Risk factors for cognitive decline following osteoporotic vertebral fractures: A multicenter cohort study

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ABSTRACT

Background: Osteoporotic vertebral fractures (OVFs) are the most common cause of intractable back pain and reduced activities of daily living (ADL), which may affect cognitive function. However, no previous studies have reported a change in cognitive function after OVFs. The purpose was to reveal cognitive function changes after OVFs and investigate the risk factors for cognitive decline.

Methods: Consecutive patients with symptomatic OVFs were enrolled in a prospective multicenter cohort study. The inclusion criteria were age >65 years, diagnosis of acute or subacute OVF, and back pain onset within 2 months prior to presentation. Cognitive function was assessed with the mini-mental state examination. Medical history, radiological findings, and ADL were investigated as risk factors for cognitive decline.

Results: We recruited a sample of 339 patients (58 men and 281 women) who met the inclusion criteria. Patients underwent examinations and completed questionnaires at both the time of enrollment and at 6-month follow-up. At 6-month follow-up, cognitive decline was observed in 26 (7.7%) patients. Medical history, including comorbidities and sports activities, did not affect odds ratios (ORs). However, elevated ORs were associated with delayed union (OR: 4.67, 95% Confidence interval: 1.22–17.87). In addition, significantly increased ORs were associated with reduced ADL at 6-month follow-up.

Conclusions: The current results revealed the incidence of cognitive decline after the onset of OVF. Delayed union and reduced ADL at 6-month follow-up were associated with cognitive decline. Patients with cognitive decline experienced significantly reduced quality of life. These results highlight the importance of preventing cognitive impairment in patients with symptomatic OVF. Physical treatment or early surgical treatment may provide appropriate options, particularly for patients with suspected delayed union.

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1. Introduction

The rate of major osteoporotic fractures has declined in developed countries in recent years [1]. In contrast, the prevalence of dementia increased within the same time period [2]. Among osteoporotic fractures, osteoporotic vertebral fractures (OVFs) are the most common, often causing intractable back pain and reduced activities of daily living (ADL), which may affect cognitive function. For most patients with OVFs, the primary goal of treatment is the return to their pre-fracture functional level. However, some patients suffer from back pain after the usual healing period because of kyphosis and nonunion [3,4]. A study by Chang et al. suggested that osteoporosis patients have a higher risk of dementia compared with patients without osteoporosis [5]. Osteoporosis could thus be considered a risk factor for dementia. However, it has been suggested that both low bone mineral density (BMD) and poor cognitive function are likely to result from another process, such as low estrogen status [6]. Therefore, the observation that
osteoporosis is associated with poor cognitive function suggests a link between the mechanisms underlying two of the most common diseases affecting older women [6]. In addition, in some cases, patients with OVFs require hospital admission for severe pain. Heruti et al. [7] reported that cognitive impairment upon admission was associated with poorer rehabilitation outcomes of elderly hip-fractured patients, although absolute motor gain appeared to be independent of cognitive status.

In a 12-year follow-up study of patients with OV F [8], 6 of 76 surviving individuals were considered by relatives or healthcare staff to be incapable of participating in any follow-up examination because of dementia. However, cognitive function was not assessed in all patients. There no previous studies have examined changes in cognitive function after OV F in detail. The current study sought to reveal cognitive functional changes following OV F, investigating the factors related to cognitive functional decline.

2. Materials and methods

2.1. Patient population

A total of 485 consecutive patients with symptomatic OVFs were enrolled in a prospective multicenter cohort study that included 25 institutes, after providing written informed consent. The inclusion criteria were an age of >65 years, diagnosis of acute or subacute OV F, and back pain onset within 2 months prior to presentation. The exclusion criteria were pathological fractures, multiple fractures, cancer, and high-energy injury. At an initial visit to an institute, fresh vertebral fracture was diagnosed based on acute back pain, a deformed vertebral body detected with radiography, and abnormal intensity within the vertebral bodies detected with magnetic resonance imaging (MRI). The study design was approved by the ethics committees for clinical research at each institute.

Calcaneal BMD was evaluated in quantitative ultrasound measurements, ultrasonic bone assessment equipment AOS-100 made by Hitachi Aloka Medical, Ltd. A structured self-administered questionnaire was used to collect background data for each patient. Medical histories included cerebrovascular events, diabetes mellitus, steroid administration, and the duration and type of medication for osteoporosis. Final education age (≥22 or <22 years old), living situation (living with or without another person), smoking habits (non/current/former), and regular sports habits were also evaluated. We defined regular exercise as daily or regular activity (more than several times a month) such as walking, jogging, or participating in various sports within the past year. Severity of pain was assessed subjectively by patients using a visual analogue scale (VAS). The proportion and duration of analgesics use after the onset of OV F was assessed. The 36-Item Short Form Health Survey (SF-36) questionnaire was applied to assess QOL. To evaluate patients’ ADL, we used the criteria proposed by the long-term care insurance system of the Japanese Health and Welfare Ministry for evaluation of the degree of independence of disabled elderly individuals. ADL classifications were ranked as follows: in rank J, although some disability is present, daily life was almost independent and patients could go outside without assistance from other individuals; in rank A, patients lived independently indoors but required assistance to go out; in rank B, patients required some assistance living indoors and spent most of the day in bed but were able to sit up, and in rank C, patients spent all day in bed and required assistance with urination/defecation, getting dressed, and meals. At the final visit after the 6-month follow-up, the SF-36 was readministered to assess patients’ QOL. All physicians were specialist orthopedic surgeons. We therefore considered these treatment options as standard conservative treatment for OV F at the time of enrollment in Japan.

2.2. Image assessment

At the time of enrollment and 6-month follow-up, patients were examined using plain radiography (X-ray) and MRI of the spine. The plain X-rays were assessed based on the lateral views between the flexion and extension positions. The percentage height of the anterior wall was calculated using the following formula: \(\frac{[2 \times \text{affected vertebral height} - \text{lower vertebral height} + \text{upper vertebral height}]}{100}\). If the adjacent vertebral body, either cranial or caudal, was deformed due to an old fracture, the vertical height of the anterior wall of the fractured vertebral body was divided by the vertical height of the anterior wall of the adjacent non-deformed vertebral body. Delayed union was defined as a recognizable intravertebral cleft and apparent segmental motion on dynamic plain X-rays at the 6-month follow-up, as assessed by two spine surgeons.

2.3. Data analysis

Mini-mental examination (MMSE) was divided into three categories: 25–30 = no cognitive impairment; 21–24 = mild cognitive impairment; and 0–20 = severe cognitive impairment [9]. Cognitive decline was defined when the MMSE classification declined from one class to the one below between the enrollment and 6-month follow-up. Patients with severe cognitive impairment at the time of enrollment were excluded from the analysis. A logistic regression model was used to compute odds ratios (ORs) and 95% confidence intervals (CIs) for cognitive decline. In addition, we conducted a sensitivity analysis by using 4 point decrease of MMSE scores as worsening cognitive performance [10].

The chi-squared test or Fisher’s exact test were used for analyzing categorical variables, and the Wilcoxon rank-sum test was used for continuous variables. A mixed-effects model was used to adjust baseline score and compare change in VAS of back pain and SF-36. The statistical test results were considered significant at \( p < 0.05 \). All \( p \)-values were two-sided. All analyses were performed using the SAS software package, version 9.4 (SAS Institute, Inc., Cary, NC).

Fig. 1. Flow chart.
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