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Prospective cohort protocol examining the perioperative indicators for complications and early mortality following hip fracture surgery in the frail patient

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ABSTRACT

Introduction The primary aim is to validate earlier suggested risk factors and to find new associated risk factors for (30-day) mortality after a hip fracture in the frail population. The secondary aim is to determine the factors associated with perioperative complications. At last we want to develop and validate a more specific 30-day mortality prediction tool compared with the Nottingham Hip Fracture Score. The 30-day mortality prediction can help inform surgical risk and guide shared decision-making among patients, family and physicians.

Methods and analysis The study is designed as a prospective multicentre cohort study within the area of Rotterdam, the Netherlands starting from January 2018. All patients over 65 years of age, with an acute proximal hip fracture, are included. Treatment of patients will be by standard practice of care using the latest national and international guidelines. Inclusion will be continued at least until January 2021 and including at least 2500 patients. In this large cohort we hope to have sufficient strength and quality to identify risk factors of 30-day mortality and to compare them to known risk factors in literature. Moreover, we plan to develop and validate a 30-day mortality prediction tool, which identifies patients with a high probability of 30-day mortality.

Ethics and dissemination Ethical approval for this protocol was given by the Ethics Committee of the Maasstad Hospital (TWOR). Patient data are stored anonymously using the Castor data management system. No external funding is used for this study. Results will be published in peer-reviewed publications and at international conferences.

Trial registration number NL8313.

Strengths and limitations of this study

- Large and comprehensive prospective hip fracture database.
- The design of a prospective ongoing database, research questions related to complications and clinical outcomes can be answered.
- This study is not a randomised controlled trial focusing on specific research questions.

INTRODUCTION

Fractures of the hip are associated with high overall morbidity and mortality rates. Following a hip fracture, even frail patients with major comorbidities are in need for surgery, aiming for pain relief and early mobilisation.[1 2] Complications after surgery are inevitable in this fragile population and high incidence rates of delirium (23%–39%), pneumonia (5.9%), surgical site infections (5%) and myocardial infarction (1.9%) have been reported.[1–6] In addition to high complication rates, high mortality rates are reported after hip fracture surgery. Early postoperative mortality is particularly high, with reported 30-day mortality rates of 5.4%–13.3%.[6–10] Age, comorbidities, perioperative management and postoperative complications mostly influence the risk of mortality.[6 11–14] Determination of risk factors supports clinicians to identify patients at high risk for mortality and enables accurate preoperative risk assessment. A known high risk for mortality can support appropriate informed consent (patient and family), timing of surgery, and enable possibilities for intervention with respect to perioperative management.

Risk factors for mortality identified in previous literature are age, male gender, cognitive impairment, multiple comorbidities, diabetes, cancer, abnormal ECG, institutionalisation, functional impairment (prefracture mobility), body mass index, a high American Society of Anesthesiologists classification and infections during admission.[12 13 15]

The primary aim of the present study is to validate earlier suggested risk factors and find

new associated factors for 30-day mortality. The secondary aims are:

- To collect epidemiological data about the background and incidence of patients with a hip fracture in the Rotterdam area between 2018 and 2022.
- To analyse clinical outcomes such as in-hospital mortality, length of hospital stay and complications after surgery to gain a more complete insight in the postoperative outcome.
- To monitor the implementation and functioning of a geriatric trauma unit within orthopaedic trauma units.
- To develop a more specific 30-day mortality prediction tool compared with the Nottingham Hip Fracture Score (NHFS) for clinical usage.

PATIENTS AND METHODS

Project context

Based on the results of our previous studies in the FranciscusHospital and Maasstad Hospital in Rotterdam we found a 30-day mortality rate of 9.5% after hip hemiarthroplasty in patients with proximal femur fractures.[16] In that study baseline characteristics and clinical outcomes were retrospectively obtained from the hospital records. For a more specific and definitive answer to prognostic factors for 30-day mortality in our population, we will have to include patients with a proximal femur fracture in a prospective study design with all types of proximal femur fractures included (femoral neck, pertrochanteric and subtrochanteric fractures). The primary outcome is mortality within 30 days after admission. This time frame is chosen because 30 days is the common follow-up period after surgery to study the association between perioperative mortality and a hip fracture.[10 17 18] Mortality at 3 and 12 months after surgery will be analysed as secondary outcomes.

