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# Silent myocardial ischaemia and haemoglobin concentration: a randomized controlled trial of transfusion strategy in lower limb arthroplasty

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Vox Sanguinis

**Background and Objectives** Red cell transfusion is commonly used in orthopaedic surgery. Evidence suggests that a restrictive transfusion strategy may be safe for most patients. However, concern has been raised over the risks of anaemia in those with ischaemic cardiac disease. Perioperative silent myocardial ischaemia (SMI) has a relatively high incidence in the elderly population undergoing elective surgery. This study used Holter monitoring to compare the effect of a restrictive and a liberal red cell transfusion strategy on the incidence of SMI in patients without signs or symptoms of ischaemic heart disease who were undergoing lower limb arthroplasty.

**Materials and Methods** We performed a multicentre, controlled trial in which 260 patients undergoing elective hip and knee replacement surgery were enrolled and randomized to transfusion triggers that were either restrictive (8 g/dl) or liberal (10 g/dl). Participants were monitored with continuous ambulatory electrocardiogram (ECG) (Holter monitoring), preoperatively for 12 h and postoperatively for 72 h. The tapes were analysed for new ischaemia by technicians blinded to treatment. The total ischaemia time in minutes was divided by the recording time in hours and an ischaemic load in min/h was calculated. Haemoglobin levels were measured preoperatively, postoperatively in the recovery room, and on days one, three and five after surgery.

**Results** The mean postoperative haemoglobin concentration was 9·87 g/dl in the restrictive group and 11·09 g/dl in the liberal group. In the restrictive group, 34% were transfused a total of 89 red cell units, and in the liberal group 43% were given a total of 119 red cell units. A postoperative episode of silent ischaemia was experienced by 21/109 (19%) patients in the restrictive group and by 26/109 (24%) patients in the liberal group [mean difference −4·6%; 95% confidence interval (CI): −15·5% to 6%, $P = 0{\cdot}41$). There was no significant difference ($P = 0{\cdot}53$) between the overall ischaemic load in the restrictive group (median 0 min/h, range 0–4·18) and the liberal group (median 0 min/h, range 0–19·48). In those patients who did experience postoperative SMI, the mean ischaemic load was 0·48 min/h in the restrictive group and 1·51 min/h in the liberal group (ratio 0·32, 95% CI: 0·14–0·76, $P = 0{\cdot}011$). The median postoperative length of hospital stay in the restrictive group was 7·3 days [range 5–11; interquartile

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range (IQR) 6–8] compared with 7·5 days (range 5–13; IQR 7–8) in the liberal group. The numbers were not large enough to conclude equivalence.

**Conclusions** In patients without preoperative evidence of myocardial ischaemia undergoing elective hip and knee replacement surgery, a restrictive transfusion strategy seems unlikely to be associated with an increased incidence of SMI. A proportion of these patients experience moderate SMI, regardless of the transfusion trigger. Use of a restrictive transfusion strategy did not increase length of hospital stay, and use of this strategy would lead to a significant reduction in red cell transfusion in orthopaedic surgery. Our data did not indicate any potential for harm in employing such a strategy in patients with no prior evidence of cardiac ischaemia who were undergoing elective orthopaedic surgery.

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**Key words:** haemoglobin, ischaemia, transfusion.

## Introduction

The benefits and problems associated with allogeneic blood transfusion in the elderly have been discussed in the recent medical literature [1]. The use of transfusion thresholds and optimal target haemoglobin concentrations attempt to balance the potential benefits against possible risk [2]. There are cogent reasons to avoid blood transfusion, including haemolytic reactions, immunomodulation [3–5] and transmission of infectious agents [6,7]. Furthermore, red blood cells (RBCs) are a perishable, finite resource, the cost of which is escalating, as production costs that include increasingly sophisticated screening assays for infectious agents, as well as techniques such as universal leucodepletion, soar. In the UK, the perceived risk of transfusion-transmitted variant Creuzfeldt–Jacob Disease (vCJD) has increased the cost further as some plasma for fractionation and for clinical use in children is now sourced from outside the UK. vCJD might also threaten the UK blood supply as a result of extended criteria for donor deferral [8,9]. Against all of the known and identifiable risks must be set the potential consequences of anaemia, in particular cardiac ischaemia. These risks are poorly defined. Commensurate with this has been the re-evaluation of thresholds for transfusion in critical care [10]. Clearly, concerns remain over the effect of a restrictive transfusion threshold on patients with ischaemic heart disease. The available data on which to confidently decide transfusion triggers are limited.

