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Research Article

Peripheral IL-6 Levels but not Sarcopenia Are Predictive of 1-Year Mortality After Hip Fracture in Older Patients

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Abstract

Background: Sarcopenic patients may have an increased risk of poor outcomes after a hip fracture. The objective of this study was to determine whether sarcopenia and a set of biomarkers were potential predictors of 1-year-mortality in older patients after a hip fracture.
Methods: About 150 patients at least 80 years old were hospitalized for the surgical treatment of a hip fracture. The primary outcome measure was the death in the first year after the hip fracture. Sarcopenia was defined at baseline by having both low muscle mass (bioimpedance analysis) and handgrip and using the updated European Working Group on Sarcopenia in Older People (EWGSOP2) definition of probable sarcopenia. Janssen's (J) and Masanés (M) cutoff points were used to define low muscle mass.
Results: Mortality 1 year after the hip fracture was 11.5%. In univariate analyses, baseline sarcopenia was not associated with mortality, using neither of the muscle mass cutoff points: 5.9% in sarcopenic (J) versus 12.4% in non-sarcopenic participants (p = .694) and 16% in sarcopenic (M) versus 9.6% in non-sarcopenic participants (p = .285). Probable sarcopenia (EWGSOP2) was not associated with mortality. Peripheral levels of IL-6 at baseline were significantly higher in the group of participants who died in the year after the hip fracture (17.14 ± 16.74 vs 11.42 ± 7.99 pg/mL, p = .026). TNF-α peripheral levels had a nonsignificant trend to be higher in participants who died. No other biomarker was associated with mortality.
Conclusions: Sarcopenia at baseline was not a predictor of 1-year mortality in older patients after a hip fracture. IL-6 was associated with a higher risk of mortality in these patients, regardless of sarcopenia status.

Key Words: Fragility fracture, Preoperative, Predictor, Outcomes, TNF-α

Sarcopenia (1) has been recognized as an independent condition by the International Classification of Disease-10 (2). Both sarcopenia and fragility hip fractures are common in older patients and can be linked with the recent concept of osteosarcopenia (3). It has been suggested that sarcopenic patients may have an increased risk of poor outcomes after a hip fracture, including worse functional recovery, institutionalization, and higher mortality (4,5). However, mortality has been explored in these studies as a composite outcome or in postacute settings, not when sarcopenia is assessed shortly after the hip fracture has occurred.

Very few studies have explored the role of blood biomarkers in predicting mortality after a hip fracture. A recent study identified biomarker signatures of all-cause and disease-specific mortality, from a comprehensive range of cytokines, chemokines, growth factors, glucose metabolism regulators and adipokines, adhesion molecules, acute-phase response, pathogen-specific antibodies, and bone remodeling. Stem cell growth factor-β and gastric inhibitory polypeptide were identified as specific biomarkers of mortality risk (6). A small prospective study with severe hip fracture patients exploring a large set of blood biomarkers found that plasmatic neopterin levels could predict mortality (7). We

have been unable to find prospective studies exploring the role of biomarkers that were performed in unselected hip fracture patients.

We have previously reported the prevalence of sarcopenia in very old patients admitted to an Orthogeriatric Unit for the surgical treatment of a hip fracture and the relationship of a range of neuromuscular and peripheral blood pro-inflammatory and oxidative stress markers with sarcopenic status (8,9). In this setting, we prospectively followed up participants for 1 year after the hip fracture. Here we report the value of sarcopenia and of blood biomarkers in predicting mortality in the year after the hip fracture occurred, based on their significance in previously published research and expert opinions regarding their potential prognostic value and/or their association with trauma/fracture/sarcopenia and practicability of assessment in a hospital routine.

Dysregulation of the posttraumatic inflammatory response may contribute to a high perioperative mortality rate of the older patients suffering from a hip fracture. For instance, it has been found that increased interferon gamma (IFN-γ)-induced inflammation presurgery is predictive of nonsurvival post-hip fracture and may even predict the time of survival after hip fracture surgery (7). In general, biochemical markers of inflammation are associated with increased mortality in older patients with hip fracture as high levels of the cytokines interleukin-6 and tumor necrosis factor alpha (TNF-α) are associated with a poor outcome, following hip surgery, and are related with an increased rate of bone resorption and incidence of hip fractures (10).

