

General *versus* regional anaesthesia for hip fracture surgery: a meta-analysis of randomized trials

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Hip fracture surgery is common and the population at risk is generally elderly. There is no consensus of opinion regarding the safest form of anaesthesia for these patients. We performed a meta-analysis of 15 randomized trials that compare morbidity and mortality associated with general or regional anaesthesia for hip fracture patients. There was a reduced 1-month mortality and incidence of deep vein thrombosis in the regional anaesthesia group. Operations performed under general anaesthesia had a reduction in operation time. No other outcome measures reached a statistically significant difference. There was a tendency towards a lower incidence of myocardial infarction, confusion and postoperative hypoxia in the regional anaesthetic group, and cerebrovascular accident and intra-operative hypotension in the general anaesthetic group. We conclude that there are marginal advantages for regional anaesthesia compared to general anaesthesia for hip fracture patients in terms of early mortality and risk of deep vein thrombosis.

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Hip fracture is a common condition and is increasing in incidence. In 1990, there were an estimated 1.7 million hip fractures worldwide. Predictions for numbers presenting in 2050 are as high as 6.3 million globally.¹ Females predominate, at a ratio of 4:1, indicating their increased susceptibility to fractures due to osteoporosis.²

Most hip fractures are treated surgically, either by internal fixation of the fracture or by replacement of the femoral head with an arthroplasty. The high incidence of hip fracture confers a considerable load on surgical and anaesthetic services. Furthermore, this group of patients has an average age of approximately 80 yr and intercurrent illnesses such as cardiac and respiratory disease are common. These problems result in hip fracture being associated with significant morbidity and mortality.

Anaesthesia for hip fracture most commonly involves either a general or a regional anaesthetic. General anaesthesia may be induced and maintained by a number of drugs, depending on the anaesthetist's preference and the condition of the patient. The airway may be maintained using a face mask, laryngeal mask or endotracheal tube, and ventilation may be spontaneous or mechanical. Regional anaesthesia usually takes the form of a spinal injection of local anaesthetic to induce surgical anaesthesia, but epidural anaesthesia may also be used. Sedatives are often used in conjunction with regional anaesthesia to help the patient tolerate posi-

tioning during placement of the spinal or epidural needle and also during the intra-operative period. Previous studies have failed to establish a benefit of one form of anaesthetic over another.^{3–4} A previous meta-analysis of 11 trials³ showed no difference in outcome with different anaesthetic methods but not all published randomized trials were included. In addition, data from one trial was duplicated in two other trials by the same author. The purpose of this study was to extend and correct the work done previously using a more comprehensive search of the literature in order to determine if there is a difference in outcome depending on the type of anaesthetic used in hip fracture patients.

Methods

Search strategy and study selection

Randomized and quasi-randomized trials were identified using the search strategy of the Musculoskeletal Injuries Review Group of the Cochrane Collaboration.⁵ This included searching the computer databases of Medline, Embase, CINAHL, Current contents and the Cochrane controlled trials register. In Medline the search method used was that described by Dickerson.⁶ In addition we searched using the references of all identified trials and review articles along with hand-searching of core journals and

abstract books of orthopaedic conferences. Articles in all languages were included and translations were obtained for any trials published in foreign languages. Where relevant, further information was sought from trial authors. Trials comparing different anaesthetic techniques for hip fracture repair that reported mortality or any aspect of morbidity were considered for inclusion. Trials were excluded if they compared outcome following different doses of drug for the same anaesthetic technique, and those comparing different general anaesthetic techniques.

Data extraction and quality assessment

Independent reviewers (SCU, RG) assessed methodological quality using a nine item scoring system. The items assessed were:

- (i) the method of randomization,
- (ii) inclusion and exclusion criteria for patients entered into the study,
- (iii) adequate description of treatment and control groups at entry to the study,
- (iv) if the care programmes were identical between the groups other than the anaesthetic type,
- (v) clear definition of the outcome measures in the text,
- (vi) blinding of the assessors to the treatment group,
- (vii) adequate patient follow-up (a minimum of 3 months was taken as adequate),
- (viii) number of patients lost to follow-up (less than 5% lost to follow-up was taken as acceptable) and
- (ix) statistical analysis on an intention-to-treat basis.

