Longitudinal Study on Functional and Cognitive Outcomes in Patients with Postoperative Delirium after Femoral Fracture

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Research article

Keywords: Hip fracture, delirium, cognition, clinical outcome

Posted Date: July 3rd, 2019

DOI: <https://doi.org/10.21203/rs.2.11021/v1>

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Abstract

Background Proximal femoral fractures are frequent injuries of elderly people and are often associated with declines in physical function and high rates of morbidity and mortality. A severe and frequent complication after hip surgery is postoperative delirium (POD), potentially associated with poorer clinical outcomes. We hypothesized that elderly patients with POD after hip fracture showed significantly worse clinical outcomes within one year after the fracture, compared to patients not suffering from POD. Additionally, relevant predictors of POD were evaluated. **Methods** Patients with proximal femoral fractures aged ≥ 60 years were included in a prospective, single-center observational study in Germany and followed up for 12 months. POD was evaluated by daily application of the Confusion Assessment Method (CAM) during the acute hospital stay. A variety of standardized instruments were used to evaluate patients' functional and cognitive capacity, mobility, quality of life (HrQoL), depression, pain, etc., at baseline, discharge, and follow-up. A multiple logistic regression analysis was conducted to determine socio-demographic and clinical predictors of POD. **Results** Among 402 included patients (mean age: 81.3 ± 8.2 years), 184 (45.8%) developed POD (mean duration: 6.5 ± 4.4 days). At baseline, POD patients were significantly older, more often institutionalized, cognitively and physically more impaired, reported lower HrQoL, and had significantly more complications during the hospital stay. Multiple logistic regression analyses explained 22% of the variance, while prolonged intensive care unit stays, level of pain after surgery, and diminished pre-operative physical and cognitive state were significant predictors of POD. In-hospital mortality and overall mortality after 12 months were significantly higher in POD patients. Twelve months after the fracture, POD was significantly associated with diminished mobility, HrQoL, cognitive and functional capacity, and higher risk of falls. **Conclusions** Pain management is an important and controllable variable during hospital stay and should be a specific focus of the postoperative period, especially in functionally and cognitively impaired patients. Since patients with POD showed significantly worse clinical outcomes at discharge and 12 months post-fracture, prevention and effective treatment of POD should be of high priority in elderly patients with hip fractures.

Background

Postoperative delirium (POD) manifests in patients after surgical procedures and/or general anaesthesia. The current Diagnostic and Statistical Manual of Mental Disorders (DSM-V) defines POD as an acute beginning and fluctuating disturbance of consciousness with reduced ability to focus, maintain, or shift attention, accompanied by cognitive and perceptual disturbances. The definition of delirium in the International Classification of Diseases 10th edition (ICD-10) additionally includes psychomotor dysfunction, alteration of the sleep-wake cycle, and emotional disturbances [1].

POD prevalence rates vary widely, ranging from 9 to 87%, depending on the patients' age and the type of surgery [2]. The overall prevalence of POD in elderly patients is reported to be between 10 and 37% [3]. Despite improvements in surgical and anaesthetic techniques and patient selection for surgical procedures, orthopedic surgery is a clinical procedure with high incidence of delirium. Especially, hip

surgery has a high concomitant incidence of POD, which is more frequent in emergency hip fracture surgery (5.0 – 53.3%) compared to elective hip surgery (3.6 – 28.3%) [4].

Femoral fractures are common in the elderly. In Germany, the incidence is 100/100,000 per year [5]. Due to demographic changes in Western countries, the incidence rates of femoral fracture are expected to rise. Concomitantly, the number of postoperative complications is expected to increase, since POD is the most frequent complication after hip surgery [6]. Moreover, the diagnostic procedure should include the evaluation of risk factors for POD in patients with hip fracture, including cognitive impairment, age, sex, institutionalization, functional impairment, body mass index (BMI), comorbidities, polypharmacy, and vision impairment [7].

Several earlier studies longitudinally evaluated associations between POD and functional and cognitive outcomes, duration of hospital stays, and healthcare costs [8-10]. However, the prognostic relevance of POD for the survival as well as the clinical outcomes of elderly patients with hip fractures remains unclear [11]. The availability of data from prospective studies helps elucidate this relationship. Therefore, in 2009 the RePrOF study (Rehabilitation after Proximal Femoral Fracture) was set up as the largest prospective, observational study on clinical outcomes of patients with hip fracture in Germany and one of the largest international evaluations. Here, we hypothesized that the development of POD in a large cohort of patients with hip fracture was associated with the patients' functional and cognitive outcomes, quality of life, and further clinical characteristics on admission to the hospital, at discharge and 12 months after the fracture. Additionally, we evaluated clinical and socio-demographic predictors of POD.

