EFFECT OF RISEDRONATE ON THE RISK OF HIP FRACTURE IN ELDERLY WOMEN

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ABSTRACT

Background Risedronate increases bone mineral density in elderly women, but whether it prevents hip fracture is not known.

Methods We studied 5445 women 70 to 79 years old who had osteoporosis (indicated by a T score for bone mineral density at the femoral neck that was more than 4 SD below the mean peak value in young adults [−4] or lower than −3 plus a nonskeletal risk factor for hip fracture, such as poor gait or a propensity to fall) and 3886 women at least 80 years old who had at least one nonskeletal risk factor for hip fracture or low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 plus a hip-axis length of 11.1 cm or greater). The women were randomly assigned to receive treatment with oral risedronate (2.5 or 5.0 mg daily) or placebo for three years. The primary end point was the occurrence of hip fracture.

Results Overall, the incidence of hip fracture among all the women assigned to risedronate was 2.8 percent, as compared with 3.9 percent among those assigned to placebo (relative risk, 0.7; 95 percent confidence interval, 0.6 to 0.9; P=0.02). In the group of women with osteoporosis (those 70 to 79 years old), the incidence of hip fracture among those assigned to risedronate was 1.9 percent, as compared with 3.2 percent among those assigned to placebo (relative risk, 0.6; 95 percent confidence interval, 0.4 to 0.9; P=0.009). In the group of women selected primarily on the basis of nonskeletal risk factors (those at least 80 years of age), the incidence of hip fracture was 4.2 percent among those assigned to risedronate and 5.1 percent among those assigned to placebo (P=0.35).

Conclusions Risedronate significantly reduces the risk of hip fracture among elderly women with confirmed osteoporosis but not among elderly women selected primarily on the basis of risk factors other than low bone mineral density. (N Engl J Med 2001; 344:333-40.)

HIP fractures cause substantial disability and are associated with a high rate of death among elderly women,[1] but there have been few studies of the effects of drug treatment on the risk of hip fracture. Observational studies suggest that estrogen may reduce the risk of hip fracture.[2-4] Alendronate reduced the risk of hip fracture in postmenopausal women with low bone mass at the femoral neck or with previous vertebral fractures, but not in women without those risk factors.[5,6] Numerous risk factors for hip fracture have been identified.[7-13] In general, these risk factors can be categorized as skeletal (e.g., a low bone mineral density or a previous fracture) or nonskeletal (e.g., age, a poor gait, or a propensity to fall). The effects of drug therapy in women identified solely on the basis of risk factors other than low bone mineral density have not been determined.

Risedronate (Actonel, Procter & Gamble, Cincinnati), a pyridinyl bisphosphonate, decreases the risk of vertebral and nonvertebral fractures in postmenopausal women with osteoporosis.[14,15] We conducted a clinical trial designed to evaluate the effects of risedronate on the risk of hip fracture in elderly women with osteoporosis or with risk factors for hip fracture other than low bone mineral density.

METHODS

Study Design and Subjects

The study was conducted between November 1993 and April 1998. We enrolled two groups of ambulatory postmenopausal women in two identical protocols at 183 study centers in North

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America, Europe, New Zealand, and Australia. One group consisted of women 70 to 79 years old who had osteoporosis, indicated by either a bone mineral density at the femoral neck (T score) that was more than 4 SD below the mean peak value in young adults (−4) or a femoral-neck T score lower than −3 plus at least one risk factor for hip fracture. These risk factors (hereafter referred to as clinical risk factors) included difficulty standing from a sitting position, a poor tandem gait, a fall-related injury during the previous year, a psychomotor score of 5 or less on the Clifton Modified Gibson Spiral Maze test (a test of hand–eye coordination, with scores ranging from 1 to 12, where scores of 5 or less are considered to indicate an increased risk of falling),[16] current smoking or smoking during the previous five years, a maternal history of hip fracture, a previous hip fracture, and a hip-axis length of 11.1 cm or greater. The other group consisted of women 80 years of age or older who had at least one nonskeletal risk factor for hip fracture, a femoral-neck T score lower than −4, or a femoral-neck T score lower than −3 plus a hip-axis length of 11.1 cm or greater. For purposes of enrollment, femoral-neck T scores were calculated according to the densitometer's manufacturer's reference data base. The femoral-neck T scores at base line were later recalculated according to reference data from the Third National Health and Nutrition Examination Survey.[17] The women identified their race.

