

# Evaluation and Management of Osteoporosis and Sarcopenia in Patients with Distal Radius Fractures

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Distal radius fractures (DRFs) are one of the most common fractures seen in elderly people. Patients with DRFs have a high incidence of osteoporosis and an increased risk of subsequent fractures, subtle early physical performance changes, and a high prevalence of sarcopenia. Since DRFs typically occur earlier than vertebral or hip fractures, they reflect early changes of the bone and muscle frailty and provide physicians with an opportunity to prevent progression of frailty and secondary fractures. In this review, we will discuss the concept of DRFs as a medical condition that is at the start of the fragility fracture cascade, recent advances in the diagnosis of bone fragility including emerging importance of cortical porosity, fracture healing with osteoporosis medications, and recent progress in research on sarcopenia in patients with DRFs.

Keywords: Radius fractures, Osteoporosis, Sarcopenia, Osteoporotic fractures, Porosity

The World Health Organization has defined osteoporosis as a metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk.<sup>1)</sup> It has been estimated that more than 200 million people are suffering from osteoporosis.<sup>2)</sup> In 2008, about 40% of women in Korea were reported to have osteoporosis.<sup>3)</sup> On the other hand, sarcopenia is defined as the loss of muscle mass and muscle strength and functional impairment of muscles with aging, which compromises physical performance. It is closely associated with fractures and has been investigated as a new independent risk factor for fragility fractures, leading to a condition known as osteosarcopenia.<sup>4,5)</sup> Osteoporosis and sarcopenia are predominantly common in older individuals,

Received July 29, 2019; Accepted October 21, 2019

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Department of Orthopedic Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82 Gumi-ro 173beongil, Bundang-gu, Seongnam 13620, Korea Tel: +82-31-787-7198, Fax: +82-31-787-4056 E-mail: hsgong@snu.ac.kr resulting in increased morbidity, mortality, and healthcare costs.  $^{\rm 6,7)}$ 

Distal radius fractures (DRFs) are the most common upper extremity fracture in middle-aged and elderly people with an overall higher incidence in women.<sup>8)</sup> The incidence of DRFs is rising in recent decades. A study from the USA found a 17% increase in the incidence of this injury over a 40-year period, and in Sweden the incidence almost doubled for the older population over a 30-year time span.<sup>9,10)</sup> The proportion of DRFs treated by surgery tended to increase over time, from 32.6% in 2011 to 38.3% in 2015 in Korea.<sup>11)</sup>

Osteoporosis is an independent risk factor for lowenergy DRFs in the elderly population and hence should not be missed in managing DRFs. Studies have shown that patients with DRFs have a high incidence of osteoporosis and an increased risk of subsequent fractures, subtle early physical performance changes, and a high prevalence of sarcopenia.<sup>12,13)</sup> Since DRFs typically occur 15 years earlier than hip fractures, they reflect early changes of the bone and muscle frailty and provide physicians with an opportunity to prevent progression of frailty and secondary fractures.<sup>13,14)</sup> Since our last review on the evaluation of bone

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frailty in DRF patients,<sup>15)</sup> new information has emerged, including the importance of cortical porosity and muscle frailty in these patients. Therefore, in this review, we will discuss the concept of DRFs as a medical condition that starts the fragility fracture cascade, recent advances in the diagnosis of bone fragility including emerging importance of cortical porosity, fracture healing with osteoporosis medications, and recent progress in research on sarcopenia in DRF patients.

## DIAGNOSIS OF OSTEOPOROSIS AND ITS INCIDENCE IN PATIENTS WITH DRFs

The diagnosis of osteoporosis is based on dual-energy Xray absorptiometry (DXA), which is the reference standard for determining bone mineral density (BMD).<sup>16)</sup> Several previous studies have shown that BMD is lower in patients with a DRF than in those without a fracture.<sup>17-20)</sup> However, a few studies have found no difference between patients and controls.<sup>21,22)</sup> Table 1 shows the prevalence of osteoporosis in patients with DRFs.<sup>18-20,22-28)</sup> A study by Lee et al.<sup>24)</sup> in a Korean female population found that patients aged 50 to 59 years and 70 to 79 years who had DRFs had statistically significantly lower BMD at the hip than did the reference Korean female population.

