Original article

Risk factors of mortality during the first year after low energy osteoporosis fracture: a retrospective case-control study

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Summary

Introduction. **Osteoporotic fractures are a major public health problem because of the morbidity and mortality of fracture complications. The objective of this study was to examine predictive factors of mortality during the first year after an osteoporotic fracture.**
Methods. **It is a retrospective case-control study using data of a group of 1081 patients aged over 50 years with severe osteoporotic fractures by the Rennes university hospital emergency department from August 2007 to September 2008. Patients (cases) who died during the year following the fracture were compared with others who had survived (controls) one year after the fracture, matched on age, sex and type of fracture. Pre-fracture comorbidities and complications after the fractures were studied.**
Results. **Forty-two cases and 126 controls were analyzed without significant differences in age, sex or type of fracture. On univariate analysis, previous neoplasia, neurodegenerative disease, walking aids, thromboembolic complication, post fracture infection, post fracture heart failure, post fracture acute respiratory failure were associated with more mortality after osteoporotic fracture. After multivariate analysis, only previous neoplasia (OR = 4.63 [1.79 – 11.95]; p = 0.02) and acute respiratory failure after fracture (OR = 28.15 [5.75 – 137.9]; p<0.001) were retained as predictive factors during the year following the fracture.**
Conclusion. **Patients died more often from their co-morbidities than direct complications of their fractures. Osteoporotic fracture seems to be a marker of poor health status and a factor which may hasten the death.**

KEY WORDS: osteoporosis; fracture; mortality; comorbidities; epidemiology.

Introduction

The population aged over 65 with osteoporosis is growing constantly and this affects public health, because of fracture complications, decreasing life quality and increasing mortality, when it's a severe osteoporotic fracture (1). Osteoporosis affects 1 out of 3 women after the menopause and 1 out of 8 men over 50. Post osteoporotic fracture mortality was studied between 30 days and over 20 years after fracture (2-4), and on several fractures (2, 4, 5). Nevertheless, the comparison was more often with a control group without osteoporotic fracture. All studies conclude on greater mortality after osteoporotic fracture but causes of death were not clear and even less so when the comparison was made with patients who also had suffered from an osteoporotic fracture. However, a comparative analysis between patients who died after an osteoporotic fracture and those who also had a fracture but are still alive is likely to show mortality risk factors other than the fracture itself.
The objective of this retrospective study was to evaluate mortality risk factors during the first year after a severe osteoporotic fracture.

Patients and Methods

Patients

This retrospective case-control study, included patients from a group of 1081 patients aged over 50 years with a severe low energy fracture detected by the Rennes university hospital emergency department from August 2007 to September 2008 (5). "Cases" were 42 patients who died during the year following the fracture. We selected 3 controls for 1 case, thus 126 patients from the same initial group still alive one year after the fracture, were selected and matched on age, sex and fracture type. The severe osteoporotic fractures are hip, pelvis, proximal humerus, spine, proximal tibia or distal femur, 3 ribs fractures.

Methods

Following data were collected retrospectively from medical records:
- Co-morbidities before fractures: cardiovascular disease (myocardial infarction, cerebrovascular accident, lower limb arteriopathy), neurodegenerative disease (dementia, Parkinson disease, multiple sclerosis), neoplasia defined as an evolutive neoplasia or solid neoplasia written on the medical records, chronic obstructive pulmonary disease (COPD), cirrhosis, alcohol dependence defined as a harmful consumption with physical or affective consequences, chronic kidney disease defined as a renal clearance < 60ml/min (MDRD), diabetes, institutionalization, technical assistance in walking (stick, zimmer), prevalent osteoporotic fracture.
- Post-fracture complications: thromboembolic complications (phlebitis, pulmonary embolism), infection defined as a fever with a bacterial infection, heart failure, acute respiratory failure defined as the use of high dose of oxygen , acute renal failure, cirrhosis complication, anemia defined as anemia which need transfusion.

Table 1 - Characteristics of 42 deceased patients and 126 patients alive one year after a low energy fracture.

