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Nutrition and Inflammation Influence 1-Year Mortality of Surgically Treated Elderly Intertrochanteric Fractures: A Prospective International Multicenter Case Series

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Abstract

Introduction: Hip fracture is a common and devastating event in older adults causing increased dependence, comorbidity, and mortality. Since new surgical techniques have not significantly improved the mortality rate, a better understanding of patient risk factors could improve the treatment algorithm and outcomes. This prospective study aimed to document the 1-year survival rate of patients with intertrochanteric fracture treated surgically in Latin America and to investigate risk factors associated with 1-year mortality. **Patients and Methods:** Between January 2013 and March 2015, 199 patients were prospectively enrolled. Inclusion criteria were aged 60 years or older, isolated intertrochanteric fracture (AO/OTA 31-A), and time to surgery within 10 days after injury. The follow-up period was 1 year. The association between mortality and patient demographics, comorbidity, surgical details, and preoperative laboratory parameters was assessed using log-rank tests. **Results:** Twenty patients died by 365 days after surgery (including 5 that died within 30 days of surgery) resulting in a 1-year survival rate of 89.8% (95% confidence interval = 84.6-93.3). The 1-year mortality was significantly associated with age ($\geq$85 years old, $P = .032$), existing comorbidity ($P = .002$), preinjury mobility level ($P = .026$), mental state (Mini-Mental State Examination > 23, $P = .040$), low preoperative plasma albumin level ($P = .007$), and high preoperative blood C-reactive protein level (CRP; $P = .012$). At the 1-year follow-up, patients on average did not regain their preinjury hip function and mobility, although the self-assessed quality of life was equal or better than before the injury. **Discussion:** As a prospective study, the current patient population had clear inclusion and exclusion criteria and was relatively homogeneous. The resulting associations between 1-year postoperative mortality and preoperative hypoalbuminemia and preoperative elevated CRP level are therefore especially notable. Previously identified risk factors such as male gender and time to surgery showed no significant association with 1-year mortality—the overall favorable condition of the current population or the lack of statistical power maybe responsible for this observation. **Conclusion:** The current results showed that under the condition of optimal surgical treatment and low surgery-related complication, preinjury health status as indicated by the blood level of albumin and CRP has a direct and significant impact on 1-year mortality rate.

Keywords
hip fracture, mortality, albuminemia, C-reactive protein, CRP, risk factor

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Introduction

Hip fracture is a common and serious event in older adults. About 40% of all hip fractures in older adults are inter- (per-) trochanteric fractures, and women seem to be at greater risks of intertrochanteric fractures than men. In the United States, intertrochanteric femoral fractures occur in over 80 per 100 000 patients annually, with almost constant mortality rates of 15% to 30%.[1] Due to hospitalization and increased patient dependence, comorbidity, and mortality, such fractures pose a serious burden to the society.[2] The increase in life expectancy

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and high prevalence of osteoporosis are associated with an alarming forecast that estimates up to 20 million cases by 2050.[3] Worldwide, health-care costs associated with hip fractures can reach roughly 130 billion dollars by 2050.[2] A registry in Argentina showed an increase in the incidence of hip fractures by 1.4% in 2015, afflicting 64.6 per 10 000 individuals.[4]

It must be noticed, however, that the mortality rates can vary widely among studies, presumably due to geographical or regional differences, different health-care practices in different countries, and socioeconomic settings.[5,6] This leads to the question what the variables are that contributed to the differences. Presumably, both the general health of patients before the injury and the quality of care affect the outcome.

A large body of literature has been published on the subject of predictors for postoperative mortality after hip fractures. In combination, these publications have identified a long list of potential predictors such as age, gender, type of residency, American Society of Anesthesiologists (ASA) grading, mental state, prefracture mobility, degree of comorbidity, time to surgery, type of fracture, and surgical details. Unfortunately, the results from studies don't always agree with one another (very likely due to the retrospective nature of most of the studies), leaving the predictive power of many of these "predictors" questionable. In addition, some of these better-accepted predictors, such as age and gender, are "patient" factors that health-care practitioners have no influence over and cannot optimize. Not to mention from one study to another, the palette of risk factors assessed could be quite different except for the common ones such as patient demographics and the type of fracture.

Preoperative patient optimization is another area of discussion. It has been pointed out that surgery delay may be justified under conditions when preoperative optimization (eg, to correct anemia or electrolyte imbalance) could improve the outcome.[7-9] However, several recent studies pointing to an association between excessive mortality and laboratory results such as hyponatremia and low hemoglobin count[10-12] led to the criticism that these conditions are simply markers of other underlying diseases, and they may or may not be risk factors associated mortality on their own.[7,13,14]

It has been shown previously that mortality and functional outcomes after hip fracture surgery vary according to fracture types.[15,16] Such differences were observed not only between intra versus extracapsular fractures but also between intertrochanteric versus femoral neck fractures. Patients with intertrochanteric fractures were suspected to be older and had less functional recovery.[16,17] These interpretations, however, could not be confirmed due the differences in baseline characters of different study populations.[16] In the current study, we decided to focus on this presumed more fragile population of intertrochanteric fracture patients and attempted to address the role of a broad spectrum of potential mortality predictors (demographic, surgery aspects, and a comprehensive preoperative evaluation) via a prospective study. With stringent inclusion and exclusion criteria, we expect that the results may better establish laboratory parameters in predicting outcomes after hip fracture surgery.