While areal BMD (aBMD) measurement is a significant predictor of fracture risk, its value is limited because it is a two-dimensional technique and affected by the size and position of the subject and it cannot distinguish between cortical and trabecular compartments.<sup>25,29,30</sup> Moreover, BMD is not consistently lower in patients with a DRF than in normal controls and over 80% of fractures occur in women who would not be classified as osteoporotic according to current BMD criteria.<sup>21,22,24</sup> These suggest that factors other than BMD, such as bone microarchitecture, bone geometry, microdamage, mineralization, bone turnover, and propensity to fall, influence bone strength and fracture risk.<sup>13,30</sup>

## RECENT ADVANCES IN THE DIAGNOSIS OF BONE FRAGILITY IN PATIENTS WITH DRFs

Trabecular bone score (TBS) was introduced as a tool for assessing trabecular microarchitecture and has been used in many clinical and research fields. TBS is a textural index that evaluates pixel gray-level variations in the lumbar spine DXA image (Fig. 1).<sup>31)</sup> It provides an indirect index of trabecular microarchitecture and bone quality. TBS has shown significant association with fractures in several studies.<sup>32,33)</sup> In patients with DRFs, however, Shin et al.<sup>15)</sup>

found that TBS was not different from that in those without a fracture, although hip BMD was significantly lower in patients with DRFs. Their result suggests that TBS measured at the lumbar spine does not reflect early microarchitectural changes of the distal radius and only hip BMD is associated with the risk of DRFs.

BMD measured by quantitative computed tomography (QCT) provides a true volumetric BMD measure and it is not size dependent as in DXA. DXA measures integral (cortical and trabecular) aBMD, whereas QCT allows separate measurement of BMD of the trabecular and cortical bone compartments, enabling greater understanding of the effects of disease and treatment on bone.<sup>34</sup>

CT determines X-ray attenuation coefficient normalized to Hounsfield unit (HU) values (Fig. 2). HU values are measured by using the standard PACS (Picture Archiving and Communication System) software tool. A calibration phantom is required to be scanned with the patient to convert the HU into the bone mineral unit. This phantom contains various concentrations (g/cm<sup>3</sup>) of calcium hydroxyapatite or equivalent and is used to interpolate BMD based on the HU.<sup>35,36)</sup> Previous biomechanical study has shown that an increase in the HU value is correlated linearly with an increase in material density. HU values showed a decreasing trend with increasing age and decreasing BMD.<sup>37,38)</sup> Johnson et al.<sup>38)</sup> found that BMD and T-scores significantly correlate with the capitate trabecular HU in patients with wrist fractures. A capitate threshold of 307 HU maximizes sensitivity and specificity for detecting osteoporosis. High radiation exposure and low resolution imaging are the greatest disadvantages of this method.<sup>39)</sup> Currently, CT performed for other reasons such as fracture assessment is termed as opportunistic use. Such use of CT may increase screening rates or preclude DXA screening in some individuals.<sup>40)</sup>

High-resolution peripheral QCT (HR-pQCT) is a noninvasive approach, which enables *in vivo* three-dimensional analysis of bone microstructure at the appendicular skeleton.<sup>41)</sup> HR-pQCT allows the analysis of geometric, microstructural, densitometric, and mechanical properties of the trabecular and cortical bone architecture in the distal radius and tibia.<sup>41,42)</sup> In addition, the micro-finite element analysis permits the estimation of bone strength.<sup>43)</sup>

#### **CORTICAL POROSITY AND DRFs**

Cortical bone comprises approximately 70% mineralized matrix, and trabecular (spongy) bone comprises 10%–30% mineralized bone matrix fashioned as plates and rods occupying the medullary canal.<sup>44)</sup> As 80% of the skeleton

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is cortical bone, the size and number of porosity in this region play a critical role in bone strength.<sup>45)</sup> Even a small increase in porosity of cortex compromises stiffness to a greater extent than does the similar increase in an already highly porous trabecular bone.<sup>46)</sup>

