PROGNOSTIC FACTORS OF FUNCTIONAL OUTCOME AFTER HIP FRACTURE SURGERY: A SYSTEMATIC REVIEW

ABSTRACT

Objective: This systematic review aimed to identify immutable and modifiable prognostic factors of functional outcomes and their proposed mechanism after hip fracture surgery.

Design: Systematic search of MEDLINE, Embase, CINAHL, PEDRO, OpenGrey and ClinicalTrials.gov for observational studies of prognostic factors of functional outcome after hip fracture among surgically treated adults aged ≥ 50 years. Study selection, quality assessment, and data extraction were completed independently by two reviewers. The Quality in Prognosis Studies Tool was used for quality assessment and assigning a level of evidence to factors. Proposed mechanisms for reported associations were extracted from discussion sections.

Results: From 33 studies of 9,552 patients, we identified 25 prognostic factors of functional outcome after hip fracture surgery. We organised factors into groups: demographics, injury and comorbidities, body composition, complications, and acute care. We assigned two factors a weak evidence level - anaemia and cognition. We assigned Parkinson's disease an inconclusive evidence level. We could not assign an evidence level to the remaining 22 factors due to the high risk of bias across studies. Frailty was the proposed mechanism for the association between anaemia and functional outcome. Medication management, perceived potential, complications, and time to mobility were proposed as mechanisms for the association between cognition and functional outcome.

Conclusion: We identified one modifiable and one immutable prognostic factor for functional outcomes after hip fracture surgery. Future research may target patients with anaemia or cognitive impairment by intervening on the prognostic factor or the underlying mechanisms.

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KEY POINTS

- Hip fracture leads to functional impairment, institutionalization, and death.
- Variation in outcomes of rehabilitation may result in part from differences between patients who undergo hip fracture surgery.
- The strongest prognostic factors for functional outcomes were cognitive impairment and anaemia.
- Potential to target these patients for intervention of intensive rehabilitation or more liberal transfusion strategy.
- Need for high-quality prognostic studies of additional factors of functional outcome after hip fracture surgery.

INTRODUCTION

In the United Kingdom (UK), 75,000 men and women over the age of 60 years are admitted to acute care with hip fracture each year.[1] The injury has been dubbed the "hip attack", due to its clinical severity and adverse consequences.[2] Even with treatment, up to 10% of patients die postoperatively in hospital.[3] Among survivors, 25% never recover their pre-fracture function, and 22% transition from independent living to long-term care.[4-6]

Clinicians take steps to improve functional outcomes changing how patients are assessed and rehabilitated after hip fracture surgery.[7-9] Yet the most effective rehabilitation remains unclear.[7-9] This uncertainty may be due to limited understanding of the extent of prognostic factors.[10, 11] For example, studies suggest sex,[12] fracture type,[12] surgery type,[13] and time to surgery[14] are associated with functional outcomes after hip fracture. Indeed, outcomes may vary between women treated early for transcervical fracture with arthroplasty and men treated late for intertrochanteric fracture with internal fixation.

Uncertainty over the most effective rehabilitation may also be due to limited understanding of the nature of prognostic factors. Prognostic factors are immutable when interventions cannot change the factor level.[15] Knowledge of immutable prognostic factors would enable clinicians to adopt a stratified care approach by prioritizing those at high risk of poor functional outcomes for more intensive rehabilitation.[11] In contrast, prognostic factors are modifiable when interventions may change the factor level.[15] Indeed, in the UK, Best Practice Tariffs target modifiable prognostic factors of mortality after hip fracture surgery for health care improvement.[16]

No attempt has been made to synthesize the extent and nature of prognostic factors for functional outcomes after hip fracture surgery. Therefore, we conducted a systematic review of the literature to identify both modifiable and immutable prognostic factors for functional outcomes of hip fracture surgery. We further summarised these factors on the proposed underlying mechanism for the reported associations.

METHODS

Search Strategy

The protocol for this systematic review was registered on the International Register of Systematic Reviews (PROSPERO) (CRD42017069148).[17] Databases were searched for published (MEDLINE, Embase, CINAHL, and PEDRO) and unpublished (OpenGrey) studies and protocols (ClinicalTrials.gov) (see Appendix 1, Supplementary File). The search was developed using terms for *hip fracture* and *functional outcome* employed by previous Cochrane Systematic Reviews.[18-21]

Reference lists of retrieved studies were screened to identify additional studies that may have been missed during database searches. Authors were contacted for further information, if required.

Selection Criteria

We exported citations from databases into Covidence for de-duplication and screening.[22] Two reviewers independently screened all abstracts against inclusion and exclusion criteria (R1, R2). Conflicts were resolved by a third reviewer (R3). Full texts of potentially eligible studies were independently screened by 2 reviewers (R2, R3) with conflicts resolved by a third reviewer (R1).

