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Increased risk of hip fracture among patients with end-stage renal disease

ASTIER M. ALEM, DONALD J. SHERRARD, DANIEL L. GILLEN, NOEL S. WEISS, SHIRLEY A. BERESFORD, SUSAN R. HECKBERT, CRAIG WONG, and CATHERINE STEHMAN-BREEN

Division of Nephrology, University of Washington; Division of Nephrology, Puget Sound Health Care System; Department of Biostatistics, University of Washington; Fred Hutchinson Cancer Research Center; School of Public Health and Community Medicine, and Department of Epidemiology, University of Washington, Seattle, Washington, USA

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Background. Although patients with end-stage renal disease (ESRD) are at increased risk for bone loss, the risk of hip fracture in this population is not known. We compared the risk of hip fracture among dialysis patients with the general population.

Methods. We used data from the United States Renal Data System (USRDS) to identify all new Caucasian dialysis patients who began dialysis between January 1, 1989, and December 31, 1996. All hip fractures occurring during this time period were ascertained. The observed number of hip fractures was compared with the expected number based on the experience of residents of Olmstead County (MN, USA). Standardized incidence ratios were calculated as the ratio between observed and expected. The risk attributable to ESRD was calculated as the difference between the observed and expected rate of hip fracture per 1000 person-years.

Results. The number of dialysis patients was 326,464 (55.9% male and 44.1% female). There were 6542 hip fractures observed during the follow-up period of 643,831 patient years. The overall incidence of hip fracture was 7.45 per 1000 person years for males and 13.63 per 1000 person years for females. The overall relative risk for hip fracture was 4.44 (95% CI, 4.16 to 4.75) for male dialysis patients and 4.40 (95% CI, 4.17 to 4.64) for female dialysis patients compared with people of the same sex in the general population. While the age-specific relative risk of hip fracture was highest in the youngest age groups, the added risks of fracture associated with dialysis rose steadily with increasing age. The relative risk of hip fracture increased as time since first dialysis increased.

Conclusions. The overall risk of hip fracture among Caucasian patients with ESRD is considerably higher than in the general population, independent of age and gender.

In the general population, hip fractures are an important public health problem. In 1991, there were an estimated 300,000 hip fractures in the United States [1], with an associated cost of close to $10 billion per year [2]. In addition to the economic impact, hip fractures are associated with an increase risk of morbidity and mortality [3–5]. Several investigators have shown that patients with end-stage renal disease (ESRD) have reduced bone mineral density, a risk factor for fracture in the general population [6–8]. In addition, a cross-sectional study reported that osteopenia among Japanese men with renal failure was associated with an increased risk for vertebral fracture [9]. However, the incidence and relative risk of hip fracture in dialysis patients compared with the general population are not known. We conducted a population-based cohort study to estimate the risk of hip fracture among Caucasian dialysis patients compared with the general U.S. population.

METHODS

Patients

This study used data from the United States Renal Data System (USRDS). The details of the USRDS data collection techniques are described elsewhere [10]. Briefly, the USRDS collects information on the incidence, prevalence, treatment, morbidity, and mortality of ESRD patients who have survived more than 90 days on dialysis. Data are derived from the ESRD Medical Evidence Form, Medicare billing records, United Network for Organ Sharing transplant records, ESRD Network Census reports, and ESRD death notification reports. All Caucasian patients who began dialysis between January 1, 1989, and December 31, 1996 (N = 326,464), were included in the analysis. NonCaucasian dialysis patients were excluded because race-specific incidence rates of hip fracture in the comparison group were not available and the racial distribution was known to differ from that of the ESRD population. We were unable to choose a comparison group that reported the racial distribution because our comparison group was the only pub-

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lished report of hip fracture rates that included younger patients. Patients who lack any evidence of payment activity in the Medicare database for one year are classified by the USRDS as lost to follow-up; they were censored in our analysis at that time.

Hip fracture

Hip fractures were determined by identifying International Classification of Diseases, 9th Revision (ICD-9) codes indicating first cervical, intertrochanteric, or subtrochanteric hip fracture. The ICD-9 codes are derived from Health Care Financing Administration Standard Analytical Files, which contain data on inpatient hospital stays. ICD-9 codes were available in the USRDS database for the period January 1, 1989, to December 31, 1996. The observed number of hip fractures was compared with that expected based on the experience of residents in Olmstead County (MN, USA) [11].

