New quantitative ultrasound techniques for bone analysis at the distal radius in hip fracture cases: differences between femoral neck and trochanteric fractures

Motoyuki Horii¹
Hiroyoshi Fujiwara¹
Ryo Sakai¹,²
Koshiro Sawada³
Yasuo Mikami³
Syogo Toyama¹
Etsuko Ozaki⁴
Nagato Kuriyama⁴
Masao Kurokawa²
Toshikazu Kubo¹

¹Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan
²Department of Orthopaedics, Saiseikai Suita Hospital, Japan
³Department of Rehabilitation Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Japan
⁴Department of Epidemiology for Community Health and Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Japan

Address for correspondence:
Motoyuki Horii
Department of Orthopaedics
Graduate School of Medical Science
Kyoto Prefectural University of Medicine
Kyoto, Japan
E-mail: horii@koto.kpu-m.ac.jp

Summary

Background. Ample evidence on etiological and pathological differences between femoral neck and trochanteric fracture cases suggests the possibility of individualized treatment. There are many issues related to areal bone mineral density and other quantitative computed tomography parameters of the proximal femur. Although osteoporosis is a systemic problem, little has been reported regarding differences in bone structural parameters, including bone mineral density, between them in regions other than the proximal femur.

Methods. Participants were consecutive female patients >50 years of age admitted to the Saiseikai Suita Hospital (Osaka prefecture, Japan) for their first hip fracture between January 2012 and September 2014. Cortical thickness (CoTh, mm), volumetric trabecular bone mineral density (TBD, mg/cm³), and elastic modulus of trabecular bone (EMTb, GPa) were obtained as the new QUS parameters using the LD-100 system (Oyo Electric, Kyoto, Japan). The mean values of these parameters were compared between femoral neck and trochanteric fracture cases. In addition, correlations between age and each QUS parameter were investigated for each fracture type. A receiver operating characteristic (ROC) curve analysis was performed to examine the degree of effect each parameter on the fracture types. The area under the curve (AUC) for each parameter was compared to the AUC for age.

Results. There were 63 cases of femoral neck fracture (mean age, 78.2 years) and 37 cases of trochanteric fracture (mean age, 85.9 years). Mean TBD and EMTb were significantly higher for femoral neck fractures. There were significant negative correlations between QUS parameters and age for femoral neck fractures (P < 0.005). The regression lines for femoral neck fractures were above those for trochanteric fractures for TBD and EMTb. AUCs were 0.72 for age, and 0.61, 0.65, and 0.65 for CoTh, TBD, and EMTb, respectively.

Conclusions. The new QUS parameters indicated that TR fracture cases were more osteoporotic than were FN fracture cases, even at the distal radius. There might be systemic differences between them, in addition to localized factors at the proximal femur.

KEY WORDS: hip fracture; femoral neck fracture; trochanteric fracture; quantitative ultrasound; distal radius; osteoporosis.

Background

Hip fracture, one of the primary osteoporotic fractures, has a profound influence not only on decreasing healthy life expectancy but also the length of the lifespan overall. Although the recent decline of its incidence has been suggested even in Japan, the number of new patients continues to increase tremendously due to the rapid increase in the elderly population (1). Fracture prevention is a major health and socioeconomic concern in many countries. There are two types of hip fracture, namely femoral neck fracture (FN fracture) and trochanteric fracture (TR fracture). There is a lot of evidence to indicate etiological and pathological differences between them, suggesting the possibility of individualized treatment to improve prevention of hip fractures (2, 3). Among these differences, there are many issues related to areal bone mineral density (areal BMD) as measured by dual energy X-ray absorptiometry (DXA) and other quantitative computed tomography (QCT) parameters on the proximal femur (4-6). Apart from these radiation methods, quantitative ultrasound (QUS) is easily utilized for health examination purposes, even outside of medical institutions, because it does not involve exposure to ionizing radiation. Recently, a new ultrasound method to assess bone densitometry at the distal radius based on two longitudinal waves (new QUS) was developed (LD-100 system, Oyo Electric, Kyoto, Japan), and it was proven to show significant correlations with peripheral QCT (pQCT) measurement values (7).Al-
though osteoporosis is a systemic problem, little has been reported about differences in bone structural parameters, including bone mineral density (BMD), between FN and TR fractures in regions other than the proximal femur. The aim of this study was to investigate the differences between FN and TR fractures using the new QUS parameters obtained at the distal radius.