Patients and Methods

Registration and Ethics

Ethical approval from all local authorities was obtained. This study was conducted in accordance with the ethical principles set forth in the Declaration of Helsinki including amendments as well as the International Council for Harmonization Good Clinical Practice guidelines, the European Standard EN ISO14155/2003-2011, and the laws and regulations of the individual countries where the research was conducted. The ClinicalTrials.gov Identifier is NCT01650064NCT01316289.

Study Design

The current study was a prospective multicenter observational consecutive case series study with a follow-up (FU) period of 12 months (up to 425 days).

Setting. Between January 2013 and March 2015, patients were enrolled in 6 different medical institutions from 5 Latin America countries, namely, Argentina, Chile, Colombia, Ecuador, and Uruguay. The eligibility of patients was determined by each institution. Of the 6 participating institutions, 4 were dedicated to private patients, one included both private and public patients, and one was designated for public patients. All source data were entered by the study site staff into a web-based Electronic Data Capture system, which is managed by the AO Foundation Clinical Investigation and Documentation.

Inclusion criteria. Patients included in the study were those 60 years or older, diagnosed according to the AO/OTA Fracture and Dislocation Classification with an isolated intertrochanteric fracture (31-A) confirmed by radiographic evaluation, without history of prior fractures or surgical treatment in the affected hip, and underwent surgical repair within 10 days after injury. Patients (or their legally authorized representatives) must be able to understand and sign the informed consent form (ICF) and be willing and able to participate in the study according to the study protocol.

Exclusion criteria. Patients who sustained pathological fracture or polytrauma were excluded from the study. Additional exclusion criteria were patients with active malignancy, neurological and/or psychiatric disorders, physical status of class V or VI according to the ASA classification, recent history of substance abuse or prior implant on the fractured hip, participated in other medical study within the previous month, or failed to complete the patient baseline questionnaire were excluded from the study. Prisoners were also excluded from the study.

Intervention. Patients participating in this study received treatments according to the standard practice of individual clinics. The intertrochanteric fracture fixation surgeries were performed according to the routine treatment protocol at the clinics, and surgical approach was done according to the treating surgeon's preference. Similarly, postoperative care was done according to the standard practice of the institutions.

Patient demographics, comorbidities, and other baseline data. Aside from patients' gender, age, and body mass index (BMI), their baseline (preinjury) status was documented using the ENhancing Recovery In Coronary Heart Disease patients (ENRICHD) social support inventory,[18] Barthel index,[19,20] Mini-Mental State Examination (MMSE),[21,22] Charlson comorbidity index (CCI),[23,24] and ASA classification.[25] Fractures were classified by the investigators according to the AO/OTA system using the preoperative radiographs. Injury and surgical details such as fracture type (open or close), time between injury and surgery, type of anesthesia, and duration of surgery were recorded. Blood sodium, potassium, C-reactive protein (CRP) levels, plasma troponin T, albumin levels, and creatinine clearance were included as part of the routine preoperative blood tests.

Outcome Measures

Primary outcome measure. The primary outcome of this study was time to death up to 365 days after surgery.

Secondary outcome measure. Comorbidities, surgical, and laboratory parameters were evaluated for mortality analysis; functional outcomes were assessed using Modified Harris Hip Score (MHHS)[26,27] and Parker Mobility Score (PMS);[28] and quality of life (QoL) was assessed using EQ-5D-5 L (EQ-5D index) and EQ visual analogue scale[29,30] (EQ VAS) questionnaires (validated Spanish patient questionnaires were employed for the study).EQ-5D index, EQ VAS, and PMS were assessed at baseline (preinjury), 90-day (±21 days) FU, and 365-day (up to 425 days) FU. Modified Harris Hip Score was assessed at baseline and the 90-day (±21 days) FU.

Adverse events. The timing and handling of adverse events (AEs) were recorded and assessed for their cause and relation to the surgical treatments.

Statistical Analysis

A sample size of 200 patients was chosen on the grounds of feasibility and based on the expected precision of the survival rate estimate. Assuming a 10% dropout rate for reasons other than mortality and a plausible range of survival proportions between 0.95 and 0.70, the width of the exact binomial 95% confidence interval (CI) was expected to be between 0.07 and 0.14. This precision was considered adequate to meet the primary objective of the study.

All enrolled patients deemed eligible were included in the analysis for both the primary and secondary outcomes. For the survival analysis, the data from the 37 patients who completed the 365-day follow-up before 365 days were considered censored after their last visits. These data, however, still contributed to the analysis. To ensure that punctuality of the FUs did not influence the results of the secondary outcomes, a sensitivity analysis excluding unpunctual assessments was performed for the secondary end points. Survival rates were calculated using the Kaplan-Meier method. Kaplan-Meier curves and log-rank tests were used to analyze the association between 1-year mortality and potential risk factors. For the analysis of secondary outcomes measured at more than 2 time points, mixed effects models for repeated measures with an unstructured covariance matrix were used. Change in MHHS between preinjury and 90 days after surgery was analyzed using a paired *t* test. Value of $P < .05$ was considered statistically significant. All analyses were performed using the software SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