Inclusion criteria

We included observational studies which reported the association between a prognostic factor and any measure of functional outcome (function, mobility, or balance) on discharge from acute care. We included observational studies of adults with mean age of 65 years and older who underwent surgery after non-pathological closed hip fracture, published in English between 1st January 2007 and 30th June 2017.

Exclusion criteria

We excluded studies of adults with mean age less than 65 years , admitted with an injury other than hip fracture, treated conservatively for hip fracture, treated surgically for a pathological or open hip fracture, or which reported on non-functional outcomes or outcomes following discharge. We excluded intervention-based studies on the premise they do not reflect prognostic factors of functional outcome following usual care, as well as case studies, editorials, commentaries, and conference proceedings.

Quality assessment

Selected studies were assessed independently for methodological quality by two reviewers (R1, R2) using the Quality in Prognosis Studies (QUIPS) tool.[23] The QUIPS tool assesses risk of bias in 6 domains - participation, attrition, prognostic factor measurement, outcome measurement, confounding, and statistical analysis and reporting.[23] Conflicts were resolved by consensus (R1, R2). We assigned a level of evidence for each factor according to guidelines developed by Hayden et al. '*that studies of acceptable quality for inclusion in the synthesis would at least partly satisfy each of the 6 biases (that is, studies from the analysis that are at high risk for any important bias would be omitted)*.'[24] This guideline was adapted for use with the QUIPS tool by Burton et al.[25] Studies were assigned an overall high risk of bias if one or more domains were considered high risk.[24] Studies were assigned a moderate risk of bias if three or more domains were moderate risk and none were high risk.[24, 25] Studies were assigned a low risk of bias if three or more domains were low risk and none were high risk.[24, 25]

Data extraction

Data extraction was completed by one reviewer onto tables designed a priori (R2). All data was checked for accuracy by a second reviewer (R1). Data extracted included the author's name, publication date, study population, age, sample size, eligibility criteria, prognostic factor measurement, outcome measurement, length of stay, analysis type, and effect estimate. The proposed mechanisms for reported associations were extracted from the discussion sections by one reviewer (R1). The extraction was checked for accuracy by a second reviewer (R3).

Analysis

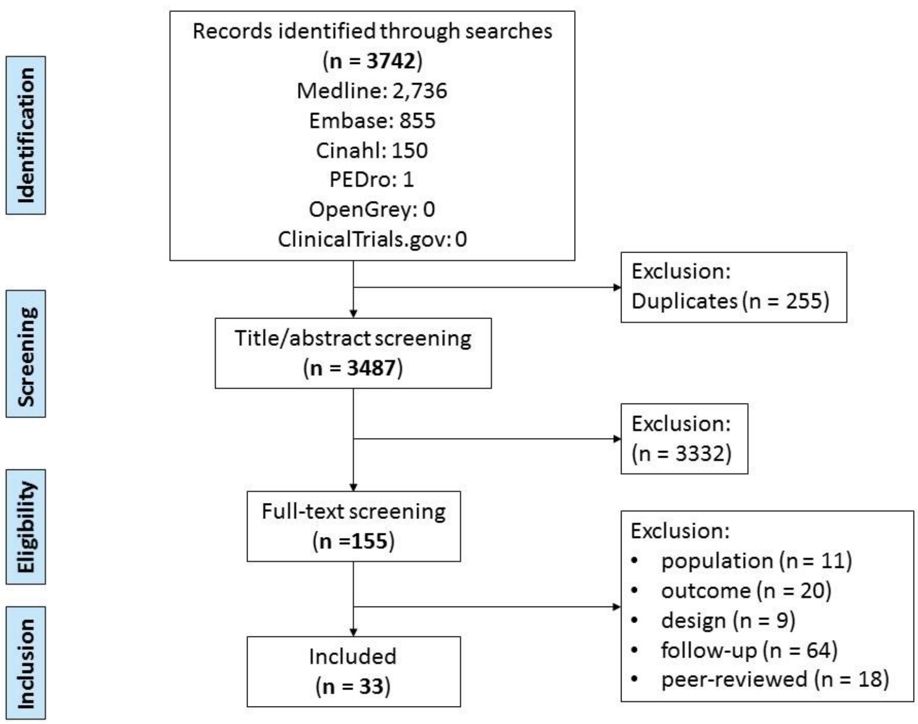
We reported study characteristics as counts and proportions. We reviewed the data extraction tables to assess for study heterogeneity. There was variation in eligibility criteria, prognostic factor measurement, and outcome measurement across studies. Therefore, we analysed the association between prognostic factors and functional outcomes using a narrative review approach.[26] We summarised the evidence on prognostic factors and their underlying mechanisms in tables. We further summarised factors and their proposed mechanisms in a dependency graph to represent relationships among assembled factors.[27] We synthesized the evidence for prognostic factors where the overall risk of bias was low.[24]

RESULTS

Study selection

Figure 1 presents a flow diagram of study selection. We identified 3,487 studies after de- duplication. Following title and abstract screening 155 full-text studies progressed to full-text review. We subsequently included 33 studies in this review.

