

# Cover page

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Associations between time to reduction and complications in patients with dislocated total hip arthroplasty: A protocol for an observational cohort study

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# Associations between time to reduction and complications in patients with dislocated total hip arthroplasty:

## A protocol for an observational cohort study

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## *Background*

Total hip arthroplasty (THA) is one of the most performed surgical procedures worldwide, with well-established efficacy in relieving joint pain and enhancing patient mobility.<sup>1-4</sup> Between 1995 and 2023, around 241,000 primary THA's were recorded in Denmark, averaging over 8,000 procedures annually.<sup>3</sup> An increasing number of THAs are performed in Denmark, with, approximately 14,000 in 2023, caused by a growing elderly population.<sup>3,5,6</sup> In Denmark, the proportion of patients experiencing a dislocation of their primary THA is around 3%, and 23% of 1,400 THA revision surgeries performed in 2023 were due to dislocation.<sup>3,7</sup>

Dislocation of THA is painful and can result in neurovascular damage, making immediate reduction essential. Furthermore recurrent dislocations, can lead to a decrease in quality of life.<sup>8,9</sup> Patients are usually elderly and frail with multiple comorbidities, making them susceptible to perioperative complications.<sup>10</sup> Delirium is a common postoperative complication in elderly patients and can lead to increased length of stay, admission to Intensive care unit and incidence of other complications such as pneumonia and death.<sup>11-13</sup>

In Denmark, the standard treatment for dislocated THA is closed reduction, mostly performed in the operating theatre under general anesthesia and with potential additional use of a neuromuscular blocking agent.<sup>14</sup> However, general anesthesia presents both logistical and clinical challenges. It requires the availability of an operating theatre and experienced personnel, consideration of fasting regimes, and carries an increased risk of cardiovascular and respiratory complications.<sup>14,15</sup> Despite the widespread use of general anesthesia, there is currently a lack of consensus on how to provide anesthesia for patients with THA dislocations in Denmark.<sup>14</sup>

Outside of Denmark, closed reduction of dislocated THA is increasingly being performed in the emergency department under sedation.<sup>9,16</sup> This strategy presents potential advantages of reducing time to reduction along with hospital costs and length of stay, while freeing up resources in operating theatres.<sup>17-21</sup> However, sedation may induce complications such as, respiratory depression, apnea, aspiration, and other adverse events, that can be safely avoided in an operating theatre using general anesthesia.<sup>16,22,23</sup>

It remains unclear whether time to reduction, type of anesthesia and strategy for airway management are associated with increased risks of postoperative complications after closed reduction of dislocated THA.

## *Objective*

The aim of the study is to investigate the impact of time to closed reduction on both patient related and organizational factors. These include, length of stay, hospitalization, admission to intensive care unit, rehospitalizations, delirium, all-cause mortality, infection requiring hospital contact, and cardiovascular complications. We also intend to investigate whether different anesthetic strategies and airway management are associated with different complication rates.

We hypothesize that longer waiting time until reduction increase the post procedure length of stay, readmissions, and risk of complications.

## *Methods*

This protocol is developed in accordance with the principles outlined in STROBE (Strengthening the Reporting of Observational Studies in Epidemiology).<sup>24</sup>

### *Study design*

We will conduct a retrospective cohort study based on prospectively collected clinical data on patients presenting with THA dislocations who were treated with closed reduction in an operating theatre.

### *Setting and Population*

The cohort contains all adults presenting with a dislocated THA, who underwent closed reduction in an operating theatre with anesthesiology being involved, in public hospitals in the Capital and Zealand Regions of Denmark.

The study population is extracted from a dataset retrieved from the Electronic Health Record (EHR) system 'Sundhedsplatformen' (Epic Systems Corporation, WI, USA) from 1 January 2017 to 31 December 2024, including granular data from approximately 1.1 million anesthetic procedures.

## Inclusions Criteria

Patients are eligible for inclusion if they are 18 years of age or above, presented in the emergency department with a dislocated THA, and underwent subsequent closed reduction in the operating theatre with the involvement of anesthesiology.

## Exclusion Criteria

Patients are excluded if they:

- Were primarily booked for open surgical reduction.
- Did not have a complete case log (i.e. time of admission; referral to the operation theatre; anesthesia induction; discharge, etc.) and we were unable to recreate the log using simple code rules.

## Exposure and Outcomes

Exposure variables.

- Time in minutes from admission to closed reduction.
- Time of day
- Weekday vs. weekend
- Airway management
- Anesthesia method(s)
- Neuromuscular blocking agent (Yes/No)

Outcome measures

### Primary outcome

- Post procedure length of stay in minutes from closed reduction until discharge from the hospital.