The exclusion criteria were any major medical illness, a recent history of cancer, another metabolic bone disease within the previous year, important abnormalities in the results of routine laboratory tests, recent use of drugs known to affect bone, allergy to any bisphosphonate, a history of bilateral hip fractures, and any physical or mental condition that would preclude participation in a clinical trial. There were no specific criteria for exclusion on the basis of previous or ongoing upper gastrointestinal tract disorders or concomitant use of nonsteroidal antiinflammatory drugs, aspirin, proton-pump inhibitors, or antacids.

The women in each of the two enrollment groups were randomly assigned to take either a 2.5-mg or a 5.0-mg risedronate tablet or an identical-appearing placebo tablet daily for three years. The women were instructed to take the tablets with a cup (240 ml) of water on an empty stomach, 30 to 60 minutes before breakfast, and to remain upright for 60 minutes thereafter. The women also received supplemental calcium carbonate (1000 mg of elemental calcium daily) to be taken with the midday or evening meal. Vitamin D (≤500 IU daily) was given if the serum 25-hydroxyvitamin D concentration at the time of screening was below 16 ng per milliliter (40 nmol per liter), as determined at one of the two central laboratories (Quintiles [Smyrna, Ga.] for the North American study centers and Bioanalytical Research [Ghent, Belgium] for the other study centers). The protocol was approved by the ethics committee or institutional review board at each center, and all the women gave written informed consent.

Measurements of Efficacy

The primary end point was the incidence of radiographically confirmed hip fractures. A secondary end point was the incidence of nonvertebral osteoporotic fractures, defined as all radiographically confirmed fractures of the wrist, leg, humerus, hip, pelvis, or clavicle. Bone mineral density, another secondary end point, was measured at base line and at six-month intervals by dual-energy x-ray absorptiometry with a densitometer (Lunar, Madison, Wis., or Hologic, Waltham, Mass.) in the women who were enrolled at 44 of the study centers. The scans were obtained according to procedures established by a central analysis and quality-assurance facility (Oregon Osteoporosis Center, Portland). The presence or absence of a vertebral fracture at base line was determined by examination of spinal radiographs, according to published methods.[18]

Assessments of Adverse Events

The women underwent physical examinations at the beginning and end of the study. Hematologic tests and tests of serum chemistry were performed and information about adverse events was collected at regular intervals during the study.

Statistical Analysis

Women who received at least one dose of either risedronate or placebo were included in the analysis. Women who discontinued treatment before the end of the three-year treatment period were requested to return to their study center at the time of the scheduled third-year visit. We performed analyses of fractures that occurred during the treatment period as well as those that occurred during treatment or follow-up. We planned to compare the women who were assigned to risedronate at each dose with those assigned to placebo. However, because the incidence of hip fractures was lower than expected and because another study of risedronate showed that both a 2.5-mg dose and a 5.0-mg dose were effective in reducing the risk of vertebral fractures,[14] we modified the analysis of efficacy and compared the women assigned to risedronate at either dose with those assigned to placebo.

Because two groups of women (those with confirmed osteoporosis and those with primarily nonskeletal risk factors) were enrolled, we undertook a prospective analysis of the data according to the enrollment group. On the basis of data indicating that the presence of a vertebral fracture at base line affects the subsequent incidence of hip fractures in women with low bone mineral density at the femoral neck,[5,6] we performed a retrospective analysis of the risk of fracture among the women 70 to 79 years old who had a history of vertebral fracture.

