



Reducing Blood Transfusions in Primary Total Hip Replacement Patients: Effectiveness of Near-patient Testing and a Dedicated Preoperative Anemia Clinic*

Reduzindo as transfusões de sangue em pacientes com artroplastia total primária do quadril: A eficácia dos testes rápidos de Hb e uma clínica especializada em anemia pré-operatória

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Abstract

Objective Preoperative anemia in orthopedic patients is associated with higher allogeneic blood transfusion rates and poorer outcomes. Up to 25% of the patients listed for major orthopedic surgery have some degree of anemia. Good perioperative patient blood management is essential to reduce the sequelae of anemia and the need for transfusions. We assessed the efficacy of rapid near-patient testing in conjunction with a dedicated preoperative anemia clinic for screening and treating primary total hip replacement (THR) patients for anemia.

Methods A comparison of overall allogeneic blood transfusion rates was made for patients undergoing primary total hip replacement before and after the implementation of near-patient testing and of a dedicated preoperative anemia clinic over 1 year. A comparison was also performed between anemic patients who were referred to the clinic with those who were not referred. Preoperative hemoglobin levels, allogeneic blood transfusion rates and clinic treatment for 1,095 patients were reviewed.

Results There was a significant decrease in transfusion rates in patients undergoing primary THR from 10.0 to 6.2% ($p < 0.05$; χ^2 test) after the implementation of near-patient testing and of a dedicated preoperative anemia clinic pathway. The allogeneic

Keywords

- ▶ blood transfusion
- ▶ anemia
- ▶ arthroplasty, replacement, hip
- ▶ preoperative period

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blood transfusion rate for anemic patients who were treated in the clinic was 6.7% compared with 26.9% for patients who were anemic preoperatively but were not treated in the clinic ($p < 0.05$; Fisher exact test). On average, treatment in the pathway increased the hemoglobin of the patients by 20 g/L, from 104 g/L to 124 g/L ($p < 0.001$).

Conclusions Near-patient testing, in conjunction with a dedicated preoperative anemia clinic, reduces perioperative allogenic blood transfusion requirements for patients undergoing primary THR by providing rapid identification and effective treatment of preoperative anemia.

Resumo

Objetivo A anemia pré-operatória em pacientes ortopédicos, está associada a maiores taxas de transfusão de sangue alogênico, resultando em desfechos mais desfavoráveis. Até 25% dos pacientes encaminhados para cirurgia ortopédica de grande porte, apresentam algum grau de anemia. O controle adequado do sangue do paciente no perioperatório é essencial, a fim de reduzir as sequelas da anemia e a necessidade de transfusões. Avaliamos a eficácia do teste rápido, em conjunto com uma clínica especializada no tratamento da anemia pré-operatória, com o objetivo de detectar e tratar a anemia dos pacientes a serem submetidos a artroplastia total primária do quadril.

Métodos A comparação das taxas totais de transfusão de sangue alogênico, foi realizada em pacientes submetidos a artroplastia total primária do quadril, antes e depois da implementação dos testes rápidos e da clínica especializada no tratamento da anemia pré-operatória ao longo de um ano. Também foi feita uma comparação entre os pacientes com anemia, que foram encaminhados para a clínica, com aqueles que não foram encaminhados. Foram revisados os níveis de hemoglobina pré-operatória, as taxas de transfusão de sangue alogênico e o tratamento clínico em 1.095 pacientes.

Resultados Houve uma redução significativa nas taxas de transfusão, em pacientes submetidos à ATQ primária, caindo de 10,0% para 6,2% ($p < 0,05$, teste χ^2), após a implementação do teste rápido e da clínica especializada em anemia pré-operatória. A taxa de transfusão de sangue alogênico para pacientes anêmicos tratados na clínica foi de 6,7%, em comparação com 26,9% para pacientes anêmicos no pré-operatório, que não foram tratados na clínica ($p < 0,05$, teste exato de Fisher). Em média, o tratamento na clínica aumentou a taxa de hemoglobina dos pacientes em 20 g/L, passando de 104 g/L para 124 g/L $p < 0,001$.

