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# PROGNOSTIC FACTORS OF IN-HOSPITAL COMPLICATIONS AFTER HIP FRACTURE SURGERY: A SCOPING REVIEW

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## ABSTRACT

### Purpose

To examine prognostic factors that influence complications after hip fracture surgery. To summarise proposed underlying mechanisms for their influence.

### Methods

We reported according to Preferred Reporting Items for Systematic Review and Meta-Analysis Scoping Review extension. We searched MEDLINE, Embase, CINAHL, AgeLine, Cochrane Library, and reference lists of retrieved studies for studies of prognostic factor/s of postoperative in-hospital medical complication/s among patients 50 years and older treated surgically for non-pathological closed hip fracture, published in English January 2008 - January 2018. We excluded studies of surgery type or in-hospital medications. Screening was duplicated by two independent reviewers. One reviewer completed extraction with accuracy checks by a second. We summarised extent, nature, and proposed underlying mechanisms for prognostic factors of complications narratively and in a dependency graph.

### Results

We identified 44 prognostic factors of in-hospital complications after hip fracture surgery from 56 studies. Of these, we identified 7 patient factors– dehydration, anaemia, hypotension, heart rate variability, pressure risk, nutrition, indwelling catheter use; and 7 process factors– time to surgery, anaesthetic type, transfusion strategy, orthopaedic versus geriatric/comanaged care, and multidisciplinary care pathway, potentially modifiable during index hospitalisation. We identified underlying mechanisms for 15 of 44 factors. The reported association between 12 prognostic factors and complications was inconsistent across studies.

### Conclusions

Most factors were reported by one study with no proposed underlying mechanism for their influence. Where reported by more than one study, there was inconsistency in reported associations and the conceptualisation of complications differed, limiting comparison across studies. It is therefore not possible to be certain whether intervening on these factors would reduce the rate of complications after hip fracture surgery.

## INTRODUCTION

The age standardized rate of hip fracture ranges from lows of 2/100,000 in Nigeria (women) and 35/100,000 in Ecuador (men), to highs of 574/100,000 in Denmark (women) and 290/100,000 in Denmark (men).[1] Patients with hip fracture often present with a reduced capacity to overcome the physiologic stress of their injury and subsequent surgery. Therefore, 30% die in the first postoperative year,[2] with 7% dying in hospital.[2-4] This increased risk of death is often attributed to characteristics of the patient, and structures and processes of healthcare delivery.[5]

The occurrence and opportunity to prevent postoperative complications has more recently become a focus of care after hip fracture surgery.[6] Over 20 years ago, Silber and colleagues argued for *death after postoperative complications* as a powerful indicator of care quality.[7] Attributing postoperative mortality to complications requires first to identify factors that might influence the occurrence of both complications and death. Failure to account for these factors could result in observing a statistical association between complications and death in the absence of causation.

We previously summarised prognostic factors for mortality after hip fracture surgery and anticipate a heterogeneous body of evidence on prognostic factors of complications.[5] Therefore, we conducted a scoping review to summarize the available literature on prognostic factors for post-operative complications. Further, we will summarise the proposed underlying mechanisms of their influence. Knowledge of the extent and nature of prognostic factors of postoperative complications will inform future interventions, quality improvement initiatives, and risk stratification.

## METHODS

A scoping review framework is appropriate when summarizing a body of knowledge that is heterogeneous to identify consistencies and potential gaps for future research.[8] The review was

reported in adherence to the Scoping Review extension of the Preferred Reporting Items for Systematic Review and Meta-Analysis statement.[8]

## Search Strategy

We searched the electronic databases MEDLINE, Embase, CINAHL, AgeLine, and the Cochrane Library. The search was developed using terms for the population (*hip fracture)* and outcome (*complications)* (see Supplementary File 1). Reference lists of retrieved studies were screened to identify additional studies that may have been missed during database searches.

## Eligibility Criteria

We included studies which reported the association between a prognostic factor and any measure of postoperative in-hospital medical complication/s among patients aged 50 years and older who underwent surgery for non-pathological closed hip fracture, published in English between 1st January 2008 and 24th January 2018. We defined prognostic factors as those which relate to characteristics of the patient, structures of care, and/or processes of preoperative and postoperative care.