Each study could score a maximum of 11 for methodological quality. The method of randomization was considered the most important factor and could score a maximum of three points. All other items could score one point only. Any difference in opinion between the assessors was resolved by discussion with a third reviewer (MJP).

Outcome measures sought in each paper included intra-operative details and data related to post-operative morbidity and mortality. Intra-operative details included length of operation, blood loss, transfusion requirements and the occurrence of hypotension. Morbidities included post-operative hypoxia, pneumonia, thromboembolism, confusion, renal failure, myocardial infarction, congestive cardiac failure, urinary retention and vomiting. Complications relating to the type of anaesthesia, such as dental damage in general anaesthesia and post-dural puncture headache for spinal anaesthesia were sought. Length of hospital stay, long term functional and quality of life outcomes were also sought.

Data analysis

Review Manager software⁷ was used to analyse the outcome data. Heterogeneity between comparable trials was tested using a standard chi-square test. Where $P < 0.1$ for heterogeneity, a random effects analysis was carried out. Pooled Peto odds ratios (OR) were calculated for dichotomous outcomes, and pooled weighted mean differences for con-

tinuous variables. Ninety five per cent confidence intervals were derived in both cases. Full details of the data analysis and methodology are presented elsewhere.⁵

Results

Patients and studies included

Fifteen trials involving a total of 2162 patients with hip fracture were included.⁸⁻²⁵ Details of these trials are summarized in Table 1. A full list of the excluded trials considered for review is available elsewhere,⁵ as are full data of the individual studies included in this meta-analysis. The majority of excluded studies involved comparisons outside the scope of this review, and one trial was excluded because all patients receiving a regional anaesthetic also had a general anaesthetic.²⁶ Two excluded trials involved neuroleptanaesthesia which was considered to be no longer appropriate for hip fracture surgery, and were therefore excluded.^{27 28} One study was excluded as it recorded injected indocyanine green clearance as its only outcome measure.²⁹ Attention is drawn to the three trial reports by McKenzie and colleagues.¹⁹⁻²¹ All of these involve patients from one trial.²⁰ This study contains results from the whole trial population, whereas the other two trials involved only subgroups of patients. For the purpose of this review, all three papers are referred to as 'McKenzie 1984', and data from the 1980 and 1985 papers were only included if these were unavailable in the original paper. A spinal anaesthetic was used in all trials except one which used an epidural technique.¹⁴

Outcome measures

Tables 2 and 3 summarize the comparison of outcome between regional and general anaesthesia for all outcome measures studied.

Mortality was reported in 11 studies, data being available at 1 month or beyond in eight studies.^{9 14-16 20 22 23 25} Table 2 shows the significant reduction in mortality at 1 month, but this advantage did not extend to 3 months or beyond.

Most studies reported the length of operation. Pooling of results was possible for six studies,^{9-11 18 20 23} indicating a significant reduction in the surgical times for general anaesthesia (weighted mean difference 4.8 min, 95% CI 1.1-8.6 min).

Summation of the reported occurrence of intra-operative hypotension was possible from six studies.^{9 14 15 18 22 23} There was significant heterogeneity of these results (chi-square 11.9, $P < 0.05$). Using fixed effects analysis, hypotension was significantly less frequent in the general anaesthetic group: 116/447 (26.0%) in the general anaesthetic group compared with 146/426 (34.3%) in the regional anaesthetic group (Peto OR 1.5, 95% CI 1.1-2.0). However, analysis using a random effects model, revealed a non-significant tendency to a lower incidence of hypotension in the general anaesthetic group (OR 1.21 and 95% CI 0.65-2.02).

