Mortality Following the Diagnosis of a Vertebral Compression Fracture in the Medicare Population

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Background: Vertebral compression fractures in women are associated with increased mortality, but the generality of this finding, as a function of age, sex, ethnicity, and region, among the entire elderly population in the United States remains unclear. The objective of this study was to assess the survival of the Medicare population with vertebral compression fractures.

Methods: We conducted a retrospective data analysis of Medicare claims generated by a 5% sample of all Medicare enrollees from 1997 through 2004. The patient sample consisted of all 97,142 individuals with a new diagnosis of vertebral compression fracture from 1997 through 2004. Controls were matched for age, sex, race, and Medicare buy-in status, with a five-to-one control-case ratio. The survival of a patient was measured from the earliest date of a new fracture until death or until the end of the study. The patients with a fracture were compared with the controls by calculation of the mortality rates, with use of Kaplan-Meier analysis and the Cox regression method. Demographic subpopulation analysis and analysis by comorbidity levels were performed as well.

Results: Medicare patients with a vertebral fracture had an overall mortality rate that was approximately twice that of the matched controls. The survival rates following a fracture diagnosis, as estimated with the Kaplan-Meier method, were 53.9%, 30.9%, and 10.5% at three, five, and seven years, respectively, which were consistently and significantly lower than the rates for the controls. The mortality risk following a fracture was greater for men than for women. The difference in mortality between the patients with a vertebral compression fracture and the controls was greatest when the patients were younger at the time of the fracture; this difference declined as the age at the time of the fracture increased.

Conclusions: This study establishes the mortality risk associated with vertebral fractures for elderly patients of all ages and ethnicities and both sexes in the Medicare population; however, it does not imply a causal relationship. The difference in mortality between patients with a fracture and controls is higher than previously reported, even after controlling for comorbidities.

Level of Evidence: Prognostic Level III. See Instructions to Authors for a complete description of levels of evidence.

A vertebral compression fracture is a serious complication associated with osteoporosis of the spine. The prevalence of osteoporosis in the United States is high, especially among women, and it increases rapidly with age. According to one estimate, osteoporosis affects as many as one in three women and one in eight men over the age of fifty years worldwide[1]. In patients with a vertebral compression fracture, the structural strength of the vertebral body is weakened by the loss of mineral and bone mass, and it is no longer able to sustain the compressive load from the weight of the upper body and additional stress brought on by body movements and other activities. Vertebral body fractures due to compression cause pain, deformity, and restricted mobility. In the U.S., about 1.5 million fractures occur annually, and 700,000 of these occur in the spine[2]. Each year, 250,000 new vertebral compression fractures are diagnosed, and >80% of these

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are related to weakened vertebral bodies secondary to osteoporosis[3].

The adverse effects associated with a vertebral compression fracture have been studied and reported by several researchers. In addition to increased back pain, the overall quality of life[4,5] may be diminished. Patients with a vertebral compression fracture are more likely to fall and are five times more likely to sustain subsequent fractures than individuals without such a fracture[6].

Although a decrease in the quality of life has been documented in a number of studies, the association between vertebral compression fracture and patient longevity has been less well studied. In one study of the effect of vertebral compression fracture on survival[7], the authors found a 23% increase in mortality risk after a mean duration of follow-up of 8.3 years and an even higher increase (110%) in the risk of death from pulmonary disease. The purpose of the present study was to examine the survival of a broad group of patients with a vertebral compression fracture, including men, nonwhite patients, and patients from rural and suburban communities, and to examine differences in survival among these subpopulations.

Materials and Methods

Patient Cohort

The cohort of patients with a symptomatic vertebral compression fracture was identified from Medicare claims submitted by physicians, hospitals, and outpatient clinics from January 1, 1997, through December 31, 2004. We included both pathologic and traumatic fractures. One or more claims listing an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code of 733.13 (pathologic fracture of vertebrae) or 805.0, 805.2, 805.4, 805.6, or 805.8 (cervical, thoracic, lumbar, sacrum/coccyx, and other unspecified vertebral fractures) was required for inclusion in the study.

