CLINICAL RESEARCH STUDY

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Obesity Is Not Protective against Fracture in Postmenopausal Women: GLOW

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ABSTRACT

OBJECTIVE: To investigate the prevalence and incidence of clinical fractures in obese, postmenopausal women enrolled in the Global Longitudinal study of Osteoporosis in Women (GLOW).

METHODS: This was a multinational, prospective, observational, population-based study carried out by 723 physician practices at 17 sites in 10 countries. A total of 60,393 women aged ≥55 years were included. Data were collected using self-administered questionnaires that covered domains that included patient characteristics, fracture history, risk factors for fracture, and anti-osteoporosis medications.

RESULTS: Body mass index (BMI) and fracture history were available at baseline and at 1 and 2 years in 44,534 women, 23.4% of whom were obese (BMI ≥30 kg/m^2). Fracture prevalence in obese women at baseline was 222 per 1000 and incidence at 2 years was 61.7 per 1000, similar to rates in nonobese women (227 and 66.0 per 1000, respectively). Fractures in obese women accounted for 23% and 22% of all previous and incident fractures, respectively. The risk of incident ankle and upper leg fractures was significantly higher in obese than in nonobese women, while the risk of wrist fracture was significantly lower. Obese women with fracture were more likely to have experienced early menopause and to report 2 or more falls in the past year. Self-reported asthma, emphysema, and type 1 diabetes were all significantly more common in obese than nonobese women with incident fracture. At 2 years, 27% of obese women with incident fracture were receiving bone protective therapy, compared with 41% of nonobese and 57% of underweight women.

CONCLUSIONS: Our results demonstrate that obesity is not protective against fracture in postmenopausal women and is associated with increased risk of ankle and upper leg fractures.

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Fractures are a major cause of morbidity and mortality in postmenopausal women, and incur huge economic costs for health services. One in 3 women aged ≥50 years will sustain ≥1 fracture during her remaining lifetime, with an estimated annual cost of €30 billion in Europe and $17 billion in the US.[1-3] The social and economic burden resulting from fractures is predicted to increase at least 2-fold in the next few decades as a result of demographic changes in the population.[4]

Low body mass index (BMI) is an important risk factor for fractures in postmenopausal women—an effect mediated predominantly, although not exclusively, through low bone mineral density (BMD).[5] In contrast, obesity is widely believed to be protective against fracture because of higher BMD and reduced impact of falls as a result of increased soft-tissue padding.[6,7] However, in a recent audit of postmenopausal women presenting to a Fracture Liaison Clinic, 27.7% of women presenting with a fracture had a BMI ≥30 kg/m^2.[8] This suggests that fractures in obese women may contribute significantly to the overall fracture burden in the postmenopausal population.

The Global Longitudinal study of Osteoporosis in Women (GLOW)—a prospective, multinational, observational, population-based study of postmenopausal women—provides an ideal setting in which to investigate the epidemiology and pathogenesis of fractures in obese postmenopausal women.[9] The aim of this study was to document the prevalence of clinical fractures in obese women in the GLOW cohort at baseline, and to establish the incidence of fractures in this population after 2 years of follow-up. Further aims were to examine the skeletal sites of fracture and underlying risk factors in obese women, and to compare these with corresponding data in nonobese and underweight women with fractures.

CLINICAL SIGNIFICANCE

- Nearly 1 in 4 postmenopausal women with clinical fracture is obese, a finding that has major public health implications in view of the rapidly rising incidence of obesity.
- Obesity is a risk factor for ankle and upper leg fractures.
- Increased risk of falls and reduced physical mobility are likely to be important pathogenetic factors in fractures in obese individuals.

METHODS

GLOW is a prospective cohort study involving 723 physician practices at 17 sites in 10 countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, UK, and US). The study methods have been described previously.[9] In brief, practices typical of each region were recruited through primary care networks organized for administrative, research, or educational purposes, or by identifying all physicians in a geographic area. Each site obtained local ethics committee approval to participate in the study. The practices provided the names of women aged ≥55 years who had been seen by their physician in the past 24 months. Approximately 3000 women were sought at each site. Self-administered questionnaires (baseline surveys) were mailed to 140,416 subjects between October 2006 and February 2008, with a 2:1 oversampling of women aged ≥65 years. Nonresponders were followed-up with a series of postcard reminders, a second questionnaire, and telephone interviews. After appropriate exclusions, 60,393 women agreed to participate in the study. Follow-up questionnaires were mailed 1 and 2 years later to women who had participated in the baseline survey. Women without both 1 and 2 years of follow-up (lost to follow-up or died) and women with incomplete BMI data were excluded from the analysis.

Data Collection

Questionnaires were designed to be self-administered and covered domains that included: patient characteristics and risk factors, fracture history, current medication use, and other medical diagnoses. Data on height and weight were collected to allow calculation of BMI. Women were defined as obese if BMI was ≥30 kg/m^2, nonobese if BMI was 18.5-29.9 kg/m^2, and underweight if BMI was <18.5 kg/m^2.

Information was gathered on previous fractures (fractures that had occurred since the age of 45 years) during the baseline survey and on incident fractures during the 1- and 2-year follow-up surveys. All surveys included report of fracture location, including spine, hip, wrist, and other nonvertebral sites (clavicle, upper arm, rib, pelvis, ankle, upper leg, lower leg, foot, hand, shoulder, knee, and elbow), and occurrence of single or multiple fractures. Self-reports of personal risk factors included: history of parental hip fracture; premature menopause (age ≤45 years); number of falls in the past 12 months; use of arms to assist standing from a sitting position; current use of cortisone; fair or poor general health; current cigarette smoking; and consumption of ≥3 units of alcohol daily. Subjects were considered to be taking anti-osteoporosis medication if they reported current use of alendronate, calcitonin, estrogen, etidronate, ibandronate, pamidronate, recombinant human parathyroid hormone (1-84), raloxifene, risedronate, strontium ranelate, teriparatide, tibolone, or zoledronate. Information also was obtained about other diagnoses, including asthma, emphysema, osteoarthritis, rheumatoid arthritis, colitis, stroke, Parkinson's disease, multiple sclerosis, cancer, and type 1 diabetes.

Statistical Analysis

Age was compared across BMI groups using the Kruskal-Wallis test for continuous variables. Fracture rates are reported as rates per thousand women. Only women with