The Effects of Postoperative Delirium

on Outcomes in Hip Fracture Patients

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Abstract

Background

Hip fractures have reached epidemic levels in an ever-ageing population. Based on this increase, the rate of postoperative delirium (POD) is simultaneously expected to rise as it seems to be a disproportionate hazard post-hip surgery. POD is purported to have detrimental effects, but prevention and screening efforts remain inadequate. Therefore, examination of recent evidence for negative outcomes, including decreased survival and increased complications, is critical if we seek best practice.

Objectives

This review examines the most recent evidence for the effect of POD on mortality of hip fracture patients and other outcomes such as length of stay, discharge destination and functional outcomes.

Methods

Two electronic databases searches resulted in selection and critical appraisal of ten studies.

Results

Across the ten articles selected for review, the prevalence of POD ranged from 18-53.3%. Nine studies focused on mortality. In unadjusted analysis, mortality was found to have a significantly increased association with POD. However, several papers showed with effective adjustment for confounding or contributory variables, no independent association was observed. Medical complications was a focus in four of the articles, and the association with POD was observed following adjustment. Similar results were reported for increased non-home discharge and length of hospital stay.

Conclusion

POD has some effect on outcomes in hip surgeries but future research needs coherence of methods across the field and comprehensive accounting for the increased age and comorbidities of POD patients. Determining whether factors like increased length of stay are themselves the cause, rather than the result, is imperative. The lack of consistent high-quality research frustrates the validity of many of the papers conclusions on increased mortality. While we await such research an effort still needs to be made to prevent POD, especially given the more valid evidence of other less fatal effects.

Introduction

Hip fractures have been termed a modern epidemic [1] as the second leading cause of hospitalization in the growing cohort of '65 years and older' [2]. In 2000 there were 1.6 million hip fractures worldwide, with predicted increase to 4.5–6.3 million by 2050 [3]. A hip fracture can be a fatal turning point. One-year mortality rate is reportedly 20–24%. It is shown that 40% were unable to walk independently, while 60% required assistance with activities of daily living [4]. This crisis is stretching healthcare costs and rehabilitation services. This is evident in Ireland, where from 2000 to 2014, there has been a 51% increase in bed days for osteoporotic fractures, and hip fractures making up 47% of those bed days [5].

There is growing understanding of the various perioperative factors that predict poorer outcomes and increased mortality post hip surgery. These include age, ASA score [6], time to surgery,[7] comorbidities, pre-fracture mobility[8], and cognitive impairment [9]. However, there is scope to further scrutinize and delve into perioperative variables, in order to guide advances in hip fracture management.

POD is defined as an 'acute brain dysfunction,' which shows similar symptoms to dementia, but is expected to improve when 'causative factors' are normalized [10]. It varies in severity and duration, and it has been noted specifically that symptoms may differ if POD co-exists with dementia [11]. Symptoms are screened for using diagnostic tools noting onset, course, inattention, disorganized thinking and consciousness.

There seems to be a disproportionate risk post hip surgery, with reported incidence up to 53.3% [12]. It is postulated that this is due to the increased age of hip patients and the 'threshold theory of cognitive decline' which describes the elderly as having a diminished brain reserve capacity, or on a 'functional cliff' for developing POD when experiencing a strain such as hip surgery [13].

This review aims to examine the reported effect POD can have, mainly on mortality, length of stay, and institutionalization – the most popular measured outcomes in the literature.

Glossary of Abbreviations

AOR: Adjusted Odds Ratio

ASA: American Society of Anesthesiologists

CAM: Confusion Assessment Method

CI: Confidence Interval

DOSS: Delirium Observation Screening Scale

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

FNF: Femoral neck fracture

HR: Hazard Ratio

IF: Internal Fixation

IQR: Interquartile Range

LOS: Length of Stay

MMSE: Mini Mental State Exam

NOF: Neck of Femur

OR: Odds Ratio

ORIF: Open rotation internal fixation

P: p-value

POD: Postoperative Delirium

THA: Total Hip Arthroplasty

Objectives

This systematic review aims to evaluate recent literature within the following objectives:

1. Examine the evidence for the effect of POD on mortality of hip fracture patients.
2. Determine the reported impact of POD on other outcomes such as length of stay, functionality, readmission.