Participants and methods

Participants

The participants were consecutive female patients >50 years of age admitted to the Saiseikai Suita Hospital (Osaka prefecture, Japan) for first hip fracture between January 2012 and September 2014. Patients with a history of systemic administration of corticosteroid were not included. Women with hip fractures secondary to tumors were also excluded.

New QUS measurements

The transducers of the LD-100 system were set at the distal radius of each participant with ultrasound gel. The non-dominant side was generally assessed, except in cases with a previous fracture at the corresponding site. Cortical thickness (CoTh, mm), volumetric trabecular BMD (TBD, mg/cm²), and elastic modulus of the trabecular bone (EMTb, GPa) were obtained as the new QUS parameters and were calculated from the propagation speed (m/s) and the attenuation (dB) of both fast and slow waves (7). T-score results were also automatically provided.

Data analysis

T-scores were used for the data analysis. The mean values of these parameters were compared between FN and TR fracture cases. In addition, correlations between age and each QUS parameter were investigated for FN and TR fractures.

A receiver operating characteristic (ROC) curve analysis was performed to examine the degree of effect of each parameter on the fracture types. The area under the curve (AUC) for each parameter was compared to the AUC for age.

The Mann-Whitney U-test was used to compare parameters between FN and TR fracture cases. A P-value of <0.05 was regarded as significant. Statistical analyses were conducted with StatFlex Ver. 6.0 (Artech Co., Ltd., Osaka, Japan).

Results

A total of 100 fractures from 100 subjects was included. There were 63 cases of FN fracture and 37 cases of TR fracture. The mean age (SD) was 78.2 (10.1) years for FN fracture cases. A higher ratio of FN fractures than of TR fractures is observed in Japan (13). A significantly higher mean age than other fracture patients. Our results showed that TR fracture cases had a greater extent of osteoporosis than FN fractures (8). In addition to a lower BMD, a thinner cortex has also been recognized for TR fracture cases in the proximal femur (5, 9, 10).

Our results showed that TR fracture cases had a greater extent of osteoporosis, even in the distal radius. There were significant differences not only for TBD but also for EMTb, which is directly related to mechanical bone strength (7). Numerically, CoTh was thinner for TR fracture cases. Those results in the distal radius may indicate that the differences between these fracture cases are systemic.

General concern that TR fractures have a significantly lower mean age than FN fracture cases. The ROC analysis showed the highest AUC of 0.722 for age compared to those for the QUS parameters. These results suggest a strong correlation between age and fracture type. On the other hand, moderate correlations between TBD and EMTb related to the fracture types were indicated by the respective AUCs of 0.649 and 0.652, which were not significantly different when compared to the AUC for age. The regression lines for FN fractures were above those for TR fractures on the scatter plots for TBD and EMTb.

Previously, the rate of increase was shown to be more remarkable for FN fractures than for TR fractures in Japan (13). A higher ratio of FN fractures than of TR fractures is observed in Western countries, in contrast to the ratios observed in Japan (14, 15). A higher incidence was also recognized among urban populations compared to that in rural populations (16, 17).

Previous studies suggest that patients who experience FN fractures have higher body fat percentages (18), higher body mass indices (BMIs), and are more likely to have undergone treatment for hypertension (19). Arakaki et al. reported about differences in bone structural parameters, including bone mineral density, between FN and TR fractures in regions other than the proximal femur.

Table 1 - Areas under the curve for age and each quantitative ultrasound parameter.

| Parameter | AUC  | SE   |
|-----------|------|------|
| Age       | 0.72 | 0.05 |
| CoTh      | 0.61 | 0.06 |
| TBD       | 0.65 | 0.06 |
| EMTb      | 0.65 | 0.06 |

AUC, area under the curve; CoTh, cortical thickness; EMTb, elastic modulus of trabecular bone; SE, standard error; TBD, volumetric trabecular bone mineral density.
of FN fracture (20). Worsening collagen crosslinking is a major candidate related to bone fragility other than BMD, which is strongly affected by metabolic syndrome, such as diabetes (21).

Among our cases, there were no differences in height, weight, or BMI between fracture types. With respect to complications, a greater number of FN fracture patients had taken medication for diabetes (Table 2).
TR fractures may be best prevented by increasing bone density (2). For FN fractures, the risk profile is considerably more complex than that for TR fractures (3). Because of the variety and complexity of osteoporotic fractures, the precise determination of risk factors for each osteoporotic fracture might be virtually impossible (22). However, research specifically focusing on FN fractures could facilitate more effective individualized preventive measures. Our results indicate that systemic factors should be taken into consideration in future research, in addition to local factors.

