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Should patients with exceptional longevity be treated for osteoporosis after a hip fracture?

Abstract

Background

There are no studies focusing on treatment for osteoporosis in patients with exceptional longevity after suffering a hip fracture.

Objective

To assess the advisability of initiating treatment for osteoporosis after a hip fracture according to the incidence of new fragility fractures after discharge, risk factors for mortality, and long-term survival.

Design

Retrospective review.

Setting

A tertiary university hospital serving a population of about 425,000 inhabitants in Barcelona.

Subjects

All patients older than 95 years admitted with a fragility hip fracture between December 2009 and September 2015 who survived admission were analyzed until the present time

Methods

Pre-fracture ambulation ability and new fragility fractures after discharge were recorded. Risk factors for 1 year and all post-discharge mortality were calculated with multivariate Cox regression. Kaplan Meier survival curve analyses were performed.

Results

One hundred and seventy-five patients were included. Median survival time was 1.32 years (95% CI 1.065-1.834), with a maximum of 9.2 years. Male sex (HR 2.488 95% CI 1.420-4.358) and worse previous ability to ambulate (HR 2.291, 95%CI 1.417-3.703) were predictors of mortality. After discharge and up to death or the present time, 10 (5.7%) patients had a new fragility fracture, half of them during the first 6 months.

Conclusions

Few new fragility fractures occurred after discharge and half of these took place in the first 6 months. The decision to start treatment of osteoporosis should be individualized, bearing in mind that women and patients with better previous ambulation ability will have a better chance of survival.

1. Introduction

The number of centenarians and almost centenarians is increasing in most countries, especially in Western societies [1]. Falls and osteoporosis are risk factors for hip fractures, and both are more frequent at older ages, so that an increase in hip fractures in patients with exceptional longevity is to be expected [2, 3]. It is well-established that after one fragility fracture, the risk of a new one is greatly increased. Nevertheless, many patients do not receive treatment for osteoporosis [4, 5]. In patients older than 80 years, the number of prescriptions for these drugs is even lower, despite the fact that they have been shown to be effective in preventing new fractures, that there is no evidence that they are associated with more age-related adverse effects [6, 7], and that clinical guidelines for osteoporosis in our setting do not limit the age at which treatment should be started [8, 9].

As treatments for osteoporosis need time, estimated to be between 6 and 24 months, before their efficacy in fracture reduction starts to take effect [10], it is not considered appropriate to initiate them if the estimated survival time of the patient is less than one year [10, 11]. The few studies conducted in patients with exceptional longevity who have had a hip fracture have focused mainly on describing baseline characteristics, outcomes during admission, short- and long-term mortality and functional recovery. Only one, to our knowledge, concerns osteoporosis treatment, and the authors found an increased number of prescriptions to centenarian patients compared to before the fracture, although it was much lower than in younger patients [12]. Although mortality in centenarians is higher than in patients in the most common age group for hip fractures [13] and, approximately 50% of patients with exceptional longevity will still be alive one year after the fracture [14, 15], some surviving for relatively long periods [16, 17], no studies have reviewed the risk of new fragility fractures in these patients, or whether it is necessary or even advisable to start treatment in patients who have not previously received it.

The objectives of our study were to analyze the incidence of new fragility fractures, risk factors for 1-year and all post-discharge mortality, and long-term survival in patients with exceptional longevity after a hip fracture, in order to assess the appropriateness of initiating osteoporosis treatment in an understudied population that will increase in the coming years.

2. Methods

2.1 Setting

The study was conducted in the Orthopedic Surgery Ward of the Hospital de la Santa Creu i Sant Pau, a tertiary university hospital serving a population of about 425,000 people in Barcelona.

2.2 Subjects

All patients older than 95 years discharged from the Orthogeriatric Unit with a diagnosis of fragility hip fracture between December 2009 and September 2015 were retrospectively reviewed and data analysis was performed up to the present time or date of death of the patient.