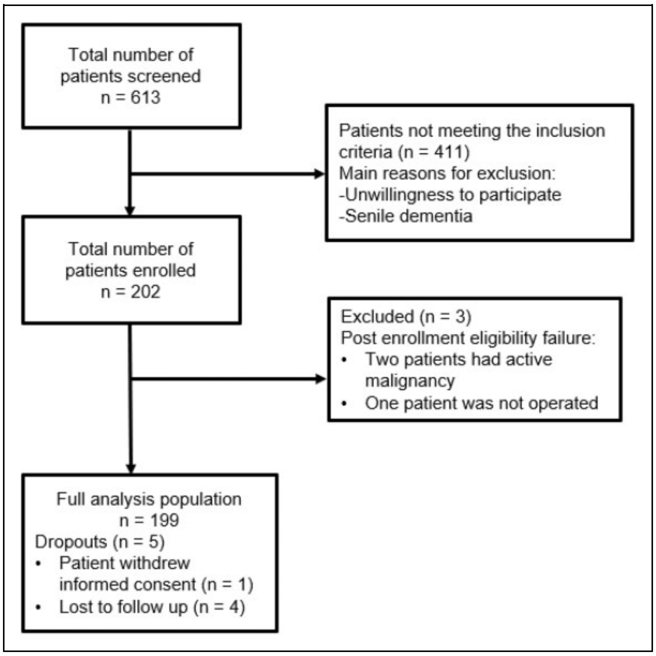

Figure 1. Patient recruitment flow diagram.

Results

Patients

In total, 613 patients with intertrochanteric fractures were screened, and 202 patients signed an ICF. Among these, 3 were excluded due to active malignancies or the cancelation of surgical treatment. Of the remaining 199 eligible patients and excluding the deaths, 5 eventually dropped out (1 withdrew the consent and 4 for unknown reasons, 2.51%; Figure 1).

Patients were predominantly female (87.9%), and the mean (standard deviation) patient age was 83.5 (7.5) years (Table 1). Before the injuries, the majority of the patients were of good mental health (normal mental state, 36.0% and mildly impaired, 31.5%) and relatively independent in performing

Table 1. Baseline Patient Demographic and Comorbidity.

	N = 199
Gender, n (%)	199
Female	175 (87.9)
Male	24 (12.1)
Age, years, n	199
Mean (SD)	83.5 (7.5)
Body mass index, kg/m^2, n (%)	197
Mean (SD)	24.4 (3.4)
<18.5	5 (2.5)
18.5 to <25.0	112 (56.9)
25.0 to <30.0	69 (35.0)
≥30.0	11 (5.6)
ENRICHD social support inventory score, n (%)	194
Mean (SD)	28.1 (4.1)
6-18	2 (1.0)
19-34	192 (99.0)
Barthel Index, n	199
Mean (SD)	84.0 (18.5)
Mini-Mental State Examination score, n	197
Mean (SD)	21.4 (6.5)
≤9	16 (8.1)
10-20	48 (24.4)
21-24	62 (31.5)
25-30	71 (36.0)
Charlson Comorbidity Index,[a] n (%)	197
Median (Q1; Q3)	1.0 (0.0; 1.0)
0	97 (49.2)
1	52 (26.4)
2	24 (12.2)
3	15 (7.6)
4	6 (3.0)
5	2 (1.0)
6	1 (0.5)
ASA score, n (%)	199
I A normal healthy patient	5 (2.5)
II A patient with mild systemic disease	133 (66.8)
III A patient with severe systemic disease	56 (28.1)
IV A patient with severe systemic disease that is a constant threat to life	5 (2.5)
Place of residence prior to admission, n (%)	199
At home without support (independent)	153 (76.9)
At home with caregiver support	40 (20.1)
Nursing home	5 (2.5)
Other	1 (0.5)

Abbreviations: ASA, American Society of Anesthesiologists; ENRICHD, ENhancing Recovery In Coronary Heart Disease patients.
[a]The minimum possible score is 0 and maximum, 29. A higher score indicates a greater burden of comorbid conditions. ENRICHD social support inventory: The scores range from 6 to 34; higher scores indicate greater level of social support. Scores between 6 and18: low social support, 19-34: reasonable social support. Barthel Index measures patients' functional independence in activities of daily living. Scores range from 0-100; higher score reflects greater degree of independence. Mini-Mental State Examination evaluates patients' cognitive state; scores range from 0 to 30; lower scores indicate greater deficits. Scores greater than or equal to 25 points: effectively normal. Scores ≤ 9 points: severe cognitive impairment, 10-20 points: moderate cognitive impairment, 21-24 points: mild cognitive impairment. Charlson Comorbidity Index: Scores range from 0 to 29. A higher score indicates a greater burden of comorbid conditions.

Table 2. Injury and Surgical Details.

