


Frailty, post-operative delirium and functional status at discharge in patients with hip fracture

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Abstract

Objective: To explore the effect of frailty, alone and in combination with post-operative delirium (POD), on the risk of poor function at discharge in patients with hip fracture (HF).

Methods: This is a prospective cohort study of patients with HF admitted to an Orthogeriatric Unit (OGU) between October 1, 2011 and March 15, 2019. POD was assessed using the 4AT and the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5-edition criteria. A 22-items Frailty Index (FI) was created using the data collected on admission. The outcome measure was the Cumulated Ambulation Score (CAS) score at discharge. A log-binomial regression model was used to assess the effect of frailty and POD on CAS.

Results: A total of 988 patients (median age = 84.9 years, Interquartile range = 80.6-89.2) were included: 360 patients (36.4%) were frail and 411 (42%) developed POD. Poor functional status at discharge (CAS score ≤ 2) was more common in frail than non-frail patients (68.3% vs. 53.8%, $p < 0.001$). In a regression adjusted for confounders, frailty alone (Relative Risk, RR = 1.33, 95% Confidence Intervals, CI = 1.14-1.55) and POD alone (RR 1.38, 95% CI = 1.2-1.59) were associated with poor functional status at discharge; when combined, frailty and POD had an interaction, yielding a mild increase in the risk of poor outcome (RR 1.47, 95% CI = 1.28-1.69).

Conclusions: In older patients undergoing HF surgery, frailty, POD and their combination, are associated with poor functional status at discharge.

KEYWORDS

delirium, elderly, frailty, functional outcome, hip fracture, orthogeriatric

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Key Points

- Studies that investigate the joined effect of frailty and post-operative delirium (POD) on functional outcome of hip fracture (HF) patients after surgical repair are lacking
- In this prospective cohort study on 988 older patients with HF, we demonstrated that frailty, POD and their combination are associated with poor functional status at discharge from an Orthogeriatric Unit
- Assessing frailty could help early detecting the onset of POD, promoting its prevention and reducing the negative impact on function at discharge
- The results of this study emphasize the need to improve geriatric knowledge across hospitals that assist older patients with HF

1 | INTRODUCTION

Yearly 1.6 million hip fractures (HFs) occur worldwide, with over 610,000 cases in Europe and more than 123,000 in Italy.¹ HFs are a major issue for National Health Systems worldwide:² within one year after HF, nearly one third of all patients die and about 50% of the survivors do not regain their pre-fracture functional status.³⁻⁵

Frailty is a condition of increased vulnerability towards stressors, with limited ability to maintain or regain homeostasis.⁶ Several studies have demonstrated that frailty is a predisposing factor for falls (and thus for HF) and other adverse events, including functional decline, emergency hospitalisation, nursing home admission and death.⁷⁻⁹ It is also a risk factor for postoperative complications among HF patients.¹⁰

Post-operative delirium (POD) is common among older patients undergoing HF surgery and is associated with poor short and long-term outcomes, including prolonged length of hospital stay, institutionalization, functional and cognitive decline, and death.¹¹⁻¹⁴

Frailty is strongly associated with the development of delirium,^{14,15} which indirectly suggests that these two conditions may jointly contribute to affect the patient's outcomes. However, studies that investigated the joined effect of frailty and POD on an important outcome of HF patients after surgical repair (i.e., the functional one)⁹⁻¹² are lacking.

The aim of this study is to explore the effect of frailty, alone and in combination with POD, on the risk of poor function at discharge in patients with HF. These findings may have important implications for the provision of care to HF patients.

2 | METHODS**2.1 | Setting and sample**

This is a prospective observational study of patients consecutively admitted to the Orthogeriatric Unit (OGU) at S. Gerardo University Hospital, Monza, Italy from October 1, 2011 to March 15, 2019. The OGU has been described in previous studies.^{5,12}

All patients admitted to the OGU were eligible for this study if they were aged 65 years and above, had a diagnosis of proximal

HF and underwent surgical repair. Patients with a diagnosis of distal HF, metastatic cancer or those with an expected lifespan lower than one month (according to physician's judgement) were excluded.

