Recognising anaemia and malnutrition in vascular patients with critical limb ischaemia

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ABSTRACT

INTRODUCTION Anaemia is a common problem in surgical patients. Patients with critical limb ischaemia (CLI) suffer chronic inflammation, repeated infection, require intervention, and can have a protracted hospital stay. The aims of this study were to assess anaemia and nutritional status in patients presenting with CLI.

PATIENTS AND METHODS Two observational studies were undertaken, initially a retrospective series of 27 patients with CLI. Patient demographics, clinical details, transfusion status and in-patient laboratory haemoglobin values (Hb) were recorded. In a prospective series of 32 patients, laboratory markers to identify the cause for anaemia were assessed. Further nutritional status was assessed by records of height, weight, body mass index and a validated scoring system.

RESULTS In the retrospective series, 15 patients (56%) were anaemic. Ten (37%) were transfused a median of 2 units (range, 2–13), a total of 35 units. Patients who were transfused had lower Hb on admission ($P = 0.0019$), most were anaemic on admission (90%). At discharge, most patients were anaemic ($n = 23$; 83%). In the prospective series of 32 patients, 20 (63%) were anaemic. Nutritional assessment was performed on 18, only seven patients were scored undernourished. This was increased to 23 by an independent assessor. Anaemia was associated with malnutrition ($n = 17$; $P = 0.049$) and an increased hospital stay (mean 25 days [SD 16] vs mean 12 days [SD 8], $P = 0.0125$; total 513 vs 144 bed days).

CONCLUSIONS Anaemia and poor nutrition are common and not recognised in vascular patients presenting with critical limb ischaemia. Anaemia is associated with and increased length of hospital stay.

KEYWORDS

Critical limb ischaemia – Anaemia – Malnutrition

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Anaemia is a common problem in surgical patients.^{1–3} Prevalence is reported from 5–78.5%.⁴ Anaemia is an independent risk factor for blood transfusion, peri-operative infection, mortality and a longer in-patient stay.^{1–8}

Two main types of anaemia affect surgical patients, iron-deficiency anaemia (IDA) and anaemia of chronic disease (ACD);¹² the latter is more common in chronically ill and hospitalised patients.^{19–21} ACD can be difficult to diagnose, often being regarded as a diagnosis of exclusion.²⁰ A key feature of ACD is a disruption of normal iron homeostasis initiated by a cytokine-mediated immune response,^{4–6} such as in chronic inflammatory disease, during infection or following surgery.

Patients with critical limb ischaemia (CLI) suffer from chronic inflammation, repeated infection, often undergo several invasive or operative treatments, and can have a protracted hospital stay. We hypothesised that, for these reasons, many patients with CLI may suffer anaemia, require blood transfusion and suffer from poor nutrition.

The aims of this study were to assess anaemia and nutritional status in patients presenting with CLI. Further, to assess

what laboratory markers determine the type of anaemia, and current transfusion practice.

Patients and Methods

Two series of vascular patients were assessed at a regional vascular centre, where five vascular surgeons serve a population of 450,000. Initially, a retrospective case series of 27 patients with CLI was performed over 4 months in 2007. Patient demographics, clinical details, transfusion status and in-patient laboratory haemoglobin values (Hb) were recorded. Data were prospectively collected over the subsequent 4 months on 32 patients admitted with CLI. In addition to the first series, we aimed to identify the cause for anaemia by haematological and chemistry markers (mean red cell volume [MCV], vitamin B₁₂, folate, serum ferritin, zinc protoporphyrin [ZnPP], reticulocyte count, creatinine, C-reactive protein [CRP], and glomerular filtration rate [GFR]). On admission, all patients should have their nutritional status assessed by a hospital protocol that involves records

of height, weight, body mass index (BMI) and a validated scoring system. The scoring system was divided into three sections (Table 1). Scores of 1–2 denoted mild nutritional deficiency, 3–5 moderate and >5 severe malnutrition. The authors (TR and MS) then reviewed the assessment with the ward dietician to assess if the nutritional assessment was performed and also accuracy of the score. Douglas score for risk assessment was also recorded for comparison.

For the purposes of this study, anaemia was defined as a laboratory haemoglobin concentration of less than 11.5 g/dl for females and 13 g/dl for males, values that were the lower limit of normal for each sex. Trigger index was defined as the Hb at which patients were transfused. Patients on dialysis or with known renal dysfunction (creatinine > 180 µmol/l) were excluded.

Statistical analysis

Data were entered into a Microsoft Excel spreadsheet (Microsoft Office Excel 2003, Microsoft Corporation). Results were reported as mean (SD) or median (range). Paired and unpaired *t*-tests, Mann–Whitney test, one-way analysis of variance (ANOVA) with post-test, and Kruskal–Wallis test with post-test (GraphPad

InStat; GraphPad Software, Inc., San Diego, CA, USA) were used as appropriate.

