Effect of comorbidities on the association between age and hospital mortality after fall-related hip fracture in elderly patients.

A Padrón-Monedero, T López-Cuadrado, I Galán, E V Martínez-Sánchez, P Martin, R Fernández-Cuenca.

Osteoporos Int. 2017 May;28(5):1559-1568.

https://doi.org/10.1007/s00198-017-3926-2

Padrón-Monedero A, López-Cuadrado T, Galán I, Martínez-Sánchez EV, Martin P, Fernández-Cuenca R. Effect of comorbidities on the association between age and hospital mortality after fall-related hip fracture in elderly patients. *Osteoporosis International*. 2017; 28(5): 1559-1568. Impact Factor: 3.857 (Q2) (doi: https://doi.org/10.1007/s00198-017-3926-2)

Effect of comorbidities on the association between age and hospital mortality after fall-related hip fracture in elderly patients.

Alicia Padrón-Monedero [a], Teresa López-Cuadrado [a], Iñaki Galán [a,b], Elena V. Martínez-Sánchez [a,c], Pilar Martin [d], Rafael Fernández-Cuenca [a,c].

[a] National Centre for Epidemiology. Instituto de Salud Carlos III. Madrid. C/ Monforte de Lemos 5, Madrid (Spain).

[b] Department of Preventive Medicine and Public Health. School of Medicine. Universidad Autónoma de Madrid/ IdiPAZ. C/Arzobispo Morcillo 2, Madrid (Spain).

[c] CIBER of Epidemiology and Public Health (CIBERESP). C/ Melchor Fernandez Almagro 3-5, Madrid (Spain).

[d] Adelphi University, College of Nursing and PH. Garden City, NY 11530, USA.

Short title: Comorbidities and mortality after hip fracture in the elderly.

Word count: 3540

Address for correspondence:
Alicia Padrón-Monedero, MD, OMS, PhD.
National Centre for Epidemiology,
Instituto de Salud Carlos III,
C/ Monforte de Lemos 5,
28029 Madrid, Spain
Phone: 918222622
FAX: 913877815
E-mail: a.padronm@isciii.es

ABSTRACT

Purpose To analyze the impact of Elixhauser comorbidities on the relation between age and mortality after hip fracture in elderly patients.

Methods Cross-sectional study of the population ≥65 years old hospitalized in Spain in 2013 with a diagnosis of fall-related hip fracture in the Basic Minimum Set Data (BMSD). The impact of Elixhauser comorbidities on the association between mortality and age groups (65-74, 75-84, ≥85) was analyzed by logistic regression models with progressive adjustment for demographic variables and comorbidities introduced individually.

Results We identified 31,884 patients, 5.5% of which died during hospitalization. Compared with those 65-74 years old, the multivariate odds ratio (OR) of mortality for those 75-84 and ≥85 years old decreased from 2.23 (95% CI: 1.71-2.90) and 4.57 (95% CI: 3.54-5.90) to 2.11 (95% CI: 1.61-2.77) and 4.10 (95% CI: 3.14-5.35) respectively after adjustment for comorbidities. The OR of mortality for men was 1.77 (95% CI: 1.58-1.98) compared to women. The comorbidities with higher OR for mortality were: congestive heart failure (OR: 3.88; 95% CI: 3.42-4.41), metastasis (OR: 3.44; 95% CI: 2.27-5.20), fluid and electrolyte disorders (OR: 2.95; 95% CI: 2.47-3.52), coagulation deficiencies (OR: 2.87; 95% CI: 2.08-3.96) and liver disease (OR: 2.40; 95% CI: 1.82-3.17).

Conclusions The association between age and mortality after hip fracture remains after adjusting for numerous comorbidities. However some potentially controllable disorders are associated with an increased risk for mortality, thus improving their management could benefit survival.

Abbreviations. BMDS: Basic Minimum Data Set. CI: Confidence Interval.

Keywords. Elderly, falls, mortality, comorbidities.

MINIABSTRACT

The relation between age and mortality after hip fracture was analyzed in elderly patients. 5.5% of 31,884 patients died. Compared to those 65-74 years old the multivariate odds ratio (OR) for mortality for those 75-84 and ≥85 were 2.11 (95% CI: 1.61-2.77) and 4.10 (95% CI: 3.14-5.35)

INTRODUCTION

Hip fracture in elderly population is a major cause of mortality [1-3] and a burden to the healthcare system being the most frequent reason for hospital admission in trauma services. In Spain, it is estimated that the average hospital cost per patient is 8.365 € [4].

Mortality after a fall-related hip fracture in older people increases with age [5-10], and it is considered one of its main predictors [6, 8, 9, 11], so the progressive aging of the population means that mortality following a hip fracture is likely to increase in the future. However, since age is not a modifiable variable, it has been suggested that assessing the impact of other variables correlated with age and mortality, as comorbidities and fragility [5-7], that might be controlled, would be more useful.

Some authors have found associations between the number of comorbidities and a higher mortality risk after a fall-related hip fracture in the elderly [5, 6, 10] although the association between mortality and increasing age remains after adjustment for the number of comorbid conditions [10].