	N = 199
AO fracture classification, n (%)	
AO 31-A1	59 (29.6)
AO 31-A2	114 (57.3)
AO 31-A3	26 (13.1)
Fracture type, n (%)	
Closed	199 (100.0)
Open	0 (0.0)
Time from injury to hospital admission (days)	
Median (Q1; Q3)	0.0 (0.0; 0.0)
Time from injury until surgery (days)	
Mean (SD)	2.2 (1.8)
Type of anesthesia, n (%)	
General	51 (25.6)
Regional	148 (74.4)
Duration of surgery (skin-to-skin time, minutes), n	
Mean (SD)	55.4 (24.8)
Duration of hospital stay (nights)	
Median (Q1; Q3)	7.0 (5.0; 10.0)
Implant type, n (%)	
Nail	151 (75.9)
Plate	25 (12.6)
Plate MIPO	23 (11.6)

Abbreviation: MIPO, minimally invasive plate osteosynthesis; SD, standard deviation.

daily living activities (mean Barthel index score = 84.0 [18.5]). Of the 199 eligible patients, 160 (80.4%) patients were from private hospitals, 35 (17.6%) were from a hospital with mixed private and public patients, and 4 (2.0%) were from a public hospital.

All fractures in the study were closed fractures, with AO 31-A2 being the majority (57.3%) type, followed by AO 31-A1 (29.6%), and AO 31-A3 (13.1%). The majority of the patients (142 of 199) received surgery within 2 days of injury (mean = 2.2 [1.8] days) with a mean surgical time of 55.4 (24.8) minutes (Table 2). Except for 1 patient, all patients had suffered low-energy trauma. After discharge, 178 (89.4%) patients lived at home either independently (26.1%) or at home with caregiver (63.3%). Other demographic/health details and injury/surgical details are provided in Tables 1 and 2, respectively.

Primary Outcome

The 1-year survival rate for the current study was 89.8% (95% CI = 84.6-93.3); among the 20 patients who died by 365 days after surgery, 5 of them died within 30 days of surgery (Figure 2). The causes of death varied and were of no discernible patterns (Table 3). Four patients were reported by the families to have died at home with unknown causes.

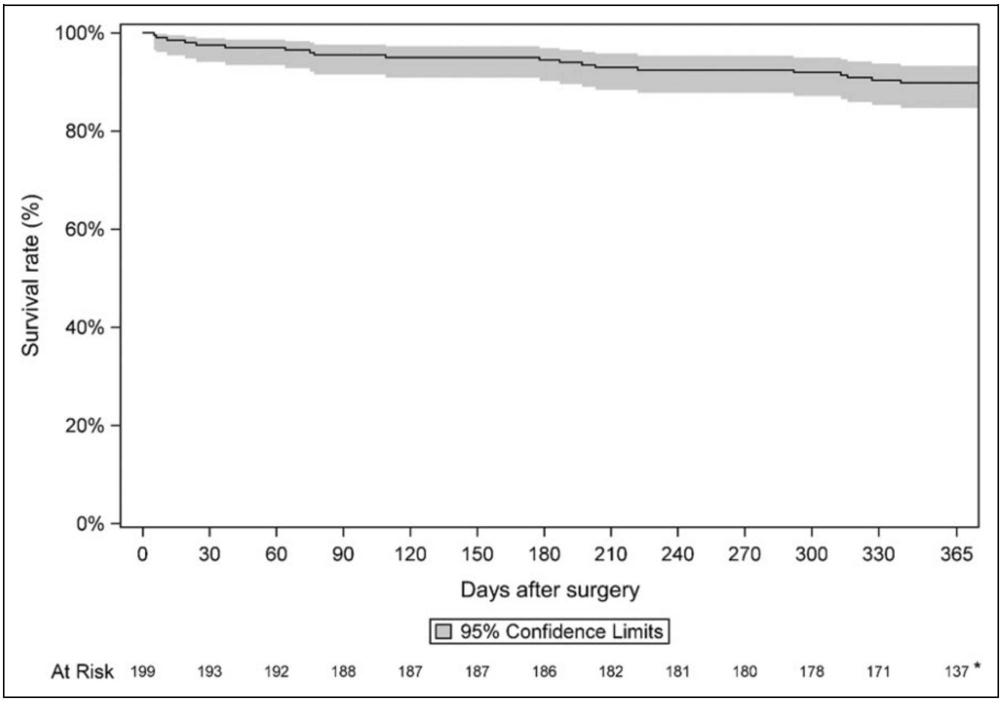

Figure 2. One-year survival rate: Kaplan-Meier analysis with number of patients at risk.
*Thirty-seven patients completed their 1-year visit too early (259–364 days after surgery), therefore the number of patients at risk at 365 days was 137 patients.

Table 3. Cause of Deaths Within 365 Days After Surgery.

Adverse Event (AE)	N = 20[a]
AE that lead to death, n (%)	20
Sepsis	1
Pneumonia	2
Bleeding (gastrointestinal, cerebral)	1
Cardiac (myocardial infarction, new arrhythmia)	1
Stroke	1
Unknown respiratory failure	1
Symptomatic hyponatremia	1
Heart failure, multiple organ dysfunction syndrome	1
Pancreas carcinoma	1
Bedsores	1
Acute pulmonary oedema	1
Bowel obstruction	1
Cardiogenic shock	2
Diabetic ketoacidosis	1
Unknown	4

[a]One patient died after the 365 days visit was done. As the death was caused by an adverse event started before the 365 days visit, the death was included in the analysis.