The ubiquitin–proteasome system (UPS) is a tightly regulated system responsible for the removal of short-lived normal proteins and misfolded and dysfunctional proteins (11). Increased proteolytic rates are a determinant of protein loss in direct muscle trauma. Thus, UPS is critical during muscle wasting and in critically ill blunt trauma patients, in which large proportions of muscle are exposed to direct trauma (12).

Glutathione (reduced form: GSH; oxidized form: GSSG) is a major contributor to the defense against reactive oxygen species. It has been shown that antioxidant status of serum correlate with trauma severity and its assessment may be useful to predict outcome after traumatic brain injury. For instance, higher serum GSH levels found on admission are associated with a better outcome (13). Reduction of plasma GSH level is a sensitive indicator for disturbed redox potential of the cells after polytraumatic injury in multiple organ failure patients (14).

After the occurrence of a fracture, lipid peroxidation levels are increased in older patients. A significant association between the plasma redox system and mortality has been observed. To contribute to tissue repair and survive in necrotic and ischemic tissue, cells express intrinsically high levels of antioxidative enzymes, including glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase activity (CAT) (15). Plasma GPx activity in participants who die within 1 year of screening is lower than those of survivors. In addition, the association of SOD activity with mortality in community-dwelling older adults has been studied and is considered as a prognostic biomarker for mortality in older women (16).

Butyrylcholinesterase (BuChE) is a performance metric of liver function, with lower activity reflecting more extensive liver injury (17). Decreased BuChE activity has been associated with severity and mortality in critically ill patients, with varying prognostic values for different diseases. Importantly, reduced BuChE activity indicates severe systemic inflammation in critically ill patients (18) and a higher risk of mortality within 1 year in HIV/AIDS patients (19).

Finally, C-terminal agrin fragment (CAF) has been proposed as a biomarker for age-associated sarcopenia originating from the degeneration of the neuromuscular junctions. In fact, elevated serum levels of CAF are associated with sarcopenia in older hip-fractured patients (20) and in multimorbid community-dwellers (21).

In short, there is ample evidence about the association of biochemical markers of inflammation with increased mortality in hip fracture patients. However, to the best of our knowledge, none has explored the relationship between the plasma proteasome activity, glutathione, BuChE activity, and CAF levels, respectively, and mortality in a select population of older adults with hip fracture. Then, we hypothesize that levels of each one of these biomarkers in the preoperative period are associated with 1-year mortality in our older hip fracture population.

Method

Setting and Participants

We prospectively recruited 150 older patients of at least 80 years old (mean age 87.6 ± 4.9 years, 78.7% were women) who were hospitalized in an acute orthogeriatric ward of a Spanish tertiary hospital for the surgical treatment of a fragility hip fracture and who agreed to participate in the study. Exclusion criteria were (a) emergency surgery before informed consent could be collected, (b) pacemaker carriers, (c) patients with active cancer, (d) patients who had received a blood transfusion before a blood sample for biomarkers' assays could be obtained, and (e) those who were unable to understand instructions to measure handgrip strength. A full description of the characteristics of these patients and peripheral biomarkers' levels have been published elsewhere (8,9). The prevalence of sarcopenia was 11.5% (10.3% in women and 16.1% in men), with Janssen's cutoff points and 34.9% (36.5% in women and 29% in men), with Masanés cutoff points, respectively. The concordance between both measures was low, with a kappa index of 0.316. Of the 77.5% who had independent ambulation before the fracture, 40% reported three or more recent falls. Before admission, 38% had dementia and 80.4% had mild to moderate dependence to basic activities of daily living (BADL) before admission; 14.2% were independent for all BADL. Mininutritional Assessment was suggestive of malnutrition in 12.6%, and 85.2% were on four or more prescribed drugs. Sarcopenic (Masanés) participants had a lower body mass index (BMI) than non-sarcopenic participants (18.6 vs 24.3, $p = .003$), but no other significant differences were found between both groups. The phase angle was also unrelated to sarcopenia status.