According to Elixhauser *et al.* [12], comorbidities may have different effects on different diseases, so it is advisable to consider them individually and not simplify them as an index. Therefore, the analysis of the impact of individual comorbidities on mortality could be particularly important. A limited number of studies have examined the association between mortality after a fall-related hip fracture in elderly population and age, after adjusting for a limited number of comorbidities entered individually into the models [6-9, 11]. Besides none of them included some potentially controllable comorbidities considered of interest in the evolution of in-hospital patients such as coagulation deficiencies and fluid and electrolyte disorders [12]. It has also been suggested that one of the causes of in-hospital mortality that could most benefit from an explanatory model adjusting for Elixhauser comorbidities could be hip fracture [13].

Therefore the aim of this study was to assess whether the association between age and mortality after fall-related hip fractures in an elderly population remains after adjusting for the individual Elixhauser comorbidities. It also tests the hypothesis that some potentially controllable comorbidities could be associated with an increased mortality.

METHODS

Study population

Data were collected from hospital discharges from the Basic Minimum Set of Data of Hospitalization (BMSD-H) from January 2013 to December 2013, which includes all hospital discharges from both public and private hospitals within the consortium included in the Spanish National Health System.

The inclusion criteria were individuals aged 65 years or older, who had an emergency admission with a primary diagnosis of hip fracture (femoral neck or intertrochanteric), corresponding to codes 820.xx of the International Classification of Diseases 9th Clinical Modification (ICD-9CM) together with a secondary diagnoses of an accidental fall corresponding to codes E880-E888. The patients from our original database, that were not included in the analysis because they had a primary diagnosis of "pathological hip fracture" (733.14 of ICD-9CM), which did not meet our inclusion criteria, were 677. Thus, we collected data from 34,286 patients.

We excluded for the analyses data for patients in which type of discharge, our dependent variable, was not specified (n = 545). We also excluded the records of patients transferred to another hospital (n = 1533). The records of 3 patients in which sex was not collected were excluded leaving 32,205 patients. Finally, when the records of a patient showed readmissions in the same Hospital for the same cause in the same year (n = 321) we selected only the last episode and excluded the rest. Therefore, the total sample for analysis included 31,884 patients.

To ensure confidentiality of the patients, data were anonymized prior to analyses.

Study variables

The dependent variable, in-hospital mortality, was defined as those in which type of discharge was coded as death in the BMSD-H.

The independent variables considered for the analyses were: age at admission (65-74, 75-84 and ≥85), sex, and the individual Elixhauser comorbidities classified dichotomously as included or not in any of the secondary diagnoses, according to the recommended codes for ICD-9CM of the Agency for Healthcare Research and Quality (version 3.5) [13] (Table 1). According to the BMSD-H data collection protocol, secondary diagnoses should include those, that not being the main diagnosis, coexist with it at the time of admission or are developed throughout in-hospital stay, and could influence the duration or the treatment administered [14].

Statistical analysis

Chi-square tests were used to compare the mortality distribution by demographic and clinical variables.

Logistic regression models with progressive adjustment were run to analyze the impact of other variables on the association between in-hospital mortality and age groups (65-74, 75-84, ≥85). Model (A): crude model; model (B): multivariate model adjusting for sex; model (C): multivariate model with additional adjustment for Elixhauser comorbidities (congestive heart failure, arrhythmia, valvular disease, pulmonary circulation disorders, peripheral vascular disease, chronic pulmonary disease, renal failure, liver disease, lymphoma, metastatic cancer, solid tumor without metastases, coagulation deficiency, fluid and electrolyte disorders and depression).

The Elixhauser comorbidities retained in the final model were those that had a significant association with the dependent variable.

A sensitivity analysis, replicating the model with the maximum adjustment (model C), was run with the population of 32,205 patients (including patients with readmissions for the same cause).

To further study the association between in-hospital mortality and age groups (65-74, 75-84, ≥85) we replicated a fully adjusted model that included sex and Elixhauser comorbidities introduced only as an aggregate dichotomous variable (<3 or ≥3) (model D). We also analyzed possible interactions between: sex and age groups, 3 or more comorbidities and sex and 3 or more comorbidities and age groups.
Statistical significance was set at $p < 0.05$. The data were analyzed using STATA software release 14 (StataCorp LP, College Station, Texas 77845 USA).

RESULTS

The demographic and clinical characteristics of patients hospitalized for fall-related hip fracture, their distribution according to mortality and the comparison of proportions by Chi-squared test are shown in Table 2. Most of the 31,884 patients selected for the analyses were women (75.9%) and aged 75 years or older (40.7% 75 to 84 and 49.0% 85 and over). The mean age was 83.8 years (standard deviation 7.03) with a range of 65 to 107 years. Overall 1,766 (5.5%) died during hospitalization. The most frequent comorbidities were cardiac arrhythmias that were present in 19.5% of patients, chronic pulmonary disease in 10.2%, renal failure in 9.6% and depression in 8.9%.

The association between age and mortality increased with increasing the age group and was significant in all models (Table 3). In the crude model (model A) OR of mortality for those 75-84 and ≥85 years old compared to those 65-74 years were 2.08 (95% CI: 1.60-2.70) and 4.14 (95% CI: 3.21-5.34) respectively. In model B after adjusting for sex the OR increased to 2.23 (95% CI: 1.71-2.90) and 4.57 (95% CI: 3.54-5.90) respectively. In model C with additional adjustment for Elixhauser comorbidities the OR decreased to 2.11 (95% CI: 1.61-2.77) and 4.10 (95% CI: 3.14-5.35), respectively (p for linear trend <0.001).

