

Epidemiology of Hip Fracture: The MEDOS Study

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Introduction

Osteoporosis is recognized by the World Health Organization (WHO) as a major health problem that imposes a considerable burden on health-care resources worldwide. Osteoporosis produces a reduction in bone mass and subsequently in bone strength which finally results in unexpected fractures. Hip fracture is due in most cases to osteoporosis and it is a significant fracture from a socio-economic point of view, because it gives rise to the greatest morbidity and costs associated with the disease. It is estimated that 1.66 million hip fractures occur each year worldwide [1]. An exponential increase in the incidence of fractures is reported in the countries of the developing world as well as those of the Western world [2] that is mainly due to an age-related reduction in bone mass and to an increase in the risk of falling with age [3].

There is a marked difference in hip fracture rates between communities; according to retrospective studies, rates vary by 10-fold or more within Europe [4]. This difference suggests that factors other than the menopausal or gonadal status are important in the aetiology of hip fracture. It is important to identify these factors because, if these are reversible lifestyle factors, they may have a significant effect on approaches to prevention.

The MEDOS Study

The lack of reliable data on the incidence of osteoporotic hip fractures and the risk factors associated with osteoporosis were the impetus for MEDOS, the Mediterranean Osteoporosis Study, which was set up in 1986

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with the collaboration of the WHO and the European Foundation for Osteoporosis [5]. The MEDOS study was a prospective, multicentre study of the incidence of hip fractures carried out in six Mediterranean countries (14 centres): Portugal (Porto), Spain (Madrid, Seville), France (Paris, Toulouse), Italy (Rome, Siena, Parma), Greece (Crete) and Turkey (Istanbul, Samsun, Erzurum, Diyarbakir, Ankara). The duration of the study in each centre was 12 months, within the period 1988–9.

The purpose of the study was to determine the incidence rates and risk factors associated with hip fracture over the age of 50 years. The project comprised three parts: (a) a collection of existing register data on hip fracture occurrence from 31 European ministries of health; (b) a study of hip fracture incidence in the areas covered by the participating centres in the Mediterranean countries in age groups above 50 years; (c) a case-control study comparing 8185 individuals (2816 cases and 5369 controls; two controls per case).

A number of measures were taken to obtain high-quality data. The first task in the preparation of the project was to draw up a protocol, which was finalized after 13 versions [6–8]. According to the protocol, cases were excluded if patients had life-threatening medical conditions and cases and controls were excluded if no reasonably reliable interview data were obtained. Controls were obtained mainly from population registers and from neighbours of the cases.

The case-control questionnaire [6,7] was designed to characterize risk factors for hip fracture and to identify any protective factors. Sets of questions were included on physical characteristics, socio-demographic features, reproductive history, lifestyle, existing medical conditions, previous diseases and medications. The responses from hip-fracture patients were compared with those of age-matched and sex-matched controls from the same catchment area.

The Register Study

In the first part of the study 17 European countries responded to the request for existing data on the number of hip fracture patients by age and sex, between

the years 1983 and 1985. As expected, hip fracture was most frequently found amongst the elderly, particularly women. The incidence of hip fracture rose exponentially with age in both sexes. It was higher in women than in men and there was a 3-fold range between countries in the female-to-male sex ratio. There was an 11-fold range in apparent incidence amongst women and a 7-fold range amongst men between the various countries. The highest incidence of hip fracture was found in the northern part of Europe and the lowest in the Mediterranean area. There was a significant positive correlation between the age-standardized incidence rates reported in men from each country and that in women. There was a larger difference in incidence between countries, which suggests important genetic or environmental factors in the causation of hip fracture, the extent of which reflects imperfect capture of data [9].

The Incidence Study

In the second part of the MEDOS study the incidence of hip fracture in the abovementioned 14 European centres was assessed. Hip fracture cases were recorded prospectively in defined catchment areas over a 1-year interval. During the years 1988–9 a total of 3629 men and women over the age of 50 years were identified with hip fracture from a catchment of 3 million. In all communities the fracture rate increased exponentially with age. There were large and significant differences between centres in the doubling time of hip fracture risk with age and in crude and age-standardized rates. Greater than 4-fold and 13-fold differences in age-standardized risk were found amongst men and women respectively. The lowest rates were observed from Turkey and the highest from Seville (Spain), Crete (Greece) and Porto (Portugal). Fractures were significantly more frequent among women than men with the exception of three rural Turkish centres. Indeed, in rural Turkey the normal female/male ratio was reversed. Variations in incidence between regions were greater than the differences within centres between sexes, and there was a close and significant correlation between incidence rates for men and those for women in the regions studied. Excess female morbidity increased progressively from the age of 50 years but attained a plateau after the age of 80 years, suggesting a finite duration of the effect of menopause (Fig. 1).