Data Collection

Assessment of participants at baseline (hospital admission) included socio-demographic data, cognitive status (Pfeiffer's questionnaire (22) and Global Deterioration Scale [Reisberg] (23)), pre-fracture (2 weeks prior to the fracture) functional status (Barthel index (24) and Functional Ambulation Categories [FAC] (25)), pre-fracture nutritional status (Mininutritional Assessment-short form (26); BMI, using the last reported weight and the Height Heel-Knee measure technique, to avoid mobilization with the fracture), number of reported falls, and medications.

Assessment of Sarcopenia

Diagnosis of sarcopenia was based on the European Working Group on Sarcopenia in Older People (EWGSOP) criteria (27), adapted to this setting, where physical performance (gait speed or the Short Physical Performance Battery) could not be measured, as all participants are unable to walk. Muscle mass was estimated preoperatively

using bioelectrical impedance analysis (BIA, Quantum/S Bioelectrical Body Composition Analyzer; Akern). Skeletal muscle index (kg/m^2) was calculated dividing absolute muscle mass by squared height. Two different cutoff points were used to define low muscle mass, proposed by Janssen (28) and Masanés (29) (these are based on a Spanish reference population). Muscle strength was also assessed preoperatively in all participants. It was assessed with handgrip strength using a handheld dynamometer (Jamar). The patients were bedridden, so they had to adopt a half-sitting position in bed and hold the dynamometer in the hand to be tested, with the arm at right angles and the elbow by the side of the body. The maximal value of three consecutive measurements in the dominant arm was used for the analysis. Low grip strength was defined as values less than 30 kg and less than 20 kg for men and women, respectively (27). The updated version of the European Working Group on Sarcopenia in Older People criteria (EWGSOP2) was published after the study was started (30), emphasizing the role of muscle strength, so we decided to add the EWGSOP2 definition of probable sarcopenia, with the new proposed cutoff points for handgrip strength (<27 kg for men and <16 kg for women, respectively) and no muscle mass measure in a new post hoc analysis.

Blood Sampling and Biochemical Measures

Fasting venous blood samples were collected from each patient in the morning, usually within 24 h after arrival and always before surgery.

Peripheral markers (pro-inflammatory and oxidative stress parameters) were determined either in the plasma or in the erythrocyte fraction obtained from peripheral whole blood of every patient.

IFNγ, IL-1β, IL-6, and TNFα cytokines

These cytokines were quantitatively determined using the Milliplex Multi-Analyte Profiling Human Cytokine/Chemokine Kit for 96-well assay (Millipore Corp., St. Louis, MO) run on a Luminex platform.

Chymotrypsin-like activity of the 20S proteasome

It was quantified in plasma fraction by monitoring the accumulation of the fluorescent cleavage product 7-amino-4-methylcoumarin (AMC) from a synthetic fluorogenic substrate (Suc-Leu-Leu-Val-Tyr-AMC; Sigma-Aldrich).

GSH, GSSG, and GSH:GSSG

Reduced glutathione (GSH) and its oxidized form (GSSG) were measured spectrofluorometrically in the erythrocyte fraction by using the *o*-phthalaldehyde method. The glutathione redox ratio GSH:GSSG was calculated from the determined GSH and GSSG.

Endogenous antioxidant enzymes

SOD was assayed by quantifying the inhibition of pyrogallol autoxidation at 420 nm. CAT was assayed in Triton X-100 (1%)-treated supernatants following the disappearance of H_2O_2 at 240 nm. One IU of SOD refers to the amount of enzyme that produces 50% inhibition in pyrogallol autoxidation. One IU of CAT is defined as the amount of enzyme that transforms 1 μmol of H_2O_2 per minute at 25°C and pH 7.4. Total GPx was determined following reduced Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidation at 340 nm in the presence of excess GR, GSH, and cumene hydroperoxide as substrate. GPx activity was expressed as substrate (nmol NADPH) transformed·per minute·per milligram protein.

BuChE activity

Assessment of BuChE activity was carried out using the Ellman's reaction, adapted for use with microtiter plates, by which the BuChE present in the plasma sample catalyzes the hydrolysis of butyrylthiocholine iodide and the resulting thiocholine product reacts with 5,5′-dithiobis (2-nitrobenzoic acid) (Sigma-Aldrich) to form a colored anion, 5-thio-2-nitro-benzoic acid.

C-terminal agrin fragment

It was determined in plasma fraction using a commercially available Enzyme-Linked Immunosorbent Assay kit (NT total CAF ELISA kit; Neurotune AG, Schlieren, Zurich, Switzerland) following the manufacturer's instructions.