Secondary Outcome

Mortality analysis. The association between potential risk factors and 1-year mortality was investigated using the Kaplan-Meier analysis and log-rank test (Figure 3A-F and Table 4). Results showed that patients aged 85 years or older ($P = .032$) with existing comorbidity according to CCI ($P = .002$), PMS scoring ≤ 6 ($P = .026$), low preoperative plasma albumin level ($P = .007$), high preoperative blood CRP ($P = .012$), and cognitive impairment (MMSE score $\leq$ 23,[31] $P = .040$) had lower expected 1-year survival rate. A closer examination of Figure 3F also indicates that blood CRP level was associated with late (60 days postoperative) mortality. Factors such as gender, BMI, history of diabetes, history of cardiovascular diseases, time to surgery, and preoperative blood sodium level showed no statistically significant association with 1-year mortality (Table 4).

A sensitivity analysis was also performed to compare the Argentinian against other study centers (the Argentinian site alone contributed 99 of the 199 patients enrolled), and the result showed that there was no statistical difference in the 1-year mortality rates ($P = .578$).

Mobility, pain, and hip function. The preinjury PMS results (mean score = 6.7, 95% CI = 6.35-7.05) showed that patients were on average relatively mobile and could handle indoor/outdoor walking and shopping with some aid. The preinjury MHHS results (mean score = 81.6, 95% CI = 78.7-84.6) showed that patients had on average relatively low level of hip pain and good hip functions (Table 5). Table 5 also shows that patients on average did not regain their mobility at the 365-day FU. In comparison to preoperative PMS, the 365-day PMS had decreased by 1.02 points (95% CI = 0.63-1.42, $P < .001$). Modified Harris Hip Score was assessed at admission and at the

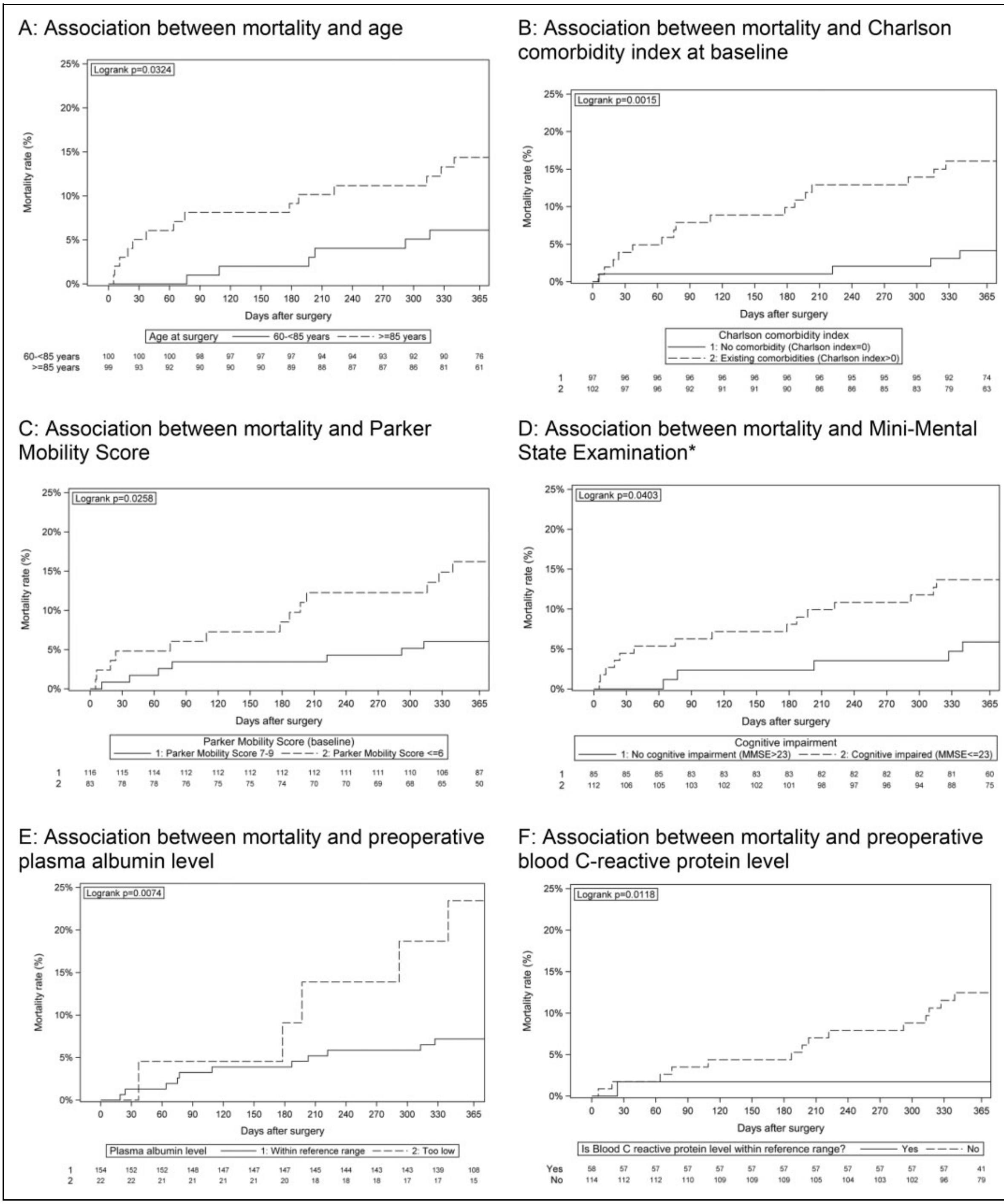

Figure 3. One-year mortality analyses: Kaplan-Meier curve with number of patients at risk.
*The cut-off point for the Mini-Mental State Examination was set at 23 based on the prevailing opinion and usage.[31]

90-day FU. Compared to preinjury, the mean MHHS at 90 days decreased by 10.8 points (95% CI = 7.3-14.4, $P < .001$).