Data collection complied fully with Italian law on personal data protection. Informed consent for participation in clinical studies was obtained from all patients or proxy respondent on admission to the OGU and the study protocol was approved by the Brianza Institutional Review Board.

2.2 | Frailty index

A Frailty Index (FI) of health deficits was operationalized following a standard procedure.¹⁶ Upon admission, all patients underwent a Comprehensive Geriatric Assessment (CGA) including socio-demographics, functional and somatic health status. Most of CGA variables were used to construct a FI including 21 variables. The FI score was calculated for each patient by dividing the sum of the altered items for the sum of all items measured. As an example, if a person presented with 10/21 altered items, the corresponding FI score was $10/21 = 0.48$. As in a previous study,¹⁷ a cut-off ≥ 0.25 was used to define frail patients.

2.3 | Diagnosis of POD

The occurrence of POD was evaluated daily, from the first day after surgery to discharge, by three expert geriatricians (MC, PM and GB) and 11 trained fellows. Delirium was screened with the 4AT,¹⁸ a tool with a sensitivity of 88% and a specificity of 88% for the diagnosis of delirium,¹⁹ and then diagnosed in accordance to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.²⁰ To be classified as having POD, the patient had to show symptoms of delirium for at least two consecutively days after surgery. On Sundays and on holidays, when the assessors were not always available at the OGU, information concerning delirium was obtained from a review of daily medical and nursing notes, as in previous studies.^{12,13}

2.4 | Medical care and rehabilitation

All patients received a daily visit by a geriatrician and an orthopaedic surgeon while postoperative rehabilitation was provided from postoperative day one by a team of physical therapists for 30 min per day, five days per week. Exercises included mainly ability to perform standing and walking exercises aimed at improving the patient's functional status.

2.5 | Outcome measure

The outcome measure was the patient's Cumulated Ambulation Score (CAS), as evaluated by physical therapists at hospital discharge.²¹ The CAS is a composite score reflecting independence in ambulation in three essential functions of transfer: from-sitting-to-supine-to-sitting, from-sitting-to-standing-to-sitting and the walking ability with an appropriate aid. For each function, 2 points are given if patients could complete the task without help, 1 point if help is needed and 0 point if he/she could not complete the task.

2.6 | Statistical analyses

Continuous variables are reported as median and interquartile range (IQR) whereas qualitative variables were reported as frequencies and percentages. Statistical significance between groups was evaluated using Wilcoxon test for continuous variables and chi-square test for categorical variables. Each patient was classified by a categorical variable with levels defined by the combination of frailty and POD presence. This variable was included in a log-binomial regression model to evaluate the association of its levels with functional outcome at hospital discharge, taking into account the problem of the overestimation in association estimates due to common outcome. Unadjusted and adjusted association estimates were reported as relative risk (RR) and corresponding 95% confidence intervals (CI). The adjustment was made for covariates selected a priori (age, sex, type of fracture, 48-h delay of surgery, type of anaesthesia). All tests were two-sided, and we considered as significant p -value <0.05 . All analyses were carried out using SAS software (version 9.4; SAS Institute).

