Foreword

The editors have great pleasure in the publication of a new edition of the Preoperative Association’s Evidence-based Guidelines for Preassessment Units. We had originally planned a new edition in 2020, four years after the previous one, but it has had a prolonged gestation due to the pandemic and the inevitable extra call on authors’ time.

We hope you agree it has been worth the wait. We have excluded the chapters on diabetes and preoperative fasting, purely because they both have established international guidelines in place already which do not need to be repeated here. However, we have included five new excellent chapters: guidelines on biological agents, herbalists, alcohol, consent and the use of preoperative respiratory function tests, all of which have been the subject of lectures at recent Preoperative Association national conferences and have practical answers for everyday queries.

We also have engaged new authorship of existing topics namely, hypertension and anaemia by authors who have been involved in guideline working groups. All the other chapters have been updated by their authors to bring them bang up to date with the latest developments.

We are confident you will find this volume an invaluable resource of practical information for pre-assessment staff of all grades.

Nick Lavies & Rob Hill
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Summary and Key Recommendations

- Anaemia and allogenic blood transfusion are associated with poor outcomes for surgical patients.
- The WHO definition of anaemia has been criticized recently. Expert opinion favours a Haemoglobin (Hb) of 130g/l or more, in both males and females.
- Patients should be screened for anaemia and iron deficiency at the earliest opportunity in the surgical care pathway.
- Surgical procedures with a moderate to high risk of blood loss >500ml or a transfusion risk of >10% are deemed the most suitable.
- Anaemia and iron deficiency are easily treated in the preoperative setting. All patients should be offered iron therapy in line with NICE guidance.
- Patients with absolute iron deficiency and >6 weeks from surgery should be given a trial of oral iron.
- Patients <6 weeks from surgery, identified with Functional Iron deficiency or have a failed oral iron treatment should be offered intravenous iron.
- Strict adherence to preoptimization pathways reduces allogenic transfusion however significant cost benefit realization requires adherence to all of the pillars of Patient Blood Management.
INTRODUCTION

Anaemia affects 2.36 billion people worldwide with the prevalence of iron deficiency estimated to be around 1.46 billion individuals. [1] In the surgical setting, prevalence varies between surgical specialties ranging between 20-45% [2]. The WHO recommends that measures should be taken to optimise patients' own blood volume using a patient blood management (PBM) approach [3]. Optimisation of anaemia status is the first pillar in this proposal and supported by a wealth of guidance from international expert groups including the National Institute of Clinical Excellence (NICE) [4,5], the Association of Anaesthetists of Great Britain and Ireland [6] and The Society for Advancement of Blood Management [7].

More recently, the international consensus statement on the perioperative management of anaemia and iron deficiency challenges how we have previously defined anaemia in the preoperative setting [8]. Munoz et al. suggest that the preoperative haemoglobin should be ≥130 g/l in both men and women based upon 2 large studies where outcomes in women worsened when the preoperative haemoglobin was below 130 g/l [9,10]. The following guidelines pull together these opinions and available evidence.

Why is optimising anaemia important in the perioperative setting?

Patients presenting with anaemia at the time of surgery show increased postoperative morbidity and mortality [11,12]. Mussallam et al. analysed data from 211 hospitals and over 200,000 patients in the American College of Surgeons National Surgical Quality Improvement Programme, looking at the prevalence and outcomes of patients across a range of surgical disciplines. An increased risk of 30 day mortality and morbidity was demonstrated in patients who were anaemic compared to those that were not anaemic on the day of surgery [9]. Klein et al. showed similar results in cardiac surgery and also showed that women were at higher risk. It is difficult to separate the cause and effect of anaemia over the effect of an increased requirement for allogenic blood transfusion that leads to poorer outcome [10]. Evidence of poorer outcome in patients that require a blood transfusion during their surgery for cancer is compelling, blood transfusion being an independent risk factor for survival and tumour recurrence [13,14]. The updated Cochrane review by Preston et al in 2012 supports this conclusion and moreover there was no evidence of benefit in preoperative transfusion [15].

Clearly, maintaining freedom from transfusion is more likely if the patient presents in a non-anaemic state. Implementation of the 3 pillars of PBM [16] improve patient outcome, reduces health care costs and saves blood [17]. Making provision to implement PBM could not be more timely in light of the COVID 19 pandemic, where the donor pool has reduced and supply may outstrip demand as the NHS returns to full operative capacity [18,19]. All 3 pillars should be implemented to optimise haemoglobin in the perioperative setting.

What is the cause of anaemia in the surgical patient?

Iron deficiency is the commonest cause of anaemia in the surgical population. Chronic kidney disease and nutrients such as B12 and folate deficiency are less common causes [20,21]. The origin of iron deficiency is complex. Absolute iron deficiency exists when iron stores are severely depleted e.g. chronic ongoing blood loss from menstruation, a tumour, or chronic non-steroidal anti-inflammatory use. Functional iron deficiency is the inability to mobilise iron from stores. Patients may have normal or elevated iron stores in this state. The inflammatory process, chronic in the preoperative state and acute in the postoperative state lead to upregulation of the hormone hepcidin [22]. This hormone is regulated by interleukin 6. Increased hepcidin downregulates the ferroportin receptor in the gastrointestinal tract preventing iron uptake from the diet or iron supplements. It is important to understand the mechanism of iron deficiency in order to treat the patient appropriately. Preoperative pathways should reflect these differences.

What is the definition of anaemia and iron deficiency, who needs investigation?

All patients presenting for surgery with a moderate to high blood loss (>500ml) or a transfusion risk of >10% should be investigated for anaemia and iron status [2,8]. The WHO continue to define anaemia as Hb <130g/l in men and <120g/l in women whereas Blaudszun et al. consider that the haemoglobin threshold should be identical for both sexes. Women have a lower circulating blood volume, lower body surface area and are more likely to require allogenic blood transfusion and this is supported by data on women with haemoglobin 120-129 g/l requiring more transfusions. It is now more widely accepted that the haemoglobin threshold prior to surgery should be 130g/l in both sexes [23].

The definition of absolute iron deficiency is a serum Ferritin < 30mcg/l, Ferritin > 30mcg/l and Transferrin saturation <20% and/or elevated CRP are suggestive of functional iron deficiency. If these tests are normal in the presence of anaemia, B12, folate and serum creatinine should be evaluated. This is demonstrated in an ideal pathway by Munting et al [2], and we have adapted this for our Pre-optimisation and assessment clinic locally. (See Figure 1)

Timing of investigation and treatment

Preoperative testing for anaemia and iron deficiency should be done as early as possible in the patient pathway. Ideally this should be done in the primary care setting but this is rarely achieved. Services differ between surgical specialties and hospitals but as a routine the patient should be tested at the point of diagnosis or ‘listing’ for surgery. Pre-assessment is generally too late in the patient pathway. Minimum tests should include a full blood count (FBC), anaemia screen (to include ferritin, B12 and folate if indicated) and CRP. It is important to remember that patients identified with absolute iron deficiency in a non-urgent surgical specialty should be sent via their GP for urgent endoscopy.

