Prognostics of recovery in hip fracture patients

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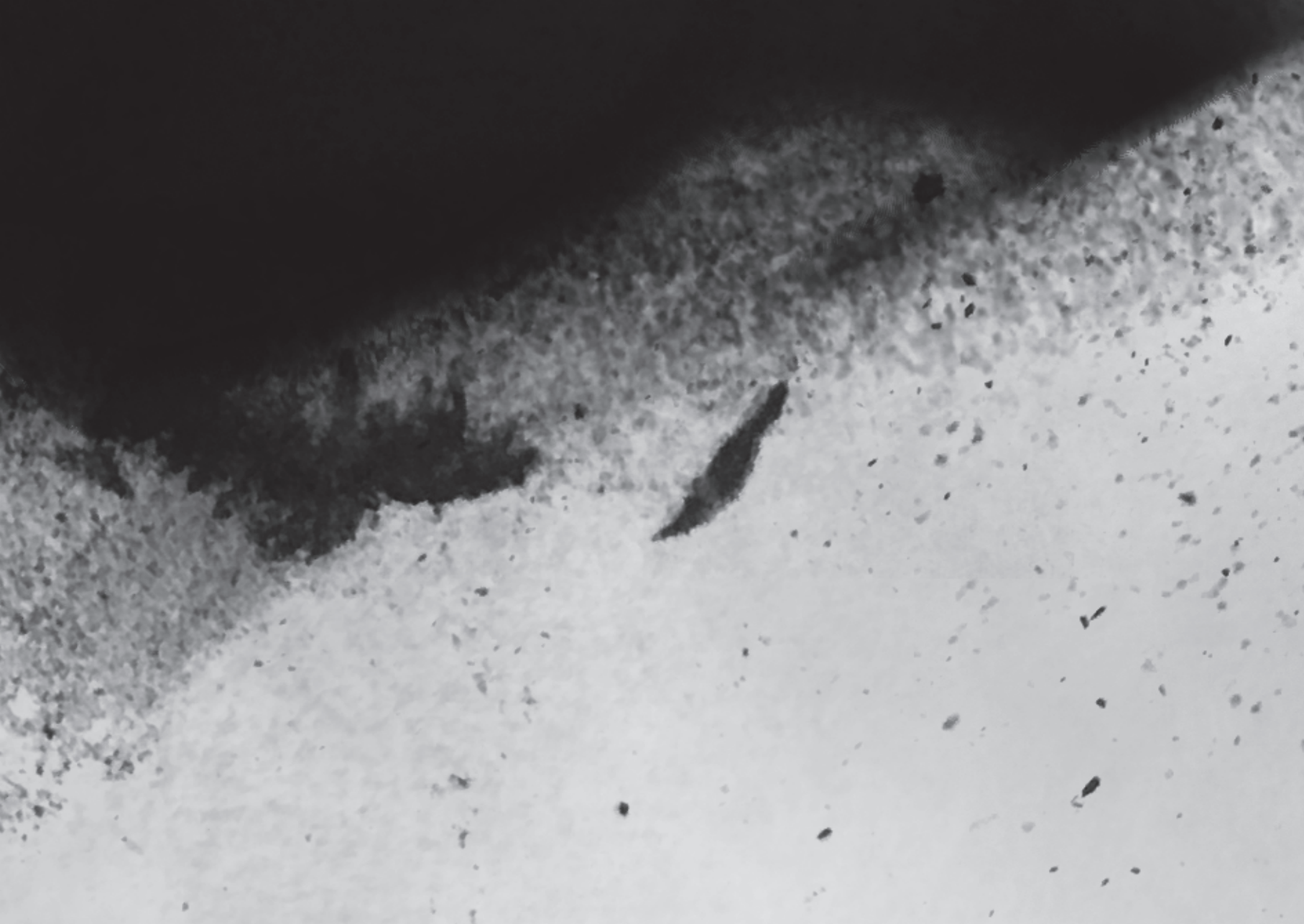


Chapter 6

Short-term recovery of independence in a multi-state model

Prognostic factors for short-term recovery of independence in a multi-state model for patients with a hip fracture. van der Sijp M.P.L., van Eijk M., Niggebrugge A.H.P., Putter H., Blauw G.J., Achterberg W.P. *J Am Med Dir Assoc. 2020 Sep 19;S1525-8610(20)30696-4.*

Abstract

Objectives: This study investigates the transitions of community-dwelling patients with a proximal femoral fracture towards recovery of independence using multistate modeling. The prognostic value of factors affecting the short-term rate of recovery of independence in activities of daily living was assessed for the resilient portion of the population.

