Bone 117 (2018) 123–129

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Influence of demographic and clinical characteristics of elderly patients with a hip fracture on mortality: A retrospective, total cohort study in North-East Spain

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ARTICLE INFO

Keywords:
Hip fractures
Aging
Comprehensive health care
Public health

ABSTRACT

Importance: The increased mortality after hip fracture (HF) is caused by multiple factors, and large samples are needed to assess the weight of each factor. To date, few studies have investigated these factors through a total cohort approach, and the complexity of underlying medical conditions has not been considered.
Objective: To investigate the influence of demographic and clinical characteristics on increased mortality risk in elderly patients with hip fracture (HF).
Design: Retrospective, total cohort study collecting 4-year data.
Setting: All hospitals and primary care units owned by, or associated with, Catalonia's local health department (CatSalut) (north-east Spain).
Participants: All patients aged ≥65 years, admitted to Catalan hospitals from CatSalut because of a HF between 1st January 2012 and 31st December 2015.
Exposure: Hip fracture.
Main outcome measures: The main outcome was survival. Measures regarding demographic and clinical characteristics at the moment of hospital admission included age, sex, osteoporosis treatment, previous fractures, type of intervention, nutritional status, and comorbidities.

Patients were stratified using the Adjusted Morbidity Groups (GMA) risk assessment tool.
Results: Of the 30,552 patients included in the study sample, 10,439 (34%) died during follow-up, 6821 (22%) within the first year after hospital admission. Mean (SD) age was 84 (7) years; 75% were female.

Baseline factors with greater influence on survival were age (HRs 1.44 [95% CI 1.22–1.70], 2.38 [2.03–2.79], and 4.38 [3.73–5.15] for age groups 70–79, 80–89, and > 89, respectively), underweight (HR 1.65 [1.36–2.01]), lack of surgical intervention (HR 2.64 [2.47–2.83]), and very high risk stratum of GMA risk (HR 1.58 [1.45–1.73]). Vitamin D/calcium supplementation and osteoporosis treatment showed a significant but moderate influence on mortality (HRs 0.84 (0.79–0.88) and 0.92 [0.85–0.99], respectively).
Conclusions and relevance: In elderly patients with HF, age and health status factors at hospital admission have the greatest impact on mortality risk after hospital admission. Our findings encourage a comprehensive intervention aimed at improving underlying medical conditions of HF patients.

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https://doi.org/10.1016/j.bone.2018.09.002
Received 2 April 2018; Received in revised form 30 August 2018; Accepted 5 September 2018
Available online 14 September 2018

1. Introduction

Proximal femoral fracture, or hip fracture (HF), is a major worldwide public health issue, with high incidence in the elderly [1–3]. Although age has been considered a major independent risk factor for HF, world age-standardized rates show a > 10-fold range between countries, suggesting that the probability of experiencing a HF depends on environmental rather than genetic factors [2]. Like other First World countries, Spain has experienced a progressive increase in HF incidence over the last decades, with over 35,000 cases in 2012, and its regions (autonomous communities) have shown remarkable differences in HF incidence that cannot be explained by age, sex, and rurality [4,5].

In addition to causing functional disability, HF is associated with a greater mortality risk, particularly in patients over 60 years old [6–8]. Several observational trials have shown that the risk of death for patients with HF is 3–8 times greater than for age-matched subjects in the general population. In Spain, in-hospital mortality rate of HF patients aged 65 or more—accounting for nearly 90% of all HF—ranges from 2% to 8%, depending on specific regions [9]; similar variability has been found when comparing mortality rates between countries [10,11].

Differences in the mortality risk reported in various trials have prompted the investigation of factors influencing mortality after HF. Besides age, identified as the primary predictor of mortality 3–12 months after HF [12], the patient's comorbidity burden has been postulated as a key factor determining mortality risk following HF [13–17]. Individual conditions such as low body mass index (BMI), dementia, cardiovascular disease, diabetes, and liver disease appeared to have a remarkable influence on mortality risk during the years following the HF [12–14]. In addition to patient's clinical, nutritional and functional statuses before the fracture, variables related to HF management such as type of surgical intervention and osteoporosis treatment may also influence the patient's survival odds [18,19].

