


Preoperative patient blood management during the SARS-CoV-2 pandemic

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Remote pathways and priorities for care in pandemic times

The COVID-19 pandemic, caused by the coronavirus SARS-CoV-2, has forced examination of much of routine healthcare provision in the UK, and necessitated changes in practice to protect patients from the virus while continuing to deliver high-quality care for their other health needs. This has been highlighted by the challenges in provision of elective surgical services while SARS-CoV-2 remains prevalent in communities. NHS providers have moved from preoperative assessment pathways routinely involving face-to-face appointments to remote (telephone, digital or combination) assessments.^{1,2} Telehealth-based solutions provide an innovative option to provide patient care during pandemic times while helping prevent and contain the spread of infection.³ They are also convenient for the patient and medical staff and are likely to become part of routine care in the future. This reduction in face-to-face contacts means there is a pressing need to rethink how best to prepare patients for elective surgery, ensuring comprehensive assessment is performed within the limitations imposed by pandemic-related changes to working practices. It is also an opportunity to review the evidence for best care to evaluate the benefit of certain aspects of what may have become routine practice in consideration of risk balance to the patient.

In designing and redesigning clinical pathways, the following general principles should be applied:

1. Minimise the number of exposure events
 - a Only carry out interventions with clear or proven benefit
 - b Combine interventions wherever possible, for example, blood tests at the time of any face-to-face outpatient consultation or radiology test, or coincident with SARS-CoV-2 screening swabs; carry out interventions during inpatient stay to avoid readmission

- c Consider oral treatments rather than parenteral treatments that necessitate a healthcare setting visit
 - d Reduce length of hospital admission (and therefore exposure) by application of evidence-based patient blood management (PBM) interventions.

2. Minimise exposure risk during interventions using personal protective equipment (PPE), and COVID secure areas.

Patient blood management

Surgical PBM has become standard of care over the last decade and involves preoperative, operative and postoperative phases, to manage anaemia, minimise blood loss and ensure appropriate transfusion practices, with benefits for both patient outcomes and the blood supply chain. Appropriate use of blood is critical to mitigate the negative impact of the pandemic on blood collection and resulting blood stocks at a time of great challenge for blood services.⁴ A systematic review and meta-analysis of 393 randomised controlled trials ($n = 54\,917$) showed that PBM interventions reduced exposure to allogeneic blood components, length of stay and intensive care usage. In a network meta-analysis of the randomised controlled trials most of the effects were explained by the use of tranexamic acid and restrictive transfusion triggers; there was less additive effect of other preoperative interventions.⁵

This Good Practice Paper (GPP) reviews the aspects of preoperative PBM and how they may be implemented in the setting of remote assessment pathways. The body of evidence which informs the recommendations made in this GPP is from the 'pre-COVID' era where current limitations on face-to-face contact were not an issue. This paper identifies best practice and offers solutions as to how to adapt practice to ensure patients continue to benefit from maximal PBM in spite of the changes to preoperative pathways. In some instances, practice will be unchanged, for example the need for a clear perioperative PBM plan is also crucial in the non-pandemic setting. Other recommendations are modified to

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accommodate pandemic-enforced changes in practice, for example, those relating to preoperative investigations. It is intended that this guidance is read in conjunction with other British Society for Haematology (BSH) guidance on the topics of diagnosis and management of preoperative anaemia⁶ and perioperative management of anticoagulation and antiplatelet therapy.⁷ The following aspects of care are discussed:

1. An assessment of the patient
 - a Preoperative anaemia
 - b Their risk of bleeding
 - i History of abnormal bleeding in response to haemostatic challenges
 - ii Antiplatelet therapy
 - iii Anticoagulant therapy
 - c Their tolerance of postoperative anaemia
2. An assessment of the likely blood loss at surgery incorporating
 - a The nature of the procedure (e.g. open surgery vs minimal access surgery)
 - b Need for anticoagulant therapy
3. Postoperative pathway
 - a Transfusion plan
 - b Anticoagulant and antiplatelet therapy
 - c Postoperative adjunct therapies for anaemia