We excluded studies with a population of patients less than 50 years of age, treated conservatively, with pathological and/or open hip fracture, a primary exposure of surgery type or the administration of medications in hospital (as the volume of research indicated specific sub-questions for surgical type and medications are suited for their own reviews), a control/comparison group that was free of hip fracture, an outcome of surgical complications (e.g. dislocation, malunion), a study endpoint outside of the hospital setting (without explicit reporting of in-hospital complications), and those published in a language other than English and outside of the predetermined date ranges.

## Study Selection

We exported citations from databases into Covidence for de-duplication and screening.[9] Three reviewers independently screened all abstracts against inclusion and exclusion criteria (KS, EG, DT). Conflicts were resolved by a fourth reviewer (RMC). Full texts of potentially eligible studies were independently screened by four reviewers (KS, EG, DT, PS) with conflicts resolved by two reviewers (RMC, JAB).

## Data extraction

Data extraction was completed by two reviewers independently onto tables designed a priori (RMC, KS). Conflicts were resolved by consensus. Data extracted included the author's name, publication date, country, method, sample size, participants, prognostic factor measurement, control, outcome, duration of follow up (length of stay), analysis type, and effect estimate. We extracted the effect of the primary study factor from multivariable analysis or from univariable analysis when multivariable analysis was not available. We included estimates from univariable analyses only, when a primary prognostic factor was not stated in the title and/or aim of the study. This was done to avoid misclassification of covariates in multivariable analyses as primary factors.[10] The proposed mechanisms for reported associations were extracted from the discussion sections by one reviewer (RMC). The extraction was checked for accuracy by a second reviewer (KS).

## Analysis

We reported findings as counts and proportions and summarised factors with a reported association and with a reported no association with complications in text and tables using a narrative review approach.[11] We also summarized the extent and the nature (modifiable vs. nonmodifiable) of these factors during an index hospitalisation for hip fracture. We selected this caveat of 'during an index

hospitalisation' to distinguish factors that are amenable to intervention during the hospital stay to reduce the occurrence of complications from those that are not. For example, while body mass index is modifiable it is not a modifiable risk factor for in-hospital complications after hip fracture surgery as the time between surgery and the occurrence of complications is too short for a change in body mass index. Factors and their proposed underlying mechanisms were further summarised in a dependency graph. A dependency graph depicts the factors (nodes) and relationships among then (single-headed arrows).[12] The dashed arrows indicated conflicting evidence for the presence of an association.

## RESULTS

### Study selection

We identified 7,341 studies from electronic databases after de-duplication. We excluded 6,731 on title and abstract screening. We excluded 554 on full text screening for the following reasons: population (n = 60), exposure (n = 42), control (n = 13), outcome (n = 168), design (n = 118), follow-up after discharge from hospital (n = 125), publication date (n = 26), and language (n = 2). This left 56 studies for inclusion in the current review (See Figure 1).

### Study characteristics

This scoping review of 56 studies included 2,457,050 patients with sample size ranging from 35[13] to 2,121,215.[14] Overall, 23 studies reported the association between prognostic factor/s and a single complication,[15-37] six studies reported the association between prognostic factors/s and multiple complications,[13, 38-42] and 27 studies reported the association between prognostic factor/s and a composite measure of complications (Supplementary File 2). [14, 43-68] Length of stay ranged from 4[13, 15, 34, 37, 48, 55, 63] to 36[52] days across studies. Additional details related to the studies included in this review may be found in Supplementary File 3.

**Figure 1**: Study selection

**[insert figure here]**

## Prognostic factors

*Prognostic factors of composite measures of medical complications*

In total, 12 prognostic factors of composite measures of medical complications were reported by 15 studies included in this review (Table 1, Figure 2). Of these factors, seven related to nonmodifiable patient factors –comorbidity count,[63] dementia,[66] Parkinsons disease,[47] BMI ($\geq 30 kg.m^2$),[58] frailty (Fried Frailty Criteria),[13] serum albumin (<35 g/l),[64] and surgical readiness (preoperative risk score incorporating the American Society of Anesthesiologists Score);[52, 53] two related to potentially modifiable patient factors –nutrition (preoperative Mini Nutritional Assessment Short Form),[43] and pressure risk (admission Norton scale) [51]; two related to modifiable care processes - time to surgery,[14, 61] and multidisciplinary care pathway[56, 57]; and one related to a nonmodifiable care structure - hospital type(teaching status).[60]