This study has some limitations. First, there was no comparison with femoral neck BMD, which is recommended by WHO for the diagnosis of osteoporosis (23). Second, information about medication usage for osteoporosis was not available, though many of the cases were estimated to have been left untreated. Third, there was no control population, such as one without fractures. Our data do not indicate any candidate criteria to target to prevent hip fracture. Fourth, data were analyzed only from female patients because of the small amount of cases.

Conclusions
The new QUS parameters indicated that TR fracture cases were more osteoporotic than were FN fracture cases, even at the distal radius. There might be systemic differences between them, in addition to localized factors at the proximal femur.

Abbreviations
AUC: area under the curve  
BMD: bone mineral density  
BMI: body mass index  
CoTh: cortical thickness  
DXA: dual energy X-ray absorptiometry  
EMTb: elastic modulus of trabecular bone  
FN fracture: femoral neck fracture  
pQCT: peripheral quantitative computed tomography  
QCT: quantitative computed tomography  
QUS: quantitative ultrasound

Table 2 - Body characteristics and complications.

| Body characteristics       | Femoral neck fracture | Trochanteric fracture |
|----------------------------|-----------------------|-----------------------|
| Height, cm, mean ± SD      | 149.8 ± 7.5           | 148.2 ± 6.1           |
| Weight, kg, mean ± SD      | 48.4 ± 7.6            | 47.3 ± 9.5            |
| BMI, kg/m², mean ± SD      | 21.7 ± 3.3            | 21.5 ± 4.0            |

Complications
- Diabetes, n (%): 16 (25.4%) for FN, 5 (13.5%) for TR
- Hypertension, n (%): 38 (60.3%) for FN, 22 (59.5%) for TR
- Rheumatic arthritis, n (%): 2 (3.2%) for FN, 0 (0%) for TR
- Vertebral fracture*, n (%): 4 (6.3%) for FN, 0 (0%) for TR
- Dialysis, n (%): 1 (1.6%) for FN, 0 (0%) for TR

* Prevalent fractures. BMI, body mass index; SD, standard deviation.
New quantitative ultrasound techniques for bone analysis at the distal radius in hip fracture cases: differences between femoral neck and trochanteric fractures

ROC: receiver operating characteristic
TBD: volumetric trabecular bone mineral density
TR fracture: trochanteric fracture

Declarations

Ethic approval and consent to participate
Ethical approval was obtained from the ethics committee of Kyoto Prefectural University of Medicine, and written informed consent was obtained from all patients prior to inclusion.

Consent for publication
Not applicable.

Availability of data and materials
The dataset supporting the conclusions of this article is available upon readers request - please contact corresponding Author (horii@koto.kpu-m.ac.jp).

Acknowledgement
None of the Authors reports any relevant financial conflict of interest. The Authors would like to thank Dr. Isao Mano of Oyo Electric for his technical support for the LD-100 system.

Competing interests
The Authors declare that they have no competing interests.

Author’s contributions
MH, HF, NK, and TK contributed to the conception and design of the study. RS and MK participated in the data collection. MH, KS, NK, and EO performed the statistical analysis. MH, YM, and ST drafted the manuscript. All Authors read and approved the final manuscript.