Methods

On 20/01/2020, electronic database searches were undertaken using the following terms:

PubMed: All (Title/Abstract)

I. delirium or POD or cognitive dysfunction or cognitive impairment or POCD

II. postoperative or after surgery or post-op or post-surgery or surgical or after hip surgery

III. hip fracture or neck of femur or femoral neck or hip fracture or neck of femur fracture or femoral neck fracture or NOF fracture or proximal femur or fractured neck of femur

IV. outcomes or predictor or impact or mortality or indicator or sequelae or complications

EBSCO (MEDLINE)

I. (Abstract) delirium or POD or cognitive dysfunction or cognitive impairment or POCD

II. (Abstract) postoperative or after surgery or post-op or post-surgery or surgical or after hip surgery

III. (Abstract) hip fracture or neck of femur or femoral neck or hip fracture or neck of femur fracture or femoral neck fracture or nof fracture or proximal femur or fractured neck of femur

IV. (Title) outcomes or predictor or impact or mortality or indicator or sequelae or complications

Inclusion Criteria

- Published 2010-2020
- Evaluates hip fracture patients post-operatively
- Examines mortality or other outcomes postoperatively
- Includes POD as a variable

Exclusion Criteria

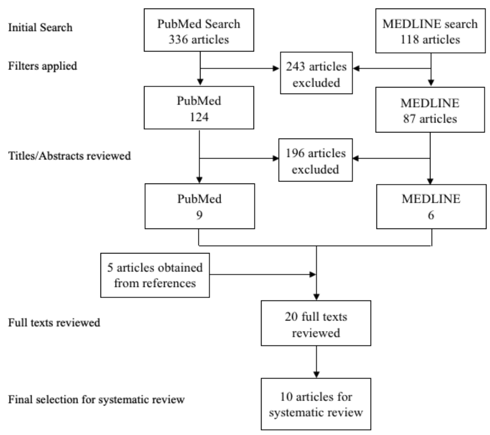
- No full text or English available
- Included knee fracture patients
- Focus on analgesia, anesthesia, or surgery
- Systematic reviews, meta-analyses, case studies

Selection Process

The initial search results and filter applications are shown in Figure 1. The remaining papers were reviewed by title and/or abstract to select the most relevant. Many were excluded by title alone due to obvious exclusion criteria breaches. The more appropriate articles were reviewed by abstract, until twenty full texts were examined, including five from references. Finally, ten articles were selected for systematic review.

After selection, the details of these papers were summarized using a table of results with the headings: Author, (Year) Location, Title, Study Design, Sample Size, Population, Key Findings, Strengths and Limitations. Critical appraisal for each article was by the EBL checklist, found in the appendix, and subsequent validity score, found in Table 1. This is a standardized checklist that determines study quality and validity using specific questions on sampling, data collection, results and design.

Figure 1
Selection process



Results

The prevalence of POD across the articles ranged from 18%-53%.

Mortality

Nine studies dealt with mortality, many giving results that backed an increased mortality rate with POD. Arshi et al. reported POD patients had a significantly higher risk-adjusted 30-day mortality (OR 2.22 [1.74-2.84]). [13] De Jong et al. stated POD was a significant predictor of 1-year mortality, remaining after multivariate analyses, (OR 1.93, P=0.016). [16] Choi et al described that All POD patients had significantly lower survival rates at 2-year follow-up than control (77.1% vs 87.8%; p<0.001). This study also reported that immediate POD had significantly lower survival (71.0%) than control

Table 1
Validation scoring based on EBL Critical Appraisal Checklist
Four of the studies were found to be invalid (< 75%).

Article	Population (%)	Data Collection (%)	Study Design (%)	Results (%)	Overall (%)
Arshi et al. (2018) Predictors and Sequelae of POD in Geriatric Hip Fracture Patients	66.7	50.0	80.0	83.3	67.8
Belleli et al (2014) Duration of POD Is an Independent Predictor of 6-Month Mortality in Older Adults After Hip Fracture	66.7	62.5	80.0	100.0	75.0
Choi et al. (2017) Early POD after hemiarthroplasty in elderly patients aged over 70 years with displaced FNF	44.4	87.5	100.0	83.3	75.0
De Jong et al. (2019) Delirium after hip hemiarthroplasty for proximal femoral fractures in elderly patients: risk factors and clinical outcomes	44.4	75.0	100.0	66.7	67.8
Gottshalk et al. (2015) The Impact of Incident POD on Survival of Elderly Patients After Surgery for Hip Fracture Repair	55.6	75.0	100.0	66.7	71.4
Krogseth et al. (2013) Delirium is a risk factor for institutionalization and functional decline in older hip fracture patients	55.6	75.0	100.0	100.0	75.0
Malik et al. (2018) Incidence, risk factors and clinical impact of POD following ORIF for hip fractures: an analysis of 7859 patients from the ACS-NSQIP hip fracture procedure targeted database	75.0	62.5	100.0	66.7	74.1
Mosk et al. (2017) Dementia and delirium, the outcomes in elderly hip fracture patients	75.0	62.5	100.0	100.0	81.4
Radinovic et al. (2015) Estimating the effect of incident delirium on short-term outcomes in aged hip fracture patients through propensity score analysis	44.4	87.5	80.0	83.3	75.0
Tahir et al (2018) Risk factors for onset of delirium after NOF fracture surgery: a prospective observational study	66.7	75.0	100.0	66.7	75.0

