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Anaemia impedes functional mobility after hip fracture surgery

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Abstract

Background: the impact of anaemia on the outcome after a hip fracture surgery is controversial, but anaemia can potentially decrease the physical performance and thereby impede post-operative rehabilitation. We therefore conducted a prospective study to establish whether anaemia affected functional mobility in the early post-operative phase after a hip fracture surgery.
Patients and Methods: four hundred and eighty seven consecutive hip fracture patients, treated according to a well-defined multimodal rehabilitation programme with a uniform, liberal transfusion threshold, were studied. Hb was measured on each of the first three post-operative days, and anaemia defined as Hb <100 g/l. Functional mobility was measured with the Cumulated Ambulation Score (CAS).
Results: the results were obtained from 170, 132 and 116 patients who were found anaemic on the first, second and third post-operative day, respectively. A significant association between anaemia and the ability to walk independently before the correction of anaemia was present on each of the 3 days separately ($P<0.05$). A significant correlation was also found on each day between the functional score and the Hb level. A multivariate analysis integrating the type of surgery, medical complications and prefracture function showed that anaemia at the time of the physiotherapy session was an independent risk factor for not being able to walk on the third post-operative day [OR 0.41 (0.14–0.73) $P = 0.002$].
Conclusion: anaemia impedes functional mobility in the early post-operative phase after a hip fracture surgery and is an independent risk factor for patients not being able to walk post-operatively. The potential for a liberal transfusion policy to improve the rehabilitation potential in hip fracture patients with anaemia should be investigated.

Keywords: *hip fracture, anaemia, rehabilitation, elderly*

Introduction

Patients with a hip fracture are often the elderly with a high degree of comorbidity rendering them especially susceptible to the effects of perioperative physiological stress and the associated post-operative morbidity and mortality [1–3]. In this context perioperative anaemia occurring as a result of intra and post-operative bleeding may represent a further physiological insult due to increased cardiac demand and potential tissue hypoxia [4–6]. Severe anaemia with Hb levels below 80 g/l is associated with an increased post-operative mortality [7], especially in those with a pre-existing cardiac disease [8]. The impact of moderate anaemia with Hb levels between 80 and 100 g/l is controversial, especially in hip fracture patients [9, 10]. Although moderate anaemia has not been demonstrated to increase mortality in hip fracture patients [10, 11], anaemia will potentially decrease physical performance and thereby impede post-operative rehabilitation [6]. Thus, post-operative anaemia in hip fracture patients has been associated with decreased walking distance on discharge [12] and post-operative delirium [13], but no data exists on the day to day effect of anaemia on functional capacity during the initial phase of rehabilitation. We therefore conducted a prospective study of hip fracture patients treated according to a well-defined multimodal rehabilitation programme and uniform transfusion guidelines, in order to establish the impact of anaemia on functional mobility in the early post-operative phase.

Patients and methods

Inclusion

From September 2002 to July 2004, all hip fracture patients admitted to the hip fracture unit at the department of

orthopaedics at Hvidovre University Hospital were studied prospectively. The inclusion criteria were primary hip fracture occurring in the community in patients with a prefracture walking function independent of human assistance regardless of walking aids used, no pathological fracture or surgery resulting in a Girdlestone status. Patients were excluded from the analysis if they were not able to participate in the physical therapy programme due to mobilisation restriction on the advise of the operating surgeon or transfer to another ward for medical complications.

This study is part of Hvidovre University Hospitals Hip Fracture Project, which was evaluated by the local ethical committee, who had no objections to the project and concluded that no written patient consent was necessary. The study was approved by the Danish data protection agency.

Perioperative procedures

All patients admitted to the unit received surgical intervention for their fracture. Patients were treated perioperatively in a special hip fracture unit with a multimodal rehabilitation program. The rehabilitation program included surgery within 24 h, epidural anaesthesia and epidural analgesia initiated immediately after admittance and continued for 96 h post-operatively [14]. From admission until the fourth post-operative day patients received supplemental oxygen therapy 2 l min^{-1} whenever supine. All patients received antibiotics with cefuroxim 1.5 g immediately preoperatively and antithrombotic prophylaxis with low-molecular weight heparin (enoxaparin 40 mg^{-1} SC once daily) from the time of admission. Patients were on a regular diet supplemented by three daily protein drinks in the entire perioperative period excluding 6 h of preoperative fasting.