The incidence of hip fracture was calculated with use of Kaplan–Meier survival estimates. The log-rank test was used to test the significance of differences between treatment groups. P values were not corrected for multiple comparisons. Proportional-hazards regression analysis was used to estimate the relative risk (with the 95 percent confidence interval) of hip fracture in the risedronate group as compared with the placebo group; nonvertebral fractures were analyzed by similar methods. Comparisons of the percent change from base line in bone mineral density according to treatment assignment were performed by analysis of variance. All tests were two-sided.

RESULTS

Characteristics of the Subjects

A total of 9331 women were enrolled in the study and received at least one dose of study medication (Fig. 1). Within each enrollment group, the base-line characteristics of those assigned to risedronate and those assigned to placebo were similar (Table 1). Measurements of bone mineral density were available at base line for only 31 percent of the women 80 years of age or older. Almost all the women (98 percent) were white.

Complete follow-up data were available for 64 percent of the women (69 percent of those with confirmed osteoporosis and 58 percent of those with mainly clinical risk factors). The duration of follow-up was similar for the women assigned to risedronate and those assigned to placebo (mean, 2.3 years), as was the mean duration of therapy (2.0 years). The clinical characteristics, including the bone mineral density at the femoral neck, of the women who discontinued treatment early and of those who received treatment for all three years of the study were similar, except that the former tended to be slightly older and to weigh less and were more likely to smoke than the latter. There were no significant differences between the women assigned to risedronate and those assigned to placebo with respect to the reasons for discontinuation of treatment (data not shown).

