Original Article

Spinal or general anaesthesia for surgical repair of hip fracture and subsequent risk of mortality and morbidity: a database analysis using propensity score-matching*

L. Morgan,[1] **T. M. McKeever,**[2] **J.Nightingale,**[3] **D. E. Deakin**[4] and **I. K. Moppett**[5]

1 Medical Student, 2 Professor, Division of Epidemiology and Public Health, 5 Professor, Anaesthesia and Critical Care, Division of Clinical Neuroscience, University of Nottingham, UK
3 Research Manager, 4 Consultant, Department of Trauma and Orthopaedics, Nottingham University Hospitals NHS Trust, Nottingham, UK

Summary
Around 76,000 people fracture their hip annually in the UK at a considerable personal, social and financial cost. Despite longstanding debate, the optimal mode of anaesthesia (general or spinal) remains unclear. Our aim was to assess whether there is a significant difference in mortality and morbidity between patients undergoing spinal anaesthesia compared with general anaesthesia during hip fracture surgery. A secondary analysis examined whether a difference exists in mortality for patients with pre-existing cardiovascular disease or chronic obstructive pulmonary disease. This was a clinical database analysis of patients treated for hip fracture in Nottingham, UK between 2004 and 2015. Propensity score-matching was used to generate matched pairs of patients, one of whom underwent each mode of anaesthesia. Data were analysed using conditional logistic regression, with 7164 patients successfully matched. There was no difference in 30- or 90-day mortality in patients who had spinal rather than general anaesthesia (OR [95%CI] 0.97 [0.8–1.15]; p = 0.764 and 0.93 [0.82–1.05]; p = 0.247 respectively). Patients who had a spinal anaesthetic had a lower-risk of blood transfusion (OR [95%CI] 0.84 [0.75–0.94]; p = 0.003) and urinary tract infection (OR [95%CI] 0.72 [0.61–0.84]; p < 0.001), but were more likely to develop a chest infection (OR [95%CI] 1.23 [1.07–1.42]; p = 0.004), deep vein thrombosis (OR [95%CI] 2.18 [1.07–4.45]; p = 0.032) or pulmonary embolism (OR [95%CI] 2.23 [1.16–4.29]; p = 0.016). The mode of anaesthesia for hip fracture surgery resulted in no significant difference in mortality, but there was a significant difference in several measures of postoperative morbidity.

Correspondence to: I. Moppett
Email: iain.moppett@nottingham.ac.uk
Accepted: 9 March 2020
Keywords: anaesthesia, general; anaesthesia, spinal; hip fracture; mortality; transfusion
*Presented in part at the Royal Medical Society's National Student Conference, Edinburgh, UK, January 2019.
Twitter: @iainmoppett

Introduction
Hip fractures, or fractures of the proximal third of the femur [1], are one of the most common serious injuries that occur in the older population. In 2016, more than 70,000 patients aged ≥ 60 years were treated for a hip fracture in hospitals around the UK, costing the NHS and social care £1 billion (€1.13 billion, US$1.26 billion) annually [2]. Furthermore, one projection indicates that by 2033, despite the incidence of hip fractures in older people decreasing, the increase in the at risk population during the intervening period means around 100,000 patients annually will have a hip fracture fixed surgically in England [3]. The older population account

for the vast majority of hip fractures and these patients present additional anaesthetic considerations and concerns; this may be a reflection of the reduced 'functional reserve' in ageing organ systems [4]. This means that additional physiological demands, whether they be intra- or peri-operative, can lead to considerable impairment [5].

There are a number of anaesthetic options for patients having hip fracture surgery, but spinal or general anaesthesia are the two used most commonly in the UK [6]. One of the main benefits of a general anaesthetic is the patient's lack of knowledge or memory of the procedure, which could potentially increase patient satisfaction, given the unfamiliar and often daunting operating theatre environment [7]. However, there are potential benefits associated with spinal anaesthesia, notably less intra-operative hypotension, avoidance of neurologically active drugs and a possible reduction in early delirium [8]. Decisions regarding anaesthesia are taken on a case-by-case basis; current National Institute of Health and Care Excellence (NICE) guidelines state that patients should be offered the choice between general and spinal anaesthesia following a discussion on the respective benefits and drawbacks [9]. In practice, anaesthetist preference probably plays a central role in this decision-making.