At discharge, recommendations for adequate dietary calcium intake were made (3 units of dairy products per day) and all patients were prescribed 1000 units per day of vitamin D. Although vitamin D levels were not available in our patients, the prevalence of vitamin D deficiency in the oldest old in our setting was over 90% [18]. Treatment was maintained in patients already taking bisphosphonates, but no new treatment for osteoporosis was initiated in any patient.

The study was approved by the institutional ethics committee and conducted according to the ethical principles of the Declaration of Helsinki for medical research involving human subjects.

2.3 Data collection

We retrospectively recorded the following data: age, sex, comorbidities measured by the Charlson index [19], functional ambulation classification category (FAC) [20] prior to admission, place of residence, number of drugs prior to admission (including vitamin D, calcium and osteoporosis medications), previous fragility fractures, and hemoglobin and albumin levels at admission. Length of hospital stay, delay to surgery, type of fracture, assessment of surgical risk based on ASA (American Society of Anesthesiologists) risk score, type of surgery, type of anesthesia, complications during admission, final discharge destination and treatments for osteoporosis at discharge were also noted.

Short- and long-term survival were recorded. The date of death was obtained from the patient's medical records and the Ministry of Health**'s** National Death Index website (https://www.mscbs.gob.es/estadEstudios/estadisticas/estadisticas/estMinisterio/IND_TipoDifusion.htm), after authorization. ,

We recorded new fragility fractures and the date on which the new fracture occurred. We considered fragility fractures: hip, spine, forearm, humerus, ribs, tibia (excluding the ankle), pelvis and other femoral fractures, as described in the paper by Kanis et al. [21].

We used the FAC classification, even though it was originally created for neurologically impaired patients, because it has been used in other studies conducted in our setting [12, 14] and provides a useful measure of the patient's ambulation ability. We dichotomized the scale with a cut-off point at FAC < 3 and ≥ 3 to differentiate between patients who need physical help from another person and those who do not.

2.4 Statistical analysis

Continuous variables were presented as means and standard deviations, and compared using Student's t-test with the Welch correction. For categorical variables, absolute numbers, relative frequencies or proportions were calculated and compared using Fisher's exact test. Multivariate Cox regression analysis was performed with statistically significant variables in the univariate analysis (proportional hazards model) to determine the independent variables. A Kaplan Meier post-discharge survival analysis was calculated. Statistical analysis was performed with the IBM SPSS Statistical Package (version 27) (SPSS Inc., Chicago, IL, USA). Statistical significance was $p \leq 0.05$ in all cases.

3. Results

Between December 2009 and September 2015, one hundred and seventy-five patients aged over 95 years of age were discharged after a hip fracture.

Cumulative mortality at one year was 76 (43.45%). The baseline characteristics and comparison of surviving and non-surviving patients at one year are shown in Tables 1 and 2.

Four patients were already taking bisphosphonates, with a mean of 2.76 (SD 0.66) years of treatment (minimum 1.82 years, maximum 3.35 years). Any of hip fractures was considered atypical. Patients already taking calcium carbonate or cholecalciferol were taking between 1000 and 1500 mg a day and between 880 and 2000 units a day respectively.

The results of the multivariate Cox regression analysis for independent variables associated with mortality during the first year and in the entire post-hip fracture period are shown in Table 3. Sex and previous FAC score were the only variables associated with mortality at 1 year and all mortality after discharge in the multivariate regression analysis.

The median survival time was 1.3 years (95% CI 1.065-1.834) with a maximum of 9.26 years. The survival curve for patients is shown in Figure 1a. Figures 1b and 1c show survival curves by sex and previous FAC score. One patient (0.6%) could not be located after the second year, and another is still alive today.

After discharge 10 (5.7%) patients sustained a fragility fracture (7 hip, 1 pelvis, 1 proximal humerus, 1 distal radius). No patient had more than one subsequent fracture.