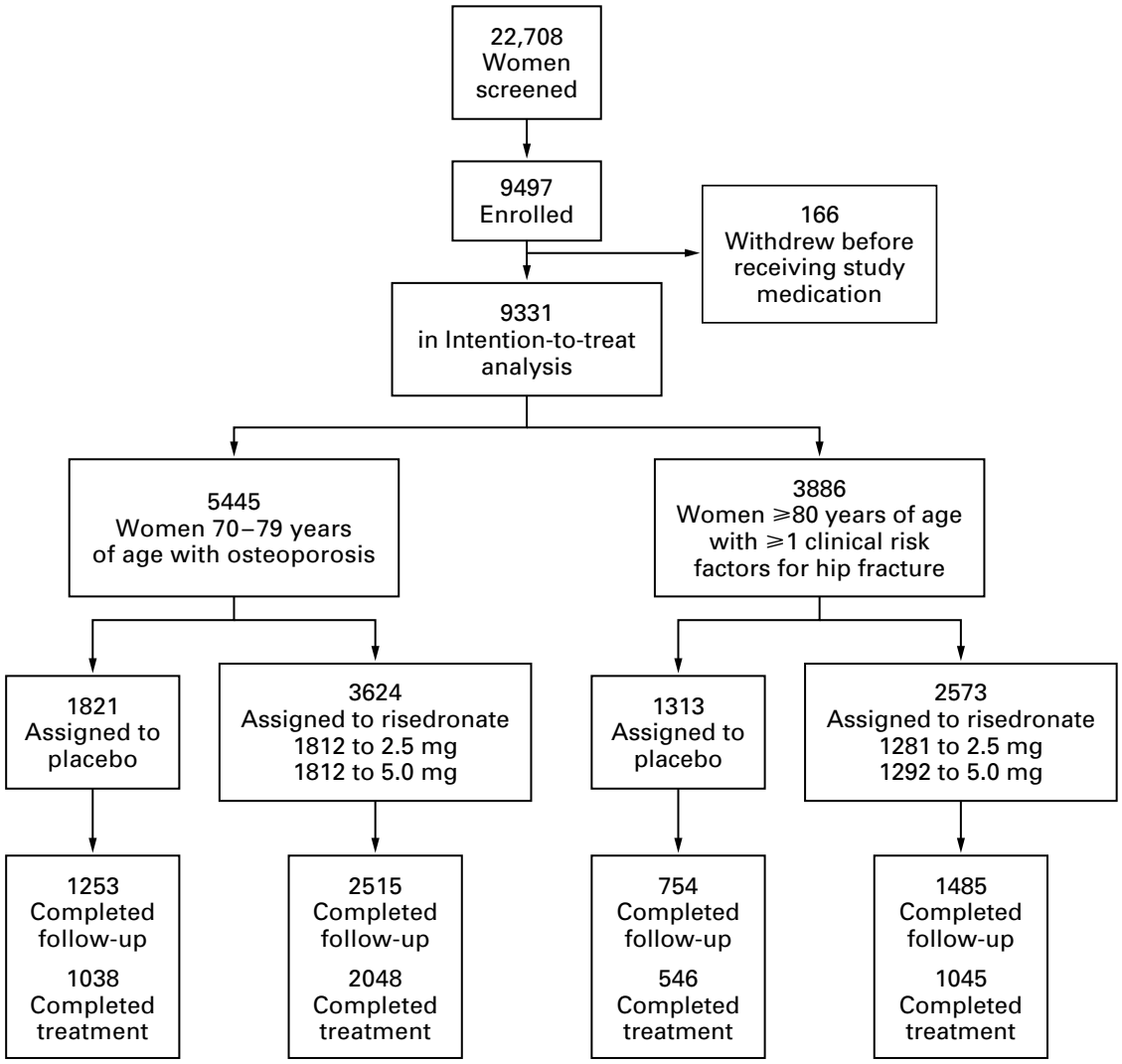

Figure 1. Design of the Study.

Women 70 to 79 years of age were enrolled if they had a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with at least one nonskeletal risk factor for hip fracture). Women ⩾80 years of age were enrolled if they had at least one nonskeletal risk factor for hip fracture or a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with a hip-axis length ⩾11.1 cm). The following numbers of women had withdrawn by 12, 24, and 36 months: 842, 1365, and 1677 of the women 70 to 79 years old and 820, 1317, and 1647 of the women 80 years of age or older. Some women stopped taking their assigned treatment before the end of the study but were followed until the end of the study (i.e., completed follow-up).

Hip Fractures

Of the 9331 women who received at least one dose of study medication, 232 had a hip fracture. Of these fractures, 60 percent were at the femoral neck, 33 percent were intertrochanteric, 3 percent were at the femoral head, and no specific information on the site of the fracture was available for 4 percent. In an analysis of all women, the incidence of hip fracture was 2.8 percent among the women assigned to risedronate, as compared with 3.9 percent among those assigned to placebo (Table 2).

The incidence of hip fracture in the group of women 70 to 79 years old was 1.9 percent among those assigned to risedronate and 3.2 percent among those assigned to placebo (relative risk, 0.6; 95 percent confidence interval, 0.4 to 0.9; P=0.009) (Table 2 and Fig. 2A). In this younger group, the effects of the 2.5-mg and 5.0-mg doses of risedronate were similar; the relative risk of hip fracture for the 2.5-mg dose was 0.5 (95 percent confidence interval, 0.3 to 0.9) and that for the 5.0-mg dose was 0.7 (95 percent confidence interval, 0.4 to 1.1). Information on the presence or

TABLE 1. BASE-LINE CHARACTERISTICS OF THE WOMEN IN THE STUDY, ACCORDING TO AGE AT ENROLLMENT.*

CHARACTERISTIC	WOMEN 70–79 YR OF AGE WITH OSTEOPOROSIS		WOMEN ≥80 YR OF AGE WITH ≥1 CLINICAL RISK FACTORS FOR HIP FRACTURE	
	RISEDRONATE (N=3624)	PLACEBO (N=1821)	RISEDRONATE (N=2573)	PLACEBO (N=1313)
Age — yr	74±3	74±3	83±3	83±3
Time since menopause — yr	28±8	28±8	37±7.0	37±7
Height — cm	156.6±7.0	156.4±6.9	154.6±7.2	154.7±7.3
Weight — kg	61.1±11.0	61.3±10.9	60.4±11.6	60.3±11.2
Evidence of vertebral fractures — no. (%)†	1100 (38)	562 (39)	743 (44)	394 (45)
Femoral-neck T score‡	−3.7±0.6	−3.7±0.6		
Serum 25-hydroxyvitamin D — ng/ml	23±11	23±11	20±11	20±11
Low serum 25-hydroxyvitamin D — no. (%)§	1040 (29)	547 (30)	1128 (44)	577 (44)

