Timing matters in hip fracture surgery: patients operated within 48 hours have better outcomes - a meta-analysis and meta-regression of over 190,000 patients


CRD summary
This review evaluated the relationship between surgical delay and mortality in elderly patients with hip fracture. The authors concluded that surgical delay was associated with a significant increase in the risk of death and pressure sores, but results should be considered suggestive and not conclusive. The authors’ cautious conclusion is appropriate and seems reliable.

Authors' objectives
To evaluate the relationship between surgical delay and mortality in elderly patients with hip fracture.

Searching
MEDLINE, EMBASE and CINAHL were searched up to December 2011. A search strategy was reported to be available. The reference lists of included studies, reviews, meta-analyses, and guidelines on high fracture surgery and prognostic factors were also searched. Studies published in English, French, Italian or Spanish after 1980 were sought.

Study selection
Eligible for inclusion were randomised, quasi-randomised, prospective and retrospective cohort and case controlled studies in patients (average age per study was 65 years or older) with the reported timing of hip fracture operation. Studies also had to provide sufficient data on survival status to enable meta-analysis.

Included were controlled observational studies conducted worldwide, with four carried out in the United Kingdom. The mean age of study participants was 80 years (range 76 to 83 years) and the mean proportion of women was 74%. The primary outcome was overall mortality. Secondary outcomes were post-operative complications: infections, pressure sores, post-operative chronic pain, hospital length of stay and readmission. The optimal surgical time delay ranged from 12 hours to more than 72 hours.

Two reviewers independently selected the studies for inclusion. Disagreements were resolved by consensus, or with the involvement of a third reviewer.

Assessment of study quality
The quality of observational studies was assessed using the Newcastle-Ottawa scale which covered selection, exposure/outcome and comparability. Observational studies that met eight or nine of the criteria were considered to be high quality. For randomised controlled trials (RCTs), quality was assessed on sequence generation, allocation concealment, and completeness of outcome data. RCTs that met two or more criteria were considered to be high quality.

Two independent reviewers assessed study quality.

Data extraction
Data were extracted or converted for all outcomes to enable the presentation of odds ratios and 95% confidence intervals.

One reviewer extracted data and this was checked by a second reviewer. Disagreements were resolved by discussion or with the involvement of a third reviewer.

Methods of synthesis
Odds ratios were pooled for the primary outcome in a random-effects meta-analysis (DerSimonian and Laird), using the inverse variance method and ordered by study year. Statistical heterogeneity was assessed using I². The robustness of the analysis was tested using Bayesian techniques. Meta-regression analysis was carried out to explore the influence
of study design (prospective or retrospective), type of data (administrative or clinical), methodological quality (high versus low), study location (USA and other), different optimal time cut-points, age, female prevalence, study year, and optimal time treated as a continuous variable. A fixed-effect model with a funnel plot and Harbord's test, were applied to explore the influence of small study effects.

**Results of the review**

Thirty-four cohort studies (14 prospective; 20 retrospective; 191,802 patients) and one RCT (71 patients) were included in the review. Sample sizes ranged from 65 to 57,315. The quality of observational studies ranged from 5 to 9 points (median 7). The RCT was considered to be at high risk of bias. A risk of small study bias could not be ruled out, despite Harbord's test failing to reach statistical significance.

Early surgery (within 24 to 48 hours) was associated with a significantly lower risk of death (OR 0.74, 95% CI 0.67 to 0.81; 34 studies; $I^2=84.7\%$). A fixed-effect analysis gave a slightly smaller benefit (OR 0.79, 95% CI 0.77 to 0.81) which suggested slight small study bias. Bayesian analysis showed the likelihood of no effect or an adverse effect of early surgery could have been anticipated in approximately 20% of future studies. There were no statistically significant effects on mortality for any of the covariates in meta-regression analysis. A reduction in pressure sores was reported as a result of early surgery (OR 0.48, 95% CI 0.38 to 0.60; six studies; $I^2=0\%$). Further meta-analyses on secondary outcomes were not possible due to substantial heterogeneity.

**Authors' conclusions**

Surgical delay was associated with a significant increase in the risk of death and pressure sores in elderly patients with hip fracture. Due to potential methodological weaknesses in the included studies, results of this review should be considered suggestive and not conclusive.

**CRD commentary**

The review question and inclusion criteria were clearly reported. Three relevant databases were searched. There were language restrictions, and no apparent search for unpublished material. This meant that relevant studies might have been overlooked, and publication/language biases could not be ruled out. The possibility of publication bias was found in formal analysis. The review process was conducted with sufficient attempts to minimise error and bias.

Appropriate quality assessment criteria were applied to the included studies, which indicated that study quality (on average) was moderate to good. Study results were synthesised in meta-analyses, but there was considerable heterogeneity across studies. The impact of this heterogeneity was explored and no firm conclusions were possible.

The review contained a large number of studies and patients, with carefully conducted analyses and appropriate sensitivity testing. Therefore, the authors' cautious conclusion is appropriate and seems reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that orthopaedic surgery should be scheduled to ensure that most patients were operated on within one or two days. Conservative timing strategies should be avoided, except (for example) in patients requiring stabilisation.

**Research:** The authors did not state any implications for research.

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