These fractures occurred between 15 and 1,166 days after discharge, and 5 (2.9%) occurred in the first six months after discharge (figure 2). Four of these 5 fractures were hip fractures. All patients with a new fragility fracture were female. There were no statistically significant variables in the comparison between patients who sustained a new fragility fracture and those who did not, nor in the comparison between those who had fractures more than 6 months after discharge and those who did not.

4. Discussion

This study shows that 10 (5.7%) of all patients with exceptional longevity had new fragility fractures, all of them within the first 3.2 years after discharge. Most of these were not taking treatment for osteoporosis. Half of the new fractures occurred during the first months after discharge, which is the time of maximum risk, as other authors have pointed out. In a 5-year follow-up study of non-vertebral fragility fractures, Huntjens et al. found that the absolute risk of sustaining a new non-vertebral fracture was 17.6% and that the period of highest risk was within the first year, when 6.4% of patients had a new fracture; this was despite the fact that all patients had started antiosteoporosis treatment [22]. Van Helden et al., found that the cumulative incidence of clinical fractures at two years was 10.8%, and 6.48% of these occurred during the first year, although the authors do not indicate whether the patients were receiving treatment for osteoporosis [23]. Both studies were performed in patients younger than ours, with a mean age in females of about 73 years and 67 in males.

A study conducted in Iceland showed that women had a higher risk of a subsequent fracture immediately after the first major osteoporotic fracture and that the increase in risk became more pronounced with increasing age [24].

In studies focusing on patients who had sustained a hip fracture, the risk of a new fragility fracture was much higher. Schemitsch et al. observed a second hip fracture in one in every three patients (median age 81 years) within a mean of 1.5 years [25]. In a 22-year follow-up study in women of different ages conducted in Sweden, almost half of all women with a hip fracture suffered a new fracture during their remaining lifetime, with a 10-year fracture risk of 40%. The number of patients over 90 years with at least one fracture during follow-up was 14 (16%), which was lower than in other age groups. The authors concluded that the risk of a new fracture was highly influenced by survival time [26]. Other authors have suggested that the reason why patients with exceptional longevity have fewer new fractures could be explained not only by their shorter expected survival time but also by the relationship between functional recovery and functional status. One study found an increased association between high functional status and second fractures. While high functional status is predictive of better physical recovery after the initial fracture, more second fractures occur in patients with high functional status because there are more opportunities for falls [27].

We found a single study mentioning bone health prescriptions in centenarian patients, and although the percentage was lower than in other age groups, there was an increase in prescriptions after hip fracture compared to before (pre-fracture antiosteoporosis medication 1.6%, at discharge 14.1%). However, the criteria for starting treatment in some patients and not in others were not stated [12], nor were the outcomes of new fragility fractures.

We noted the number of fragility fractures occurring after 6 months post-discharge because the effects of osteoporosis treatment are not immediate. It is estimated that it takes about 6 months to prevent vertebral fractures and between 18 and 24 months to prevent hip fractures; consequently, it is recommended not to initiate this treatment in patients with an estimated survival time of less than one year [10]. In our study, most new fragility fractures were hip fractures, and half of these occurred during the first 6 months. It is likely therefore that most of the new fragility fractures could not have been prevented even if we had initiated treatment at discharge.

At the time of the study, a fracture liaison service (FLS) had not yet been established in our center, nor did we have orthogeriatric care guidelines from our Geriatric Society, as we have now [28]. While treatment for osteoporosis was recommended routinely for patients who had had hip fractures, no new treatment for osteoporosis was initiated in patients with exceptional longevity, considering that they had little chance of surviving more than one year.

As expected, long-term survival in these patients was low. However, the survival curve shows that 3 years after discharge, more than 25% of patients were alive. We have found only two other studies reporting mortality more than two years after discharge in this group of patients: Tarity et al. in 2013, found a survival rate of 10% at 3 years [16], and Mosfeld et al. in 2019, a survival rate of 22% at 2 years [17].