*Plus–minus values are means ±SD. Women 70 to 79 years old were enrolled if they had a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with at least one nonskeletal risk factor for hip fracture). Women 80 years of age or older were enrolled if they had at least one nonskeletal risk factor or a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with a hip-axis length ≥11.1 cm). Within each age group, there were no significant differences between treatment groups in any characteristic. To convert the values for serum 25-hydroxyvitamin D to nanomoles per liter, multiply by 2.5.

†The percentages are based on the number of women for whom vertebral-fracture status was known (of the women 70 to 79 years old, 2873 and 1437 assigned to risedronate and placebo, respectively, and of those ≥80 years old, 1692 and 874 assigned to risedronate and placebo, respectively).

‡Measurements of bone mineral density were available for 5375 of the women 70 to 79 years old (3575 of those assigned to risedronate and 1800 of those assigned to placebo). These measurements were not available for most (69 percent) of the women 80 years of age or older, and hence their T scores were not analyzed. The T scores shown were calculated with use of the manufacturer's reference data at the time of screening; mean values were the same regardless of the instrument used (the Lunar instrument in 43 percent of the women and the Hologic instrument in 57 percent of the women). Recalculation of the femoral-neck T scores at base line with data from the Third National Health and Nutrition Examination Survey yielded T scores of approximately −2.9 to −2.7 in both groups of women 70 to 79 years old.

§A low value was defined as one below 16 ng per milliliter (40 nmol per liter).

absence of a history of vertebral fracture at base line was available for 4351 of the younger women, 1703 (39 percent) of whom had evidence of at least one vertebral fracture at base line. Among the latter women, the relative risk of hip fracture associated with risedronate treatment was 0.4 (95 percent confidence interval, 0.2 to 0.8; P=0.003). Among the younger women who were known not to have a history of vertebral fracture at base line, the relative risk was 0.6 (95 percent confidence interval, 0.3 to 1.2; P=0.14).

In the group of women 80 years of age or older, risedronate had no effect on the incidence of hip fracture (Table 2 and Fig. 2B). The majority (58 percent) of the women in this group were recruited solely on the basis of clinical risk factors, such as a recent fall-related injury; only 16 percent were recruited on the basis of low bone mineral density at the femoral neck. Information on bone mineral density was not available for most of the women in this age group. Among the 1313 older women who were assigned to the placebo group, 316 were known to have osteoporosis (T score, −2.5 or lower according to reference data from the Third National Health and Nutrition Examination Survey; mean T score, −3.3). The incidence of hip fracture among the women with confirmed osteoporosis was 9.7 percent, as compared with 5.6 percent among the 89 women without osteoporosis (T score, higher than −2.5) and 3.6 percent among the 908 women whose bone mineral density was not known. Among the 941 older women who were known to have low bone mineral density (T score, −2.5 or lower), the incidence of hip fracture was 7.2 percent among those assigned to risedronate and 9.7 percent among those assigned to placebo (P=0.37).

Nonvertebral Fractures

In an analysis of all the women, the incidence of nonvertebral fractures was 9.4 percent among those assigned to risedronate, as compared with 11.2 percent among those assigned to placebo (relative risk, 0.8;

TABLE 2. INCIDENCE OF HIP FRACTURE IN SUBGROUPS OF THE WOMEN, ACCORDING TO TREATMENT WITH RISEDRONATE OR PLACEBO.*

GROUP	RISEDRONATE			PLACEBO			RELATIVE RISK (95% CI)	P VALUE†
	TOTAL NO.	NO. WITH HIP FRACTURE	INCIDENCE	TOTAL NO.	NO. WITH HIP FRACTURE	INCIDENCE		
			%			%		
Overall	6197	137	2.8	3134	95	3.9	0.7 (0.6–0.9)	0.02
Women 70–79 yr of age with osteoporosis	3624	55	1.9	1821	46	3.2	0.6 (0.4–0.9)	0.009
Presence of vertebral fracture at base line‡	1128	22	2.3	575	25	5.7	0.4 (0.2–0.8)	0.003
Absence of vertebral fracture at base line	1773	14	1.0	875	12	1.6	0.6 (0.3–1.2)	0.14
Women ≥80 yr of age with ≥1 clinical risk factors for hip fracture	2573	82	4.2	1313	49	5.1	0.8 (0.6–1.2)	0.35