In the UK, the majority of red cells are used in surgical patients. A multicentre survey showed that 594 810 transfused RBC units were successfully traced to their respective clinical specialties, representing 91·9% of all RBC units issued to the study hospitals. Of the RBC units transfused, 51·2% were transfused in surgical specialties and 60 470 (10·17% of the total) were used in patients undergoing orthopaedic surgical procedures. Based on National Blood Transfusion Service figures for 1998, when 2·24 million units of blood were issued nationally, this suggests that ≈ 224 000 units of blood per year are used nationally for orthopaedics. In 24 of the hospitals studied in more detail over the same 12-month period, it was shown that 38·7% of the orthopaedic red blood cell usage was for primary hip and knee replacement surgery [11].

The volume and complexity of elective orthopaedic surgery is continuing to grow because of an increasingly elderly population, many of whom have comorbidities, including ischaemic heart disease. There is a clear need to define the risk of ischaemia in these patients. The incidence of cardiac events is extremely small in patients with no underlying cardiac disease, and massive studies would be required to explore the effects of anaemia on such events. However, the incidence of myocardial ischaemia, which may be considered a surrogate for myocardial events, is relatively much higher and can be detected and quantified by Holter continuous ambulatory electrocardiogram (ECG) monitoring [12–14]. Previous studies have reported that silent myocardial ischaemia (SMI) can be found in up to 30% of patients during the perioperative period following non-cardiac surgery [15–20]. Both increased incidence and duration of perioperative SMI are associated with adverse outcomes [21–23]. Anaemia may increase the risk of SMI, but there is sparse information about the relationship between haemoglobin concentration and SMI in this population of patients. To address this issue, patients undergoing elective hip and knee joint replacement surgery were recruited in order to assess the influence of a restrictive or a liberal transfusion strategy on the incidence of perioperative SMI.

## Patients and methods

We undertook a randomized, controlled, multicentre equivalence trial. Our proposal, following a statistician's advice, was to recruit 660 patients. Local and Regional Ethics Committee approval was obtained for all three participating acute hospitals in southeast England (Chelsea and Westminster, Royal London and Oldchurch hospitals). Written, informed consent was obtained from patients undergoing elective lower limb joint replacement.

Exclusion criteria were age < 55 years, digoxin therapy, ECG evidence of conduction defects, ST segment depression, left ventricular hypertrophy or left bundle branch block. Any

patient with anaemia was also excluded. The following patient information was collected: age; gender; smoking status; cardiovascular risk factors; history of hypertension; angina; previous myocardial infarction; diabetes; and cardiac drug therapies.

At the preoperative visit, Holter monitors (Delmar Reynolds Tracker I; Reynolds Medical Limited, Hertford, UK) were connected to the patients using bipolar leads and silver/silver chloride skin electrodes. The electrode configuration used was CM3 and CM5. The Reynolds Pathfinder 700 was used to analyse the output data. Patients were randomized preoperatively using permuted blocks that were derived from random number tables. Envelopes containing the number and allocation sequence remained sealed until the patient was assigned to intervention. The patient and technician analysing the Holter tapes were unaware of treatment allocation. The anaesthetists and surgical team responsible for the patient were informed of treatment allocation. Each patient was monitored for 12 h preoperatively, intraoperatively and then for a 72-h postoperative period.

A benzodiazepine premedication was administered at the discretion of the anaesthetist. General anaesthesia was induced using propofol and fentanyl. Paralysis was achieved with rocuronium, vecuronium or atracurium. Analgesia was administered with a morphine patient-controlled pump, via an epidural (for the postoperative period only), or by a nerve block.

All patients received postoperative oxygen while being Holter monitored. Transfusion was guided by an algorithm (Fig. 1). Normovolaemia was maintained. Patients assigned to the restrictive group were transfused when haemoglobin concentrations fell below 8 g/dl and were then maintained at haemoglobin concentrations between 8 and 9·5 g/dl. Patients allocated to the liberal transfusion group received blood when the haemoglobin concentration fell below 10 g/dl and were then maintained at haemoglobin concentrations of 10–12 g/dl.