Results

Retrospective case series

In the retrospective case series of 27 patients, there were 16 men and 11 women. Average age was 68 years (SD 13.8). All underwent either operation (70%) or angioplasty (30%) with none undergoing both. Median length of stay was 14 days (range, 1–38 days), with a total of 399 hospital bed-days. On admission, 15 patients (56%) were anaemic with an average Hb of 2.5 g/dl (SD 1.7) below the lower limit of normal for the sex of the patients. Eleven patients (41% male) were not anaemic on admission with an average Hb of 1.9 g/dl (SD 1.1) above the lower limit of normal for the sex of the patients.

Ten patients (37%) were transfused a median of 2 units (range, 2–13 units), a total of 35 units. The average trigger Hb index was 8.4 g/dl (SD 0.8). Patients were transfused an average of 6 days (SD 6.2) after admission. Patients who were transfused had lower Hb on admission ($P = 0.0019$), and most were anaemic on admission (90%). Transfusion produced an average rise in Hb of 1.1 g/dl. Seventeen patients (63%) were not transfused; average admission Hb was 0.4 g/dl (SD 2.4) above the lower limit of normal for the sex of the patients. On average, their Hb fell 1.4 g/dl (SD 0.5) during admission (Fig. 1). Overall, at discharge, most patients were anaemic ($n = 23$; 83%).

Table 1 The scoring system

Body mass index (kg/m²)

> 20	0
18–20	2
< 18	3

Food intake^a

No	0
Yes	2
Not known	1

Unintentional weight loss^b

No	0
Up to 3 kg	1
More than 3 kg	2

Stress factor/illness severity^c

None	0
Moderate	1
Severe	2

Nutritional screening tool, scores (0–9) were repeated on a weekly basis.

^aHad the patient had decreased food intake over the last month, since last scoring, or if they were nil by mouth.

^bHad the patient unintentionally lost weight over the previous 3 months or since last assessment.

^cStress factor was moderate if: minor or uncomplicated surgery, minor infection, presence of chronic disease, CVA, any gastrointestinal disease. Major was: multiple injuries, pressure sores, severe sepsis, pancreatitis, malignant disease, major surgery or postoperative complications.

Figure 1 Mean haemoglobin fall in non-transfused CLI patients ($n = 17$) during their hospital stay. There was a significant difference in haemoglobin at admission and discharge ($P = 0.029$). Haemoglobin difference* is referred to as the difference between the laboratory haemoglobin concentration, and the lower limit of normal for the sex of the patient.

Table 2 Risk factors at admission of patients with critical limb ischaemia (*n* = 32)

Risk factor	<i>n</i> (%)
Diabetes mellitus	8 (26%) ^a
Smoking	23 (77%) ^b
Hypertension	20 (67%)
High cholesterol	16 (53%)
Previous MI/CVA	11 (37%)
Relevant past vascular history	22 (85%)

^aTwo patients (7%) were on insulin.^bAn average of 38 pack-years (SD 35) were smoked per patient.

Prospective case series

In the prospective case series of 32 patients, there were 21 men and 11 women. Average age was 75 years (SD 12). Ten patients underwent operation, seven angioplasty and two both. Overall median length of stay was 15 days (range, 3–77 days), with a total of 657 hospital bed-days. Admitting diagnosis was rest pain (21) or tissue loss (11); risk factors are given in Table 2.

On admission, 20 patients (63%) were anaemic. Anaemic patients had a lower average MCV than non-anaemic patients but only three patients had microcytosis (Table 3). Furthermore, anaemic patients had a higher CRP and a lower albumin level. When comparing other haematological markers by admitting diagnosis, there was no difference between the groups.

Douglas risk score was performed in most (21) with average score of 16 (SD 3). Eighteen patients were on regular opiate analgesia at admission. Nutritional assessment had been performed on 18 patients, height measured in 14

Table 3 Haematological markers at admission for anaemic and non-anaemic critical limb ischaemia patients (*n* = 32)

Haematological marker	Anaemic	Non-anaemic	<i>P</i> -value
MCV (fl)	89 (6.9)	95 (4)	0.0095*
Vitamin B ₁₂ (ng/l)	529 (308.5)	450 (84)	NS
Folate (µg/l)	611 (269)	559 (283.6)	NS
Ferritin (µg/l)	198 (155)	162 (179.5)	NS
ZnPP	77 (27.4)	52 (12.7)	NS
Reticulocyte count (10 ⁹ /l)	64 (43.9)	43 (0)	NS
CRP (mg/l)	72 [§] (61.8)	25 [§] (22.6)	0.0495*
Albumin (g/l)	33 (5.5)	40 (63)	0.0113*
Creatinine (µmol/l)	114 (47)	84 (22.7)	0.0579

Data are mean (SD). *Significant difference (*P* ≤ 0.05).[§]Above normal range. NS, not significant.

and weight in 15, BMI was calculated in 16 (although incorrectly in two). Whereas only seven patients had been scored undernourished, this increased to 23 on review with a dietitian (Fig. 2). Patients who presented anaemic were more likely to be malnourished (nutritional score > 3; *n* = 17; *P* = 0.049). Length of hospital stay was longer in those patients who presented with anaemia (mean 25 days [SD 16] vs mean 12 days [SD 8] *P* = 0.0125; total 513 vs 144 bed-days).