*Women 70 to 79 years old were enrolled if they had a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with at least one nonskeletal risk factor for hip fracture). Women 80 years of age or older were enrolled if they had at least one nonskeletal risk factor or a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with a hip-axis length ≥11.1 cm). The incidence is the proportion of the total group at risk at a given time with a hip fracture, according to the Kaplan–Meier survival estimates for the three-year period of the study.

†P values are for the comparison between risedronate and placebo by the log-rank test (two-sided).

‡The presence or absence of a vertebral fracture at base line was known for 4351 (80 percent) of the women 70 to 79 years old.

95 percent confidence interval, 0.7 to 1.0; P=0.03). When only the women with confirmed osteoporosis were considered, the incidence of nonvertebral fractures among those assigned to risedronate was 8.4 percent, as compared with 10.7 percent among those assigned to placebo (relative risk, 0.8; 95 percent confidence interval, 0.7 to 1.0; P=0.03). Among the women in this enrollment group who had a vertebral fracture at base line, the incidence of nonvertebral fracture was 10.3 percent among those assigned to risedronate, as compared with 16.1 percent among those assigned to placebo (relative risk, 0.7; 95 percent confidence interval, 0.5 to 0.9; P=0.01). Among the women selected primarily on the basis of nonskeletal risk factors, the treatment assignment had no effect on the incidence of nonvertebral fracture (10.8 percent with risedronate, as compared with 11.9 percent with placebo; P=0.43).

Bone Mineral Density

Bone mineral density was measured during treatment in a total of 1765 women (19 percent of those who received at least one dose of study medication), including 1236 of the women in the younger enrollment group, who had confirmed osteoporosis, and 529 of those in the older group. In the younger group, the mean bone mineral density at the femoral neck and trochanter among those assigned to risedronate was higher at six months than at base line and was higher than the mean value among those assigned to placebo at six months and at all time points thereafter. At three years, the bone mineral density at the femoral neck in this group was 2.1 percent and 3.4 percent higher among the women assigned to 2.5 mg and 5.0 mg of risedronate, respectively, than among those assigned to placebo, and the bone mineral density at the trochanter was 3.8 percent and 4.8 percent higher, respectively. At three years there was no change in the bone mineral density at either site among the younger women assigned to placebo. These changes in bone mineral density were similar to those observed in the older enrollment group (data not shown).

Adverse Events

In an analysis of all the women, the proportion of women who had any adverse event, who had a serious adverse event, or who withdrew because of an adverse event was similar regardless of treatment assignment (Table 3). The incidence of adverse events involving the upper gastrointestinal tract was similar among the women assigned to risedronate and those assigned to placebo.

The women in the older enrollment group, who ranged in age from 80 to 100 years, had a slightly higher incidence of death, other serious adverse events, and withdrawals due to adverse events than the younger women. However, the overall frequency and types of adverse events, including those involving the up-

