RESEARCH ARTICLE

Effect of postoperative anemia on functional outcome and quality of life after hip and knee arthroplasties: a long term follow-up [version 1; peer review: 1 approved, 1 not approved]

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Abstract

Background: Postoperative anemia is frequent in patients undergoing hip and knee arthroplasty. While it is legitimate to think that anemia could decrease postoperative vigor and, consequently, limit the patient's rehabilitation, our previous study showed that anemia does not impair functional recovery in patients during the immediate postoperative period (10 days). Here we investigate the possible relationship between the postoperative hemoglobin (Hb) concentration and long-term (6 months or more) functional recovery and quality of life (QoL) in patients.

Study design and methods: A follow-up, observational study was conducted in the 305 patients 60 years and older who underwent major hip or knee arthroplasty and participated in the Transfusion Requirements in Orthopedic Surgery (TRIOS) study (phase 2). The relationship between postoperative Hb concentration (or variation thereof) and primary outcomes (Functional Status Index (FSI) score, scores in the two categories of the Short Form 36 (SF-36) test and adverse events) was established by linear regression.

Results: 160 patients responded to long-term follow-up. There were no significant correlations between the postoperative Hb concentration (or the variation in perioperative Hb) and either the FSI or SF-36 scores or adverse events. Consequently, moderate postoperative anemia does not appear to affect long-term (6 months or more after surgery) functional recovery or QoL in patients undergoing a major arthroplasty.

Conclusion: Our results confirm the lack of longer-term effects of anemia on functional recovery observed in the immediate postoperative period in the TRIOS phase 2 study.

Keywords

postoperative anemia, arthroplasties

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Immediate postoperative anemia is common in patients who undergo a major hip or knee arthroplasty¹. Consequently, clinicians have to decide whether or not a patient should receive a transfusion to counter postoperative anemia that may affect recovery. However, opinions are divided regarding the true need for, and benefit of, transfusions after major orthopedic surgeries. Several studies have suggested that the risk of postoperative morbidity is higher in patients with cardiovascular disease or those with a major illness and anemia after surgery^{2,3}. These results prompted physicians to adopt a more liberal transfusion strategy by regularly transfusing patients to hemoglobin (Hb) concentrations higher than 100 g/L⁴.

In contrast, a more conservative transfusion strategy is chosen by many clinicians, including those of the Centre Hospitalier de l'Université de Montréal (CHUM)⁵, due to the fact that patients are subject to frequent microcirculatory or immunosuppressive complications after a blood transfusion⁴. Furthermore, the risk of blood-transmitted pathogens (known and unknown) and the limited availability of blood products renders the liberal approach less attractive. A restrictive approach intended to limit transfusions only to patients with an Hb level lower than 70 g/L is, at the moment, favored considering these potential risks associated with blood transfusions⁵. An important randomized study including 838 intensive care patients showed that the use of a transfusion threshold of 70 g/L (with the aim of keeping the concentration of Hb between 70 and 90 g/L) was at least as safe as the use of a liberal strategy with a transfusion threshold of 100 g/L⁴. The 30 day postoperative death rate and the rates of cardiovascular complications and organ dysfunction were not significantly different with a restrictive strategy (and were even significantly lower in some subgroups), suggesting that patients who undergo surgery are able to tolerate Hb levels much lower than those previously admitted. According to these results, it seems that the use of a restrictive transfusion strategy does not affect mortality or morbidity in the immediate postoperative period (30 days after surgery). In addition, as described in the meta-analysis by Alvarez *et al* 2001, many studies have shown that the human body can adapt to lower [Hb] by increasing cardiac output and oxygen extraction along with a decrease in blood viscosity⁶. These adaptive changes could explain the similar results observed when using restrictive and liberal transfusion strategies.

The results of the recent Transfusion Requirements in Orthopedic Surgery (TRIOS) phase 2 trial also support a restrictive transfusion strategy⁷. They suggest, contrary to our initial hypothesis, that anemia does not affect functional recovery and quality of life (QoL) in patients immediately (1 to 10 days) after their surgery. Here we ask whether the lack of effects of anemia observed in our patients during the immediate postoperative period persists in the long-term period (6 months or more after surgery).