Females and patients with better previous ambulation ability were the most likely to survive one year after hip fracture. The difference in survival in both parameters was maintained throughout the post-discharge period. Very few studies have described risk factors for mortality in patients with exceptional longevity. Higher comorbidity has been described as predictive of in-hospital, 30-day and 6-month mortality [14, 29], and dementia and higher

ASA score have been associated with an increased risk of 30-day mortality [12, 14]. Worse pre-injury walking ability was observed to be a risk factor for short- and long-term mortality in centenarian patients [14, 30].

In many studies worldwide, mortality after hip fracture is higher in men [31, 32]. Men who sustain a hip fracture tend to be younger than women, and also have a higher short-term [33] and long-term mortality [34]. In recent years, one-year mortality has decreased in women, but not in men [35]. It is not clear why men have worse survival. Some studies have associated it with poorer health, higher comorbidity and polypharmacy [36,37]. Wehren et al. found that the risk of dying in the first two years after hip fracture was twice as high in men as in women and that infections such as pneumonia, influenza and septicemia were largely responsible for the gender difference [38]. These gender differences in survival were maintained in our study, although it has also been described that males who do reach very old age are often fit and delay or escape potentially lethal illnesses [39].

Other authors have also found associations between poorer pre-fracture ambulation ability and increased mortality after discharge, although this was measured in different ways depending on the study. Meyer et al., in a 3 1/2-year follow-up after a hip fracture, described a marked increase in mortality in patients who did not walk outdoors regularly before admission [40]. Gonzalez-Marcos et al. found that mortality at 6 months in patients who could not walk before the hip fracture was ten times higher than in those who could [41]. Previous walking ability is also directly related to capacity for functional recovery. A study conducted in Norway found that functional recovery in patients with hip fractures was better in those with good or very good baseline functionality [42]. It is reasonable to assume that patients with better functionality survive longer, as lower physical capacity has been associated with increased frailty, mortality [43], and with all-cause mortality in older adults [44].

Delirium, on the other hand, was not an independent predictor of one-year mortality, although it was statistically significant in the univariate test. Delirium is a widely reported risk factor for mortality [32]. Some risk factors for developing delirium are shared with those for mortality, such as advanced age, male sex and preoperative functional dependency [45]. In our study, the number of patients presenting delirium was not very high despite the advanced age of our patients. Reasons for this may be that delirium was underdiagnosed as it tends to fluctuate, or that it was not recognized in patients with hypoactive delirium, as some authors have pointed out [46, 47].

The main limitations of our study are that the number of patients was small, and that the study was performed in a single hospital. The main strengths are the description of risk factors for mortality, the analysis of long-term survival of patients with exceptional longevity, for whom there are practically no references in the literature, and especially, that this is, to our knowledge, the first time that appropriateness of osteoporosis treatment in patients with exceptional longevity has been considered, a challenge faced by clinicians nowadays.

5. Conclusions

After hip fracture, patients with exceptional longevity had fewer fragility fractures, half of them in the first 6 months after discharge, which does not allow us to recommend treatment with anti-osteoporosis drugs.

Further studies are needed to confirm these findings, but our results support that the decision to start osteoporosis treatment in patients with exceptional longevity should be made on an individualized basis, taking into account that women and patients with better ambulatory capacity have the best chances of survival.