Timing of surgery is important. If time to surgery is more than 6 weeks, patients should be given a trial of oral iron as per NICE recommendations. All patients should have a repeat FBC and offered intravenous iron if the haemoglobin response has been inadequate or the patient has had significant side effects [5]. Oral iron is ineffective in the postoperative setting secondary to acute inflammation, emphasizing the need to investigate and treat in the preoperative period.

Oral iron – recommendations for dosing

There are many preparations of oral iron. The recommended daily dose is 40-60mg of elemental iron per day which varies between brands [8]. The table below represents the iron content of the commonly used iron tablets and the elemental iron content per tablet. Tablets can be given at a higher dose on an alternate day basis. However, we have found that patients forget which day they have taken the tablet and then avoid taking the iron, leading to treatment failure. Monitoring for efficacy of oral iron is essential and should be undertaken 4 weeks following the start of treatment. A longer treatment period with up to 6 months is required to replace iron stores completely.
Side effects of oral iron are frequent, between 30-70% in one systematic review [24], with patients describing constipation, change of bowel habit, loss of appetite, abdominal pain and dyspepsia.

<table>
<thead>
<tr>
<th>IRON PREPARATION</th>
<th>AMOUNT</th>
<th>ELEMENTAL IRON CONTENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous Fumarate</td>
<td>200mg</td>
<td>65mg</td>
</tr>
<tr>
<td>Ferrous Gluconate</td>
<td>300mg</td>
<td>35mg</td>
</tr>
<tr>
<td>Ferrous Sulphate</td>
<td>300mg</td>
<td>60mg</td>
</tr>
<tr>
<td>Ferrous Sulphate, dried</td>
<td>200mg</td>
<td>65mg</td>
</tr>
</tbody>
</table>

Intravenous Iron - recommendations, when to use

NICE guidance (NG 24) recommends intravenous iron should be started in the following circumstances:

- Short time to surgical intervention <6 weeks
- Poor tolerance to oral iron
- Oral iron ineffective at 4 weeks
- Functional Iron deficiency

Intravenous iron is a safe treatment. Safety data from a review of over 19,000 patients by Avni et al demonstrated that there was no increase in serious adverse events [25]. Infection was identified as a possible association but this was with a rarely used iron preparation (Ferrous Gluconate). Anaphylaxis is a possible complication of intravenous iron preparations and needs to be indicated in the drug safety information produced by the pharmaceutical companies. The risk however is extremely small [25,26].

With this in mind, intravenous iron should be delivered in a setting where patients can be monitored for blood pressure, heart rate and oxygen saturation prior to, 15mins and 30 minutes into an infusion and 30 minutes after the infusion. This could be a medical or surgical day case unit, an endoscopy unit or an intravenous drug suite; there are many options. The Cardiff prescription, pre infusion questionnaire and patient monitoring proforma are shown in Figure 2. The newer preparations of iron allow full replacement of iron stores at one sitting and this proforma has the ability to be adapted and apply in your own perioperative care setting.

As for any intravenous drug, a reaction management algorithm should be in place. Nursing teams should be trained to manage minor reactions such as flushing described as a Fishbane reaction, chest tightness and back discomfort. All patients should be given information on the drug before consenting to the procedure.

Erythropoetin

Ideally, a transferrin saturation (TSAT) >20% should be used to identify patients with functional iron deficiency. Those with a mixed picture or an element of bone marrow failure which is common in the elderly may not have the same response to intravenous iron as those with absolute iron deficiency. These patients may be suitable for treatment with Erythropoietin, but this is dependent on the surgery type, risk of transfusion and patient risk factors. A separate pathway for these patients should be developed in liaison with local haematologists. This would also be a suitable treatment option for patients who refuse blood for religious beliefs [29].

Postoperative Anaemia

In major surgical interventions anaemia maybe present in up to 90% of patients in the post operative period. This is multifactorial in origin, untreated preoperative anaemia, perioperative blood loss, blunted erythropoesis secondary to the acute inflammatory response and haemodilution being contributory factors [27]. Monitoring of post-operative haemoglobin is dependant on the severity of blood loss and destination of the patient postoperatively. However, as a minimum, all patients should have a post-op Day 3- 4 FBC.

The nature of postoperative anaemia does not lend itself to oral iron. Intravenous iron is the first choice in patients with significant blood loss or iron deficiency identified in the preoperative setting [28]. Serum Ferritin is a poor marker for iron deficiency post operatively and transferrin saturation should be performed if iron status is unknown. Patients who are symptomatic when they reach the transfusion trigger, usually 75-80g/L, may be considered for a packed red cell transfusion as per local transfusion policy, whereas asymptomatic patients should be considered for intravenous iron.

Monitoring outcome data

Data from patients in Cardiff treated in the preoperative setting with intravenous iron who achieved Hb >130 g/L at the time of surgery showed a mean increase of 16.9 g/L (6-44 g/L IQR). These patients had lower serum ferritin and CRP at presentation. The group that had an increased haemoglobin with IV iron but did not reach Hb 130g/L at the time of surgery, had a lower Hb at presentation, higher ferritins and higher creatinine suggestive of a mixed iron deficiency picture.

Treating anaemia with intravenous iron in the preoperative setting has limited randomised controlled trial evidence. The results of the PREVENT study - intravenous iron versus placebo in major non cardia surgery [30] do not show a statistical difference in packed red cell use but do demonstrate an increase in haemoglobin and improvement in functional status. The authors acknowledge the criteria for inclusion did not assess the iron status of patients preoperatively, only the haemoglobin. The dosing of intravenous iron and time to surgery, which were too low and too short in this study are other contributory factors as to why this study does not demonstrate significant results.

Our own experience gives us the view that haemoglobin and transfusion are poor measurements of patient outcome. The integral role that iron has at a cellular level means the outcome measures used in this study were not subtle enough to show the true benefits of iron treatment. Further work on the benefits of perioperative iron are essential to unravel the complex mechanisms and cellular benefits that iron treatment affords. In the meantime a wealth of expert guidance on identification and management exist to adapt and apply in your own perioperative care setting [31,32].
References

5. NICE Blood Transfusion. NICE Guideline NG24 2015 nice.org.uk/guidance/ng24 (accessed 01/07/2020)

Figure 1: Pre-operative anaemia pathway

- **Pre-op bloods**
  - **Major Surgery?**
    - Yes: Estimated blood loss >500ml
    - No: Transfusion risk >10%
    - GBS required
  - Intermediate/low risk surgery
    - Standard pre-op bloods if indicated: FBC, anaemia screen

- **Ferritin**
  - <30mcg/L
    - Iron deficiency anaemia
      - Asses assess (note 1)
    - >30mcg/L
      - IV iron therapy
      - >6 weeks until surgery
        - Start oral iron (ferrous fumarate 333mg OD)
        - Preoperative therapy ceased 4 weeks before surgery
        - Patient listed on POAG database for follow-up up in 6 weeks
        - If HP improves proceed to surgery
        - If poor response, consider IV iron
  - Ferritin 30-100mcg/L
    - TSAT < 20% or CRP >5mg/L
    - Anemia of chronic inflammation with iron deficiency
      - IV iron therapy
      - Consider cause and refer as appropriate (note 2)
    - Ferritin >100mcg/L
      - TSAT <20% or CRP >5mg/L
      - Anemia of chronic inflammation
        - Consider IV iron therapy
        - Consider cause, check B12 and folate and refer as appropriate (note 2)
      - Ferritin >100mcg/L
        - TSAT >20% or CRP <5mg/L
        - Other causes - Chronic kidney disease, B12/Folate deficiency
          - Check B12, Folate, Creatinine
          - Refer to nephrologist if kidney disease