Methods

Patients were eligible for the study if they were at least 60 years of age and had suffered a proximal femoral fracture (ICD-10 codes: S 72.0–72.2). Exclusion criteria were multiple trauma (Injury Severity Score ≥ 16) and malignoma-associated fractures. All patients were surgically treated with either internal fixation or hip arthroplasty at the Centre for Orthopedics and Trauma Surgery, University Hospital Giessen and Marburg, Germany. Approval of the Ethics Committee of the University of Marburg (AZ 175/08) for the study protocol was obtained prior to the study. All patients or their legal representatives gave their written consent before study participation and the study conforms to recognized standards as detailed in the Declaration of Helsinki.

Data collection

Data were collected by trained study personnel (research nurses, senior physicians, and/or trained medical doctoral students). On admission to the hospital, participating patients were examined by a senior physician, the patients' history was documented, and they were asked to report their (pre-fracture) health status with regard to their functional and psychological status, cognitive capacity, and health-related quality of life. During the surgery, data on treatment duration, occurring complications, and surgical procedures were recorded. After the surgery, patients were examined daily during their hospital stay. Patients were visited and examined again twelve months after discharge from the hospital.

Regarding the instruments used, patients were assessed pre-operatively for cognitive impairment (Mini-Mental State Examination, MMSE), depression (Geriatric Depression Scale, GDS-15), functional abilities before the fracture (Karnofsky index, Barthel index, Lawton Instrumental Activities of Daily Living, IADL) as well as health-related quality of life (EuroQol). The patient's histories comprised data on the accident and fracture details, medication, comorbidities (Charlson Comorbidity Index, CCI), mobility, family and residential status before the accident, American Society of Anaesthesiologists score (ASA), Glasgow Coma Scale (GCS), weight, height, and body mass index (BMI). During the hospital stay, data on the patients' stay at the intensive care unit (ICU), complications, pain (visual analogue scale), and mobilization (Timed "up and go" test (TUG), Harris Hip Score (HHS), Tinetti Test (TT)) were recorded and the development of POD was assessed daily by means of the Confusion Assessment Method (CAM).

CAM assesses the presence, severity, and fluctuation of nine delirium characteristics: acute onset, attention deficits, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and altered sleep-wake cycle. The CAM diagnostic algorithm is based on four cardinal features of delirium: 1) acute onset and fluctuating course, 2) inattention, 3) disorganized thinking, and 4) altered level of consciousness. A diagnosis of delirium according to CAM requires the presence of features 1, 2, and either 3 or 4 [12]. All raters were trained to use the CAM instrument for the assessment of delirium as well as all other measurements before the start of the study. For a more detailed description of methods used in this study, please see [13].

Data entry and statistics

Data were recorded in a Filemaker database (FileMaker Inc., Santa Clara, CA, USA). Double entry by two individuals with an automatically generated plausibility check was performed to ensure data quality. IBM SPSS statistics 24 (Statistical Package for the Social Sciences, IBM Cooperation, Armonk, N.Y., USA) was used for statistical analysis. All data concerning socio-demographic and clinical characteristics of the study population are presented as means with standard deviation (SD), minimum, median, and maximum or number of cases (percentages), where appropriate. Due to the non-normal distribution of the dependent variables according to the Kolmogorov-Smirnov test, differences between two independent groups were investigated using non-parametric tests (Mann-Whitney U test). Differences in relative frequency were evaluated by Chi-square tests.

A multiple logistic regression analysis was conducted to determine socio-demographic and clinical predictors of POD as a binary dependent variable. Crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were determined and the Hosmer-Lemeshow test was used to assess the goodness of fit for the logistic regression model. After controlling for multicollinearity, the following independent variables resulting from the baseline and in-hospital assessment were included: Age, sex, living situation, the use of psychotropic drugs, length of stay in the intensive care unit, patients' physical status (ASA classification), cognitive capacity (MMSE), comorbidities (CCI), ability to perform daily activities (Barthel Index), health-related quality of life (EQ-5D index), and the extent of pain after surgery.

Results

A total of 402 patients were enrolled in the RePROF study. Of these, 72.9% were female and the mean age was 81.3 ± 8.2 years (Table 1). During their hospital stay, 184 patients (45.8%) developed POD with a mean duration of 6.5 ± 4.4 days. The majority of affected patients ($n = 152$, 37.8%) developed POD within the first four days after surgery: at day 2 = 55 patients (29.9%), day 3 = 74 (40.2%), day 4 = 23 (12.5%), and days 5 to 12 = 32 (17.3%). Patients with POD were significantly older than patients without POD. There were no differences between the two groups concerning the patients' sex, their family status or education level (POD: 11.2 ± 2.2 years of education vs. non-POD: 11.1 ± 1.8 years, $p = 0.685$). In Germany, the statutory health insurance classified patients in need of care into three different levels at the time when this study was set up. On admission, significantly more POD patients were at care level I or II compared to the non-POD patients (Table 1).