The objective of the present study was to establish the relationship between the postoperative Hb concentration, and functional recovery and QoL in the long-term after a major arthroplasty. Should there be a relationship between anemia and these two outcomes, we would be able to determine a minimal Hb level below which long-term functional recovery and QoL is affected. Should it exist, this threshold could help clinicians and patients decide between a liberal or a restrictive transfusion strategy after major orthopedic surgery.

We hypothesized that patients with a lower postoperative Hb concentration have a diminished functional recovery and QoL in the long-term after surgery, compared to those who have higher postoperative Hb concentration.

Materials and methods

Study design and population

We conducted a follow-up, observational study at the CHUM – Hôpital Notre-Dame to evaluate the long-term postoperative evolution of the 305 patients who participated in TRIOS phase 2 trial. The inclusion criteria of the initial TRIOS phase 2 trial were: being over the age of 60 at the time of surgery, candidacy for a knee or hip arthroplasty or a non-urgent prosthesis revision, the ability to walk prior to surgery and to provide informed consent to participate in the study. Additionally, an exclusion criterion implemented in this present follow-up study was that patients should not have had another surgery since the one for which they had been recruited originally. The protocol was evaluated and accepted by the ethics committee of the CHUM. Each patient was sent a letter inviting him/her to participate in the follow-up study by phoning one of the investigators (ACL). Verbal consent from each of the 160 patients who agreed to participate was obtained prior to completing the interview by telephone.

Primary outcomes

Functional recovery was measured with the Functional Status Index (FSI), a reliable and valid instrument allowing auto-evaluation of physical function in adults⁸. This tool informs the clinician on three aspects of the physical function of the patient during a given activity. These three aspects include the need for assistance, the level of pain and the difficulty of performing a given activity. The sum of the results of these three aspects gives a global score describing how a patient perceives his or her physical condition. A high FSI score corresponds to a poor functional status⁹. Scores range from 54 for fully autonomous patients to 234 for patients experiencing a weak recovery.

Equally, the [Short Form 36 \(SF-36\)](#) was used to evaluate the QoL of patients¹⁰. This test provides a physical components score (PCS) and a mental components score (MCS) that evaluate these two functions. Scores range from 0–100, with higher scores indicating better health. On the physical components score, low scores indicate many limitations in physical

activities; on the mental components score, low scores indicate problems with work or other daily activities as a result of emotional health¹⁰.

At the same time, patients were asked about complications or morbidities associated with postoperative anemia such as: cardiovascular, respiratory or neurological adverse events, major infections and non-specific symptoms of anemia (dizziness, weakness and fatigue). Hb concentrations were recorded on several occasions during the patient's stay at the hospital during the initial TRIOS phase 2 trial. We selected two of these recordings (taken during the preoperative medical consultation and after surgery, at the time of the 6 Minute Walk Test^{11,12}) for each patient to establish correlations with long-term postoperative recovery.

Data collection

Each patient's file was consulted to obtain details on his/her general recovery, postoperative morbidities or mortality using surgery and physiotherapy notes. All this information was noted in a database.

For the evaluation of functional recovery and QoL using the FSI and the SF-36, each patient was asked to complete these questionnaires during a telephone interview. If a patient had not called back within 10 days after receiving the letter, a member of the team (ACL) called the patient to obtain his/her consent to participate in the study.

During the phone call to the patient, a member of the team (ACL) would read every question and note the patient's answers. Data for FSI, SF-36 and postoperative complications were all obtained during the same phone call. Time from the original TRIOS phase 2 trial to follow-up ranged between 6 months to 3 years. Twenty six to 36 patients completed the questionnaire each week during 7 consecutive weeks, making a total of 160 respondents.

SF-36 scores (PCS and MCS) were calculated using Quality-Metric Inc. SF Health Outcomes™ Scoring Software (Lincoln, RI <http://www.qualitymetric.com>).

Statistical analysis

Data were analyzed in order to determine a Hb concentration below which functional recovery and QoL in patients are impaired. Relationships between Hb concentrations and FSI or SF-36 scores were studied by linear regression using two main models. The first investigated scores in association with postoperative Hb concentration and the second investigated scores in association with individual changes between the preoperative and postoperative [Hb] recordings. An eventual non-linear effect of postoperative Hb on FSI scores was also verified. A p value < 0.05 was considered statistically significant. All analyses were completed using LaTeX and R version 2.13.0 software by the CHUM's statistician (MPS).