In the sensitivity analysis including patients with readmissions for the same cause, the fully adjusted model (Model C), provided similar results with OR of 2.10 (95% CI: 1.60-2.76) and 4.09 (95% CI: 3.14-5.34) for 75-84 and ≥85 years respectively when compared to those 65-74 years old (p for linear trend <0.001).

In the fully adjusted model (model C) the OR of mortality for men compared to women were 1.77 (95% CI: 1.58-1.98) (Table 3).

In the complete model (model C) the comorbidities significantly associated with higher in-hospital mortality after hip fracture were: congestive heart failure (OR: 3.88; 95% CI: 3.42-4.41), metastatic cancer (OR: 3.44; 95% CI: 2.27-5.20), fluid and electrolyte disorders (OR: 2.95; 95% CI: 2.47-3.52), coagulation deficiency (OR: 2.87; 95% CI: 2.08-3.96), liver disease (OR: 2.40; 95% CI: 1.82-3.17), pulmonary circulation disorders (OR: 1.95; 95% CI: 1.45-2.63), peripheral vascular disease (OR: 1.90; 95% CI: 1.47-2.45), lymphoma (OR: 1.82; 95% CI: 1.02-3.27), renal failure (OR: 1.74; 95% CI: 1.53-1.98), solid tumor without metastasis (OR: 1.68; 95% CI: 1.29- 2.19) and arrhythmias (OR: 1.59; 95% CI: 1.42-1.78) (Table 3). The sensitivity analysis including patients with readmissions for the same cause provided similar OR for all significant comorbidities.

In model D, when adjusting for the number of comorbidities (<3 and 3 or more) the OR of mortality for those 75-84 and ≥85 years compared to those 65-74 years old decreased from 2.23 (95% CI: 1.71-2.90) and 4.57 (95% CI: 3.54-5.90) to 2.04 (95% CI: 1.56-2.65) and 4.29 (95% CI: 3.32-5.54) respectively (p for linear trend <0.001) (Table 4).

No significant interactions for mortality were found between age groups and sex, or presenting three or more comorbidities and sex. In the stratified analysis, presenting 3 or more comorbidities showed a lower association with mortality in patients 85 or more years with OR of 2.35 (95% CI: 2.09-2.65) (p for interaction= 0.006 compared to those 65-74). In the stratified analysis the OR for those 75-84 and 65-74 years old were 3.10 (95% CI: 2.58-3.73) and 4.96 (95% CI: 2.94-8.38), respectively.

DISCUSSION

After adjustment for Elixhauser comorbidities, mortality after a fall-related hip fracture has a significant association with age with a positive linear trend. The comorbidities that have an association with mortality are in descending order: congestive heart failure, metastatic cancer, fluid and electrolyte disorders, coagulation deficiency, liver disease, pulmonary circulation disorders, peripheral vascular disease, lymphoma, renal failure, tumor without metastases and arrhythmias. Some of these disorders significantly associated with mortality, such as some fluid and electrolyte disorders, coagulation deficiencies and arrhythmias, could be potentially controllable and could provide a survival benefit for the patients. This is consistent with our second hypothesis. Mortality is significantly higher for men than for women.

The 5.5% of our patients died during admission. This is consistent with other studies that establish mortality after hip fracture between 5 and 10% in the first month [1, 6, 8, 15].

Few studies have assessed the association between mortality after fall-related hip fractures in the elderly and age, adjusting for a limited number of comorbidities included as individual variables [6-9]. Moreover population size in other studies was smaller than in our study and in their analyses they did not include the Elixhauser comorbidities, some of which, such as coagulation deficiencies and fluid and electrolyte disorders have been described as important predictors of outcomes for in-hospital patients [12]. According to Roche *et al* [6] the association between age and mortality in patients with hip fracture remained significant after adjusting for 11 comorbidities. The conditions significantly associated with a higher risk of mortality were the presence of renal disease and respiratory disease. Tosteson *et al.* [7] found that the association between age and mortality remained significant after adjustment for 13 comorbidities and those that presented a greater association with mortality were lymphoma, severe chronic liver disease, solid tumor, congestive heart failure, chronic renal failure, chronic pulmonary disease, history of diabetes, stroke and dementia. They also suggested that the increased mortality could be partly explained by a worse pre-fracture health and functional status [7] that could be manifestations of fragility. Castronuovo *et al.* [8] adjusting for 6 morbidities as individual variables, found associations between increased mortality and history of heart disease, chronic lung disease and renal disease. Paksima *et al.* [9] after adjusting for 14 comorbidities found that mortality in older patients after fall-related hip fracture was associated with present history of cancer, chronic obstructive pulmonary disease and congestive heart failure. Kannengaard et al. analyzing specific Charlson index components, found that the most powerful baseline risk factors for mortality after a hip fracture were metastatic solid tumours, renal disease, liver disease and chronic obstructive pulmonary disease [16].