Quality of life. The EQ-5D index scored showed that after a decline in patient QoL at 90 days (mean change from baseline, −0.11, 95% CI = −0.16 to −0.06, $P < .001$, Table 5), the QoL had returned to preinjury status at 365 days (mean change from baseline = −0.02, 95% CI = −0.08 to −0.03, $P = .444$). In contrast to the EQ-5D index results, EQ VAS results showed that patients' self-rated postoperative health state at 90 days ($P = .977$) did not change significantly compared to that at preinjury. At 365 days after surgery, the mean EQ VAS increased by 5.2 points (95% CI = 1.6-8.9,

Table 4. Association Between Potential Risk Factors and 1-Year Mortality.

Risk Factor	n	365 Days Survival in % (95% CI)	*P* Value (Log-Rank Test)
Age			.032
60-<85 years	100	93.9 (86.9-97.2)	
≥85 years	99	85.6 (76.9-91.2)	
Gender			.393
Female	175	90.7 (85.3-94.2)	
Male	24	83.3 (61.5-93.4)	
Body mass index			.973
<25	117	90.4 (83.4-94.6)	
≥25	80	88.6 (79.2-93.9)	
History of diabetes			.229
No	125	91.9 (85.5-95.6)	
Yes	45	84.2 (69.6-92.1)	
Cardiovascular disease			.109
No	168	91.6 (86.3-94.9)	
Yes	31	79.5 (59.9-90.3)	
Charlson comorbidity index			.002
>0	100	84.6 (75.8-90.4)	
0	97	95.9 (89.3-98.4)	
Parker Mobility Score (baseline)			.026
≤6	83	83.8 (73.7-90.3)	
7-9	116	94.0 (87.8-97.1)	
Cognitive impairment according to Mini-Mental State Examination[a]			.040
No (MMSE > 23)	85	94.1 (86.4-97.5)	
Yes (MMSE ≤ 23)	112	86.3 (78.3-91.5)	
AO fracture classification			.216
AO 31-A1	59	94.9 (85.1-98.3)	
AO 31-A2	114	88.5 (81.0-93.2)	
AO 31-A3	26	83.9 (62.6-93.7)	
Time between injury and surgery (days)			.735
≤2 days	142	90.8 (84.7-94.6)	
≥3 days	57	87.2 (75.0-93.7)	
Type of anesthesia			.369
General	51	92.0 (80.0-96.9)	
Regional	148	89.0 (82.7-93.1)	
Preoperative plasma troponin T level[b] within reference range			.742
No	48	91.6 (79.1-96.8)	
Yes	124	88.6 (81.6-93.1)	
Preoperative creatinine clearance			.202
Standardized creatinine clearance ≥ 30, mL/min	115	92.0 (85.3-95.8)	
Standardized creatinine clearance < 30, mL/min	81	86.3 (76.6-92.1)	
Preoperative blood sodium level[b]			.213
Within reference range	155	91.5 (85.8-95.0)	
Too low	38	86.8 (71.2-94.3)	
Preoperative blood potassium level[b] within reference range			.335
No	27	85.2 (65.2-94.2)	
Yes	166	91.4 (86.0-94.8)	
Preoperative plasma albumin level[b]			.007
Within reference range	154	92.8 (87.4-96.0)	
Too low	22	76.6 (52.5-89.5)	
Preoperative blood C-reactive protein level[b] within reference range			.012
No	114	87.5 (79.9-92.4)	
Yes	58	98.3 (88.4-99.8)	

Abbreviation: MMSE, Mini-Mental State Examination.
[a]The cut-off point for the Mini-Mental State Examination (MMSE) was set at 23 based on the prevailing opinion and usage.[31]

$P = .005$) in comparison to the preinjury value, indicating that on average patients felt better than before the injury. To assess the influence of FU punctuality on the secondary outcomes, the same analyses were performed using only the punctual data. Results showed that punctuality did not change the results of the analyses.

Table 5. Patient Recovery During Follow-Up.

Visit	Mean (95% CI)	Change (95% CI)[a]	P Value
Parker Mobility Score[b]			
Preinjury, n = 199	6.70 (6.35-7.05)		
90 days, n = 139	4.72 (4.33-5.11)	−1.98 (−2.40 to −1.55)	<.001
365 days, n = 156	5.67 (5.31-6.04)	−1.02 (−1.42 to −0.63)	<.001
Modified Harris Hip Score			
Preinjury, n = 198	81.6 (78.7-84.6)		
90 days, n = 143	70.8 (68.1-73.5)	−10.8 (−14.4 to −7.3)	<.001[c]
EQ-5D index score[b]			
Preinjury, n = 198	0.71 (0.67-0.76)		
90 days, n = 143	0.60 (0.56-0.65)	−0.11 (−0.16 to −0.06)	<.001
365 days, n = 155	0.69 (0.65-0.74)	−0.02 (−0.08 to 0.03)	.444
EQ-5D VAS[b]			
Preinjury, n = 192	67.8 (65.1-70.5)		
90 days, n = 121	67.8 (64.4-71.3)	0.1 (−3.7 to 3.8)	.977
365 days, n = 137	73.0 (70.4-75.6)	5.2 (1.6 to 8.9)	.005