Design: An inception cohort was recruited between 2016 and 2019.

Setting and Participants: Only community-dwelling older patients admitted with a proximal femoral fracture were included.

Measures: Follow-up was performed at 6 weeks and 3 months, when the patients' living situation and level of independence were recorded. Multistate modeling was used to study the transition rates of the population through prespecified states of the recovery process. Using this model, prognostic factors for the recovery of independence were identified for resilient patients (defined as those patients who managed to return home at any point in the follow-up after discharge).

Results: A total of 558 patients were included, and 218 (40.9%) recovered to prefracture levels of independence. Of the resilient patients, 20.7% were discharged home directly, and 79.3% via a rehabilitation home. In this patient group, a more favorable American Society of Anesthesiologists classification, better prefracture mobility, and the absence of a prefracture fear of falling were statistically significantly associated with a successful recovery. A low level of prefracture independence was inversely associated, meaning that patients with a low level of prefracture independence had a higher chance of successful recovery.

Conclusions and Implications: This study identified 4 factors with an independent prognostic value for the recovery of independence in resilient patients after a proximal femoral fracture. These factors could be used to construct clinical profiles that contribute to the assessment of the patient's post-acute care needs and recovery capacity. In addition, multistate modeling has been shown to be an effective and versatile tool in the study of recovery prognostics.

Introduction

Despite the frequent presence of frailty characteristics, the majority of patients admitted with a proximal femoral fracture were independently living patients with a high level of independence in activities of daily living (ADL) before the occurrence of the fracture.1 Of these patients, an estimated 12-19% dies within one year after surgery and another 10-20% becomes permanently institutionalized.2, 3 Those who do regain sufficient independence and avoid institutionalization display considerable physical resilience.[4] Regardless, up to 80% of patients who are able to return to their independent living situation do not fully recover to prefracture level of independence in ADL.[3] This has substantial personal and social implications for the patient as an individual and a significant economic impact on the healthcare system.

This combination of recovery goals (survival, returning home and recovering independence) is often studied using separate analyses for each of the alternative outcomes (events). This may, however, not be completely correct, since this approach fails to reveal possible relationships between the different events. Events may be competing with one another, meaning they could influence each other if and when another event occurs.[5] In the case of the recovery of independence in patients with a hip fracture, the alternative events of mortality or admission to a nursing home may compete with each other. Previous studies of functional recovery have often either excluded patients who died during follow-up, as their functional status couldn't be assessed after that event, or have opted to allocate these patients to an unfavorable outcome category.[6-8] In those studies, no adjustment was made for competing events.

Multistate modeling is a novel technique that takes patient transitions throughout the recovery process into account. As such, multistate models allow inclusion of all potentially competing events. In addition, the probability and rate of patient transitions through the states of the model can be estimated for each time point in the process. The prognostic value of patient and treatment factors can be assessed in relation to each transition and the rate of a particular transition, allowing the relevance of each factor to be estimated at every step of the recovery process.[9]

A recent review by Sheehan et al. (2018) identified 25 factors for which the prognostic value of short-term functional outcome was tested. Sufficient but still only weak levels of evidence were found for anemia and impaired cognition, and both were negatively associated with regaining function.[10] Previously identified prognostic factors for loss of independence include age, comorbidity scores, cognitive status and pre-fracture functionality.[11-14] Besides these predominantly biological factors, some psychosocial factors have also been associated with functional outcome, including fear of falling and presence of an informal caregiver.[15, 16]

A better understanding of the relevance of these factors for the recovery of independence would improve prognostics, which is valuable for the management of patient expectations and helps to anticipate the need for appropriate care appropriately when a prolonged functional deficit

is expected. For the more resilient patients who are discharged home, this information would be relevant to homecare and the burden on informal caregivers such as partners and family.