Footnotes
- **Note 1**: Possible causes include iron deficiency, chronic inflammation, malignancy, infection, liver disease, renal failure, haemosidotic heart, cholestatic liver, malignancy
- **Note 2**: Possible causes include iron deficiency, malignancy, infection, liver disease, renal failure, haemosidotic heart, cholestatic liver, malignancy
- **Note 3**: Various assays of blood ferritin and refer to appropriate or refer to ferritin in advanced disease and discuss timing of samples with a gastroenterologist.
Figure 2: The Cardiff prescription, pre infusion questionnaire and patient monitoring proforma

| Prescription Chart for Monofer (iron(III) isomaltoside 1000) in Cardiac Surgery |
|---------------------------------|---------------------------------|
| Allergy                         | Please circle as appropriate   |
| NONE KNOWN                      |                                 |
| Signature                       | Date                            |
| Name                            | Drug/allergy                    |
| Description of reaction         |                                 |

Prescriber to complete all boxes shaded in grey

Monofer to be prescribed if haemoglobin < 130 g/L and ferritin <100 mcg/L.

In patients having complex valve/aortic surgery or a redo procedure, Monofer to be prescribed in all patients with a ferritin <100 mcg/L (even if Hb greater 130g/L) – see Preoperative Anaemia Pathway.

**Step 1 Justify need for parenteral iron therapy**

<table>
<thead>
<tr>
<th>Hb (&lt;130 g/L)</th>
<th>Ferritin (&lt;100mcg/L)</th>
<th>Planned surgery</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex valve/aortic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Redo valve/graft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (specify indication)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Step 2 Dose = 20mg/kg – tick dose as appropriate (calculate if weight <50kg)**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose 20mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 kg</td>
<td>1g</td>
</tr>
<tr>
<td>50-59 kg</td>
<td>1.2g</td>
</tr>
<tr>
<td>60-69 kg</td>
<td>1.4g</td>
</tr>
<tr>
<td>70-79 kg</td>
<td>1.6g</td>
</tr>
<tr>
<td>80-89 kg</td>
<td>1.8g</td>
</tr>
<tr>
<td>90-99 kg</td>
<td>2g</td>
</tr>
<tr>
<td>≥100 kg</td>
<td></td>
</tr>
</tbody>
</table>

**Step 3 Complete the Monofer Prescription Schedule**

<table>
<thead>
<tr>
<th>DATE</th>
<th>Drug name and infusion</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>Prescriber signature</th>
<th>TIME GIVEN</th>
<th>GIVEN BY</th>
<th>CHECKED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sodium Chloride 0.9% for flushing cannula</td>
<td>5ml</td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iron (III) Isomaltoside (Monofer®) in 500ml Sodium Chloride 0.9% over 60 minutes</td>
<td>IV infusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium Chloride 0.9% for flushing cannula</td>
<td>5ml</td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Step 4 Prescriber’s signature**

<table>
<thead>
<tr>
<th>PRIN T name</th>
<th>Designation</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
</table>

**Step 5 Clinical Check by Pharmacist, dispensing and accuracy check**

<table>
<thead>
<tr>
<th>Clinical check</th>
<th>Dispensing</th>
<th>Final check</th>
</tr>
</thead>
</table>

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**Pre-administration questionnaire and monitoring**

<table>
<thead>
<tr>
<th>Past medical history</th>
<th>Liver disease</th>
<th>Rheumatoid arthritis/SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>asthma</td>
<td>Previous sensitivity to iron</td>
</tr>
<tr>
<td></td>
<td>eczema</td>
<td>Other drug allergies</td>
</tr>
</tbody>
</table>

If any of the above apply, the patient will be at a greater risk of hypersensitivity reactions. Please be aware that the infusion may need to be slowed down or stopped (see Reaction Management Algorithm).

**Monitoring**

<table>
<thead>
<tr>
<th>Time</th>
<th>Temperature</th>
<th>Respiratory rate</th>
<th>Blood pressure</th>
<th>Pulse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Infusion</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 30 minutes</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 60 minutes</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 minutes after completion of infusion</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Anaphylaxis**

Acute severe anaphylactic reactions may occur with parenteral iron administration. They usually occur within the first few minutes of administration and are characterised by sudden onset respiratory failure and/or cardiovascular collapse.

Urticaria, rashes, itching, nausea and shivering may also occur.

Administration must be stopped immediately if signs of an anaphylactic reaction are observed.

Appropriate resuscitation medication must be available including hydrocortisone IV and adrenaline. See Reaction Management Algorithm.
INTRODUCTION

Hypertension is defined as a systolic blood pressure (SBP) equal to or greater than 140 mmHg or a diastolic blood pressure (DBP) equal to or greater than 90 mmHg. Over a quarter of the UK’s adult population have hypertension which may be controlled with medication, inadequately controlled on medication or chronically untreated [1]. It is widely accepted that uncontrolled hypertension is one of the most important preventable risk factors for premature morbidity and mortality [2].

Hypertension is almost always asymptomatic and is most commonly diagnosed following screening in the primary care setting. Hypertension may be classified into four categories and management options are influenced by the stage of hypertension (Table 1), the estimated cardiovascular risk as well as evidence of target organ damage (Table 2).

Table 1. Categorisation of the stages of hypertension

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic blood pressure; mmHg</th>
<th>Diastolic blood pressure; mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160–179</td>
<td>100–109</td>
</tr>
<tr>
<td>Stage 3</td>
<td>180–209</td>
<td>110–119</td>
</tr>
<tr>
<td>Stage 4</td>
<td>≥ 210</td>
<td>≥ 120</td>
</tr>
</tbody>
</table>

Table 2. Hypertension-related target organ damage

<table>
<thead>
<tr>
<th>Organ</th>
<th>Common manifestations of hypertension-related organ damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Left ventricular hypertrophy</td>
</tr>
<tr>
<td></td>
<td>Heart failure, both reduced ejection fraction (systolic) and preserved ejection fraction (diastolic)</td>
</tr>
<tr>
<td></td>
<td>Ischaemic heart disease</td>
</tr>
<tr>
<td>Brain</td>
<td>Ischaemic stroke</td>
</tr>
<tr>
<td></td>
<td>Intracerebral haemorrhage</td>
</tr>
<tr>
<td></td>
<td>Small vessel cerebral ischaemic disease</td>
</tr>
<tr>
<td></td>
<td>Vascular dementia</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Proteinuria</td>
</tr>
<tr>
<td></td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Vascular</td>
<td>Aortic dissection</td>
</tr>
<tr>
<td></td>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>Eyes</td>
<td>Hypertensive retinopathy</td>
</tr>
</tbody>
</table>

Most cases of hypertension are primary and are not associated with any underlying medical cause. Some secondary causes for hypertension may be associated with the indication for proposed surgery and these groups of patients are excluded from this guidance, although many of the general points covered in this chapter may apply (Table 3).
Managing hypertension pre-operatively is a complex matter. Important considerations include whether the detection of hypertension should lead to further investigation and treatment, with the possibility of postponement of the proposed surgery. Conversely, if the surgery does proceed, consideration should be given to the impact of untreated hypertension on the perioperative outcome. Cancellations and postponements of planned surgical procedures have significant psychological, social and financial implications for patients, their families and the NHS. In view of this, diligent care should be taken to avoid unnecessary cancellations.

