

Regional Variation in Hip Fracture Incidence among Japanese Hemodialysis Patients

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Abstract

Background

Hip fracture incidence in Japanese hemodialysis patients is five fold higher than in the general population, although the mechanisms underlying this difference are not fully understood. Substantial regional variation exists in hip fracture incidence in the general Japanese population, despite a uniform health care and insurance system and lack of ethnic and racial variation. In this study, we determined whether the regional variation seen in the general population also applies to hemodialysis patients in Japan.

Methods

Standardized incidence ratios were calculated for each regional district, and regional variations of hip fracture incidence among hemodialysis patients were evaluated using data obtained from the Japanese Society for Dialysis Therapy registry (data collected from December 2007 to December 2008).

Results

Standardized hip fracture incidence ratios across the districts ranged from 0.71 to 1.29 for male and 0.49 to 1.36 for female hemodialysis patients. Incidence ratios tended to be higher in western Japan and lower in eastern Japan, suggesting that regional variation also exists among hemodialysis patients.

Conclusions

Our findings suggest that common risk factors for hip fracture may be shared among the general population and hemodialysis patients. Further research aimed at identifying factors, including those associated with regional variation, may help decrease hip fracture incidence in both the general population and hemodialysis patients in Japan.

Introduction

Despite the universal health care and insurance system and lack of racial and ethnic variation in Japan, substantial regional variation in hip fracture incidence exists in its general population [1-4]. Hip fracture incidence is reportedly higher in western Japan than in eastern Japan for both men and women. This trend has continued since 1987, when the first nationwide survey was carried out [5]. The etiology of the regional variation remains unclear, but may reflect regional differences in lifestyle and/or customs.

Hip fracture is an important cause of death and loss of function in hemodialysis (HD) patients and the general population [6,7], and its incidence in HD patients is four to five fold higher than in the general population [8,9]. However, the mechanism underlying this higher risk is not well understood.

Although the general population and HD patients may share common risk factors for hip fracture [6,7], it is unclear whether the regional variation observed in the general population also applies to HD patients in Japan. Therefore, this study aimed to determine whether HD patients exhibit regional variation in hip fracture incidence in Japan using data from the Japanese Society for Dialysis Therapy (JSDT) registry.

Materials and Methods

Data sources

This retrospective cohort study involved two consecutive data panels from the JSDT registry. The registry has conducted annual questionnaire surveys of dialysis facilities throughout Japan since 1968, and several publications are based on data from this registry [10, 11]. Data collection has been described previously [12]. Briefly, year-

end survey questionnaires are sent to all dialysis facilities in Japan, requesting information on each patient. The response rate was 99.0% in the 2008 survey [12]. This study used data collected between December 31, 2007 and December 31, 2008.

Study Population

The study population consisted of patients without a history of hip fracture who received HD three times per week as of December 31, 2007. The data extraction process has been described previously [9]. Briefly, the 2007 JSDT registry included 275,119 dialysis patients, of which 200,529 were undergoing dialysis three times per week. We excluded 3,540 patients due to history of hip fracture and 68,848 due to incomplete pertinent clinical data. Therefore, we analyzed data from 128,141 HD patients. There were no differences in characteristics such as age, gender, dialysis vintage, primary cause of ESRD, and prevalence of cardiovascular diseases between the selected 128,141 patients and all dialysis patients listed in the JSDT registry as of December 31, 2007.

Outcome

Detection of new hip fracture events has been described previously [9]. In brief, a question regarding history of hip fracture was included in the surveys conducted at the ends of 2007 and 2008, so that new hip fracture events could be detected.

Statistical Analyses

Hip fracture incidence was calculated as the total number of hip fractures divided by the total patient-years at risk. Details of the calculation have been described previously

[9]. Briefly, we applied the following estimation method for total patient-years at risk, since exact dates of fracture incidents were not available. If a patient did not suffer a hip fracture, the patient's time at risk was calculated as being equal to the patient's survival time during the one-year study period. If a patient suffered a hip fracture, we assumed the patient-years at risk were equal to half the patient's survival time during the study period. Application of this estimation method did not significantly affect the study results in a previous study [9].

The inverse of hip fracture incidence, i.e., the total patient-years at risk divided by the total number of hip fractures, indicates the number of patients needed to suffer one additional hip fracture event in a year. For example, if the number is 100 per 1 patient per year, this means that one additional hip fracture will occur among 100 HD patients in a year.

An indirect standardization method was used to compare regional differences in hip fracture incidence [1, 4, 9]. To evaluate the influence of regional differences, Japan was divided into 12 districts according to the classification set forth in a previous report [4], as shown in Table 1. The standardized incidence ratio (SIR) was calculated for each district. Regional differences among HD patients were evaluated by comparisons with the general Japanese population [13].

All data were unlinked to patient identifiers and the study was conducted in accordance with Japan's privacy protection laws and ethical guidelines for epidemiological studies published by the Ministry of Education, Science, and Culture and the Ministry of Health, Labour, and Welfare in 2005. Statistical analyses were performed using SPSS for Windows (Version 18.0; SPSS, Inc., Chicago).

Results

Among a total 128,141 patients (men, 61.9%), there were 1,437 hip fractures (men, 595; women, 842) during the one-year follow-up. Age- and gender-specific hip fracture incidence rates are shown in Table 2. Hip fracture incidence for patients aged 25-29 years was higher than that for patients in their 30s for both male and female HD patients. The incidence tended to increase exponentially with increasing age after the 30s. Hip fracture incidence remained lower among male HD patients relative to female HD patients for all age groups. The inverse of hip fracture incidence revealed that one in 132 male and 57 female HD patients suffered additional hip fracture events in a year (Table 2).