On admission, 333 (82.8%) participants were community-dwelling, but significantly more patients who developed POD later were living in a nursing home ($n = 42$, 22.8%) compared to those who did not suffer POD ($n = 22$, 10.9%, $p = 0.003$). A total of 18 (5.4%) of 333 community-dwelling participants at baseline were institutionalized within the 12 months of the study period. There was no significant difference between POD and non-POD patients concerning the rate of institutionalization within the 12-month duration of the study ($n = 10$, 7.0% vs. $n = 8$, 4.5%, $p = 0.213$).

During the study period 102 participants (25.4%) died. In total, 25 patients (6.2%) died in hospital, 56 (13.9%) died during the first six months, and 21 (7.9%) between follow-up after six and 12 months (FU 6 and FU 12). As shown in Table 2, the in-hospital mortality as well as the overall mortality over the study period was significantly higher in the POD group.

The overall prevalence of pre-operative cognitive impairment in the RePROF cohort (MMSE scores below 27) was 66.4%. Patients who developed POD during the hospital stay scored significantly worse in the MMSE on hospital admission than the non-POD group: 142 patients (78.5%) of the POD group scored less than 27 points, compared to only 110 patients (54.7%) of the non-POD group ($p < 0.001$). Additionally, dementia was more often reported for nursing-home patients than for community-dwelling participants ($n = 42$, 60.9% vs. $n = 45$, 13.5%, $p < 0.001$).

CCI scores, ASA classification, and GCS on admission to the hospital were significantly worse in patients who developed POD (Table 1). A total of 258 patients (64.2%) of the cohort had two or more comorbid diseases according to CCI. The CCI showed significantly more chronic heart failure, diabetes mellitus, renal and cerebrovascular diseases in the POD group (Table 1).

As shown in Table 3, there were no significant differences between the groups concerning types of fracture, surgical procedures, time from admission to surgery (total mean $\pm$ SD: 18.3 ± 13.3 hours) or duration of surgery. In contrast, POD patients required post-surgical treatment in the ICU more often and stayed significantly longer in the ICU. Additionally, the self-reported pain levels were significantly higher in

POD patients. Especially during days 3 to 10 after surgical treatment, the median level of pain was considerably higher in POD patients.

After 12 months, patients who had suffered POD showed significantly worse outcomes in all clinical scales applied (Tables 2 and 4). The participants' functional and cognitive outcome as well as their HrQoL on admission and at FU 12 is detailed in Tables 2 and 4. On admission and at FU 12, POD patients had significantly decreased ability to perform daily activities (Karnofsky-Index, Barthel-Index, Lawton IADL) and diminished cognitive capacity according to the MMSE.

In contrast, there was no considerable difference in the presence of depression (GDS-15) between the groups (POD and non-POD) at baseline or at FU 12 (Table 4). Regarding the participants' HrQoL, POD patients had significantly lower values in the EQ-5D index at baseline and at FU 12. Although the results of the EQ VAS were higher for the non-POD patients at both assessments, the differences were not significant (Table 4).

Furthermore, we assessed the patients' mobility at discharge from the acute care hospital and at FU 12 with TUG, TT, and HHS. Patients with POD showed significantly worse results in the TUG at FU 12, in the TT, and the HHS at both assessments, and were at a significantly higher risk of falling at discharge and 12 months later (Table 2). In summary, patients with POD showed significantly worse clinical outcomes in all scales applied (Tables 2 and 4). But it is of note that all POD patients had – with the exception of the timed “up and go” test – significantly worse test results on admission or at discharge from the hospital, respectively.

Finally, we assessed predictors for the development of POD using multiple logistic regression analysis. As depicted in Table 5, the longer the patients were treated in the ICU, the higher the risk of developing POD (OR 1.174, 95% CI: 1.021 – 1.351). Additionally, patients suffering from more severe physical constraints on admission (ASA score) were at higher risk of developing POD (OR 2.140, 95% CI: 1.072 – 4.272). Also, restrictions in the patients' functional ability before hospital stay were correlated with a higher risk of POD (Barthel-Index: OR 0.980, 95% CI: 0.960 – 0.998). Furthermore, participants who scored higher in the MMSE on admission, indicating less impaired cognitive function, had lower risk of POD (OR 0.940, 95% CI: 0.885 – 0.999). The patients' self-reported extent of pain after surgery was also strongly associated with the development of POD (OR 1.140, 95% CI: 1.014 – 1.281). In total, the independent variables explained 22% of the variance in the regression model.

Discussion

Although POD is a common complication after orthopedic surgery, there is no consensus on the incidence rates in the literature. A meta-analysis of 26 studies focused on POD after orthopedic surgery reported an incidence ranging from 4% to 53% [4]. In our cohort, 184 of 402 patients (45.8 %) developed POD, which is higher than reported in other recent studies and can only partly be explained by differences in recruitment or the diagnostic method of delirium [14]. The highest level of POD incidence was on postoperative day 2, which is in accordance with data from other studies [15].

