. The software uses the raw DXA images of the anteroposterior spine for the same region of interest as the lumbar spine BMD measurements.

3. Hip geometry parameters

Geometric bone structure properties in all scans were further analyzed using the advanced hip assessment (AHA) program included with the GE Lunar Prodigy software, as described previously.[13,14] The AHA program automatically sets the region of interest, defined as the narrow neck (NN), transversing the narrowest width of the femoral neck. The AHA program yielded data for hip axis length (HAL), neck shaft angle (NSA), mean cortical thickness (mm), femur neck width (mm), cross-sectional area, cross-sectional moment of inertia (cm⁴), section modulus (cm³), and buckling ratio at the NN. The short-term coefficients of variance of AHA indices calculated from the images used for the precision assessment of BMD appeared to be slightly greater than those of conventional BMD, but were approximately 2%, similar to the previously reported precision data.[15]

4. Cortical thickness of the distal radius

Cortical bone thickness was measured and analyzed based on a previously described method of analyzing the relationship between the BMD and cortical thickness of the distal radius.[16] In patients with initial DRF or recurrent DRF on the same side, an image of the contralateral side was selected. In patients with subsequent DRF on the side contralateral to that of the previous DRF, an old DRF side image was selected. In patients with bilateral subsequent DRF, an image of the dominant hand was selected. All images were randomly sorted after removing the personal information of patients and were reviewed by 1 orthopedic surgeon and 1 orthopedic resident. All radiographic measurements were performed using the picture archiving and communication systems program of our institute (PetaVision; Asan Medical Center, Seoul, Korea). Varying image magnification was normalized by standardizing longitudinal capitate lengths on all radiographs to 21.65 mm.[17] BCT was measured 50 and 70 mm proximal to the distal radio-ulnar joint, with the mean of the 2 measurements defined as average BCT. The mean value of each measurement was used for the analysis.

5. FRAX

FRAX[®] is a simple fracture risk assessment tool developed by the WHO.[11] FRAX algorithms calculate the 10-year probability of major osteoporotic fractures and hip fractures. We calculated the 10-year probability of fracture by

including clinical risk factors such as previous fracture, hip fracture in parents, smoking habits, steroid medicine, rheumatoid arthritis, secondary osteoporosis, and alcohol habits. FRAX scores were acquired using the web-based calculation tool for Korean. We adjusted the FRAX score with TBS in each patient.

6. Statistical analysis

All statistical analyses, including propensity score matching analysis, were performed using the R statistical software (version 3.1.0; The R Foundation for Statistical Computing, Vienna, Austria), with *P* less than 0.05 considered significant. Descriptive statistics, including means and standard deviations, were estimated for both groups. After assessing the normality of the distribution of the tested parameters, between-group differences in continuous variables were assessed using the Student's *t*-test or Mann-Whitney U-test, as appropriate. Categorical variables, including the proportions of women and those with underlying diseases, were compared in the 2 groups using the χ^2 test or Fisher's exact test. The reliability of measurements of distal radius BCT was calculated using the single measures intraclass correlation coefficient (ICC) from a 2-way random effect analysis of variance. For propensity score matching, we used nearest neighbor matching with the caliper 0.25.

RESULTS

1. Characteristics of subsequent DRF patients

The mean time from initial DRF to subsequent DRF was 121.5 ± 82.3 months (range, 1-240 months). Of the 24 patients with subsequent DRF, 16 experienced recurrent DRF of the same wrist, 7 had subsequent DRF on the contralateral side of the initial DRF, and one experienced bilateral DRF simultaneously after an initial unilateral DRF. Patients in the subsequent DRF group were older than those in the initial DRF group, but this difference was not significant (*P*=0.091). The portion of patients receiving osteoporosis medications was significantly higher in the subsequent than in the initial DRF group (41.7% vs. 19.2%, *P*=0.011). Other demographic factors and the proportions of patients with underlying diseases were similar in the 2 groups, except that the rate of asthma was significantly higher in the subsequent DRF group (*P*=0.009) (Table 1).

Table 1. Baseline patient characteristics

Variables	Primary DRF group (N=203)	Subsequent DRF group (N=24)	P-value
Age (yr)	64.7±10.3	68.4±8.2	0.091
Body mass index (kg/m ²)	23.3±3.1	23.4±3.1	0.969
Hypertension	85 (41.9%)	9 (37.5%)	0.681
Dyslipidemia	84 (41.4%)	7 (29.2%)	0.248
Diabetes mellitus	22 (10.8%)	3 (12.5%)	0.734
Stroke history	12 (5.9%)	1 (4.2%)	0.999
Renal insufficiency	7 (3.4%)	0 (0.0%)	0.999
Thyroid or parathyroid disease	22 (10.8%)	2 (8.3%)	0.999
Rheumatoid arthritis	9 (4.4%)	1 (4.2%)	0.999
Asthma	5 (2.5%)	4 (16.7%)	0.009 ^{a)}
Malignancy	21 (10.3%)	4 (16.7%)	0.314
Steroid medication history	11 (5.4%)	0 (0.0%)	0.612
Proton pump inhibitor medication history	10 (4.9%)	3 (12.5%)	0.146
Smoking history	2 (1.0%)	0 (0.0%)	0.999
Osteoporosis medication history	39 (19.2%)	10 (41.7%)	0.011 ^{a)}
Vitamin D medication history	88 (43.3%)	11 (45.8%)	0.817
Calcium medication history	24 (11.8%)	2 (8.3%)	0.999

The data is presented as mean ± standard deviation or number (%).