In our study, coagulation deficiencies (mainly due to congenital deficiencies of coagulation factors) are associated with an increased risk for mortality. The availability of treatments and prophylactic protocols for many congenital coagulation disorders [17-19] could be a benefit for the survival of these patients. On the other hand some congenital coagulopathies if uncontrolled could lead, among others, to joint injuries [18], thus we cannot dismiss the fact that patients with coagulopathies present with fractures with increased joint destruction. However, it has been assessed that appropriate long-term prophylaxis in patients with bleeding disorders could preserve joint integrity and reduce the need for future orthopedic surgery [18].

Few studies have evaluated the relation between electrocardiographic abnormalities and mortality after hip fracture in older population even though it has been suggested that they are an important indicator of mortality [5, 20]. Atrial fibrillation is the most common cardiac arrhythmia in the population with a prevalence of 5 to 10% and is a major cause for mortality. *Adunsky et al.* found associations between long-term mortality and chronic atrial fibrillation in patients with hip fracture [20]. Consistent with this we have found significant associations between the presence of arrhythmias and an increased mortality, specifically between the presence of atrial fibrillation (ICD-9CM code 427.31) and higher ORs for hospital mortality (1.62, 95% CI 1.44-1.83) (data sub-analyses of different types of arrhythmias not shown) independent of other associated comorbidities. It may be of interest to analyze whether the increased mortality associated with arrhythmias is due to natural complications in managing the arrhythmia itself during the process (such as suspension of anticoagulation and the risk of peripheral embolism, or use bridge therapies with heparins of low molecular weight with a subsequent increased risk for fatal bleeding); or simply that atrial fibrillation was identifying a group of patients with a higher risk as a marker of advanced cardiovascular impairment and therefore that few modifiable elements may exist in the acute phase. In any case we suggest that future studies consider the potential interest of a management protocol for this condition adapted not only to the special needs of elderly patients, as has already been established [21], but further adapted to aged patients that have suffered a trauma.

In our population, the prevalence of fluid and electrolyte disorders is low, although they have a significant association with mortality in elderly patients after hip fracture. Although proper fluid and electrolyte replacement is necessary to stabilize blood pressure and tissue perfusion, some studies have reported that administration of a large volume of fluid, in particular saline solutions, could have counterproductive effects, contributing to the development of hypernatremia [22]. Hypernatremia, among other electrolyte disorders, could contribute to a worse prognosis and has been considered a quality-of-care marker [22]. To persevere in preventing hypernatremia, could benefit the outcome of in-hospital patients [22]. According to the last Cochrane revision [23] it is advisable that future studies analyze the optimal perioperative management protocol of fluid and electrolyte replacement in hip fracture surgical patients that could improve their outcome. That recommendation appears to be supported by our results.

We have found an association between depression and lower mortality. Since other studies have found no relation between mortality after a hip fracture and preoperative depression [5] future studies that further analyze this finding would be necessary.

Our study has also provided additional information on the association between mortality after hip fracture in an elderly population and sex, with higher mortality among men than women. Other studies have also found that mortality, after fall-related hip fracture in the elderly, is higher for men than for women [3, 5, 6, 8-10, 16, 24, 25]. Some studies have hypothesized that increased mortality for men could be partly explained because men have more comorbidities [10] and poorer health than women of the same age so increasing the harmful consequences of fractures [5, 26, 27]. However, consistently with our results, other authors have shown that excess mortality after hip fractures in older men persists even after adjusting for comorbidity synthetic indices [10, 16] and even after adjusting for some individual comorbidities [7, 8] [16]. This is consistent with our results. Several studies have shown that the higher mortality risk in men, compared to women, was not supported by the hypothesis that men have poorer health [28] and a higher prevalence of comorbidities [16], but suggested that future studies with a comprehensive collection of secondary diagnoses would be needed. We have considered in our analysis a greater number of diagnoses and the gender differences are maintained. Thus, our data make it advisable to further explore possible causes of this increased mortality risk for men apparently independent of men presenting more comorbidities, what has hitherto been considered one of the main hypotheses explaining the differences in mortality between the sexes. It has been hypothesized that these gender differences might be due to increased consumption of tobacco and alcohol by men compared to women [16, 24] but up till now no association has been found between alcohol and tobacco consumption and mortality after a hip fracture in the elderly [24, 29].

Some studies suggest that in younger age groups the presence of comorbidities could have a greater association with mortality after hip fracture than in older age groups [10, 11]. This is consistent with our results and could be partially explained because in older populations other variables not taken into account in our analysis, like the concept of fragility, could make the relative impact of comorbidities on mortality lower than in younger populations. However, we cannot also rule out that health professionals collect more detail on comorbidities in younger patients.

On the other hand, given the limited effect of comorbidities on the association between age and mortality after hip fracture, other confounders not considered may partly explain the association. Possibly the concept of fragility, and the low physiological reserve that implies, would be one of the most important to consider. Joseph *et al.* found that a Frailty index calculated by the integration of various comorbidities, performance of daily activities, healthy attitudes, and variables related to function and nutrition, was a predictor of the type of discharge (home, transfer to a nursing facility and/or mortality) in geriatric trauma patients [30]. Tosteson *et al.* found that limitation for daily activities prior to fracture was associated with an increased mortality after adjustment for 13 comorbidities [7] and Paksima *et al.* also showed that the worse the prefracture ambulatory level the higher the mortality risk [9]. Meyer *et al.* also found that low physical ability was associated with a higher mortality after hip fracture [29].