Study design and population

The study is designed as a prospective cohort study within the area of Rotterdam, the Netherlands starting from January 2018 (figure 1). All patients over 65 years of age, with an acute proximal hip fracture (intracapsular, trochanteric or subtrochanteric), are included. Excluded are patients with multitrauma injuries, pathological fractures without sufficient trauma mechanism, or patients with no understanding of the Dutch or English language. Table 1 provides an overview of the planned collection of baseline characteristics of the patients. Treatment of patients will be by standard practice of care using the latest national and international guidelines. After admission at the emergency department a pelvic X-ray is made as soon as possible. After diagnosing a hip fracture, the patient is transferred to orthopaedic trauma department. A geriatrician is consulted prior to surgery for each patient with a hip fracture. If the patient is known with cognitive impairment or suspected of having it, the patient will be admitted to the geriatric trauma unit within the orthopaedic trauma department. Within the geriatric trauma unit a dedicated geriatric team of nurses is present to treat the patient in an environment which aims to imitate a nursing home facility as close as possible. From day 1 after surgery the patient is mobilised with physiotherapy and the patients are eating and staying in a living room during the day to facilitate a day and night rhythm. Our previous studies showed that 30% of patients were admitted from a semi-independent nursing home or nursing home facility.[19] The remaining patients were in need of recovery in a nursing home facility after surgery. Therefore, from day 1 after surgery there is an inventory and application for aftercare and revalidation in a nursing home facility.

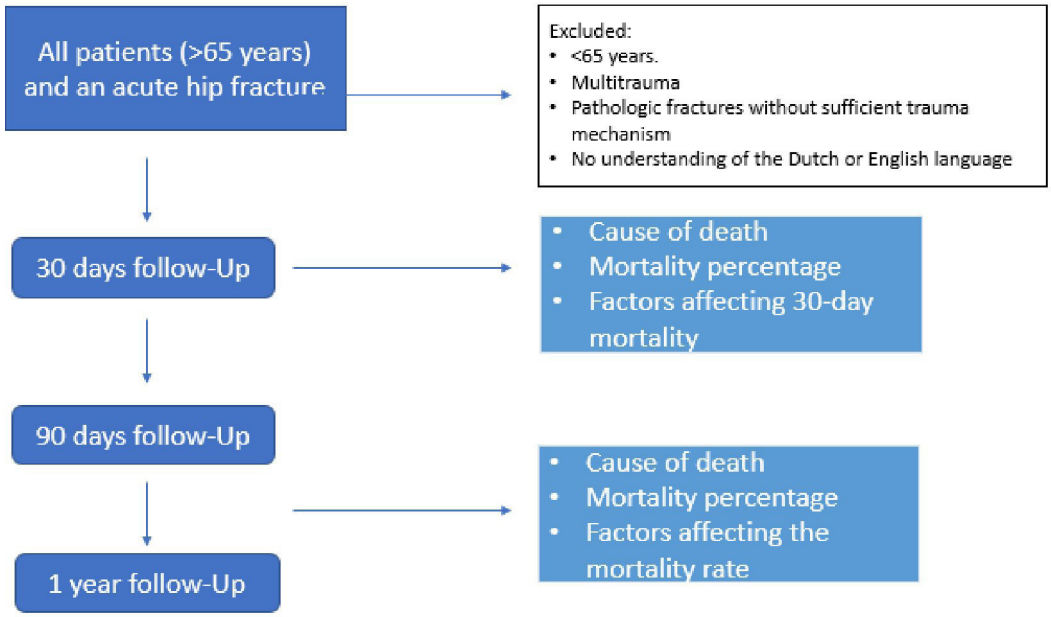

Figure 1 Flow chart. Overview of planned inclusion and follow-up.

Table 1 Collection of baseline characteristics of the patients

Factor				
Baseline characteristics				
Age				
Gender				
BMI				
ASA score				
NHFS				
Residential status				
Walking aids (inside/outside)				
Katz ADL index				
Cardiac comorbidities	Rhythm anomalies	Valve insufficiency	Myocardial infarction	Hypertension
Pulmonary comorbidities	COPD			
Brain comorbidities	Cerebrovascular accident	Parkinson's		
Cognitive dysfunction	Dementia	Psychiatric disorders		
Malignancy				
Musculoskeletal	Osteoporosis	Previous fractures		
Kidney failure	GFR			
Endocrine failure	Diabetes mellitus			
Autoimmune disease	Rheumatoid arthritis			
Vascular disease				
Use of medication				

ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate (in mL/min/1.73 m^2); Katz ADL, Katz Index of Independence in Activities of Daily Living; NHFS, Nottingham Hip Fracture Score.