Patient factors of BMI ($<18.5 kg/m^2$ ; $\geq 30 kg/m^2$),[38] cognitive impairment,[46] and time to surgery[55, 67, 68] were also reported as not associated with complications after hip fracture surgery. No association between admission on anticoagulation,[54] orthopaedic versus medical primary service,[48] time of day of surgery,[65] and liberal transfusion strategy[50] with postoperative complications were reported (Table 1).

*Prognostic factors of cardiac, respiratory, and/or kidney/urinary measures of medical complications*

*Cardiac*: In total, one nonmodifiable patient factor –troponin (>0.03 ng/mL),[39]; two potentially modifiable patient factors – heart rate variability (time and frequency domains),[49] and hypotension (more than 3 occurrences of systolic pressure under 90mmHg intraoperatively);[59] and two modifiable

process factors –time to surgery,[14, 68] transfusion strategy (liberal)[50] of cardiac complications were reported by 14 studies included in this review (Table 2, Figure 2). No association between admission on anticoagulation,[42] nutrition (preoperative Mini Nutritional Assessment Short Form score; Mini Nutritional Assessment),[41, 43] BMI ($\geq$ 30kg/m$^2$),[58] dementia,[66] frailty (Fried Frailty Criteria),[13] orthopaedic versus geriatric primary service,[44] orthopaedic versus comanaged service,[44] timing of orthogeriatric care,[62] with cardiac complications were reported after hip fracture surgery.

*Respiratory*: In total, six nonmodifiable patient factors – age,[59] bedbound prefracture,[59] neurological comorbidity,[59] BMI ($\geq$ 30kg/m$^2$),[58] dementia,[66] and renal failure;[59] one potentially modifiable patient factors – heart rate variability (time and frequency domains),[49] and three modifiable process factors - time to surgery,[14, 68] orthopaedic versus geriatric primary service,[44] orthopaedic versus comanaged service,[44] of respiratory complications were reported by 11 studies included in this review (Table 2, Figure 2). No association between admission on anticoagulation,[42] nutrition (Mini Nutritional Assessment),[41] frailty (Fried Frailty Criteria),[13] and timing of orthogeriatric care,[62] with respiratory complications were reported after hip fracture surgery.

*Kidney/urinary*: In total, 10 nonmodifiable patient factors – age,[34] sex, (female[15], male[18, 34]) comorbidities (count),[15, 34] vascular disease,[18] dementia,[66] diabetes,[18, 20] chronic kidney disease,[15, 18] glomerular filtration rate (eGFR),[15, 18, 34] previous coronary revascularization,[34] and serum potassium;[15] two potentially modifiable patient factors – heart rate variability (time and frequency domains),[49] and indwelling catheter (duration);[33] and two modifiable process factors – time to surgery[14, 68] and orthopaedic versus comanaged service[44] of kidney/urinary complications were reported by 15 studies included in this review (Table 2, Figure 2). Patient factors age,[18, 20, 33, 34] sex,[20, 34] diabetes,[33, 34] dementia,[33] and serum potassium[34] were also reported as not

associated with kidney/urinary complications after hip fracture surgery. No association between cerebrovascular disease,[34] hypertension,[33, 34] smoking status,[34] BMI (mean),[34] history of myocardial infarction,[34] neurological comorbidities,[33] admission on anticoagulants,[34, 42] nutrition (Mini Nutritional Assessment),[41] frailty (Fried Frailty Criteria),[13] overactive bladder,[33] orthopaedic versus geriatric primary service,[44] and timing of orthogeriatric care,[62] with kidney/urinary complications were reported after hip fracture surgery.