Outcomes

The information on mortality, functional situation, and the number of visits to the emergency department and hospitalizations a year after the hip fracture was collected from the hospital's electronic medical record, the electronic medical record of the primary care physician, and from a telephone call made to the contact telephone number provided at the beginning of the study.

Regarding the date of death, the electronic medical record of the hospital and that of the primary care physician was reviewed; the phone call was only made in those cases where there was no record of the date of death.

During those phone calls, the patient himself or the main caregiver was asked about the functional situation a year after the hip fracture. The following data were collected: Barthel, Lawton, FAC, type of technical assistance at home as well as for going out into the street, number of falls in the last year, number of visits and hospitalizations in the last year, and, finally, with whom the person lived a year after the hip fracture. In the cases that institutionalization had been required, the date of admission into the nursing home was also recorded.

Statistical Analyses

All analyses were performed using Stata software version 13.0 (Stata Inc., College Station, TX). Results for quantitative variables were described by mean and standard deviation and for qualitative variables by the absolute and relative frequency.

Bivariate analysis was used to compare the results from participants with and without sarcopenia, using the three definitions. The Student's *t* test or the Mann–Whitney test was applied for quantitative variables, and the chi-square (χ^2) test was used for qualitative variables. A *p* value of less than .05 was considered significant.

Both the analysis of the main outcome measure and the analysis of the secondary measures have been approached by performing (a) a univariate analysis in order to find possible associations of markers and basal variables with the dependent variable and (b) an analysis to test whether the effect is maintained simultaneously among all possible independent variables identified.

A multivariate Cox regression analysis of all variables that showed statistical significance in the preceding bivariate analysis was performed. The probability of death was calculated using the Kaplan–Meier survival analysis and Cox regression (hazard ratio [HR], 95% confidence interval [CI]).

Ethical Approval

The study was approved by the Ethical Committee of the Hospital Universitario Ramón y Cajal in July 2014. All participants signed a

written consent before enrollment. For participants with cognitive impairment, a proxy family member signed the consent.

Results

Characteristics of Participants

A full description of the baseline characteristics of the 150 participants has been already published (8). In brief, the mean age was 87.6 ± 4.9 years, 78.7% were women. The prevalence of sarcopenia depends on the cutoff points used to define low muscle mass, that is, 11.5% using Janssen's U.S. cutoff points and 34.9% using Masanés' cutoff points for Spain. Sarcopenic and non-sarcopenic participants were similar in most baseline characteristics; the only exception was a lower BMI in sarcopenic participants with sarcopenia defined by Masanés' cutoff points. The prevalence of probable sarcopenia using the EWGSOP2 definition was 93.3% (94% and 90.3% in women and men, respectively).

Biomarkers

A set of biomarkers was explored, and the baseline findings and the relationship between biomarkers and sarcopenia have been published elsewhere (9). We found no associations of sarcopenia with most neuromuscular, pro-inflammatory or oxidative stress markers, except for lower peripheral TNF-α levels and CAT in sarcopenic participants.

Mortality

One-year mortality was 11.5%, as the acute inhospital mortality was 1.3%. Median survival was 11.2 months (95% CI 10.8–11.7) (Figure 1). In univariate analyses, baseline sarcopenia was not associated with mortality, using either of the muscle mass cutoff points: 5.9% in sarcopenic (Janssen) versus 12.4% in non-sarcopenic participants (p = .694) and 16% in sarcopenic (Masanés) versus 9.6% in non-sarcopenic participants (p = .285). Using the reference cutoff points for probable sarcopenia measured with handgrip strength, following the recommendations of EWGSOP2 criteria, baseline probable sarcopenia was also not associated with mortality (Table 1).

IL-6 peripheral levels were significantly higher in the group of participants who died in the year after the hip fracture (17.14 ± 16.74 vs 11.42 ± 7.99 pg/mL, p = .026). Similarly, TNF-α peripheral levels had a nonsignificant tendency to be higher in participants who died (Table 2). No other biomarker was associated with mortality. The median survival in participants with IL-6 less than 13 was 11.4 months (95% CI 10.8–11.9), whereas it was lower in participants with IL-6 at least 13, with a median survival of 11.1 months (95% CI 10.2–11.9) (Figure 2).