3 | RESULTS

The socio-demographic and clinical characteristics of the study population, both overall and according to frailty status are shown in Table 1. A total of 988 patients were included in this study. The median age was 84.9 (IQR 80.6–89.2) years and 250 (25.3%) of the participants were male. Of these, 906 (92.5%) were community dwellers, 60 (6.1%) were nursing home residents and 6 (0.6%) were already hospitalized at time of HF. Intracapsular fracture occurred in 489 patients (50.1%), inter-trochanteric in 435 patients (44.5%) and

sub-trochanteric in 53 patients (5.4%). Intramedullary nailing was used in 387 patients (39.3%), endoprosthesis in 372 patients (37.8%), sliding screw fixation in 178 patients (18.1%), cannulated screw fixation in 31 patients (3.2%) and total hip arthroplasty in 12 patients (1.2%). Most of the patients underwent a regional anaesthesia (81.5%) and both endoprosthesis and intramedullary nails were the commonest types of surgery. Surgical delay (i.e., ≥ 48 h from fracture to surgery) was found in 37.9% of patients. POD occurred in 42% of patients and, at discharge, 59.1% of all individuals had a CAS score ≤ 2 .

Upon admission, 628 (63.6%) patients had a FI score <0.25 and were thus defined as frail, whereas 360 (36.4%) had higher FI scores and were defined as non-frail. The values (median and IQR or number and percentages) of the variables used to compute the FI, overall and by the presence of frailty on admission, are reported in the Table S1. If compared to their counterpart, frail patients had a higher average ASA score, preferably underwent general than regional anaesthesia and waited more than 48 h before undergoing surgery. After the surgical intervention, the frail patients developed more frequently POD than others and at discharge, the proportion of patients with CAS score ≤ 2 was higher in this group. The length of stay was longer in frail than non-frail patients (10 days, IQR 8–15 vs. 9 days IQR 7–12, $p < 0.0001$).

Using a log-binomial regression model (Table 2), we obtained the unadjusted and adjusted association estimates between the combination of frailty, POD and their risk of poor function at discharge. We found that frailty alone (RR 1.33, 95% CI = 1.14–1.55) and POD alone (RR 1.38, 95% CI = 1.2–1.59) were both associated with poor functional status (CAS ≤ 2) at discharge. Additionally, there was a significant interaction of frailty and POD, albeit with an antagonist effect, which mildly increased the risk of negative outcome (RR 1.47, 95% CI = 1.28–1.69).

4 | DISCUSSION

This study shows that frailty, POD and their combination are associated with poor functional status at discharge in a large cohort of older patients undergoing HF surgery. We also found an interaction between frailty and POD which slightly increased the risk of poor outcome.

The association of frailty with the post-operative functional status at hospital discharge in patients with HF is largely underestimated, given that only a few studies have been conducted until now to examine it. In a cohort of 274 patients who underwent post-HF surgery, Inoue et al. found that frailty, as defined using a 19-item modified FI, was independently associated with increased likelihood of lower functional recovery at discharge.¹⁶ In another study, Low et al. found that pre-morbid frailty (as measured with the Clinical Frailty Scale) was the strongest independent predictor of poorer Functional Independence Measure efficiency, inability to recover pre-fracture mobility and return to community dwelling.²² Dementia and delirium were also independently predictive of poor outcomes across all measures.²² Frailty was cited as a predictor of poor functional

TABLE 1 Clinical features of 988 older patients recruited according to Frailty Index (FI) score at hospital admission