Conclusões O teste rápido, juntamente com a clínica especializada no tratamento da anemia pré-operatória, reduziu a necessidade de transfusão de sangue alogênico perioperatório, em pacientes submetidos a artroplastia total primária do quadril, proporcionando uma identificação rápida e um tratamento eficaz da anemia pré-operatória.

Palavras-chave

- ▶ transfusão de sangue
- ▶ anemia
- ▶ artroplastia de quadril
- ▶ período pré-operatório

Introduction

The World Health Organization (WHO) defines anemia as an hemoglobin (Hb) concentration of < 120 g/L in nonpregnant women and of < 130 g/L in men.¹ Untreated preoperative anemia is associated with increased morbidity, mortality, length of stay,²⁻⁵ and a 3-fold risk of requiring allogeneic blood transfusion (ABT).⁶ Allogeneic blood transfusion is associated with its inherent risks, including infections, delayed wound healing, fluid overload, and transfusion-

related lung injury (TRALI).^{7,8} Studies have also linked ABT to prolonged hospital stay.⁹ Moreover, blood products are costly and are a limited resource. Therefore, addressing preoperative anemia makes sense from a clinical and health economic perspective.

An estimated 15 to 25% of patients listed for major elective orthopedic surgery have some degree of anemia preoperatively, and this may reach 80% in the postoperative period.^{10,11} Orthopedic surgery accounts for 10% of transfused red blood cells, with total hip replacement (THR) accounting

for 4.6%.¹² In 2017, the National Joint Registry recorded just over 105,000 THRs performed in England and Wales that year.¹³ Hip arthroplasty is, therefore, one of the most relevant fields for addressing preoperative anemia, since it often involves significant blood loss, and the time between listing and surgery is often long enough to detect and treat anemia. Moreover, an aging population means more hip arthroplasties in patients with increasing frailty and comorbidities, including anemia.

In 2011, the WHO endorsed Patient Blood Management (PBM) to optimize preoperative anemia and reduce unnecessary blood transfusions. The three sustaining pillars of PBM are management of preoperative anemia, minimization of blood loss, and rational use of allogeneic blood products.¹⁴ Patient Blood Management has been shown to improve outcomes by reducing transfusion rates, length of stay, morbidity, and readmission rates.¹⁵ Numerous health organizations support preoperative correction of anemia. A report by the WHO on the availability, safety and quality of blood products recommends that every reasonable measure should be taken to optimize¹⁶ the blood volume of the patient preoperatively, while the UK Department of Health recommends that policies should be in place for the identification and treatment of preoperative anemia in hospitals.¹⁷

The present paper describes our preoperative strategy of PBM for screening and treating anemic patients listed for elective primary THR using rapid near-patient testing in conjunction with a dedicated preoperative anemia clinic. We analyzed retrospectively ABT rates for patients undergoing primary THR before and after the implementation of near-patient testing and of the preoperative anemia clinic. We believe this rapid screening and dedicated treatment pathway is the first of its kind for patients undergoing hip replacement surgery.

Materials and Methods

At the time of listing for a primary THR, all patients undergo a near-patient Hb measurement (HemoCue, ►Fig. 1) in the orthopedic clinic, which provides an instantaneous reading and, therefore, rapid identification of anemia. A low result prompts further investigation with a laboratory full blood count if the Hb of the patient is low (< 130 g/L for men or < 115 g/L for women). The patient is also started on oral iron therapy and referred to the Rapid Access Preoperative Anemia Clinic (RaPAC), and a letter explaining the findings and treatment is also sent to the general practitioner of the patient. Surgery is put on hold until the anemia of the patient is optimized (►Fig. 2). In our department, all patients should undergo Hb screening with instant results using the HemoCue at the time of listing in the orthopedic clinic. Unfortunately, some patients were missed and, subsequently, were not treated on this pathway. These omitted patients served as a control group, thus providing an opportunity for comparing the efficacy of the pathway, albeit in a nonrandomized manner.