Existing research in this area has not shown clinically significant differences in mortality and morbidity between spinal and general anaesthesia for hip fracture surgery. In part, this may be due to the problem of confounding by indication; people at higher risk of adverse outcomes may be more likely to get one form of anaesthesia than another. Propensity score-matching is a statistical technique which aims to provide a quasi-experimental analysis where groups are similar across possible confounding factors. The aim of this observational study was to use propensity score-matching to investigate whether there was a clinically relevant difference in outcomes between spinal and general anaesthesia across the population.

Methods

The data were obtained from the Nottingham Hip Fracture Database, a clinical registry that contains data on pre-admission health status, surgical intervention and post-discharge complications for all patients who have undergone surgery to repair a hip fracture in Nottingham University Hospitals NHS Trust since 1999. Approval for the use of the fully anonymised dataset for this project was gained from the local Clinical Quality Risk and Safety Team. Patient identifiable data (including date of birth, age and date of admission) were excluded from the dataset to ensure anonymity. A pseudo-identifier was provided in order to allow clarification of data between the clinical audit team and the investigators. Patients who were admitted between 2004 and 2015 were included in the study. Patients who underwent epidural anaesthesia were not included. The nature and quality of these data have been described in detail in previous reports [10]. Comorbidities and outcomes are recorded based on the admission clerking and medical records.

The primary exposure was a dichotomy between general and spinal anaesthesia. General anaesthesia included those with and without regional nerve blocks. Similarly, spinal anaesthesia included those with and without regional nerve blocks.

The postoperative outcome measures of morbidity were recorded if documented in the patient's notes by the treating clinician. Data regarding 30-day mortality are obtained and cross-referenced from hospital data, as well as data from the Office for National Statistics (ONS), as has been described previously [10]. Cross referencing hospital data with ONS data allows identification of all patients who have died in the community, or in other hospitals.

The primary outcome measure was 30-day mortality. Secondary outcomes defined a priori were: 90-day mortality; requirement for blood transfusion; postoperative infections (deep wound infection, urinary tract infection (UTI) and *Clostridium difficile* infection); cardiac failure; deep vein thrombosis (DVT); pulmonary embolism (PE); myocardial infarction; cerebrovascular accident; wound haematoma; renal failure; and gastro-intestinal haemorrhage. Two non-exclusive sub-groups were defined a priori based on a known higher risk of adverse outcomes. These were patients with documented cardiovascular disease (pre-existing cardiovascular conditions including: previous myocardial infarction; ischaemic heart disease; atrial fibrillation; valvular heart disease; or hypertension) and chronic obstructive pulmonary disease (COPD) [11].

Raw data were cleaned before analysis. Clearly erroneous values were back-checked with the original data and corrected. Missing data that could not be corrected were coded as a dummy missing variable. Discharge location was recoded into: hospital; residential home; own home; or other.

Propensity score-matching was used to simulate attributes of a randomised controlled trial within an observational study design. Eighteen different covariates were used in the propensity score model: year of admission; age at admission (banded to 5 years); sex; fracture type, ASA physical status; whether the patient required help to walk before admission; abbreviated mental test score [12]; presence of cardiovascular disease; previous

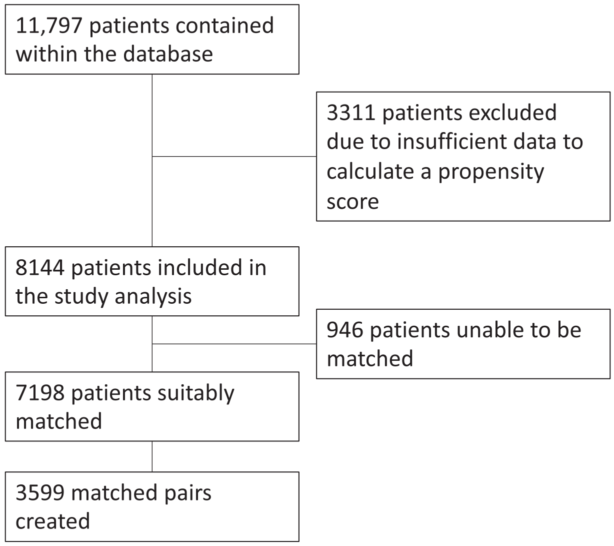

Figure 1 Flowchart to indicate inclusion/exclusion throughout the study.