(87.8%), while delayed POD survival (83.6%) did not differ significantly from control (87.8%), p=0.579. [15] Mosk et al. mentioned POD patients had a higher incidence of mortality < 6 months (30.1%, P<0.001) [20]. Malik et al. showed that POD gave OR 2.04 for 30-day mortality (p < 0.001) [19]. Belleli et al. revealed that POD was independently associated with 6-month mortality and that each POD day increased hazard of dying by 17% [14].

Several articles were unable to find the results significant for increased mortality. Gottshalk et al. initially reported decreased survival, yet on Cox regression this became insignificant; HR 1.25 (CI [0.92-1.48]) [17]. Krogseth et al. combined institutionalization with mortality for composite risk analysis, which failed to reach statistical significance (AOR: 2.07, CI 0.88-4.89) [18]. Tahir et al. claimed 1-year mortality was significantly higher with POD (25.7%) compared to patients without delirium (15%) p = 0.026. Mortality within 30-days followed the same trend (10% vs. 6%) however did not reach statistical significance [22]. In Randovic et al. neither models of confounding showed 1-month mortality as a statistically significant hazard[21].

Medical Complications

Four studies dealt with medical complications. Arshi et al reported POD independent associations with higher coincidence of postoperative pneumonia, UTI, CVA, MI, hospital readmission and sepsis within 30 days[13]. Mosk et al. also displayed a higher rate of complications (48.5%, P<0.001) [20] while Malik et al. reported increased 30-day readmissions with POD (OR 1.80; p < 0.001) [19]. In Randovic et al., POD was a higher age adjusted risk of re-intervention plus death (OR 2.56), complications (OR 2.66) and higher severity complications (B = 0.83, P = 0.027). With more variate adjustments, a higher risk of re-intervention plus death (OR 7.16) and a longer LOS (B = 5.08) remained [21].

Institutionalization

Five studies investigated discharge location following POD. Arshi et al. mentioned POD was associated with greater discharge to (OR 1.65), and prolonged stay in, inpatient facilities (OR 1.79) [13]. In De Jong et al., POD patients without dementia, vs. control (no POD), were significantly more often discharged to nursing homes (OR 7.06) or semi-independent nursing homes (OR 11.4) [16]. Mosk et al reported that POD was significantly associated with nursing home admission (91.8%, P<0.001) [20]. Malik et al. stated POD lead to significantly higher odds of non-home discharge (OR 1.79) [19]. Krogseth et al. through logistic regression analysis concluded delirium remained a significant predictor of institutionalization (AOR: 5.50) [18].

Length of Hospital Stay (LOS)

6 studies examined the effect on LOS. Arshi et al. reported increased LOS [13]. However De Jong et al. stated greater LOS for the non-dementia POD group was not significant (P=0.128) [16]. Mosk et al described an increased LOS (median 6 days [IQR: 6], P=0.002) for POD patients [20]. For Malik et al. LOS was also significantly associated with POD. Compared with 0-3 day stay POD was associated with LOS 4-6 days (OR 1.63; p<0.001 and >6 days (OR 3.30; p< 0.001). [19] Tahir et al stated that the presence of delirium was associated with significantly increased LOS (average 13 days vs. 10 days, p = 0.001). [22] Randovic et al. also reported a prolonged LOS in POD (B = 5.75, P < 0.001) [21].