This chapter only applies to the period before planned surgery and clarifies what can be regarded as a 'safe' high blood pressure threshold for elective surgery. The guidance focuses on blood pressures which may cause an increased risk of harm during the perioperative period rather than those that may increase morbidity and mortality in the longer term. It has been demonstrated that the implementation of the AAGBI/BHS guidelines reduces the number of elective surgical patients being cancelled solely due to hypertension [3,4].

However, improvement in practice is still required and it is hoped that the guidance set out in this chapter will: 1) continue to reduce the number of cancellations of elective surgery due to hypertension alone; 2) improve detection of significant hypertension before elective surgery; and 3) reduce the number of patients referred from preoperative assessment clinic back to primary care for the management of hypertension. It is important to note that the blood pressure values cited and the treatments recommended in this chapter are based on the current NICE guidance [2], and if this guidance were to change, then so would the advice provided in this chapter.

### Table 3. Groups of surgical patients excluded from this guidance

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Reasons for exclusion from this guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-elective surgery</td>
<td>Urgent and emergency surgery should not be delayed by the presence of hypertension. Blood pressures greater than 180 mmHg systolic and 110 mmHg diastolic should be managed by the perioperative team as guided by the clinical situation. The incidental finding of hypertension during an emergency surgical admission should be communicated to the General Practitioner for follow-up.</td>
</tr>
<tr>
<td>Cardiac, endocrine, neurosurgery, renal and vascular surgery</td>
<td>Peri-operative hypertension is often present secondary to the underlying pathology. Specialist management will be required and is beyond the scope of this guidance.</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>Childhood hypertension is uncommon. Specialist management will be required and is beyond the scope of this guidance.</td>
</tr>
</tbody>
</table>

### ASSOCIATION BETWEEN HYPERTENSION AND PERI-OPERATIVE HARM

The association between uncontrolled hypertension and adverse perioperative outcomes is well established [5,6]. Higher incidence of myocardial ischaemia [7], perioperative cardiovascular death [8], renal dysfunction [9] and cerebral vascular disease [10] are seen in patients with uncontrolled hypertension undergoing anaesthesia. Diastolic hypertension [11] and raised pre-operative pulse pressure is associated with an increased risk of myocardial injury, even when SBP is controlled [12]. There is very little data regarding the degree of hypertension and subsequent risk of perioperative mortality. However, it appears that patients with a SBP of less than 180 mm Hg or DBP less than 110 mmHg (i.e. stage 1 or 2 hypertension) and no associated target organ damage do not experience an increased risk of perioperative cardiovascular morbidity or mortality. [13].

Patients with stage 3 or 4 hypertension are more likely to have target organ damage. There is some evidence to suggest that hypertension with target organ damage is associated with a small increased incidence of peri-operative major adverse cardiovascular events [14]. However, it is not known whether or not reducing blood pressure in these patients during a short postponement of elective surgery will result in a reduction of their perioperative risk. Any decision should take into account factors other than blood pressure, namely: comorbidity, functional capacity, frailty, and the urgency and indication for surgery. Therefore, the anaesthetist needs to consider whether the blood pressure should be reduced before surgery and consider whether doing this for a short period of time preoperatively actually reduces the patients' perioperative risk.

Patients with hypertension (controlled or uncontrolled) demonstrate a more labile haemodynamic profile than their non-hypertensive counterparts [15]. The induction of anaesthesia and airway instrumentation can lead to a pronounced increase in sympathetic activation, which may lead to a significant increase in blood pressure and heart rate. A reduction in systemic vascular resistance soon after the induction of anaesthesia commonly leads to varying degrees of hypotension. Reduction in vascular resistance is multifactorial and may be secondary to loss of the baroreceptor reflex control, central neuraxial blockade, and direct effects of anaesthetic agents. The effect on vascular tone will be exaggerated by 'deep' or excessive anaesthesia and in patients who are fluid-depleted. This, and the often exaggerated haemodynamic response to surgery, pain and emergence from anaesthesia, have also been described as being more common in the hypertensive population [16].

In order to mitigate the effects of labile haemodynamics in hypertensive patients, there are a number of available anaesthetic techniques which can be adopted to attain haemodynamic stability during surgery, such as choice of induction drugs, depth-of-anaesthesia monitoring and invasive arterial and cardiac output monitoring with targeted vasopressor and fluid therapy. There is growing evidence that the intra-operative management of blood pressure, particularly the avoidance of hypotension, has a significant effect on morbidity, and this effect may be greater than pre-operative hypertension, other than extremes described in this guidance [17].

### How to measure blood pressure

Blood pressure should be measured in a calm and comfortable environment with calibrated and validated equipment. Before commencing measurement, the patient should be seated with their supported arm outstretched for at least one minute and the pulse rate and rhythm should be recorded. When the pulse is irregular, blood pressure should be measured by auscultation over the brachial artery during manual deflation of an arm cuff since automated sphygmomanometers are inaccurate in this situation.

The patient is considered to be normotensive if the blood pressure measurement is less than 140/90 mmHg. If the initial measurement is found to be equal to or higher than 140/90 mmHg, the blood pressure should be measured a further two times at least one minute apart to mitigate the effect of ‘white coat hypertension’. Of these 3 blood pressure readings, the lower of the last two should be recorded.
**BLOOD PRESSURE IN PRIMARY CARE BEFORE REFERRAL FOR SURGERY**

Non-urgent surgical referrals from primary care should not be made without blood pressure measurement (Fig. 1) and surgical outpatients should arrange for primary care to supply blood pressure readings if these have not been documented in the referral letter. Blood pressure should be measured in pre-operative assessment clinic for all patients who attend without documented blood pressure readings from the last 12 months.

If the reading in primary care is between 140/90 mmHg and 179/109 mmHg, the patient may have stage 1 or 2 hypertension and should be offered ambulatory (ABPM) or home blood pressure monitoring (HBPM) to establish their true blood pressure.

Lifestyle advice and pharmacological treatment may be offered in primary care after a diagnosis of hypertension is made. The blood pressure target in primary care prior to referral to surgery is SBP less than 160 mmHg and DBP less than 100 mmHg. Patients found to be incidentally hypertensive during this referral process should undergo the same hypertension management pathway as any other primary care patient. The referral letter to surgeons should include details if the patient has declined hypertension treatment or where all appropriate attempts have been made to reduce persistently high blood pressure, which might have included specialist investigations.