*Prognostic factors of delirium complications*

In total, 22 prognostic factors of delirium complications were reported by 14 studies included in this review (Table 3, Figure 2). Of these factors, 17 related to nonmodifiable patient factors – age,[29, 59] sex (male),[29] frailty (Fried Frailty Criteria),[13] comorbidities (count),[29] neurological comorbidity,[59] congestive heart failure,[29] atrial fibrillation,[29] cognitive impairment,[24, 37, 40, 45] dementia,[29] depression,[45] neuroticism,[32] Parkinson's disease,[29] BMI (< 20 $kg/m^2$),[24] preoperative serum metabolites,[22] plasma cortisol,[23] surgical readiness (American Society of Anesthesiologists score),[29] outdoor injury;[24] two related to potentially modifiable patient factors – nutrition (postoperative cumulative energy balance),[27] anaemia (Hg level ≤9.7 g/dL during hospitalisation);[35] and three related to modifiable care processes – orthopaedic versus geriatric care,[44] orthopaedic versus comanaged care,[44] and delirium friendly pre-printed orders.[21]

Patient factors of age,[28, 45] sex,[45] cognitive impairment,[28] dementia,[45] depression,[29, 32] nutrition (preoperative Mini Nutritional Assessment Short Form),[43] surgical readiness (American Society of Anesthesiologists score);[45] and process factors - orthopaedic versus comanaged care[16] were also reported as not associated with delirium complications after hip fracture surgery. No association between education (illiterate, elementary, middle, higher),[28] race,[29] BMI,[29] comorbidities (count) [28, 45], congestive heart failure,[29] pulmonary disease,[29] cerebrovascular

disease,[29] hypothyroidism,[29] chronic renal insufficiency,[29] syncope,[29] atrial fibrillation,[29] hypertension,[29] cancer,[29] anxiety,[32, 36] psychiatric illness,[29] psychological factors - extraversion, agreeableness, conscientiousness, or openness,[32] diabetes,[29] cerebrospinal fluid melatonin,[31] fracture type,[28, 45] time to admission,[28] time to surgery,[28, 68] surgical duration,[28] anaesthetic type (spinal, epidural, general),[45] or timing of orthogeriatric care,[62] with delirium complications were reported (Table 3).

*Prognostic factors of pressure ulcers and other complications*

In total, two nonmodifiable patient factors –cognitive impairment,[40] and diabetes,[25] and one potentially modifiable patient factors – dehydration (preoperative dry lips, thirst, and skinfold test)[25]; and two potentially modifiable process factors – time to surgery,[19, 61, 68] and anaesthetic type (other than general),[19] of pressure ulcers were reported by studies included in this review (Table 4, Figure 2). No association between admitted on anticoagulant,[42] and surgical duration,[19] with pressure ulcers were reported after hip fracture surgery.

One study reported education (elementary versus university degree), cognitive impairment, depression and anaemia (Hg level <12 g/dL in women and Hg level <13 g/dL in men during hospitalisation) were prognostic of pain.[30] The same study reported age, sex, diabetes, surgical readiness (American Society of Anesthesiologists score), anaesthetic type (general versus regional), and surgical duration were not prognostic of pain.[30] Two studies reported that time to surgery was not prognostic of pain.[30, 68] One study reported age, prefracture residence, comorbidity count, respiratory comorbidities, and neurological comorbidities were prognostic of dysphagia while cardiac comorbidities, ear, nose and throat comorbidities, and anaesthetic type were not prognostic of dysphagia.[26] One study reported that BMI ($\geq 30 kg/m^2$) was prognostic of electrolyte abnormalities.[58] Admission on anticoagulants,[17, 42] BMI ($\geq 30 kg/m^2$),[58] and timing of

orthogeriatric care,[62] were not associated with anaemia. One study reported dementia was not prognostic of sepsis.[66]

### Underlying mechanisms

We identified underlying mechanisms for 15 (34.1%) of the 44 prognostic factors of in-hospital complications (Table 5, Figure 2).

**Figure 2:** Prognostic factors of complications after hip fracture surgery. Nodes represent factors and arrows represent dependencies between nodes. Dashed arrows indicate conflicting evidence for the presence of an association.