Our findings suggest that further studies assessing the impact of indicators of fragility in the association between age and mortality after a fall-related hip fracture in the elderly after adjusting for Elixhauser comorbidities included as individual variables are worthwhile.

Strengths

This study included all patients admitted to public hospitals with the diagnosis of hip fracture in the country during 2013 so is nationally representative.

It is also the first study that has analyzed the independent impact of each Elixhauser comorbidity in the association between in-hospital mortality after fall-related hip fracture and age. Thus, it offers an added value with important practical implications; because regardless of whether the association between age and mortality declines very slightly after adjusting for comorbidities, some comorbidities not previously studied, present a significant association with mortality, and could be considered, in specific cases, as potentially controllable. These could include certain coagulation deficiencies, fluid and electrolyte disorders and certain arrhythmias among others.

The main diagnoses selected have been an intertrochanteric fracture or a fracture of the femoral neck, excluding the femoral diaphysis, so the study population had an acceptably homogeneous type of injury.

Limitations

First, no information was available on socioeconomic and educational level, although other studies have found no association with the risk of death form overall accidental falls or specifically with hip fracture in the elderly, so the lack adjusting for these variables is unlikely to have an impact in our analysis [5, 7].

Second, we had no information on marital status which has been associated with mortality after a hip fracture in the elderly in some studies [7, 8] but not in others [31].

Third, in the elderly population accidental falls, even those milder, could produce a deferred death attributed to another cause [32], thus the cases of death due to fall-related fractures may be underestimated. On the other hand it has been reported that the increased risk for mortality occurs very soon after the fracture [2, 3, 8, 28] and that out-hospital mortality after hip fracture in elderly is only 15.5% [10] so the possible underestimation of mortality was probably not very large. In addition this possible bias, if any, would lead mainly in the direction of not finding associations with the studied variables.

Fourthly, we had no information on the degree of fragility of patients, so this variable with potential interest has not been included in the adjustment.

Fifth, although we have analyzed the relationship between mortality and type of surgery we did not include this variable in the analysis, since almost all treatments consisted of internal fixation or joint replacement, which is consistent with other studies [5]. Besides, consistently with other studies, we did not find differences between different surgical procedures and increased mortality [33, 34].

Sixth, we have not adjusted for other variables associated with treatment like a waiting period longer than 24 hours before surgery, although it is interesting to note that this was not found to be significantly associated with mortality in previous studies [15, 35, 36].

Seventh, we had no information about functional and nutritional status, so this potential confounder has not been included in the adjustment.

Eighth, our database did not allow us to categorize between early versus late mortality, so we only registered in-hospital mortality.

Finally, we cannot rule out that data from patients who died during admission presented greater thoroughness in the collection of the number of associated diseases, which could lead to an overestimation of the impact of comorbidities on mortality risk.

CONCLUSIONS

After adjustment for comorbidities, age is independently associated with an increased in-patient mortality after a fall-related hip fracture in older population. Although an adequate treatment of certain potentially controllable comorbidities could improve the prognosis of some patients, the reduction of the association between age and in-patient mortality that occurs after adjusting for comorbidities is limited. Additional factors associated with age, including the concept of fragility, could explain this excess of in-patient mortality in the elderly and would require specific approaches.

Conflict of interest: Alicia Padrón-Monedero, Teresa López-Cuadrado, Iñaki Galán, Elena V. Martínez-Sánchez, Pilar Martin and Rafael Fernández-Cuenca declare that they have no conflict of interest.

Ethics approval: This study was approved by the Institutional Review Board of the Carlos III Institute of Health.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