**MEASUREMENT OF BLOOD PRESSURE DURING PREOPERATIVE ASSESSMENT**

If the blood pressure measured in preoperative assessment clinic is raised above 180 mmHg systolic or 110 mmHg diastolic, the patient should be referred back to primary care for assessment and management of their blood pressure, unless there is documented evidence of blood pressures less than 160 mmHg systolic and 100 mmHg diastolic measured in primary care (Fig. 2). If the blood pressure is above 140 mmHg systolic or 90 mmHg diastolic, but below 180 mmHg systolic and below 110 mmHg diastolic, the GP should be informed for the concurrent determination of whether hypertension is present, but elective surgery should not be postponed. If the reading is equal to or higher than 180/110 mmHg in primary care, the patient should be screened for red flags (Table 4) which may indicate a hypertensive crisis and will require immediate treatment.

**Table 4. Red flags which may indicate a hypertensive crisis**

<table>
<thead>
<tr>
<th>System</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>Generalised neurological symptoms, such as agitation, delirium, stupor, seizures, or visual disturbances</td>
</tr>
<tr>
<td></td>
<td>Nausea and vomiting, which may be a sign of increased intracranial pressure</td>
</tr>
<tr>
<td></td>
<td>Focal neurological symptoms that could be due to an ischaemic or haemorrhagic stroke</td>
</tr>
<tr>
<td></td>
<td>History of acute head injury or trauma</td>
</tr>
<tr>
<td>Eyes</td>
<td>Fresh flame haemorrhages, exudates (cotton-wool spots), or papilloedema seen on direct fundoscopy</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Chest discomfort or pain, which may be due to myocardial ischaemia or aortic dissection</td>
</tr>
<tr>
<td></td>
<td>Dyspnoea, which may be due to pulmonary oedema</td>
</tr>
<tr>
<td></td>
<td>Acute, severe back pain, which might be due to aortic dissection</td>
</tr>
<tr>
<td>Other</td>
<td>Acute use of drugs that can produce a hyperadrenergic state (e.g. cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors)</td>
</tr>
<tr>
<td></td>
<td>Recent discontinuation of clonidine or, less commonly, other antihypertensive agents</td>
</tr>
</tbody>
</table>

Pre-operative assessment clinics should inform general practitioners when they measure raised blood pressures in patients who have not had readings taken in primary care in the preceding 12 months. The letter should request that the general practitioner investigate whether patient has hypertension and whether or not surgery will proceed without a diagnosis of hypertension being made or treatment commenced.
**Hypertension Treatment in Primary Care**

This section summarises the recommendations for antihypertensive pharmacological therapy in primary care following the diagnosis of hypertension and are summarised in Figure 3. There is good evidence for the treatment of hypertension with one or more of the following: diuretics (thiazide, chlorothalidone and indapamide); beta-blockers; calcium channel-blockers (CCB); angiotensin converting enzyme (ACE) inhibitors, or an angiotensin-2 receptor blocker (ARB). The threshold for treating high blood pressure might change according to cardiovascular risk.

**Step 1 Treatment**

Patients aged less than 55 years should be offered an ACE inhibitor, or an ARB. If an ACE inhibitor is prescribed but is not tolerated (for example, because of cough), offer an ARB. ACE inhibitors and ARBs are not recommended in women of childbearing potential and should not be used in combination.

Patients aged over 55 years and patients of African or Caribbean family origin of any age should be offered a CCB. If a CCB is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure or a high risk of heart failure, a thiazide-like diuretic should be offered.

Beta-blockers are not a preferred initial therapy for hypertension. However, beta-blockers may be considered in younger patients, particularly those with an intolerance or contraindication to ACE inhibitors and ARBs, or women of childbearing potential or patients with evidence of increased sympathetic drive. If beta-blockers are started and a second drug is required, add a CCB rather than a thiazide-like diuretic to reduce the person’s risk of developing diabetes.

---

**White-coat Hypertension**

A finding of significant hypertension (greater than 180 mmHg systolic and/or 110 mmHg diastolic) on the day of surgery should be judged in context of the presence or absence of: i) evidence of previously controlled blood pressure; ii) clinical features of a hypertensive crisis and; iii) anxiety. In a patient with documented evidence of satisfactory control of blood pressure in the 12 months leading up to surgery, the presence of significant hypertension (without any red flag signs) is most likely secondary to anxiety i.e. ‘white coat hypertension’. In this scenario, clinical judgement should be applied and surgery may proceed (some may consider a trial of anxiolytic medication prior to induction of anaesthesia). It is particularly important in these patients, that intraoperative blood pressure targets are based on the patient’s usual preoperative blood pressure rather than the blood pressure measured on the day of surgery.

---

*Figure 2*

Secondary care blood pressure assessment of patients after referral for elective surgery. *The GP should be informed of blood pressure readings in excess of 140 mmHg systolic or 90 mmHg diastolic, so that the diagnosis of hypertension can investigated and treated as necessary. DBP and SBP diastolic and systolic blood pressure. Adapted with permission from the ‘AAGBI/BHS Hypertension Guidelines’.

*Figure 3*

Summary of the recommendations for antihypertensive pharmacological therapy in primary care following the diagnosis of hypertension. angiotensin converting enzyme (ACE) inhibitors, or an angiotensin-2 receptor blocker (ARB), calcium channel blockers (CCB).
Beta-blockers

Beta-blockers should not be commenced in the perioperative period due to increases in postoperative mortality, secondary to hypotension and stroke [22]. Conversely, those patients established on beta blockade therapy should continue this treatment as omission may be associated with myocardial ischaemia.

Table 5. Pre-operative management of antihypertensive medication

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-operative advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin converting enzyme inhibitors / angiotensin 2 receptor blockers</td>
<td>Hold 24 h pre-operatively</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Continue</td>
</tr>
<tr>
<td>Thiazide and thiazide-like diuretics</td>
<td>Continue</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Continue</td>
</tr>
<tr>
<td>Other (clonidine, moxonidine, alpha-methyldopa)</td>
<td>Continue – abrupt withdrawal can be associated with adverse events</td>
</tr>
</tbody>
</table>

FUTURE OF HYPERTENSION TREATMENT: ASSESSING CARDIOVASCULAR RISK

The extent by which cardiovascular disease is reduced by treatment for hypertension is dependent on the composite cardiovascular risk, not the blood pressure alone. It is likely that future treatment of hypertension will be based on the composite 5 or 10 year risk of stroke; myocardial infarction; heart failure; and cardiovascular morbidity and mortality [23]. This change in perspective is driven partly by the uncertainty in how long it takes for cardiovascular risk to fall with antihypertensive medication as opposed to how long it takes for blood pressure to fall. This should be balanced against the 1% relative increase in perioperative cardiovascular risk due to the patient ageing that accompanies each delayed month. Nevertheless this chapter has been written based on current guidance and best practice where hypertension is diagnosed before elective surgery.

PRE-OPERATIVE MANAGEMENT OF ANTIHYPERTENSIVE MEDICATION

Each antihypertensive agent has different pharmacological properties and may be used as monotherapy or in combination. The decision to stop or continue antihypertensive agents pre-operatively must involve balancing the risks of withholding the agent with continuing it. Unfortunately, there are no large randomised controlled trials on which to base advice in this setting. The guidance in Table 2 is based on balancing the patient’s perioperative cardiovascular risk and the anticipated effect of the drug on the patient’s haemodynamic stability during anaesthesia.