Bala et al.<sup>47)</sup> analyzed HR-pQCT in 100 postmenopausal women aged above 50 years with a forearm fracture and 105 controls and found that women with a fracture

Table 1. Incidence of Osteoporosis in Patients with Distal Radius Fractures (DRFs)							
Study	No. of subjects	Mean age (yr)	Osteoporosis based on lumbar BMD or T-score	Osteoporosis based on hip BMD or T-score	Overall osteoporosis	Comment	
Earnshaw (1998) <sup>18)</sup>	106	65.7	< 65 yr: 17% ≥ 66 yr: 24%	< 65 yr: 24% ≥ 66 yr: 55%	50%		
Hegeman et al (2004) <sup>19)</sup>	. 94	69	< 65 yr: T-score, -1.41 (SD, 1.49) ≥ 66 yr: T-score, -2.16 (SD, 1.53)	< 65 yr: T-score, −1.17 (SD, 1.00) ≥ 66 yr: T-score, −1.75 (SD, 0.92)	51% Low BMD: 85%		
Sosa et al. (2005) <sup>22)</sup>	469	62.6	Calcaneus Quantit DRF gro Z-score: –0.55 ± T-score: –1.52 ±	tative Ultrasound index up Control <i>p</i> -value 0.90 –0.52 ± 1.03 0.707 0.86 –1.41 ± 0.97 0.254		<i>p</i> -values were not significant.	
Lofman et al. (2007) <sup>20)</sup>	171	67		50–59 yr: 19% 60–69 yr: 15% 70–79 yr: 83%	Osteoporosis: 37% Osteopenia: 52%		
Lashin and Davie (2008) <sup>23)</sup>	186	65.5		50–64 yr: 31.1% 65–74 yr: 34.4% > 75 yr: 40%	33.9%		
Lee et al. (2010) <sup>24)</sup>	54	64	50–59 yr: 38% 60–69 yr: 34% 70–79 yr: 67%		57.4%		
Oyen et al. (2011) <sup>25)</sup>	664 Women, 85 men	66	Women Mer Osteoporosis: 39% 23% Osteopenia: 34% 42%	N Women Men 50–59 yr: 18%/59% 50–59 yr: 17%/64% 60–69 yr: 25%/46% 50–64 yr: 14%/- 65–90 yr: 51%/40% 64–90 yr: 20%/-	Women: 34% OR (95% CI) Osteoporosis: 7.1 (4.3–11.6) Osteopenia: 2.7 (1.9–3.9) Men: 17% Osteoporosis: 8.5 (1.6–4.7) Osteopenia: 3.4 (1.1–10.5)	Osteoporosis was significantly associated with low-energy distal radial fracture.	
Jang et al. (2012) <sup>26)</sup>	104 Women	65		Femoral neck BMD DRF Group: 0.65 ± 0.16 (0.20–1.07) Control: 0.70 ± 0.14 (0.28–1.01) (p = 0.03	3)	Hip BMDs were significantly lower in the DRF group than in the control group.	
Massey et al. (2015) <sup>27)</sup>	128 Women	Group 1 (35–50 yr) Group 2 (> 50 yr)	Group 1: Osteoporosis, 17% Osteopenia, 23% Group 2: Osteoporosis, 26% Osteopenia, 27%	<ul> <li>Group 1: Osteoporosis, 6%</li> <li>Osteopenia, 43%</li> <li>Group 2: Osteoporosis, 27%</li> <li>Osteopenia, 48%</li> </ul>			
Jung et al. (2016) <sup>28)</sup>	206	Group 1 (50–59 yr) Group 2 (60–69 yr) Group 3 (70–79 yr)	Lumbar BMD Group 1: $0.928 \pm 0.14$ Control: $1.004 \pm 0.15$ ( $p = 0.13$ ) Group 2: $0.831 \pm 0.12$ Control: $0.892 \pm 0.14$ ( $p = 0.52$ ) Group 3: $0.816 \pm 0.17$ Control: $0.848 \pm 0.16$ ( $p = 0.72$ )	Femoral neck BMD Group 1: $0.802 \pm 0.10$ 2) Control: $0.889 \pm 0.12$ ( $p < 0.001$ ) Group 2: $0.745 \pm 0.09$ 7) Control: $0.774 \pm 0.09$ ( $p = 0.473$ ) Group 3: $0.670 \pm 0.08$ 4) Control: $0.707 \pm 0.12$ ( $p = 0.325$ )	51.5%	Only the BMD in the femur area was significantly lower in group 1 (50–59 yr) than in age-matched controls.	