The conclusion from the MEDOS incidence study was that there are marked and sizeable differences in the incidence rates of hip fracture throughout southern Europe. The reasons for these differences are likely to be related to lifestyle or genetic factors rather than to differences in endocrine status [10].

An interesting finding was that the risk of hip fracture was almost 3 times higher among women in long-term residential care than in women living at home. Analysis of data of the Paris centre [11] on women without dementia (107 cases and 225 neighbourhood controls)

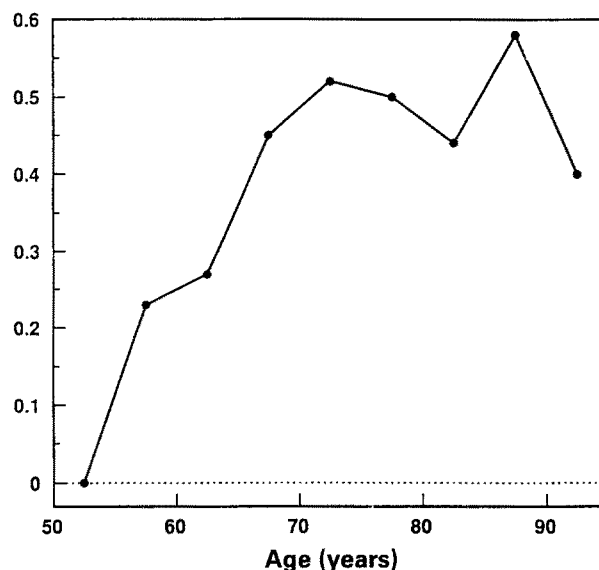


Fig. 1. A progressive increase with age in the excess female morbidity was obvious only up to the age of 75 years, suggesting a finite duration of a menopause effect. (From Elffors et al. [10].)

showed that age, level of activity and morbidity were important factors in determining whether the elderly were in residential care.

The Case–Control Study

In the third part of the MEDOS study the risk factors for developing a hip fracture were studied. Fractured patients were compared with age-matched people selected from the neighbourhood or population registers who served as control. Cases and controls were interviewed using a structured questionnaire on work, physical activity, exposure to sunlight, reproductive history and gynaecological status, height, weight, mental score and consumption of tobacco, alcohol, calcium, coffee and tea.

Several significant risk factors were identified by univariate analysis, including low body mass index (BMI), short fertile period, low physical activity, lack of sunlight exposure, low milk consumption, no consumption of tea and a poor mental score [12]. No significant adverse effects of coffee or smoking were observed. Moderate intake of spirits was a protective factor in young adulthood, but otherwise no significant effect of alcohol intake was observed. For some risks, a threshold effect was observed. A low BMI and milk consumption were significant risks only in the lowest 50% and 10% of the population respectively (Fig. 2).

A late menarche, poor mental score, low BMI and physical activity, low exposure to sunlight and a low consumption of calcium and tea remained independent risk factors after multivariate analysis, accounting for 70% of hip fractures. Excluding mental score and age at menarche and attributable risk was 56%. Thus, the majority of hip fractures could be explained on the basis of the potentially reversible risk factors sought. A