Using multistate modeling, this study investigates the transitions related to the recovery of independence in community-dwelling patients with a proximal femoral fracture. Focusing on the resilient portion of the population, the prognostic value of factors related to the short-term rate of recovery of independence in activities of daily living are assessed.

Methods

This prospective cohort study was performed and documented in agreement with the 'Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)' statement guidelines for reporting observational studies.[17] Data were handled in accordance with 'Good Research Practice' guidelines. Data were registered prospectively in a coded database, concurrently with clinical registrations during admission. Details of the routine data collection and outcomes have been published previously and apply to all patients with a proximal femoral fracture.[18]

The methodology of data collection and of any subsequent observational studies was approved by the institutional Medical Research Ethics Committee and the study hospital's board of directors without the need for individual patient consent.

Patients

An inception cohort was constructed that included all patients admitted with a proximal femoral fracture between December 2016 and December 2019. Inclusion in the final study cohort was limited to older patients (aged 70 years or more) who were community-dwelling, which was defined as not permanently residing in a nursing home before admission. Exclusion criteria included patients with high-energy traumas or pathological fractures.

Treatment and assessments

Baseline characteristics and details of treatment were registered during admission. These included age, sex, general health status using the American Society of Anesthesiologists (ASA) classification (categorized as I-II and III-V)[19], nutritional status using the Mini Nutritional Assessment - Short Form (MNA®-SF, categorized as normal, 14-12 or abnormal 11-0)[20, 21], prefracture residence (categorized as at home, at home with homecare or a residential home), the availability of an informal caregiver at home, fracture type and treatment type. Cognition was rated using the Six-item Cognitive Impairment Test (6CIT) upon admission, with cognitive impairment defined as a score ≥11 or as a previous diagnosis of dementia.[22] The (prefracture) baseline of independence in

activities of daily living (using the Katz Index of Independence in Activities of Daily Living, Katz ADL)[23], mobility (using the Parker Mobility Score, PMS)[24], and fear of falling[25] were retrospectively assessed during admission, taking the period directly before the fracture. Anemia was recorded based on routine bloodwork during admission and categorized as a hemoglobin level below 8.1 mmol/L (12 g/dL) for men and below 8.1 mmol/L (13 g/dL) for women.

During the acute hospital phase, postoperative patients were discussed twice weekly in a multidisciplinary meeting that included an orthopedic trauma surgeon, ward doctor, geriatrician, trauma nurse, physiotherapist and transfer nurse. Patients were preferably discharged 3 days after surgery, if pain was manageable and no active complications were present. For prefracture community-dwelling patients, discharge home was generally possible when mobility was adequate for independent living (meaning that the patient could safely make indoor transfers) or if home care was available and sufficient (or redundant). If not, or if rehabilitation goals were too complex to be dealt with through ambulatory therapy, discharge to a geriatric rehabilitation nursing home was planned.[26] In the Netherlands, geriatric rehabilitation is a form of temporary inpatient care at a specialized nursing home, led by an elderly care physician for an intended period of 6 weeks to 3 months. Nursing staff and an occupational therapist are involved in the recovery of independence in ADL, such as transferring and bathing. Patients receive on average 3-6 sessions of physiotherapy per week, though intensity varies depending on the patients' physical endurance and formalized agreements employed by the rehabilitation units.[27] Additional treatment aspects during geriatric rehabilitation concern general medical care, fall prevention, osteoporosis, nutrition and fear or depression.

Patients were invited for routine outpatient check-ups 6 weeks and 3 months after surgery. Patients not attending the outpatient check-ups were called to reschedule or, if not possible, to arrange a check-up by phone. Patients for whom an outpatient checkup was deemed too burdensome, due to severe cognitive or physical impairments also had a phone check-up. The Katz ADL and current living situation were assessed and recorded.