Table 1 Characteristics of included trials. R=regional anaesthesia; G= general anaesthesia; N/A= not available

Trial	Country	Mean age (years) R/G	Gender % female	Number of patients R/G	Methodology score
Adams 1990 ⁸	Germany	81/79	82	24/32	2
Berggren 1987 ⁹	Sweden	77/78	81	28/29	7
Bigler ¹⁰	Not stated	80/78	82	20/20	7
Bredahl 1991 ¹¹	Denmark	80/79	100	15/13	6
Brichant 1995 ¹²	Belgium	N/A	N/A	54/52	4
Brown 1994 ¹³	Hong Kong	75/79	50	10/10	6
Couderc 1977 ¹⁴	France	86	86	50/50	4
Davis 1981 ¹⁶	New Zealand	81/78	85	64/68	7
Davis 1987 ¹⁵	New Zealand	79.5	78	259/279	6
Maurette 1988 ¹⁸	France	81/84	N/A	19/16	6
McKenzie 1984 ²⁰	England	75/74	N/A	73/75	6
McLaren 1978 ²²	England	79/76	N/A	26/29	4
Racle 1986 ²³	France	82/82	100	35/35	7
Tasker 1983 ²⁴	England	N/A	N/A	100	2
Valentin 1986 ²⁵	Denmark	79	80	251/297	7

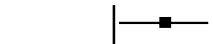
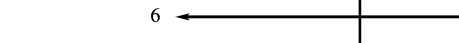


Table 2 Comparison of outcome between regional and general anaesthesia for dichotomous variables. All results were derived using fixed effects analysis except those marked * which were derived using random effects analysis. Statistically significant results are indicated by +. Results to the left of the vertical line indicate an advantage for regional anaesthesia over general anaesthesia and conversely for those lying to the right. Results show the incidence of each outcome measure. T=number of trials; P=number of patients; OR=odds ratio; CI=confidence intervals

Outcome	T/P	Incidence (regional)	Incidence (general)	Peto OR (95% CI)	Peto OR (95% CI)
Mortality—1 month	7/1578	49/766 (6.4%)	76/812 (9.4%)		0.66 (0.47–0.96)
Mortality—3 months	6/1491	88/726 (12.1%)	98/765 (12.8%)		0.91 (0.67–1.24)
Mortality—6 months	3/1264	103/613 (16.8%)	105/651 (16.1%)		1.05 (0.78–1.41)
Mortality—12 months	2/726	80/354 (22.5%)	78/372 (21.0%)		1.10 (0.77–1.57)
Operative hypotension	7/873	146/426 (34.3%)	116/447 (26.0%)		1.51 (1.12–2.02)+
Patients receiving transfusion	3/228	63/108 (58.3%)	68/120 (56.7%)		1.02 (0.58–1.80)
Post-operative hypoxia	1/57	10/28 (35.7%)	14/29 (48.3%)		0.60 (0.21–1.71)
Pneumonia	8/1096	27/529 (5.1%)	31/567 (5.5%)		0.92 (0.53–1.59)
Myocardial infarction	4/888	4/431 (0.9%)	8/457 (1.8%)		0.51 (0.16–1.63)
Cerebrovascular accident	7/1085	10/529 (1.9%)	6/556 (1.1%)		1.72 (0.64–4.63)
Congestive cardiac failure	6/902	11/439 (2.5%)	12/463 (2.6%)		0.97 (0.42–2.23)
Renal failure	4/796	2/382 (0.5%)	3/414 (0.7%)		0.77 (0.13–4.50)
Acute confusional state	3/167	10/83 (12.0%)	19/84 (22.6%)		0.47 (0.21–1.06)
Urine retention	2/97	10/48 (20.8%)	10/49 (20.4%)		1.02 (0.39–2.71)
Nausea and vomiting	2/95	2/46 (4.3%)	3/49 (6.1%)		0.69 (0.12–4.13)
Deep vein thrombosis	4/259	39/129 (30.2%)	61/130 (46.9%)		0.41 (0.23–0.72)+
Pulmonary embolism	9/1184	8/575 (1.4%)	10/609 (1.6%)		0.84 (0.33–2.13)