An episode of silent ischaemia was defined as horizontal or down-sloping ST segment depression of at least 1 mm occurring 60 ms after the J point on an ECG complex for at least 1 min and returning to baseline for at least 1 min. The ischaemic load for each patient was calculated by dividing the minutes of ischaemia by number of hours that the patients were monitored. This method of calculating ischaemic load was based on previous studies of SMI.

Each patient was visited daily by a research fellow when a history was taken and an examination carried out. Any patient displaying signs or symptoms consistent with anaemia, for example shortness of breath, had a full blood count taken that day (if not one of the protocol blood test days), and if anaemia was confirmed they were transfused to improve their clinical condition. At no point was the patient's care compromised for the sake of the study.

Further measurements recorded were blood loss, haemoglobin concentration in the recovery room and on postoperative days 1, 3 and 5, number of units transfused, length of postoperative hospital stay, adverse events and new infections requiring antibiotic therapy. Twelve-lead ECGs were recorded daily for the first three postoperative days.

Compliance with the transfusion protocol was ensured by blood transfusion being prescribed only by the research fellows involved in the study.

## Statistical analyses

The study was originally powered to demonstrate equivalence between the liberal and restrictive groups. Assuming the incidence of silent ischaemia to be 30 ± 10%, 330 patients were required per arm, for an 80% power at a 5% significance level.

To verify that the transfusion trigger protocols were adequately implemented, haemoglobin concentrations in each group were summarized over the entire postoperative monitoring period, as shown in Table 1.

Patient characteristics and baseline measurements were summarized by transfusion trigger group. The primary outcome (i.e. ischaemic load over the whole postoperative monitoring period) was compared for the two trigger groups by three approaches: first, the proportion of patients with any ischaemic

**Table 1** Postoperative haemoglobin levels per day

| | Liberal transfusion group | | | | | Restrictive transfusion group | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Mean | SD | Hb < 8[a] | Hb < 10[b] | *n* | Mean | SD | Hb < 8[a] | Hb < 10[b] | Difference | 95% CI for difference | *P*-value |
| Preoperative | 107 | 13·6 | 1·22 | 0 | 1 | 110 | 13·1 | 1·22 | 0 | 1 | 0·43 | | |
| Recovery | 105 | 11·5 | 1·63 | 1 | 21 | 110 | 10·6 | 1·54 | 7 | 36 | 0·90 | 0·47–1·32 | 0·0001 |
| Day 1 | 107 | 11·0 | 1·41 | 2 | 18 | 110 | 9·7 | 1·52 | 10 | 65 | 1·29 | 0·89–1·68 | < 0·0001 |
| Day 3 | 107 | 11·0 | 1·26 | 0 | 25 | 110 | 9·6 | 1·36 | 9 | 69 | 1·35 | 1·00–1·70 | < 0·0001 |
| Day 5 | 107 | 11·1 | 0·93 | 0 | 7 | 109 | 9·8 | 1·23 | 1 | 67 | 1·34 | 1·05–1·63 | < 0·0001 |

[a]Number of patients with a haemoglobin level of < 8 g/dl.

[b]Number of patients with a haemoglobin level of < 10 g/dl.

CI, confidence interval; Hb, haemoglobin; SD, standard deviation.