Variable	Full sample (n = 988)	FI < 0.25 (n = 628)	FI ≥ 0.25 (n = 360)	p value
Socio-demographics				
Age, years, median (IQR)	84.9 (80.6–89.2)	84.7 (79.9–88.6)	85.3 (81.4–89.5)	0.0248 ^b
Male, n (%)	250 (25.3)	141 (22.5)	109 (30.3)	0.0065
Source of admission				
Community dwelling	906 (92.5)	588 (94.5)	318 (88.8)	0.0002 ^a
Nursing home	60 (6.1)	23 (3.7)	37 (10.3)	
Hospital	6 (0.6)	5 (0.8)	1 (0.3)	
Other	8 (0.8)	6 (1.0)	2 (0.6)	
Related to intervention				
Fracture type				
Intracapsular	489 (50.1)	328 (53.0)	161 (45.0)	0.0533
Inter-trochanteric	435 (44.5)	260 (42.0)	175 (48.9)	
Sub-trochanteric	53 (5.4)	31 (5.0)	22 (6.1)	
ASA physical status classification, median (IQR)	3.0 (2.0–3.0)	3.0 (2.0–3.0)	3.0 (3.0–3.0)	<0.0001 ^b
Type of anaesthesia				
General/sedation	182 (18.4)	107 (16.7)	78 (21.6)	0.0463
Regional	816 (81.5)	532 (83.3)	284 (78.5)	
Type of surgery				
Endoprosthesis	372 (37.8)	245 (39.2)	127 (35.4)	0.2333 ^a
Intramedullary nail	387 (39.3)	240 (38.4)	147 (40.9)	
Sliding hip screw	178 (18.1)	108 (17.3)	70 (19.5)	
Cannulated screw	31 (3.2)	19 (3.0)	12 (3.3)	
Total hip arthroplasty	12 (1.2)	11 (1.8)	1 (0.3)	
Other	4 (0.4)	2 (0.3)	2 (0.6)	
Surgical delay (≥48 h)	405 (37.9)	239 (35.1)	166 (43.0)	0.0007 ^a
Related to post-surgical course				
Postoperative delirium, n (%)	411 (42.0)	228 (36.5)	183 (51.3)	<0.001
Mobilization on the first postoperative day	971 (98.4)	623 (99.2)	348 (97.0)	0.0066
Collected at discharge				
CAS, median (IQR)	2.0 (1.0–3.0)	2.0 (2.0–3.0)	2.0 (1.0–3.0)	<0.0001 ^b
CAS ≤ 2, n (%)	584 (59.1)	338 (53.8)	246 (68.3)	<0.001
Length of hospital stay, days, median (IQR)	10.0 (8.0–13.0)	9.0 (7.0–12.0)	10.0 (8.0–15.0)	<0.0001 ^b

Note: Values are reported as median and (interquartile range) or number (%).

Abbreviations: ASA, American Society of Anaesthesiologists; CAS, Cumulated Ambulation Score; FI, Frailty Index.

^aFisher exact test.

^bWilcoxon test.

outcomes also in a previous systematic review on patients with HF.²³ However, among the 81 articles included in the review, there was only one study that demonstrated a role of frailty in influencing patient's functional recovery²⁴ and there was no mention of a potential association between frailty and post-HF functional recovery in previous reviews.²⁵

The relationship between POD and functional outcome at discharge is supported by larger evidence. One of the most recent studies in this field showed that patients who developed POD after HF surgical repair had an increased risk of low Barthel Index (a tool to measure functional status) at discharge than those without POD; within the delirium cohort, those suffering from dementia had the

Variable	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Frailty index and post-operative delirium		
Frailty no/delirium no	1	1
Frailty yes/delirium no	1.33 (1.14 to 1.56)	1.33 (1.14 to 1.55)
Frailty no/delirium yes	1.41 (1.23 to 1.63)	1.38 (1.20 to 1.59)
Frailty yes/delirium yes	1.55 (1.35 to 1.78)	1.47 (1.28 to 1.69)
Socio-demographic variables		
Age	-	1.00 (0.99 to 1.01)
Sex		
Females	-	1
Males	-	0.93 (0.82 to 1.05)
Fracture and intervention covariates		
Fracture type		
Intracapsular	-	1
Inter-trochanteric/sub-trochanteric	-	1.0 (0.90 to 1.11)
Other	-	1.20 (1.03 to 1.04)
48-h delay in intervention		
No	-	1
Yes	-	1.19 (1.08 to 1.32)
Anaesthesia		
Other	-	1
General/Sedation	-	0.93 (0.83 to 1.05)

Abbreviations: RR, relative ratio; 95%CI, confidence intervals.