REFERENCES

1. Parker M, Johansen A (2006) Hip fracture. BMJ 333:27-30
2. Melton LJ (2003) Adverse outcomes of osteoporotic fractures in the general population. Journal of bone and mineral research 18:1139-41
3. Hindmarsh DM, Hayen A, Finch CF, Close JC (2009) Relative survival after hospitalisation for hip fracture in older people in New South Wales, Australia. Osteoporos Int 20:221-9. doi: 10.1007/s00198-008-0641-z
4. Ministerio Sanidad Servicios Sociales e Igualdad (2014) Documento de consenso sobre prevención de fragilidad y caídas en la persona mayor. Ministerio Sanidad Servicios Sociales e Igualdad. Centro de Publicaciones. Madrid http://www.msssi.gob.es/profesionales/saludPublica/prevPromocion/Estrategia/docs/FragilidadyCaidas_personamayor.pdf. Accessed 31 August 2016.
5. Smith T, Pelpola K, Ball M, Ong A, Myint PK (2014) Pre-operative indicators for mortality following hip fracture surgery: a systematic review and meta-analysis. Age and Ageing 43:464-71. doi:10.1093/ageing/afu065
6. Roche JJ, Wenn RT, Sahota O, Moran CG (2005) Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. BMJ 331:1374. doi:10.1136/bmj.38643.663843.55
7. Tosteson AN, Gottlieb DJ, Radley DC, Fisher ES, Melton LJ (2007) Excess mortality following hip fracture: the role of underlying health status. Osteoporos Int 18:1463-72
8. Castronuovo E, Pezzotti P, Franzo A, Di Lallo D, Guasticchi G (2011) Early and late mortality in elderly patients after hip fracture: a cohort study using administrative health databases in the Lazio region, Italy. BMC Geriatrics 11:37
9. Paksima N, Koval KJ, Aharanoff G, et al (2008) Predictors of mortality after hip fracture: a 10-year prospective study. Bulletin of the NYU Hospital for Joint Diseases 66:111-7
10. Hindmarsh D, Loh M, Finch CF, Hayen A, Close JC (2014) Effect of comorbidity on relative survival following hospitalisation for fall-related hip fracture in older people. Australasian journal on ageing 33:E1-7 doi: 10.1111/j.1741-6612.2012.00638.x
11. de Luise C, Brimacombe M, Pedersen L, Sorensen HT (2008) Comorbidity and mortality following hip fracture: a population-based cohort study. Aging Clin Exp Res 20:412-8
12. Elixhauser A, Steiner C, Harris DR, Coffey RM (1998) Comorbidity measures for use with administrative data. Medical care 36:8-27
13. Ministerio Sanidad Servicios Sociales e Igualdad (2011) Estudio de las comorbilidades que componen el índice de Elixhauser. Análisis de prevalencia y fiabilidad en los registros del CMBD estatal de hospitalización. Madrid. http://icmbd.es/docs/informe-comorbilidades-1.pdf. Accessed 31 August 2016.
14. Ministerio Sanidad Servicios Sociales e Igualdad (2015) Registro de altas- CMBD estatal. Hospitalización CMBD-H. Manual de definiciones y glosario de términos. Madrid. http://pestadistico.inteligenciadegestion.msssi.es Accessed 21 April 2016.
15. Franzo A, Francescutti C, Simon G (2005) Risk factors correlated with post-operative mortality for hip fracture surgery in the elderly: a population-based approach. European journal of epidemiology 20:985-91. doi: 10.1007/s10654-005-4280-9
16. Kannegaard PN, van der Mark S, Eiken P, Abrahamsen B (2010) Excess mortality in men compared with women following a hip fracture. National analysis of comedications, comorbidity and survival. Age and ageing 39:203-9. doi: 10.1093/ageing/afp221
17. Mannucci PM (2008) Prophylaxis in congenital coagulation disorders: past, present and future. Blood Transfus 6 Suppl 2:S1-3.
18. Makris M (2012) Prophylaxis in haemophilia should be life-long. Blood Transfus 10:165-8. doi: 10.2450/2012.0147-11
19. Bhat R, Cabey W (2014) Evaluation and management of congenital bleeding disorders. Emerg Med Clin 32:673-90
20. Adunsky A, Arad M, Koren-Morag N, Fleissig Y, Mizrahi EH (2012) Increased 1-year mortality rates among elderly hip fracture patients with atrial fibrillation. Aging Clin Exp Res 24:233-8
21. The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC) (2010) European society of cardiology guidelines. European Heart Journal (2010) 31, 2369–2429 http://eurheartj.oxfordjournals.org/content/ehj/31/19/2369.full.pdf doi:10.1093/eurheartj/ehq278

22. Besen BA, Gobatto AL, Melro LM, Maciel AT, Park M (2015) Fluid and electrolyte overload in critically ill patients: An overview. World J Crit Care Med 4:116-29
23. Brammar A, Nicholson A, Trivella M, Smith AF (2013) Perioperative fluid volume optimization following proximal femoral fracture. Cochrane Database of Systematic Reviews Issue 9. Art. No.: CD003004. doi: 10.1002/14651858.CD003004.pub3.
24. Trombetti A, Herrmann F, Hoffmeyer P, Schurch MA, Bonjour JP, Rizzoli R (2002) Survival and potential years of life lost after hip fracture in men and age-matched women. Osteoporos Int 13:731-7
25. Holt G, Smith R, Duncan K, Hutchison JD, Gregori A (2008) Gender differences in epidemiology and outcome after hip fracture: evidence from the Scottish Hip Fracture Audit. J Bone Joint Surg 90:480-3
26. Yoshida S (2007). A Global Report on Falls Prevention. Epidemiology of Falls. Ageing and life course family and community health WHO. Geneva. http://www.who.int/ageing/projects/1.Epidemiology%20of%20falls%20in%20older%20age.pdf. Accessed 31 August 2016.
27. WHO (2007) WHO global report on falls prevention in older age. Ageing and life course family and community health WHO. Geneva. http://www.who.int/ageing/publications/Falls_prevention7March.pdf. Accessed 31 August 2016.
28. Robbins JA, Biggs ML, Cauley J (2006) Adjusted mortality after hip fracture: From the cardiovascular health study. JAGS 54:1885-91. doi: 10.1111/j.1532-5415.2006.00985.x
29. Meyer HE, Tverdal A, Falch JA, Pedersen JI (2000) Factors associated with mortality after hip fracture. Osteoporos Int 11:228-32
30. Joseph B, Pandit V, Zangbar B, Kulvatunyou N, Hashmi A, et al (2014) Superiority of frailty over age in predicting outcomes among geriatric trauma patients: a prospective analysis. JAMA Surg 149:766-72.. doi:10.1001/jamasurg.2014.296.
31. Fernandez-Ruiz M, Guerra-Vales JM, Trincado R, Medrano MJ, Benito-Leon J, Bermejo-Pareja F (2014) Hip fracture in three elderly populations of central Spain: data from the NEDICES study. Intern Emerg Med 9:33-41. Doi: 10.1007/s11739-011-0728-y
32. Stevens JA, Rudd RA (2014) Circumstances and contributing causes of fall deaths among persons aged 65 and older: United States, 2010. JAGS 62:470-5. doi: 10.1111/jgs.12702
33. Cheng T, Zhang GY, Liu T, Zhang XL (2012) A meta-analysis of percutaneous compression plate versus sliding hip screw for the management of intertrochanteric fractures of the hip. J Trauma 72:1435-43. doi: 10.1097/TA.0b013e318247252a
34. Heetveld MJ, Rogmark C, Frihagen F, Keating J (2009) Internal fixation versus arthroplasty for displaced femoral neck fractures: what is the evidence? J Orthop Trauma 23:395-402
35. Williams A, Jester R (2005) Delayed surgical fixation of fractured hips in older people: impact on mortality. J Adv Nurs 52:63-9
36. Franzo A, Simon G, Francescutti C (2006) Mortality associated with delay in operation after hip fracture: ... but Italian data seem to contradict study findings. BMJ 332:1093