Claims records from the 5% Medicare Beneficiary Encrypted File (BEF) were used in this study. This file is a random sample compiled from claims from beneficiaries whose health insurance claims number contains the requisite digits in the sampling plan developed by the Centers for Medicare and Medicaid Services. Medicare is the largest nationwide insurance program that provides hospital insurance (Part A) or medical insurance (Part B) to the elderly. The 5% systematic sample reflects the claims generated by approximately two million Medicare enrollees. Although the Medicare data include some claims from nonelderly patients with a vertebral compression fracture who belong to special populations (for example, those with end-stage renal disease), this study included only patients with a vertebral compression fracture who were sixty-five years of age or older at the time of the diagnosis. Patients enrolled in health maintenance organizations, those not enrolled in both Part A and Part B of Medicare, and those residing outside of the U.S. were excluded.

For each patient diagnosed with a vertebral compression fracture, we defined an index event, which was the earliest diagnosis of a vertebral compression fracture identified from any of the three claim sources examined. To ensure that the index event indeed represented a new fracture, we required that the index event had occurred after the patient was enrolled in Medicare and that the patient had not had a vertebral compression fracture for at least 180 days prior to the index event. On the basis of the above criteria, 97,142 elderly patients with a new diagnosis of vertebral compression fracture were identified for the study.

TABLE I Demographic Characteristics of Patients with Vertebral Compression Fracture and Controls

	Patients with Vertebral Compression Fracture (N = 97,142)		Controls (N = 428,956)	
	No.	%	No.	%
Sex				
Male	24,846	25.6	119,387	27.8
Female	72,296	74.4	309,569	72.2
Age				
65-69 yr	10,182	10.5	50,875	11.9
70-74 yr	15,448	15.9	75,851	17.7
75-79 yr	21,122	21.7	99,870	23.3
80-84 yr	22,229	22.9	97,936	22.8
≥85 yr	28,161	29.0	104,424	24.3
Race				
White	91,114	93.8	400,286	93.3
Black	2446	2.5	12,104	2.8
Other/unknown	3582	3.7	16,566	3.9
Charlson index categories				
0	17,842	18.4	276,437	64.4
1-2	34,746	35.8	89,867	21.0
3-4	23,532	24.2	39,426	9.2
≥5	21,022	21.6	23,226	5.4
Buy-in				
Yes	19,124	19.7	81,966	19.1
No	78,018	80.3	346,990	80.9

Comparison Cohort

To evaluate the survival of patients following a vertebral compression fracture, a comparison cohort, or control group, was also selected. The ratio of controls to patients with a vertebral compression fracture was five to one. Eligible controls were selected from the same 5% sample of Medicare enrollees. Each patient in the final fracture cohort was matched with patients, from the eligible pool of controls, whose ages were within three years of the age of the "case" patient and who were at least sixty-five years of age. If more eligible controls were available than the five required for each case, the controls closest in age were selected. Eligible controls were also of the same sex and race (white, black, or other/unknown) as the case patient. Eligible controls had to be enrolled in both Part A and Part B of Medicare and could not be enrolled in a health maintenance

TABLE II Summary of Mortality of Patients with Vertebral Compression Fracture and Controls

	Patients with Vertebral Compression Fracture			Controls			
	Person-Years	Deaths	Rate	Person-Years	Deaths	Rate	Ratio
Overall	171,444	39,707	231.6	1,109,763	94,982	85.6	2.71
Sex							
Male	38,039	11,922	313.4	291,826	27,736	95.0	3.30
Female	133,405	27,785	208.3	817,937	67,246	82.2	2.53
Age							
65-69 yr	17,768	2,545	143.2	121,957	2727	22.4	6.41
70-74 yr	28,767	4,743	164.9	199,767	6552	32.8	5.03
75-79 yr	38,880	7,481	192.4	265,473	13,935	52.5	3.67
80-84 yr	39,786	9,294	233.6	259,464	22,783	87.8	2.66
≥85 yr	46,244	15,644	338.3	263,101	48,985	186.2	1.82
Race							
White	161,430	37,531	232.5	1,041,154	90,168	86.6	2.68
Black	3861	1087	281.5	29,127	2509	86.1	3.27
Other/unknown	6154	1089	177.0	39,482	2305	58.4	3.03
Charlson index categories							
0	29,618	2114	71.4	553,936	24,467	44.2	1.62
1-2	62,660	10,729	171.2	353,201	30,874	87.4	1.96
3-4	44,233	11,838	267.6	138,354	21,898	158.3	1.69
≥5	34,933	15,026	430.1	64,272	17,743	276.1	1.56
Buy-in							
Yes	37,129	8998	242.3	222,070	26,360	118.7	2.04
No	134,315	30,709	228.6	887,693	68,622	77.3	2.96