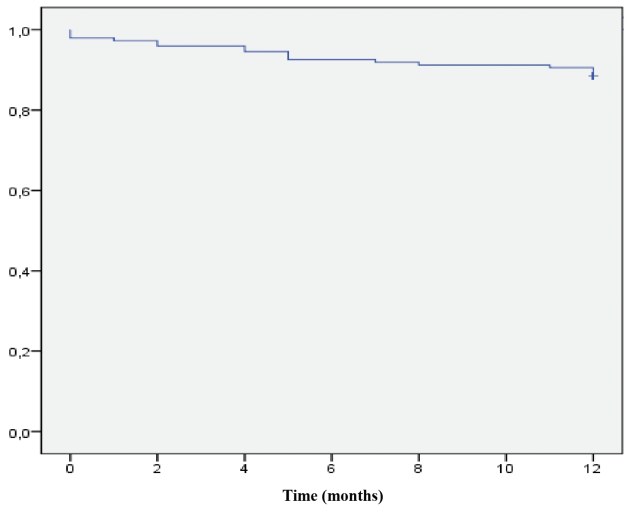

Figure 1. Cox survival regression (Kaplan–Meier curves).

Discussion

In the present study, we assessed outcomes 1 year after discharge in older people who were admitted for the surgical treatment of an osteoporotic hip fracture. Particularly, we only correlated laboratory variables recorded at admission to hospital (presurgery) to 1-year mortality in this study. Therefore, possible effects on mortality because of medications added later, complications, or later surgical or endovascular interventions cannot be evaluated from this study but might be elucidated by further follow-up.

One-year mortality after discharge was low in our participants (11.5%) and certainly lower than the prevalence found in other studies in which it ranged from 12.1% to 36% (31–37). Even in a study performed in a population quite similar to ours, mortality was 23.2% (36). This difference could be partly due to our exclusion of patients with cancer or in need of palliative care. Only one study from Ireland found the 1-year mortality of 12.1%, very close to the one we found (37). In those studies, mortality during acute hospital stay ranged from 2% to 4.1%, whereas in our study it was 1.3%. In a systematic review and meta-analysis of 75 included studies with 94 publications involving 64,316 patients, the follow-up period varied from discharge to 5 years and 48% of the included studies were 12 months. The 1-month inpatient mortality was 13.3% (calculated by a total of 20,988 patients, 1.2%–16.3%) and 1 year was 24.5% (total 31,895 patients, 7.8%–35%).

In our study, sarcopenia (defined as low muscle mass with alternative cutoff points and low muscle strength) was not associated with 1-year mortality. In contrast, previous studies found that sarcopenia on hospital admission, defined by EWGSOP2 criteria, was associated with an increased risk of 3-year mortality (HR 2.08; 95% CI 1.38–3.16) (38). A recent systematic review showed that sarcopenia is a risk factor for mortality (pooled OR 3.596), with a higher effect in those older than 80 years, with only 2 of 12 studies not showing this association (39). Furthermore, another recent study showed that sarcopenia strongly predicts all-cause mortality and composite adverse outcomes (falls, emergency department visits, institutionalization, and hospitalization) among older Taiwanese adults, in a cohort of 728 older participants with a mean age of 73.4 and nearly 53% males, during a mean follow-up of 32.9 months (40). It is therefore evident that the association between sarcopenia and mortality seems to be reduced with shorter follow-up periods (41). To date, most studies have been performed in nonacute settings. Moreover, studies of the association of sarcopenia and mortality performed in surgical settings usually define sarcopenia as low muscle mass and, therefore, participants may well have other conditions defined by low muscle mass, such as malnutrition or cachexia, which have been found to predict death (42,43). In some of those studies, only hospital mortality was considered (44). Two retrospective studies in hip fracture patients have shown an association between some computed tomography scan muscle parameters (psoas cross-sectional area, decreased thoracic paravertebral muscle size, and attenuation) and 1-year mortality (45,46). The only study using a definition

Table 1. Relationship Between Probable Sarcopenia (EWGSOP2 Criteria) and 1-Year Mortality

	Women			Men		
Mortality	Probable Sarcopenia (n = 103)	Non-Sarcopenic (n = 16)	p	Probable Sarcopenia (n = 127)	Non-Sarcopenic (n = 3)	P
No	88.3%	89.5%		88.2%	100%	
Yes	11.7%	10.5%	1.000	11.8%	0%	1.000

Note: EWGSOP = European Working Group on Sarcopenia in Older People.