Taken together, these data suggest that the mortality risk after HF is caused by multiple factors. However, addressing the influence of various clinical and demographic factors on mortality risk requires large study samples to gain enough statistical power to clearly assess the weight of each individual factor. In countries with public healthcare systems covering the whole population, large administrative datasets provide clinical data from a massive number of patients, allowing for a whole-population approach to healthcare issues. Using this approach—commonly regarded as total cohort studies—some authors have provided relevant information regarding the impact of measures taken after hospital admission on mortality of HF patients [10,11,20]. In an attempt to provide new insights regarding the influence of patients characteristics on mortality after suffering HF, we have analyzed a database of a public healthcare entity that provides healthcare services to virtually the entire population of Catalonia (north-east of Spain) to describe the HF incidence in the elderly, and to dissect the components of a multivariate model of HF mortality risk.

2. Methods

2.1. Study design and population

In this observational, retrospective study we have gathered sociodemographic and clinical data from the local health department (CatSalut) dataset of Catalonia (north-east Spain). CatSalut provides free healthcare services to the entire population of Catalonia through a network of 62 public hospitals and 369 primary care units. Since 2011, the CatSalut surveillance system collects detailed information on healthcare usage for the entire population of Catalonia. As part of this surveillance system, the Minimum Basic Dataset for Healthcare Unites registry compiles data on hospitalization, primary care, skilled nursing facilities and mental health network, information on pharmacy prescriptions and expenditure, and a registry on billing records, which includes outpatient visits to specialists, emergency department visits, non-urgent medical transportation, ambulatory rehabilitation, home oxygen therapy, and dialysis [21]. The registry has an automated data validation system that checks data consistency and identifies potential errors. Furthermore, as this information is used for provider payment purposes, external audits are regularly performed to ensure the quality and reliability of the data.

In our primary analysis, searches were restricted to women and men aged 65 years or more, who were admitted to any public hospital because of a HF between 1st January 2012 and 31st December 2015. For reference, we also gathered clinical data from the total population of Catalonia, which in 2012 amounted to 7,553,650 inhabitants. Data regarding HF inpatient care at private health centers could not be collected because said centers use different patient identification codes. Nevertheless, a small percentage of HF patients are admitted to private hospitals; for reference, of 1,016,190 all-cause hospitalizations that occurred in Catalonia in 2015, 808,908 (80%) were in public hospitals, whereas the rest occurred in private hospitals. In the case of HF, 10310 hospitalizations were registered in Catalonia in 2015: 9628 in public hospitals and only 682 (7%) in private hospitals.

Data retrieved from the CatSalut surveillance system was unlinked to personal information, which would potentially allow patient identification. The study protocol was approved by the Independent Ethics Committee of the Jordi Gol Primary Care Research Institute (Spain) (ref. P17/127). Based on sample size and absence of personal information in the dataset used for analysis, the Ethics Committee determined that it was not necessary to obtain a written informed consent from each patient.

2.2. Variables and endpoints

Demographic characteristics of study patients included sex and age. The patient's comorbidity burden at the time of experiencing the HF was assessed using the adjusted morbidity groups (GMA) health-risk assessment tool, which considers the type of disease (i.e. acute or chronic), number of systems affected, and complexity of each disease, which is coded by the International Classification of Diseases (ICD-9-CM) [22,23]. Patients were classified into five GMA strata based on their morbidity-associated risk. The baseline risk (healthy stratum) was assigned to the GMA score range encompassing 50% of the total population. Subsequent cutoffs at 80%, 95%, and 99% were used to define the population at low, moderate, and high and very high risk, respectively. In addition to the morbidity-associated risk, the occurrence of specific conditions considered relevant to describe the health status of our population was reported. The HF causing hospital admission was classified as either femoral neck fracture or intertrochanteric fracture. History of previous fractures included fractures (ICD-9 categories) associated with increased risk of a second fracture: [24,25] vertebral (805 or 806), rib (807), pelvis (808), clavicle (810), scapula (811), humerus (812), radius/ulna (813), carpal (814 to 817), femur/hip (820 or 821). Surgical variables included the need for blood transfusion and type of intervention: no intervention, internal or external fixation, and prosthetic replacement. Information on active treatments at the time of hospital admission was gathered for all drugs indicated for osteoporosis treatment and prevention, including supplementation with calcium and vitamin D. To be considered an active treatment, the patient had to account for at least 6 scripts dispensed in the pharmacy for a given drug within 12 months prior to hospital admission. Polypharmacy was considered when the patient was given 8 different medicines according to the anatomical therapeutic chemical classification system (fourth level) [26]. Based on their nutritional status, patients were classified into 4 categories: underweight, normal weight, overweight, and obesity. Institutionalization of the patient in a nursery home at the time of experiencing the HF was recorded. The primary endpoint was survival time after HF.