Values are presented as mean  $\pm$  SD or mean  $\pm$  SD (range). BMD: bone mineral density, SD: standard deviation, OR: odds ratio, CI: confidence interval.

had micro-architectural deterioration, increased cortical porosity, and decreased trabecular bone volume fraction. They found significant correlations between the risk of a major fracture and cortical porosity. In women with osteopenia, the source of over 50% of all fractures, fracture risk was increased if high porosity was present. They found that only cortical porosity measured at ultradistal radius predicted fracture risk, independently of aBMD alone. Thus, measuring cortical porosity is clinically useful in identifying patients at risk for fractures, who can be considered at low risk on the basis of their aBMD measurement alone.<sup>47)</sup>

Biver et al.<sup>48)</sup> investigated the independent contribution of cortical and trabecular volumetric BMD (vBMD) and microstructure as risk factors of incident fractures in a cohort of 740 community-dwelling postmenopausal women. They found that two-thirds of the women with fractures were not classified as osteoporotic by conventional DXA. For major osteoporotic fractures, the highest hazard ratio was obtained for the inner cortical porosity of the radius, which might reflect both cortical and trabecular compartments. They concluded that peripheral (ultradistal radius and tibia) cortical and trabecular vBMD and microstructure would predict a fracture independently of each other and other currently used tools such as femoral neck BMD, fracture risk assessment tool, and TBS.

## RISKS OF SUBSEQUENT FRACTURES IN PATIENTS WITH DRFs

Many studies have shown that patients with DRFs have a greater probability of a subsequent fracture in later life



**Fig. 2.** Hounsfield unit measurement of the capitate in the coronal section of computed tomography with a circular region of interest with a diameter of 1 cm. Min: minimum, Max: maximum, Avg: average, SD: standard deviation.



**Fig. 1.** The trabecular bone score (TBS) examination shows that the two patients with the same age (52 years) and similar bone mineral density (BMD) have different trabecular bone qualities.

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than those without previous DRFs. The association of prior wrist fractures and subsequent fractures is shown in Table 2.  $^{49-58)}$ 

A meta-analysis study by Haentjens et al.<sup>53)</sup> highlights that DRFs increased the relative risk (RR) of hip fractures more significantly in men than in women. The impact of a spine fracture, in contrast, did not differ between gen-

ders). Owen et al.<sup>54)</sup> showed that a DRF associated with minor trauma is indicative of an overall 50% increase in the risk of a subsequent hip fracture. The RR of a subsequent hip fracture is greater for men with DRFs (RR, 6.4) than for women with DRFs (RR, 1.3). Other studies show similar results in which male have a greater chance of subsequent fractures than women irrespective of age.<sup>54,58)</sup>