Table 2. Peripheral Biomarkers From Participants Within 1 Year of Hip Fracture

	Mortality		
Biomarker	Yes	No	p
IFNγ (pg/mL)	6.46 ± 6.14	8.32 ± 7.93	.181
IL-1β (pg/mL)	1.7 ± 2.6	1.26 ± 1.14	.156
IL-6 (pg/mL)	**17.14 ± 16.74**	**11.42 ± 7.99**	**.026**
TNFα (pg/mL)	10.28 ± 9.59	7.62 ± 4.81	.058
20S (nmol AMC/mg protein)	14.22 ± 4.33	13.23 ± 5.22	.834
Nanomole GSH/mg protein	67.81 ± 26.24	51.53 ± 26.16	.748
Nanomoles GSSG/mg protein	2.95 ± 1.85	2.54 ± 1.45	.975
GSH:GSSG	33.18 ± 25.65	24.55 ± 14.93	.709
CAT activity (IU/min/mg protein)	3,798.19 ± 1,606.76	3,358.31 ± 1,463.97	.276
SOD activity (IU/mg protein)	11.86 ± 6.15	16.75 ± 11.75	.165
GPx activity (nM NADPH/min/mg protein)	102.27 ± 41.67	104.51 ± 89.86	.456
BuChE activity (IU/mg protein)	2.21 ± 0.67	2.43 ± 1.05	.229
CAF (pM)	730.28 ± 1,140.37	391.47 ± 554.69	.52

Note: AMC = 7-amino-4-methylcoumarin; GPx = glutathione peroxidase; SOD = superoxide dismutase; CAT = catalase activity; BuChE = butyrylcholinesterase; CAF = C-terminal agrin fragment; GSH = reduced glutathione; GSSG = oxidized form of glutathione IFN=interferon; IL=interleukin; TNF=tumor necrosis factor.

of sarcopenia that included muscle function did not find higher mortality in sarcopenic but did so in osteosarcopenic participants (47).

In fact, there may be a differential effect on mortality according to the different elements that are part of the definition of sarcopenia. In our study, probable sarcopenia defined as low grip strength was not associated with 1-year mortality. However, a recent cohort study with 509 older hip fracture patients (mean age 85.6 years) using a multivariate model found eight independent mortality risk factors including grip strength, but none of the body composition parameters remained significant after adjustment for other baseline characteristics (36).

We found that most of the biomarkers measured at hospital admission were not either associated with 1-year mortality. The only biomarker associated with mortality was IL-6, along with a nonsignificant trend for TNF-α. In our sample of patients, we have already reported that there was no correlation between IL-6 peripheral levels and sarcopenia (9), in contrast to the report shown by Bian and colleagues (48).

Although preoperative IL-6 levels were a possible predictor of mortality in our study, this was not confirmed in the study of Saribal and colleagues (49). They have only demonstrated higher postoperative plasma levels of IL-6 and TNF-α compared with healthy controls in a small sample of hip fracture patients (n = 40) with a lower mean age (74 ± 1 years) than ours (87.6 ± 4.9 years). Otherwise, previous studies with a higher number of participants have found a relationship between those cytokine levels and mortality (50).

Somewhere else, in the MEMO Study, with a more or less balanced ratio of men and women, IL-6 plasma levels at baseline have been associated with all-cause mortality in older male participants, whereas in women, no associations with mortality for IL-6 were found (51). In the fact that we did not find differences between women and men, we should point out that the percentage of women in our study was much higher (78.7%) and the absence of a detectable effect of sex could be explained by the small number of men.

Interestingly, an association between frailty and pro-inflammatory cytokines differing in a sex-specific manner has been found in naturally aging mice (52), which has not been well explored in humans. What is more, the recent ability to quantify frailty in animal models with tools developed for use in humans provides a translational platform for understanding the value of the sex-specific inflammatory cytokine profile as a predictive factor of mortality in humans. In light of this, we suggest that a future approach is needed to accomplish the assessment of a representative panel of either sex-specific peripheral cytokines in order to obtain a more real prognostic factor pattern for 1-year mortality.