organization. Patients with a vertebral compression fracture who received state payment assistance with their Medicare premium (that is, state buy-in) were matched with controls with the same status. Although not ideal, this buy-in indicator was used as a marker of individuals with limited financial resources, which may affect survival. Eligible controls could not have been diagnosed with a vertebral compression fracture at any time during the study period. The sampling plan for the controls was designed so that the controls for each patient with a vertebral compression fracture were not used again—i.e., a control in a case-control set appeared only once in the study. A small number of patients with a vertebral compression fracture (for example, black ninety-year-old men in Western states) did not have a sufficient number of matching controls for the five-to-one sampling plan. In those cases, all of the eligible controls were used. A total of 428,956 controls were selected for the 97,142 patients with a vertebral compression fracture (average, 4.4 controls per case). These frequency-matched case-control groups formed the basis of the survival comparison. The general characteristics of the patients and controls are summarized in Table I.

Follow-up

The death of an enrollee was ascertained by the Centers for Medicare and Medicaid Services with use of data from the Social Security Administration and other sources. The date of death was available from the annual Medicare "denominator" file for enrollees in the 5% sample who had died in that year. Survival of a patient with a vertebral compression fracture was calculated as the time from the index date until death or until the end of follow-up on December 31, 2004. Patients with a vertebral compression fracture who were alive on December 31, 2004, were considered censored. Similarly, survival of the five matching controls was calculated from the index date of the case patient in each of the case-control groups. This study afforded a minimum duration of follow-up of one day and a maximum duration of 7.5 years from July 1, 1997, until December 31, 2004.

Comorbidity Adjustment

To account for the health status of each patient in this comparison, the Charlson comorbidity index (Dartmouth-Manitoba version[8]) was calculated. Because all of the diagnoses and procedures received by a Medicare beneficiary are identified in the claims data, the Medicare data are well suited for characterizing the overall health status of a patient. All disease diagnoses and surgical procedures performed in a six-month period prior to the index event were compiled from the Medicare claims. The Charlson comorbidity algorithm utilizes nineteen categories of diseases based on diagnoses and surgical procedures received by a patient, and the final index is a composite value representing the overall degree of comorbidity. In this analysis, the Charlson index values were grouped into four categories[9]: 0 (none), 1 to 2 (low), 3 to 4 (moderate), and ≥5 (high).

TABLE III Results of Kaplan-Meier Analysis Comparing Patients with Vertebral Compression Fracture and Controls

	Patients with Vertebral Compression Fracture			Controls		
	8-Year Survival Rate *(%)*	Mean Duration of Survival *(mo)*	Median Duration of Survival *(mo)*	8-Year Survival Rate *(%)*	Mean Duration of Survival *(mo)*	Median Duration of Survival *(mo)*
Overall	6.8	42.0	39.8	49.7	66.1	89.1
Sex						
Male	7.4	35.1	29.7	47.0	63.9	83.4
Female	7.6	44.3	43.0	50.7	66.8	—
Age						
65-69 yr	28.2	54.0	61.5	82.8	82.4	—
70-74 yr	21.4	50.9	54.0	75.6	79.3	—
75-79 yr	15.4	46.7	47.4	63.5	74.0	—
80-84 yr	8.5	41.5	39.7	49.8	65.3	83.6
≥85 yr	1.2	32.2	28.1	21.7	48.3	45.3
Race						
White	6.6	41.8	39.6	49.2	65.9	88.2
Black	16.9	37.4	34.2	54.4	65.4	—
Other/unknown	30.4	47.7	49.4	64.7	71.7	—
Charlson index categories						
0	42.5	65.4	77.6	69.8	76.3	—
1-2	16.7	48.9	49.9	48.9	66.0	87.7
3-4	6.8	38.1	34.8	29.7	52.7	52.7
≥5	0.5	27.0	19.8	14.3	38.0	30.0
Buy-in						
Yes	6.0	40.3	38.3	37.8	59.3	67.2
No	7.9	42.6	40.3	53.3	68.0	—

Statistical Analysis

Two types of analyses were performed: calculations of mortality rates and multivariate proportional hazard regressions. The mortality status of patients with a vertebral compression fracture and controls was summarized by calculating the total person-years of follow-up, total deaths, and death rates (deaths per 1000 person-years). The overall survival of the patients with a vertebral compression fracture and the controls was