Data analysis

The incidence of hip fracture was calculated as observed hip fractures identified per total patient time at risk. Patient time at risk is the sum of the time contributed by each person in the population over the risk period. Exposure time was defined as the period 90 days after the first dialysis treatment to the time of hip fracture or censoring (death, loss to follow-up, or end of study). Since the results of the analysis did not change after censoring patients at the time of transplant, person time that occurred after transplant was not excluded from the analysis.

The expected number of hip fractures was calculated by multiplying the number of appropriate person years at risk by the corresponding age-specific hip fracture incidence rate for the reference population (Olmstead County). Standardized incidence ratios (SIRs) were computed as the ratio of the number of observed hip fractures to the number of expected hip fractures. SIR can be interpreted as the relative increase in the incidence rate in the ESRD population compared with that of the comparison population. Confidence intervals were calculated using the normal approximation to the Poisson distribution [12]. The added rate of hip fracture caused by ESRD, that is, the risk attributable to ESRD, was calculated as the difference between the observed rate of hip fractures per 1000 person years and the expected rate of hip fractures per 1000 person years. It may be interpreted as the incidence of hip fracture that is due to ESRD and is useful for estimating the magnitude of the public health problem.

To determine whether an association between the incidence of hip fracture and the time since first dialysis treatment for ESRD existed in these data, age-adjusted incidence ratios were again computed. Time since the start of ESRD included time on any form of dialysis, as well as time accrued after transplantation. Time since the first treatment of ESRD was categorized into zero to one year, one to two years, two to four years, and more than four years. For each of these groups, hip fracture incidence and total observed patient years were calculated. These rates were then compared with the Olmstead County population via SIRs.

RESULTS

There were 6542 hip fractures during the follow-up period of 643,831 patient-years. The age-specific incidence rates of hip fracture for both the ESRD patients and the general population, by gender, are described in Tables 1 and 2. The overall incidence of hip fracture was 7.45 per 1000 person-years among men and 13.63 per 1000 person-years among women. The incidence increased with increasing age and remained lower among men than among women for all age groups.

For both men and women, the overall age-adjusted incidence for the ESRD population was approximately fourfold higher than that of the general population; the relative risk for hip fracture was 4.44 (95% CI, 4.16 to 4.75) among males and 4.40 (95% CI, 4.17 to 4.64) among females (Tables 1 and 2). The relative risk of hip fracture was greatest in the youngest age group for both men and women and approached that of the general population in the oldest age group. However, the added incidence of hip fracture associated with ESRD increased with age and was greater for women than men. The magnitude of the added risk of hip fracture ranged from approximately 2 per 1000 per year in persons under 45 years to 20 per 1000 person years in those 85 years and older.

The incidence ratios for hip fracture stratified by time since first dialysis treatment for ESRD for men and women, standardized for age, are shown in Table 3. The risk of hip fracture rose with increasing duration since first dialysis for both men and women. This trend was seen among all age groups.

DISCUSSION

The overall incidence of hip fracture among patients who had undergone renal dialysis was about fourfold higher than what would be expected in the general population. This increased risk of hip fracture was found among both men and women. Whereas the SIR was highest in the youngest age group and decreased with increasing age, the risk attributable to dialysis increased with increasing age.

Our data are consistent with data from the general population in which the incidence of hip fracture increases with age and is greater in women than men [13–17]. The increased risk of hip fracture compared with the general population is also consistent with studies demonstrating relatively lower bone mineral density

Table 1. Observed and expected incidence of hip fracture among male ESRD patients

Age *years*	Patient-years	Observed number of hip fractures	Hip fracture incidence[a]	Olmstead County hip fracture incidence	Expected number of hip fractures	Observed/expected ratio (95% C.I.)[b]	Added rate of hip fracture in dialysis patients[a]
<45	100,801	263	2.61	0.03	3.02	87.0(29.4, 424.4)	2.58
45–54	54,904	177	3.22	0.13	7.14	24.8(14.1, 47.5)	3.09
55–64	69,092	364	5.27	0.54	37.31	9.8(7.3, 13.2)	4.73
65–74	87,130	867	9.95	1.33	115.88	7.5(6.2, 9.1)	8.62
75–84	44,648	835	18.70	7.81	348.70	2.4(2.2, 2.6)	10.89
>85	4,693	185	39.42	19.94	93.58	2.0(1.7, 2.3)	19.48
Total	361,268	2,691	7.45	4.96	1793.09	4.44(4.16, 4.75)[c]	