2.3. Statistical analysis

Continuous variables are expressed as the mean (standard deviation) and/or median (interquartile range [IR], defined as percentiles 25 and 75), and categorical variables as the number and percentage. Comparisons between categorical variables were carried out using the chi-square test. The primary outcome variable was time to death. The survival analysis was carried out using the actuarial method. Subsequently, using the variables with a significant difference between categories (Gehan test), a multivariate model was generated by calculating the Cox proportional hazards with robust standard errors using a stepwise backward elimination method, by means of the Likelihood ratio test, solely for operated patients. The Schoenfeld's global test was used to assess the proportionality of hazard functions over time. Given the high number of cases included in the analysis, and in order to avoid minimal - although significant - violations of the proportionality of hazard functions, variables were also inspected graphically using the scaled Schoenfeld residuals with $p < 0.05$, and the goodness of fit was compared using the Likelihood ratio test. The threshold for statistical significance was set at a 2-sided α-value of 0.05, and all analyses were performed in R (version 3.4.3) and SPSS (IBM SPSS Statistics for Windows, Version 18.0. Armonk, NY: IBM Corp.).

3. Results

3.1. Characteristics of the study population

Between 2012 and 2015, 30,552 patients aged 64 years or more were admitted to public health centers (either owned by, or associated with CatSalut) with a HF diagnosis. Overall, 10,439 (34.2%) of HF patients included in our analysis died during the entire study period; 6821 (22.3%) within the first year after hospital admission.

Table 1 shows the main demographic and clinical characteristics of the study population, as well as the survival associated with each subgroup. Mean (SD) age of the study population was 84 (7) years (median 85, IR 80–89): 83 (7) years for men and 85 (7) years for women (median 84 [IR 79–89] and 85 [IR 81–90] years for men and women, respectively). History of previous fractures, observed in 9.4% of patients, and type of fracture did not yield significant differences regarding survival. On the other hand, the presence of all medical conditions investigated resulted in significant survival differences. Fig. 1 summarizes the distribution of patients across the five GMA strata for the total population and HF patients. Subjects in the high- and very-high risk strata accounted for 5% of the overall population and 45% of HF patients.

3.2. Mortality after hip fracture

Survival rate in the years following a HF, assessed only in patients who had surgery (n = 28,889; 95%), declined more rapidly as age and GMA risk increased (Fig. 2). Table 2 summarizes the result of the Cox proportional hazards model, which was built based on all variables showing significant differences in the survival analysis. Estimated HRs were statistically significant for all conditions except for the variables hipocalcemia and supplementation with calcium/vitamin D and the categories obesity and moderate risk strata of the variables nutritional status and GMA grouper, respectively. Baseline factors showing greatest influence on survival (i.e. variables associated with an HR increase over 50%) were age, underweight, and upper stratum of GMA morbidity risk. Osteoporosis treatment showed a significant, but moderate protective effect.

The assessment of the proportionality of hazard functions revealed small deviations (although significant at $p = 0.003$) of this assumption, mostly due to the large sample size. Table S1 (Supplementary file 1) provides the model including time interactions of the affected variables.

4. Discussion

In this retrospective analysis of a public health dataset, which included most cases of HF in a population of over 7.5 million people, we found that age and health status (characterized by the patient's nutritional status and comorbidity burden) at the moment of experiencing the HF were the two factors with greater influence on mortality for a few years after hospital admission. Other baseline factors such as type of fracture, type of intervention, or osteoporotic treatment showed either lesser or no significant impact on mortality risk.