Results

From February to March 2011, the 305 patients who participated in the TRIOS phase 2 were asked to contact a member of the research team (ACL) to complete FSI and SF-36 questionnaires. Among those 305 patients, 184 were available and accepted to take part in the study at the moment of the phone call but 24 of them were excluded because they had had another surgery since their original operation. As a result, the information of 160 patients was considered.

Table 1 presents the main demographic characteristics of the 160 patients who participated in the follow-up study. The average age of the patients was 72.4 years (range 60–91) and 64% of them were women. The average patient's body mass index (BMI) was 30.5 kg/m² (range 16.2–51.5) and the average (range 1–3) American Society of Anesthesiologists' (ASA) physical status score was 2 (patients with a systemic pathology that does not limit his/her activities) in the majority of patients (61.3%). Eighty-two patients underwent a total knee arthroplasty (TKA) and 78 underwent a total hip arthroplasty (THA).

Table 2 shows average preoperative and postoperative (1 to 10 days after surgery – average 4.6 days) Hb concentrations, average FSI and SF-36 scores and the number of patients who had major complications after surgery. There was a 36.2 g/L

Table 1 Patient characteristics (n=160).

Characteristic	
Age (years)	72.4 ± 7.0
Sex	
Male	57 (35.6)
Female	103 (64.4)
Weight (kg)	78.5 ± 16.5
Height (m)	1.60 ± 0.09
BMI* (kg/m ²)	30.5 ± 6.1
ASA*	
1	11 (6.9)
2	98 (61.3)
3	51 (31.9)
4	0 (0.0)
Surgery	
Total knee arthroplasty	82 (51.3)
Total hip arthroplasty	78 (48.7)

*Data are reported as mean ± SD for continuous variables and as number (%) for categorical variables.
ASA = preoperative physical status according to the American Society of Anesthesiologists; BMI = body mass index

Table 2 Mean Hb concentrations and primary outcomes.

Preoperative Hb (g/L)	133.8 ± 14.0
Postoperative Hb (g/L)	97.6 ± 12.0
FSI score (range 51–179)	76.0 ± 24.9
SF-36 PCS score (range 21.4–64.9)	45.1 ± 9.5
SF-36 MCS score (range 8.2–72.5)	57.1 ± 10.7
Cardiovascular adverse events	7 (4.4)
Respiratory adverse events	12 (7.5)
Neurological adverse events	3 (1.9)
Major infections	10 (6.3)
Non-specific symptoms of anemia	13 (8.1)

Data are reported as mean ± SD for continuous variables and as number (%) for categorical variables. *FSI = Functional Status Index; PCS = Physical Component Summary score; MCS = Mental Component Summary score; SF-36 = Short Form 36 quality of life assessment.

difference between mean preoperative and postoperative Hb concentrations. The average postoperative Hb concentration (97.6 ± 12.0 g/L) was below the threshold for anemia as defined by the [World Health Organization](#) (120 g/L in women and 130 g/L in men). The percentage of patients who had adverse events of any type (cardiovascular, respiratory or neurological adverse events, major infections and non-specific symptoms of anemia - dizziness, weakness and fatigue) was low, ranging between 1.9 to 8.1%.

Table 3 presents the relationship between the postoperative Hb concentration and each patient's long-term primary outcome

scores. There were no significant associations between postoperative [Hb] and FSI, PCS or MCS. Preoperative Hb concentrations ($p = 0.0000$) were associated with postoperative [Hb]. Postoperative [Hb] tended to be (but were not significantly) associated with cardiovascular complications ($p = 0.0771$) and female gender ($p = 0.0752$). There was no significant association between postoperative Hb concentrations and patients' other characteristics. The relationships between postoperative [Hb] and FSI and PCS or MCS components of the SF-36 are shown on a scatter plot in [Figure 1](#).

As shown in [Figure 1](#), there was no statistically significant association between postoperative [Hb] and FSI, PCS or MCS scores. The distribution of the dots in [Figure 2](#) reflects a similar lack of association between Hb concentration and postoperative complications (marked by filled circles).