Mortality prediction tools

Preoperative risk factors for mortality have been identified,[6 12 13 19] and various risk stratification tools assessing patients' risk of morbidity and mortality, such as the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity, the Charlson Comorbidity Index, the NHFS and modifications (Almelo Hip Fracture Score), have been developed to predict 30-day mortality risk after surgery.[8 20–26] In comparison to other models the NHFS shows the most promising results after extensive validation and with reasonable discrimination.[21 27] To verify whether the mortality after an intracapsular hip fracture was higher compared with the predicted mortality score according to the NHFS, a validation of the NHFS in patients with a hemiarthroplasty after an intracapsular hip fracture was performed in one of our previous studies.[16] Findings suggest that for a patient with a hemiarthroplasty following an intracapsular hip fracture, there could be an underestimation for the 30-day mortality rate following the NHFS prediction model.[16] In our prospective database the NHFS will be calculated and used as a benchmark model for prediction of 30-day mortality.

Data analyses and statistical power

After 3 years of inclusion there will be an estimated number of 2500 patients in the prospective database. After completing follow-up, the primary aim is to search for factors associated with 30-day mortality. A prediction model for 30-day mortality will be fitted by logistic regression. Variable selection will be performed by applying the lasso or elastic net methodology in conjunction with 10-fold cross-validation to prevent overfitting. To describe the characteristics of included patients, categorical variables will be presented as frequencies and percentages. Continuous variables will be presented as mean (±SD). The nature of the correlation (eg, linear and quadratic) between candidate mortality predictors and outcome will be graphically assessed by locally weighted scatterplot smoothing curves. For a non-linear correlation, cut-off points are determined based on the observed distribution, clinical grounds and literature. Table 2 describes the planned collection of perioperative variables. Mortality and clinical outcome parameters such as delirium, wound infections and factors affecting length of hospital stay will be analysed. Mortality rates and differences in 30-day mortality influenced by complications and clinical outcomes will be estimated and displayed using the Kaplan-Meier estimator. Statistical analyses will be performed using Stata (StataCorp, College Station, TX, USA). All statistical tests will be two sided with a significance level of $p<0.05$.

Table 2 Planned collection of perioperative variables

Factor	
1. Preoperative characteristics	**3. Treatment characteristics**
Date and time of fracture	Type and use of anaesthesia
Date and time of admission	Type of implant
Cause of accident	Date and time of surgery
Location of accident	Duration of surgery
Fracture type	Use of drain
Fracture side	Anticoagulation
Pathological fracture	Complications during surgery
	Blood loss intraoperative medication
2. Admission details	**4. Discharge**
Department	Mortality during admission
Involvement of geriatrician	Date ready for discharge
Complications during admission	Date of discharge
Clinical outcomes of admission	Discharge location
Involvement of physiotherapy	Walking aids at discharge
SNAQ score	

SNAQ, Short Nutritional Assessment Questionnaire.

Time plan of the study

The study is designed as a prospective cohort study within the area of Rotterdam, the Netherlands starting from January 2018. Inclusion will be continuing at least until January 2021. During this period patients will be included in at least two level II trauma hospitals in Rotterdam (the Franciscus Hospital and the Maasstad Hospital). If inclusion is started and well on time in these two hospitals the inclusion can be extended to more level II trauma centres in the region of Rotterdam. In the first two hospitals an estimated number of 900 patients per year receive surgery for their hip fracture. During the 3 years of inclusion an estimated number of at least 2700 patients will be included.

Follow-up

Each patient will have at least 6 weeks of follow-up at the outpatient clinic. In case of a fragile or cognitively impaired patient the follow-up will be performed by calling the nursing home facility. Table 3 describes the variables collected at 6 weeks and 1 year of follow-up. If a patient has died during follow-up, the cause and date of death will be noted.

Patient and public involvement

Patients and/or the public were not involved in the development of the study protocol.

Table 3 Planned collection of follow-up variables at 6 weeks and 1 year

Factor	
Follow-up at 6 weeks	**Follow-up at 1 year**
Date of follow-up	Date of follow-up
Alive or deceased	Alive or deceased
Complications	Complications
Mobility level	Mobility level
Residential status	Residential status
Osteoporosis screening	
Katz ADL index	

Katz ADL, Katz Index of Independence in Activities of Daily Living.

DISCUSSION

In the present paper we cover the design, outcome measures and timeline of the Rotterdam hip fracture study Factors affecting mortality and morbidty rates after hip fracture surgery, FAMMI study). After completion of 3 years of inclusion with at least 30 days of follow-up the prospective database will include an estimated 2700 patients, with a minimum of 2500 included patients. The primary objective of the study is to validate earlier suggested risk factors and to identify new associated factors for 30-day mortality after hip fracture surgery. Using penalised logistic regression using the lasso or elastic net procedure, factors will be selected and combined to develop a 30-day mortality prediction model. Moreover, epidemiological data on the background and incidence of patients with hip fracture in the Rotterdam area will be analysed and combined with clinical outcomes such as: in-hospital mortality, length of hospital stay and complications after surgery to gain a more complete insight in the postoperative outcome.