Several preoperative risk factors for POD have been described: Cognitive impairment, age, sex, institutionalization, functional impairment, BMI, comorbidities, ASA classification, acute medical conditions, polypharmacy, and vision impairment [7]. Our cohort reflected most of the previously described risk factors: POD patients had more often a pre-existing diagnosis of dementia, scored lower on the MMSE on hospital admission, were older and lived more often in nursing homes at the time of the fracture. Additionally, our findings add that they also had higher care levels, lower functional capacity as well as higher CCI and ASA scores on admission to the hospital.

In our cohort, patients who developed POD reported significantly more often chronic heart failure, diabetes mellitus, cerebrovascular disease, and dementia, which are known to increase the risk of POD [16]. Especially, conditions either increasing cerebrovascular risk or indicating vascular damage were shown to increase the risk of POD. Rudolph and colleagues found that, in patients with cerebrovascular risk factors and impaired cognition, the risk of POD doubled compared with those with either of these risk factors alone [17]. In a systematic review by Oh and colleagues, cognitive impairment was one of the strongest preoperative risk factors for POD after hip fracture surgery [7]. In our cohort, this was also true: Patients who developed POD had significantly more often a pre-existing diagnosis of dementia and scored significantly worse on the MMSE on admission. Preoperative cognitive assessment may be one of the most useful methods to identify those at a high risk of POD and to take preventive measures.

Other studies have identified depression as an independent risk factor for the development of POD [18]. Patients with preoperative depressive symptoms are at higher risk for developing POD of longer duration. In our cohort, POD patients had significantly higher mean scores in the GDS, although notably, both groups had identical median scores. Therefore, GDS was not included as an independent variable in the multiple regression analysis.

One of the risk factors for POD that can easily be influenced during the hospital stay is pain. Bilge and co-workers detected higher pain VAS values in delirium-developing patients and showed that pain scores influenced the development of delirium [16]. Björkelund et al. suggested that effective pain treatment would decrease the incidence of delirium in patients surgically treated due to hip fractures [19]. In our cohort, the median level of pain was considerably higher in POD patients on postoperative days 3 to 10. Developing and implementing guidelines for the management of effective pain treatment may be a preventive method in POD, especially in the early postoperative period. Although a lot of scientific effort has been invested in the elucidation of potential risk factors for the development of postoperative delirium in elderly patients, there is still no final, conclusive set of risk factors or predictors for POD [7, 10].

One aim of the longitudinal RePrOF study was to examine associations between the occurrence of POD in patients with hip fracture and their HrQoL as well as their functional and cognitive capacities. POD patients' HrQoL (EQ-5D index) was significantly lower on admission and at FU 12. We were not successful in identifying earlier studies on geriatric hip fracture patients to examine the association of HrQoL and POD in these. Chen et al. published data from a study on POD (diagnosed by CAM) and HrQoL (measured with the SF-36 questionnaire) in patients undergoing coronary artery bypass graft. The

authors reported that impaired cognitive function was associated with poorer HrQoL. However, no relationship between POD and poorer HrQoL was found, while HrQoL was associated with impaired cognitive function [20].

The long-term cognitive and functional outcomes of hip fracture patients with POD are poorer than those of non-POD patients [21]. Contrasting earlier reports, there is increasing evidence that POD is not a transient, reversible phenomenon, but it has been shown that the occurrence of POD leads to further cognitive decline in affected patients. Inouye and colleagues examined the cognitive trajectories of more than 560 elderly patients without dementia who underwent major surgery and found greater immediate impairment as well as significantly greater long-term cognitive decline relative to the non-delirium group, which was further corroborated by proxy reports [22].

The necessity of institutionalization of patients after hip surgery implies a high burden for patients, their families, and society. An American claims data analysis showed that 34% of patients were admitted to a nursing home within one year after surgery, hinting at an increased risk of nursing home placement for POD patients compared to non-POD patients [23]. However, in our cohort a similar proportion of POD patients were institutionalized within one year after surgery compared to the non-POD group. One recent approach to prevent institutionalization was based on Comprehensive Geriatric Assessment (CGA) by Inpatient Geriatric Consultation Teams (IGCT) to detect geriatric problems and to address the specific needs in 171 frail older adults undergoing hip fracture surgery [24].

In our cohort, POD patients showed a significantly higher in-hospital mortality as well as overall mortality over the study period. Although other studies have reported higher mortality rates in POD patients, a recent systematic review by Hamilton and colleagues found that only a few studies exist estimating the impact of POD on mortality in adult non-cardiac surgery patients. Among these, studies controlling for confounders failed to demonstrate significant independent associations of delirium and mortality [25]. In contrast, Moskowitz et al. found an overall incidence of delirium of 44% in POD patients and a 7.4-fold higher risk of five-year-mortality in a cohort of 172 patients undergoing elective surgery [26].

Our study has several limitations. First, the participants were consecutively recruited in only one study site, posing a risk of selection bias. Additionally, the cohort examined may not be representative of the German population. Second, although the interviewers were extensively trained in the appropriate application of the instrument, misdiagnoses cannot be fully excluded. Third, the pre-fracture IADL and BI were assessed retrospectively, posing a risk of recall bias regarding the patients' self-rating of their functional abilities. However, we think this was the best method to assess the patients' pre-fracture function as used in earlier studies [27, 28].