Diagnosis of anaemia

Preoperative anaemia is common, affecting 10–15% of patients before elective orthopaedic surgery,⁸ a third of those undergoing abdominal surgery and half of those undergoing colorectal surgery.⁹ Several large database analyses have associated preoperative anaemia with worse patient outcomes with regard to postoperative complications, morbidity and mortality.^{10,11}

The most common cause of anaemia is absolute, or classical iron deficiency due to nutritional deficiency, reduced iron uptake or blood loss.¹² Absolute iron deficiency results in reduced ferritin levels, with low circulating iron, raised total iron binding capacity (TIBC) and reduced transferrin saturation (TSAT or iron saturation).

It is necessary to distinguish anaemia associated with absolute iron deficiency, that is likely to respond to iron replacement therapy, from anaemia of chronic disease associated with functional iron deficiency (FID). Functional iron deficiency is characterised by low circulating iron levels and TSAT, with normal or reduced TIBC and normal or increased serum ferritin levels. Systemic markers of inflammation C-reactive protein (CRP) may also be elevated.

The diagnosis of anaemia necessitates a blood test, and the potential for additional SARS-CoV-2 exposure. Testing in

advance of surgery should therefore be limited to those patients in whom it is likely to be of benefit with regard to their surgery. Screening for anaemia should be undertaken in all patients who are themselves high risk or those undergoing major surgery or in whom significant blood loss may be anticipated.¹³ It should not be undertaken in those who are undergoing minor or intermediate surgical procedures, or in patients who are otherwise well and in whom anaemia would not normally prevent or delay surgery, nor affect the outcome of surgery. Where waiting times for surgery are anticipated to be prolonged, early identification and treatment of anaemia will allow the patient to proceed directly to surgery when a slot becomes available. This may be achieved through close liaison with primary-care teams to enable timely investigations.

Patients may have had recent blood tests for other purposes and where these are present, acceptable, and the patient remains clinically stable, repetition may not be necessary. These tests may have been performed by their general practitioner as part of routine care or for instance in the case of cancer surgery in their pathway before operation. Coordination with other health care providers will minimise duplication. Studies in healthy volunteer blood donors suggest haemoglobin results remain steady even after a prolonged inter-test period of up to two years, suggesting that in otherwise healthy patients undergoing elective surgery, it is reasonable to use historic results to assess for anaemia.¹⁴ Where blood tests are required, these should be carried out as early in the surgical pathway as possible to allow adequate time for interpretation and effective intervention in those in whom anaemia is identified. Coordination between departments is critical, as such opportunities may be in diverse areas, for example, radiological investigations or appointments for unrelated problems.

To avoid multiple visits for blood tests, blood for all diagnostic tests should preferably be taken during one visit. Where laboratory systems allow, automatic reflex testing based on the initial haemoglobin and red-cell indices will provide the relevant diagnostic tests with the minimum of delay, and avoid unnecessary tests. Where this is not possible, samples may still be taken together and additional testing requested manually on the samples held. Alternatively, requesting all diagnostic tests 'up front' will ensure that results are available without delay but may incur additional cost and use of resources.

In the preoperative setting, tests must be directed at detection of treatable causes of anaemia, for which effective interventions can be delivered. In the first instance this should include as a minimum full blood count, renal and liver profile. Where there is anaemia associated with a normal or low mean corpuscular volume (MCV) and/or mean corpuscular haemoglobin (MCH), additional diagnostic tests should be directed at diagnosis of iron deficiency and anaemia of chronic disease and include ferritin, iron studies (serum Fe, TIBC, TSAT) and inflammatory markers. Where the MCV is

raised, B12 and folate assays should be requested. In most circumstances it is out with the scope of preoperative assessment to investigate and treat anaemia due to other causes and referral for management will be necessary. Further testing can however be undertaken at this stage to prevent the need for further blood tests and infection risk. Consideration should also therefore be given to completion of a full anaemia screen where a simple deficiency is not found. This should include the addition of: thyroid stimulating hormone (TSH), a haemolysis screen (lactate dehydrogenase, reticulocytes, blood film, haptoglobin and direct antiglobulin test) and immunoglobulins. Pathways and individual responsibilities should be agreed for follow-up, particularly for patients for whom the cause of anaemia remains undiagnosed or is found to be unrelated to the reason for surgery. This may require onward referral to a haematologist, gastroenterologist or gynaecologist as indicated, as preoperative assessment clinics will not have the necessary expertise to pursue a diagnosis in such cases.