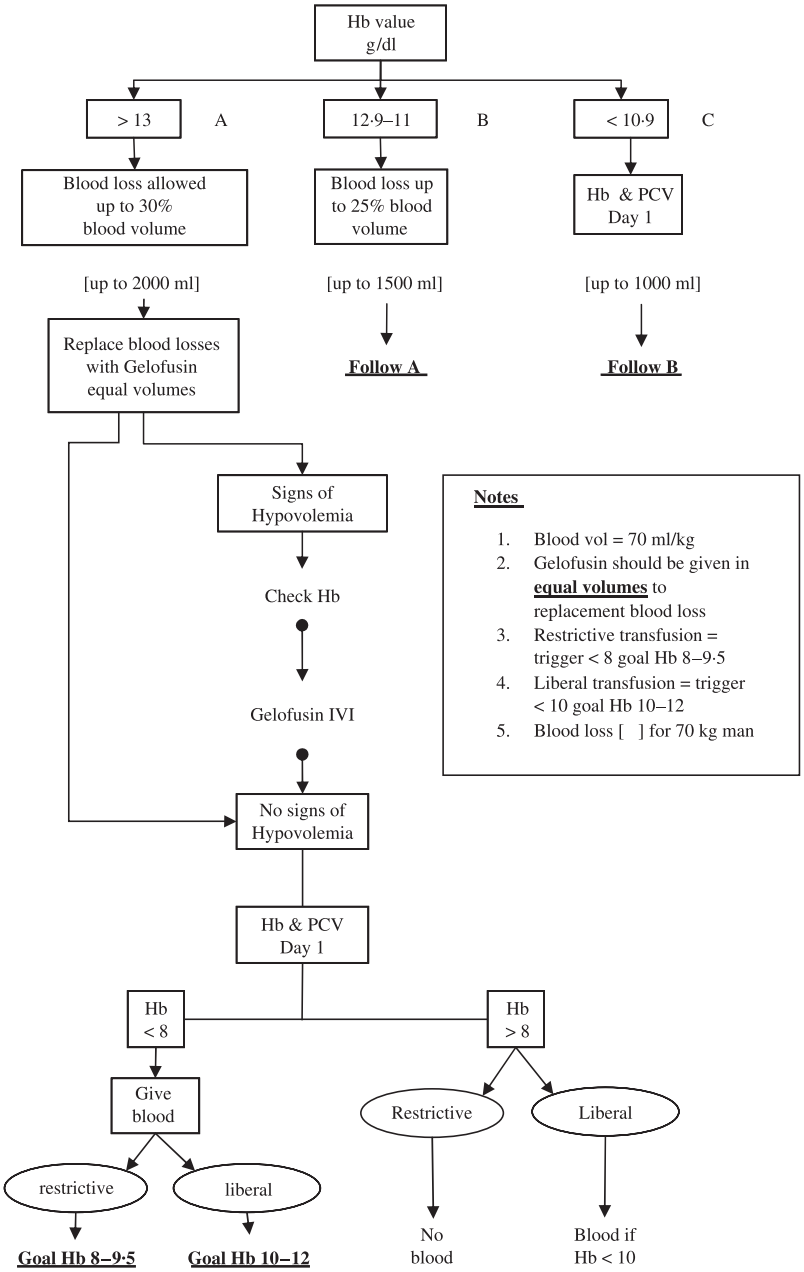


**Fig. 1** Transfusion algorithm.

load was assessed by a two-sample $\chi^2$ of proportions; second, the ischaemic load (in min/h) was compared, assuming a non-parametric distribution, using the Kolmogorov–Smirnov equality of distributions test; and, third, the same data were compared with a two-sample *t*-test. Secondary outcomes were summarized by group.

## Results

Unfortunately, the study recruited only 260 participants, from a target of 660 to achieve sufficient statistical power. As recruitment commenced it became clear that the strict exclusion criteria, specifically the ECG criteria, meant that the proportion of patients eligible to participate in the study was much lower than anticipated. This, in turn, prolonged the time during which recruitment took place. With a fixed amount of funding and time available to research fellows in subspecialty training in England, the study had to be curtailed after 2 years.

The total number of patients recruited into the study was 260, of whom 218 had analysable tape recordings. The total ECG recording time for the whole study was 936 786 min. Patient demographics are summarized in Table 2. There was no difference in any characteristics between the two groups. Median baseline preoperative haemoglobin levels in the study

**Table 2** Patient demographics

| | Liberal ($n$ = 109) | Restrictive ($n$ = 109) |
|---|---|---|
| Age (in years) | 71·5 (7·6)[a] | 70·7 (7·1)[a] |
| Men | 55 (49·5%) | 48 (44·0%) |
| Smokers | 14 (12·8%) | 14 (12·8%) |
| Diabetic | 10 (10·9%) | 7 (6·4%) |
| Hypertensive | 40 (36·7%) | 45 (41%) |
| Angina | 8 (7·3%) | 6 (5·5%) |
| Previous MI | 6 (5·5%) | 6 (5·5%) |
| Beta blockers | 10 (10·9%) | 9 (8·25%) |
| ACE inhibitors | 18 (16·5%) | 21 (19·2%) |

[a]Standard deviation.

ACE, angiotensin-coverting enzyme; MI, myocardial infarction.