Table 1: ICD-9CM coding for Elixhauser comorbidities (Agency for Healthcare Research and Quality (version 3.5)).

Definitions of Comorbidities	ICD9-MC
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0-428.9.
Arrythmia	426.10, 426.11, 426.12, 426.13, 426.2-426.53, 426.6-426.89, 426.9, 427.0, 427.2, 427.31, 427.32, 427.41, 427.42, 427.60, 427.61, 427.81, 427.89, 427.9, 785.0, V45.00, V45.01, V45.02, V45.09, V53.31, V53.32, V53.39.
Valvular disease	093.20-093.24, 394.0-397.1, 397.9, 424.0-424.99, 746.3-746.6, V42.2, V43.3.
Pulmonary circulation disorders	415.11-415.19, 416.0-416.9, 417.9.
Peripheral vascular disease	440-440.9, 441.00-441.9, 442.0-442.9, 443.1-443.9, 444.21-444.22, 447.1, 449, 557.1, 557.9, V43.4.
Hypertension (complicated and uncomplicated)	401.1, 401.9, 642.00-642.04, 401.0, 402.00-405.99, 437.2, 642.10-642.24, 642.70-642.94.
Paralysis	342.0-344.9, 438.20-438.53, 780.72.
Other neurological disorders	330.1-331.9, 332.0, 333.4, 333.5, 333.7, 333.85, 333.94, 334.0-335.9, 338.0, 340, 341.1-341.9, 345.00-345.11, 345.2-345.3, 345.40-345.91, 347.00-347.01, 347.10-347.11, 649.40-649.44, 768.70-768.73, 780.3, 780.31, 780.32, 780.39, 780.97, 784.3.
Chronic pulmonary disease	490-492.8, 493.00-493.92, 494-494.1, 495.0-505, 506.4.
Diabetes uncomplicated	249.00-249.31, 250.00-250.33, 648.00-648.04.
Diabetes complicated	249.40-249.91, 250.40-250.93, 775.1
Hypothyroidism	243-244.2, 244.8, 244.9.
Renal failure	403.01, 403.11, 403.90, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585, 586, V42.0, V45.1, V56.0-V56.32, V56.8
Liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 456.0, 456.1, 456.20, 456.21, 571.0, 571.2, 571.3, 571.40-571.49, 571.5, 571.6, 571.8, 571.9, 572.3, 572.8, V42.7.
Chronic peptic ulcer disease excluding bleeding	531.41, 531.51, 531.61, 531.70, 531.71, 531.91, 532.41, 532.51, 532.61, 532.70, 532.71, 532.91, 533.41, 533.51, 533.61, 533.70, 533.71, 533.91, 534.41, 534.51, 534.61, 534.70, 534.71, 534.91.
AIDS/HIV	042-044.9.
Lymphoma	200.00-202.38, 202.50-203.01, 203.02-203.82, 203.8-203.81, 238.6, 273.3.
Metastatic cancer	196.0-199.1, 209.70, 209.71, 209.72, 209.73, 209.74, 209.75, 209.79, 789.51.
Solid tumor without metastasis	140.0-172.9, 174.0-175.9, 179-195.8, 209.00-209.24, 209.25-209.3, 209.30-209.36, 258.01-258.03.
Reumathoid artritis/collagen vascular diseases	701.0, 710.0-710.9, 714.0-714.9, 720.0-720.9, 725.
Coagulation deficiency	286.0-286.9, 287.1, 287.3-287.5, 289.84, 649.30-649.34.
Obesity	278.0, 278.00, 278.01, 649.10-649.14, 793.91, V85.30-V85.39, V85.54.
Weight loss	260-263.9, 783.21, 783.22.
Fluid and electrolyte disorders	276.0-276.9.
Blood loss anemia	280.0, 648.20-648.24.
Deficiency anemias	280.1-281.9, 285.21-285.29, 285.9.
Alcohol abuse	291.0-291.3, 291.5, 291.8, 291.81, 291.82, 291.89, 291.9, 303.00-303.93, 305.00-305.03.
Drug abuse	292.0, 292.82-292.89, 292.9, 304.0-304.93, 305.20-305.93, 648.30-648.34.
Psychoses	295.00-298.9, 299.10, 299.11.
Depression	300.4, 301.12, 309.0, 309.1, 311.