^{a)}P<0.05.

DRF, distal radius fracture.

2. Bone fragility parameters in initial and subsequent DRF patients

BMDs, TBS, hip geometry parameters, and BCT of the distal radius did not differ significantly in the initial and subsequent DRF groups. The lowest T-score in the DXA, along with BMDs and TBS, were higher—and the rate of osteoporosis was lower—in the subsequent DRF group than those in the initial DRF group. However, the 10-year probability of major osteoporotic fracture in FRAX was significantly higher in patients with subsequent DRF (7.5% vs. 10.8%, *P*<0.001) (Table 2). Similar results were observed when propensity score-matched patients with initial DRF and subsequent DRF were compared (Table 3). The ICC was 0.867 (95% confidence interval, 0.828–0.897) for inter-observer reliability of distal radius BCT.

DISCUSSION

All subsequent DRFs occurred after minor trauma like initial DRFs, but the characteristics of the initial and subsequent DRFs differed. The age distribution and the periods between initial and subsequent DRFs ranged widely in

Table 2. Bone mineral density, trabecular bone score, hip geometry parameters, cortical thickness of the distal radius and 10 years probability of osteoporotic fracture in patients with primary and subsequent distal radius fracture

Variables	Initial DRF group (N=203)	Subsequent DRF group (N=24)	P-value
Lumbar BMD (g/cm ²)	0.910±0.145	0.918±0.124	0.682
Femur neck BMD (g/cm ²)	0.742±0.115	0.748±0.108	0.835
Trochanter BMD (g/cm ²)	0.618±0.103	0.639±0.111	0.369
Total hip BMD (g/cm ²)	0.790±0.116	0.808±0.109	0.456
Lowest T score in DXA	-2.3±1.0	-2.1±0.8	0.351
Osteoporosis	82 (40.4%)	7 (29.2%)	0.378
Trabecular bone score	1.366±0.082	1.367±0.090	0.594
HAL (mm)	100.9±5.1	100.6±4.8	0.762
NSA (°)	125.1±4.1	125.5±3.3	0.444
Cortical width (mm)	4.6±1.5	4.6±1.2	0.663
CSA (cm ²)	108.3±17.3	107.4±17.8	0.795
CSMI (cm ⁴)	6,969.5±1,642.5	6,396.1±1,624.3	0.209
SM (cm ³)	421.1±87.7	393.4±97.1	0.149
BR	4.1±1.6	3.8±1.0	0.580
Mean bicortical thickness of distal radius (mm)	5.0±0.9	5.1±0.8	0.471
10 years probability of major osteoporotic fracture on FRAX (%)	7.5±4.1	10.8±4.3	<0.001 ^{a)}
10 years probability of hip fracture on FRAX (%)	2.5±2.7	3.3±2.6	0.050

The data is presented as mean ± standard deviation or numbers (%).

^{a)}P<0.05.

BMD, bone mineral density; DXA, dual energy X-ray absorptiometry; HAL, hip axis length; NSA, neck shaft angle; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; SM, section modulus; BR, buckling ratio; FRAX, fracture risk assessment tool; DRF, distal radius fracture.

Table 3. Bone mineral density, trabecular bone score, hip geometry parameters, cortical thickness of the distal radius and 10 years probability of osteoporotic fracture in propensity score matched patients with primary and subsequent distal radius fracture