Conclusions

In conclusion, the RePrOF cohort provided data for 402 geriatric patients with hip fractures. A multiple logistic regression analysis revealed that the pre-operative physical and cognitive state and the patients'

self-reported level of pain after surgery have to be considered as significant predictors of POD. Especially patients suffering from POD during their hospital stay showed significantly diminished outcomes in terms of function, mobility, cognition, HrQoL and mortality at discharge and 12 months post-fracture. Since POD is one of the most frequent and burdening complications after surgery in geriatric patients, further efforts should be made to develop screening tools for the prediction of adverse postoperative events as well as specific treatment schedules to prevent the occurrence of POD in this vulnerable population. In case of POD development, an effective treatment is essential to maintain patients' clinical outcomes longitudinally.

To our best knowledge, this is the first primary data analysis in Germany assessing a large cohort of hip fracture patients from admission to the acute care hospital, during hospital stay, and re-evaluating the patients 12 months after fracture.

List Of Abbreviations

ASA: American Society of Anesthesiologists Score

BI: Barthel Index

BMI: Body mass index

CAM: Confusion Assessment Method

CCI: Charlson Comorbidity Index

CGA: Comprehensive Geriatric Assessment

DSM: Diagnostic and Statistical Manual of Mental Disorders

EQ-5D: EuroQol – 5 Dimensions

GCS: Glasgow Coma Scale

GDS-15: Geriatric Depression Scale (15 items)

HHS: Harris Hip Score

HrQoL: Health-related quality of life

IADL: Lawton Instrumental Activities of Daily Living

ICD-10: International Classification of Diseases 10th edition

ICU: intensive care unit

IGCT: Inpatient Geriatric Consultation Teams

KI: Karnofsky Index

MMSE: Mini-Mental State Examination

POD: Postoperative Delirium

RePrOF: Rehabilitation after Proximal Femoral fracture

SD: Standard Deviation

TT: Tinetti Test

TUG: Timed Up and Go Test

VAS: Visual Analogue Scale

Declarations

Ethics approval and consent to participate

Approval of the Ethics Committee of the University of Marburg (AZ 175/08) for the study protocol was obtained prior to the study and the study conforms to recognized standards as detailed in the Declaration of Helsinki.

Consent for publication

All patients or their legal representatives gave their written consent before study participation.

Availability of data and material

The dataset supporting the conclusions of this article is included within the article.

Competing interests

Monika Balzer-Geldsetzer, Benjamin Buecking, Steffen Ruchholtz, Bernhard Kis, and Philipp Hessmann have no conflicts of interest to declare. Richard Dodel reports personal fees from Abbott / Abbvie, grants from Baxter, non-financial support from Betreuungsverein Biedenkopf, grants and non-financial support from BMBF (DLR), non-financial support from Deutsche Gesellschaft für Neurologie, non-financial support from Deutsche Parkinson Gesellschaft, grants from Deutsche Parkinson Vereinigung, personal

fees from DZNE Deutsches Zentrum für neurodegenerative Erkrankungen, non-financial support from EBC European Brain Council, grants from Faber-Stiftung, grants from Internationale Parkinson Fonds, non-financial support from KNDD Kompetenznetz Degenerative Demenzen, personal fees from Lilly, non-financial support from Medizinische Hochschule Hannover, grants from M.J.Fox Foundation, personal fees from Movement Disorder Society, personal fees from Novartis, personal fees from Octapharma, personal fees from Pfizer, personal fees from Thieme Verlag, other from Transmit GmbH, grants from UKGM, personal fees from Med Update, personal fees from Studienstiftung des deutschen Volkes, non-financial support from National Board of Health and Healthcare Schweden, grants from EU Horizon 2020, personal fees from Axon Neuroscience, non-financial support from Universitätsklinikum Tübingen, non-financial support from Forschungszentrum Jülich, non-financial support from European Academy of Neurology (EAN), non-financial support from Universität Regensburg, grants from AOK Gesundheitskasse Hessen, grants from AOK Gesundheitskasse Sachsen und Thüringen, non-financial support from Kliniken Beelitz GmbH, non-financial support from Rudi Assauer Initiative Demenz und Gesellschaft, personal fees from Klinikum Fulda, personal fees from Krankenhaus der Barmherzigen Brüder Trier, non-financial support from Universitätsklinikum Hamburg Eppendorf, non-financial support from Klinikum Bad Hersfeld, non-financial support from Deutsche Gesellschaft für Gerontologie und Geriatrie e. V., non-financial support from Kurpfalzkrankenhaus Heidelberg, non-financial support from Universitätsklinikum Ulm, non-financial support from Westpfalz-Klinikum Kaiserslautern, non-financial support from Universitätsklinikum Schleswig-Holstein, non-financial support from Universitätsklinikum Aachen, non-financial support from Universitätsklinikum Ulm, non-financial support from Bayer Vital GmbH, non-financial support from Deutscher Hausärzteverband, non-financial support from Gemeinsamer Bundesausschuss, personal fees from Ono Pharma UK Ltd., personal fees from Dr. Willmar Schwabe GmbH & Co. KG, personal fees from Kohlhammer GmbH, personal fees from Akademie für medizinische Fortbildung, personal fees from Johanniter GmbH, outside the submitted work.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit-sectors.