Table 2. Risks of Subsequent Fractures in Patients with Distal Radius Fractures (DRFs)							
	Study	Population	Country	Study type	Subsequent fragility fracture (RR/RH/HR/OR/SIR)	Comment	
	Owen et al. (1982) <sup>54)</sup>		USA	Retrospective study	Hip fracture RR: 6.4 for men, 1.3 for women	Overall 50% increase in the risk of a subsequent hip fracture.	
	Mallmin et al. (1993) <sup>52)</sup>	1,126 Women, 212 men > 40 yr	Sweden	Cohort study	RH: 2.27 for men, 1.54 for women	The increased risk in the women was independent of age at inclusion, but that in the men was more pronounced in the younger age groups.	
	Lauritzen et al. (1993) <sup>55)</sup>	1,162 Women 20–99 yr	Denmark		Hip fracture RR: 60–79 yr, 1.9 (95% Cl, 1.3–2.6) RR: 20–99 yr, 1.8 (95% Cl, 1.3–2.2)	The relative risk of hip fracture was highest within the first years after a fracture of the radius or the humerus.	
	Tuppurainen et al. (1995) <sup>57)</sup>	3,140 Women 53.4 ± 2.8 yr	Finland	Prospective study	Wrist fracture RR: 2.25 (95% Cl, 1.10–4.62)	Former history of fractures, low baseline BMD, and use of alcohol are predisposing factors associated with premenopausal fractures, while hormone replacement therapy is protective in this respect.	
	Honkanen et al. (1997) <sup>56)</sup>	12,162 Women	Norway	Retrospective study	HR: 1.9 (95% CI, 1.6–2.3)	Early premenopausal low-energy wrist fracture is an indicator of low peak BMD, which predisposes to subsequent fractures in general.	
	Cuddihy et al. (2002) <sup>58)</sup>	1,288 (243 Men, 1,045 women) ≥ 35 yr	USA	Retrospective cohort study	Hip fracture RR: 1.4 for women (95% Cl, 1.1–1.8) 2.7 for men (95% Cl, 0.98–5.8) Vertebral fracture RR: 5.2 for women (95% Cl, 4.5–5.9) 10.7 for men (95% Cl, 6.7–16.3)		
	Haentjens et al. (2003) <sup>53)</sup>	499 Men, 3,683 women	USA, Europe	Meta-analysis study	Hip fracture RR: 1.53 (95% Cl, 1.34–1.74) In older men RR: 3.26 (95% Cl, 2.08–5.11)	Fractures of the distal part of the radius increased the RR of hip fracture more significantly in men than in women.	
	Schousboe et al. (2005) <sup>50)</sup>	9,704 Women > 50 yr	USA	Cohort study	Vertebral fracture OR: 1.72 (95% Cl, 1.31–2.25) Hip fracture HR: 1.43 (95% Cl, 1.17–1.74)		
	Oyen et al. (2010) <sup>51)</sup>	218 Men,1,576 women ≥ 50 yr	Norway	Cohort study	RR with a T-score ≤ -2.5 Men: 16.3% risk of hip fracture 25.1% risk of other osteoporotic fractures Women: 18.2% hip fracture 34.7% risk of other osteoporotic fractures	There is an increase in fracture risk with increasing age and number of previous fractures.	
	Amin et al. (2013) <sup>49)</sup>	1,776 Adolescents, $\leq$ 18 yr 1,086 Boys, 11 $\pm$ 4 yr 690 Girls, 10 $\pm$ 4 yr	USA	Cohort study	At least one fragility fractures at $\ge$ 35 yr: 144 (13%) in boys and 74 (11%) in girls Boy: SIR, 1.9 (95% CI, 1.6–2.3) Girl: SIR, 1.0 (95% CI, 0.8–1.2)	DRF in boys, but not in girls, is associated with an increased risk for fragility fractures as older adults.	

RR: relative risk, RH: relative hazard, HR: hazard ratio, OR: odds ratio, SIR: standardized incidence ratio, CI: confidence interval, BMD: bone mineral density.

Thus, a previous low-energy DRF in middle-aged and elderly patients have shown to be a predictor of osteoporosis and greater risk of subsequent fractures.

Hip geometry is known as a risk factor of osteoporotic hip fractures.<sup>59)</sup> Shin et al.<sup>60)</sup> reported that DRF patients had lower hip BMD; lower cortical thickness, crosssectional area, and section modulus; and higher buckling ratio than a control group. They suggested that mechanical factors, specifically the geometry of the weak proximal femur, may increase the risk of subsequent hip fractures in patients with DRFs. On lumbar geometry, Melton et al.<sup>61)</sup> showed that the lumber spine vBMD, bone geometry (vertebral apparent cortical thickness), bone microstructure, bone strength, and spine load to bone strength ratio can be correlated with a predictor of vertebral fractures. These parameters have not been correlated with DRFs and will be a subject of further studies.