References
1. Orimo H, Yaegashi Y, Hosoi T, Fukushima Y, Onoda T, Hashimoto T, Sakata K. Hip fracture incidence in Japan: Estimates of new patients in 2012 and 25-year trends. Osteoporos Int. 2016 Jan 5. [Epub ahead of print].
2. Fox KM, Cummings SR, Williams E, Stone K. Study of Osteoporotic Fractures. Femoral neck and intertrochanteric fractures have different risk factors: a prospective study. Osteoporos Int. 2000;11(12):1018-1023.
3. Pulkkinen P, Gürer CC, Jämäö T. Investigation of differences between hip fracture types: a worthy strategy for improved risk assessment and fracture prevention. Bone. 2011;49(4):600-604.
4. Greenspan SL, Myers ER, Maillard LA, Kido TH, Krasnow MB, Hayes WC. Trochanteric bone mineral density is associated with type of hip fracture in the elderly. J Bone Miner Res. 1994;9(12):1889-1894.
5. Johannesdottir F, Poole KE, Reeve J, Siggeirsdottir K, Aspelund T, Mogensen B, Jonsson BY, Sigurdsson S, Harris TB, Gudnason VG, Sigurdsson G. Distribution of cortical bone in the femoral neck and hip fracture: a prospective case-control analysis of 143 incident hip fractures; the AGES-REYKJAVIK Study. Bone. 2011;48(6):1268-1278.
6. Hey HO, Sng WJ, Lim JL, Tan CS, Gan AT, Ng JH, Kang FH. Interpretation of hip fracture patterns using areal bone mineral density in the proximal femur. Arch Orthop Trauma Surg. 2015;135(12):1647-1653.
7. Sai H, Iguchi G, Tobimatsu T, Takashiki K, Otsu T, Horii K, Mano I, Nagai I, Ito H, Fujita T, Yoh K, Baba H. Novel ultrasonic bone densitometry based on two longitudinal waves: significant correlation with pQCT measurement values and age-related changes in trabecular bone density, cortical thickness, and elastic modulus of trabecular bone in a normal Japanese population. Osteoporos Int. 2010;21(10):1781-1790.
8. Watt J, Cox L, Crilly RG. Distribution of vertebral fractures varies among patients according to hip fracture type. Osteoporos Int. 2015;26(3):885-890.
9. Museyko O, Bousson V, Adams J, Laredo JD, Engelke K. OCT of the proximal femur—which parameters should be measured to discriminate hip fractures? Osteoporos Int. 2016 Mar;27(3):1137-1147.
10. Szulc P, Duboeuf F, Schott AM, Dargent-Molina P, Meunier PJ, Delmas PD. Structural determinants of hip fracture in elderly women: re-analysis of the data from the EPIDOS study. Osteoporos Int. 2006 Feb;17(2):231-236.
11. Committee for Osteoporosis Treatment of The Japanese Orthopaedic Association. Nationwide survey of hip fractures in Japan. J Orthop Sci. 2004;9(1):1-5.
12. Lofman O, Berglund K, Larsson L, Toss G. Changes in hip fracture epidemiology: redistribution between ages, genders and fracture types. Osteoporos Int. 2002;13(1):18-25.
13. Hagino H, Sakamato K, Harada A, Nakamura T, Mutoh Y, Mori S, Endo N, Nakan O, Ito E, Kita K, Yamamoto N, Aoyagi K, Yamazaki K. Committee on Osteoporosis of The Japanese Orthopaedic Association. Nationwide one-decade survey of hip fractures in Japan. J Orthop Sci. 2010;15:737-745.
14. Hagino H, Yamamoto K, Ohshiro H, Nakamura T, Kishimoto H, Nose T. Changing incidence of hip, distal radius, and proximal humerus fractures in Tottori Prefecture, Japan. Bone. 1999;24:265-270.
15. El Maghraoui A, Kumba BA, Joundi I, Achermil L, Bezza A, Tazi MA. Epidemiology of hip fractures in 2002 in Rabat, Morocco. Osteoporos Int. 2005;16:597-602.
16. Horii M, Fujiwara H, Ikeda T, Ueshima K, Ikoma K, Shirai T, Terauchi R, Nagae M, Kuriyama N, Kubo T. Urban versus rural differences in the occurrence of hip fractures in Japan’s Kyoto prefecture during 2008-2010: a comparison of femoral neck and trochanteric fractures. BMC Musculoskelet Disord. 2013;304. doi: 10.1186/1471-2474-14-304.
17. Finsen Y, Benum P. Changing incidence of hip fractures in rural and urban areas of central Norway. Clin Orthop Relat Res. 1987;218:104-110.
18. Di Monaco M, Valiero F, Di Monaco R, Mautino F, Cavanna A. Body composition and hip fracture type in elderly women. Cln Rheumatol. 2004;23:6-10.
19. Stewart A, Porter RW, Primrose WR, Walker LG, Reid DM. Cervical and trochanteric hip fractures: bone mass and other parameters. Clin Rheumatol. 1999;18:201-206.
20. Arakaki H, Owan I, Kudoh H, Horizono H, Arakaki K, Ikoma K, Shinjo H, Hayashi K, Kanaya F. Epidemiology of hip fractures in Okinawa, Japan. J Bone Miner Metab. 2011;29:309-314.
21. Saito M, Marumo K. Effects of Collagen Crosslinking on Bone Material Properties in Health and Disease. Calcif Tissue Int. 2015;97(3):242-61.
22. Rubin KH, Friis-Holmberg T, Hermann AP, Abrahamsen B, Brixen K. Risk assessment tools to identify women with increased risk of osteoporosis: a prospective case-control analysis of the data from the EPIDOS study. Osteoporos Int. 2006 Feb;17(2):231-236.
23. World Health Organization. WHO scientific group on the assessment of osteoporosis at primary health care level. 2007. http://www.who.int/chp/topics/Osteoporosis.pdf. Accessed 13 Feb 2016.