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Table 1. Comparison between surviving and non-surviving patients older than 95 years during the first year after hip fracture: Baseline characteristics

Patients = 175	Total n=175	Survivors n=99	Non-survivors n=76	p value
Age, in years (SD)	97.23 (2.38)	97.06 (2.32)	97.46 (2.45)	0.276
Female sex *n* (%)	152 (86.9)	92 (92.9)	60 (78.9)	0.006
Charlson index (SD)	1.18 (1.20)	1.07 (1.05)	1.32 (1.36)	0.198
Previous FAC score* ≥ 3 *n* (%)	132 (75.4)	83 (83.8)	49 (64.5)	0.003
Dementia	58 (33.1)	35 (35.4)	23 (30.3)	0.293
Place of residence: *n* at home (%)	101 (57.7)	61 (61.6)	40 (52.6)	0.150
Previous fragility fracture *n* (%)	42 (24)	22 (22.2)	20 (26.3)	0.325
Number of drugs (SD)	4.95 (2.9)	4.85 (2.86)	5.08 (2.96)	0.606
Vitamin D *n* (%)	20 (11.4)	10 (10.1)	10 (13.2)	0.346
Calcium *n* (%)	14 (8)	7 (7.1)	7 (9.2)	0.403
Bisphosphonate *n* (%)	4 (2.3)	1 (1)	3 (3.9)	0.218
Intracapsular fracture *n* (%)	79 (45.1)	41 (41.4)	38 (50)	0.164
Hemoglobin at admission in g/L (SD)	119.5 (15.01)	121.04 (15.05)	117.47 (14.82)	0.125
Albumin at admission in g/L (SD)	28.17 (3.24)	28 (3.05)	38 (3.47)	0.443
ASA score** classification (SD)	2.82 (0.58)	2.77 (0.58)	2.88 (0.58)	0.205

Note: SD = *standard deviation*

** Functional ambulation classification*

*** American Society of Anesthesiologists*

Table 2. Comparison between surviving and non-surviving patients older than 95 years during the first year after hip fracture: in-hospital results and outcomes during the first year after discharge

Patients = 175	Total n=175	Survivors n=99	Non- survivors n=76	p value
Length of hospital stay, in days (SD)	12.89 (8.29)	12.07 (6.26)	13.96 (10.31)	0.161
Delay to surgery, in days (SD)	3.51 (2.42)	3.30 (2.22)	3.79 (2.65)	0.2
Prosthesis *n* (%)	62 (35.4)	34 (34.3)	28 (36.8)	0.427
Spinal anesthesia *n* (%)	171 (97.7)	96 (97)	75 (98.7)	0.415
Transfusion *n* (%)	102 (58.3)	57 (57.6)	45 (59.2)	0.475
Delirium *n* (%)	53 (30.3)	23 (23.2)	30 (39.5)	0.016
Patients with other complications *n* (%)	84 (48)	48 (48.5)	36 (47.4)	0.503
Discharge to a center *n* (%)	72 (41.1)	42 (42.4)	30 (39.5)	0.406
New fragility fracture	10 (5.7%)	8 (8.1)	2 (2.6)	0.111