Figure 1: Study selection



Study characteristics

This systematic review included 9,552 patients (mean age 68 – 89 years). Sample size ranged from 55[28] to 1114[29] patients (Table 1). Functional outcome was measured by Functional Independence Measure in 11 studies,[29-39] Barthel Index in 8 studies,[40-47] Modified Barthel Index in 6 studies,[48-53] Tinetti[44, 54] and Timed Up and Go in two studies,[28, 55] and Elderly Mobility Scale[56] and Cumulated Ambulation Score[30] in one study. Four studies developed their own functional outcome measure.[57-60] Length of stay after hip fracture surgery ranged from 1 [30] to 55 [36] days across studies.

Quality assessment

The results of the quality assessment are presented in Appendix 2, Supplementary File. The agreement between two independent reviewers regarding the risk of bias domains was 90%. Following discussion 100% consensus was reached. In total, 3 studies (9%) had low overall risk of bias[33, 42, 44] and 30 studies (91%) had high overall risk of bias.[28-32, 34-41, 43, 45-60] The main reasons for high bias assignment were study confounding, participation, and attrition. Failure to control for important potential confounders (e.g. pre-fracture function, comorbidity) was a high risk of bias in 13 studies (39%).[30, 31, 35, 40, 43, 48, 50-54, 57, 59] Overall, 9 studies (27%) did not adjust for any potential confounders.[30, 31, 40, 43, 51, 52, 57-59] For 21 studies (64%) participant eligibility criteria were narrow.[28, 30-32, 34-39, 45-50, 52, 53, 55, 59, 60] In particular, 8 studies (24%) excluded patients with cognitive impairment.[31, 36-38, 48, 49, 51, 53] Additional detail on participant exclusions may be found in Appendices 3-8, Supplementary File. A total of 6 studies (18%) failed to provide reasons for loss to follow-up, or a comparison between those lost to follow-up and those observed for the study duration.[41, 48, 50, 51, 55, 60]

Prognostic factors

Overall, 25 prognostic factors of functional outcome after hip fracture surgery were identified by 33 studies (Table 1).

Three factors were reported by studies with low overall risk of bias. We assigned a weak level of evidence for an association between functional outcome and cognitive impairment,[42] and between functional outcome and anaemia on admission.[33] We assigned an inconclusive level of evidence for an association between functional outcome and Parkinson's disease.[44]

Prefracture function,[42, 49] perceived potential,[49] medication management,[42] complications,[42] and time to mobilisation[30] were proposed as underlying mechanisms for the association between cognitive impairment and functional outcome. Frailty and weakness were proposed as underlying mechanisms for the association between anaemia on admission and functional outcome.[33] Medication management and complications were proposed as underlying mechanisms for the association between Parkinson's disease and functional outcome (Table 2, Figure 2).[58]

We organised the remaining 22 factors reported by studies of high risk of bias into 5 groups: demographics, injury and comorbidities, body composition, complications, and acute care factors. A total of 38 potential underlying mechanisms were proposed for 14 factors (Table 2, Figure 2).

Demographics

Age,[30, 31, 53-55] sex,[30] and prefracture residence[59] were associated with functional outcome. Age[52] and sex[55] were also reported as not associated with functional outcome. Prefracture function,[52] cognitive impairment,[42] and pain[28] were proposed as underlying mechanism for the association between age and functional outcome. Depression,[37] urinary retention,[35] age,[37] comorbidity,[37] and cognitive impairment[37] were proposed as underlying mechanisms for the association between sex and functional outcome. Cognitive impairment,[59] comorbidity,[53] complications[53] and time to mobilisation[53, 59] were proposed as underlying mechanisms for the association between prefracture residence and functional outcome (Table 2, Figure 2).