Across all 12 districts, overall unadjusted hip fracture incidence rates for female HD patients were approximately two to four fold higher than that for male HD patients (Table 3). The mean age (standard deviation) of HD patients did not differ across the 12 districts. SIRs of hip fracture ranged from 0.71 to 1.29 for male and 0.49 to 1.36 for female HD patients across the 12 districts. SIRs were relatively high in western Japan and low in eastern Japan among both male and female HD patients (Fig. 1).

Discussion

This study revealed that hip fracture incidence among HD patients tended to be higher in western Japan than eastern Japan, which is similar to the trend observed in the general Japanese population. This suggests that common risk factors for hip fracture may be shared among the general population and HD patients.

The observed regional variation in hip fracture incidence among HD patients was unexpected because several HD patient-specific factors, such as secondary hyperparathyroidism [14] and Abeta-2M-amyloidosis and related osteopathy [15], would be expected to contribute to the increased risk of hip fracture among HD patients. What factor(s) may account for the regional variation? Several administrative, climatic, and cultural differences are observed between eastern and western Japan, although these have not been formally defined. For example, Japan's radio frequency differs between eastern and western Japan (50 hertz in eastern Japan and 60 hertz in western Japan). Moreover, winter in eastern Japan is generally colder than in western Japan. We speculate that the responsible factors may be environmental. This is supported by the uniform health care and insurance system and lack of ethnic or racial variation in Japan. Below we present some possible explanations for our findings.

First, a discussion of factors associated with dietary elements, including vitamin K and vitamin D, is warranted. In a previous ecological study, significant correlations were found between SIR by region and intake of magnesium, vitamin D, and vitamin K in both men and women, and calcium in women. In that study, a strongest inverse correlation was found in vitamin K in both men and women in the general population [4]. Indeed, a high proportion of HD patients suffer from a deficiency of vitamin K compounds [16, 17]. Vitamin D insufficiency and/or deficiency is also prevalent among HD patients [18, 19]. A number of studies have reported that vitamin K1 deficiency [17] and vitamin D insufficiency and/or deficiency [20] are associated with bone fracture in HD patients. These studies collectively suggest that dietary factors, such as vitamin K and/or vitamin D status, may be associated with an increased risk of hip fracture among

HD patients relative to the general population. Despite the studies discussed above, little is known about the regional variation in these dietary factors among HD patients. In fact, dietary restrictions imposed on HD patients may result in different dietary habits than that of the general population [21]. Moreover, associations observed at the population level may not necessarily apply at the individual level, particularly with ecological studies [22]. While ecological studies are useful for setting forth hypotheses, rigorous research is needed to explain the regional variation.

Second, climate-related factors should also be considered, as they may impact hip fracture incidence. For instance, European hip fracture data show a clear north-south gradient with the highest hip fracture incidence occurring in Scandinavian countries and the lowest in Spain. This may reflect the fact that cold winters induce more falls in elderly populations [23]. However, we observed just the opposite in the present study. Although winter in eastern Japan is generally colder than in western Japan, hip fracture incidence in eastern Japan was lower than in western Japan. The Tohoku region in eastern Japan, where hip fracture incidence was lower than other regions for both male and female HD patients, is a snowy region. Moreover, there is less sunlight in Tohoku than in other regions in Japan. This suggests that regional differences in climate cannot completely explain the regional variation in hip fracture incidence observed among HD patients. One potential reason climate-related factors may have a relatively small effect on hip fracture incidence in Japan, compared to the clear north-south gradient seen in Europe, is that the difference in latitudes between Scandinavian countries and Spain is larger than that between eastern and western Japan. Further studies will be necessary to identify factors associated with the observed regional variation.

Data presented in Table 2 reveal a J-curve association between hip fracture incidence and age. The nadir of the J-curve in age was at the 30s, with an increase of hip fracture incidence on either side of this range. Although the number of fracture events in younger groups was too small to draw any conclusions, HD patients in their 20s may be affected by other factors, such as steroid therapy and chronic kidney disease-mineral bone disorder in childhood, since most would have been affected by chronic kidney disease from childhood [24]. Alternatively, the increased risk of hip fracture might be associated with more involvement in outdoor activities by patients in younger groups or those living in the warmer western Japan. A prospective study will be needed to further address this.

There are some limitations to this study. First, this was an ecological study with many potential sources of bias due to the group-level analysis (e.g., the ecological fallacy) [22]. Second, the regional variation shared by the general Japanese population and HD patients might not have resulted from the same cause.

Despite these limitations, this study has several strengths. To our knowledge, this is the first report addressing the regional variation in hip fracture incidence among HD patients. Previous reports have been limited to showing regional variation in the general population [23]. Second, our study is a nationwide survey of Japanese dialysis facilities with a large sample size. Finally, our study also assessed the inverse of hip fracture incidence stratified by age and gender. We believe that this parameter may serve as a useful tool to explain hip fracture incidence among HD patients.

Conclusions

We found that regional variation in hip fracture incidence exists not only in the general Japanese population, but also among HD patients. This suggests that there may be some risk factors for hip fracture in common between the general Japanese population and HD patients. Further studies will be needed to identify factors that decrease hip fracture incidence in both of these populations.

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