## **TREATMENT OF OSTEOPOROTIC DRFs**

Traditionally, stable DRFs have been treated with closed reduction and cast immobilization with satisfactory clinical outcomes.<sup>62)</sup> However, osteoporosis can compromise the maintenance of reduction achieved by cast application or pinning.<sup>63)</sup> Molded casts frequently fail to prevent loss of reduction and, in particular, shortening of the radius, and percutaneous pinning is reported as ineffective in osteoporotic bone.<sup>64,65)</sup> Therefore, open reduction and internal fixation with a volar fixed-angle locking plate has become a popular option for the treatment of unstable DRFs.<sup>66-68)</sup> In a recent randomized trial comparing nonoperative treatment with volar locking plate fixation for DRFs in elderly patients ( $\geq$  70 years), the Patient Rated Wrist Evaluation score, the Disabilities of Arm, Shoulder and Hand (DASH) score, and grip strength were better for the volar locking plate group at 3 months and 12 months whereas the complication rates were similar, suggesting a benefit of volar plating in the elderly patient.<sup>69)</sup>

Interestingly, conflicting results have been seen in literatures regarding the influence of osteoporosis on radiological and clinical outcomes of DRFs treated with open reduction and internal fixation with a volar locking plate.<sup>68,70-75)</sup> Several studies have mentioned that rigid fixation using volar locking plates in DRF patients with osteoporosis provided radiological and clinical outcomes similar to those in DRF patients without osteoporosis.<sup>5,70,75,76)</sup> However, some studies have shown that patients with osteoporosis have worse clinical outcomes than nonosteoporotic patients despite similar radiological outcomes.<sup>73,74)</sup> Fitzpatrick et al.<sup>73)</sup> reported that osteoporosis by BMD was a strong independent predictor of high DASH scores, and a decrease in BMD was associated with reduced grip strength.<sup>74)</sup> Osteoporotic bone can negatively affect the mechanical property of fracture callus and impairs fracture healing especially in the early and later periods.<sup>77)</sup>

Several investigators have shown improved anatomic and functional outcomes with the use of autologous bone grafts to reconstruct the radial metaphysis.<sup>78,79)</sup> However, harvesting bone grafts results in increased operative time, blood loss, postoperative pain, cost, and surgical complications.<sup>79)</sup> Bone graft substitutes have been introduced, but with respect to outcome improvement, need for fixation, or healing time, which of the numerous types of bone graft substitutes can best replace autografts in DRFs remains to be elucidated.<sup>79)</sup>

## OSTEOPOROSIS TREATMENT AND FRACTURE HEALING

Pharmacologic options for the treatment of osteoporosis include bisphosphonates, calcitonin, estrogens, estrogen agonist/antagonist, parathyroid hormone, and the receptor activator of nuclear factor kappa-B ligand inhibitor (denosumab) and humanized monoclonal antibody to sclerostin (romosozumab).<sup>80,81)</sup>

Controversies exist regarding osteoporosis therapy and fracture healing. Rozental et al.<sup>14)</sup> compared healing rates assessed by radiographic union of DRF in patients on bisphosphonate therapy at the time of the injury to those not on the therapy. They found that bisphosphonate use was associated with a slightly longer time of fracture healing (approximately 6 days) compared to no therapy. However, a randomized study by Gong et al.<sup>82)</sup> showed that early initiation of bisphosphonate treatment for patients with an osteoporotic DRF treated with volar locking plate fixation does not affect fracture healing or radiographic or clinical outcomes. Similarly, denosumab showed neither delay of the fracture healing nor contributions to other complications, even when it is administered at or near the time of the fracture in nonvertebral fractures.<sup>83)</sup> One possible explanation is that although bisphosphonate and denosumab are antiresorptive by action, they (denosumab at high doses) delay callus remodeling and thus increase callus volume and provide mechanical strength.<sup>83)</sup> Anabolic agents like teriparatide were shown to shorten time to healing of DRFs. However, due to high cost and good healing by the conventional management, routine use of teriparatide is not recommended in DRFs.<sup>84)</sup>