Outcomes and the multistate model

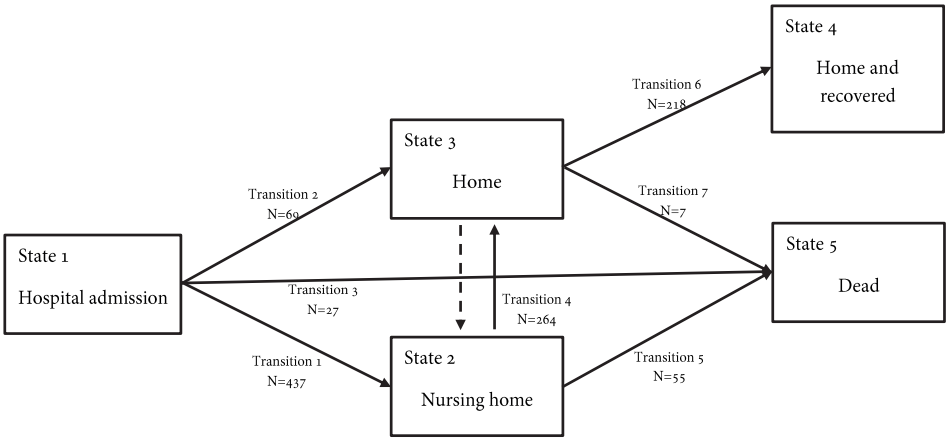
The primary outcome and endpoint of recovery in this study is a combined outcome measure for the recovery of independence in ADL. Recovery was considered successful when patients simultaneously met all three criteria stated below on at least one of the two outpatient check-ups (6 weeks or 3 months after surgery) during follow-up;

- No mortality due to any cause.
- Independent living: the patient returned to an independent form of residency. Residence was grouped binomially as dependent (included residence in a geriatric rehabilitation home or a nursing home) or independent (living in a private residency with or without homecare, or in a residential home).

- Recovery of independence in ADL: assessed using the Katz ADL score, and patients who returned to their prefracture level of independence in ADL (follow-up Katz ≤ prefracture Katz) were considered successful.

Here, the criteria 'mortality' and 'independent living' are considered inherent aspects of the recovery of independence in ADL. In the multistate model, each of these events is an individual state. The model consists of 5 states in total: (1) hospital admission from surgery to discharge, (2) residing in a nursing home, either temporarily for geriatric rehabilitation, or secondarily and permanently after unsuccessful rehabilitation, (3) residing in an independent living situation (including homecare or a residential home), (4) independent living with recovered independence in ADL and (5) deceased (Figure 1). States 4 and 5 were included as absorbing states, meaning patients are censored when reaching these states. The transition from home to a nursing home (3 à 2) was observed for only 3 (0.6%) cases and excluded from the model. Hospital readmission (a return to state 1) was not included in the model.

Figure 1. Multi-state model representing the states from admission to recovery or dead and their interlinking transitions within 3 months.



Each box represents a possible postoperative state. The arrows represent the observed transitions of patients between states within the 3-month follow-up period. The dotted arrow was a state transition that was rarely observed and therefore excluded from further analyses. Patients were only considered 'recovered' (state 4) when they were alive, lived independently, and had a recovered independence in activities of daily living.

Statistical analyses

No missing data were imputed. Univariate analyses were used to compare the baseline characteristics with regard to the primary outcome. An unpaired two-sample t-test was used to compare means, with standard deviations (SD), of continuous data with a normal distribution. Data with

a non-normal distribution (Kolmogorov-Smirnov test of $p< 0.05$), are presented as medians with interquartile ranges (IQR) and compared using the Mann–Whitney U test. Categorized characteristics were compared using crosstabs and the Chi-square test if the groups were sufficiently large (expected cell-count <5) or Fishers-exact test if this condition was not met.

Multistate analyses were used to assess the influence of factors on the participants' transition rates to a recovered independence in ADL and to independent living.[5, 28] In order to model effects on the functional recovery of the more resilient patients who returned to their prefracture independent living situation, all 11 patient characteristics were included as factors in the multistate analyses for patients transitioning to the 'home and recovered' state (state 6).

All statistical analyses were performed using IBM SPSS statistics PC software version 25.0 and the package mstate (de Wreede et al. 2010) version 0.2.11, for R version 3.6.1 (R Development Core Team 2006).[29] A p-value smaller than 0.05 was considered statistically significant. A convenience sample size was used by including all patients from the prespecified inclusion period.