Preoperative care

If a patient is admitted from a nursing home with the suspicion of a hip fracture, the pelvic X-ray is made at the emergency department as soon as possible. In case of a hip fracture the patient will be admitted to the hospital at the orthopaedic trauma department, and in case of cognitive dysfunction or multiple comorbidities the patient will be admitted at the geriatric trauma unit within the orthopaedic trauma department. On admission the patient's medication and comorbidities are verified and if necessary other specialists are consulted prior to surgery. Anticoagulation use is verified and inhibitors are administered if necessary. In our earlier study between 2011 and 2016 the mean time to surgery was 27 hours, and 93% (851 patients) had surgery within 48 hours on admission.[6] The time from arrival at the emergency department until admission at the department should be as short as possible in order to reduce waiting time for surgery. By fast-tracking patients with hip fracture straight to the orthopaedic ward, Eriksson *et al* were able to decrease the mean time from arrival to start of surgery

and the majority of these patients underwent surgery within 24 hours.[28] Pincus *et al*[18] investigated in over 42 000 patients whether 30-day mortality was higher if the operation was delayed for more than 24 hours. Indeed, they showed that an increased risk of mortality was present if more than 24 hours between admission and surgery had expired.[29] In most national guidelines and literature a time to surgery of less than 48 hours is advised to reduce postoperative mortality. In the recent publication of the randomised controlled trial of the HIP ATTACK investigators there was no benefit in accelerated surgery within 6 hours after diagnosis compared with 24 hours (standard care group 10–42 hours).[30] We want to measure and validate the optimal time to surgery within the 48 hours before the risk of postoperative complications increases. Moreover, we wish to study whether the time to surgery should be strictly within 24 hours on admission or can be extended to 48 hours. Besides the time to surgery, timing of surgery will be studied. For example, whether surgery during evenings or weekends will cause more complications such as delirium compared with planned surgery during the day.

Perioperative care

As mentioned before, dedicated geriatric trauma units within hospitals are needed to provide the surrounding care during an admission of a hip fracture and to reduce postoperative complications.[31] From 2015 onwards, a geriatrician was consulted prior to surgery as standard practice of care for each patient (>70 years) presenting with hip fracture. The consultation of a geriatrician became standard practice of care because most fragile patients with hip fracture have multiple physical comorbidities in combination with cognitive impairment. Multiple factors lead to a delirium percentage of 26% in our population after hip fracture surgery.[19] In our prospective study we will investigate whether admission at the geriatric trauma unit combined with the consultation of geriatrician prior to surgery will reduce the percentage of complications, more specifically the incidence and length of delirium.

Postoperative care

Early mobilisation after surgery with a physiotherapist is needed to reduce postoperative complications such a pneumonia and delirium. As mentioned before, from day 1 after surgery an application is made for further revalidation outside the hospital in order to reduce the length of in-hospital stay. During admission at the geriatric trauma unit an activity mentor is present who will try to facilitate a normal day schedule as much as possible for all patients with hip fracture during their admission, including eating, crafting and playing games together in the living room.

Strengths and limitations

To our knowledge the present study will be a large and comprehensive prospective database compared with known literature studying factors effecting 30-day mortality after proximal femur fracture. With the design of a prospective ongoing database, more research questions related to complications and clinical outcomes can be answered. However, since its design is a prospective cohort, differential loss to follow-up can introduce bias and absence on data on potential confounding factors can lead to false conclusions. The follow-up for patients with a hip fracture is in general short since a high percentage of patients will die within a few years after surgery. Moreover, this study is no randomised controlled trial focusing on specific research questions. The level of evidence is therefore lower for these specific questions. However, our study could provide new clinical information necessary for the start of randomised controlled trials.

Trial status

When this manuscript was submitted, recruitment has started.

ETHICS AND DISSEMINATION

Ethical approval for this protocol was given by the Ethics Committee of the Maasstad Hospital (TWOR). Patients will receive standard practice of care after their hip fracture. Because of the high percentage of cognitive dysfunction and no changes are made to the standard practice of care, the local ethics committee (TWOR Rotterdam) decided that patients' consent to review their medical records is not required. Patient data are stored anonymously using the Castor data management system, and all the protocols are to be conducted in compliance with the Declaration of Helsinki. No external funding is used for this study.

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Contributors LdJ acted as trial principal investigator. VvR and LdJ enrolled patients and collected data. MK performed statistical analysis of the trial data. LdJ drafted the manuscript. GRR, TMALK, VvR and MK critically revised the manuscript. All authors have read and approved the final manuscript.

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