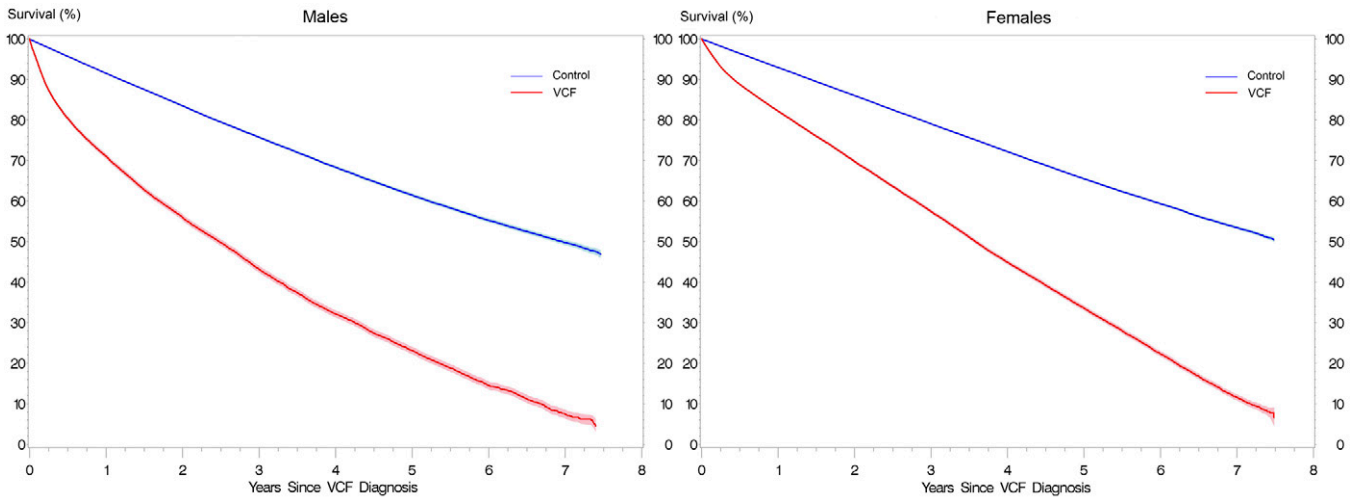

Fig. 1

Survival curves for men (left) and women (right). VCF = vertebral compression fracture.