The strong influence of age on mortality after HF has been extensively reported, with consistent results indicating an age-dependent increase in mortality risk in patients older than 60 years [6,27,28]. Similarly, previous studies observed a cross-contribution of sex, with greater mortality in men despite a higher presence of older women [6,14,27,28]. Besides age and sex, there is an overall agreement that both nutritional status and comorbidity burden somehow influence the mortality risk after HF [13–17,29,30]. However, conclusions on the extent of this influence are not clear, particularly regarding the comorbidity burden. Traditionally, the Charlson Comorbidity Index (CCI) has been the preferred indicator for stratifying HF patients according to their comorbidity burden [13–17]. Although most studies report significant relationships between CCI and mortality risk after HF, in some cases the significance appears only in patients with CCI score > 3 or 4, which often implies the presence of severe diseases with a strong impact on mortality in the overall population [13,17]. To prevent this potential bias and overcome the lack of stratification of the disease severity in the CCI scale, some authors have implemented algorithms, which combine the CCI score with age and lifestyle variables [13,15], while others have used a rough number of pre-selected clinically significant comorbidities as a predictor of mortality after HF [14]. Alternatively, we graded the comorbidity burden of our patients using the GMA risk assessment tool. The GMA is a population-based health risk assessment tool developed to design healthcare strategies and manage chronic patients [22]. Unlike CCI, which rates each patient based on the presence or absence of preselected diseases, the GMA tool considers all medical conditions and takes into account the complexity of each disease and the number of systems affected. Our multivariate analysis revealed a significant and progressive increase in the mortality risk across the upper GMA groups, with 30% and 60% greater HRs in the high-risk and very high-risk strata, respectively. Also, as patients dealing with multiple comorbidities are expected to have more complex treatments, polypharmacy was included as a potential influencing factor on mortality; as expected, this was the scenario for most patients in our sample (68%). However, polypharmacy showed little influence on mortality (HR 1.07), suggesting that rather than the rough number of treated medical conditions, it is the severity and complexity of these conditions that determine the influence of the comorbidity burden on survival in HF patients. It is noteworthy that the influence of health status on mortality risk is consistent with the fact that receiving no intervention after HF was associated with a higher HR for mortality. Although there is no record of a specific reason for not receiving intervention, our healthcare system guarantees emergency intervention of HF, and the "no intervention scenario" is most common for patients with very poor health status and little chance to survive surgical intervention.

In the past decade, various authors have investigated the clinical and demographic factors influencing mortality after HF. However, whereas some studies have been performed on population-based cohorts [13,31,32], other are based on modest cohorts with limited statistical power for analyses exploring multiple influencing factors [33–36]. Our record included clinical and demographic data from 30,552 patients experiencing a HF in our region. Furthermore, the universal nature of the public health system coverage reduced the likelihood of missing data from patients treated outside the public health system, leading to a study sample that gathered almost all HF

Table 1
Baseline characteristics and survival of the study population.