A newer anabolic agent romosozumab has been introduced and clinical trial data show its significant

antifracture benefits.<sup>85)</sup> Romosozumab is a humanized monoclonal antibody to sclerostin, an inhibitor of Wnt signaling pathways. When romosozumab binds to sclerostin, sclerostin cannot bind to the LRP-5/6 receptors and cannot exert its inhibitory effect, permitting the engagement of Wnt ligands with their coreceptors, resulting in an increase in bone formation and BMD.<sup>86)</sup>

# **CARE GAP IN PATIENTS WITH DRFs**

Many studies show that rates of evaluation to identify osteoporosis and treatment following fragility fractures are inadequate, especially for patients with nonvertebral fractures (Table 3).<sup>14,58,87-90)</sup> Only 2.8% of women over the age of 50 years with a DRF underwent a BMD scan, and only 22.9% were managed with osteoporosis medication in the USA.<sup>87)</sup> In Korea, Gong et al.<sup>90)</sup> used the national cohort in 2007 and found that 8.7% the patients with DRFs underwent diagnostic bone density scans, whereas 22.5% with a hip fracture and 28.8% with a spine fracture underwent a bone density scan. Regarding reasons for this gap between fragility fractures and osteoporosis care, Andrade et al.<sup>88)</sup> suggested that the problem may be at the level of the healthcare delivery system. There may be a clinical disconnection between the physicians who treat fragility fractures and physicians who are responsible for detecting and treating osteoporosis.

Studies have been also conducted regarding patient

adherence to medication. Poor adherence to osteoporosis medication is often observed in postmenopausal women, and limited health literacy appears to be associated with this poor adherence.<sup>91)</sup> In a study by Roh at al.,<sup>91)</sup> inadequate health literacy among patients who had sustained a DRF was associated with poor adherence to weekly oral, but not quarterly intravenous, bisphosphonates. Another study by Roh et al.<sup>92)</sup> stated that younger age and unmarried status are significant factors for avoiding a test for osteoporosis while younger age and lower level of annual income are associated with discontinuing osteoporosis treatment.

#### FRACTURE LIAISON SERVICE

A fracture liaison service (FLS) is a multidisciplinary system approach to reduce subsequent fracture risk in patients with a recent fragility fracture by identifying them at or close to the time when they are treated at the hospital for fracture and providing them with easy access to osteoporosis care.<sup>93)</sup> In this model of care, a patient is automatically enrolled in the assessment of risk for a secondary fracture and treatment is initiated to improve bone quality and strength. Kaufman et al.<sup>94)</sup> have shown that compared to other models such as referral letters to primary care physicians or endocrinologists, the FLS model results in a higher rate of diagnosis and treatment with less attrition in the post fracture phase. The international Osteoporosis

Table 3. Care Gap in Patients with Distal Radius Fractures (DRFs)							
Study	Sample size	Wrist fracture evaluated for osteoporosis (%)	Wrist fracture treated for osteoporosis (%)	Not evaluated/ advised (%)	Comment		
Freedman et al. (2000) <sup>87)</sup>	1,162		24		There was a significant decrease in the rate of treatment of osteoporosis with increasing patient age at the time of the fracture.		
Cuddihy et al. (2002) <sup>58)</sup>	343			70.8			
Andrade et al. (2003) <sup>88)</sup>	1,620		23		44% of vertebral fractures and 21% of hip fractures treated for osteoporosis. Increasing age was associated with a reduced likelihood of receiving osteoporosis treatment.		
Rozental et al. (2008) <sup>14)</sup>	240	21.3	27.5	78.7	Ordering a BMD can dramatically improve osteoporosis evaluation and treatment rates following DRF.		
Gong et al. (2009) <sup>90)</sup>	61,234		7.5		30.1% of vertebral fractures and 22.4% of hip fractures treated for osteoporosis.		
Sarfani et al. (2014) <sup>89)</sup>	82	15					

BMD: bone mineral density.