Injury and comorbidities

Fracture type was associated with functional outcome after hip fracture surgery.[53, 55] Comorbidity as measured by Charlson Comorbidity Index was associated with functional outcome after hip fracture surgery.[54] Prefracture function, [30, 31, 42, 53-56] diabetes,[38] atrial fibrillation,[29] and Vitamin D level[47] were associated with poor functional outcome after hip fracture surgery. Polypharmacy was also associated with functional outcome.[42] Vitamin D level[50] was also reported as not associated with functional outcome. Pain[28] and time to mobilisation[30] were proposed as underlying mechanisms for the association between fracture type and functional outcome. Prefracture function,[38] history of stroke,[38] and complications[35] were proposed as underlying mechanisms for the association between diabetes and functional outcome. Weakness was the proposed underlying mechanism for the association between vitamin D and functional outcome (Table 2, Figure 2).[47]

Body composition

Body mass index[31] and malnutrition,[45, 46] were associated with functional outcome after hip fracture surgery. Sarcopenia was not associated with postoperative functional outcome.[43] Comorbidity,[45] cognitive impairment,[45] complications,[46] and frailty[46] were proposed as underlying mechanisms for the association between malnutrition and functional outcome (Table 2, Figure 2).

Complications

Pain,[36, 55] elevated blood urea,[34, 35] perioperative urinary retention,[34, 35, 42] pressure ulcers,[42] and delirium[42] were associated with functional outcome. Emotional distress[53] and new onset depression[37, 49] were associated with functional outcome after hip fracture surgery. Deep vein thrombosis and anaemia on discharge[30, 32] were not associated with functional outcome.[51] Admission albumin level was not associated with functional outcome.[39] Pain,[36] frailty,[37] perceived rehabilitation potential,[37, 48] and rehabilitation adherence[36, 48, 54] were proposed as underlying mechanisms for the association between new onset depression and functional outcome. Fatigue,[36] cognitive impairment,[36] time to mobilisation,[30] and rehabilitation adherence[36] were proposed as underlying mechanisms for the association between pain and functional outcome. Malnutrition and dehydration were proposed as underlying mechanisms for the association between blood urea and functional outcome (Table 2, Figure 2).[34]

Acute care factors

Time to surgery,[54, 57] time to mobilisation,[30] and overall length of stay[53, 60] were associated with functional outcome. Length of stay[31] and procedure type[30] were also reported as not associated with functional outcome. Time to mobilisation was the proposed underlying mechanism for the association between time to surgery and functional outcome (Table 2, Figure 2).[54]

Figure 2: Prognostic factors and their proposed underling mechanisms for their association with functional outcome after hip fracture surgery. Nodes represent factors and their underlying mechanisms while arrows represent dependencies between nodes.