### Secondary outcomes

- All-cause mortality at 90 days. (Y/N)
- Post procedure admission to the intensive care unit within 30 days (Y/N)
- Readmissions to hospital within 30 days (Y/N)
- Diagnosis with delirium or administration of haloperidol, olanzapine, risperidone, or quetiapine (as a surrogate for new onset delirium) (Y/N)

- Serum creatinine increase of more than 25  $\mu\text{mol/L}$  within a period of less than 48 hours (as a surrogate for acute kidney failure) (Y/N)
- Infection requiring hospital contact.
- Cardiovascular complications (diagnosed arrhythmia, myocardial infarction, cerebral ischemia or hemorrhage, pulmonary embolism or deep venous thrombosis)

### Variables

Patient demographics like age, sex, weight, height, BMI, American Society of Anesthesiology (ASA) classification, location (hospital), first-time dislocation/recurrent dislocation and comorbidity (diagnose codes at admission) will be retrieved for baseline statistics and adjustment in our multivariate statistical analyses.

A detailed list of variables is provided in **Appendix 1**.

### Data collection

The data is extracted from the EHR-system Sundhedsplatformen validated and cleaned. The patients are recorded when they are admitted to a public hospital in the Capital and Zealand Regions of Denmark, which contains one or more operations CSN-ID linked to an anesthesia CSN-ID (indicating that a procedure was performed with anesthesia).

The initial database extraction has been approved by 'Team for journaldata, videnskabsetik og forskningsstøtte, Region Hovedstaden' (Approval number R-23038250; 14 July 23). Furthermore, approval has been granted for the transfer of medical record data from the database to this research project (Approval number R-24079695; 13 December 24).

### Data handling

The dataset will undergo preprocessing and validation before analysis, including checks for missing values, duplicates, and errors. Only validated data will be used in the analysis to ensure accuracy and reliability.

Data will be stored in a secure database with restricted access. The dataset will be retained for a period and will be deleted once the study is completed.

## Statistical Analysis

Baseline data will be presented using descriptive statistics. For continuous variables, means and standard deviations (SDs) will be used to summarize data with normal distributions, and medians and interquartile range (IQR) for non-normally distributed data. Counts and percentages will represent categorical variables.

Linear regression models will be applied to assess the primary outcome of post procedure length of stay and other continuous outcomes.

Logistic regressions models with corresponding odds ratios (ORs) will be applied to assess the dichotomous secondary outcomes. To mitigate bias, we will adjust for relevant confounders in our statistical models and ensure data validation for the key variables, age, BMI, ASA-classification, comorbidities, site etc.

For all analyses we will present statistical tests as two-sided and consider a  $p$  value less than 0.05 statistically significant. For precision 95% confidence intervals will be presented.

For exposure variables with more than 10% missing data, multiple imputation will be employed to reduce potential bias. We will use baseline demographics (age, sex, BMI, ASA-classification, first-time dislocation/recurrent dislocation, site, and comorbidity) for imputation

In cases where a patient undergoes multiple closed reductions during the observation period, we will conduct two analyses. The primary analysis will be based on each patient's first reduction event. A secondary analysis will utilize a linear mixed model for all reduction events regardless of multiple events by the same patient. In this latter analysis, patients will be included for each hospitalization that involves a dislocation requiring closed reduction.

In cases where missing data on outcome variables exceed 10%, we will impute worst-case and best-case scenarios and conduct sensitivity analyses to assess the impact of these imputations on our findings.

Statistical analyses will be performed using latest available stable version of R (R Core Team, Vienna, Austria).



## *Strengths and limitations*

This study offers several strengths. First, the retrospective design allows for a quick and cost-effective study, as data are already available. This allows for analysis of a large cohort of patients with dislocated THA and explores the impact of timing on outcomes such as length of stay, readmissions, and complications. Additionally, the use of an extensive patient database increases statistical power, enabling assessment of multiple outcomes across a broad sample.

Several limitations should be considered.

Selection bias may arise since the study relies on existing patient records potentially resulting in incomplete or non-representative data particularly for specific patient groups, e.g. those treated in emergency settings outside an operating theatre. This could limit the generalizability of the findings to a broader patient population.

Information bias may be present as clinical documentation might be inconsistent or incomplete, particularly regarding timing of reduction or complications. Additionally, patient identification relied on specific procedural codes for orthopedic surgery, which may have led to misclassification and potentially eligible patients being not correctly registered.

Confounding factors, such as comorbidities, may influence both the timing of reduction and clinical outcomes. Confounding by indication may occur if patients with more severe conditions are either delayed in receiving treatment or receive specific types of airway management, which may in turn affect both the timing of reduction and clinical outcomes. As an example, more frail or acute patients may experience shorter waiting times or specific airway interventions, while more healthy patients might face delays in treatment due to the less urgent nature of their condition. This could falsely appear to influence outcomes, when in fact, their poorer prognosis is due to their underlying condition rather than the treatment provided.

## *Publications*

Findings will be submitted for publication in an international, peer-reviewed journal relevant to the field of study.