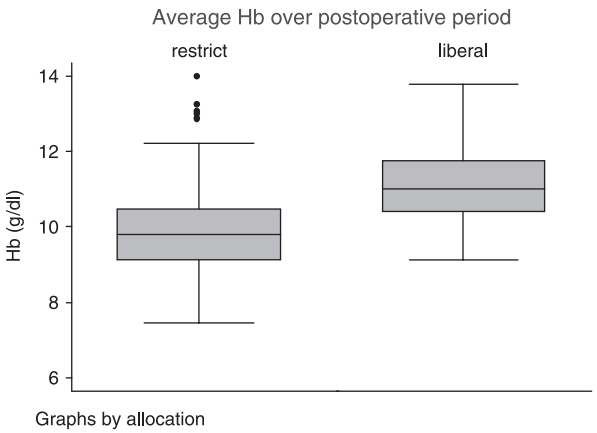


**Fig. 2** Average haemoglobin (Hb) level during the postoperative period.

groups were as follows. Liberal group: not transfused, 14 ($n$ = 65); transfused, 13·2 ($n$ = 38). Restrictive group: not transfused, 13·2 ($n$ = 78); transfused, 12·7 ($n$ = 32).

The mean haemoglobin concentrations over the postoperative recording period are summarized in Table 1 and Fig. 2. The mean haemoglobin concentration was 9·87 g/dl in the restrictive group and 11·09 g/dl in the liberal group. Of the 109 patients in the restrictive group, 37 (34%) were transfused a total of 89 red cell units (median 0, range 0–5 units). Of those in the liberal group, 46 out of 109 (43%) received a total of 119 units (median 0, range 0–10).

The number of patients presenting with any silent ischaemia during the postoperative monitoring period was 21/109 (19%) in the restrictive group and 26/109 (24%) in the liberal group (mean difference −4·6%, 95% CI −15·5% to 6%, $P$ = 0·41). There did not appear to be a temporal relationship between ischaemia on Holter recordings and transfusion levels, in particular ischaemic changes did not appear to occur when the haemoglobin level was at its lowest.

The median ischaemic load was 0 min/h (range 0–4·18) in the restrictive group and 0 min/h (range 0–19·48) in the liberal group. There was no significant difference in distribution, as measured by using the Kolmogorov–Smirnov test ($P$ = 0·53), for non-inferiority. Of the small number of patients with postoperative SMI, the data followed a log-normal distribution. The data were therefore log transformed before carrying out a two-sample $t$-test on this subset of patients. The mean ischaemic load was 0·48 min/h in the restrictive group and 1·51 min/h in the liberal group (ratio 0·32, 95% CI 0·14–0·76, $P$ = 0·011), indicating that amongst those with ischaemia, the ischaemic load was significantly less in the restrictive group than in the liberal group. Median length of hospital stay in the restrictive group was 7·3 days (range: 5–11) compared with 7·5 days (range: 5–13) in the liberal group.

For the entire randomized population there was no evidence of an overall difference in the incidence of ischaemia between the liberal and restrictive groups. The numbers were not large enough to conclude equivalence. Indeed, a far larger study of 660 patients would be needed to provide conclusive evidence of no difference.

Patient adverse events are summarized in Table 3. In the restrictive group, 16 adverse events occurred and in the liberal group 13 adverse events occurred.

These events were for the 260 patients randomized in the study. One death occurred during the study. The patient in whom death occurred was randomized to the liberal transfusion strategy and died as a result of a myocardial infarction, which was confirmed electrocardiographically and by analysis of cardiac enzymes.

**Table 3** Postoperative adverse events

| Event | Liberal ($n$ = 109) | Restrictive ($n$ = 109) |
|---|---|---|
| Deep vein thrombosis | 4 | 5 |
| Pulmonary embolism | 1 | 2 |
| Left bundle branch block | 1 | 2 |
| Ventricular tachycardia | | 2 |
| Heart block | | 1 |
| Myocardial infarction | 1 | |
| Death | 1 | |
| Chest infection | 3 | 2 |
| Wound infection | 2 | 2 |

## Discussion

The main findings of the study are that the rate of SMI was 22%, which is lower than reported in previous studies. This is not likely to be a result of the exclusion criteria because all studies measuring new ischaemic changes on Holter monitoring traces are subject to the same exclusion criteria for ECGs. In the 218 patients no difference was demonstrated between the restrictive and the liberal transfusion strategy in

terms of either SMI or length of postoperative stay. In those patients who demonstrated ischaemia, there was a significantly greater ischaemic load (0·48 vs. 1·51) associated with a liberal transfusion strategy. The actual incidence of myocardial events in this study was extremely low, as was the incidence of postoperative infection.