Angiotensin converting enzyme inhibitors / angiotensin 2 receptor blockers

Withholding angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) 24 h before surgery appears to be associated with fewer significant peri-operative haemodynamic fluctuations [18].

Calcium channel blockers

Data from small randomised controlled trials suggest that calcium channel blockers may be associated with improved outcomes [19,20].

Thiazide and thiazide-like diuretics

Limited evidence to suggest continuing these agents is not associated with harm [21]. However a diuresis on the day of surgery can be both a nuisance for the patient and counter-productive to keeping good preoperative hydration.
References

5. Smithwick RH, Thompson JE. Splanchnectomy for essential hypertension: results in 1,266 cases. Journal of the American

Guidelines for the Pre-Operative Assessment and Management of Patients with Obstructive Sleep Apnoea

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2 Consultant in Anaesthesia and Sleep Medicine, South Tees Hospitals NHS Foundation Trust. Honorary Professor, Hull York Medical School and Teesside University. Clinical Lead for South Tees Prehabilitation Implementation and Strategy group

Acknowledgements: Sharon Avery, Robert Hill, Anita Baldea and Angie Habgood who co-authored previous versions of the guidance document on behalf of the Preoperative Association

Summary and Key Recommendations

- Obstructive Sleep Apnoea (OSA) is common and preoperative assessment should include a risk assessment such as the STOP-BANG screening tool to facilitate diagnosis and treatment.
- A high index of suspicion for OSA should exist in all morbidly obese patients, as the prevalence is substantially higher in this patient group.
- Untreated OSA is associated with more than doubling the risk of perioperative complications and increased hospital length of stay.
- If OSA is strongly suspected on clinical grounds, or a screening tool, patients should be referred for Sleep Medicine assessment where surgery is non-urgent.
- If OSA is strongly suspected on clinical grounds, or screening tool, and either sleep studies are not readily available or surgery is urgent, then patients should be treated as if they have a positive diagnosis, and managed accordingly.
- It is recommended that agreed, expedited referral pathways should be established between preoperative assessment clinics and local Sleep Medicine services to minimise delays where significant OSA is suspected.
- If OSA has been diagnosed or is strongly suspected, the postoperative care provided should include the ability to institute CPAP except in selected minor day-case surgery.
- Patients who have their own treatment devices e.g. CPAP machines, should bring them into hospital on admission.
- OSA should not preclude patients from day case surgery; however, detailed perioperative management & discharge planning should be put into place in advance and central neuraxial techniques or loco-regional anaesthesia used wherever possible.
- A co-ordinated perioperative management plan should be agreed through the preoperative assessment process.
Table 1. Predisposing factors for OSA

- Obesity (BMI ≥ 35)
- Male gender
- Neck circumference >40 cm in males, or >39 cm in females
- Family history of OSA
- Enlarged tonsils
- Anatomical nasal obstruction
- Smoking
- Advancing age
- Craniofacial abnormalities e.g. Down’s Syndrome, Micrognathia, Acromegaly

Table 2. OSA Classification*

<table>
<thead>
<tr>
<th>AHI</th>
<th>Severity of OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>Normal</td>
</tr>
<tr>
<td>5-14</td>
<td>Mild</td>
</tr>
<tr>
<td>15-30</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>Severe</td>
</tr>
</tbody>
</table>

* See reference [11]
1.5 Diagnosis

Formal diagnosis of OSA is through Sleep medicine evaluation. Diagnosis is usually based on:

- History of presenting symptoms (above)
- Evidence of daytime sleepiness – this is usually assessed by completing an Epworth Sleepiness Score (see Appendix 1). A score of > 12 is strongly suggestive of increased daytime somnolence
- Diagnostic sleep studies – a range of studies can be used to aid diagnosis. Complexity of studies ranges from simple overnight pulse oximetry to in-patient polysomnography and may depend on local expertise and availability

1.6 General clinical management

- Mild OSA – lifestyle advice including weight loss is first line, with mandibular advancement devices also having been shown to be effective. Consideration of Continuous Positive Airways Pressure (CPAP) if unresponsive to above or if symptoms are impacting on quality of life.
- Moderate/Severe OSA – mainstays are weight loss and CPAP. Mandibular advancement devices can be used but are generally less effective than CPAP.

The above management applies to all patient groups diagnosed with OSA and is not only applicable to patients presenting for elective surgery. Above treatment recommendations are based on National Institute for Health and Clinical Excellence (NICE) guidance [12].

1.7 General perioperative considerations

Greater numbers of elderly and morbidly obese patients are now presenting for surgery. This has been compounded over recent years with the development of government initiatives to treat morbid obesity through surgical intervention (bariatric surgery). In bariatric patients, OSA screening and treatment should be a routine part of preassessment [13].

Untreated OSA is associated with a range of co-morbidities (see above), which increases risk to patients in the perioperative period. A cohort study of 1,058,710 hospitalised adult patients undergoing elective surgeries has highlighted significant adverse postoperative outcomes associated with OSA [5] – Table 3.

Table 3. Postoperative risk of complications in patients with OSA compared to non-OSA patients [5]. RR – relative risk. Risks of pneumonia and tracheostomy were not increased in OSA vs. no OSA group.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No OSA (%)</th>
<th>OSA (%)</th>
<th>RR (p-value)</th>
<th>No OSA (%)</th>
<th>OSA (%)</th>
<th>RR (p-value)</th>
<th>No OSA (%)</th>
<th>OSA (%)</th>
<th>RR (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Orthopaedic surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate surgery</td>
<td>0.3</td>
<td>3.9</td>
<td>13 (&lt;.01)</td>
<td>0.3</td>
<td>3.5</td>
<td>11.7 (&lt;.01)</td>
<td>3.3</td>
<td>6.6</td>
<td>2 (&lt;.01)</td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td>0.3</td>
<td>3.5</td>
<td>13 (&lt;.01)</td>
<td>0.3</td>
<td>3.5</td>
<td>11.7 (&lt;.01)</td>
<td>3.3</td>
<td>6.6</td>
<td>2 (&lt;.01)</td>
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<tr>
<td>Post-operative complication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergent intubation</td>
<td>0.3</td>
<td>3.9</td>
<td>13 (&lt;.01)</td>
<td>0.3</td>
<td>3.5</td>
<td>11.7 (&lt;.01)</td>
<td>3.3</td>
<td>6.6</td>
<td>2 (&lt;.01)</td>
</tr>
<tr>
<td>Emergent CPAP/NIV</td>
<td>0.1</td>
<td>3.5</td>
<td>13 (&lt;.01)</td>
<td>0.3</td>
<td>3.5</td>
<td>11.7 (&lt;.01)</td>
<td>3.3</td>
<td>6.6</td>
<td>2 (&lt;.01)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>0.5</td>
<td>1.5</td>
<td>3 (&lt;.03)</td>
<td>0.5</td>
<td>1.2</td>
<td>2.4 (&lt;.01)</td>
<td>4.2</td>
<td>5.1</td>
<td>1.2 (&lt;.03)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4.9</td>
<td>6.7</td>
<td>1.4 (&lt;.01)</td>
<td>2.9</td>
<td>5.8</td>
<td>2 (&lt;.01)</td>
<td>8.3</td>
<td>9.2</td>
<td>1.1</td>
</tr>
</tbody>
</table>

One limitation highlighted in this study, was a lack of information regarding patient use of CPAP therapy at home, which the Nationwide Inpatient Sample database did not specify. However, it is clear that a diagnosis of OSA (with or without home CPAP treatment) is associated with a range of highly significant perioperative complications. Abdominal surgery appears to convey the highest absolute risk.