Existing national guidance and local maximum blood ordering schedules (MSBOS) should be followed when determining which patients should have samples taken for group and screen or cross match. Where these are necessary, they should be taken at the same time as other interventions as far as is possible. The recommendation for isolation for 14 days before surgery during the pandemic¹⁵ (though in some cases shorter preoperative isolation may be deemed appropriate in accordance with local public health guidance) necessitates that transfusion samples be taken on admission for surgery where this is required.

Recommendations

- **Perform anaemia screening and investigation only where this is justified by national guidance, local MSBOS or clinical need (2B)**
- **Take blood tests as early in the pathway as possible to allow effective intervention (1C)**
- **Take all diagnostic blood tests in one session to avoid further visits (2B)**
- **Do not perform routine follow-up tests that require additional visits, unless these will alter decision-making (2B)**
- **Patients found to have unexplained iron deficiency require referral for investigation (1B)**
- **Take group and screen or crossmatch samples (when required) at the time of admission for surgery to comply with preoperative isolation requirements (2B)**

Treatment of anaemia

When anaemia is identified, this should be investigated and managed accordingly. Patients should be enrolled and managed within clinical trials where possible; however, trial activity has been significantly curtailed during the pandemic, and the

added infection risk incurred due to trial-related hospital attendances must be considered when discussing such options with the patient.

Those patients with iron deficiency should be treated, in the preoperative setting as in any other setting. If time allows then a course of oral iron can be effective and does not require hospital attendance. When oral iron is not tolerated, or found to be ineffective, intravenous iron can be used though this will require a hospital attendance and associated exposure risk. The Cochrane review on the use of iron therapy to treat anaemia has recently been updated.¹⁶ One hundred and twelve randomised controlled trials (RCTs) totalling 22 169 patients were included. Overall, iron therapy was efficacious in increasing haemoglobin levels and reducing need for blood transfusion. However, patient outcomes were heterogeneously reported.

The management of surgical patients in whom the cause of anaemia has not been determined is less clear. The PREVENTT trial¹⁷ randomised 487 anaemic patients undergoing major abdominal surgery at multiple UK sites to receive intravenous iron (ferric carboxymaltose, 1 000 mg) or placebo (saline) a median of 15 (12–22) days preoperatively. No diagnostic process was mandated before randomisation. Intravenous iron was efficacious to increase haemoglobin [mean difference, 4.7 g/l; 95% confidence interval (CI), 2.7–6.8] but did not result in a reduced need for blood transfusion (risk ratio, 1.03; 95% CI, 0.78–1.37; $P = 0.84$). There were no differences between the groups in postoperative complications, hospital stay or days alive and out of the hospital at 30 days. Secondary results from PREVENTT showed significant differences in patients after surgery and on discharge from hospital. The intravenous iron group had significantly higher haemoglobin concentrations at eight weeks following surgery (mean difference, 10.7 g/l; 95% CI, 7.8–13.7), and re-admission to the hospital following surgery was significantly less likely; 31 (13%) vs 51 (22%), risk ratio, 0.61; 95% CI, 0.40–0.91, 38 in the intravenous iron group vs 71 in the placebo group (rate ratio, 0.54; 95% CI, 0.34–0.85). This study indicates that anaemic patients who do not have confirmed iron deficiency should not be treated with empirical intravenous iron.