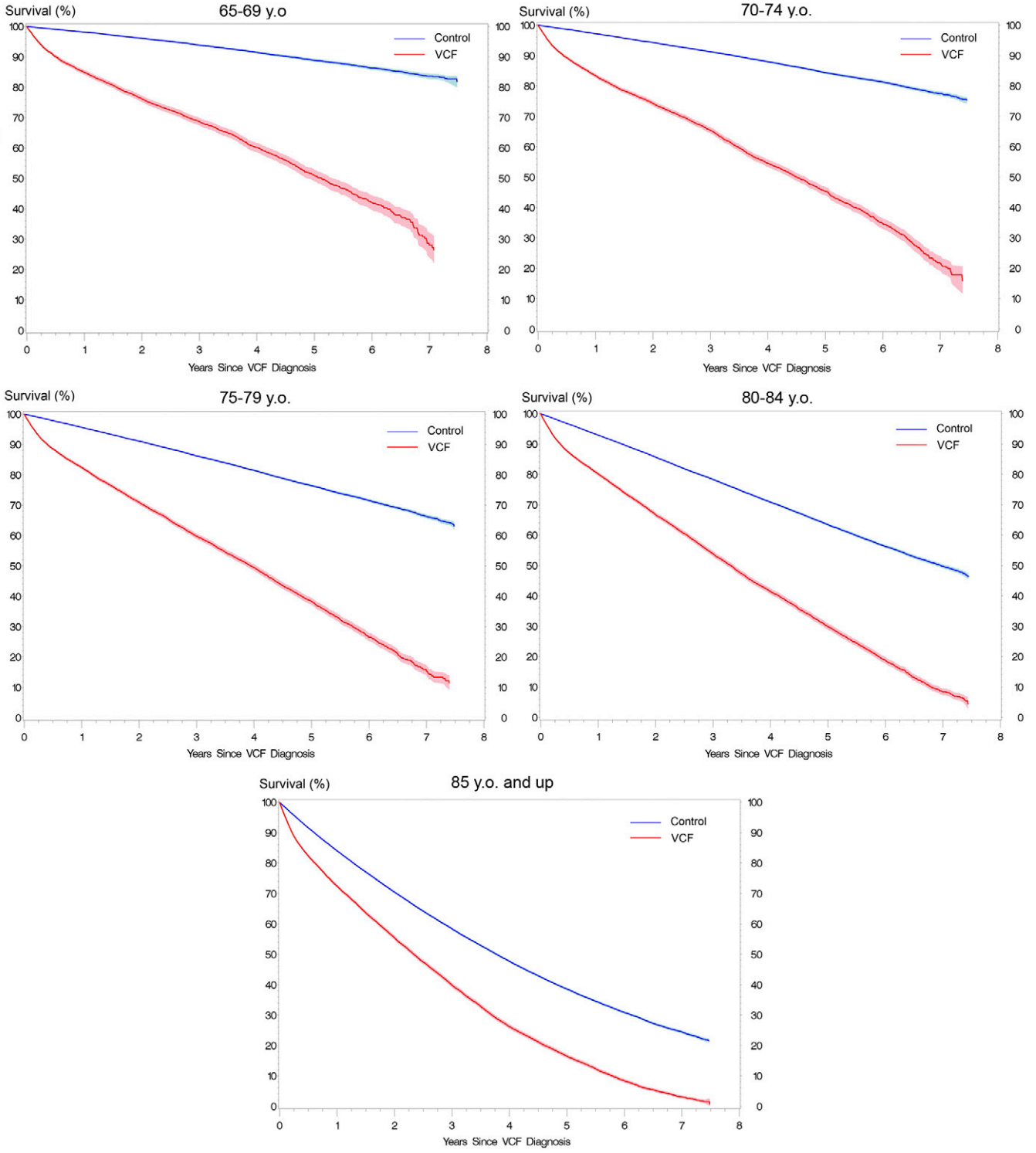

Fig. 2

Survival curves for different age groups. VCF = vertebral compression fracture, and y.o. = years old.

estimated with the Kaplan-Meier method along with means and standard deviations of survival time. Kaplan-Meier survival curves following the diagnosis of a vertebral compression fracture were constructed for the fracture and control cohorts and various demographic subpopulations. Differences in survival were assessed with the log-rank test. The Kaplan-Meier survival curves provided a graphical view of the difference in mortality between the patients with a vertebral compression

TABLE IV Summary of Hazard Ratios Determined with Cox Regression Analysis Comparing Patients with Vertebral Compression Fracture and Controls

	Unadjusted		Adjusted for Comorbidity	
	Ratio	95% Confidence Interval	Ratio	95% Confidence Interval
Overall	2.80	2.77-2.84	1.83	1.80-1.86
Sex				
Male	3.51	3.42-3.60	2.17	2.11-2.24
Female	2.57	2.53-2.61	1.72	1.69-1.75
Age				
65-69 yr	6.88	6.47-7.31	2.99	2.78-3.22
70-74 yr	5.41	5.19-5.64	2.62	2.49-2.75
75-79 yr	3.93	3.80-4.05	2.17	2.09-2.25
80-84 yr	2.85	2.78-2.93	1.84	1.79-1.90
≥85 yr	1.88	1.84-1.92	1.45	1.42-1.48
Race				
White	2.78	2.74-2.82	1.83	1.80-1.85
Black	3.38	3.12-3.67	1.96	1.79-2.16
Other/unknown	3.16	2.92-3.43	1.89	1.72-2.08
Charlson index categories				
0	1.37	1.29-1.47	—	—
1-2	2.35	2.27-2.44	—	—
3-4	1.87	1.79-1.96	—	—
≥5	1.59	1.51-1.67	—	—
Buy-in				
No	3.13	3.08-3.18	1.98	1.94-2.01
Yes	2.03	1.98-2.09	1.47	1.43-1.51

fracture and the controls. The log-rank test results and the survival curves described variations in survival characteristics among these subgroups.

A more comprehensive assessment of the survival characteristics was accomplished with the Cox regression analysis. Consistent with the study design, the Cox regression was stratified by the individual matched case-control set. This use of the Cox regression allowed non-proportionality to exist across different strata while still providing an estimate of the overall hazard ratio for the difference between the patients with a vertebral compression fracture and the controls.