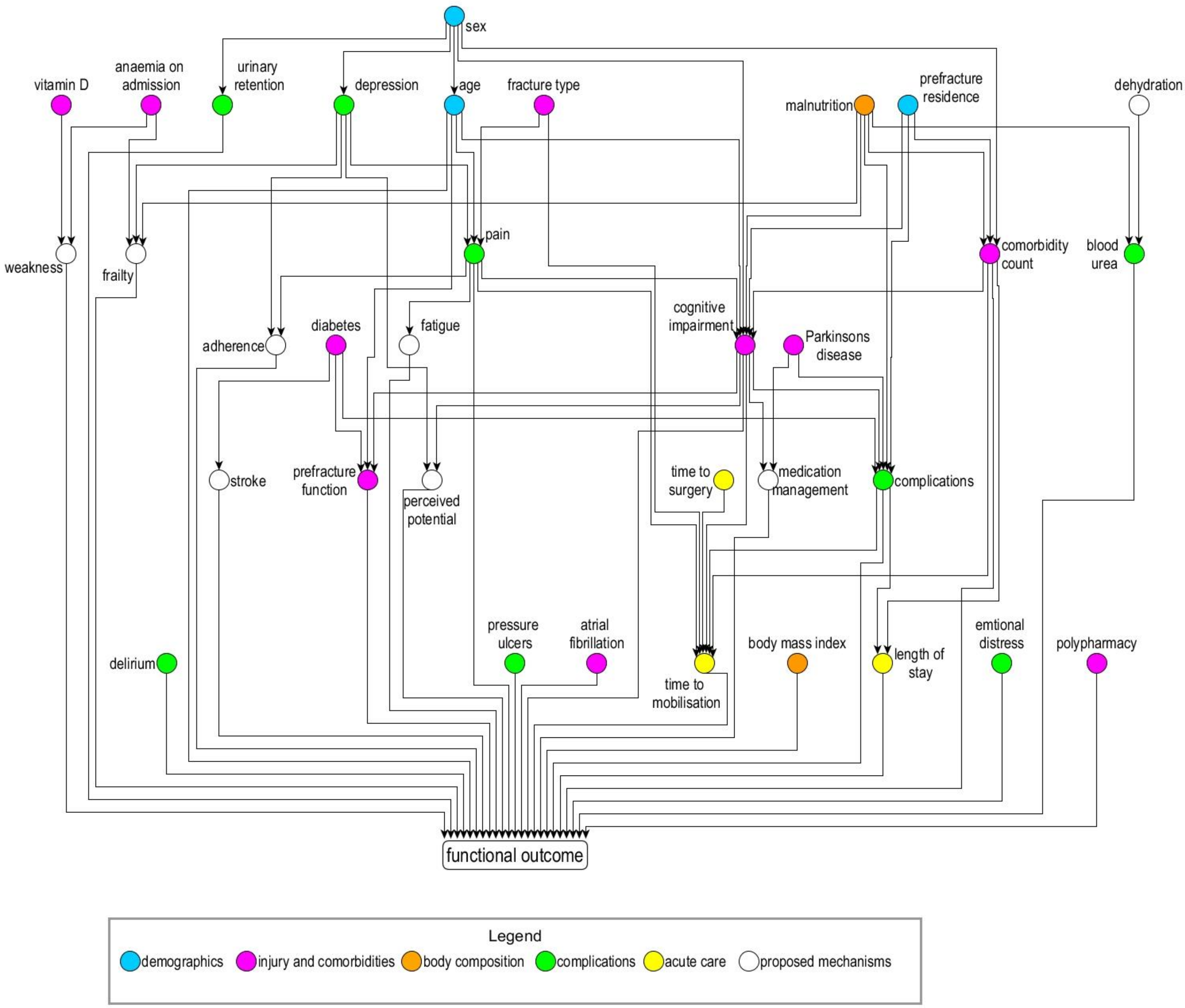


Table 1 Prognostic factors assessed for association with functional outcome after hip fracture surgery

Author/ Year	Risk of Bias	Sample size	Prognostic Factor	Outcome	LOS (days)	Effect estimates (95% CI)
Adam 2013	High	90	EMS	EMS, LEFS	NA	1.4 (CI NA)
Adunksy 2008	High	NA	Anaemia on discharge	FIM	32	0.8 (0.3-1.8)
Adunksy 2011	High	606	Change in GFR	FIM	31-32	1.0 (1.0 to 1.0)
Adunksy 2015	High	707	Post- voiding residual volume	FIM	30-31	-1.8 (-3.8 to -0.2)
Adunksy 2012	High	1114	Atrial fibrillation	FIM	29-33	NA
Arinzon 2007	High	165	VAS	FIM	42-55	-6.7 (-12.2 to -1.3)
Benedetti 2015	High	249	SPMSQ	BI	10	0.6
Bliemel 2015	Low	402	Parkinson's disease	BI, POMA, TUG	14-17	p = 0.1
Bliemel 2015B	High	402	MMSE	BI	12-15	-16.1 (-21.5 to -10.5)
Buecking 2015	High	392	Age, BI, CCI, anaemia on admission, MMSE, time to surgery	POMA	NA	Age: -0.2 (-0.3 to -0.1) BI: 0.1 (0.1 to 0.2) CCI: -0.4 (-0.8 to -0.0) Anaemia on admission: 0.1(0.0 to 0.1) MMSE: 0.2 (0.1 to 0.4) Time to surgery: -0.1 (-0.1 to -0.0)
Doshi 2014	High	179	Age	MBI	10	p >0.05
Dubljanin-Raspopovic 2011	Low	343	Anaemia on admission	FIM	31	1.3 (1.0 to 1.3)
Dubljanin Raspopovic 2014	High	112	GDS	FIM	28	GDS -0.2 (-11.5 to 0.1)
Enemark 2017	High	73	Parkinson's disease	Mobility*	12	p=0.1
Goisser 2015	High	117	Dietary intake	BI	13	p=0·003
Goisser 2015	High	117	MNA	BI	5-45	p=0.2
Gonzalez-Montalvo 2016	High	479	Sarcopenia	FAC, BI	10	1.7 (0.99 to 2.8)
Horikawa 2014	High	99	Prefracture residence	ADL†	34-49	p <0.001
Hulsbaek 2015	High	167	Age, sex, NMS, procedure type, time to mobilisation, anaemia on discharge	CAS	1-18	Age: 4.3 (1.8 to 10.1) Sex: 0.9 (0.4 to 2.4) NMS: 7.0 (2.9 to 17.0) Procedure type: 1.6 (0.7 to 3.9) Time to mobilisation: 3.3(1.3 to 8.0) Anaemia on discharge: 5.8 (CI NA)
Kondo 2010	High	211	LOS	Mobility‡	8-44	0.2 (0.0 to 0.9)
Kristensen 2009	High	436	Age, NMS, fracture type	TUG	NA	Age: 0.5 (0.2 to 0.8) NMS: -10.8 (-16.5 to -5.0) Fracture type: 6.6 (1.9 to 11.1)
Kristensen 2013	High	55	VAS	TUG	NA	VAS: 8.7 (2.1 to 15.2)¶
Lee 2013	High	293	DVT	MBI BBS	NA	MBI p=0.8 BBS p=0.2
Lieberman 2007	High	224	Diabetes	FIM	29-32	p=0.001.
Liu 2015	High	261	Vitamin D	BI	10-33	5.2 (3.1 to 8.2)
Martin-Martin 2015	High	186	Age, MBI, fracture type, GHQ-28, LOS	POMA	NA	Age: -0.1 (-0.2 to 0.1) MBI: 0.1 (0.1 to 0.1) Fracture type: -1.5 (-2.8 to -0.2) GHQ-28: -0.2 (-0.3 to -0.1) LOS: -0.1 (-0.1 to -0.0)
Mizrahi 2007	High	449	Albumin	FIM	31-32	p=0.4
Morghen 2011	High	386	MMSE	MBI	28-29	NA
Morghen 2011	High	423	GDS	MBI	27-29	Mild 1.6 (0.8 to 3.3) Moderate/Severe 1.6 (1.3 to 7.8)
Seng 2015	High	210	Vitamin D	MBI	NA	NA
Shakouri 2009	High	117	Age, FIM, BMI, LOS	FIM	NA	NA LOS: p >0.05
Uriz-Otano 2015	Low	285	Prefracture function, delirium, medications, pressure ulcers, urinary retention, MMSE	BI	9-10	Prefracture function: 5.6 (2.4 to 12.7) Delirium: 3.2 (1.1 to 9.5) Medications: 1.6 (1.2 to 2.1) ** Pressure ulcers: 11.1 (2.9 to 43.3) Urinary retention: 3.9 (1.0 to 15.0) MMSE 1.1 (1.0 to 1.2)
Yonezawa 2009	High	203	Time to surgery	Mobility§	38-40	p=0.04