In the anemia clinic, a full history, examination, and additional blood tests are performed. Patients undergo a



Fig. 1 Near-patient hemoglobin testing device.

full blood count including reticulocyte count and Reticulocyte Hemoglobin Content (CHr), serum iron, ferritin, transferrin levels, transferrin saturation, B12, folate, kidney, liver and thyroid functions tests, serum LDH and C-reactive protein as a marker of inflammation. If the history is suggestive of any neoplastic red flag symptoms, further appropriate imaging such as endoscopy or computed tomography (CT) is ordered.

These tests help to determine the cause of anemia in the preoperative patient, which can be complex, and guide further treatment. Most patients have iron deficiency anemia (IDA), which may be due to absolute or functional iron deficiency. In absolute iron deficiency, iron stores are depleted from either inadequate dietary intake, inadequate absorption, or increased loss from occult bleeding. In contrast, functional iron deficiency is usually present in patients with chronic inflammation and is secondary to abnormal iron metabolism. Inflammation causes an upregulation of hepcidin, which leads to reduced intestinal absorption and promotes sequestration of iron in the liver and by macrophages; this is commonly referred to as anemia of chronic disease. The next most common cause of preoperative anemia is B12/folate deficiency, which is often secondary to reduced dietary intake, malabsorption such as parietal anemia, or to the use of certain drugs such as methotrexate.

Depending on the cause of anemia, comorbidities, and on the response to the oral iron therapy, a target Hb level is set. This is most often above the threshold for anemia; however, if there are significant comorbidities such as cardiac impairment, ischemic heart disease, cerebrovascular disease, advanced chronic kidney disease, or severe anemia of chronic disease, this may not be safe or achievable, and the individual