Note: SD = *standard deviation*

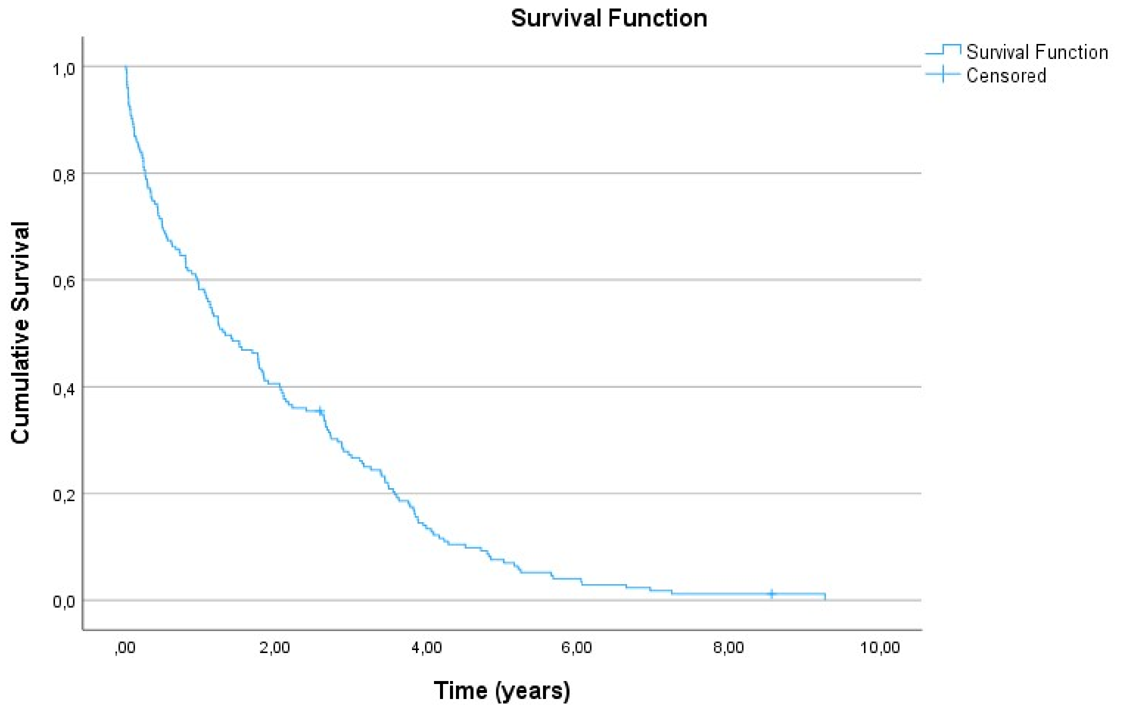
Table 3. Multivariate Cox regression analysis for risk factors for mortality at 1 year, and all post-discharge mortality.

	Hazard ratio	95% confidence interval	p
One year after discharge			
Male sex	2.488	1.420 - 4.358	0.001
Previous FAC* ≥ 3	2.291	1.417 - 3.703	0.001
Delirium	1.465	0.920 – 2.331	0.108
All post-discharge mortality			
Male sex	1.873	1.183 – 2.966	0.007
Previous FAC* ≥ 3	1.549	1.078 – 2.228	0.018
Delirium	1.003	0.718 – 1.400	0.988

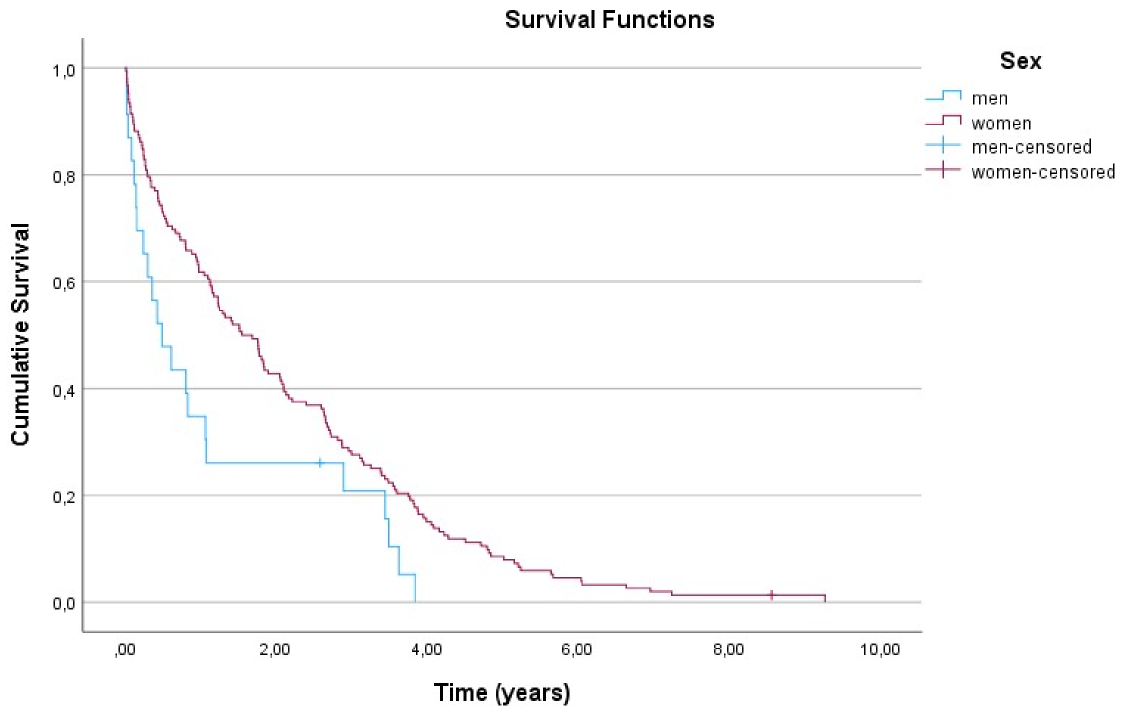
** Functional ambulation classification*