Discussion

Mortality

The results on mortality were far from conclusive, damaged by inconsistencies in follow-up periods, sampling size, and analysis. The articles showed weak statistical evidence for POD as a predictor of increased mortality [16], or it failed to achieve significance based on Kaplan-Meier survival analysis [17]. In Randovic et al., both extensive risk adjusted models failed to show that POD was a statistically significant hazard for 1-month mortality [21]. Yet a study with fewer confounding variables, Malik et al., found an association with 30-day mortality [19]. The exclusion of preoperative delirium perhaps explains Gottshalk et al. finding that, on Cox regression, POD was not significant for mortality [17]. This patient group has been shown in other studies to be at significant risk of POD [16, 20, 22]. Some studies perhaps lacked a substantial sample size to reach statistical significance. For example, in Tahir et al. 70 patients had POD, and 30-day mortality trends, while consistent, were insignificant [22]. Similarly certain papers deemed a p-value of <0.05 was enough for statistical significance which may redefine some results [15, 16]. Furthermore, the quality of statistical analysis differed, some lacking confounding [13, 19].

There is a certain inclination towards an association between POD and early mortality, yet this review is relatively consistent in showing that following adjustment for confounders significant associations of POD with mortality were unlikely [14].

Other Outcomes

There is more coherence, but perhaps less scrutiny, when dealing with other measured outcomes. POD was shown to have associations with complications [20], and hospital readmissions [13,19]. Arshi et al. also showed a greater rate of specific complications with POD [13]. The two models in Randovic et al. provided further backing to this, showing higher risk when adjusted for age for both of the aforementioned variables. The presence of POD was also associated with a higher severity complication score. With adjustment, POD remained a high risk for re-intervention plus death and a longer LOS [21].

LOS was conclusively associated with POD [13, 18, 19, 20, 22] Yet one study which stratified for dementia patients – a strongly associated risk for POD, had a non-significance to this association [16]. Most of these studies recognised the limitation of this for LOS as an outcome, due to the inability to establish the direction of the relationship between both variables.

Similarly, with institutionalisation, there was a relatively consistent association with POD across studies that measured it. [13, 16, 18, 19, 20,]. While many lacked conclusive confounding, Krogseth et al. through logistics regression analysis showed POD as the initiation of a detrimental functional process [18]. POD was also shown to have the greatest impact on patients who were already impaired. Thus, with all outcomes it is difficult to definitively establish POD as the cause.

Limitations

Throughout the studies there were certain issues with external validity, and other aspects of quality. Often sample sizes were small, only three papers having over 500 participants [13, 19, 20], with POD patients a smaller subset within these samples. Four papers were deemed unrepresentative in critical appraisal [15, 16, 17, 18]. Some acknowledged a reason for exclusion, but there is a benefit instead to stratifying these patients when included to get a proper picture.

Most of the studies acknowledged the difficulty in concluding that any of the outcomes were a direct cause from POD, given an admission that healthier patients are less vulnerable to the development of delirium and more resistant to its adverse outcomes if they become delirious [18]. Again assessment of confounding variables is a crucial issue here.

The field of knowledge itself must also be critiqued. There was a frustrating contrast in results based on lack of consistency and comparability of study design. A primary example of this was the diagnosis of POD. Most used the established DSM-IV tools and CAM algorithm but within this, there was variety. These assessments were carried out differently, e.g. every day [21] or once off [17]. Some also used additional techniques such as clinical notes reviewing and DOSS scores [20]. There were more disparities including stratifying dementia patients, delirium subtyping, missing hypoactive delirium, exclusion of certain surgical techniques, which all adds to the complexity involved in answering the review question. There is the possibility of bias within the papers, particularly single-centre studies performed by service providers e.g. Choi et al [15].
Other limits of this review would be time constraints while on full time placement, personal research and review inexperience, lack of access to full texts. As the sole reviewer, author bias is a major limitation on my part.

Conclusion

This review cannot draw any distinct conclusions from papers reviewed, and is forced instead to examine the state of the research field, which is seemingly clouded by low-quality outcome measurement – particularly of mortality - statistical variance, and general lack of consistency across the field. Thus, future research needs to focus on effective external validity of mortality claims. [24] Similarly there is a gap in the literature for measurement of personal impacts on patients, such as PTSD and depression. The issue of increased age and comorbidities associated with POD clouds the interpretations of these statistics and only multivariate regression models can address these issues.

Nevertheless, the need for prevention of POD was echoed throughout, given relative coherence on the less fatal negative effects, queries over increased mortality rate, and a background of increasing hip fracture prevalence. This should force action in the current lack of structured follow-up for these patients, [15] due to the great burden of POD on healthcare costs, patients, and families.

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