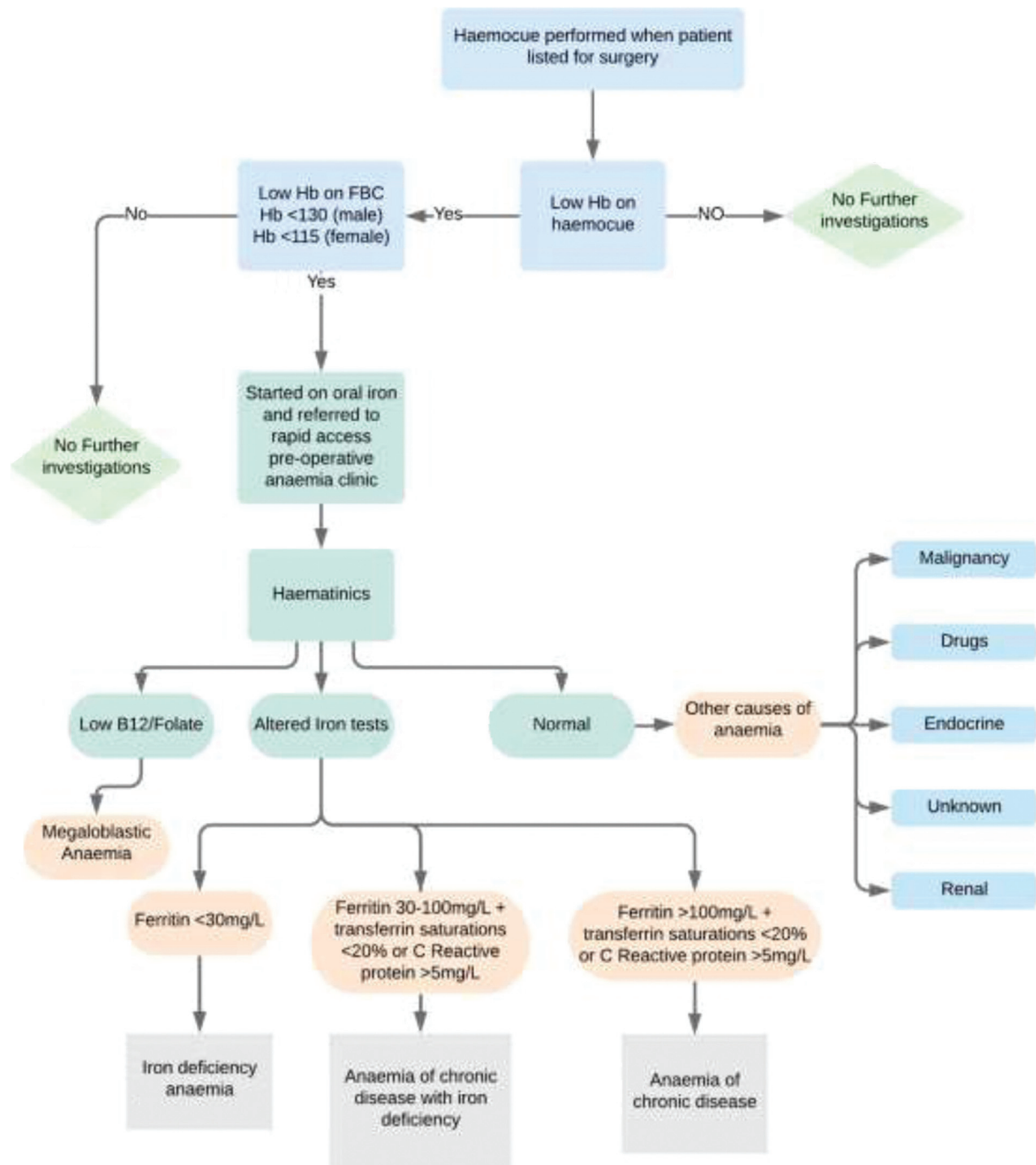


Fig. 2 Preoperative anemia diagnosis.

target Hb of the patient may be lowered. Treatment options include continuing oral iron, intravenous iron when the response to oral iron is suboptimal, or CHr remains low, or a short course of erythropoietin with oral/parenteral iron therapy. Patients who responded well to the oral iron therapy, who did not have any red flag symptoms, and were no longer anemic were discharged from the clinic and advised to continue oral iron therapy until 3 months postsurgery.

The patients who were still anemic were either given further oral iron treatment if there had been some improvement or were started on parenteral (IV) iron if the scheduled surgery date was within 4 weeks or if the patient could not

tolerate oral iron. Patients requiring parenteral iron attended as a day-case procedure. Patients who had anemia of chronic disease and those not responding adequately to iron therapy were treated with a short course of erythropoietin, which typically consisted of weekly doses over 3 to 6 weeks (median: 4 weeks) to reach the target Hb level.

The project was registered as an audit with the trust's audit department. The preoperative anemia clinic was set up in 2011, and all patients who underwent primary THR in 2009 and 2017 were identified from the trust's NJR database. From a list of patients who attended the preoperative anemia clinic, all patients who underwent primary THR were

identified. The hospital blood transfusion department was able to provide the transfusion data for all patients who underwent primary THR in our institution. We cross-analyzed the lists to identify patients who required an ABT within 2 weeks of their operation. The Integrated Clinical Environment (ICE) system of the hospital was used to determine the preoperative Hb levels of all patients in the study groups undergoing THR; therefore, to identify patients who were anemic preoperatively. The statistical analysis for the comparison blood transfusion rates was performed using the Chi-Square test or the Fisher Exact test; comparison for Hb levels, age and ASA between groups was performed using the Mann-Whitney U test.

Our trust policy advises ABT if Hb levels drop to <70 g/l, or to <80 g/l if there are significant cardiac comorbidities or if the patient is symptomatic. There were no changes in blood transfusion policy between 2009 to 2017. Dalteparin as an inpatient followed by 6 weeks of aspirin 150 mg daily was commonly used for postoperative venous thromboembolism (VTE) prophylaxis, unless the patients were already on regular anticoagulants or deemed to be at higher risk of VTE, in which

case prophylactic dalteparin was continued. Tranexamic acid 15mg/kg pre- and postoperatively was routinely given to patients undergoing hip replacement surgery, unless there were contraindications. The implant of choice for primary THR in our trust is the cemented Exeter femoral stem (Stryker) and the Contemporary cemented acetabular cup (Stryker) inserted by the posterior approach to the hip, and this remained unchanged during the study period. There were also no significant changes in the consultant surgeons performing primary THRs in our institution during this period.