The risk of major cardiac complications (including cardiac death, myocardial injury, heart failure, thromboembolism, stroke and atrial fibrillation) within 30 days of non-cardiac surgery has been shown to increase significantly in undiagnosed, severe OSA [14].

The impact of CPAP treatment on perioperative complications is discussed in further detail in section 2.4.

Other perioperative challenges in patients with OSA include:

- 8-fold increase in the incidence of difficult intubation [8]
- Increased sensitivity to use of perioperative opioids and sedation
- Complications associated specifically with obesity – refer to further reading
- Increased length of hospital stay

1.8 Obesity Hypoventilation Syndrome (OHS)

Obesity is also associated with the ‘obesity hypoventilation syndrome’. Along with the characteristics seen in OSA, there is chronic awake hypercapnia, but a diminished ventilatory drive despite an elevated PaCO2 (diagnosis requires arterial blood gas analysis during wakefulness). Individuals tend to have lower daytime oxygen saturations, lower quality of life, increased daytime somnolence, and at the extreme, pulmonary hypertension and right heart failure. These patients are clinically very similar to patients with OSA, but with potentially more severe cardio-pulmonary co-morbidities, and mandate a high index of suspicion to identify them pre-operatively. Low daytime oxygen saturations and raised plasma bicarbonate levels are clues to the presence of OHS. OHS usually requires treatment with non-invasive ventilation (NIV) rather than CPAP. See recommendations for further reading for a comprehensive overview of OHS.

2. SCREENING, DIAGNOSIS AND PERIOPERATIVE MANAGEMENT OF OSA

Given the reported prevalence of OSA in patients presenting to the preoperative assessment clinic, and increased incidence of postoperative complications, it is essential to employ strategies to identify and diagnose patients at highest risk. Successful diagnosis allows treatment and optimisation of OSA in the perioperative period thereby allowing appropriate perioperative planning and minimisation of associated complications.

2.1 Preoperative Screening

Appropriately targeted preoperative assessment prior to elective surgery provides an ideal opportunity to identify and refer patients identified as being ‘at risk’ of suffering from OSA. This should be underpinned by:

**History and symptoms** – ‘triple S’ symptoms (above) are a quick and simple way of achieving this. A positive response to these symptoms should raise a high index of suspicion that OSA may be present and prompt a more in depth assessment. A formal Epworth Sleepiness Score (ESS) represents an ideal way to assess daytime somnolence with a score > 12 abnormal (Appendix 1). As part of delivery of the ESS, it is critical to ask patients to demarcate true ‘sleepiness’ from fatigue when answering questions.
Patients with newly diagnosed moderate to severe OSA should be commenced on CPAP as per [0%].

### 0.9%

0.6%

1.6%

**Area of uncertainty**

No OSA

2.7%

has anyone observed that you stop breathing during sleep?

do you have a history of high blood pressure, with or without treatment?

do you feel tired or fatigued during the daytime almost every day?

### 0.6%

1.4

0.6%

male gender

OSA treated

OSA untreated

2.5

Body mass index >35kg/m²

28

CPAP treatment should be commenced 8-12 weeks in advance of surgery, with flexibility required.

do you snore loudly, enough to be heard through closed door?

Age >50 years

OSA likely

0.6%

4.9%

OSA unlikely.

2.5

2.5

appendix 2 [18].

It is worth considering the main limitation of the STOP-BANG questionnaire - despite its high sensitivity it has only moderate specificity for predicting OSA. Recent work has shown an improvement in the specificity of STOPBANG if a stepwise approach to its use is taken [17].

Raised bicarbonate in a patient with a STOPBANG >3 is highly indicative for moderate-severe OSA [17]. Certain combinations of risk factors appear to confer a disproportionate risk for OSA e.g. it has been found that the predictive probability of diagnosing OSA is significantly higher when using 2 positive items of STOP + BMI >35 or male gender [18]. This is particularly pertinent in the group of patients with a STOP-BANG score 3-4 (intermediate risk). This is highlighted in appendix 2 [18].

### 2.2 Preoperative management following diagnosis

The American Society of Anaesthesiologists (ASA) has published guidelines for the perioperative management of patients with OSA [7], however the optimal clinical pathway for newly diagnosed patients is yet to be determined. At the time of writing expert opinion recommends:

- Patients with newly diagnosed moderate to severe OSA should be commenced on CPAP as per nice guidance [12] (depending on urgency of surgery)
- CPAP treatment should be commenced 8-12 weeks in advance of surgery, with flexibility required (depending on the urgency of surgery)

### 2.3 Preoperative management of patients with established OSA

Table 4. Unadjusted incidence rates and adjusted odds ratios (OR) of postoperative cardiopulmonary complications for treated and untreated obstructive sleep apnoea patients [19]. (Treatment = CPAP)

Appendix 3 offers a treatment algorithm for this patient group preoperatively.

### 2.4 Benefits of CPAP treatment in the perioperative setting

CPAP treatment has been shown to reduce or reverse the cardiovascular structural changes induced by severe OSA. It also improves AHI scores, oxygen saturation levels and functional status. A large cohort study from 2015 has demonstrated the significant benefits of perioperative CPAP use, versus no CPAP, in patients with OSA undergoing major vascular and general surgical procedures [19]. In this study, patients with OSA but not on CPAP therapy had a risk of postoperative complications 2-3 times higher than the patient cohort on CPAP. Patients treated with CPAP encouragedly had a risk of postoperative complications comparable to the group without OSA. Complication rates are summarised in table 4. This risk has been proven across several other studies, whilst also demonstrating significant reductions in hospital length of stay in patients using CPAP peroperatively [20].

### 2.5 Sleep Medicine referrals

It is strongly recommended that formal links be established between preoperative assessment, and local Sleep Medicine services at an early stage. Agreed, expedited pathways of care should be drawn up between relevant clinicians to provide objective referral and re-assessment criteria. This provides the ideal platform to optimise patient care, whilst minimising surgical waiting time.

---

**Thresholds for STOP-BANG implementation** offer different diagnostic validity in identifying individuals with possible OSA, and conversely when attempting to rule out the condition. The scheme below represents a pragmatic clinical approach to utilising the STOPBANG score achieved based on best available evidence:

- **S** do you Snore loudly, enough to be heard through closed door?
- **T** do you feel Tired or fatigued during the daytime almost every day?
- **O** has anyone observed that you stop breathing during sleep?
- **P** do you have a history of high blood pressure, with or without treatment?