In the study of Sun and colleagues (53), cytokine levels (TNF-α, IL-6, and IL-10) represent independent outcome predictors for adverse postoperative outcomes (mortality and complications) in older hip fracture patients. The authors concluded that the inflammatory response might play an important role in postoperative organ dysfunction in older hip fracture patients and suggested further studies to define whether decreasing the inflammatory response through cytokine antibodies or damage control strategies would decrease mortality and complications following hip fracture.

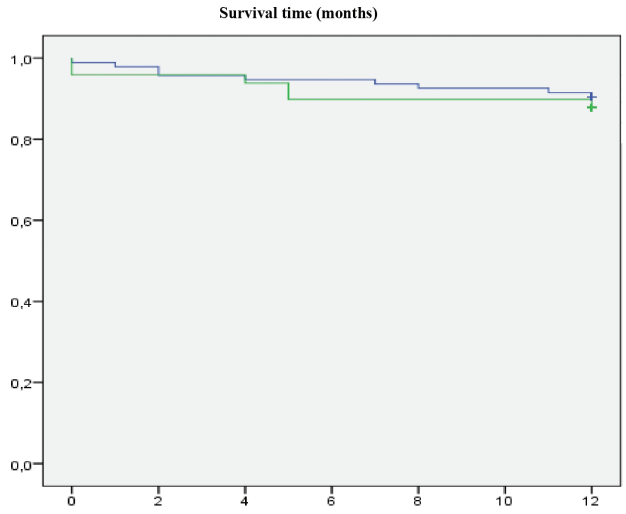

Figure 2. Cox survival regression (Kaplan–Meier curves) related to IL6 levels.

We acknowledge that this study had some limitations. Older age may attenuate differences between groups, as aging is associated with many of the proposed mechanisms that produce sarcopenia. The fact that all participants had an acute severe disease that triggers its own inflammatory and repair mechanisms may act as an additional confounder. For instance, based on the known association between high serum levels of IL-6 and cognitive decline from longitudinal population-based studies, it has been shown that older patients with hip fracture and hyperactive characteristics of delirium had higher IL-6 levels than the matched patients with hypoactive delirium (54). Also, hydro and electrolyte disturbances may appear after a hip fracture that may bias body composition assessment by BIA. Muscle mass measures may also have been altered in participants with heart or renal failure. Preoperative changes in BIA in hip fracture patients have not been well studied, but muscle mass has been found to be lower in such patients compared with healthy age, gender, and BMI-matched controls. The presence of infections, delirium or pain, and the use of medications that can affect the muscle strength may also falsely increase the number of participants with sarcopenia. Previous comorbidity could be a confounder in the multivariate analysis (37) and it was not assessed. Finally, we did not obtain a measure of frailty, which may have helped in the categorization of participants. Therefore, an increased risk for type 1 error may have resulted for not having measured the confounding variables referred and adjusted for them.

An important strength of this study lies in a large number of participants at a specific situation (a well-defined sample of older patients, with three different definitions of sarcopenia explored). Moreover, there were a few follow-up losses. Despite the results and conclusions achieved, our study included a wide panel of biomarkers and data on pre-hip fracture health and functional status with the aim of stratifying patients. Although the determination of biomarkers in the preoperative period might seem a limitation of the study because its pattern cannot be extrapolated to other settings, two aspects highlight the importance of determining them in this stage: (a) clinical significance, because their levels reflect the inflammatory state of the patients at admission and (b) hip fracture itself or pressure damage to muscles due to immobilization seems to play an important role in the excess inflammatory response. Nevertheless, we acknowledge that the inflammatory marker measurement may be of interest if performed prospectively, after surgery, as an association of them with increased mortality has been found by others.

Conclusions

Sarcopenia did not predict postdischarge 1-year mortality in this sample of older patients hospitalized for the surgical treatment of a hip fracture.

This study identified IL-6 peripheral levels as a potential biomarker for patients with a high risk of mortality after a hip fracture surgery, regardless of the sarcopenia status. Therefore, IL-6 may be considered as a possible predictor of 1-year mortality in this small sample of older hip fracture patients.

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Conflict of Interest

None declared.

The authors certify that they comply with ethical guidelines for authorship and publishing of the Journal.

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