Results

Before the introduction of the preoperative anemia clinic, our trust performed 598 primary THRs in 2009 and 497 in 2017. Sixty patients required ABTs in 2009 compared with 31 in 2017. There was a significant reduction in ABT rates for patients undergoing primary THR, from 10.0 to 6.2% ($p < 0.05$; χ^2 test) from 2009 to 2017.

A total of 110 of the 598 patients in 2009 (18.4%) undergoing a primary THR had Hb < 130 g/L (male)s or Hb < 115

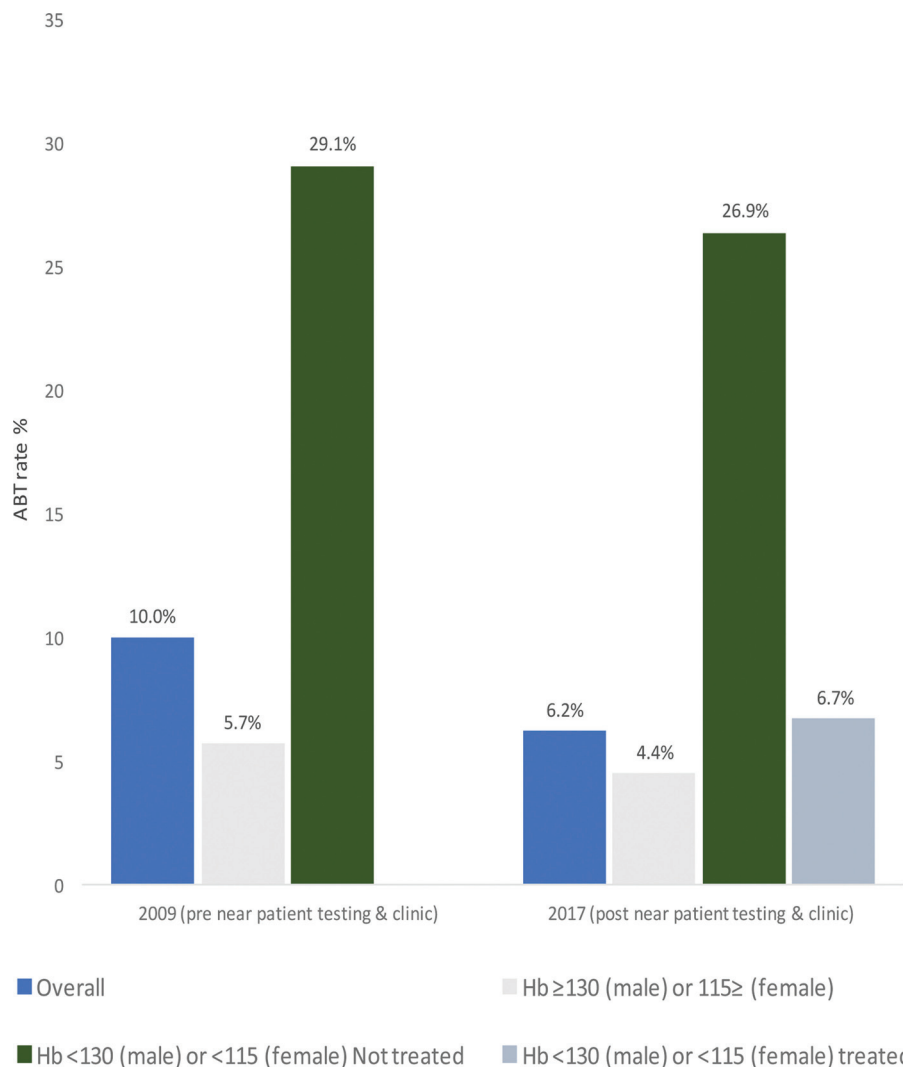


Fig. 3 ABT rates for primary THR patients before and after implementing near-patient testing and a dedicated anemia clinic.