Results

Between December 2016 and December 2019, a total of 558 eligible patients were admitted with a proximal femoral fracture. Sufficient follow-up data were obtained for 533 (95.5%) patients, and 97.5% of all characteristics data were available for these patients. The median age of patients was 85 (IQR 77-90) and a majority were female (n=235, 71.5%). Regarding fractures, 282 (52.9%) patients had a femoral neck fracture, 234 (43.9%) patients had a pertrochanteric femoral fracture and 17 patients (3.2%) a subtrochanteric fracture. An osteosynthesis was performed for 297 (55.7%) patients, a prosthesis for 226 (42.4%) patients, and 11 (2%) patients were treated conservatively (Table 1).

The median follow-up for all patients was 87 (IQR 11) days, and the 3-month follow-up was planned a mean 90 (SD ±9.3) days after treatment. Regarding the baseline characteristics of included patients, those who recovered within 3 months of surgery (n=218, 40.9%) were significantly younger and had a more favorable ASA classification, mobility, independence in ADL, cognition, nutritional status, prefracture living situation and fear of falling status (Table 1). Sixty-nine (12.9%) patients were discharged home directly, 438 (82.0%) were discharged to a nursing home (either for rehabilitation or for permanent stay), and 27 (5.1%) patients died during their hospital stay (Figure 1). Of the patients discharged to a nursing home, 264 (60.4%) were discharged home within the study period. Of the patients who returned home after discharge, 218 (65.5%) recovered to their prefracture level of independence in ADL.

The distribution of patients in each state over time is presented in Figure 2. The transition of patients to the 'recovered' state at 45 and 90 days (seen as inversed sigmoid curves in the graph) corresponds to the outpatient check-ups assessing patient independence of ADL at 6 weeks and 3 months after surgery.

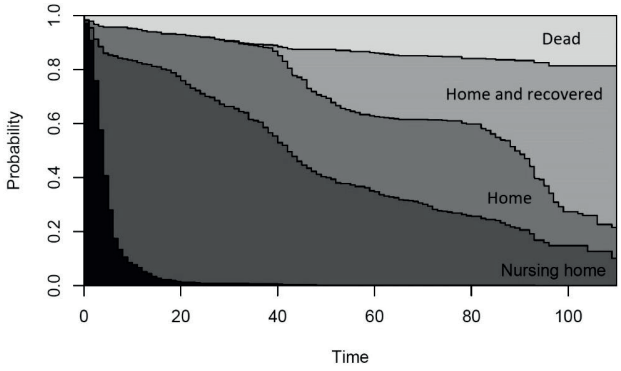
Table 1. Baseline characteristics for patients with a proximal femoral fracture stratified for functional outcome.

Characteristic	Unrecovered N=315 (59.1%)	Recovered N=218 (40.9%)	All patients N=533 (100%)	P-value
Patient characteristic				
Age, years (median, IQR)	87 (80-91)	80 (75-87)	85 (12)	*<0.001*
Sex, female	231 (73.3)	150 (68.8)	381 (71.5)	0.26
ASA classification				
I-II	87 (27.6)	105 (48.2)	192 (36.0)	
III-V	228 (72.4)	113 (51.8)	341 (64.0)	*<0.001*
Parker mobility score				
7-9	93 (30.0)	147 (67.7)	240 (45.5)	
4-6	164 (52.9)	57 (26.3)	221 (41.9)	
0-3	53 (17.1)	13 (6.0)	66 (12.5)	*<0.001*
Katz ADL score				
0-1	183 (58.7)	163 (74.8)	346 (65.3)	
2-3	71 (22.8)	37 (17.0)	108 (20.4)	
4-6	58 (18.6)	18 (8.3)	76 (14.3)	*<0.001*
Cognitive impairment	138 (47.6)	53 (25.9)	191 (38.6)	*<0.001*
Malnourished	146 (49.8)	55 (25.9)	201 (39.8)	*<0.001*
Living situation				
Independent	160 (50.8)	163 (74.8)	323 (60.6)	
Homecare or residential home	155 (49.2)	55 (25.2)	210 (39.4)	*<0.001*
Informal caregiver				
Yes	190 (62.3)	124 (57.1)	314 (60.2)	0.24
Fear of falling				
Yes	153 (56.7)	77 (37.9)	230 (48.6)	*<0.001*
Anemia				
Yes	154 (49.0)	89 (41.0)	243 (45.8)	0.068

ASA, American Society of Anesthesiologists; IQR, interquartile range. Higher ASA scores represent more severe comorbidities; higher Katz ADL scores represent lower levels of independency; and higher Parker Mobility Scores represent better levels of mobility. Recovered patients regained their individual prefracture level of independence in ADL. Italics indicate a P value of < .05.