cerebrovascular accident; diagnosis of COPD; presence of renal disease; diagnosis of diabetes; existing malignancy; smoking status; polypharmacy (≥ four medications prescribed); haemoglobin concentration on admission; grade of operating surgeon; and grade of caring anaesthetist. Matched pairs were formed by using nearest neighbour matching, minimising the difference between the propensity scores of the paired patients [13]. Propensity score-matching was performed separately for the cardiovascular and COPD patient sub-groups. Conditional logistic regression was then carried out, comparing spinal anaesthesia with general anaesthesia. All analyses were carried out using the statistical software package Stata/SE 15.1 (StataCorp LLC, College Station, TX, USA).

Results

In total, 8144 patients were included in the initial analysis, all of whom had a propensity score calculated (Fig. 1). Of these, 6054 (74.3%) were women, and the most common age bracket on admission was 85–89 years (24.6%). In terms of comorbid conditions, 4965 patients had cardiovascular disease (61.0%) and 1391 (17.1%) had COPD. During surgery, 1312 (16.1%) patients had their operation performed by a consultant surgeon, whereas 5253 (64.5%) had a consultant anaesthetist. The prevalence of the various outcome measures in the general and spinal anaesthetic cohorts is detailed in Table 1. Nearest-neighbour matching attempted to match patients with a suitable counterpart, and 7164 patients were matched into 3582 pairs.

There was no significant difference in 30- or 90-day mortality in patients who had spinal rather than general anaesthesia (OR [95%CI] 0.97 [0.8–1.15]; $p = 0.764$ and 0.93 [0.82–1.05]; $p = 0.247$) respectively (OR < 1 favours spinal anaesthesia). Given that national guidance, management protocols and other systematic factors change over time, we repeated the analysis using only the 72.8% of pairs where operations were within 3 years of each other. Again, there was no significant difference in 30- or 90-day mortality in patients who had spinal rather than general anaesthesia (OR [95%CI] 0.92 [0.74–1.15]; $p = 0.460$ and 0.95 [0.81–1.13]; $p = 0.580$) respectively.

The impact of spinal compared with general anaesthesia on the incidence of the secondary outcome measures is shown in Table 2. Spinal anaesthesia was found to be protective for two factors: postoperative blood transfusion (OR [95%CI] 0.84 [0.75–0.94]; $p = 0.003$); and postoperative UTI (OR [95%CI] 0.72 [0.61–0.84]; $p < 0.001$). However, those patients receiving spinal anaesthesia were more likely to develop a postoperative chest infection (OR [95%CI] 1.23 [1.07–1.42]; $p = 0.004$), pulmonary embolism (PE) (OR [95%CI] 2.23 [1.16–4.29]; $p = 0.016$) or deep vein thrombosis (DVT) (OR [95%CI] 2.18 [1.07–4.45]; $p = 0.032$). No other measures of postoperative morbidity showed a statistically significant difference.

The use of spinal anaesthesia did not affect 30-day mortality in patients with either cardiovascular disease (OR [95%CI] 0.91 [0.74–1.12]; $p = 0.372$) or COPD (OR [95%CI] 0.98 [0.66–1.45]; $p = 0.920$). However, spinal anaesthesia was associated with a statistically significant reduction in 90-day mortality in patients with cardiovascular disease (OR [95%CI] 0.84 [0.72–0.98]; $p = 0.026$) but not for those with COPD (OR [95%CI] 0.92 [0.68–1.24]; $p = 0.590$).

Table 1 Comparison of the prevalence of postoperative outcome measures stratified by method of anaesthesia for surgical repair of a hip fracture.