The use of a combination of erythropoietin and intravenous iron to treat preoperative anaemia in patients undergoing non-cardiac surgery has been the subject of a number of trials reviewed recently by Cochrane.¹⁸ Conclusions were limited by the quality of evidence, but suggest that administration of recombinant erythropoietin plus iron reduced the risk of red-cell transfusion and when erythropoietin was administered at higher doses, haemoglobin levels were increased. No differences in length of hospital stay or adverse events were identified but further RCTs are required to fully assess this treatment approach.

Novel approaches during the inpatient stay that may benefit the patient should be considered. In the setting of cardiac surgery, Spahn randomised 505 patients with anaemia or

iron deficiency to a combination of 20 mg/kg ferric carboxymaltose, 40 000 U subcutaneous erythropoietin alpha, 1 mg subcutaneous vitamin B12, and 5 mg oral folic acid or placebo on the day before surgery.¹⁹ The primary end-point demonstrated a reduction in the median number of blood transfusions during the first seven days [odds ratio (OR) of 0.70 (95% CI 0.50–0.98)]. However, there was no difference in patient-reported end-points of postoperative complications or length of hospital stay. Perioperative intravenous (IV) iron in non-anaemic patients undergoing cardiac surgery has been shown to result in reduced postoperative anaemia and has the potential to reduce contact with healthcare settings during the postoperative period, reducing potential exposure events.²⁰

Following treatment, response assessment must be undertaken. Ideally this should not incur an additional potential exposure event, and should be undertaken at the same time as another mandatory intervention whenever possible. A decision should be made at the diagnosis of anaemia how this test will be done and whether it will affect the decision to proceed to surgery. Where the decision is made to proceed to treatment regardless of the effectiveness of the treatment, and there is little or no opportunity for additional treatment, there would be little justification for an additional blood test before the day of surgery.

Recommendations

- **Patients with preoperative anaemia should be treated within a clinical trial where possible (1C)**
- **Individualised treatment plans should be formulated based on the results of investigations of anaemia (2B)**
- **Generic treatment with intravenous iron should not be offered to all anaemic patients preoperatively (1A)**
- **Patients diagnosed with absolute iron deficiency anaemia should be treated with iron replacement. Oral therapy should be offered first line to minimise the need for hospital attendance (1B)**
- **Assessment of response to treatment should be performed at the time of admission for surgery to assess whether the desired effect has been obtained and to inform peri- and postoperative management (2C)**

Minimising blood loss — preoperative considerations

When considering maximising preoperative PBM interventions while minimising patient face-to-face contact, the preoperative elements of the second pillar of PBM, minimising blood loss, gain added importance. Many factors which contribute to a patient's bleeding risk can be readily assessed by history taking which can be undertaken remotely. A review should be performed of the patient's medical notes and electronic records. A management plan to modify features identified in the history which may increase a patient's bleeding

risk can then be formulated and communicated to the patient, the operative team and primary care prior to the planned surgery.

The patient's past medical history should be reviewed including any personal or family history of inherited bleeding disorders. Conditions which may increase bleeding risk, for example renal or liver impairment, should also be considered. National Institute for Health and Care Excellence (NICE) Guidance recommends blood tests to assess haemostasis should not be performed routinely, but should be considered in patients with chronic liver disease.¹³ The optimal method for screening for bleeding disorders in the preoperative population is not well defined, though this practice is endorsed by national and international guidelines.^{21,22} The International Society on Thrombosis and Haemostasis (ISTH) bleeding assessment tool (BAT) aims to identify people with inherited bleeding disorders (including mild disorders) by using a questionnaire to identify a personal history of non-trivial bleeding.²³ While this tool standardises the evaluation of bleeding symptoms, it may be lengthier and more detailed than is required in the preoperative setting but could be employed if initial screening questions raised concerns.