There was marked heterogeneity of values for blood loss and volumes of blood transfused. Three studies^{11 16 25} reported an increased operative blood loss for general anaesthesia whilst two studies^{8 20} reported an increase for regional anaesthesia. Pooling of results was possible for

only three studies,^{11 16 20} demonstrating a tendency to an increased blood loss with general anaesthesia (weighted mean difference 81 ml, 95% CI 216–53 ml). Three studies^{8 10 16} reported on the number of patients requiring transfusion with no significant difference between anaes-

Table 3 Comparison of outcome between regional and general anaesthesia for continuous variables. All results were derived using fixed effects analysis except those marked * which were derived using random effects analysis. Statistically significant results are indicated by +. Results to the left of the vertical line indicate an advantage for regional anaesthesia over general anaesthesia and conversely for those lying to the right. T=number of trials; P=number of patients; WMD=weighted mean difference; CI=confidence intervals

Outcome	T/P	Regional	General	WMD (95% CI)	WMD (95% CI)
Length of operation (min)	6/376	189	187		4.82 (1.08–8.56)*
Blood loss (ml)	3/308	152	6		64.6 (–138.5 to 9.3)
Transfusion (ml)	2/218	103	100		168.9 (98.5 to 239.4)
Length of hospital stay (days, additive)	2/218	108	10		–0.21 (–5.21 to 4.78)

thetic methods (63/108 (58%) for general anaesthesia compared with 68/120 (57%) for regional anaesthesia, (Peto OR 1.01, 95% CI 0.6–1.8). Three studies reported this outcome as mean volume of blood transfused.^{14 18 23} Two studies^{14 23} showed no significant difference but in one study patients who had a regional anaesthetic had twice the mean volume of blood transfused.¹⁸

Deep vein thrombosis was specifically recorded in one study,¹² in a subgroup of patients in two further studies,^{16 20} and mentioned in one further study.²² Summation of these four studies gave a reduced incidence for regional anaesthesia: 39/129 (30%) for regional anaesthesia compared with 61/120 (51%) for general anaesthesia (Peto OR 0.41, 95% CI 0.23–0.72). Pulmonary embolism was reported in nine studies.^{8–10 12 15 16 20 22 23} Summation of all results showed no difference in incidence between the regional and general anaesthetic groups (8/575 (1.3%) for regional anaesthesia compared with 10/609 (1.6%) for general anaesthesia). However, subdivision of the results into fatal and non-fatal embolism showed a significant reduction in incidence of fatal pulmonary embolism following regional anaesthesia.

Data for many morbidities such as pneumonia, congestive cardiac failure, myocardial infarction and cerebrovascular accident were only available as causes of death in some of the trial reports. The incidence of pneumonia (including aspiration pneumonia) was given in eight studies,^{8–10 15 16 20 22 23} congestive cardiac failure in six studies,^{8–10 15 16 22} renal failure in four studies,^{8 15 16 23} urine retention in two studies^{9 10} and vomiting in two studies.^{10 22} For all these outcomes there was no tendency to any difference between anaesthetic techniques. Myocardial infarction was reported in four studies^{15 16 20 23} and confusional states in three studies.^{9 10 23} These outcomes had a tendency to be more common after general anaesthesia, but the results did not reach statistical significance. Cerebrovascular accident was reported in seven studies^{9 10 14–16 20 23} with a tendency for this complication to be more common after regional anaesthesia, but again the result did not reach statistical significance.

Post-operative arterial oxygen tension was reported in

six studies.^{9 13–15 20 22} Three of these^{13 16 20} reported lower oxygen tension in the immediate post-operative period after general anaesthesia in comparison to regional anaesthesia. The other three^{9 14 22} reported no significant difference between techniques. Pooling of data was not possible due to the varying methods of presenting outcomes. Stress hormones were measured in two studies^{8 24} both of which reported greater increases after general anaesthesia. Time to ambulation was only recorded in two studies,^{10 24} one of which showed no difference between the groups²⁴ whilst the other¹⁰ noted a reduction in the time to ambulation of 5.1 days in the general anaesthetic group to 3.3 days for regional anaesthesia. Summation of the five studies which reported length of hospital stay showed no difference between the two groups.^{8 9 15 20 23} Maurette and colleagues¹⁸ showed no differences between the groups on psychological evaluation and Bredahl and coworkers¹¹ showed no difference in intra-operative temperature between the groups, although more patients had a core temperature in recovery of <36°C in the spinal group (47% vs 23% in the general anaesthesia group).