Outcome measure	General anaesthesia n = 4186	Spinal anaesthesia n = 3958
Blood transfusion	903 (21.6%)	739 (18.7%)
Chest infection	468 (11.2%)	523 (13.2%)
Urinary tract infection	474 (11.3%)	338 (8.5%)
Renal failure	296 (7.1%)	240 (6.1%)
Myocardial infarction	90 (2.2%)	89 (2.2%)
Cardiac failure	77 (1.8%)	58 (1.5%)
Haematoma	67 (1.6%)	48 (1.2%)
Clostridium difficile infection	39 (0.9%)	28 (0.7%)
Deep infection	39 (0.9%)	26 (0.7%)
Gastro-intestinal haemorrhage	32 (0.8%)	28 (0.7%)
Cerebrovascular accident	20 (0.5%)	23 (0.6%)
Pulmonary embolism	18 (0.4%)	29 (0.7%)
Deep vein thrombosis	12 (0.3%)	24 (0.6%)

Table 2 Comparison of postoperative morbidity for spinal anaesthesia vs. general anaesthesia for patients having surgical repair of a hip fracture. Odds ratio < 1 favours spinal anaesthesia.

Outcome measure	Discordant pairs	Odds ratio (95%CI)	p value
Blood transfusion	2306	0.84 (0.75–0.94)	0.003
Chest infection	1540	1.23 (1.07–1.42)	0.004
Urinary tract infection	1306	0.72 (0.61–0.84)	< 0.001
Renal failure	844	0.83 (0.68–1.00)	0.052
Myocardial infarction	318	0.99 (0.72–1.35)	0.937
Cardiac failure	230	0.77 (0.53–1.11)	0.163
Haematoma	194	0.76 (0.51–1.14)	0.188
Deep infection	118	0.69 (0.41–1.15)	0.155
Clostridium difficile infection	114	0.73 (0.43–1.23)	0.235
Gastro-intestinal haemorrhage	104	0.93 (0.54–1.60)	0.782
Pulmonary embolism	84	2.23 (1.16–4.29)	0.016
Cerebrovascular accident	72	1.25 (0.65–2.41)	0.506
Deep vein thrombosis	70	2.18 (1.07–4.45)	0.032

Discussion

In this study, the mode of anaesthesia did not affect 30- or 90-day mortality in the general population of patients having a hip fracture surgically repaired. Those patients receiving spinal anaesthesia were less likely to require a postoperative blood transfusion or develop a UTI. However, they were at increased risk of developing a postoperative chest infection or venous thromboembolism. There was no convincing evidence for an impact of mode of anaesthesia on mortality for the pre-specified sub-groups of patients with cardiovascular disease or COPD.

These findings with regards to mortality are in line with current evidence. A systematic review of adult patients with hip fractures found no difference in 30-day mortality with regional vs. general anaesthesia, based on 11 studies incorporating 2152 participants [14]. The same systematic review also found no difference in mortality at 3 months based on five studies and 953 participants [14]. This is concordant with another systematic review including 14 studies [15] and a large American study (> 50,000 patients) [16] that both showed that anaesthetic technique had no effect on 30-day mortality.

The secondary outcome data are hypothesis-generating and should be interpreted with caution, particularly the sub-group analyses of patients with cardiovascular disease and COPD. There was a reduction in postoperative blood transfusions after spinal anaesthesia. There are a number of potential explanations for this finding. It is possible a true relationship between spinal anaesthesia and requirement for postoperative blood transfusion exists. A study found that patients undergoing spinal anaesthesia for hip arthroplasty were 35% less likely to require a postoperative transfusion, and the authors postulated that spinal anaesthesia led to lower intra-operative blood pressure and therefore a reduction in blood loss [17]. However, the findings of the anaesthetic sprint audit of practice suggested that intra-operative arterial blood pressure was lower with general anaesthesia in patients having hip fracture surgery [6]. In addition, our results are concordant with a meta-analysis of 66 randomised controlled trials that found the mean difference of estimated blood loss to be 335 ml lower with spinal compared with general anaesthesia in a variety of surgical procedures [18]. It is also possible that a degree of residual confounding may have led to this finding as no data were available to match patients based on existing coagulopathy; this condition is a relative contra-indication to spinal anaesthesia, due to the increased risk of vertebral canal haematoma and subsequent spinal cord compression [19]. Given that patients with an existing coagulopathy have an increased likelihood of requiring a postoperative transfusion [20], and are also more likely to be deemed unsuitable for a spinal anaesthetic, it is possible that this had a confounding effect.