Preoperative fluid therapy consisted of rehydration fluid (Na 40 mmol/l, K 20 mmol/l, glucose 250 mmol/l) 20 ml/kg immediately upon admission; intraoperatively, an infusion of isotonic saline 5 ml/kg/h was provided, supplemented by 6% hydroxyethyl starch 130/0.4 on signs of hypovolaemia. Intraoperative blood loss was replaced by 6% hydroxyethyl starch 130/0.4, at a rate of 1:1 until Hb fell below 100 g/l, at which point transfusion of red blood cells (RBC) was initiated. In the post-anaesthesia care unit (PACU) all patients received 500 ml IV glucose (278 mmol/l). Post-operative fluid therapy was standardised and intravenous fluids were only administered if daily oral intake was <1,500 ml, or in the case of hypovolaemia when 500 ml of 6% hydroxyethyl starch 130/0.4 was given.

Transfusion therapy

Hb was as a standard measured immediately upon admission via venous sampling and analysed with cyano-methaemoglobin method (Advia, Bayer, Lyngby, Denmark), again in the PACU 1 h after the end of anaesthesia and every morning until the fifth post-operative day via venous sampling with Hemocue (Hemocue, Vedbæk, Denmark). A standardised liberal transfusion threshold was in place, with all patients scheduled to receive RBC transfusion if the patient had a measured Hb level <98 g/l at *any* point during their admission. In the following, anaemia will, for convenience refer to a measured Hb < 100 g/l.

Guidelines for transfusions were one unit of RBC, which at our institution contains an average of 55 g of Hb, if measured Hb was between 89 and 97 g/l; two units if Hb was between 72 and 88 g/l and three units if it was below 72 g/l; extreme anaemia was to be treated with a number of transfusions at the discretion of the attending physician. White blood cell (WBC) depleted transfusions were not given.

Intraoperatively Hb was only measured and transfusions given when excessive blood loss was observed. In the PACU any transfusions ordered as a consequence of anaemia, were to be initiated before the patients left the PACU. In the ward the Hb values were measured in the morning and any indication for transfusion was to be acted upon immediately. Hospital logistics dictated that this usually was effectuated in the early afternoon of the same day.

Rehabilitation

Prefracture functional level expressed by the New mobility score (NMS) (0–9, with 0–5 indicative of poor walking function) was recorded upon admission [15]. The NMS is a composite score of the patient's ability to perform: indoor walking, outdoor walking and shopping. Post-operatively, the patients were mobilised if at all possible on the day of operation, and an intensive physiotherapy programme comprising two daily 30-min sessions, was initiated either on the day of operation or on the first post-operative day. The attending physiotherapists had the first session of the day with the patients before noon.

During the physiotherapy session, the patients were evaluated on their ambulatory capacity via the Cumulated Ambulation Score (CAS) [16], which allows day-to-day measurements of functional mobility in hip fracture patients in the early post-operative phase. At this point of their rehabilitation most hip fracture patients have not yet gained functional independence allowing the use of more elaborate measurements. The CAS describes the patients' independence in ambulation in transfer from supine-to-sitting-to-supine, sitting-to-standing-to-sitting and the patient's walking ability with an appropriate aid. Each function is assessed on a three-point scale; 2: independent of human assistance, 1: patient requiring human assistance to perform the function and 0: patient is unable to perform the function despite human assistance.

Discharge criteria from the hip fracture unit were standardised: the ability to independently get in and out of bed and walk to- and fro from a place of eating, the ability to independently perform bathroom visits and the ability to walk with the help of a walking aid to be used in the home. Patients were primarily rehabilitated in the orthopaedic ward. Patients, who after initial rehabilitation in the hip fracture unit, still required an excessive length

of intensive rehabilitation, were only then transferred to a secondary rehabilitation facility.

Data collection

Data were gathered prospectively. Medical conditions, American Society of Anaesthesiologists (ASA) classification, type of surgery, as well as complications, length of stay and 30-day mortality were all registered, the latter established via the Danish civil register. A complication was defined as being present in any patient that post-operatively developed any of the following: cerebrovascular accident, delirium, acute myocardial infarction or unstable angina, acute congestive heart failure, new onset arrhythmia, pneumonia, respiratory insufficiency, gastric or duodenal ulceration, renal dysfunction, septicaemia, pulmonary embolism, deep venous thrombosis or wound infection. For the analysis of the impact of complications on early post-operative functional mobility, only those complications occurring before the fourth post-operative day were included.