Table 4 presents the relationship between the difference between pre and postoperative Hb, FSI and SF-36 components scores, and shows that this difference in Hb concentration was not associated with FSI, PCS and MCS. Only non-specific symptoms of anemia ($p = 0.0418$) and age ($p = 0.0106$) were statistically associated with the difference in [Hb]. The difference in Hb concentrations tended to be (but was not significantly) correlated with female gender ($p = 0.0684$).

A possible non-linear effect of postoperative [Hb] on FSI scores was investigated ([Table 5](#)). To do so, a quadratic transformation of FSI was added (FSI^2). Again, there was no statistically significant relationship between postoperative Hb concentration and FSI scores. Finally, the effect of time between surgery and

Table 3 Linear model for the relationship between the postoperative Hb concentration and each patient's characteristic.

	Estimate	Std. Error	95% CI	95% CI	t value	P value
Intercept	45.2085	20.0361	5.6125	84.8045	2.2564	0.0255
HbPre	0.3503	0.0747	0.2027	0.4979	4.6894	0.0000
FSI	-0.0542	0.0561	-0.1651	0.0568	-0.9651	0.3361
PCS	-0.0871	0.1362	-0.3563	0.1821	-0.6395	0.5235
MCS	-0.0248	0.0967	-0.2160	0.1663	-0.2568	0.7977
Cardiovascular adverse events	7.8503	4.4099	-0.8646	16.5652	1.7802	0.0771
Respiratory adverse events	3.4453	3.6746	-3.8166	10.7073	0.9376	0.3500
Major infections	1.9188	3.8866	-5.7620	9.5995	0.4937	0.6223
Non-specific symptoms of anemia	0.8243	3.6342	-6.3577	8.0062	0.2268	0.8209
Neurological adverse events	-2.8670	7.0231	-16.7463	11.0123	-0.4082	0.6837
Age	0.1903	0.1313	-0.0692	0.4497	1.4493	0.1494
BMI	0.0945	0.1485	-0.1989	0.3879	0.6365	0.5255
Female gender	-3.7300	2.0812	-7.8430	0.3830	-1.7922	0.0752

HbPre = Preoperative Hb; FSI = Functional Status Index; PCS = Physical Component Summary score; MCS = Mental Component Summary score; BMI = Body Mass Index; intercept is the value of the outcome when all continuous variables in the model are 0 and all categorical variables are the references categories; t value is the estimated slope divided by the standard error of the estimated slope

Figure 1 Scatter plots of FSI (A), PCS (B) and MCS (C) scores according to postoperative [Hb]. FSI = Functional Status Index; PCS = Physical Component Summary score; MCS = Mental Component Summary score; HbPost = Postoperative Hb. The lines represent local polynomial regression fitting.

completion of the follow-up questionnaire on patients' scores was considered. Time was not statistically associated with PCS and MCS scores but it was statistically correlated with FSI scores (FSI scores worsened as time elapsed; $p = 0.0108$).

Transfusion Requirements in Orthopedic Surgery: long term outcome data

1 File

<http://dx.doi.org/10.6084/m9.figshare.156048>

Discussion

Contrary to our preliminary hypothesis, we were unable to find a relationship between the immediate postoperative Hb concentration (or the difference between pre and postoperative Hb) and functional recovery or QoL in patients in the long-term period after a major arthroplasty. Also, there were no significant correlations between postoperative Hb levels and adverse events or morbidities thought to be associated with postoperative anemia. Consequently, we could not establish a Hb threshold below which functional recovery and QoL in patients are affected.

Figure 2 Scatter plots of cardiac adverse events (A), respiratory adverse events (B), major infections (C), non-specific symptoms of anemia (D) and neurological adverse events (E) according to pre and postoperative Hb concentrations. Filled circles represent patients with adverse events. HbPre = Preoperative hemoglobin; HbPost = Postoperative hemoglobin.

