Mortality after vertebral fractures in a Japanese population

Yuzo Ikeda,1 Akihiro Sudo,1 Tomomi Yamada,2 Atsumasa Uchida1

1 Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan
2 Translational Medical Science, Social and Environmental Medicine, Mie University Graduate School of Medicine, Tsu, Mie, Japan

ABSTRACT

Purpose. To assess the association between vertebral fractures and mortality.

Methods. 419 women and 210 men aged 60 to 98 (mean, 73) years participated in an osteoporosis screening exercise. Patient age, gender, comorbidity, lumbar pain, smoking, and alcohol consumption were recorded, as were the number of vertebral fractures and bone mineral density. Vertebral fractures were evaluated using lateral radiographs and quantitative morphometry. Anterior, central, and posterior vertebral heights were measured; vertebral fractures were defined as a decrease of ≥20% in any of these heights.

Results. 131 (21%) of the participants had vertebral fractures. At the 10-year follow-up, 121 (19%) of the participants (55 men and 66 women) had died; 43 of them had vertebral fractures and 78 did not. The respective 10-year survival rates for participants with and without vertebral fractures were 69% and 86% (p<0.0001). The survival rate was lower in those with greater number of vertebral fractures (76% for those with one or 2 fractures and 50% for those with ≥3 fractures). Multiple regression analysis showed that advanced age (p<0.0001), male gender (p=0.003), and presence of vertebral fractures (p=0.013) correlated significantly with survival.

Conclusion. The presence and number of vertebral fractures were associated with mortality. Prevention of vertebral fractures may be important for improving the prognosis of patients with osteoporosis.

Key words: epidemiology; mortality; osteoporosis; spinal fractures

INTRODUCTION

Vertebral fractures are often asymptomatic, and therefore many patients with this condition do not seek medical attention. The incidences of vertebral fractures in the Wakayama and Hiroshima areas in Japan are 40 and 84 per 1000 person-years for women in their 70s and 80s, respectively.1–3 Such
incidence is higher among Japanese than European subjects.\textsuperscript{3,4} Vertebral fractures\textsuperscript{5–13} and hip fractures\textsuperscript{14,15} affect mortality. We therefore assessed the association between vertebral fractures and mortality in 633 subjects.

MATERIALS AND METHODS

In December 1997, 419 women and 210 men aged 60 to 98 (mean, 73) years from the mountain village of Miyagawa in central Mie Prefecture in Japan participated in an osteoporosis screening exercise. The ethics committee of our university approved the study protocol, and informed consent was obtained from each participant.

Patient age, gender, comorbidity, lumbar pain, smoking, and alcohol consumption were recorded (Table 1), as were the number of vertebral fractures and bone mineral density. Alcohol consumption was categorised as frequent (nearly every day), sometimes (one to 4 times per week), or seldom (less than once per week). Bone mineral density of the non-dominant, distal forearm was measured using dual energy X-ray absorptiometry.

Fractures of the thoracic and lumbar vertebrae were evaluated using lateral radiographs and quantitative morphometry. Anterior, central, and posterior vertebral heights were measured; vertebral fractures were defined as a decrease of ≥20\% in any of these heights.

The 10-year survival/mortality rate of 629 participants (4 dropped out) was assessed by reviewing medical histories, telephone interviews, and death certificates.

Univariate analysis for factors that could influence prognosis (lumbar pain and alcohol consumption) was conducted using the Kaplan-Meier graphs. Intergroup comparisons were made using the log rank test. Multiple regression analysis was performed using the stepwise Cox proportional hazards model. Time to event was computed as the number of years that elapsed between each participant’s respective final wave of testing and the date of death (for decedents) or the end of follow-up in March 2007 (for surviving participants). A p value of <0.05 was considered statistically significant.

RESULTS

131 (21\%) of the participants had vertebral fractures. At the 10-year follow-up, 121 (19\%) of the participants (55 men and 66 women) had died; 43 of them had vertebral fractures and 78 did not. The causes of death in 91 participants are shown in Table 2.

The respective 10-year survival rates for participants with and without vertebral fractures were 69\% and 86\% (p<0.0001, Fig. a). The survival rate was lower in those with greater number of vertebral fractures (76\% for those with one or 2 fractures and 50\% for those with ≥3 fractures), with the mean number of vertebral fractures being 2.3. The difference between those with ≥3 fractures and those with one or 2 fractures (p=0.004) or those without

\begin{table}
\centering
\caption{Patient characteristics at baseline}
\begin{tabular}{|l|c|}
\hline
Characteristic & No. of patients \\
\hline
No. of female:male & 419:210 \\
Mean (range) age (years) & 73 (60–98) \\
Mean (range) height (cm) & 150 (105–181) \\
Mean (range) weight (kg) & 52 (30–76) \\
Mean (range) body mass index (kg/m\textsuperscript{2}) & 23 (16–33) \\
Bone mineral density (% of young adult mean value) & \\
\quad ≥80 & 317 \\
\quad 70–79 & 121 \\
\quad <70 & 191 \\
Comorbidity & \\
\quad Diabetes mellitus & 57 \\
\quad Gout & 9 \\
\quad Lumbar pain & 327 \\
Smoking & \\
\quad Smoker & 116 \\
\quad Non-smoker & 513 \\
Alcohol consumption & \\
\quad Frequent & 87 \\
\quad Sometimes & 34 \\
\quad Seldom & 504 \\
\hline
\end{tabular}
\end{table}