Abbreviations: CI, confidence interval; VAS, visual analogue scale.
[a]Change refers to change from the baseline (preinjury) value.
[b]Estimates, confidence intervals and p-values derived from a mixed model for repeated measures with an unstructured covariance.
[c]paired t-test Parker Mobility Score (PMS) is a composite score of the patient's ability to perform indoor walking, outdoor walking, and shopping. PMS ranges 0 (no walking ability at all) to 9 (fully independent) (Parker and Palmer[28], 1993). Modified Harris Hip Score (MHHS) assesses hip pain and function (Harris[27], 1969; Byrd and Jones[49], 2000), and has a range of 0 = 100. EQ-5D index score ranges from 0 (dead) to 1 (perfect health) (Herdman et al[50], 2011, EuroQol Group[29], 1990), although negative values are possible.

Safety Outcome

During the follow-up period, 88 patients (44.2%) had at least 1 AE. Nineteen patients received surgical treatment due to the occurrence of AEs; among these, 9 were related to the surgical procedure (Table 6).

Discussion

The current study documented a 1-year mortality rate of 10.2% after surgical treatment of intertrochanteric fracture in a cohort of patients in Latin America, which is on the low end of the literature values.[32-35] The surgical condition was overall favorable (eg, short injury to surgery time and short surgical time[36,37]) and with low complication rate.[38,39]

Age (≥85 years), existing comorbidity according to CCI, reduced mobility (PMS ≤ 6), low preoperative plasma albumin level, cognitive impairment (MMSE score ≤ 23), and blood high CRP level were identified as potential risk factors for 1-year mortality in this patient population.

Many variables that have previously been identified as risk factors for mortality after hip fracture surgery showed no statistically significant association with the 1-year mortality in the current study. Among these, the 2 of the most frequently acknowledged variables were the male gender and time from injury to surgery.[8,1534] One example for the former is the report from Holt et al that found a significantly lower perioperative mortality odds ratio (0.49, 95% = CI: 0.45-0.54) for women even after controlling for the effects of confounding factors. However, the authors acknowledged that others had reported that men undergoing hip fracture surgery had increased morbidity compared to age-matched women; when factors such as health status and comorbidity were controlled, male gender was not associated with an increased perioperative mortality after hip fracture.[15] Considering the overall favorable conditions of our patient cohort, such as low comorbidity, normal cognitive function, and high level of preinjury independence in daily activities, we interpret the current result, that is, the lack of statistically significant association between male gender and increased mortality confirms the previous suggestion that male gender maybe a surrogate for overall health status and therefore the observation that it was a risk factor for postoperative mortality. Alternatively, the current study could simply lack the statistical power to conclude on the gender effect due to the low percentage of male patient.

As stated by the National Clinical Guideline Centre in The Management of Hip Fracture in Adults, "...the timing of treatment for patients sustaining fractures of the proximal femur remains one of the biggest challenges to a health care system". Although it is in general recommended that unless there are legitimate reasons, early surgeries are indicted for patients with hip fracture,[40] in the same article, it was acknowledged that the level of evidence was poor—the same sentiment voiced by Matharu and Porter[41] and was supported by the systematic literature review by Khan et al.[8] As indicated by some recent publications, skepticism still exists concerning the association between early hip fractures surgery and postoperative mortality.[6,42] The results from the current cohort of patients supports the thesis that under favorable patient conditions (low comorbidity, general good mental health, and so on), early surgery may not have such a dramatic contribution to good outcomes.

Preoperative Laboratory Parameters and Mortality

Multiple studies have investigated patient baseline conditions and concluded positive association between postoperative mortality and laboratory parameters such as hyponatraemia,[12,13,43] anemia,[44,45] basal hemoglobin level,[11] level of albumin,[38,46] level of CRP, and total lymphocyte count.[10] Aside from the question if patients died from or with these conditions,[13,14] most of these studies are retrospective studies and heterogeneity in the patient population is assumed. Some of these studies included cases spanning 20 years and some did not document confounding factors such as comorbidity, mental conditions, or preinjury mobility.

As a prospective study, the current study had clear inclusion and exclusion criteria. With a relatively homogeneous patient population such as low comorbidity, reasonable mental capacity, high preinjury functional score in daily activities, and short mean injury to surgery time, the resulting association between 1-year postoperative mortality and preoperative hypoalbuminemia and preoperative elevated CRP level are especially notable.

Table 6. Summary of Adverse Events (Patient-Level).