Figure 1

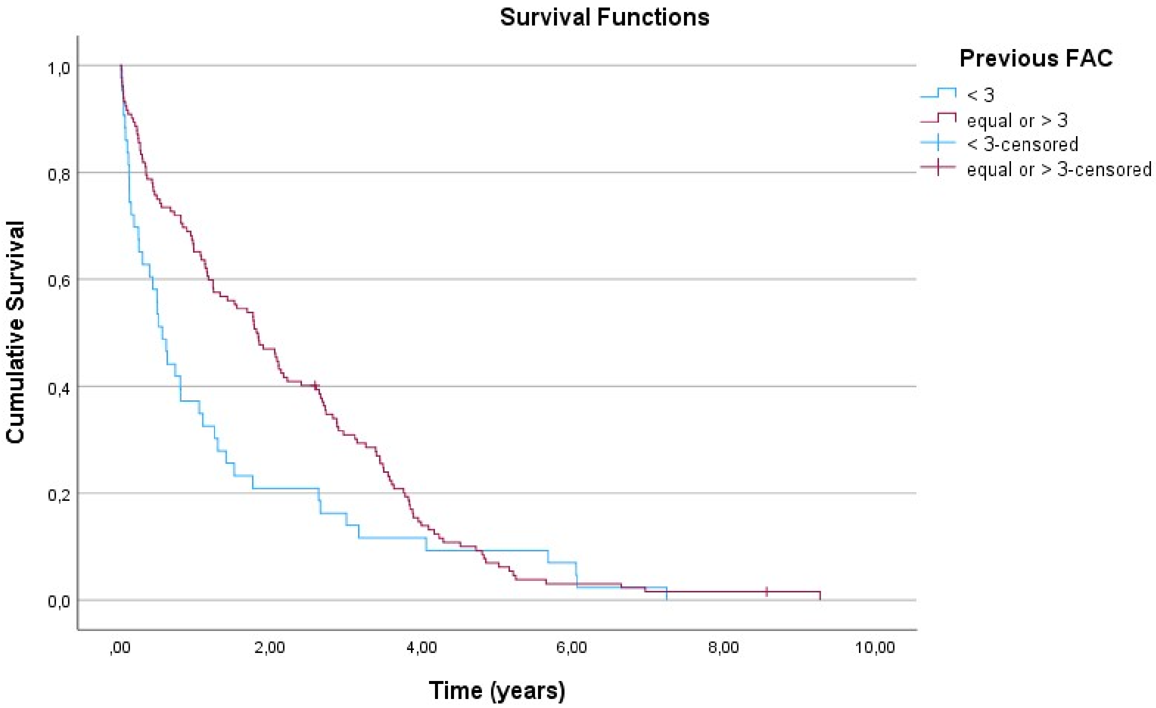
a. Cumulative survival after discharge



b. Cumulative survival after discharge according to sex



c. Cumulative survival after discharge according to previous ambulatory ability



** Functional ambulation classification*

Figure 2. New fragility fractures after discharge