学位論文の要旨

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学位論文名	Effect of Multimorbidity on Fragility Fractures in Community-dwelling Older Adults: Shimane CoHRE Study
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論文内容の要旨

INTRODUCTION

Fragility fracture (FFx), which is a common musculoskeletal injury in older adults, is associated with an increased frequency of falls. It is generally believed that the co-occurrence of multiple diseases, or multimorbidity, and the use of multiple drugs, or polypharmacy, will lead to an increased frequency of falls and the risk of fractures. Thus, we conducted this study to understand the current situation of FFx and multimorbidity in rural area in Japan and to evaluate the effects of multimorbidity on falls and FFx in the general elderly population.

The Charlson Comorbidity Index (CCI), which is an effective scale for estimating the mortality of patients with multiple comorbidities, has been used to analyze multimorbidity. Both comorbidities and the FFx risk increase with age and, therefore, we used the age-adjusted Charlson Comorbidity (AAC) index, which has better utility than CCI.

MATERIALS AND METHODS

This study was undertaken as a part of a cohort study (Shimane CoHRE Study) conducted by the Center for Community-based Health Research between 2015 and 2016 and written informed consent was obtained from all study participants. (The study protocol was approved by the Ethics Committee of Shimane University [#2888]). The data were collected from the health examinations of 1,420 community-dwelling individuals aged 60 years and older (556 men and 864 women) and the history of clinical FFx and falls was assessed using a self-reported questionnaire. For example, 1) Have you fallen during the last year: yes, or no?" and “2) Have you experienced bone fractures

during the last 5 years: yes, or no?" In addition, the participants were asked about the location, cause, and their situation of the bone fracture. We inquired about age, sex, height, weight, parent's hip fracture history, alcohol, smoking, chronic diseases, taking medication, number of teeth, denture use, and age at menopause.

The AAC Index is a weighted measure that incorporates age and different subsets of disease conditions, and the study population was classified into four ordinal categories based on the AAC Index: 0, 1–3, 4–5, and ≥6 points. We classified the participants into three groups because none of the participants had an AAC Index of 0.

The statistical analysis was conducted using SPSS (version 25.0; IBM SPSS, New York, NY, USA). Binary logistic regression analysis was performed to determine the risk of FFx and falls after adjusting for covariates.

RESULTS AND DISCUSSION

1. Clinical characteristics of the study population

Of the study participants, 27 (5%) men and 132 (15%) women experienced clinical FFx during the last five years, and 78 (14%) men and 130 (15%) women experienced falls during the last year. This suggests that the risk of FFx in elderly women is likely to be much higher than the FFx risk in elderly men, which is consistent with previous findings. The chi-square test showed a significant difference in the incidence of FFx in both men and women with rheumatoid arthritis (RA). A significant difference in the incidence of FFx among three groups of AAC index was found only in women: 22% in AAC (1–3), 41% in AAC (4–5), and 37% in AAC (≥6).

2. Association between FFx or falls and covariates

Age [odds ratio (95% of confidence interval): 1.06 (1.03–1.09)], AAC Index [2.02 (1.23–3.33) in AAC (≥6), 1.63 (1.00–2.64) in AAC (4–5), reference: AAC (1–3)], falls [2.13 (1.31–3.48)], RA [1.87 (1.23–2.87)], and antihypertensive drugs [1.50 (1.02–2.21)] were independent risk factors for FFx, although dyslipidemia [0.53 (0.34–0.82)] and antilipidemic drugs [0.58 (0.38–0.89)] were protective factors for FFx in women. In men, we found RA [3.18 (1.19–8.52)] and parent's hip fracture [2.81 (1.18–6.69)] as an independent risk factor for FFx.

The prevalence of RA or a family history of hip fractures is well known as a risk of hip fractures. In this regard, our results were consistent with the previous findings. Statins

may be beneficial for increased bone formation in rodent models, along with inducing some inhibition of osteoclastic activity. Indeed, some reports have shown that antilipidemic drugs can reduce the risk of FFx. A meta-analysis reported that hypertension is associated with reduced bone mineral density and increased fracture risk. Our findings showed that taking antihypertensive drugs, but not the presence of hypertension, increased the risk of FFx, suggesting that severe hypertension necessitating medical treatment may increase the risk for FFx in the general population, and that the impact of severe hypertension on the risk of FFx is most probably much stronger than the beneficial effects of antihypertensive drugs on the bone. In addition, we found that habitual drinking is an independent risk factor for falls in the elderly. Meanwhile, falls in men are associated with cognitive impairment.

3. AAC and potential risk factors for FFx

The chi-square test showed that participants with AAC Index (≥6) experienced significantly higher frequencies of FFx in the last 5 years, compared to those with an AAC Index (1–3). In the binary logistic regression analysis among all the elderly population, in addition to women gender [3.49 (2.27–5.37)] and falls [2.16 (1.42–3.28)], a higher AAC Index [1.77 (1.14–2.73) in AAC (≥6), 1.38 (0.90–2.11) in AAC (4–5), reference: AAC (1–3)] and history of parent's hip fracture [2.10 (1.32–3.34)] suggested a higher risk of FFx.

In general, the loss of cancellous bone in both men and women begins in the third decade of life and further accelerates with menopause in women. Later, because of menopause or deficiency of sex steroids, cortical bone loss is accompanied by increased porosity, thereby increasing the risk of FFx. Diabetes and cardiovascular disease, peripheral arterial disease, and abdominal aortic calcification are associated with a 2- to 5-fold increased risk of hip fractures. Decreased kidney function is related to abnormal bone and mineral metabolism that predisposes patients to fractures. The incidence of hip fractures among dialysis patients is 17.4-fold higher than that in the general population. Taken together, elderly people with multimorbidity are at risk of fractures, indicating the importance of multimorbidity as a contributory factor in the increased risk of FFx.

CONCLUSION

We found that older adults with a high AAC Index independently had an elevated risk of FFx, which suggests that multimorbidity increases the risk of fracture.