The association of spinal anaesthetic with a reduction in postoperative UTIs was surprising. There is very little evidence in the literature that directly supports or contradicts this finding, as previous studies have tended to focus on postoperative urinary retention (which may subsequently require catheterisation and increase the risk of the patient developing a UTI). Some of these studies have suggested that spinal anaesthesia increases urinary retention compared with general anaesthesia. However, most urinary catheters in our unit are placed pre-operatively in accordance with departmental protocols. The research in this area is inconsistent [21, 22] and the true relative effects of spinal and general anaesthesia on urinary retention and UTIs are unclear. It is possible that catheterisation rates may have altered the clinical recording of a diagnosis of UTI, which is notoriously unreliable. Positive dipstick tests in a patient who is catheterised may be ascribed less importance than if the patient was not catheterised.

We found that patients who received spinal anaesthesia were significantly more likely to suffer from DVT or PE postoperatively. A systematic review found no significant difference in the incidence of DVT when chemoprophylaxis was used [14], a practice which is now commonplace [23] and routine in our institution; however, the study did show that spinal anaesthesia increased the risk of postoperative PE although this was dependent on the type of statistical analysis performed [14]. It is possible that patients who were at greater risk of VTE (due to baseline risk or comorbidities reducing mobilisation) were more likely to be given spinal anaesthesia. There may, therefore, be support within the current evidence for an association between spinal anaesthesia and an increased risk of thromboembolic events in hip fracture operations.

The increase in postoperative chest infections within the spinal anaesthetic group is probably a consequence of two opposing factors. Spinal anaesthesia is generally believed to be protective or neutral for respiratory complications [14, 15] but this in turn may lead to greater use of spinal anaesthesia in patients at risk of respiratory complications [24]. The proportion of patients with COPD who received spinal anaesthesia was almost double that of those who had a general anaesthetic; this is likely to reflect deliberate clinical decision-making to avoid general anaesthesia in patients with pre-existing respiratory disease. However, this introduces the possibility of baseline confounding; those patients with existing COPD are more likely to develop a chest infection postoperatively and are relatively overrepresented in the population who have a spinal anaesthetic. A clinical argument is made frequently that patients with specific underlying pathology, particularly COPD, are better served by spinal anaesthesia. We could not find any convincing evidence of this benefit. As with all non-randomised studies, we cannot exclude residual confounding, particularly regarding severity of COPD.

There were limitations to this study which should be acknowledged. The pre-operative clinical characteristics and postoperative measures of morbidity recorded were not always clearly defined. As such, there is the potential for misclassification bias if data were recorded in different ways as a result of differences in interpretation and/or diagnosis between individual clinicians. The timeframe over which data were recorded into the database and the changes in clinical practice during said time-period would itself have potentially affected the concordance of different clinicians' opinions, let alone the inherent variation that would exist amongst practitioners regardless. In addition, despite the advantages of the propensity score-matching technique as a method of adjusting to limit the effects of confounding, it is possible that it may have actually increased the risk of confounding, as a result of an effect described as 'the propensity score paradox' [25, 26]. Within the context of this study, in which the covariates were already well-balanced between the two groups, the 'paradox' describes how the technique of propensity score-matching may have led to imbalance within the distribution of the clinical characteristics; this occurs through the pruning of pairs with the largest difference in propensity scores, and potentially introduces bias into the analysis [26]. In addition, the dataset does not include information about delirium rates or changes in cognitive function. Although the data are of limited quality, this may be where a benefit of spinal anaesthesia lies (if there is one to be found). Another limitation is that spinal and general anaesthesia have been considered as single entities; we were unable to consider how these were delivered. The study may have been comparing 'bad' spinal anaesthesia with 'good' general anaesthesia or vice versa. Similarly, we are unable to comment on the impact of sedation used in conjunction with spinal anaesthesia [27, 28]. Until routine data collection allows analysis of how anaesthesia was delivered, these questions are likely to remain unanswered. Finally, but perhaps most importantly, we may be simply measuring the wrong outcomes [29]. If clinical outcomes are unaffected by mode of anaesthesia, then addressing softer outcomes such as patient satisfaction, quality of life and operating theatre efficiency may be more important.