Table 1 Comparing characteristics and outcomes between different anemic groups

Referred to anemia clinic	Yes		No		
Number	30		52		
Mean age (years old)	72		72		
Median ASA	3		3		
Gender	Male	Female	Male	Female	
Number	12	18	23	29	$p = 0.71$
Mean Hb on referral to clinic (g/L)	115	98	Not referred		
Mean preoperative Hb (g/L)	124	124	117	108	
Overall mean preoperative Hb (g/L)	124		112		$p < 0.001$
Mean increase in Hb (g/L)	20		N/A		
Mean Hb pre-transfusion (g/L)	86		85		
Allogenic blood transfusion rate	2 (6.7%)		14 (26.9%)		$p < 0.05$

g/L (females), of which 32 (29.1%) required a blood transfusion, accounting for 53.3% of ABTs for primary THR that year. The transfusion rate in patients with Hb \geq 130 g/L (males) or \geq 115 g/L (females) was of 5.7% (**Fig. 3**).

In 2017, 82 out of 497 (16.5%) patients had Hb $<$ 130 g/L for males and $<$ 115 g/L for females at the time of listing. Thirty patients (36.5%) were referred to the preoperative anemia clinic (mean age: 72 years old; median ASA: 3) and 52 (63.4%) were not referred (mean age: 72 years old; median ASA: 3) (**Table 1**). Fourteen out of the 52 (26.9%) patients not seen in the clinic required a blood transfusion, accounting for 45.2% of blood transfused in primary THR patients that year. Only 2 of the 30 patients (6.7%) seen in the clinic required a blood transfusion ($p < 0.05$; Fisher exact test). The transfusion rate in the rest of the nonanemic population was of 4.4%. The mean preoperative Hb concentration was 112 g/L in the group not treated in the anemia clinic compared with 124 g/L for those treated in the anemia clinic ($p < 0.001$; Mann-Whitney U test). Preoperative Hb was considered as the latest Hb before surgery; this was, on average, 11.4 days before surgery for the group not treated and 11.0 days for the group treated in the clinic. On average, the treatment in the clinic led to a significant increase in Hb of 20 g/L, from 104 g/L to 124 g/L ($p < 0.001$).

Out of the 30 patients treated in the clinic, 19 were treated with oral iron, 3 required parenteral iron, 2 had erythropoietin therapy, and 6 were treated with erythropoietin and iron. The majority of the patients ($>$ 60%) responded to oral iron alone. Intravenous iron infusion was typically reserved for patients who had absolute or functional iron deficiency, and either could not tolerate or did not respond to oral iron. When patients were given intravenous iron, a single fixed dose of 1000 mg of either Monofer (ferric derisomaltose), or Ferrinject (ferric carboxymaltose) was administered.

A cost-effectiveness analysis has not been included in the present manuscript and will be the subject of a separate publication. We have, however, included a brief analysis for comparison. Given a significant cost reduction in erythropoietin preparations in the last decade, the average cost of 4

doses of erythropoietin alfa (Eprex) used in this cohort was £180 for a course of 10,000 units weekly for a median of 4 weeks.¹⁸ The cost of a single 1000 mg dose of intravenous iron is \sim £160.¹⁹ Only 3 patients received a single dose of intravenous iron at a total cost of £480, and 8 patients received Eprex, with an average cost of £180 per patient, resulting in a total cost of Eprex treatment of £1,440. The total cost of IV iron and Eprex in this cohort was \sim £1,920. The cost of 2 units of packed red cells in the UK is £ 332,²⁰ excluding additional costs of cross-matching and administration. Based on a transfusion rate of \sim 27% in the control group of patients who were anemic preoperatively, it is estimated that red cell transfusion of \sim 12 units amounting to £1,992 was avoided, thus achieving cost neutrality. This does not, however, consider cost savings from reduced hospital length of stay, staffing and equipment costs for blood administration, and savings from reduced complications secondary to anemia. Since the majority of the patients ($>$ 60%) in this cohort responded well to oral iron alone, we believe judicious and selective use of intravenous iron and/or of erythropoietin can be cost-effective when larger numbers are involved.