Abbreviations: EMS Elderly Mobility Score, LEFS Lower Extremity Functional Scale, BI Barthel Index, MBI Modified Barthel Index, NMS New Mobility Score, CAS Cumulated Ambulation Score, TUG Timed Up and Go, Tinetti Performance Orientated Mobility Assessment, MMSE – mini mental state exam, SPMSQ – short portable mental status questionnaire, MNA mini nutritional assessment, BMI body mass index, FAC Functional Ambulation Category, LOS length of stay, FIM Functional Independence Measure, NA – not available, CI confidence interval. * Mobility = independent – able to walk using a walker or walking stick but without the assistance from another person. Patients able to walk before hip fracture but not at discharge from the hospital were described as having 'loss of mobility'. † ADL - 1-5 1= bed rest immobilization for 24 hours, 2 = use of wheelchair with caregiver's aid, 3 = walking possible with a walking aid at home or in a geriatric health service facility, 4 = independent gait with a T-cane aid anytime and anywhere, 5 = independent gait with no aid during daily activities. ‡ Mobility 1 = walk independent without the use of equipment, 2 = walk with cane, 3 = walk with a walking frame or cart, 4 = needs assistance, 5 = use of a wheelchair, and 6 = confined to bed. § Mobility 1 = independently walking without cane, 2 = single cane walker or without cane but rather unstable, 3 = with a walker, walk while holding onto something or walk with support, 4 = move by wheelchair ¶ from multivariate regression which did not include fracture type as a covariate. **Walking component of BI only.

Table 2: Proposed mechanisms and mediators for the functional outcome effect of prognostic factors