Complications specific to the method of treatment were only very infrequently detailed (two cases of aspiration pneumonia¹⁶ and one case of headache¹⁰ after spinal anaesthesia). No study reported on differences in final functional outcomes.

Discussion

The present study has pooled the results from over 2000 patients who had either a regional or general anaesthetic for their hip fracture surgery. Many of the included studies involved only small numbers of patients and reported only limited outcome measures. Using data summation, however, it has been possible to derive results showing a significant advantage for regional anaesthetic over general anaesthetic in terms of the incidence of deep vein thrombosis and survival at one month. Surgery for hip fracture is performed in elderly patients who have multiple co-morbidities. It is not therefore surprising that a survival advantage for any

anaesthetic technique does not extend into the long term. The result for deep vein thrombosis must be treated with caution as the analysis includes some sub-group data which could lead to bias. This result does, however, correlate with the finding in the previous meta-analysis³ that deep vein thrombosis was more likely in patients who had received a general anaesthetic.

The reduced incidence of venous thromboembolism following regional anaesthesia has been described following elective hip replacement.^{30,31} Several mechanisms may be responsible. The reduction in sympathetic tone to the lower limbs during regional anaesthesia causes an increased venous blood flow³² which may reduce venous stagnation. It has also been shown that regional anaesthesia is associated with alterations in the viscosity³³ and coagulability of the blood,^{34,35} possibly as a result of modifications to the neurohumoral and metabolic responses to surgery.

In the present study there is limited evidence for a reduced incidence in venous thromboembolism following regional anaesthesia. Most of the cases of deep vein thrombosis in this study were from trials using routine venography. The high reported incidence of thrombi (30% for the spinal group and 47% for the general anaesthetic group) does not reflect the clinical rate, which is lower than that detected using radiographic methods. These results do, however, suggest that regional anaesthesia does reduce the risk of major thromboembolic complications following hip fracture surgery.

Although the results represent a sub-group analysis, the finding of a statistically significant reduction in the incidence of fatal pulmonary embolism following regional anaesthesia further suggests that regional anaesthesia may have a protective effect against major thromboembolism. The use of thromboembolism prophylaxis was mentioned in three studies^{8,12,13} but not in seven others.^{9,10,15,16,20,22,23} Its routine use might negate any benefit of regional anaesthesia in this respect.

General anaesthesia was associated with a small but statistically significant reduction in the length of the operation. There was also a non-significant reduction in the incidence of cerebrovascular accident and the incidence of intra-operative hypotension. As described above, the loss of venous tone during regional anaesthesia is associated with a reduction in blood pressure. It could be postulated that the tendency for a reduced incidence of cerebrovascular accident after general anaesthesia is a consequence of a more stable perioperative blood pressure. The more judicious use of intravenous fluid therapy and vasoconstrictor agents during regional anaesthesia may reduce the advantage of general anaesthesia in this respect.

It has previously been suggested that general anaesthesia induces more postoperative confusion than regional anaesthesia, presumably due to the central nervous system effect of anaesthetic and analgesic drugs. In this study, there was only a non-significant tendency for a greater incidence of confusion following general anaesthesia. Data

for other complications were limited, but suggests that there was no difference between the anaesthetic groups for the incidence of pneumonia, urinary retention, congestive cardiac failure and postoperative nausea and vomiting.

This meta-analysis of randomized trials has shown that regional anaesthesia for hip fracture surgery is associated with a reduced early mortality and incidence of deep vein thrombosis in comparison with general anaesthesia. General anaesthesia appears to confer no advantages other than a small reduction in surgical times. Regional anaesthesia should therefore be considered to have marginal advantages, but further randomised trials are justified to elucidate these differences. Such studies should include a protocol for the reduction of hypotension following a regional anaesthetic technique, and full reporting of all outcome measures. This meta-analysis is also published in the Cochrane Library⁵ where it will be periodically updated to include new data when available.

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