\begin{table}
\centering
\caption{Cause of death of participants}
\begin{tabular}{|l|c|c|}
\hline
Cause of death & No. of participants & \\
& With vertebral fracture & Without vertebral fracture \\
\hline
Pneumonia & 7 & 9 \\
Myocardial infarction & 5 & 8 \\
Lung cancer & 3 & 4 \\
Acute renal failure & 3 & 3 \\
Brain infarction & 0 & 5 \\
Congestive heart failure & 2 & 1 \\
Other causes & 14 & 27 \\
Unknown & 9 & 21 \\
Total & 43 & 78 \\
\hline
\end{tabular}
\end{table}
The 10-year survival rates were significantly higher in participants without vertebral fractures than (a) those with vertebral fractures (p<0.0001) or (b) those with ≥3 vertebral fractures (p<0.0001) or one to 2 fractures (p=0.004).

Fractures (p<0.0001) was significant after Bonferroni correction (Fig. b).
The respective survival rates for women and men were 86% and 77% (p=0.006). The survival rates of participants in their 60s and 70s were both significantly higher than those in their 80s (p<0.0001).
The respective survival rates for participants with ≥80%, 70–79%, and <70% of the mean bone mineral density expected in young adults were 86%, 82%, and 77%. The difference between those with <70% and ≥80% of that bone mineral density was significant (p=0.011).
The respective survival rates for participants with and without lumbar pain were 83% and 82% (p=0.868). The corresponding rates were 74% and 84% for smokers and non-smokers (p=0.012) and were 82%, 86%, and 82% for those who seldom, sometimes, and frequently drank alcohol (p=0.829).
The survival rate was significantly lower in participants of male gender, advanced age, with ≥3 vertebral fractures, low bone mineral density, and smoking habit. Neither lumbar pain nor alcohol consumption was associated with survival.

Multiple regression analysis was performed using the Cox proportional hazards model. The stepwise method showed that advanced age (p<0.0001), male gender (p=0.003), and presence of a vertebral fracture (p=0.013) correlated significantly with survival (Table 3).

| Variable                                      | Hazards ratio | 95% CI     | p Value |
|-----------------------------------------------|---------------|------------|---------|
| Vertebral fracture (yes vs. no)               | 1.72          | 1.12–2.65  | 0.013   |
| Age (years)                                   |               |            |         |
| 60s                                           | 0.07          | 0.04–0.14  | <0.0001 |
| 70s                                           | 0.18          | 0.12–0.27  | <0.0001 |
| 80s                                           | 1.00          |            |         |
| Gender (men vs. women)                        | 1.82          | 1.22–2.72  | 0.003   |
| Vertebral fracture (≥3 vs. none)              | 3.28          | 1.77–6.10  | <0.0001 |
| Vertebral fracture (1 or 2 vs. none)          | 1.33          | 0.80–2.22  | 0.271   |
| Age (years)                                   |               |            |         |
| 60s                                           | 0.08          | 0.04–0.15  | <0.0001 |
| 70s                                           | 0.18          | 0.12–0.28  | <0.0001 |
| 80s                                           | 1.00          |            |         |
| Gender (men vs. women)                        | 2.04          | 1.34–3.10  | 0.001   |

* Bone mineral density, smoking, alcohol consumption, lumbar pain are not selected
3). Participants with vertebral fractures was 1.7 fold more likely to die than those without vertebral fractures (p=0.013, Table 3), whereas participants with ≥3 vertebral fractures was 3.3 fold more likely to die than those without fractures (p<0.0001, Table 3).

DISCUSSION

The 5-year survival rates for individuals with vertebral fracture were 28% in Sweden, 5 and 61% in the United States.6 Both rates were lower than the 10-year survival rate of our participants.

The number of vertebral fractures is associated with mortality.7,8 Women with one, 2, and ≥3 vertebral deformities had 1.3, 2.5, and 3.9 fold greater risks of mortality, respectively, than those without deformities.8 In our study, the stepwise Cox proportional hazards model indicated that both the presence and the number of vertebral fractures were associated with mortality.

The effects of vertebral fractures on mortality remain unknown. Vertebral fractures may cause kyphosis, and may exacerbate dysfunction of various organs, particularly the thoracic organs. Patients may become more susceptible to lung and heart diseases, thus affecting prognosis. The degree of kyphosis is significantly associated with the risk of subsequent pulmonary death.8 Women with vertebral deformities have an increased risk of death due to cardiovascular disease and cancer, compared to women without such deformities.9 Osteoporosis is associated with atherosclerosis16–19 and cardiovascular mortality.20,21

Multiple vertebral fractures may cause esophageal hiatal hernia and esophagitis,22,23 and restrict physical function, activities of daily living, and quality of life.24,25 As the size of the elderly population grows, the incidences of osteoporosis and accompanying vertebral fractures are anticipated to increase rapidly. Preventing vertebral fractures may be important for improving patient prognosis.10

Our study had several limitations. It is necessary to follow up patients with low numbers of vertebral fractures to evaluate how their prognosis is affected compared to those with more fractures. Although patients with poor health are at increased risk of mortality and tend to become bedridden after vertebral fracture, activities of daily living do not always worsen in such patients. Thus, further investigation into the association between restriction in activities of daily living and health are warranted. Our sample was selected from a limited geographic region, which may not be representative of Japan as a whole.

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