Clearly, the study falls short of the 660 patients (330 in each limb) required in order to conclude equivalence, but it is by far the largest study of its kind to date, and analysis of the data provides no suggestion that a significant difference is likely to be found if this study were to be repeated. Indeed the trend, such as it was, favours a restrictive transfusion regime. It would be preferable if the results were conclusive, but that is not possible from this data. The authors feel that, from a clinical viewpoint, some reassurance can be gained by the absence of obvious morbidity on these numbers, although statistical certainty would have been preferable. What is worthy of note is that the transfusion requirements in critical care (TRICC) study accrued only 52% power, yet its restrictive transfusion strategy seems to have been adopted worldwide.

Other problems with the study design are that patients with obvious ECG changes that either show, or are likely to hide, new cardiac ischaemia, are excluded. Paradoxically, these patients are considered as being in a presumed high-risk category and therefore by excluding them this study is focused on the more worrying occult ischaemic population who are not readily identified. It is regrettable that the measurement of troponin I, which is released from myocytes in SMI, was not included, but the study design preceded the easy availability of this test in the study hospitals.

Calculating ischaemic load from Holter monitoring, and hence SMI, is well accepted in cardiological practice and has been documented in the anaesthetic literature. Holter continuous electrocardiography was employed with bipolar leads monitoring two channels. This had the advantages that it was relatively easy to perform, patient compliance was high and reliable results were obtained. Other studies employing two-channel Holter monitoring have reported similar rates of ischaemia [20,24]. The electrode configuration allows reliable detection of anterolateral and septal distributions of cardiac ischaemia. The disadvantage is that some ischaemia may have been missed. Monitoring over three channels would increase the yield for inferior areas of the heart, but would be more susceptible to disruption and artefacts. The problems of compliance and of artefacts are a major consideration in such studies. Owing to technical difficulties with the recording system, 44 of our traces were incomplete, yet even this was an improvement on a previously reported study, in which only 100 out of 160 tapes could be analysed. The centre analysing the tapes was remote from the participating hospitals and therefore the tapes were analysed in batches. The advantage of independence was offset by the time delay that occurred before the tapes were found to be unanalysable [25]. This design problem should be addressed when designing a future trial using Holter monitoring.

Although this was a short-term study, the clinical consequences of SMI have been widely studied [12]. As stated above, SMI is associated with the release of troponin I from myocytes [26]. In addition, the measurement of left ventricular haemodynamics in patients with SMI demonstrated an increase in left ventricular end-diastolic pressure of > 5 mmHg and an increased oxygen extraction in 63% of the patients studied [23]. In 385 elective vascular non-cardiac surgical patients, a long duration of SMI was predictive of adverse cardiac events in the perioperative period [22]. In 176 elective non-cardiac surgical patients, the adverse clinical consequences of SMI were clearly demonstrated [27]. A large study investigated the prevalence of SMI and new coronary events in elderly patients over a 45-month follow-up period. The results demonstrated a doubling of new coronary events in patients with coronary artery disease (CAD), a 1·8-fold increase in patients with hypertension, valvular disease but no CAD, and a 6·3-fold increase in those with no cardiovascular disease. The results of this study, however, need to be interpreted with caution as the mean age of the participants was 80 [28]. In addition, a long-term follow-up study of patients undergoing elective non-cardiac vascular surgery identified SMI as an independent correlate of cardiac death or myocardial infarction [29]. In these longer-term studies, perioperative SMI may be a surrogate marker for coronary insufficiency.

All of this information indicates that Holter monitoring of SMI is a reasonable surrogate for the measurement of ischaemia in the surgical population and is, by virtue of its frequency, a reasonable study end point.

Further problems in the study design were the chosen triggers. This really serves to indicate the rapidity with which the medical profession has responded to the recommendation for lower transfusion triggers. When this study was designed, the triggers chosen were considered to be low, but were acceptable to both ethics committees and orthopaedic surgeons, although with some reservations. By the completion of the studies, the triggers were considered normal. Consequently, the transfusion triggers and maintenance haemoglobin concentrations in the two groups could be interpreted as high, even for the restrictive strategy, in the light of the TRICC study. Ethics approval preceded the TRICC study and, in the absence of evidence, we may not have received approval for a more restrictive strategy than that used. It is important to emphasize that despite the studies already published, the evidence about these transfusion triggers and ischaemia is embarrassingly small.