Adverse Events	n	%[a] (95% CI[b])	Action Taken, n (%)		
			No Action	Nonoperative	Operative
Any adverse event	88	44.2 (37.2-51.4)	10 (11.6)	57 (66.3)	19 (22.1)
Cut-out of blade/screw	0	0.0 (0.0-1.8)	0 (0.0)	0 (0.0)	0 (0.0)
Cut-through of blade/screw	4	2.0 (0.6-5.1)	1 (25.0)	0 (0.0)	3 (75.0)
Poor intraoperative fracture reduction	0	0.0 (0.0-1.8)	0 (0.0)	0 (0.0)	0 (0.0)
Loss of reduction with nail/screw insertion	3	1.5 (0.3-4.3)	1 (33.3)	0 (0.0)	2 (66.7)
Iatrogenic operative femoral fracture(s)	0	0.0 (0.0-1.8)	0 (0.0)	0 (0.0)	0 (0.0)
Delayed union, nonunion	1	0.5 (0.0-2.8)	0 (0.0)	0 (0.0)	1 (100.0)
Malunion/loss of reduction leading to malalignment of the femur in frontal plane: varus/valgus	1	0.5 (0.0-2.8)	0 (0.0)	0 (0.0)	1 (100.0)
Irritation of the tractus iliotibialis	1	0.5 (0.0-2.8)	0 (0.0)	0 (0.0)	1 (100.0)
Deep wound infection	1	0.5 (0.0-2.8)	0 (0.0)	0 (0.0)	1 (100.0)
Superficial wound infection	2	1.0 (0.1-3.6)	0 (0.0)	2 (100.0)	0 (0.0)
Wound dehiscence	1	0.5 (0.0-2.8)	0 (0.0)	1 (100.0)	0 (0.0)
Hematoma (requiring revision)	0	0.0 (0.0-1.8)	0 (0.0)	0 (0.0)	0 (0.0)
Thromboembolic complications	7	3.5 (1.4-7.1)	0 (0.0)	6 (85.7)	1 (14.3)
Sepsis	3	1.5 (0.3-4.3)	0 (0.0)	2 (66.7)	1 (33.3)
Pneumonia	6	3.0 (1.1-6.4)	1 (16.7)	5 (83.3)	0 (0.0)
Renal insufficiency	0	0.0 (0.0-1.8)	0 (0.0)	0 (0.0)	0 (0.0)
Bleeding (gastrointestinal, cerebral)	3	1.5 (0.3-4.3)	0 (0.0)	3 (100.0)	0 (0.0)
Cardiac (myocardial infarction, new arrhythmia)	7	3.5 (1.4-7.1)	1 (14.3)	6 (85.7)	0 (0.0)
Stroke	4	2.0 (0.6-5.1)	0 (0.0)	4 (100.0)	0 (0.0)
Other systemic adverse event[c]	70	35.2 (28.6-42.2)	12 (17.6)	44 (64.7)	12 (17.6)

Abbreviation: CI, confidence interval.

Note: Only adverse events with onset before upper 1-year follow-up window (i.e., <= 425 days after surgery) were included.

[a]Estimated risk of developing at least one complication (calculated by dividing the number of patients experiencing at least one complication by the total number of patients.

[b]Confidence intervals were calculated using the exact method.

[c]These included conditions such as urinary tract infection, anemia, respiratory problems, and new fractures.

Hypoalbuminemia is commonly used as an indication of malnutrition and was associated with poor outcomes in patients undergoing hip fracture surgeries.[10] Malnutrition can be one component of physiological deterioration associated with aging. Currently, there is no known mechanism for how hypoalbuminemia leads to complications and increased postoperative mortality. C-reactive protein is commonly known as a serum biomarker of inflammation that reflects ongoing disease pathology such as vascular disease, poor skin health, poor oral health, and underlying malignancies. The current study demonstrated an association between blood CRP level and late postoperative mortality in geriatric hip fracture patients. This result is supported by a previous retrospective study that proposed high CRP level to be an independent predictor for 1-year mortality after hip fracture surgery.[38] Combining the results of these 2 studies, clearly the role and mechanism of CRP as a predictor for mortality in hip fractures needs further investigation.

The relevance of a comprehensive approach in managing geriatric patients with hip fractures can be exemplified in the following publications. A recent report analyzed the preventable mortality in geriatric inpatients with hip fracture and determined that 56.3% of the inpatient deaths were possibly or probably preventable. The authors suggested that measures that could potentially prevent mortality include better fluid and hemodynamic management.[47] Multidisciplinary approach with a pathway that mandated full medical evaluation with the aim to diagnose and correct reversible problems had resulted in reduced cancelation of surgery due to inadequate preoperative medical optimization and reduced mortality.[48] Such studies pointed to the importance of geriatric comanagement in caring for patients with hip fracture.

Finally, it is worthwhile to point out that, although objective tests (the PMS and EQ-5D scores) showed that the patients did not regain their preinjury mobility and QoL, they perceive that their QoL, as measured by the EQ VAS questionnaire, had surpassed the preinjury state at 1-year after surgery. This helps us to remember that patient satisfaction does not always coincide with clinical outcomes.

The strength of the current study is that it was a prospective multicenter study in several centers across Latin America; this allowed the simultaneous collection and evaluation of many important potential risk factors such as demographics, comorbidity, cognitive capacity, laboratory parameters, surgical, and outcome parameters.

The current study has 2 limitations. (1) Due to low mortality rate, important statistical analyses, that is, multivariable analyses (Cox regression) that allow to adjust for confounders could not be performed, and in-depth analyses on the cause and the timing of deaths were not feasible. (2) Patient population bias. The current study population enjoyed overall good physical and mental health in comparison to the general patient population with hip fracture. Therefore, the results may not be generalizable to all patients with hip fracture and could potentially have missed other risk factors.

Conclusion

The current results showed that under the condition of optimal surgical treatment and low surgery-related complication, preinjury health status as indicated by the blood level of albumin and CRP has a direct and significant impact on 1-year mortality rate.

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