	«Cases» *Deceased patients* N = 42	«Controls» *Patients alive* N = 126	*p*
Age N (SD) years	84.9 ± 9.2	83.3 ± 8.3	*0.27*
Women N (%)	29 (69.0%)	90 (71.4%)	*0.80*
Skeletal site N (%):			
- hip	33 (78.6%)	98 (77.8%)	*0.91*
- pelvis	2 (5.0%)	7 (5.6%)	*0.99*
- knee	3 (7.1%)	8 (6.6%)	*0.99*
- humerus	3 (7.1%)	8 (6.6%)	*0.99*
- spine	1 (2.5%)	5 (4.0%)	*0.99*
Comorbidities before fracture N (%)			
Cardiovascular disease	15 (35.7%)	32 (25.4%)	*0.20*
Neurodegenerative disease	13 (31.0%)	24 (19.0%)	*0.11*
Néoplasia	12 (28.6%)	13 (10.3%)	*0.004*
COPD	4 (10.0%)	8 (6.6%)	*0.49*
Cirrhosis	0	3 (2.4%)	*0.57*
Chronic renal failure	3 (7.1%)	5 (4.0%)	*0.41*
Diabetes	4 (10.0%)	13 (10.3%)	*0.99*
Alcohol dependence	2 (5.0%)	3 (2.4%)	*0.60*
Institutionalization	13 (31.0%)	29 (23.0%)	*0.30*
Technical assistance in walking	18 (42.9%)	30 (23.8%)	*0.02*
Prevalent fracture	14 (33.3%)	26 (20.6%)	*0.09*
Post fracture complication N (%)			
All	16 (38.1%)	16 (12.7%)	*< 0.001*
Thromboembolic complication	5 (11.9%)	1 (0.8%)	*0.003*
Infection	9 (21.4%)	7 (5.6%)	*0.002*
Heart failure	6 (14.3%)	2 (1.6%)	*0.003*
Acute respiratory failure	11 (26.2%)	2 (1.6%)	*< 0.001*
Acute renal failure	1 (2.5%)	0	*0.24*
Cirrhosis complication	0	0	-
Loss of autonomy	5 (11.9%)	14 (11.1%)	*0.81*
Anemia	4 (10.0%)	0	*0.003*

Statistical analysis

Statistical analysis was obtained using SPSS-Statistics 20.0 software. Qualitative data comparison was carried out using a statistical test of Chi-2 (χ^2) or the exact Fischer test when it was appropriate. The mean comparisons were realized using a non-parametric U test of Mann-Whitney. The difference was considered as statistically significant if $p < 0.05$. Multivariate analysis by logistic regression according to backward stepwise method was performed from data of the univariate analysis including variables if $p < 0.20$.

Results

Forty-two cases and 126 controls were analyzed (Table 1). There was no significant difference between cases and controls in terms of age and sex, respectively of 84.9 ± 9.2 *vs* 83.3 ± 8.3 years *(p = 0.27)* and of 69 *vs* 71.4% women *(p = 0.80).*

Co-morbidities before fracture or complications after fracture were associated with mortality during the first year after low energy fracture. Events significantly linked to post-fracture mortality after univariate analysis were: neoplasia (OR= 3.54 [1.47-8.54], *p=0.003*), neurodegenerative disease (OR=1.94 [0.88-4.28], *p=0.01*), prevalent walking aids (OR=2.35 [1.13-4.88], *p=0.02*), thromboembolic complication (OR=18.14 [2.05-160.4], *p=0.003*), post fracture infection (OR=5.02 [1.73-14.54], *p=0.003*), post fracture heart failure (OR=11.12 [2.15-57.57], *p=0.003*), post fracture acute respiratory failure (OR=23.71[4.98-112.8], *p<0.001*) (Table 2).

On multivariate analysis, only neoplasia (*adjusted* OR=4.63 [1.79-11.95], *p=0.02*) and post fracture acute respiratory failure (*adjusted* OR=28.15 [5.75-137.9], *p<0.001*) were significantly associated with mortality during the first year following the fracture (Table 2).

Discussion

In our study, several co-morbidities and post-fracture complications were associated with an increase in mortality during the first year following the osteoporotic fracture. On univariate analysis, neoplasia, neurodegenerative disease, technical walking aids before fracture, thromboembolic complication, infection, post fracture heart failure or acute respiratory failure were associated to increase in mortality. However, on multivariate analysis, only neoplasia (*adjusted* OR=4.63 [1.79-11.95], *p=0.02*) or acute respiratory failure (*adjusted* OR=28.15 [5.75-137.9], *p<0.001*) were predictive factors of mortality during the year following the osteoporotic fracture, whatever the fracture site.

Post osteoporotic fracture mortality has been analyzed in many studies. Nearly 20% of women and 30% of men with a hip fracture died during the year following the fracture (6) with further risk of mortality persisting up to 12 years after the fracture (7, 8). Mortality was documented for other severe fractures (4, 8).

Some studies concluded on a specific increase in mortality due

Table 2 - Risk factors of mortality one year after low energy osteoporosis fracture.

Variables	Univariate analysis Odd-Ratio (OR)	Multivariate analysis Adjusted Odd-Ratio (OR)
Neurodegenerative disease	OR 1.94 [0.88-4.28], *p = 0.10*	-
Neoplasia	OR 3.54 [1.47-8.54], *p = 0.003*	OR 4.63 [1.79-11.95], *p = 0.02*
Technical assistance in walking	OR 2.35 [1.13-4.88], *p = 0.02*	-
Thromboembolic complication	OR 18.14 [2.05-160.4], *p = 0.003*	-
Infection	OR 5.02 [1.73-14.54], *p = 0.003*	-
Heart failure	OR 11.12 [2.15-57.57], *p =0.003*	-
Acute respiratory failure	OR 23.71 [4.98-112.8], *p < 0.001*	OR 28.15 [5.75-137.9], *p < 0.001*

to osteoporotic fractures concerning vertebral fractures (9, 10) pelvis, (7) hip fracture (11) and proximal humerus (12).