Foundation in 2013 recommended setting up FLS for prevention of secondary fractures.<sup>95)</sup>

Regarding the outcomes of FLS, a study on comparative refracture rates of FLS in Ontario, Canada, reported that relative to distal radius, presenting with multiple fractures at screening was associated with a higher risk of refracture while presenting with an ankle fracture was associated with a lower risk of refracture.<sup>96</sup>

### EVALUATION OF SARCOPENIA IN PATIENTS WITH DRFs

Sarcopenia, a term first introduced in 1984 by Rosenberg, refers to age-related loss of muscle mass, and is thus a type of geriatric syndrome.<sup>97)</sup> Sarcopenia is a known risk factor for both falls and fractures. Reduced muscle strength makes it more difficult to regain lost balance and decreases the mechanical loading of the skeleton, leading to reduced adaptive bone remodeling.<sup>98,99)</sup>

Studies suggest that patients with DRFs show subtle early changes in physical performance and muscle strength.<sup>13,99</sup> Cho et al.<sup>13</sup> compared physical performance measures and fall risk factors in patients with recent DRFs and in age-matched control patients. Although there were no significant differences in the Short Physical Performance Battery Summary score, the Chair Stand score and grip strength were significantly lower in patients than in the control group. Furthermore, Fujita et al.<sup>100</sup> showed that patients with DRFs have lower grip strength, prolonged Timed Up and Go test time and lower 2-Step test score than do controls.

Roh et al.<sup>12)</sup> reported a higher prevalence of sarcopenia in patients with DRFs compared to age- and sexmatched controls. In this study, 30% of DRF patients were sarcopenic, whereas 17% of controls were within the sarcopenic criteria. The patient group had significantly lower lean body mass and weaker grip strength than the control group. However, there was no significant difference in gait speed between the two groups. Regarding the outcomes of treatment of DRFs, sarcopenic patients had similar radiologic outcomes but worse functional outcomes than control patients.<sup>101)</sup>

#### **VITAMIN D AND DRFs**

Vitamin D influences skeletal mineralization principally through the regulation of intestinal calcium absorption. Vitamin D deficiency leads to stimulation of parathyroid hormone secretion, resulting in increased bone resorption and hence bone mass loss.<sup>102</sup> It has been associated with

hip and low-energy DRFs and also has a direct effect on muscle strength modulated by specific vitamin D receptors (VDRs) present in human muscle tissue.<sup>103,104)</sup> In a study in Korean women, the mean vitamin D level was significantly lower in the DRF group than in the control group.<sup>26)</sup> Kim et al.<sup>105)</sup> assessed the VDR expression in the skeletal muscles of the forearm by immunohistochemistry in patients with DRFs and found that patients with lower muscle mass showed a significantly lower cross-sectional area of a single muscle fiber but a higher level of VDR expression. They suggested that the VDR expression is increased and the use of vitamin D is maximized in these patients to compensate for reduced muscle mass. Several studies have shown that individuals with a low vitamin D status improve in both muscle strength and performance through vitamin D supplementation.<sup>106,107)</sup>

#### CONCLUSIONS

DRFs occur on average 15 years earlier than hip fractures and are a condition that is at the start of the fragility fracture cascade. Therefore, occurrence of a DRF can be considered for physicians as an important opportunity to diagnose and treat osteoporosis and sarcopenia to prevent a secondary fracture. However, there is still a care gap between fragility fractures and osteoporosis care, especially for DRFs. Systematic approaches to address this care gap, such as FLS, are now implemented and further studies are necessary to confirm the effectiveness of such approaches.

Because DRFs can reflect early changes of bone and muscle weakness, studies on characteristics of patients with DRFs can suggest some insights on how to prevent these aging processes. Previously, measurement of BMD by DXA was considered the standard method but not all patients with DRFs have osteoporosis defined by the current BMD criteria. Recent studies using other assessment technologies such as HR-pQCT highlight the importance of cortical porosity in predicting fractures. In addition, studies on physical performance and muscles in DRF patients suggest identifiable risk factors for falls or fractures, such as decreased grip strength. Further studies are necessary to better identify patients with an increased risk of fractures or falls and intervention strategies to strength the bone and muscle.

#### **CONFLICT OF INTEREST**

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

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