Despite these limitations, there is a major strength: with the power of an 8000-patient dataset, and data on a multitude of outcomes, we were unable to demonstrate clinically-relevant differences between modes of anaesthesia. For individual clinicians to state that his or her favoured technique is optimal based on incomplete data involving only tens or hundreds of patients is an unprovable claim.

There are four ongoing randomised controlled trials of spinal vs. general anaesthesia [30–33]. We await the results of these with interest. In the meantime, it would seem the decision to use a particular mode of anaesthesia for a patient undergoing hip fracture surgery is primarily based around patient choice and the inclinations of individual practitioners [34], rather than a standardised approach. We suggest that future research should be directed towards how anaesthesia is delivered, rather than mode of anaesthesia per se.

Acknowledgements

No external funding or competing interests declared.

References

1. Petrisor B, Bhandari M. BMJ best practice: hip fractures. 2018. https://bestpractice.bmj.com/topics/en-gb/387 (accessed 27/09/2018).
2. Royal College of Physicians. National Hip Fracture Database annual report. 2017. https://www.nhfd.co.uk/files/2017ReportFiles/NHFD-AnnualReport2017.pdf (accessed 27/09/2018).
3. White S, Griffiths R. Projected incidence of proximal femoral fracture in England: a report from the NHS Hip Fracture Anaesthesia Network. *Injury* 2011; **42**: 1230–3.
4. Kanonidou Z, Karystianou G. Anesthesia for the elderly. *Hippokratia* 2007; **11**: 175–7.
5. Bowker L, Price J, Smith S. *Oxford handbook of geriatric medicine*, 2nd edn. Oxford, UK: Oxford University Press, 2012.
6. Association of Anaesthetists of Great Britain and Ireland. Anaesthetic sprint audit of practice. 2014. https://www.nhfd.co.uk/20/hipfractureR.nsf/vwContent/asapReport (accessed 20/02/2020).
7. Bodenham A, Howell S. General anaesthesia vs local anaesthesia: an ongoing story. *British Journal of Anaesthesia* 2009; **103**: 785–9.
8. Royal College of Anaesthetists. Your spinal anaesthetic: information for patients. 2014. https://www.rcoa.ac.uk/sites/default/files/documents/2020-01/03-YourSpinalweb.pdf (accessed 28/02/2020).
9. National Institute for Health and Care Excellence. Hip fracture: management. 2011. https://www.nice.org.uk/guidance/cg124/resources/hip-fracture-management-pdf-35109449902789 (accessed 28/02/2020).
10. Maxwell MJ, Moran CG, Moppett IK. Development and validation of a preoperative scoring system to predict 30-day mortality in patients undergoing hip fracture surgery. *British Journal of Anaesthesia* 2008; **101**: 511–7.
11. Buss L, McKeever TM, Nightingale J, et al. Hip fracture outcomes in patients with chronic obstructive pulmonary disease. *British Journal of Anaesthesia* 2018; **121**: 1377–9.
12. Sagar J, Blott H, Nisar P, et al. Abbreviated Mental Test (cognitive) screening in acutely ill elderly surgical patients. *British Journal of Surgery* 2015; **102**: 137–8.
13. Thavaneswaran A, Lix L. Propensity score matching in observational Studies: University of Manitoba. 2008. https://umanitoba.ca/faculties/health_sciences/medicine/units/chs/departmental_units/mchp/protocol/media/propensity_score_matching.pdf (accessed 28/02/2020).
14. Guay J, Parker MJ, Gajendragadkar PR, Kopp S. Anaesthesia for hip fracture surgery in adults. *Cochrane Database of Systematic Reviews* 2016; **2**: 1465–858.
15. Van Waesberghe J, Stevanovic A, Rossaint R, Coburn M. General vs. neuraxial anaesthesia in hip fracture patients: a systematic review and meta-analysis. *BMC Anesthesiology* 2017; **17**: 1–25.
16. Neuman MD, Rosenbaum PR, Ludwig JM, et al. Anesthesia technique, mortality, and length of stay after hip fracture surgery. *Journal of American Medical Association* 2014; **311**: 2508–17.
17. Rashiq S, Finegan BA. The effect of spinal anesthesia on blood transfusion rate in total joint arthroplasty. *Canadian Journal of Surgery* 2006; **49**: 391–6.
18. Richman JM, Rowlingson AJ, Maine DN, et al. Does neuraxial anesthesia reduce intraoperative blood loss? A meta-analysis. *Journal of Clinical Anesthesia* 2006; **18**: 427–35.
19. Harrop-Griffiths W, Cook T, Gill H, et al. Regional anaesthesia and patients with abnormalities of coagulation. *Anaesthesia* 2013; **68**: 966–72.
20. Liumbruno GM, Bennardello F, Lattanzio A, Piccoli P, Rossetti G. Recommendations for the transfusion management of