Table 2: Demographic and clinical characteristics of hospital discharge after fall-related hip fracture.

Variables	N Total	% Total	N Deaths	% Deaths	p
Total population	31,884	100	1,766	100	
Age group					<0.001
65-74	3,287	10.3	64	3.6	
75-84	12,961	40.7	514	29.1	
≥85	15,636	49.0	1,188	67.3	
Sex					<0.001
Male	7,679	24.1	669	37.9	
Female	24,205	75.9	1,097	62.1	
Comorbidities					
Number of comorbidities					<0.001
< 3	20,899	65.5	752	42.6	
≥ 3	10,985	34.5	1,014	57.4	
Congestive heart failure					<0.001
Yes	2,180	6.8	482	27.3	
No	29,704	93.2	1,284	72.7	
Arrythmia					<0.001
Yes	6,226	19.5	633	35.8	
No	25,658	80.5	1,133	64.2	
Valvular disease					<0.001
Yes	1,970	6.2	227	12.9	
No	29,914	93.8	1,539	87.1	
Pulmonary circulation disorders					<0.001
Yes	472	1.5	86	4.9	
No	31,412	98.5	1,680	95.1	
Peripheral vascular disease					<0.001
Yes	623	1.9	83	4.7	
No	31,261	98.1	1,683	95.3	
Chronic pulmonary disease					<0.001
Yes	3,235	10.2	306	17.3	
No	28,649	89.8	1,460	82.7	
Renal failure					<0.001
Yes	3,057	9.6	387	21.9	
No	28,827	90.4	1,379	78.1	
Liver disease					<0.001
Yes	600	1.9	71	4.0	
No	31,284	98.1	1,695	96.0	
Lymphoma					0.032
Yes	146	0.5	14	0.8	
No	31,738	99.5	1,752	99.2	
Metastatic cancer					<0.001
Yes	213	0.7	43	2.4	
No	31,671	99.3	1,723	97.6	
Solid tumor without metastasis					<0.001
Yes	751	2.4	96	5.4	
No	31,133	97.6	1,670	94.6	
Coagulation deficiency					<0.001
Yes	298	0.9	58	3.3	
No	31,586	99.1	1,708	96.7	
Fluid and electrolyte disorders					<0.001
Yes	1,058	3.3	200	11.3	
No	30,826	96.7	1,566	88.7	
Depression					<0.001
Yes	2,824	8.9	92	5.2	
No	29,060	91.1	1,674	94.8	

Table 3: Odds ratios (OR) and 95% confidence intervals (CI) for in-hospital death after fall-related hip fracture by demographic and individual Elixhauser comorbidities.

	Model A[a] OR (95% CI)	**Model B**[b] OR (95% CI)	**Model C**[c] OR (95%CI)
Age group* **			
65-74	1 (ref)	1 (ref)	1 (ref)
75-84	2.08 (1.60-2.70)	2.23 (1.71-2.90)	2.11 (1.61-2.77)
≥85	4.14 (3.21-5.34)	4.57 (3.54-5.90)	4.10 (3.14-5.35)
P for linear trend	<0.001	<0.001	<0.001
Sex * **			
Female		1 (ref)	1 (ref)
Male		2.16 (1.95-2.39)	1.77 (1.58-1.98)
Comorbidities [d]			
Congestive heart failure***			3.88 (3.42-4.41)
Arrythmia***			1.59 (1.42-1.78)
Valvular disease*			1.26 (1.05-1.52)
Pulmonary circulation disorders***			1.95 (1.45-2.63)
Peripheral vascular disease***			1.90 (1.47-2.45)
Chronic pulmonary disease***			1.33 (1.15-1.53)
Renal failure***			1.74 (1.53-1.98)
Liver disease***			2.40 (1.82-3.17)
Lymphoma*			1.82 (1.02-3.27)
Metastatic cancer***			3.44 (2.27-5.20)
Solid tumor without metastasis***			1.68 (1.29-2.19)
Coagulation deficiency ***			2.87 (2.08-3.96)
Fluid and electrolyte disorders***			2.95 (2.47-3.52)
Depression***			0.67 (0.53-0.83)

Table 4: Odds ratios (OR) and 95% confidence intervals (CI) for in-hospital death after fall-related hip fracture by demographic variables and aggregation of Elixhauser comorbidities.

	Model D[d] OR (95%CI)
Age group* **	
65-74	1 (ref)
75-84	2.04 (1.56-2.65)
≥85	4.29 (3.32 -5.54)
p for linear trend	<0.001
Sex* **	
Male	1 (ref)
Female	2.05 (1.85-2.27)
Comorbidities	
<3	1 (ref)
≥3	2.62 (2.38-2.90)

[d] Model D: Multivariate: Age group + sex + aggregation of Elixhauser comorbidities.

* p<0.05 ** p<0.01 *** p<0.001