worst scores.²⁶ However, the authors did not consider frailty as a risk factor for both delirium occurrence and poor functional status. This is an important limitation, given that a systematic review and meta-analysis showed that the risk of developing delirium is 2.2 times greater in frail than non-frails,¹⁵ indirectly suggesting that the existence of this condition should be taken into account as a confounder when exploring the independent association of delirium with its negative outcomes. Other studies explored the association of delirium with the functional status in patients admitted to rehabilitation wards and long-term care facilities after HF surgery, all confirming the negative effect of delirium on functional status.^{23,27,28}

Our study is the first to consider the effect of frailty alone and in combination with POD on poor functional outcome at discharge in HF patients. We found an antagonist interaction between frailty and delirium, which means that frailty and POD interfered with each other in such a way that their combined effect is less than the sum of the effect of each individual factor. This interaction suggests that both factors act in a similar fashion to determine the negative outcome. This finding suggests that preventing POD in frail patients after surgical intervention is crucial. Several reviews and clinical trials have shown that multicomponent non-pharmacological interventions can prevent delirium, decreasing its incidence in a proportion greater

than 40%.²⁹ These interventions include the assessment and corrections of precipitating factors of delirium.

Targeting frailty is also essential in patients undergoing HF surgery, in order to anticipate the negative outcomes of delirium and improve the overall health status at discharge. With an increasing contraction of the public health resources, the prevention of disability following HF is crucial. Indeed, nearly 50% of people surviving HF does not regain their pre-fracture functional status, with serious consequences in terms of healthcare costs, stress for the caregivers and negative outcomes related to disability.³⁰⁻³² Our findings may help in this context, suggesting that specific efforts should be directed towards the identification of frail patients, soon after hospital admission, on whom concentrating the interventions to prevent delirium. Future studies are expected to clarify this point.

Strengths of our study are its large sample size, the use of a CGA to assess the patients and the methods used to assess POD. Indeed, all patients were screened with the 4AT, a tool which in a recent systematic review and meta-analysis, demonstrated good overall performance in terms of test diagnostic accuracy for delirium detection.¹⁹ One limitation is that this is a single-centre study. A second limitation is the number of items used to create the FI, which is lower than suggested by Searle et al.³³ A third limitation is that a diagnosis of delirium according to the DSM-5 criteria was obtained

TABLE 2 Log binomial regression model of the variables associated with poor functional status (CAS < 2) at discharge

only in patients who screened 4-AT positive. Given that the DSM-5 criteria represent the gold standard for the diagnosis of delirium, we cannot exclude that we may have involuntarily missed some diagnoses of delirium. However, applying the DSM-5 criteria requires preliminary training and education of raters and is not always feasible in a busy setting such as an Orthogeriatric ward. Furthermore, the 4-AT has excellent properties in terms of delirium diagnostic accuracy.¹⁹ A fourth limitation is that our study's follow-up period was limited only to the acute phase following HF surgery.

In conclusion, this study showed that frailty, POD and their combination affect the functional status at discharge of older patients after HF surgery. Overall, the results of this study emphasize the need to assess both frailty and delirium in all hospitals that assist patients with HF.

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CONFLICT OF INTEREST

None.

AUTHOR'S CONTRIBUTION

Chiara Maria Gandossi, Antonella Zambon and Giuseppe Bellelli designed the study. Chiara Maria Gandossi, Giulia Oliveri, Martina Codognola, Hajnalka Szabo, Ilaria Cazzulani, Maria Cristina Ferrara, Chiara Mottadelli, Marianna Galeazzi, Isabella Amoroso, Cristina Zarcone, Giulia Principato, Maurizio Corsi, Paolo Mazzola, Giovanni Zatti, Giuseppe Foti and Giuseppe Bellelli collected the data. Giuseppe Foti performed most of the anesthesiologic and Giovanni Zatti performed most of the surgical procedures. Antonella Zambon performed the statistical analyses. Chiara Maria Gandossi, Antonella Zambon and Giuseppe Bellelli draughted the manuscript. All authors reviewed the manuscript.

DATA AVAILABILITY

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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