**[insert figure here]**

## DISCUSSION

### Main findings

We identified 44 prognostic factors of in-hospital complications after hip fracture surgery from 56 studies included in this review. Of these, 36 related to the patient and 8 related to care processes and structures. We identified 7 patient, and 7 care delivery factors, that are potentially modifiable. More specifically, the presence of dehydration, anaemia, hypotension, greater heart rate variability, higher pressure ulcer risk, malnutrition, prolonged indwelling catheter use, prolonged time to surgery, regional anaesthetic, orthopaedic (versus geriatric/comanaged) care, and multidisciplinary care pathway were associated with the occurrence of at least one in-hospital complication. The majority of factors were reported by only one study and with no proposed mechanism for their effect on complications after hip fracture surgery. Moreover, the association between 12 prognostic factors and complications was disputed across studies.

## Comparison to previous literature

From the 14 potentially modifiable factors, 3 were accompanied by a proposed underlying mechanism for their association with in-hospital complications after hip fracture surgery.

Anaesthetic type was associated with the occurrence of pressure ulcers, with patients who underwent regional anaesthetic more likely to develop pressure ulcers than those who underwent general anaesthetic.[19] In the current review we also reported anaesthetic type was not associated with composite measures of complications,[66] delirium complications,[45] or pain.[30] These findings support a 2016 Cochrane Review which indicated no difference between regional (neuraxial block) and general anaesthetic on the occurrence of pneumonia, myocardial infarction, cerebrovascular accident, or acute confusion.[69] However, the authors reported regional anaesthetic may lead to lower deep venous thrombosis and operative hypotension when compared to general anaesthetic.[69] Therefore, it is not clear whether recommending general anaesthetic to reduce pressure risk would inadvertently increase the risk of deep venous thrombosis and operative hypotension. In the current review, the proposed underlying mechanism for the association between anaesthetic type and pressure ulcers was prolonged lack of sensation preventing small shifts to redistribute pressure with regional as compared to general anaesthetic.[19] Intervening on the underlying mechanism, e.g. with higher specification foam mattresses, may mitigate the risk of pressure ulcers without changing the anaesthetic strategy for patients undergoing hip fracture surgery with regional anaesthetic.[70]

Time to surgery was associated with the occurrence of cardiac, respiratory, and/or kidney/urinary complications,[14] pressure ulcers,[19] and composite measures of complications.[14, 60] Ryan, et al. proposed medical instability as the underlying mechanism for their reported association between delay to surgery and postoperative complications.[14] In contrast, Lindholm, et al. suggested patients who undergo early surgery have less time to adjust to normal hydration preoperatively increasing their risk

of postoperative complications.[25] These contrasting proposed mechanism support the argument that there is an 'optimal' time to surgery – one which allows preoperative medical stabilization but prevents unnecessary administrative delays. Indeed, there has been considerable debate as to the optimal time to surgery with recommendations from as early as 6 hours to as late as 4 days across studies.[71, 72] Inconsistent cut-offs for *early* and *delayed* surgery may also help to explain conflicting results which reported no association between time to surgery and composite measures of complications[55, 57, 61, 67] delirium complications,[28, 31] or pain.[30]

Tsuda, et al. proposed postoperative blood transfusions for patients with anaemia may lead to immunosuppression and subsequent complications.[66] However, a randomized controlled trial of liberal versus restrictive blood transfusion strategy on long-term survival after hip fracture surgery did not support the hypothesis that blood transfusions leads to immunosuppression.[73] We previously identified frailty and weakness (a feature of frailty) as proposed underlying mechanisms for the influence of anaemia on functional recovery after hip fracture surgery.[74] Frailty could also play a role in the reported association between anaemia and complications here. Indeed, anaemia has been linked with inflammatory chronic diseases and frailty.[75] This morbidity burden may increase the risk of postoperative complications.

## Future research

The findings of this review are intended to inform future evidence synthesis and/or intervention development for clinical practice. From preliminary searches, we identified a large volume of research on the occurrence of postoperative complications after different surgical procedures, and/or the administration of medications, after index hospitalisation for hip fracture. These exposures are amenable to targeted overview of reviews to enable better understanding of their association with postoperative complications.