Modifiable risk factors for excess bleeding should then be considered, with particular attention paid to medications, namely antiplatelet agents, anticoagulants and other medications which may increase bleeding risk, for example NSAIDs. A comprehensive review of the perioperative management of these medications was published as a BSH guideline in 2016.⁷ A risk assessment should be undertaken, considering the indication for the drug, the bleeding risk associated with the procedure, and the risks associated with temporary discontinuation of relevant medications in order to formulate a patient- and procedure-specific plan. The need for bridging therapy for patients on therapeutic anticoagulation should be considered, and its requirement (or not) must be documented. It should be noted that bridging therapy is associated with increased postoperative bleeding rates, while placebo was non-inferior to low-molecular-weight heparin bridging therapy for the prevention of arterial thrombotic events in patients with atrial fibrillation anticoagulated with warfarin for stroke prevention.²⁴ Bridging therapy should therefore be reserved for patients at highest risk of thrombotic events during an interruption to anticoagulation.⁷

The antifibrinolytic drug tranexamic acid has been demonstrated to reduce blood loss and blood transfusions when used to treat patients undergoing orthopaedic surgery²⁵ and cardiac surgery²⁶ with a recent meta-analysis confirming these effects. Data from these studies are reassuring with respect to rates of thrombotic events. NICE guidance recommends its use when total surgical blood loss (which may exceed measured blood loss) is anticipated to be more than 500 mL.²⁷ The planned use of perioperative tranexamic acid should be documented following the remote assessment.

For completeness, the perioperative PBM plan should also document whether intraoperative cell salvage is to be used as

well as plans for monitoring, and correction of, perioperative body temperature and ionised calcium to help minimise risk of coagulopathy and any particular recommendations regarding patient positioning to reduce blood loss. Transfusion thresholds for red-cell transfusion should also be documented. The body of evidence supporting the safety of restrictive thresholds continues to grow,^{28,29} and these thresholds should be adopted unless there is a clear contraindication to their use. The patient should be supplied with information regarding the transfusion process, risks and benefits, alternatives to transfusion which will be considered and ultimately consent for blood transfusion should be obtained during the preoperative assessment.³⁰

Recommendations

- **Remote preoperative assessment should include assessment of the following:**
 - a **Bleeding history (1C)**
 - b **Drug history for anticoagulant or antiplatelet agents and the indication for use (1C)**
- **Coagulation screen blood tests should not be performed unless there is a history suggestive of a bleeding disorder, or a comorbidity associated with increased bleeding risk (1B)**
- **A clear perioperative patient blood management plan should be documented which includes**
 - a **When, relative to the operation, any medications should be discontinued (2B)**
 - b **When, relative to the operation, discontinued medications should be restarted (2B)**
 - c **If bridging therapy is indicated, and how it is to be managed (2C)**
 - d **If tranexamic acid is not to be administered (1A)**
 - e **If cell salvage is to be used (2C)**
 - f **Plan for perioperative monitoring of body temperature, ionised calcium levels and patient positioning to minimise blood loss (2C)**
 - g **Transfusion triggers (1A)**
- **The plan for discontinuation and restarting of medications must be communicated to the patient and to primary care (2C)**

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Author contributions

All the authors were involved in the formulation and writing of the manuscript, as well as approval of its final version.

Conflict of interest

The BSH paid the expenses incurred during the writing of this Good Practice Paper. All the authors have made a declaration of interests to the BSH and Task Force Chairs which may be viewed on request. AK has in the past five years received speaker's fees and expenses related to conference attendance, as well as consultancy fees, from Vifor Pharma and Pharmacosmos (both are pharmaceutical companies that manufacture an IV iron preparation). TR has received speaker's fees and expenses related to conference attendance from Pharmacosmos and Vifor Pharma. TR is a director of The Iron Clinic Ltd. The following members of the writing group have no conflict of interests to declare: KH, CT, SN.

Review process

Members of the writing group will inform the writing group Chair if any new pertinent evidence becomes available that would alter the strength of the recommendations made in this document or render it obsolete. The document will be archived and removed from the BSH current guidelines website if it becomes obsolete. If new recommendations are made an addendum will be published on the BSH guidelines website (<https://b-s-h.org.uk/guidelines/guidelines/>).

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