The SF-36 and FSI data were analyzed by linear regression using two main models (one studied scores in association with postoperative Hb and the second investigated scores in association with individual differences between pre and postoperative Hb concentrations). There were no significant associations of these two models with SF-36 and FSI. We also considered an eventual non-linear effect of postoperative Hb on FSI scores to ensure that all correlation models were investigated. Again, there were no associations between postoperative Hb and FSI scores.

Two recent studies support the lack of effects of postoperative anemia on functional recovery and QoL in patients undergoing a major arthroplasty. A randomized clinical trial involving 2016 patients at high cardiovascular risk demonstrated that a liberal transfusion strategy, as compared with a restrictive strategy, did not reduce the death rates, the ability to walk independently or the rates of in-hospital morbidities 60 days after hip-fracture surgery¹³. Moreover, the results of the TRIOS phase 2 trial also showed that moderate anemia does not affect functional recovery or QoL in patients during the immediate postoperative

Table 4 Linear model for the relationship between the difference in Hb concentration and each patient's characteristic.

	Estimate	Std. Error	95% CI	95% CI	t value	P value
Intercept	56.7913	19.9272	17.4126	96.1699	2.8499	0.0050
FSI	0.0573	0.0689	-0.0788	0.1934	0.8318	0.4069
PCS	0.1800	0.1666	-0.1492	0.5091	1.0804	0.2817
MCS	0.0460	0.1186	-0.1884	0.2804	0.3878	0.6987
Cardiovascular adverse events	-6.1074	5.4034	-16.7852	4.5705	-1.1303	0.2602
Respiratory adverse events	-2.4990	4.5052	-11.4019	6.4039	-0.5547	0.5799
Major infections	-0.9819	4.7653	-10.3988	8.4349	-0.2061	0.8370
Non-specific symptoms of anemia	-8.8530	4.3114	-17.3728	-0.3331	-2.0534	0.0418
Neurological adverse events	-1.9363	8.5877	-18.9067	15.0340	-0.2255	0.8219
Age	-0.4089	0.1580	-0.7212	-0.0965	-2.5870	0.0106
BMI	-0.0683	0.1821	-0.4281	0.2915	-0.3753	0.7080
Female gender	-4.2113	2.2941	-8.7447	0.3220	-1.8358	0.0684

FSI = Functional Status Index; PCS = Physical Component Summary score; MCS = Mental Component Summary score; BMI = Body Mass Index; intercept is the value of the outcome when all continuous variables in the model are 0 and all categorical variables are the references categories; t value is the estimated slope divided by the standard error of the estimated slope.

Table 5 Non-linear effect of postoperative Hb on FSI scores.

	Estimate	Std. Error	95% CI	95% CI	t value	P value
Intercept	54.8823	24.2662	6.9238	102.8408	2.2617	0.0252
HbPre	0.3501	0.0748	0.2022	0.4979	4.6787	0.0000
FSI	-0.2417	0.2702	-0.7757	0.2924	-0.8942	0.3727

HbPre = Preoperative Hb; FSI = Functional Status Index; intercept is the value of the outcome when all continuous variables in the model are 0 and all categorical variables are the references categories; t value is the estimated slope divided by the standard error of the estimated slope.

period⁷. Considering these outcomes and the fact that recovery from anemia is relatively rapid⁷, it is not entirely surprising that the long-term effects of anemia on functional recovery and QoL were minimal in the present study (Tables 3 and 4).

On the other hand, a recent literature review by Spahn suggests that an increase in postoperative mortality and morbidity could be associated with perioperative anemia¹. This review concluded that perioperative anemia is associated with postoperative infections, poorer physical functioning and recovery, and increased length of hospital stay and mortality¹. However, prospective clinical studies are required to validate these conclusions. In contrast to Spahn's review, results of the FOCUS trial demonstrated that the frequency of in-hospital morbidities (including pneumonia, wound infection, thromboembolism, stroke or transient ischemic attack and clinically recognized myocardial infarction), the inability to walk independently on a 60-day follow-up, length of hospital stay and mortality rates were not reduced by using a liberal transfusion strategy

(maintaining [Hb] over 100 g/L) as compared with a restrictive strategy (transfusion for symptoms of anemia or at physician discretion for a [Hb] below 80 g/L)¹³.