However, a large number of the se studies showed the direct impact of co-morbidities on post osteoporotic fracture mortality compared with the control group (11-14). They gave evidence of the role of cardiovascular diseases, pulmonary diseases, diabetes, neoplasia (11, 13-17), cognitive decline (16-18), sarcopenia and previous osteoporotic fractures (12). According to Morin et al. (2), 25% of patients who had a hip fracture were were institutionalized and 12% needed care at home. Institutionalization, which implies degradation of the overall state, was associated to the increase in mortality during the year following a hip fracture. This factor was more important than some co-morbidities.

The results quoted were related to studies comparing cases of osteoporotic fractures with control patients who had no osteoporotic fracture. Instead, in our study, control patients had osteoporotic fractures, and were matched on age, sex and type of fracture with cases. The layout of this study allowed a more pertinent view of co-morbidities associated with an increase in mortality because cases and control patients were matched on factors which could cause confusion. The main factor being an osteoporotic fracture.

Others studies were carried out according the same design as ours. Thus, Steven et al. (19) valuated risk factors of mortality in hospital after a hip fracture on 410 men and 1094 women and concluded that some co-morbidities on admission (heart failure or hepatopathy) were associated with an increase in mortality with a relative risk >3. Kannegaard et al. (3) found predictive factors of mortality on 1 year after hip fracture, for women and men: age, amount of drugs taken and co-morbidities including the Charlson index (COPD, heart failure, dementia, diabetes complications, hemiplegia, neoplasia, hepatopathy, renal failure, many drugs) (20). However, cerebro-vascular accidents or myocardial infarction did not influence mortality. Study of veterans with hip fractures (21) showed mortality after one year was multiplied by 4 if there was metastatic neoplasia and by 2 if there were heart failure, renal failure, hepatopathy, lymphoma or gauntness. Antecedents of metastatic cancer or renal failure were observed in other studies as a principal risk factor for mortality after fracture (22, 23).

In a study of death certificates in France from 1968 to 2004, Ziadé et al. (24) reported that cardiovascular diseases were the most frequent co-morbidities to be associated with death after an osteoporotic fracture. Other more frequent co-morbidities were diabetes, pneumonia, bedsores until 1972 and more recently, pneumonia, renal failure and dementia are the most frequent.

So, the main risk factors of mortality which recur the most often are cardiovascular disease, dementia, pulmonary disease and cancer. Our results are similar to those reported in the literature (25). The male sex is a frequent predictive factor of mortality and the risk of death is twice more than for women during the months following a hip fracture (3, 4, 19, 26-28) an increase in mortality 3 years after a pelvis fracture was also found (29). In our study, patients were matched according to their sex so this does not allow us to bring out such a difference even if it is present.

Several Authors (24, 30) reported a modification in the cause of death after an osteoporotic fracture; co-morbidities present before the fracture seem to take a larger part whereas secondary complications linked to the fracture decrease. This could be explained on the one hand by improvements in treatment of fractures, especially hip fracture surgery, which has decreased the bed-rest time and complications (31). Secondly, the aging of the population induces an increase of co-morbidities, of which cardiovascular diseases and neoplasia are in first position. Moreover, there are physio-pathological relationships between osteoporosis and atherosclerosis (32, 33) which could explain the cardiovascular disease mortality.

Our study has several limitations. It is a monocentric study concerning a small sample with therefore a low statistical power as shown by the wide confidence interval of the relative adjusted risks. The retrospective nature of the medical records didn't permit to characterize precisely the comorbidities and the complications after fracture. Particularly, concerning the main results, the neoplasia diagnosis date wasn't always known nor if it had been cured or not. This information is very important because a cured neoplasia has not the same signification than a progressive neoplasia. Acute respiratory failure after fracture probably included several different types of pulmonary diseases but we had no access to the primary diagnosis (pulmonary infection, pulmonary embolism, COPD…). We did exclude heart failure.

To conclude, in the present study, the principal predictive factors of mortality during the first year after osteoporotic fracture attested a state of bad health prior to the fracture. Direct secondary complications after an osteoporotic fracture seemed to affect mortality less, whereas comorbidities played a dominant role. However, increase in mortality after osteoporotic fractures is a real public health problem, and an osteoporotic fracture is more than ever a major sign of health deterioration and may cause a fragile balance to sway. Nowadays clinicians can supply efficient medication for osteoporosis, which have a positive impact in terms of mortality (34,35) and the treatment of osteoporotic fractures remains a priority.

Conflict of interest

All Authors declare no conflict of interest.

Ethical approval information

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