Statistical analysis

Possible correlations were tested for with the Spearmans rho. Tests for significant differences between categorical data in the univariate analyses was performed with the chi-square test, and adjusted for linear to linear association where appropriate, for ordinal and continuous data the Mann–Whitney test was used. Multivariate logistic regression analysis was done to identify independent factors associated with independent walking on the third post-operative day. The type of surgical procedure was entered in the analysis coded as dummy variables with two parallel screws chosen as control. The level of significance was set at $P<0.05$. All data analysis was performed with SPSS version 10.1.

Results

During the inclusion period, 510 consecutive patients fulfilling the inclusion criteria were admitted at the hip fracture unit. Twenty three of these patients were excluded on the first post-operative day; 11 on account of mobilization restrictions dictated by the surgeon due to the nature of the fracture, 6 were transferred to other wards because of medical complications, 1 patient refused to participate in physical therapy, 2 had died and 3 had insufficient data. Thus, on the first post-operative day, 487 patients were available for analysis of the association between anaemia and functional mobility. On the second post-operative day, 462 patients were available for analysis. Two patients had died, 8 had been discharged to nursing homes, 5 had been transferred to other wards and a further 10 had mobilization restrictions. By the third post-operative day, 1 more patient had died, 13 had been discharged, 6 transferred, 4 had mobilization restrictions and 8 had missing data leaving 430 patients for analysis. Characteristics of the included patients are shown in Table 1. Of the included patients 294 (60%) had cardiovascular disease, 110 (23%) had pulmonary disease and 365 (75%) were 75 years of age or older; overall 438 patients (90%) had cardiopulmonary disease and/or were more than 75 years of age.

Table 1. Characteristics of 487 hip fracture patients with hip fracture analysed for association between anaemia and functional mobility

Age (years)	82 (75–88)
Sex (M/F)	126/361 (74/26)
Poor prefracture functional level (new mobility score 0–5)	223 (46)
Prefracture nursing home residence	77 (16)
Weight (kg)	62 (53–70)
Height (cm)	165 (160–170)
ASA classification (III/IV)	259 (53)
Cardiovascular disease	294 (60)
Pulmonary disease	110 (23)
Haemoglobin on admission (g/l)	127 (116–137)
Fracture type	
Medial	236 (49)
Pertrochanteric	219 (45)
Subtrochanteric	32 (6)
Delay to surgery (h)	19 (14–23)
Length of surgery (min)	50 (38–70)
Intraoperative bleeding (ml)	200 (100–320)
Number of patients transfused	
Preoperatively	17 (3)
Intraoperatively	60 (12)
In postanaesthesia care unit	195 (40)
1st post-operative day	163 (33)
2nd post-operative day	130 (25)
3rd post-operative day	107 (22)
Transfusions per patient	2 (0–3)
Post-operative length of stay (days)	12 (7–23)
30-day mortality	53 (11)

Values are presented as number of patients (percentage) for nominal data and as median (25–75% quartiles) for data in scales. ASA, American society of anaesthesiologists.

Of the 487 patients, 473 (97%) had their Hb measured in the PACU; on the first, second and third post-operative days, of which 444 (91%), 388 (84%) and 392 (91%) patients, respectively had an Hb measurement in the ward. On the first post-operative day, 170 patients were found to be anaemic and 163 received transfusions; on the second post-operative day, 132 were found anaemic and 130 were transfused; and finally on the third day after surgery, 116 were anaemic and 107 patients received transfusions. From admission until the third post-operative day a total of 337 (69%) patients received transfusions (range 0–13), median number of transfusions given was two.

On each of the first three post-operative days there was a significant positive correlation between the Hb of the patients and their functional mobility measured via the day to day score of the CAS (0–6), indicating increased functional mobility with increasing measured Hb levels; (Spearmanns rho) 0.12 ($P = 0.02$), 0.18 ($P<0.001$) and 0.18 ($P<0.001$) on the first, second and third post-operative days, respectively.