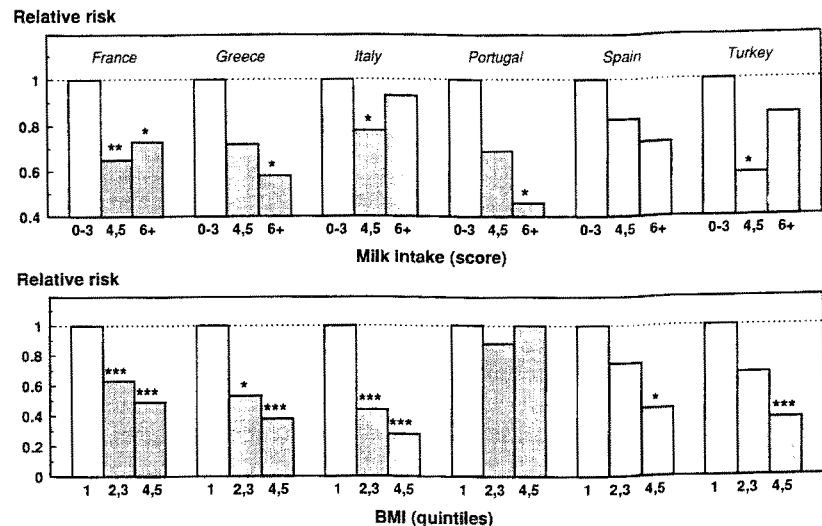


Fig. 2. Hip fracture risk according to intake of milk and BMI by country. Asterisks denote the significance of differences compared with the lowest category of intake or BMI (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$). (From Johnell et al. [12].)

multivariate model gave a relative risk for hip fracture of 0.23 for those who had a high BMI, high exposure to sunlight, a high intake of calcium and a score for physical activity above the median value. In contrast, the use of risk factors to predict hip fractures had a low sensitivity and specificity.

The coexistence of osteoarthritis reduces the risk of hip fracture [13]. Across the centres, the risk of hip fracture was reduced in the presence of osteoarthritis (relative risk 0.55 and 0.71, for men and women respectively). Osteoarthritis cases differed from hip fracture cases in that they were smaller, more obese, and had a greater BMI. If osteoarthritis cases suffered hip fractures, these occurred at a later age and were likely to be extracapsular.

Efficacy of Drugs in Preventing Hip Fracture

The preventing efficacy of bone-active drugs was also tested in the epidemiology of hip fracture. It was found that women taking drugs affecting bone metabolism had a significantly decreased risk of hip fracture [14,15]. After adjustment for differences in other risk factors it was found that oestrogen, calcium and calcitonins significantly decrease the risk of hip fracture. It is noticeable that short-term intervention late in the natural course of osteoporosis may have significant effects on the incidence of hip fractures. It was found that random treatment of 30% of the female population over 50 years of age could prevent 5% of hip fractures. If bone mineral density screening were used to select high-risk patients for treatment, 8% of fractures could be prevented [16].

Other preventive measures can be suggested to avoid a hip fracture. Using the MEDOS lifestyle data, it was possible to calculate the effects of various public health measures. Increasing milk consumption in the 10% of the population with the lowest milk index could prevent 5% of hip fractures and increasing physical activity

could prevent 16%. Implementing both measures could prevent 19% of hip fractures [16].

Orthopaedic Management of Hip Fracture

The orthopaedic management of hip fractures was also studied in the MEDOS study [17]. The majority of hip fractures recorded were extra-capsular and usually required stable internal fixation to avoid instability and deformation of pseudarthrosis. Surgery was performed in the majority of cases (85% of extracapsular and 84% of intracapsular fractures), although this proportion also varied between countries. The type of operation performed depended on the type of fracture; the most common operation for intracapsular fracture was hip replacement (67% of cases), while in extracapsular fracture the most common intervention was stable fixation (50% of cases) (Table 1). Again, there were substantial differences between centres. During the period of hospitalization, 26% of patients experienced minor complications, but only 2.4% experienced serious complications, with further surgery being required in 2%. Mortality during hospitalization was 5.1% overall (4.8% and 5.7% in intra- and extracapsular fracture cases, respectively). The average duration of hospital stay was 24 days, but it varied between centres, with a tendency for shorter stays to be associated with a greater proportion of cases treated surgically. It is known that 20–25% of orthopaedic beds are continuously occupied by elderly patients with fractures of the femur, and this percentage could rise, given the increasing rate of the incidence of the hip fractures [18].

After discharge of the fractured elderly from the hospital, mortality increases dramatically [19]. In Madrid it was found that 28% of patients died during the first year, most deaths occurring within the first 3 months. During the second year, functional capacity deteriorated in 44% of the 62 cases and in 16% of the 91 controls. At 2 years the mortality was 35% in cases compared with 18% in controls.