	n	%	No. of deaths	Survival			p[a]
				6 months	1 year	2 years	
Sex							
Male	7733	25.3	3464	75.0	66.3	53.4	< 0.001
Female	22,819	74.7	6975	85.1	79.2	69.5	
Age							
65–69	1075	3.5	159	93.5	90.5	85.5	< 0.001
70–79	5805	19.0	1251	90.1	85.7	78.7	
80–89	16,407	53.7	5434	83.7	77.3	66.7	
> 89	7265	23.8	3595	72.3	63.1	48.6	
Morbidity-associated risk (GMA groups)							
Very high risk	4244	13.9	2108	72.0	62.4	48.7	< 0.001
High risk	9475	31.0	3622	80.1	72.4	60.1	
Moderate risk	12,252	40.1	3554	86.4	80.6	70.9	
Low risk	3802	12.4	972	87.1	83.1	76.4	
Baseline risk	779	2.5	183	88.5	84.3	78.7	
Institutionalized[b]							
No	23,761	77.8	7397	84.2	78.1	68.6	< 0.001
Yes	6791	22.2	3042	77.0	68.5	54.5	
Previous fracture[c]							
No	27,689	90.6	9415	88.8	82.1	70.9	0.258
Yes	2863	9.4	1027	88.8	81.9	68.7	
Nutritional status							
Underweight	193	0.6	103	68.7	54.7	42.4	< 0.001
Normal weight	25,283	82.8	8853	82.1	75.5	64.9	
Overweight	4822	15.8	1381	85.6	79.3	69.3	
Obesity	254	0.8	93	79.2	72.1	63.2	
Specific clinical conditions							
Parkinson							
No	28,616	93.7	9672	82.7	76.1	65.7	0.001
Yes	1936	6.3	767	80.7	73.4	61.6	
Urgency							
No	18,706	61.2	5562	84.5	78.9	70.1	< 0.001
Yes	11,846	38.8	4877	79.4	71.4	58.1	
Anemia							
No	20,664	67.6	6463	84.5	78.6	68.9	< 0.001
Yes	9888	32.4	3968	78.4	70.4	57.8	
Dementia							
No	24,180	79.1	7557	83.8	77.9	68.4	< 0.001
Yes	6372	20.9	2882	78.0	68.7	54.4	
Cirrhosis							
No	30,032	98.3	10,193	82.7	76.1	65.6	< 0.001
Yes	520	1.7	246	73.9	65.5	51.9	
Ischemic heart disease							
No	25,590	83.8	8259	83.8	77.6	67.6	< 0.001
Yes	4962	16.2	2180	76.3	67.3	54.1	
Neoplasia							
No	24,060	78.8	7779	83.7	77.5	67.5	< 0.001
Yes	6492	21.2	2660	78.3	70.1	57.3	
Pressure ulcer							
No	29,324	96.0	9796	82.9	76.5	66.1	< 0.001
Yes	1228	4.0	643	74.3	62.9	48.8	
Hypocalcemia							
No	30,484	99.8	10,407	82.6	76.0	65.5	0.009
Yes	68	0.2	36	75.2	70.0	35.6	
Diabetes mellitus							
No	21,314	69.8	7029	83.1	76.9	66.9	< 0.001
Yes	9238	30.2	3410	81.3	73.7	61.9	
COPD							
No	25,456	83.3	8155	84.1	77.7	67.6	< 0.001
Yes	5096	16.7	2284	74.3	66.3	52.1	
Chronic kidney disease							
No	23,728	77.7	7569	84.4	78.3	68.4	< 0.001
Yes	6824	22.3	2870	76.0	67.6	54.6	
Type of intervention							
No intervention	1650	5.4	1003	51.2	44.3	38.2	< 0.001
Fixation	18,318	60.0	6020	84.2	77.5	66.9	
Prosthetic replacement	10,546	34.5	3401	84.7	78.2	67.0	
Needed transfusion							
No	22,939	75.1	7513	83.3	76.9	67.0	< 0.001
Yes	7612	24.9	2926	80.5	73.1	60.7	
Treatment							
Calcium and/or vitamin D supplementation							

(*continued on next page*)

Table 1 (*continued*)

	n	%	No. of deaths	Survival			p[a]
				6 months	1 year	2 years	
No	28,780	94.2	9918	81.1	74.7	64.1	< 0.001
Yes	1772	5.8	521	85.9	80.3	69.7	
Osteoporosis treatment							
No	29,106	95.3	10,069	81.0	74.5	63.8	< 0.001
Yes	1446	4.7	370	88.2	84.4	76.1	
Polypharmacy (> 8 ATC)							
No	9733	31.9	2689	85.6	80.1	71.2	< 0.001
Yes	20,818	68.1	7750	81.1	73.8	62.4	

[a] Gehan test for differences in survival.
[b] Patients institutionalized in a nursing home at the time of experiencing the HF.
[c] Included the following ICD-9 categories: vertebral (805 or 806), rib (807), pelvis (808), clavicle (810), scapula (811), humerus (812), radius/ulna (813), carpal (814 to 817), femur/hip (820 or 821).