Variables	Initial DRF group (N=48)	Subsequent DRF group (N=24)	P-value
Age (yr)	67.9±9.2	68.4±8.2	0.830
Body mass index (kg/m ²)	24.0±3.3	23.4±3.1	0.438
Lumbar BMD (g/cm ²)	0.913±0.135	0.918±0.124	0.877
Femur neck BMD (g/cm ²)	0.724±0.116	0.748±0.108	0.410
Trochanter BMD (g/cm ²)	0.613±0.103	0.639±0.111	0.334
Total hip BMD (g/cm ²)	0.771±0.121	0.808±0.109	0.212
Lowest T score in DXA	-2.4±1.0	-2.1±0.8	0.290
Osteoporosis	17 (35.4%)	7 (29.2%)	0.791
Trabecular bone score	1.352±0.093	1.367±0.090	0.313
HAL (mm)	101.1±5.1	100.6±4.8	0.538
NSA (°)	124.9±5.0	125.5±3.3	0.594
Cortical width (mm)	4.6±1.7	4.6±1.2	0.684
CSA (cm ²)	106.6±17.2	107.4±17.8	0.856
CSMI (cm ⁴)	7,018.2±1,525.3	6,396.1±1,624.3	0.115
SM (cm ³)	419.0±77.1	393.4±97.1	0.227
BR	4.3±2.1	3.8±1.0	0.459
Mean bicortical thickness of distal radius	4.9±1.0	5.1±0.8	0.280
Osteoporosis medication history	17 (35.4%)	7 (29.2%)	0.596
Asthma	1 (2.1%)	4 (16.7)	0.039 ^{a)}
10 years probability of major osteoporotic fracture on FRAX (%)	8.4±4.3	10.8±4.3	0.009 ^{a)}
10 years probability of hip fracture on FRAX (%)	3.0±2.9	3.3±2.6	0.437

The data is presented as mean ± standard deviation or number (%).

^{a)}P<0.05.

BMD, bone mineral density; DXA, dual energy X-ray absorptiometry; HAL, hip axis length; NSA, neck shaft angle; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; SM, section modulus; BR, buckling ratio; FRAX, fracture risk assessment tool; DRF, distal radius fracture.

these groups, indicating their heterogeneity. In the group comparison between the patients with initial and subsequent DRFs, the bone fragility parameters did not differ significantly. Despite the insignificant differences in bone fragility parameters and higher rates of the administration of osteoporosis medications, the 10-year probability of being affected by a major osteoporotic fracture in the FRAX analysis was significantly higher for patients with subsequent DRF than for those with initial DRF. These findings indicate that the occurrence of subsequent DRF could be dependent on multiple factors rather than those associated with bone fragility alone. Alternatively, bone fragility parameters, especially BMD, may be improved by osteoporosis medications after initial DRF, but other uncorrected or uncorrectable factors such as physical performance level, risk of falling, and sarcopenia may be associated with the development of subsequent DRF.[18-20]

Understanding the characteristics of patients who expe-

rience subsequent fragility fractures after initial fragility fractures is necessary to prevent these recurrent fractures. Several studies have evaluated the characteristics of patients who experienced subsequent fractures at other body sites. An evaluation of patients who experienced subsequent hip fracture after initial hip fracture revealed that older age, cognitive impairment, and lower bone mass might increase the risk of subsequent hip fracture.[21] In addition, subsequent vertebral fracture after initial vertebral fracture was associated with pre-existing vertebral deformities, vertebroplasty, and the location of the initial compression fracture.[22-24]

The proportion of patients taking osteoporosis medications was significantly higher in the subsequent than in the initial DRF group. This phenomenon could be explained by the effect of education and emphasis for the evaluation and management of osteoporosis provided by treating physicians after their initial DRF.[7] In addition, the discrep-

ancies between bone fragility parameters, osteoporosis medication rate, and probability of major osteoporotic fractures in the group comparisons of the initial and subsequent DRF groups could be explained by the FRAX calculation method. FRAX reflects the results of various variables including bone fragility parameters and clinical situations.[11] Although each parameter did not show significant differences in the group comparisons, the combinations of these factors could reveal significant differences.

This study has several limitations. First, its retrospective design limited its ability to prove causality for the occurrence of subsequent DRF. In addition, we could not evaluate other factors that may be related to the occurrence of subsequent DRF, such as physical performance level, risk of falling, and sarcopenia. A prospective observational study would be more suitable, but the time from initial to subsequent DRF was long and variable, and the incidence of subsequent DRF was not high. Thus, collecting a sufficient number of patients with detailed information would be difficult. Second, our institution is a tertiary referral hospital; thus, these subjects may be more diseased or injured than those in other institutions. Third, all study subjects were of Korean ethnicity. Because some hip geometry parameters, including HAL and NSA, vary according to ethnicity, the results cannot be extrapolated to other populations.[25] Finally, although we used propensity score matching to overcome the imbalances between the 2 groups, only 24 patients had experienced subsequent DRF, a much smaller number than the 203 for patients with initial DRF.

In conclusion, patients with subsequent DRF showed heterogeneity with respect to the age distribution and time interval between initial and subsequent DRF. Bone fragility parameters did not differ significantly between patients with initial and subsequent DRF. However, the ten-year probability of being affected by a major osteoporotic fracture was significantly higher for patients with subsequent DRF despite a higher number of osteoporosis treatments being performed in patients with subsequent DRF. These findings suggest that the occurrence of subsequent DRF after initial DRF can be attributed to multiple factors rather than bone fragility alone. Systematic and multidisciplinary management would be helpful for preventing the occurrence of subsequent DRF after the initial DRF.

DECLARATIONS

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Ethics approval and consent to participate

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of Asan Medical Center (2019-0686) and informed consent was waived.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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