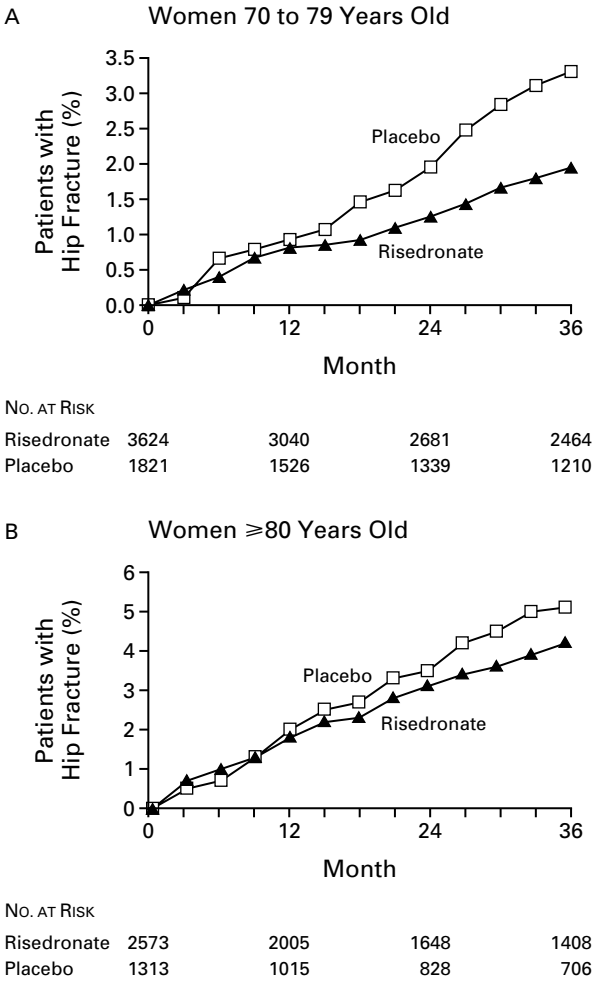

Figure 2. Kaplan–Meier Estimates of the Incidence of Hip Fracture in the Younger Women (Panel A) and the Older Women (Panel B), According to Treatment with Risedronate or Placebo.

Women 70 to 79 years old were enrolled if they had a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with at least one nonskeletal risk factor for hip fracture). Women 80 years of age or older were enrolled if they had at least one nonskeletal risk factor or a low bone mineral density at the femoral neck (T score, lower than −4 or lower than −3 with a hip-axis length ≥11.1 cm).

per gastrointestinal tract, were similar in the risedronate and placebo groups, regardless of age (data not shown).

DISCUSSION

In this large trial, risedronate prevented hip fractures in the women who had osteoporosis, indicated by a low bone mineral density at the femoral neck, but not in the women who, although they had clinical risk factors for hip fracture, did not necessarily have osteoporosis.

In the group of women with confirmed osteoporosis (those 70 to 79 years old), the observed incidence of hip fracture among those assigned to placebo (3.2 percent during the three-year study) was higher than the reported 0.6 to 0.8 percent annual incidence in unselected, untreated women of the same age,[19,20] indicating that our selection criterion of a low bone mineral density at the femoral neck successfully identified women at increased risk for hip fracture. In the group of women with confirmed osteoporosis, the incidence of hip fracture among those assigned to placebo was substantially higher among the women with a previous vertebral fracture than among those without a previous vertebral fracture (5.7 percent and 1.6 percent, respectively, during the three-year study), confirming earlier findings that a previous vertebral fracture increases the risk of hip fracture.[21] The absence of a significant effect of risedronate in the women with low bone mineral density at the femoral neck but no history of vertebral fracture is probably due to the low incidence of hip fracture and the small number of women in this group.

Our data indicating that the risk of hip fracture decreases with use of risedronate are consistent with those previously reported in trials of alendronate[5,6]; in those studies, low bone mineral density at the femoral neck and previous vertebral fracture identified women who benefited from treatment. Supplementation with calcium and vitamin D have been reported to reduce bone loss and the risk of nonvertebral fracture in ambulatory men and women over 65 years of age[22] and to reduce the risk of hip fracture among women in nursing homes.[23,24] Because supplementation with calcium and vitamin D was provided to the women in this study, the effects of risedronate treatment occurred

Table 3. Adverse Events during the Study.