cases in our region. An important advantage of the total cohort approach was the possibility of using a population-based health risk assessment tool as an alternative to other comorbidity measures, such as CCI or rough number of comorbidities. CCI was developed as an estimator of 1-year death risk in the overall population. Besides not allowing for disease severity stratification, the CCI score increases rapidly in patients with severe conditions such as metastatic cancers, which might overshadow the impact of multiple comorbid conditions —including those not listed in the CCI. Due to GMA's comprehensive nature, this stratification tool provides important advantages over CCI and other morbidity groupers, particularly in terms of prediction capacity for hospital and primary care admissions, and healthcare expenses [22,23].

Despite the multiple advantages of the total cohort population approach, the use of huge, administrative datasets has some drawbacks. Firstly, unlike clinical trials, in which committed investigators are responsible for data gathering, the reliability of our data depends on the accuracy of hundreds of physicians acting as data collectors in their routine practice. Secondly, as a retrospective study, our analyses were bounded by predefined variables included in the CatSalut surveillance system, thus preventing the investigation of other variables that could contribute to understanding the mechanisms underlying the increased mortality in HF patients. These variables include outcome measures, such as cause of death and functional recovery [16,17], and healthcare-related information such as time between fracture and intervention—this latter being subject of debate [6]. Finally, although most HF patients are treated in centers of the public health-care network, data from patients treated in private centers (7% in 2015) were missing in our analysis. Although the socio-economic profile of these patients may differ from that of the overall population, the exclusion of these cases is unlikely to severely compromise the generalizability of our results.

5. Conclusion

In summary, our analysis of 30,552 HF patients—all cases of HF treated within the framework of public health care in a population of over 7.5 million people—confirmed age as the factor with the greatest influence on survival during the years following a HF. Furthermore, our results suggest that, rather than pharmacological treatment, the general health status and the complexity of underlying diseases at the moment of experiencing the HF have an important influence on mid-term mortality in HF patients. Our findings prompted the local health department to implement integrated care pathways for secondary prevention of osteoporotic fractures, which address the patient's comorbidity burden and its complexity. Although the impact of this program on reducing mid-term mortality after HF is still under assessment, our findings encourage considering comprehensive interventions aimed at promptly detect and further improve all underlying medical conditions of HF patients, rather than targeting only issues associated with bone fragility. To better understand the mechanisms behind the increased mortality risk of HF patients, information regarding cause and functional assessment should be included in future analyses of total cohort datasets.

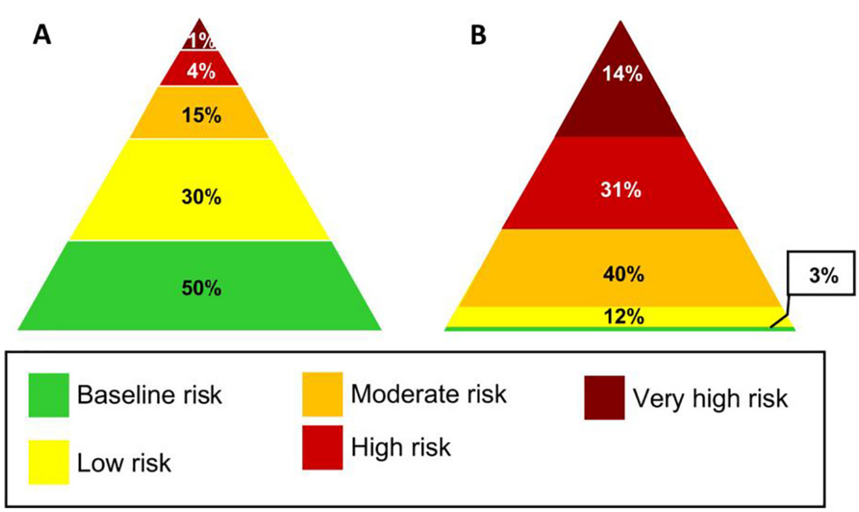

Fig. 1. Distribution of the population across the five morbidity-adjusted groups (GMA). A: the entire population of Catalonia (n = 7,503,772). B: Study population (i.e. HF patients aged ≥65 years admitted to public health centers) (n = 30,552).