[a] per 1,000 per year
[b] C.I., confidence interval
[c] Standardized for age

Table 2. Observed and expected incidence of hip fracture among female ESRD patients

Age	Patient-years	Observed number of hip fractures	Hip fracture incidence[a]	Rochester hip fracture incidence[a]	Expected number of hip fractures	Observed/expected ratio (95% C.I.)[b]	Added rate of hip fracture in dialysis patients[a]
<45	70,672	209	2.96	0.03	2.12	98.6(33.3, 481.9)	2.93
45–54	40,009	224	5.60	0.28	11.20	20.0(13.5, 30.8)	5.32
55–64	59,174	579	9.79	0.96	56.81	10.2(8.2, 12.8)	8.83
65–74	73,420	1,489	20.28	3.18	233.48	6.4(5.7, 7.2)	17.10
75–84	35,101	1,154	32.88	13.11	460.17	2.5(2.3, 2.7)	19.77
>85	4,187	196	46.81	26.84	112.38	1.7(1.5, 2.0)	19.97
Total	282,563	3,851	13.63	7.40	2090.97	4.40(4.17, 4.64)[c]	

[a] per 1,000 per year
[b] C.I., confidence interval
[c] Internally standardized

Table 3. Incidence ratios stratified by time since first dialysis treatment for men and women, standardized for age

Time since first dialysis treatment	Standardized incidence ratio[a] (95% C.I.)	
	Males	Females
3 months–1 year	3.62(3.34, 3.92)	3.75(3.52, 4.00)
1 to 2 years	3.72(3.37, 4.10)	3.76(3.47, 4.08)
2 to 4 years	6.12(5.57, 6.74)	5.80(5.37, 6.27)
More than 4 years	9.83(8.61, 11.2)	8.10(7.23, 9.07)

[a] Standardized for age

among dialysis patients [18]. Low bone mineral density is a risk factor for hip fracture in the general population [19] and has been associated with vertebral fracture in the dialysis population [9].

The relative risk of hip fracture was highest in the youngest age groups. However, the added risk of hip fracture was highest among the oldest patients. The relative risk is the relative increase in the incidence rate in the ESRD population compared with that of the comparison population. Since the incidence of hip fracture in the general population is much lower among younger people than older people, similar absolute increases in the incidence of hip fracture among younger and older patients with ESRD will result in a higher relative risk among younger persons. In contrast, the added risk—the difference between the incidence of hip fracture in the ESRD and comparison populations—reflects the incidence of hip fracture that is due to ESRD and/or its treatment, and this increases with age. The relative risk of hip fracture rose with increasing time since first dialysis in all age groups for both men and women. This suggests that there are cumulative exposures since the initiation of ESRD that predispose patients to hip fracture.

The underlying basis for the increased risk of hip fracture in the ESRD population is likely multifactorial. It has been postulated that factors specific to ESRD, such as metabolic bone disease, β2-microglobulin-related amyloidosis, hypogonadism, avascular necrosis, and chronic acidosis, may increase bone loss among ESRD patients, placing them at increased risk for fracture [18]. These processes alter bone architecture and are thought to increase bone fragility. It is also possible that the excess risk of fracture among dialysis patients is due to a greater burden of factors that are known to be risk factors for fracture in the general population, such as immobility, abnormalities in vitamin D metabolism, protein wasting, low body mass, and diabetes [19–25]. Further studies are necessary to clarify the relative contribution of these factors to the risk of hip fracture among ESRD patients.

This study has several limitations. Ascertainment of hip fracture required that a patient had been hospitalized

for the hip fracture, which may have led to an underestimate of the incidence of hip fracture. However, studies have demonstrated that the use of hospitalization data to identify hip fractures is accurate, since the vast majority of hip fractures require hospitalization for treatment [26, 27]. Second, our results pertain to only the Caucasian population and cannot necessarily be generalized to other patients with ESRD. On the other hand, this study has a number of strengths, among which is its large size. Another is its population-based character. As such, the results are not a reflection of dialysis unit-specific practices but rather practices found in the entire ESRD population.

Our study demonstrates that the risk of hip fracture among Caucasian ESRD patients is substantially higher among all age groups and both genders compared with the general population. Future studies are needed to determine the factors that increase the risk for hip fracture among dialysis patients and to identify interventions to decrease this risk.

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Reprint requests to Catherine Stehman-Breen, M.D., VA Puget Sound Health Care System, 1660 South Columbian Way, Mailstop 111A, Seattle, Washington 98108, USA.
E-mail: cos@u.washington.edu

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