Table 1. Type of operation differs between intracapsular and extracapsular hip fractures and also between countries and/or centres

	Unstable fixation ^a	Stable fixation ^a	Arthroplasty ^a	Condylocephalic nailing ^a
<i>Intracapsular hip fractures (n=827)</i>				
Paris	5 (4.8%)	19 (39.5%)	77 (74%)	3 (2.9%)
Toulouse	6 (3.8%)	21 (18.3%)	130 (82.8%)	0
Crete	3 (2.5%)	19 (13.4%)	98 (81.7%)	0
Rome	20 (16.9%)	30 (15.8%)	67 (56.8%)	1 (0.6%)
Siena	11 (17.5%)	6 (25.4%)	45 (71.4%)	1 (1.6%)
Parma	9 (11.3%)	6 (9.5%)	34 (42.5%)	31 (38.7%)
Porto	21 (42.9%)	8 (7.5%)	20 (40.8%)	0
Madrid	8 (20%)	1 (16.3%)	31 (77.5%)	0
Istanbul	5 (6.75%)	15 (2.5%)	49 (66.2%)	5 (6.8%)
Rural Turkey	-	19 (20.3%)	2 (9.5%)	0
Ankara	-	6 (90.5%)	0	0
Total	88 (10.7%)	150 (18.1%)	553 (66.9%)	36 (4.4%)
<i>Extracapsular hip fractures (n=1222)</i>				
Paris	1 (0.9%)	64 (61%)	26 (24.8%)	14 (13.3%)
Toulouse	2 (0.9%)	117 (47.7%)	74 (30.2%)	52 (21.2%)
Crete	7 (3.5%)	188 (93.5%)	5 (24.9%)	0
Rome	75 (24%)	95 (30.3%)	57 (18.2%)	86 (27.5%)
Siena	12 (17.9%)	31 (46.3%)	12 (17.9%)	12 (17.9%)
Parma	10 (20.4%)	4 (8.2%)	7 (14.3%)	28 (57.1%)
Porto	39 (66%)	14 (23.7%)	3 (5.1%)	3 (5%)
Madrid	3 (5.5%)	48 (87.3%)	9	4 (7.27%)
Istanbul	3 (3%)	27 (27.5%)	40 (40.8%)	28 (28.6%)
Rural Turkey	-	10 (52.6%)	9 (47.4%)	0
Ankara	-	11 (91%)	1 (9%)	0
Total	152 (12.4%)	609 (49.8%)	234 (19.1%)	227 (18.6%)

^a Unstable fixation was considered an osteosynthesis with one screw or pin, one nail, or ≥ 2 nails, pins or screws.

Stable fixation was considered an osteosynthesis with screws or nails and plate, nail and plate rigid fixation, nail and plate sliding fixation. Arthroplasty was either a partial hemi-arthroplasty or total hip replacement.

Condylocephalic was either intramedullary nailing or Ender's nailing.

Conclusion

In conclusion, the MEDOS study was set up to investigate the incidence of, and risk factors for, hip fractures in six countries along the northern rim of the Mediterranean. As almost all patients with a hip fracture are hospitalized, systematic data were collected during their hospital stay. These data were mainly about their past medical history and their lifestyle, the circumstances surrounding the present hip fracture, data on operation, and the evaluation at time of discharge from hospital (functional capacity, general complications). When possible, each fracture case and two controls were interviewed by trained observers in the local language using a structured questionnaire [7]. Published data [9] showed that before MEDOS there existed only scattered and incomplete retrospective information about the apparent incidence of hip fracture in Europe. The incidence study [10] showed that in all communities the fracture rate increased exponentially with age, but there were large and significant differences between centres in the doubling time for hip fracture risk with age and in crude and age-standardized rates.

Fractures were significantly more frequent among women than men, with the exceptions of three rural Turkish centres where the normal female/male ratio was reversed. The study of the risk factors for hip fracture in

southern European women [12] showed that variations in lifestyle factors are associated with significant differences in the risk of hip fracture and may predict the individuals at high risk. Preventive bone antiresorptive drugs, administered for even a short period, may have a protective effect for a hip fracture [14]. These drugs are mainly oestrogens, calcitonin and calcium. Surgical treatment for hip fractures is almost obligatory [17]. The main surgical techniques used in these cases are the pin and plate for intertrochanteric fractures and partial or total hip replacement for subcapital fractures of the femur, although small differences were found to exist between countries.

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