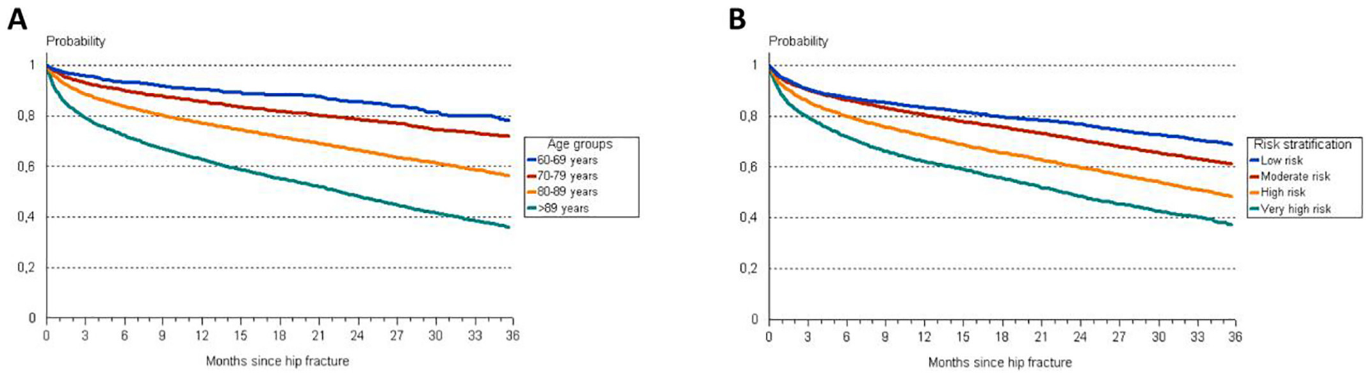

Fig. 2. Survival curves (actuarial plot) of patients allocated in each age group (A) and GMA risk group (B).

Table 2
Influence of the demographic and clinical characteristics at hospital admission on all-type mortality. Multivariate analysis (Cox Regression).

	HR (95% CI)	*p*
Sex		
Male		
Female	0.62 (0.60–0.65)	< 0.001
Age		
65–69		
70–79	1.47 (1.20–1.79)	< 0.001
80–89	2.37 (1.96–2.87)	< 0.001
> 89	4.42 (3.65–5.36)	< 0.001
Morbidity-associated risk (GMA groups)		
Very high risk	1.53 (1.39–1.68)	< 0.001
High risk	1.23 (1.14–1.33)	< 0.001
Moderate risk	1.02 (0.94–1.09)	0.473
Low risk + healthy		
Previous internalization	1.31 (1.25–1.37)	< 0.001
Nutritional status		
Underweight	1.61 (1.30–2.00)	< 0.001
Normal weight		
Overweight	0.85 (0.80–0.91)	< 0.001
Obesity	1.03 (0.82–1.29)	0.609
Specific clinical conditions		
Parkinson	1.10 (1.02–1.19)	0.003
Urgency	1.12 (1.08–1.17)	< 0.001
Anemia	1.12 (1.07–1.17)	< 0.001
Dementia	1.41 (1.34–1.48)	< 0.001
Cirrhosis	1.58 (1.38–1.82)	< 0.001
Ischemic heart disease	1.15 (1.09–1.21)	< 0.001
Neoplasia	1.16 (1.11–1.22)	< 0.001
Pressure ulcer	1.27 (1.17–1.38)	< 0.001
Diabetes mellitus	1.12 (1.07–1.17)	< 0.001
COPD	1.27 (1.20–1.34)	< 0.001
Chronic kidney disease	1.18 (1.12–1.23)	< 0.001
Needed transfusion	1.16 (1.11–1.21)	< 0.001
Treatment		
Osteoporosis treatment	0.77 (0.69–0.86)	< 0.001
Polypharmacy (> 8 ATC)	1.04 (0.99–1.09)	0.001

COPD: Chronic Obstructive Pulmonary Disease.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bone.2018.09.002.

Funding sources

Amgen Inc. provided financial support to hire medical writing services.

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