Factor	Mechanism	Mediator
Age	Functional impairment increases with age.[52]	Prefracture function
	Cognitive impairment increases with age.[42]	Cognitive impairment
	Pain scores decrease with age. Older patients may be more likely to accept the pain medication provided by their health professionals is appropriate than younger patients.[28]	Pain
Sex	Women more often present with depression than men.[37]	Depression
	For women, urinary retention is associated with functional outcome.[35]	Urinary retention
	Women with hip fracture are older than men. [37]	Age
	Women present with more comorbidities than men. [37]	Comorbidity count
	Women present with more cognitive impairment than men. [37]	Cognitive impairment
Prefracture residence	Patients admitted from long term care present with more cognitive impairment than those admitted from home.[59]	Cognitive impairment
	Patients admitted from long term care present with more comorbidities than those from home.[53]	Comorbidity count
	Patients admitted from long term care develop more complications than those from home.[53]	Complications
	Patients admitted from long term care are less likely to undergo early mobilisation than those from home.[53, 59]	Time to mobilisation
Comorbidity count	Cognitive impairment increases with comorbidity count.[42]	Cognitive impairment
	Length of stay increases with comorbidity count.[53]	Length of stay
	Patients with more comorbidities are less likely to undergo early mobilisation than those with less comorbidities.[30]	Time to mobilisation
Diabetes	Patients with diabetes are more likely to develop postoperative urinary retention than those without diabetes.[35]	Complications
	Patients with diabetes are more likely to present with history of stroke than those without diabetes.[38]	Stroke history
	Patients with diabetes present with less prefracture function than those without diabetes.[38]	Prefracture function
Cognitive impairment	For patients with cognitive impairment, prefracture function is associated with functional outcome.[42, 49]	Prefracture function
	Patients with cognitive impairment may be seen to have less potential and therapists may reduce the intensity of rehabilitation compared to patients without cognitive impairment.[49]	Perceived potential
	Patients with cognitive impairment present on more medications than those without cognitive impairment.[42]	Medication management
	Patients with cognitive impairment develop more complications than those without cognitive impairment.[42]	Complications
	Patients with cognitive impairment are less likely to mobilize early than those without cognitive impairment.[30]	Time to mobilisation
Vitamin D	Skeletal muscles require vitamin D for structural maintenance and optimal function, with deficiency causing loss of muscle mass, atrophy of type II muscle fibers, and weakness.[47]	Weakness
Parkinson's Disease	Patients with Parkinson's Disease may not receive medication on time with some omitted completely.[58]	Medication management
	Patients with Parkinson's Disease develop more complications than those without Parkinson's Disease.[58]	Complications
Dehydration	Increased urea production may reflect dehydration due to bleeding around the fracture site.[34]	Blood urea
Malnutrition	Increased urea production is associated with malnutrition.[34]	Blood urea
	Patients with malnourishment have more comorbidities than well-nourished patients.[45]	Comorbidities
	Patients with malnourishment are more likely to have cognitive impairment than well-nourished patients.[45]	Cognitive impairment
	Patients with malnourishment develop more complications than well-nourished patients.[46]	Complications
	Patients with malnourishment are more likely to be frail than well-nourished patients[46]	Frailty
Depression	Patients with depression may be less likely to comply with rehabilitation than those without depression.[36, 48, 54]	Adherence
	For patients with depression, pain is associated with functional outcome.[36]	Pain
	Patients with depression are more likely to be frail than patients without depression.[37]	Frailty
	Therapists reduce rehabilitation intensity more for patients with depression than those without depression.[37, 48]	Perceived potential
Fracture type	Patients with a trochanteric hip fracture require more pain medication than those with femoral neck fractures.[28]	Pain
	Patients with more severe fractures are less likely to mobilize early than those with less severe fractures.[30]	Time to mobilisation
Anaemia on admission	Patients with low haemoglobin on admission are more likely to be frail than those with higher haemoglobin.[33]	Frailty
	Patients with low haemoglobin on admission may have less strength than those with higher haemoglobin.[33]	Weakness
Time to surgery	Patients with longer time to surgery have a longer time to mobilisation than those with shorter time to surgery.[54]	Time to mobilisation
Complications	Patients with complications have a longer acute hospital stay than those without complications.[53]	Length of stay
	Patients with complications wait longer before mobilising than those without complications.[53]	Time to mobilisation
Pain	Patients with pain are less likely to adhere to rehabilitation than those without pain.[36]	Adherence
	Patients with pain are less likely to undergo early mobilisation than those without pain.[30]	Time to mobilisation
	Patients with pain are more likely to have disturbed sleep, appetite loss, and fatigue than those without pain. [36]	Fatigue
	Patients who report pain are less likely to be cognitively impaired than those who do not report pain.[36]	Cognitive impairment

DISCUSSION

We identified 25 prognostic factors of functional outcome after hip fracture surgery from 33 studies. We organised these factors into 5 groups; demographics, injury and comorbidities, body composition, complications, and acute care factors. Overall, the risk of bias across studies was high. There was sufficient quality evidence to assign a weak level of evidence for anaemia on admission and cognitive impairment, and an inconclusive level of evidence for Parkinson's disease. There was insufficient quality evidence to assign a level of evidence for the remaining 22 prognostic factors.

Most studies included in this review focused on immutable factors of functional outcome after hip fracture surgery. Knowledge of these factors enables clinicians to adopt a stratified care approach by prioritizing those at high risk of poor outcome.[11] We assigned a weak level of evidence for an association between cognitive impairment and functional outcome. A recent systematic review reported a positive association between rehabilitation and functional outcome after hip fracture surgery among patients with cognitive impairment.[61] Despite this cognitively impaired patients are often excluded from trials of new interventions.[62] While the presence of cognitive impairment may be considered an immutable factor,[63] all four proposed underlying mechanisms are modifiable– medication management, perceived potential, occurrence of complications, and time to mobilisation. Future high-quality prognostic studies are required to confirm or refute the proposed underlying mechanism for the reported association.