The incidence of serious adverse events in our study was low, occurring in only 17 out of 260 randomized patients. In a similar study reported by Nelson *et al.*, six adverse events were reported in 27 patients [30]. During the current study, one death from a myocardial infarction occurred and this was in

the liberal transfusion group. There is a common perception that anaemia delays mobilization of patients following lower limb joint replacement surgery and may therefore increase the length of the postoperative hospital stay. Length of stay was not statistically different between the groups in this study, although no patients in the restrictive group suffered from severe anaemia.

The postoperative infection rate was low. All blood in the current study was leucodepleted, whereas this was not the case in some previous studies. Several studies have suggested that leucodepletion reduces the incidence of infection [31–33].

Increased awareness of the deleterious effects of stored blood and the risks of transfusion have been highlighted [34,35]. During blood storage, red cells become less deformable, so blood transfusion may paradoxically decrease microcirculatory oxygen delivery and contribute to tissue hypoxia [36]. Depletion of red cell 2,3-diphosphoglycerate (2,3-DPG) and ATP, a reduction in deformability, and accumulation of bioreactive substances in storage media, are recognized consequences of blood storage. Several studies have addressed the possible adverse effects of stored red cells [37]. One review identified 14 studies evaluating the impact of RBC transfusion on oxygen kinetics. Blood transfusion consistently increased oxygen delivery, but oxygen consumption increased in only five of the studies. It is possible, although purely conjecture, that these issues may explain the paradoxical finding that the ischaemic load was greater in those patients experiencing SMI who were assigned to the liberal transfusion strategy.

Although this study was carried out in patients undergoing elective surgery, there may be useful information from the TRICC study, which showed that a restrictive transfusion policy in the critically ill is not associated with an increased mortality [38,39]. Younger patients and those with a low Acute Physiology and Chronic Health Evaluation (APACHE) score (< 20) seem to have a lower mortality with a lower transfusion threshold. However, in critically ill patients with cardiac disease and a high APACHE II score it was suggested that transfusion was associated with a lower mortality [40]. This ties in with the observations in Jehovah's witnesses with cardiovascular disease undergoing major surgical procedures where there is a higher mortality as the preoperative haemoglobin falls from 10 to 6 g/dl [41]. In a subset analysis of the TRICC study of patients with cardiovascular disease, there was a non-significant trend towards increased mortality at the lower transfusion threshold of 7 g/dl [42].

The intention of this study was to try to identify the risks of a restrictive transfusion policy. Clearly, implementing a lower transfusion threshold could lead to an important saving in the amount of blood transfused. Additional benefit could be accrued if, when a restrictive policy is in place, 'group and save' protocols were in place, rather than having crossmatched blood available, regardless of need. This may itself decrease the possibility of transfusion [43]. The potential savings of implementing a restrictive transfusion policy are impressive. Elective orthopaedic surgery accounts for the use of ≈ 200 000 units of blood per year in the UK alone. In addition, general surgeons use 13·6% of blood units issued nationally per annum (300 000 units), so a restrictive transfusion strategy applied to selected elective subgroups of these patients could achieve substantial savings. Against all of this is the spectre of potential harm. The present study is one of the few studies to be carried out comparing two transfusion strategies. It is underpowered to confirm safety, but, at a minimum, serves to describe the incidence of SMI and to highlight the important relationship between haemoglobin and SMI. In doing so it goes a little way towards providing clinical confidence in the use of this restrictive trigger. Clearly, larger randomized controlled studies are needed and this study gives a clear indication of the minimum size of such studies if confirmation of equivalence is to be sought.

In conclusion, in patients with no preoperative evidence of ischaemia on their ECG, a haemoglobin concentration of 8 g/dl as a transfusion trigger with a restrictive transfusion strategy seems unlikely to increase the risk of SMI in terms of incidence and may be associated with a lesser SMI load. Despite the belief that anaemia leads to delayed postoperative mobilization and therefore longer hospital stay, this study did not show an increased length of postoperative stay in patients assigned to the restrictive transfusion strategy

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