Event	Risedronate, 2.5 mg (N=3093)	Risedronate, 5.0 mg (N=3104)	Placebo (N=3134)
	no. of women (%)		
Any adverse event	2762 (89.3)	2786 (89.8)	2805 (89.5)
Serious adverse event*	946 (30.6)	943 (30.3)	973 (31.0)
Discontinuation of treatment due to adverse event	548 (17.7)	550 (17.7)	564 (18.0)
Adverse event involving upper gastrointestinal tract			
Any	690 (22.3)	657 (21.2)	684 (21.8)
Moderate to severe	259 (8.4)	279 (9.0)	258 (8.3)
Abdominal pain	255 (8.2)	250 (8.1)	288 (9.2)
Dyspepsia	259 (8.4)	255 (8.2)	254 (8.1)
Esophagitis	47 (1.5)	54 (1.7)	59 (1.9)
Esophageal ulcer	9 (0.3)	9 (0.3)	14 (0.4)

*Serious adverse events included death, overdose, a diagnosis of cancer, and any other event that was life-threatening or permanently disabling, that required or extended the duration of hospitalization, or that required intervention to prevent permanent impairment.

in addition to any benefit attributable to the supplementation.

The incidence of hip fracture among the older women who were assigned to placebo, who had mainly clinical risk factors, was higher than that among the younger women assigned to placebo, all of whom had confirmed osteoporosis, but it was similar to that previously reported in other groups of untreated women of similar age.[19,20] The fact that the incidence was not higher in our study may be explained by the effect of the calcium and vitamin D supplementation. It is also possible that our enrollment criteria, which allowed older women with a single clinical risk factor for hip fracture to enter the study, did not adequately identify women at increased risk of fracture, since the presence of multiple clinical risk factors more strongly predicts the risk of hip fracture than does the presence of single risk factors.[7]

Evaluation of the role of bone mineral density at the femoral neck in predicting the response to treatment among women 80 years of age or older is confounded by the facts that few of these older women were recruited on the basis of a low bone mineral density at the femoral neck and that this measurement was not available in most of these women. Among the women 80 years of age or older who were assigned to placebo, the incidence of hip fracture among those without data on bone mineral density was similar to that among those known to have T scores greater than −2.5 at the femoral neck, suggesting that the majority of the older women did not have osteoporosis.

Risedronate treatment was well tolerated in our study. Overall, the incidence and types of adverse events were similar to those observed with use of placebo, even among women 80 years of age or older. These data confirm the favorable safety profile of risedronate observed in relatively young patients in previous studies.[14,15] Fifty percent of the women completed three years of treatment, although 64 percent had complete follow-up data for the three-year study. The women who discontinued treatment early may have been at higher risk for hip fracture, since they were older, thinner, and more likely to smoke than those who completed treatment. The effect of their discontinuation of treatment would be to limit the magnitude of the treatment effect by decreasing the exposure of the treated group to the study drug. The results of the analysis of hip fracture were similar whether or not the hip fractures occurring during the follow-up period were included. The reasons for discontinuation of treatment and the adverse events associated with discontinuation among the women assigned to risedronate were similar to those among the women assigned to placebo, suggesting that poor drug tolerability was not a factor in the discontinuation of treatment.

Our results demonstrate the importance of measurements of bone mineral density in identifying women for whom drug therapy to prevent hip fracture is appropriate. Risedronate treatment reduces the risk of hip fracture among women with osteoporosis, defined as a low bone mineral density at the femoral neck, but it is not more effective than calcium and vitamin D alone in women identified primarily on the basis of clinical risk factors for hip fracture. Women with the most advanced disease (as evidenced by a low bone mineral density at the femoral neck and a history of vertebral fractures) may benefit the most from risedronate treatment.

Supported by grants from Procter & Gamble Pharmaceuticals (Cincinnati) and Aventis Pharma (Bridgewater, N.J.).

The authors have received research grants from or have served as consultants to or members of speakers' bureaus for Procter & Gamble, Aventis Pharma, and other companies that make products used in the treatment of osteoporosis.

We are indebted to Simon Pack, Ph.D., and Joseph DiGennaro, M.S., for statistical analyses; to Lisa Bosch for assistance in the preparation of the manuscript; to the members of the support staff at the study centers for their contributions; and to the women who participated in the study.

APPENDIX

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