The following factors were identified as significantly associated with a successful recovery of independence in ADL (Table 2): a less severe ASA classification (HR, 0.68; 95% CI, 0.49-0.95; P = 0.025), a better prefracture mobility (HR, 0.61; 95% CI, 0.39-0.95; P = 0.028 and HR, 0.31; 95% CI, 0.13-0.78; P = 0.013), a lower level of prefracture independence in ADL (HR, 2.53; 95% CI, 1.31-4.88; P = 0.006 and HR, 3.42; 95% CI, 1.66-7.03; P = 0.001) and the absence of prefracture fear of falling (HR, 0.65; 95% CI, 0.48-0.90; P = 0.009). Other factors (age, sex, cognition, malnutrition, presence of an informal caregiver, and anemia) did not show a significant association (P > 0.05).

Figure 2. Distribution of patients by state during short-term follow-up of patients with a proximal femoral fracture.



Each level, moving from the lower-left to the upper-right corner, corresponds to a state of the multi-state model: hospital admission, nursing home, home (meaning residing in an independent living situation, also including with homecare or in a residential home), home and functionally recovered, or dead. Time is presented in days from treatment.

Discussion

To our knowledge this is the first study to use multistate modeling to assess factors that may be independently associated with recovery after proximal femoral fracture. In addition, the model provides an overview of the transitions of patients through a set of recovery states. Of the community-dwelling older patients admitted with a proximal femoral fracture, 60.4% returned to independent living and 40.9% recovered to their prefracture level of independence in ADL.

The multistate model analyses, which focused on resilient patients who had reached an independent living situation within three months after treatment, identified four factors as being independently associated with the rate of recovery. These were prefracture mobility, comorbidity, prefracture independence in ADL, and fear of falling. Prefracture functional status and comorbidities have previously been identified as relevant, both in terms of determining a patients' resilience[4] and predicting functional outcomes.[30-32] A poorer rate of recovery in patients who experience fear of falling, especially for those with a high level of premorbid functionality, has also been observed previously.[16] A better prefracture functional status was associated with a more favorable outcome for each of the significant factors identified in this study, except for independence in ADL. We hypothesize that patients with a low level of prefracture independence in ADL lose a relatively lower degree of independence and therefore have less independence to recover, so it is less of an effort for them to return to their prefracture level. This corresponds with previous findings which indicate that most patients recover at similar rates, regardless of their prefracture functional level.[4]

Table 2. Factors independently associated with the rate of short-term recovery for independence in activities of daily living.

Characteristic	Adjusted* HR (95% CI)	P-value
Age, years	0.98 (0.96-1.00)	0.063
Sex, female	0.85 (0.61-1.19)	0.34
ASA classification		
I-II	1.0 (ref)	
III-IV	0.68 (0.49-0.95)	*0.025*
Parker Mobility Score		
7-9	1.0 (ref)	
4-6	0.61 (0.39-0.95)	*0.028*
0-3	0.31 (0.13-0.78)	*0.013*
Katz ADL score		
0-1	1.0 (ref)	
2-3	2.53 (1.31-4.88)	*0.006*
4-6	3.42 (1.66-7.03)	*0.001*
Cognitive impairment (yes)	1.26 (0.88-1.81)	0.21
Malnourished	1.44 (0.97-2.15)	0.069
Living situation		
Independent	1.0 (ref)	
Homecare or residential home	0.81 (0.47-1.42)	0.47
Informal caregiver (yes)	0.89 (0.66-1.22)	0.47
Fear of falling (yes)	0.65 (0.48-0.90)	*0.009*
Anemia (yes)	1.33 (0.98-1.82)	0.072

ASA, American Society of Anesthesiologists; ref reference category.
N=290; number of events = 188. A total of 43 observations were deleted due to absence. Italics indicate a P-value of <0.05. Higher ASA scores represent more severe comorbidities; higher Katz ADL scores represent lower levels of independency; and higher Parker mobility scores represent better levels of mobility. *Adjusted for all other factors in Table 2.