Results

Description of Cohort

The demographic characteristics of the patients with a vertebral compression fracture and their controls are summarized in Table I. Because the controls were selected by matching the case on the basis of several characteristics, the distributions of these characteristics in the patient and control groups were nearly identical. Of the 97,142 patients with a vertebral compression fracture, 74.4% were women and most (93.8%) were white. The average age of the patients with a vertebral compression fracture was 79.9 years, with a standard deviation of 7.6 years. The average age of the controls was 79.0 years, with a standard deviation of 7.5 years.

Mortality and Mortality Rates

From 1997 through 2004, the 97,142 patients with a vertebral compression fracture accumulated a total of 171,444 person-years of observation, with an average of 21.2 months per patient. The 428,956 controls accumulated a total of 1,109,763 person-years of follow-up, with an average of 31.0 months per person. By December 31, 2004, a total of 39,707 deaths of patients with a vertebral compression fracture were identified, for an overall death rate of 231.6 deaths per 1000 person-years of observation. The total number of deaths in the control group was 94,982, a death rate of 85.6 per 1000 person-years of observation. The ratio of the two mortality rates was 2.71. The person-years, deaths, death rates, and mortality ratios for the subpopulations are shown in Table II.

The survival of the patients with a vertebral compression fracture and the controls was estimated with use of the Kaplan-Meier method. The results of the log-rank test comparing the patients with a vertebral compression fracture with the controls, in the total group and in the various subpopulations, were consistently highly significant ($p < 0.001$) and therefore are not individually reported. Table III shows the percentages of subjects who were alive at the end of the study period. Because these survival percentages were estimated with the Kaplan-Meier method, the reported results were based on the last noncensored record, which may have occurred at less than the

maximum of 7.5 years between the start and end of the study period. Overall, 6.8% of the patients with a vertebral compression fracture were still alive at the end of the follow-up period, as compared with 49.7% of the controls (Table III). Survival rates following the diagnosis of vertebral compression fracture at three, five, and seven years were 53.9%, 30.9%, and 10.5%, respectively. The corresponding survival rates were much higher for the controls (78.2%, 64.5%, and 52.5%). The patients with a vertebral compression fracture and their matching controls survived for a median of 39.8 and 89.1 months, respectively. As a result of censoring, the average duration of survival (in months) was underestimated and biased downward. Nonetheless, the obvious difference in the percentages of surviving subjects and the durations of survival, coupled with the consistent gap between the survival curves for the patients with a vertebral compression fracture and the controls, demonstrated an increased mortality risk in patients with a symptomatic vertebral compression fracture.

The percentages of male and female control subjects who were still alive at the end of the study were comparable (47.0% and 50.7%, respectively). The percentages of male and female patients with a vertebral compression fracture who were alive were also similar (7.4% and 7.6%) (Fig. 1). The mortality rate increased with the age at the time of the fracture both for the patients with a vertebral compression fracture and for the controls (Fig. 2 and Table II). As expected, the difference between these two sets of rates decreased as the age at the time of the fracture increased. Patients who were sixty-five to sixty-nine years old when a vertebral compression fracture was diagnosed had a mortality rate that was 6.41 times higher than that of the age-matched controls. The mortality rate for the patients who were diagnosed with a vertebral compression fracture when they were eighty-five years of age or older was only 1.82 times higher than that for their controls. Similarly, the mortality rate for both sets of subjects increased with increasing Charlson index values. The difference between the survival of the patients with a vertebral compression fracture and that of the control subjects also decreased with increasing Charlson index values.

Survival Comparison with Cox Regression Analysis

Overall, without adjustment for differences in comorbidity, the hazard ratio between the patients with a vertebral compression fracture and their matched controls was 2.80 (95% confidence interval, 2.77 to 2.84) (Table IV). Adjustment for the baseline health of the patients lowered the hazard ratio to 1.83 (95% confidence interval, 1.80 to 1.86). Both the adjusted and unadjusted hazard ratios were significant ($p < 0.001$). The hazard (mortality) ratios between the patients with a vertebral compression fracture and the controls in the subpopulations were also calculated, and they were consistently highly significant in all of these subgroup analyses ($p < 0.001$); therefore, they are not individually reported.