Authors' contributions

All authors have read and approved the manuscript. RD, MBG, BB, and SR contributed to the study design, the data collection, and critically reviewed the manuscript. PH, RD, MBG, and BK contributed to the data analysis, data interpretation, and writing of the manuscript.

Acknowledgements

We would like to thank all participating patients and colleagues involved in planning, conducting, and analyzing the presented data evaluation. Especially, the authors want to thank Kristin Horstmann and Anna Waldermann for their support.

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Tables

Table 1: Socio-demographic and clinical characteristics of the study population on admission to the hospital.

	Total (n = 402)	POD (n = 184)	No POD (n = 201)	p-value
Age				$p < 0.001$
Mean $\pm$ SD	81.3 $\pm$ 8.2	83.2 $\pm$ 7.3	79.5 $\pm$ 8.5	
Median (range)	82.3 (60.0 – 99.0)	84.0 (60.0 – 99.0)	80.0 (60.0 – 99.0)	
Sex				$p = 0.512$
Male, n (%)	109 (27.1)	55 (29.9)	50 (24.9)	
Female, n (%)	293 (72.9)	129 (70.1)	151 (75.1)	
Living Situation				$p = 0.003$
Community dwelling, n (%)	333 (82.8)	142 (77.2)	179 (89.1)	
Nursing home, n (%)	69 (17.2)	42 (22.8)	22 (10.9)	
Family Status, n (%)				$p = 0.393$
Married	161 (40.0)	72 (39.1)	83 (41.3)	
Divorced	14 (3.5)	4 (2.2)	10 (5.0)	
Single	24 (6.0)	13 (7.1)	9 (4.5)	
Widowed	197 (49.0)	94 (51.1)	98 (48.8)	
Care Level, n (%)				$p < 0.001$
None	249 (61.9)	88 (47.8)	151 (75.1)	
Level I	79 (19.7)	47 (25.5)	29 (14.4)	
Level II	68 (16.9)	47 (25.5)	17 (8.5)	
Level III	6 (1.5)	2 (1.1)	4 (2.0)	
ASA classification, n (%)				$p < 0.001$
1	5 (1.2)	1 (0.5)	4 (2.0)	
2	72 (17.9)	18 (9.8)	51 (25.4)	
3	259 (64.4)	130 (70.7)	123 (61.2)	
4	44 (10.9)	25 (13.6)	13 (6.5)	
5	2 (0.5)	2 (1.1)	0 (0.0)	
3DS-15				$p = 0.022$
Mean $\pm$ SD	3.7 $\pm$ 3.0	4.0 $\pm$ 3.0	3.4 $\pm$ 3.0	
Median (range)	3.0 (0 – 13)	3.0 (0 – 13)	3.0 (0 – 13)	
Cognitive impairment, n (%)				$p < 0.001$
MMSE 27-30	132 (32.8)	39 (21.2)	91 (45.3)	
MMSE 20-26	134 (33.3)	62 (33.4)	71 (35.3)	
MMSE 10-19	71 (17.7)	43 (23.4)	21 (10.4)	
MMSE 0-9	62 (15.4)	37 (20.1)	18 (9.0)	
CCI				$p = 0.001$
Mean $\pm$ SD	2.4 $\pm$ 2.3	2.6 $\pm$ 2.3	2.1 $\pm$ 2.3	
Median (range)	2.0 (0 – 12)	2.0 (0 – 12)	1.0 (0 – 11)	
Comorbidities (CCI), n (%)				
Chronic heart failure	135 (33.6)	69 (37.5)	57 (28.4)	$p = 0.032$
Diabetes mellitus	99 (24.6)	58 (31.5)	34 (16.9)	$p = 0.001$
Dementia	87 (21.6)	54 (29.3)	26 (12.9)	$p < 0.001$
Cerebrovascular disease	87 (21.6)	43 (23.4)	37 (18.4)	$p = 0.003$
Renal disease	37 (9.2)	21 (11.4)	12 (6.0)	$p = 0.021$

POD: Postoperative Delirium. SD: Standard Deviation. FU: Follow-Up. ASA: American Society of Anesthesiologists.

Table 2: Mortality and clinical state of the population at discharge and at Follow-Up after 12 months.