We identified 44 prognostic factors of which only 8 related to structures of care (hospital type) and processes of care (time to surgery, anaesthetic type, transfusion strategy, orthopaedic versus geriatric primary care, orthopaedic versus comanaged care, delirium friendly pre-printed orders, multidisciplinary care pathway). This finding is supported by a recent review of orthogeriatric care models and outcomes after hip fracture which reported a dearth of evidence on the impact of orthogeriatric care on complications including delirium.[76] Structures and processes of care many be more amenable to intervention and should be explored in future prognostic studies.

There was limited replication of analyses of prognostic factors of complications across studies. Moreover, where replicated, we reported uncertainty of age, sex, BMI, cognitive impairment, diabetes, dementia, serum potassium, depression, nutrition, surgical readiness, time to surgery, and orthopaedic versus comanaged care as prognostic factors of complications across studies. Replication should be considered prior to design of an intervention or implementation of a quality improvement initiative targeting these factors.

There was a lack of consensus across studies as to an appropriate composite measure of complications after hip fracture surgery. This may be due to different goals of a composite measure, or different proposed underlying mechanisms between a given prognostic factor and composite measure of complications. However, few studies specified a goal for their composite measure or a proposed underlying mechanism for the association between prognostic factor and a composite measure of complications. It is therefore not clear whether complications selection is driven by a conceptual framework, rate of occurrence, or available data.

For elective surgical procedures, the Agency for Healthcare Research and Quality identified eight potentially fatal complications -deep vein thrombosis,  pulmonary embolism, pneumonia, sepsis, shock, cardiac arrest, gastrointestinal hemorrhage and acute ulcer.[77] We previously synthesized the evidence

on complications associated with in-hospital death after hip fracture.[5] We did not synthesize the incidence of individual complications after hip fracture surgery nor explicitly synthesize the *cause* of death. More recently, a cohort study (n=220) reported respiratory infections (35%), ischaemic heart disease (21%), and cardiac failure (13%) as the most common cause of death listed on post-mortem reports in-hospital after hip fracture surgery.[78] This supports an earlier study of isolated limb and pelvic fractures (including hip fracture) which reported bronchopneumonia as the leading cause of death (n = 45).[79] Further work should be completed to identify the most common complications causing in-hospital death after hip fracture to inform recommendations for a composite measures of complications.

We employed a scoping review adopting search terms for *complications* and not for individual complications; e.g. myocardial infarction, pneumonia, or delirium. We identified one review which focused on a specific complication after hip fracture surgery -namely delirium.[80] Their conclusion that age, overall health, and dementia were associated with postoperative delirium is reflected by the current review.[80] In the absence of a consensus as to the most appropriate composite measure of complications, it may be appropriate to generate systematic reviews and meta-analyses of specific complications informed by this review.

The dependency graph provides a framework for further discussion on intervention design.[81, 82] Therefore, we have not assessed the significance of individual factors when conflicting evidence was present. The graph depicts a network of relationships that could be statistically tested in future research. It is also important to consider the level of abstraction when considering which factors to target for intervention. Indeed, factors at a higher level of abstraction may influence the occurrence of postoperative complications through other intermediate factors and may be amenable to intervention design. In contrast, these factors may not be required for adjustment to infer causation in policy evaluations.

### Limitations of the review

There is a potential for publication bias as we limited our search to articles identified through electronic databases and to those published in English. We limited our search to complications occurring in hospital. We noted several studies which reported 30-day complications (in particular studies using the American College of Surgeons National Surgical Quality Improvement Program) but did not specify whether these complications occurred in-hospital, the community, or both.[83] Therefore, we excluded these studies from the current review. With reductions in acute length of stay, it is possible we underestimated the extent of prognostic factors of in-hospital complications. We did not assess the quality of the reviewed articles per the scoping review framework.[84] It is therefore difficult to determine whether this uncertainty reflects different methodological quality across studies, true variation in prognostication, or different conceptualisation of the composite measures (with different prognosis based on included complications).

## CONCLUSION

We synthesized the evidence on prognostic factors of complications after hip fracture surgery. We identified 44 factors from 56 articles included in this review. We identified 14 potentially modifiable factors. However, with inconsistent findings, no proposed underlying mechanism, and limited replication in the evidence base due to different conceptualisation of complications it is not possible to be certain whether intervening on these factors would reduce the rate of complications after hip fracture surgery.

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