Several studies have investigated the relationship between postoperative anemia and functional outcomes in patients after surgery. As reviewed in the study by Vuille-Lessard *et al*, the conclusions of these studies tend to diverge, but in general, most evidence-based studies indicated that the effects of anemia on functional recovery and QoL are limited⁷.

A major strength of the present study is that we used two different questionnaires to evaluate the patients' physical and psychological function. This enhances the validity of the results. Another strength of the study is the reliability and validity of the instruments used to collect data. Functional recovery was measured using the FSI, a valid and reliable instrument allowing auto-evaluation of physical function in adults⁸, while QoL was evaluated using the well-validated SF-36¹⁰.

Weaknesses of this study include the inability or the refusal of some patients to report a representative description of their physical and psychological condition. Furthermore, some interviewed patients had concurrent health problems (cancer, diabetes, renal insufficiency and arthritis for example) in addition to their orthopedic surgery that might have also affected their FSI or SF-36 scores. As a result, some patients recovering well from either THA or TKA may have presented low physical function scores due to other health problems. However, this possibility would have affected our results negatively, which was not the case since, overall, FSI scores indicated a good functional recovery. Another weakness of this study is its follow-up observational design and the variable time between surgery and follow-up. Given that total recovery from THA or TKA is relatively rapid⁷, the difference in time between surgery and the follow-up questionnaire (3 months to 6 years) may have affected the scores to the questionnaires relating to the patient's recovery and, yet, our results show that this was not the case for PCS and MCS scores and FSI scores were negatively affected by a longer time interval between surgery and the follow-up questionnaire.

In summary, postoperative anemia does not appear to affect long-term (6 months or more) functional recovery and QoL in patients undergoing THA or TKA. Our follow-up results

confirm the lack of effects of anemia on functional recovery and QoL during the immediate postoperative period observed in the TRIOS phase 2 study.

Author contributions

Alex Cormier-Lavoie interviewed the patients, collected and helped analyze the data, and wrote the manuscript. Monique Ruel helped design and conduct the study. Marie-Pierre Sylvestre analyzed the data and helped write the manuscript. Jean-François Hardy designed the study, helped conduct the study and analyze the data, and reviewed the manuscript. All authors approved the final manuscript for publication.

Competing interests

No competing interests were disclosed.

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This paper contains follow up data from patients analyzed in a previous study ([E. Vuille-Lessard et al. 2010](#)). I have great concerns about certain issues that are presented in this paper:

1. the proportion of responders was low (52%) and I suspect that selection bias was present. The authors should include the baseline characteristics of this population compared to the original study patients. The mean Hb values seem higher than in the original study. Could this study population be the better, healthier part of the original study population?
2. Data analysis was performed by regression analysis to investigate the relationship between postoperative Hb level and functional recovery (by FSI score) and quality of life by SF-36 score. The effect of time between surgery and completion of follow up questionnaires on patients' scores was evaluated. It would be more informative if the model investigating the relationship of (delta) Hb and scores was corrected for the effect of the time.
3. In my opinion p-values are not the only parameter of value. Additionally reporting R or R² would be more informative, since this parameter will explain the proportion of variation which can be explained by the variable of interest.
4. I do not agree with the strengths of the study. Using two different questionnaires is not a way to enhance the validity of the study. Perhaps the used questionnaires are not discriminative enough or are just not suitable to test the hypothesis in this patient population.
5. The authors should include possible selection bias as a major weakness, see also point 1.
6. A possible error was present in reporting the time of follow up in the weakness paragraph: 3

months to 6 years should be probably 6 months to 3 years.

7. Another possible error was present in the number of questionnaires completed. If 26 to 36 were completed during 7 consecutive weeks, > 190 questionnaires should have been available, not 184.

In this paper some essential data are lacking and together with the finding that the data was not analyzed appropriately, I conclude that the results do not add to more evidence regarding quality of life or functionality after hip- and knee arthroplasty, even after (long-term) follow up.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 07 March 2013

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The title and abstract are easy to understand and their content is a very good summary of what can be found in the full manuscript.

The methods section is operational: readers will find enough details to replicate the study.

There is no overstatement in the conclusion.

The data are original and quite unexpected: I would have guessed that elderly people would suffer from anaemia after a hip or knee surgery, and I am surprised that this is not the case.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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