In Table 2 the association between the ability of walking independently without human assistance and having a

measured Hb value below 100 g/l is shown. About 13 , 24 and 36% of the patients were able to walk independently without human assistance on the first, second and third day, respectively. A significant linear association between the ability to walk independently, requiring human assistance or not being able to walk at all and an Hb < 100 g/l was present on each of the 3 days independently. Patients with Hb < 100 g/l had significantly lower ambulation scores (day to day CAS) on the second and third post-operative day and were mobilised out of their beds for a significantly shorter time period on both the first and second post-operative day.

A multivariate analysis was performed to identify independent risk factors for not being able to walk on the third post-operative day (Table 3). Age >75 years of age, dementia, poor prefracture functional mobility (NMS 0–5) and post-operative medical complications were the most prominent risk factors followed by a haemoglobin <100 g/l which showed a 0.41 (0.14–0.73) likelihood of a patient being able to walk if anaemic. Patients who had received an intramedullar hip screw also had a significantly reduced likelihood of being able to walk on the third post-operative day.

In the early post-operative period from the end of surgery until the third post-operative day 358 patients (74%) had a measured Hb concentration below 100 g/l at some point. Anaemia was associated with a significantly increased 30-day mortality of 12.6% versus 6.3% ($P<0.05$). Finally anaemia was also significantly associated with an increased length of stay: 13 days (9–23) versus 8 days (6–18) ($P<0.001$).

Discussion

In the present study, we have demonstrated that an Hb level <100 g/l in the early post-operative period is significantly associated with a decreased functional mobility on that particular day where uncorrected anaemia is present. A multivariate analysis showed that anaemia was an independent risk factor for patients not being able to walk on the third post-operative day when uncorrected anaemia was present, independent of factors such as type of surgery, prefracture function and other complications in the analysis.

Anaemia theoretically limits functional capacity and an increased functional capacity has been shown in anaemic hemodialysis patients after treatment with erythropoietin [6]. In hip fracture patients, a large retrospective study has found post-operative Hb level to be an independent predictor for distance walked at discharge [12], but erythropoietin therapy did not lead to functional improvement in orthopaedic patients [17]. RBC transfusions can, besides the potential for transfusion complications, be immunosuppressive [18] and transfusions *per se* have been linked to an increased risk of bacterial infections in hip fracture patients [19], but no conclusive evidence exists supporting liberal as opposed to restrictive transfusion policies on morbidity and mortality after hip fracture surgery [10]. Severe anaemia has been shown to be associated with increased mortality in patients refusing transfusions [7], but no effect of RBC transfusion on mortality has been found in hip fracture patients with Hb >80 g/l [9]. One descriptive study has found a reduced readmission rate among hip fracture patients with Hb <100 g/l who received transfusion, but failed to show any effect on mortality or functional outcome 60 days after surgery [20]. A randomised study in 84 hip fracture patients compared transfusion when Hb <100 g/l with transfusion <80 g/l or 'symptomatic anaemia', but only showed a trend towards improved survival and functional outcome with a liberal transfusion trigger [10]. No previous studies have examined the impact of anaemia on physical or functional capacity at specific time points in the post-operative phase.

Our study has several strengths. Primarily the entire perioperative set-up was standardised and not subject to the variations of individual physician opinion, which allowed standardised measurements and interventions to be performed. Secondarily, the patients received a multimodal rehabilitation programme [3] including regional anaesthesia and analgesia [14], standardised restrictive fluid therapy, optimised nutrition, supplemental oxygen and an aggressive physical therapy as well as strict day to day nurse care plans; similar programmes have been shown to improve physical capacity in other types of surgery compared to conventional care [3]. Finally, transfusion therapy was standardised to both the timing of measurement of Hb concentrations and the transfusion trigger, which was specified to be Hb

Table 2. Associations between anaemia, functional mobility and mobilization on the first three post-operative days in 487 hip fracture patients

		Walking independently	Walking with human assistance	Not able to walk	*P*	Mobilisation (hours out of bed)	
1st post-operative day	No anaemia $n = 317$	52 (16%)	160 (51%)	105 (33%)	0.049	3 (1–5)	0.011
	Anaemia $n = 170$	9 (5%)	103 (61%)	58 (34%)		2 (0.5–4.5)	
2nd post-operative day	No anaemia $n = 330$	82 (25%)	175 (53%)	73 (22%)	0.007	4 (2–6)	0.024
	Anaemia $n = 132$	24 (18%)	62 (47%)	46 (35%)		3 (1–5.5)	
3rd post-operative day	No anaemia $n = 314$	124 (40%)	130 (41%)	60 (19%)	0.001	5 (3–7)	0.129
	Anaemia $n = 116$	30 (26%)	47 (41%)	39 (34%)		4 (2.5–6)	

Anaemia defined to be present in any patient who on that given day had a hb measurement of <100 g/l. Data are presented as number of patients (%) for categorical variables and as median (25–75% quartiles) for continuous data. Test for statistical significance performed with chi-square corrected for linear-by-linear association for categorical data.