Discussion

This study demonstrated the detrimental association between a vertebral compression fracture and survival in a large systematic sample of elderly patients from the Medicare population. Since enrollment in Medicare is nearly universal among the elderly population in the U.S., the results of this study apply well to all persons sixty-five years of age and older in the U.S. We found that, over a seven-year period, an elderly patient with a vertebral compression fracture had almost two times the risk of death compared with an elderly person without a vertebral compression fracture, after adjustment for comorbidity. This added mortality risk was especially detrimental if the vertebral compression fracture occurred at a younger age. Although vertebral compression fractures are more prevalent in women than in men, the mortality risk is higher among men. Even among patients with a vertebral compression fracture and a Charlson comorbidity index of 0, the hazard ratio was 1.37 ($p < 0.001$). The survival of the patients with a vertebral compression fracture and no comorbidities was actually comparable with that of their matched controls in the first twelve to twenty-four months, but it became increasingly poorer after about two years.

Previous studies have also documented an increased mortality risk following vertebral fractures[7,10,11]. Center et al. reported an increase in mortality risk for both sexes following low-trauma osteoporotic fractures[10], but they also found that men were at higher risk (a 138% increased risk) compared with women (a 66% increased risk). Mortality rates were also higher for Swedish men and women following clinical vertebral fractures, including low-energy fractures[11]. Compared with the general population, men and women who sustained such a fracture at the age of sixty years had a 4.3-fold relative risk of death at five years after the fracture. Overall, the Swedish patients with a vertebral fracture had a 28% survival rate at five years, which is comparable with our rate of 30.9% at the same time point. In a study involving elderly white women, Kado et al. determined that the rate of mortality of subjects with one or more fractures was 1.23-fold greater than that of individuals without a fracture, and this difference increased to 1.34-fold in patients with more severe fractures[7]. It is unclear to what extent the exclusion of traumatic fractures from our study might have affected the mortality risk. It has been suggested that women with vertebral fractures following low-energy or no trauma have significantly higher mortality rates (odds ratio, 2.3; $p < 0.05$) than those with high-energy trauma[12].

The age-related differences that we found in the mortality risk are in agreement with those in a previous Swedish study by Johnell et al.[11]. Those investigators showed that the risk of death for men at five years after a fracture was increased 4.3-fold when the fracture had been sustained at the age of sixty years compared with 1.3-fold when it had been sustained at the age of eighty years. In addition, the Swedish data showed that the highest mortality risk occurred immediately following the fracture and that the increase in risk lessened significantly with time ($p < 0.001$). For example, the increase in the risk of death for men who had sustained a fracture at the age of sixty years was 13.4-fold in the initial year but only 4.3-fold by the fifth year. Our study showed comparable results, as the survivorship decreased markedly in the first six months, after which

there was a more steadily declining trend. However, it is unclear if these age-related differences apply to the non-Medicare and younger patient population.

This study had several limitations. We were unable to identify the severity of each vertebral compression fracture because of the administrative nature of the Medicare data. In addition, we did not examine the number of fractures sustained by each patient. It is likely that the cumulative effect of multiple fractures may lead to progressive debilitation and ultimately the risk of complications and death. Kado et al. showed that the increase in mortality risk was 23% in patients with a fracture but 34% in those with a severe fracture and patients with multiple fractures also had a significantly greater mortality risk ($p < 0.001$)[7]. Our study included only diagnosed, symptomatic vertebral compression fractures, but as many as 80% of vertebral fractures may not be clinically apparent or may remain undiagnosed[3,7]. Even though we attempted to adjust for comorbidities and other demographic factors, there may still have been other residual confounding factors due to inadequate adjustment[13]. Part of the observed difference in mortality risk could have been due to confounding effects such as smoking, obesity, or other medical problems rather than the effects of the vertebral compression fracture itself. We also relied on administrative data, which may not have included clinical details that would otherwise be available from patient medical records. Hence, the difference in mortality could have been due to unmeasured differences between the fracture and control populations. Although patients with a vertebral compression fracture were found to have greater mortality rates, the present study did not include an investigation of the cascade of events leading to their premature deaths. A diagnosis of vertebral compression fracture could be a marker of poor health, although a vertebral compression fracture itself is seldom a direct cause of death. Further investigation is needed to clarify the sequence of health events that result in premature death of these patients.

Despite these limitations, our study encompassed a large population of patients with a vertebral compression fracture in all demographic segments who were matched with corresponding controls. This allowed us to determine the relative mortality risk for this well-controlled group of patients. Although we have demonstrated the substantial negative impact of a vertebral compression fracture on survival, the present study did not include a comparison of treatment options or efficacy of preventive regimens. ■

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