Discussion

In these two case series, we found that anaemia and malnutrition were common in patients presenting with CLI to hospital. Anaemic patients were more likely to be malnourished. Anaemia was further associated with increased hospital length of stay. Routine haematological markers did not define a cause for the anaemia, although a raised CRP may suggest ACD. Most were malnourished on admission. Many received blood transfusion during their hospital stay and most were anaemic on discharge.

Patients that were not transfused during hospital stay suffered a haemoglobin fall from admission to discharge. Although these case series did not assess blood loss at intervention, it did show that most anaemic patients underwent transfusion. If these patients could be identified prior to admission, the cause for anaemia could be assessed and treated and in-hospital blood transfusion may be reduced.

ACD is the most common anaemia of chronically ill and hospitalised patients.^{10,11} Patients with CLI suffer chronic inflammation from ulceration and gangrene;¹³ the data presented here suggest they consequently also suffer from anaemia of chronic

Figure 2 Nutritional score from nutritional screening tool in patients presenting with critical limb ischaemia. Series 1 represents the ward documented score and series 2 an independently assessed score.

disease. Various pathophysiological factors combined to cause ACD: (i) disruption in iron homeostasis; (ii) impairment of erythroid progenitor cell (EPC) proliferation and differentiation; (iii) decrease in the production and activity of erythropoietin (EPO); and (iv) a decrease in erythrocyte life-span.^{4-6,14}

Regarding the haematological investigations, most were non-diagnostic suggesting ACD. MCV, although lower, was not diagnostic. Only about half of elderly patients with an MCV below the normal range will have IDA and the majority of the remainder will have ACD.¹⁵ Serum ferritin levels are normally a good indicator of total body iron stores and are usually relatively stable.¹⁶ A serum ferritin level of < 12 µg/dl is considered a diagnostic for IDA.¹⁷ However, ferritin is an acute phase protein, and levels parallel the rise in acute phase plasma proteins such as CRP.¹⁶ The raised CRP seen in the anaemic patients here suggests that, in patients with CLI, measuring serum ferritin levels may be of limited use. In situations of iron deficiency, zinc is substituted for iron in the protoporphyrin ring, resulting in the formation of zinc protoporphyrin (ZnPP).^{18,19} Raised serum ZnPP in patients suffering from chronic inflammation usually indicates functional iron deficiency. However, no significant changes in the levels of ZnPP were seen, suggesting that these patients with CLI did not have IDA. The reticulocyte count rises in anaemia as a response to an increase in erythropoietin. A normal reticulocyte count in patients suffering from anaemia indicates either an impaired marrow function or an inadequate erythropoietin stimulus.²⁰ The anaemic patients assessed had a reticulocyte count within the normal range, which suggests an inadequate erythropoietin stimulus as seen in ACD.⁹⁻¹²

Data were also collected for nutritional status and Douglas score. The latter, a tool for risk assessment, is widely used and often acted on by nursing staff for pressure area care. However, it was clear from the results here that, although frequently malnourished, these patients were rarely properly assessed and none had nutritional input. The 2006 NICE guidance²¹ recommends simple initial assessment and referral to a multidisciplinary nutritional support team. These data suggest that nutritional status is poorly assessed on admission and, when assessed with a dietician, many patients could be assisted; further training in this areas may be required. We have since adopted a policy that all patients with CLI are started on nutritional supplements and reviewed by the nutritional support team.

The best treatment for ACD is treatment of the underlying disease.^{9,22,25} All patients with CLI seen here underwent intervention – either revascularisation or amputation. Although patients with CLI represent a small number of admissions ($n = 59$), they accounted for a significant vascular in-patient bed stay (1056 days). The data presented here high-light the need to look at every aspect of management of patients with CLI. This group of patients are frequently malnourished and anaemic. These illnesses also require treatment in addition to their vascular

disease. Management of anaemia may help to reduce their prolonged hospital stay.

Conclusions

Anaemia and poor nutrition are the normal situation in vascular patients presenting with critical limb ischaemia. Full haematological investigation and review by a dietician should be undertaken in all patients.

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