Table 3. Multivariate analysis of factors impeding functional mobility and the ability to walk independently or with human assistance on the third post-operative day ($n = 430$)

	Ability to walk on the third post-operative day			
	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
>75 years	0.16 (0.07–0.35)	<0.001	0.28 (0.12–0.67)	0.004
Prefracture NMS 0–5	0.19 (0.12–0.32)	<0.001	0.35 (0.20–0.63)	<0.001
Dementia	0.21 (0.13–0.34)	<0.001	0.36 (0.20–0.64)	<0.001
ASA 3–4	0.37 (0.23–0.60)	<0.001	0.69 (0.39–1.22)	0.20
Post-operative medical complication	0.28 (0.17–0.44)	<0.001	0.39 (0.23–0.67)	0.001
Operation is arthroplasty[a]	0.92 (0.57–1.49)	0.73	0.53 (0.17–1.60)	0.26
Operation is sliding hip screw[a]	0.78 (0.50–1.23)	0.29	0.37 (0.13–1.09)	0.07
Operation is intramedullary hip screw[a]	0.52 (0.25–1.09)	0.08	0.25 (0.07–0.91)	0.04
Hb <100 g/l 1st post-operative day	0.47 (0.29–0.75)	0.002	0.41 (0.23–0.73)	0.002

ASA, American Society of Anaesthesiologists Score; NMS, New Mobility Score.
[a] Dummy parameters, standard set as two parallel screws.

<98 g/l (6.0 mmol/l), unless the patient refused transfusion. As seen from the data, anaemia was prevalent on the first post-operative day and the compliance with the transfusion regimen was high. It was surprising that anaemia was so prevalent on both the second and third post-operative day despite our aggressive 'search and treat' approach to anaemia, suggests a continued bleeding in the post-operative phase, consistent with previously described underestimation of the total perioperative haemorrhage [5].

Our set-up allowed us to make an assessment of the detrimental effects of anaemia on physical function in the 'windows of anaemia' that occurred between the diagnosis of anaemia in the morning and the transfusion in the afternoon. As such our data allows us to conclude on the detrimental effect of anaemia when present, but it does not allow us to conclude on the potential of transfusions to correct this detrimental effect. We demonstrated an improvement in the ability to walk on all three post-operative days in non-anaemic patients, but it was evident from the data that this association was more pronounced on the third post-operative day than on the other two earlier days. This is probably due to an increased number of factors inhibiting physical function in the immediate post-operative phase such as nausea, pain, hypovolaemia and general fatigue, which becomes less prominent in the following days. Our multivariate analysis shows that anaemia is an important risk factor for patients not being able to walk, despite the heterogeneity of the patient material. Our multivariate analysis also excludes the obvious confounding factor of the type of surgery as the explanation for anaemia and low functional capacity in those patients undergoing procedures with large blood loss and surgical trauma.

In accordance with previous studies [11], we found that anaemia at *any* point in the post-operative phase was associated with increased mortality and increased length of stay. These data should be interpreted with caution in view of our consistent liberal transfusion regimen. Since almost all anaemic patients were transfused, it is impossible to conclude whether the poor outcome is a function of anaemia *per se*, a side effect of the transfusion therapy or a combination.

The present data supports the concept that all available measures should be taken to prevent the hip fracture patient from becoming anaemic. Unfortunately, it does not allow us to come to conclusion as to whether the question of transfusion in an anaemic patient will improve his/her physical and functional capacity, which requires further randomised studies within similar well-defined perioperative care programmes.

Key points

- Anaemia is prevalent after hip fracture surgery.
- Anaemia is associated with impaired post-operative ambulation.
- Post-operative anaemia is an independent risk factor for the inability to walk independently.
- Post-operative anaemia is associated with increased mortality and hospitalisation

Conflicts of interest

None declared

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