Consequently, those patients who have less function to regain, will reach their recovery endpoint sooner. Clinicians should be mindful of the expecting recovery rate and assess patients holistically to find underlying causes when a patient diverges from expectations.

Contrary to the findings of a recent systematic review on short-term prognostic factors of functional recovery, cognition and anemia showed no significant association.[10] This might indicate that these factors are relevant for the recovery of patients with proximal femoral fractures in general, but not for the recovery of independence in ADL in resilient patients who have recovered to a state of independent living. Cognitive status is an important factor with regards to discharge location, as patients with a cognitive impairment have a higher likelihood of being admitted to a nursing home. Anemia is most likely associated with elevated mortality rates rather than the re-

covery capacity of patients. In our multistate model, admission to a permanent nursing home and mortality were competing outcomes with our primary outcome. The analyses, however, focused only on resilient patients who succeeded in returning home, so risk for these competing outcomes is probably smaller in this subgroup compared to the population as a whole. This may explain why the factors cognition and anemia showed no significant associations.

Other variations in the methodology of this study compared to previous studies could in theory also contribute to the inconsistencies in findings. These include differences in overall patient selection, aspects such as the intensity of physiotherapy provided during recovery, the length of follow-up or the definition of functional recovery.

The current findings of this study emphasize the relevance of a holistic approach and systematic assessment of characteristics that have been found relevant by this study. A clinical profile could be constructed using the factors comorbidity, prefracture mobility, prefracture independence in activities of daily living and fear of falling, which help to assess the patients' post-acute care needs, including the needs for support in activities of daily living for patients who manage to return home within 3 months of treatment.

Multistate modeling seems an appropriate and flexible method which provides important insights, that might have otherwise been ignored when using an ordinary regression model.[28] The model allows for analyses of each individual transition, and multiple outcomes. This study focused on a late transition of the patients who had reached and independent form of living (defined as the resilient patients) to a recovered state of independency, in order to study their functional prognosis and the factors relevant for recovery. In addition, multistate models can be used to prognose patient outcomes at any specific moment in the recovery process. The model can take into account the patient's prefracture characteristics, aspects of treatment and all prior transition rates.[9] Future studies could use the model to predict outcomes at multiple time points, for instance at the moment of hospital discharge and geriatric rehabilitation discharge or during check-ups at specific intervals. This type of application might allow prediction of whether patients will manage independent living or walking without aides in the foreseeable future, and may lead to adjustments of rehabilitation and care aspects accordingly.

Limitations

This study describes a complete inception cohort of older patients with a proximal femoral fracture, and their transitions between states within a short-term recovery period after treatment. An adequate follow-up was achieved for most patients, and the primary combined outcome of this study ensured no loss to follow-up due to mortality.

This study included only older community-dwelling patients, so findings may be limited to this subpopulation. However, older community-dwelling patients form the majority of patients with a proximal femoral fracture. In addition, the recovery of independence in ADL has the most

significant social and economic impact in this specific patient group, as they risk additional reliance on (professional) caregivers or loss of independent living and institutionalization.

Follow-up was limited to three months, which roughly corresponds to the duration of geriatric rehabilitation provision in the Netherlands. A longer follow-up could have been considered, but this study focused on resilient patients who generally regain independent living within this time frame. A further possible limitation was that a more complex multistate model could have distinguished between a temporary stay in a geriatric rehabilitation home or discharge to permanent residence in a nursing home. Although this more elaborate model might have provided a more coherent overview, the added value for prognostic purposes could be questioned.

Conclusions and implications

This study identified 4 factors (comorbidity, prefracture mobility, prefracture independence in ADL, and fear of falling) with an independent prognostic value for the recovery of independence among resilient patients after a proximal femoral fracture. A multistate model has been demonstrated to be an effective and versatile tool in the study of recovery prognostics.

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