The average surgical time for a primary THR in 2009 was 86 (13) minutes compared with 89 (15) minutes in 2017 ($p > 0.05$). Those treated with erythropoietin in the clinic had their dates for surgery confirmed before starting treatment; this offered further protection from delays and cancellations. The clinic also provided the added benefit of providing patients with a physician review well in advance of their surgery, allowing early investigation and treatment of medical problems that could have delayed or cancelled the surgery.

Discussion

The negative impact of preoperative anemia on postoperative morbidity and mortality, length of stay, and burden on hospital resources has been well documented across surgical specialties over time.^{5,21} Preoperative anemia is a significant

modifiable risk factor for ABT requirement in the surgical patient and is also linked to increased other postoperative complications, including infections, strokes, cardiac events, death, and wound problems.^{22,23} Previously, 'top-up' transfusions were performed before surgery to boost the Hb levels of the patient; however, there is no evidence to support benefit to the patient nor a reduction in total perioperative transfusion requirements.²⁴ Moreover, this practice exposes patients to the risks of ABT and is an irresponsible use of a costly and limited health resource.

The present study has shown that a disproportionate number of transfusions is required by patients who have untreated preoperative anemia. In an ideal situation, patients should have their Hb levels checked by their general practitioner on referral, but due to time and financial constraints, this may not always be possible. The setup we described achieves rapid identification of anemic patients using a near-patient testing device (Hemocue) and effective treatment through a dedicated preoperative anemia clinic. The device model we used for screening is the Hemocue 201+, which has an accuracy of $\pm 1.5\%$ when compared with the international reference method for Hb (the ICSH method), as stated by the manufacturers.²⁵ The device has also shown excellent results when used as a screening tool for anemia²⁶ and when compared with other point-of-care Hb testing devices on the market.²⁷ Other studies have investigated the precision of the Hemocue device and reported a good correlation between instant results from this handheld device and formal laboratory testing.²⁸ In our case, the Hemocue was only used as a screening tool as patients proceeded to have formal laboratory tests before being seen in the clinic.

We have reported a retrospective study with no randomization between anemic patients for treatment or no treatment; however, the two groups were not dissimilar in terms of age, gender, and ASA. Nevertheless, the present study did provide significant evidence that rapid screening and a dedicated anemia clinic are effective in reducing transfusion requirements in primary THR patients. Interestingly, iron therapy was suitable for the majority of patients seen in the clinic, suggesting that treatment for anemia is often inexpensive and uncomplicated; the clinic was also able to recognize those patients who needed more complex treatment in the form of either parenteral iron and/or erythropoietin.

The UK National Comparative Audit of Blood Transfusion in 2016²⁹ reported that only 65% of THR patients who required a postoperative transfusion had their Hb levels checked at least 14 days before surgery. In our trust, only 36% of patients who met the criteria for referral to the preoperative anemia clinic were referred and treated. Patient compliance, however, was excellent, and all patients referred to the RaPAC attended and complied with the treatment. We hope to address the low screening and referral rate by including a box for inputting the near-patient Hb result on the listing form once surgery has been decided in order for it to serve as a prompt for the surgeon. We hope these changes, along with feedback to surgeons who are noncompliant with the screening and referral pathway, will further reduce transfusion requirements in our primary THR patients.

Such shortcomings, however, exemplify the real-world experience of suboptimal compliance amongst busy clinicians and highlights the importance of regular reminders of the benefits of the service, which are now proven.

Conclusion

A growing population with increasing life expectancy will mean more primary hip arthroplasties in older patients with increasing comorbidities, including anemia. Elective hip arthroplasty has the benefit of patients being listed months before surgery, allowing enough time for anemia to be detected and treated appropriately, thus reducing transfusions and the adverse sequelae associated with preoperative anemia and ABTs. We have described a rapid screening and treatment pathway using near-patient testing and a dedicated anemia clinic that improves patient outcomes, which is an excellent strategy for any hospital aiming to improve its preoperative patient blood management strategy and to reduce the demand for blood transfusions.

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Conflict of Interests

Dr. Chatterji reports personal fees from Consulting fees DePuy (Johnson & Johnson), outside the submitted work.

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