patients in the peri-operative period-the postoperative period. *Blood Transfusion* 2011; **9**: 320–35.

21. Chu CPW, Yap JCCM, Chen PP, Hung HH. Postoperative outcome in Chinese patients having primary total knee arthroplasty under general anaesthesia/intravenous patient-controlled analgesia compared to spinal-epidural anaesthesia/analgesia. *Hong Kong Medical Journal* 2006; **12**: 442.
22. Lingaraj K, Ruben M, Chan YH, De SD. Identification of risk factors for urinary retention following total knee arthroplasty: a Singapore hospital experience. *Singapore Medical Journal* 2007; **48**: 213–6.
23. National Institute for Health and Care Excellence. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. 2018. https://www.nice.org.uk/guidance/ng89 (accessed 28/02/2020).
24. Conde M, Lawrence V. Postoperative pulmonary infections. *BMJ Clinical Evidence* 2008; **2008**: 2201.
25. King G, Nielsen R. Why propensity scores should not be used for matching. 2018. https://gking.harvard.edu/files/gking/files/pan1900011_rev.pdf (accessed 28/02/2020).
26. Ripollone JE, Huybrechts KF, Rothman KJ, Ferguson RE, Franklin JM. Implications of the propensity score matching paradox in pharmacoepidemiology. *American Journal of Epidemiology* 2018; **187**: 1951.
27. Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. *Mayo Clinic Proceedings* 2010; **85**: 18–26.
28. Sieber FE, Neufeld KJ, Gottschalk A, et al. Effect of depth of sedation in older patients undergoing hip fracture repair on postoperative delirium: the STRIDE randomized clinical trial. *Journal of the American Medical Association Surgery* 2018; **153**: 987–95.
29. Moppett I. Hip fractures: are we asking the right questions? *Age and Ageing* 2018; **47**: 633–4.
30. ISRCTN Registry. REGARD: comparing regional and general anaesthesia and their effect on delirium in patients with hip fractures. 2017. http://www.isrctn.com/ISRCTN15165914 (accessed 28/02/2020).
31. Neuman MD, Ellenberg SS, Sieber FE, et al. Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN): protocol for a pragmatic, international multicentre trial. *British Medical Journal Open* 2016; **6**: e013473.
32. Kowark A, Adam C, Ahrens J, et al. Improve hip fracture outcome in the elderly patient (iHOPE): a study protocol for a pragmatic, multicentre randomised controlled trial to test the efficacy of spinal versus general anaesthesia. *British Medical Journal Open* 2018; **8**: e023609.
33. Li T, Yeung J, Li J, et al. Comparison of regional with general anaesthesia on postoperative delirium (RAGA-delirium) in the older patients undergoing hip fracture surgery: study protocol for a multicentre randomised controlled trial. *British Medical Journal Open* 2017; **7**: e016937.
34. White SM, Griffiths R, Moppett IK. Standardising anaesthesia for hip fracture surgery. *Anaesthesia* 2016; **71**: 1391–5.