Less studies focused on modifiable factors of functional outcomes after hip fracture surgery. To inform future Best Practice Tariffs there is a need for greater understanding of modifiable prognostic factors of functional outcomes such as rehabilitation access or staffing levels. We assigned a weak level of evidence for an association between anaemia on admission and functional outcome. However, a recent randomized controlled trial indicated that a more liberal blood transfusion policy did not lead to better recovery of activities of daily living than a more restrictive blood transfusion policy.[64] In the current review frailty and weakness (a feature of frailty) were proposed as underlying mechanisms for the reported association. Alone, a more liberal transfusion policy may be an insufficient intervention to target both anaemia and frailty. A complex intervention combining transfusion with more intensive rehabilitation may warrant further study.

The dependency graph presented here provides a framework for further discussion of prognostic factors and proposed mechanisms underlying their reported association with functional outcome after hip fracture surgery. In this review, the graph was constructed explicitly on existing literature. Therefore, the absence of nodes, or arrows between nodes, could reflect the absence of knowledge rather than the absence of dependency.[65, 66] For example, some may argue frailty is an underrepresented mechanism for the association between several factors and functional outcome. Indeed, frail adults are more likely to present as older, with cognitive impairment, incontinence, comorbidities, and poor prefracture function compared to their nonfrail counterparts.[67] Further, there was no reference to access and delivery of rehabilitation, or participation in rehabilitation, as potential mediators for the association between factors and functional outcome. This is despite evidence for an association between depression and cognitive impairment with rehabilitation participation.[68] In fact, only 16 of the 25 factors identified included any proposed mechanism underlying the studied association. We suggest this synthesis of factors on their underlying mechanisms is an important step towards transparency about underlying assumptions in prognostic analyses.

Limitations

The studies included in this review focused on prognostic factors of functional outcome on discharge after hip fracture surgery. Yet, focusing solely on functional outcome overlooks other forces influencing when and if a positive functional outcome occurs. Indeed, a positive functional outcome by discharge also depends on the death rate as patients may only recover if they remain alive.[69] Further, functional outcome on discharge also depends on the length of hospital stay, which varied across studies (range 1 to 55 days). Poor functional outcomes could reflect a higher discharge rate rather than a true difference in functional outcomes after hip fracture surgery.[69]

We assigned a level of evidence to only three prognostic factors due to the high risk of bias seen across studies. It was not possible to complete a meta-analysis due to variation in eligibility criteria, prognostic factor measurement, and outcome measurement. Several studies from the same patient cohort reported a positive association between prognostic factors and functional outcomes. This may suggest publication bias.[25] To reduce this potential bias we sought to include unpublished and incomplete studies. However, we identified no grey literature or incomplete studies. Additional studies may be indexed in databases not included in our search strategy. We included search terms for function, mobility and balance. We did not include search terms for surrogate measures of functional recovery, e.g. discharge destination. Additional prognostic factors may be identified by inclusion of these surrogate measures. Finally, we limited length of follow up to discharge from hospital to reduce the likelihood of unobserved factors confounding or interacting with functional outcomes after discharge from hospital. Patients continue to recover function for the first 6 months postoperatively.[70, 71] Therefore, additional prognostic factors for longer-term functional outcomes may not have been captured by this review.

We followed the recommendation from Hayden et al. for quality appraisal.[24] This resulted in assigning an overall level of evidence to just 3 factors. A more recent study by Hayden et al. recommends assigning overall low risk of bias if the '*most important (determined as a priori)*' of the six bias domains are rated as having low risk.[23] This would have enabled us to assign a level of evidence to additional factors. However, ranking bias domains by importance may lead to reviewer bias. More recently, overall risk was assigned based on a count of low, moderate, and high risk within a study.[25] This may result in a study being judged as low overall risk of bias even if two domains are high bias. Future research should identify the optimal approach for assigning overall risk of bias in prognostic systematic reviews.

CONCLUSION

We assigned two factors a weak evidence level – anaemia on admission and cognition. We assigned Parkinson's disease an inconclusive evidence level. Future research may target these patients by intervening directly on the prognostic factor, or the proposed modifiable underlying mechanism. We identified an additional 22 prognostic factors of functional outcomes after hip fracture surgery. However, we could not assign an evidence level to any other factors due to the high bias identified during quality assessment. Further research is required to generate high-quality prognostic studies of additional factors of functional outcomes after hip fracture surgery and their underlying mechanisms.

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