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## Appendix

### Appendix 1: Variable table

Exposure variables			
Variable	Measurement	Definition	When
Time to reduction	Minutes, as a continuous variable	From arriving time in the emergency department until the start of procedure in the operating theater.	From arriving time at the hospital until start of procedure
Time of day	Nominal categorical variable, defined as 08-16, 16-00 or 00-08	At arriving time at the hospital defined as Day (08-16), evening (16-00) or nightshift (00-08)	At arriving time at the hospital
Weekday vs weekend	Nominal categorical variable	Defined as weekday from Monday 08 to Friday 00 and weekend Friday 00 to Monday 08.	At arriving time at the hospital
Airway management	Categorical variable, defined as spontaneous breathing, mask ventilation, elective intubation, rapid sequence induction, or laryngeal mask.	The type of airway management categorized as spontaneous breathing, mask ventilation, elective intubation, rapid	At anesthesia induction

		sequence induction, or laryngeal mask.	
Anesthesia method(s)	Categorical variable, defined as propofol, etomidate, thiopental, midazolam, ketamine, sevoflurane, and desflurane.	Anesthesia method(s) categorized as propofol, etomidate, thiopental, midazolam, ketamine, sevoflurane, and desflurane.	At anesthesia induction
Neuromuscular blocking agents	Categorical variable Rocuronium, suxamethonium or non.	Neuromuscular blocking agent categorized as Rocuronium, suxamethonium or non.	At anesthesia induction
<b>Primary outcomes</b>			
Post-reduction length of stay	Minutes, as a continuous variable.	Post procedure length of stay.	From procedure start until hospital discharge up to 30 days after discharge.
<b>Secondary outcomes</b>			
All-cause mortality	Binary variable (Y/N)	90 days all-cause mortality	90 days after closed reduction
Admissions to Intensive care unit	Binary variable (Y/N)	Admissions to the intensive care unit within 30 days after the closed reduction.	30 days after the closed reduction
Readmission	Binary variable (Y/N)	Readmission within 30 days after discharge	30 days after discharge
Delirium	Binary variable (Y/N)	Defined as diagnose of delirium (F05.x, obtained from the	Post procedure, during admission up to 30 day after closed reduction.

		diagnosis codes from the given admission) <b>or</b> the non-planned administration of haloperidol, olanzapine, risperidone, or quetiapine (as a surrogate for new onset delirium)	
Acute kidney failure	Binary variable (Y/N)	Defined as serum creatinine increase of more than 25 µmol/L within a period of less than 48 hours. or an increase in serum creatinine >1.5 times the baseline value, with baseline defined as the most recent measurement within the past 12 months (As a surrogate for acute kidney failure)	Post procedure until 30 days after discharge
Infection requiring hospital contact	Binary variable (Y/N)	Defined as diagnosed infection (postoperative infection (T81.4), pneumonia (J13.x-J18.x), Cystitis (N30.x, N39.0), sepsis	Post procedure until 30 days after discharge

		(R65.x A40.x, A41.x), C. difficile (A04.7) obtained from the diagnose codes from the given admission) <b>or</b> administration of antibiotic treatment (as a surrogate for in- hospital infection	
Cardiovascular complications	Binary variable (Y/N)	Defined as diagnosed arrythmia (I47.x, I48.x, I49.x), myocardial infarction (I21.x, I22.x), cerebral ischemia (I61.x, I63.x, I64.x), hemorrhage(T81), pulmonary embolism(I26.x) or deep venous thrombosis(I80.2) (obtained from the diagnosis codes from the given admission)	From admission to 30 days after discharge.
<b>Baseline variables</b>			
Age	Years		At admission
Sex	Male or female		At admission
Weight	Kilograms		At admission
Height	Centimeters		At admission
BMI	Kg/m <sup>2</sup>		At admission
ASA-score	ASA 1-6	ASA I: Healthy patient, ASA II: Mild	At admission

		systemic disease, ASA III: Severe systemic disease, ASA IV: Severe systemic disease with constant threat to life, ASA V: Moribund patient, ASA VI: Declared brain-dead	
Comorbidity	Diagnosis codes at admission	Diagnose codes at admission (Hypertension (I10, I11, I12, I13, I14, I15), Osteoporosis (M80, M81, M82, M83), Diabetes (E10, E11, E12, E13, E14), Congestive Heart failure (I50.x), Ischaemic heart disease (I21.x, I22.x, I24.x, I25.x), Arrhythmia (I47.x, I48.x I49.x), Chronic Obst. Pulm. Disease (J44), Cancer (C00-C97), Chronic kidney disease (N18), Cerebrovascular disease (I61.x, I63.x, I64.x), Mild liver disease (K70.x, K71.x,	At admission

		K73.x, K74.x, K76.x), Moderate/severe liver disease (K72.x, I85.x), Alcohol-related disease (F10.x), Drug- related disease (F11.x, F12.x, F13.x, F14.x, F16.x), Dementia (F00, F01, F02, F03), Parkinson disease (G20), Alzheimer (G30), Depression (F32.x- F33.x), Anxiety (F40.x-F41.x), Schizophrenia (F20.x)	
Location (Hospital)	OPIAD def.	Locations categorized in The Capital Region (Site A-F) and Zealand Region (Site G-I) of Denmark.	At admission.
First-time dislocation/recurrent dislocation	Binary variable, First time or recurrent dislocation.		