	POD (at discharge: n = 170) (at FU 12: n = 81)	No POD (at discharge: n = 196) (at FU 12: n = 126)	p-value
TUG at discharge (seconds)			p = 0.337
Mean ± SD	43.2 ± 40.2	39.8 ± 45.2	
Median (range)	30.0 (9 - 240)	29.5 (7 - 370)	
TUG at FU 12 (seconds)			p < 0.001
Mean ± SD	37.3 ± 27.2	25.2 ± 23.4	
Median (range)	25.5 (10 - 120)	18.0 (8 - 197)	
Tinetti Test at discharge			p < 0.001
Mean ± SD	6.0 ± 6.2	12.8 ± 8.7	
Median (range)	3.0 (1 - 28)	12.0 (1 - 28)	
Tinetti Test at FU 12			p < 0.001
Mean ± SD	12.3 ± 9.5	19.8 ± 8.6	
Median (range)	13.0 (1 - 28)	22.0 (0 - 28)	
Harris Hip Score at discharge			p < 0.001
Mean ± SD	39.1 ± 20.4	53.3 ± 19.7	
Median (range)	41.0 (0 - 88)	57.0 (0 - 92)	
Harris Hip Score at FU 12			p < 0.001
Mean ± SD	60.2 ± 19.7	71.7 ± 22.3	
Median (range)	58.0 (0 - 96)	77.0 (0 - 100)	
Falls Assessment at discharge			p < 0.001
At risk to fall, n (%)	133 (72.3)	111 (55.2)	
Not at risk to fall, n (%)	35 (19.0)	82 (40.7)	
Falls Assessment at FU 12			p = 0.005
At risk to fall, n (%)	43 (53.0)	39 (30.9)	
Not at risk to fall, n (%)	35 (43.2)	70 (55.5)	
Mortality			
Entire study period, n (%)	59 (32.1)	32 (15.9)	p < 0.001
In-hospital, n (%)	14 (7.6)	5 (2.5)	p < 0.001
Discharge until FU 6, n (%)	33 (17.9)	20 (10.0)	p = 0.070
FU 6 months until FU12, n (%)	12 (6.5)	7 (3.5)	p = 0.190
POD: Postoperative Delirium. SD: Standard Deviation. FU: Follow-Up. TUG: Timed “Up and Go”-Test. p-value based on the Mann Whitney U test and the Chi square test.			

Table 3: Patients' treatment in the acute hospital in patients with and without postoperative delirium.

	POD	No POD	p-value
Fracture location			p = 0.375
Femoral neck, n (%)	85 (46.2)	99 (49.3)	
Trochanteric, n (%)	92 (50.0)	89 (44.3)	
Subtrochanteric, n (%)	7 (3.8)	13 (6.5)	
Time from admission to surgery (hours)			p = 0.656
Mean $\pm$ SD	18.7 $\pm$ 13.7	17.9 $\pm$ 13.2	
Median (range)	18.0 (1.3 - 92.8)	16.8 (0.75 - 91.2)	
Surgical treatment			p = 0.718
Prosthesis, n (%)	72 (39.1)	85 (42.3)	
Internal fixation, n (%)	112 (60.9)	116 (57.7)	
Duration of surgical treatment (minutes)			p = 0.948
Mean $\pm$ SD	60.5 $\pm$ 28.6	61.6 $\pm$ 31.0	
Median (range)	54.0 (15 - 215)	56.0 (13 - 193)	
Additional surgical treatment required			p = 0.326
Yes, n (%)	10 (5.4)	6 (3.0)	
No, n (%)	174 (94.6)	195 (97.0)	
Length of stay in acute hospital (days)			p = 0.069
Mean $\pm$ SD	15.0 $\pm$ 7.6	13.1 $\pm$ 3.8	
Median (range)	14.0 (2 - 50)	13.0 (3 - 28)	
Treatment in intensive care unit required			p = 0.002
Yes, n (%)	167 (90.8)	156 (77.6)	
No, n (%)	17 (9.2)	45 (22.4)	
Length of stay in intensive care unit (days)			p < 0.001
Mean $\pm$ SD	4.0 $\pm$ 4.9	2.3 $\pm$ 1.8	
Median (range)	2.0 (1 - 45)	2.0 (1 - 14)	
Reuptake in intensive care unit required			p < 0.001
Yes, n (%)	39 (21.2)	12 (6.0)	
No, n (%)	145 (78.8)	189 (94.0)	
Pain Assessment (VAS)			p = 0.041
Mean $\pm$ SD	4.3 $\pm$ 2.3	3.8 $\pm$ 2.0	
Median (range)	4.4 (0 - 10)	3.8 (0 - 10)	

POD: Postoperative Delirium. SD: Standard Deviation. VAS: Visual Analogue Scale. p-value based on the Mann Whitney U test and the Chi square test.

Table 4: Clinical state of the population on admission and at follow-Up after 12 months

	POD (on admission: n = 184) (at FU 12: n = 81)	No POD (on admission: n = 201) (at FU 12: n = 126)	p-value
Karnofsky-Index on admission			p < 0.001
Unrestricted capacity, n (%)	29 (15.8)	88 (43.8)	
Restricted capacity, n (%)	151 (82.1)	112 (55.7)	
Karnofsky-Index at FU 12			p < 0.001
Unrestricted capacity, n (%)	10 (12.3)	75 (59.5)	
Restricted capacity, n (%)	71 (87.7)	51 (40.5)	
MMSE on admission			p < 0.001
Mean $\pm$ SD	18.2 $\pm$ 9.5	23.1 $\pm$ 7.7	
Median (range)	21.0 (0 - 30)	26.0 (0 - 30)	
MMSE at FU 12			p < 0.001
Mean $\pm$ SD	16.5 $\pm$ 11.3	24.5 $\pm$ 7.3	
Median (range)	21.0 (0 - 30)	27.0 (0 - 30)	
GDS on admission			p = 0.119
Depression, n (%)	58 (31.5)	52 (25.9)	
No Depression, n (%)	101 (54.9)	141 (70.1)	
GDS at FU 12			p = 0.184
Depression, n (%)	32 (39.5)	41 (32.5)	
No Depression, n (%)	38 (46.9)	81 (64.2)	
Barthel-Index on admission			p < 0.001
Mean $\pm$ SD	73.9 $\pm$ 24.3	85.6 $\pm$ 22.8	
Median (range)	80.0 (0 - 100)	95.0 (0 - 100)	
Barthel-Index at FU 12			p < 0.001
Mean $\pm$ SD	52.8 $\pm$ 34.0	82.1 $\pm$ 24.1	
Median (range)	55.0 (0 - 100)	95.0 (0 - 100)	
IADL at admission			p < 0.001
Mean $\pm$ SD	3.4 $\pm$ 2.8	5.6 $\pm$ 2.8	
Median (range)	3.0 (0 - 8)	7.0 (0 - 8)	
IADL at FU 12			p < 0.001
Mean $\pm$ SD	2.1 $\pm$ 2.6	5.1 $\pm$ 3.0	
Median (range)	1.0 (0 - 8)	6.0 (0 - 8)	
EQ-5D Index on admission			p = 0.003
Mean $\pm$ SD	0.68 $\pm$ 0.31	0.75 $\pm$ 0.30	
Median (range)	0.80 (- 0.205 - 0.999)	0.89 (- 0.205 - 0.999)	
EQ-5D Index at FU 12			p < 0.001
Mean $\pm$ SD	0.45 $\pm$ 0.34	0.72 $\pm$ 0.30	
Median (range)	0.39 (- 0.205 - 0.999)	0.81 (- 0.205 - 0.999)	
EQ VAS on admission			p = 0.066
Mean $\pm$ SD	54.9 $\pm$ 21.0	58.0 $\pm$ 24.0	
Median (range)	50.0 (0 - 100)	57.0 (0 - 100)	

EQ VAS at FU 12

p = 0.368

Mean $\pm$ SD60.1 $\pm$ 22.263.1 $\pm$ 20.6

Median (range)

60.0 (10 – 100)

64.0 (2 – 100)

POD: Postoperative Delirium. SD: Standard Deviation. FU: Follow-Up. MMSE: Mini Mental State Examination. GDS: Geriatric Depression Scale. IADL: Lawton's Instrumental Activities of Daily Living. EQ-5D: EuroQol - 5 Dimensions. EQ VAS: EuroQol Visual Analogue Scale. p-value based on the Mann Whitney U test and the Chi square test.

Table 5: Multiple logistic regression analysis with the development of a post-operative delirium as dependent variable.

ble	Regression Coefficient	Standard Error	Odds Ratio	95%-Odds Ratio Confidence Interval	p-value
	0.032	0.024	1.032	0.984 – 1.083	0.194
male					
ale	0.062	0.392	1.064	0.493 – 2.295	0.874
g Situation (admission)					
community-dwelling					
rsing Home	0.498	0.656	1.646	0.455 – 5.953	0.447
otropropic Drugs					
)					
s	- 0.415	0.364	0.661	0.324 – 1.347	0.254
tay (days)	0.161	0.072	1.174	1.021 – 1.351	0.025
score (admission)	0.761	0.353	2.140	1.072 – 4.272	0.031
E (admission)	- 0.061	0.031	0.940	0.885 – 0.999	0.047
lmission)	- 0.020	0.010	0.980	0.960 – 0.998	0.045
admission)	0.060	0.084	1.062	0.900 – 1.252	0.476
D index (admission)	1.407	0.735	4.084	0.968 – 17.232	0.055
(VAS)	0.131	0.060	1.140	1.014 – 1.281	0.029

otropropic drugs: including antidepressants, benzodiazepines, antipsychotics, opioids, anticholinergics, epileptics, and drugs against dementia as well as Parkinson's disease. ICU: Intensive Care Unit. ASA: American Society of Anesthesiologists risk classification. MMSE: Mini-Mental State Examination. BI: Barthel-Index. CCI: Charlson Comorbidity Index. EQ-5D: EuroQol - 5 Dimensions. VAS: Visual Analogue Scale. Hosmer-Lemeshow-test: p = .221.