**B** Body mass index >35kg/m²

**A** Age >50 years

**N** Neck circumference >40cm

**G** Male gender

* Although not externally validated, replacing the “T” question with a formal ESS of >12 may in the authors’ opinion offer greater diagnostic accuracy.

### Appendix 2 offers a treatment algorithm to aid in clinical-decision making.

The Preoperative Association

Evidence-based Guidelines for Preoperative Assessment Units
2.6 Stratification of perioperative risk

In addition to a patient's risk and severity of OSA, it is important to consider the added risks of the invasiveness of the intended surgical procedure and the postoperative analgesia requirements. The ASA Taskforce recommends the following scoring system:

A. Severity of OSA

<table>
<thead>
<tr>
<th>Points</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

B. Invasiveness of surgery and anaesthesia:

- Superficial surgery under local anaesthesia or peripheral nerve block without sedation: 0
- Superficial surgery with moderate sedation or general anaesthesia: 1
- Peripheral surgery with spinal or epidural anaesthesia (with no more than moderate sedation): 1
- Peripheral surgery with general anaesthesia: 2
- Airway surgery with moderate sedation: 2
- Major surgery with general anaesthesia: 3
- Airway surgery with general anaesthesia: 3

C. Requirement for post-operative opioids:

- None: 0
- Low dose oral opioids: 1
- High dose oral, parenteral, or neuraxial opioids: 3

D. Estimation of perioperative risk:

Overall score = score for A (0-3) plus the greater of the score for either B or C (0-6)

- 4 = increased perioperative risk
- > 4 = significantly increased perioperative risk

* One point may be subtracted if a patient has been on CPAP before surgery & will continue to use own appliance consistently during the perioperative period.

** One point should be added if a patient with mild or moderate OSA also has a higher resting PaCO₂ (> 6.5 KPa)

2.7 In-patient vs. day case surgery

There are many factors that influence whether day case surgery is appropriate for patients with OSA. These include:

1. Patients' OSA status i.e. mild to severe
2. Anatomical & physiological abnormalities
3. Status of co-existing diseases
4. Nature of surgery
5. Type of anaesthesia
6. Need for post-operative opioids
7. Patients' age
8. Adequacy of post-discharge observations
9. Capabilities of the day case facilities

Owing to insufficient literature to offer recommendations, a rational approach is required when planning for day case surgery suitability. Procedures typically performed as day case surgery in non-OSA patients may also be performed for OSA patients when local or regional (loco-regional) anaesthesia is administered. Opinion is equivocal regarding whether superficial procedures may be safely performed with general anaesthesia on a day case basis. Other factors, listed above, may offer additional reasons for inpatient surgery as opposed to day case surgery. The absolute contraindications to day case surgery for OSA patients would include airway surgery and children < 3 years for tonsillectomy.

Any facility offering day case surgery should be well equipped with emergency difficult airway equipment, ability to offer non-invasive respiratory support (CPAP, NIPPV), radiological (CXR) & laboratory services (ABG, electrolytes), and a robust transfer arrangement to an inpatient facility in place.

2.8 General perioperative tips for patients requiring CPAP therapy (based on expert opinion)

- Perform surgery under central neuraxial blockade or loco-regional anaesthesia where possible to decrease risk of complications [21]. If sedation is to be used in conjunction, it is advisable to institute the patients' normal CPAP therapy during surgery.
- In patients undergoing any form of surgery under general anaesthesia it is preferable to provide loco-regional analgesia postoperatively rather than using systemic opioids. It is also advisable to institute normal CPAP therapy immediately postoperatively in the recovery area.
- Organise an inpatient bed prior to surgery for any patient scoring >4 on the ASA Taskforce risk stratification tool (described above) i.e. individuals with a high perioperative risk of complications.
- Consider postoperative Critical Care for particularly high-risk patients or for surgical procedures graded as 'Complex' by NICE [22]. This recommendation will require flexible implementation depending on resources available locally at different institutions.
- Where a high index of suspicion exists that significant OSA is likely, but surgical urgency excludes a formal diagnosis, individual patients should be assumed to be suffering from the condition and appropriate provisions made.

3. CONCLUSION

OSA is an increasingly common problem in patients presenting for surgery, with increased risk of adverse outcome where the underlying condition is not optimized. Preoperative assessment clinics provide the ideal environment to facilitate first-line diagnosis and thereby mitigate further associated risk. A coordinated, agreed, perioperative management plan should be set through the preoperative assessment process and cascaded to all relevant clinical teams in advance of surgery.
References

3. Greenstone M, Hack M. Obstructive Sleep Apnoea. BMJ. 2014 Jun 17;348:g3745
4. Peppard PE, Young T et al. Longitudinal study of moderate weight change and sleep disordered breathing. JAMA 2000;284: 3015-21
7. American society of Anaesthesiologists: Practice guidelines for the perioperative management of patients with obstructive sleep apnoea. An updated report by the American Society of Anaesthesiologists Task Force on perioperative management of patients with obstructive sleep apnoea; Anaesthesiology 2014; 120 (2): 1-19

Further Reading


APPENDIX 1: Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the situations described below, in contrast to just feeling tired?

This refers to your usual way of life in recent times.

Even if you haven’t done some of these things recently try to work out how they would affect you.

Use the following scale to choose the most appropriate number for each situation:

<table>
<thead>
<tr>
<th>Situation</th>
<th>Chance of dozing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>0 = never, 1 = Slight, 2 = Moderate, 3 = High</td>
</tr>
<tr>
<td>Watching TV</td>
<td></td>
</tr>
<tr>
<td>Sitting inactive in a public place</td>
<td></td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td></td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td></td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td></td>
</tr>
<tr>
<td>Sitting quietly after lunch without alcohol</td>
<td></td>
</tr>
<tr>
<td>In a car, as the driver, stopped in traffic for a few minutes</td>
<td></td>
</tr>
</tbody>
</table>

Outcomes

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 10</td>
<td>Normal limits</td>
</tr>
<tr>
<td>11 – 12</td>
<td>Borderline</td>
</tr>
<tr>
<td>13 – 15</td>
<td>Mild daytime sleepiness</td>
</tr>
<tr>
<td>16 – 18</td>
<td>Moderate daytime sleepiness</td>
</tr>
<tr>
<td>19 – 24</td>
<td>Excessive daytime sleepiness</td>
</tr>
</tbody>
</table>
APPENDIX 2: Recommended pathway to manage preoperative patients in conjunction with STOPBANG screening tool

Suspected OSA patients

Screening using STOP-BANG Questionnaire

Score of 0-2

Low risk of moderate/severe OSA

Proceed with planned surgery

Score of 3-4*

Area of uncertainty
Maintain High Index of Suspicion

Does patient have significant co-morbidities?

- Heart failure
- Arrhythmias
- Uncontrolled BP
- Metabolic Syndrome

NO

NICE Minor/Intermediate surgery

Proceed with planned surgery

YES

NICE Major/Complex surgery

Magnitude of surgery

Can surgery be performed under regional anaesthesia? Consider referral to Sleep Medicine

APPENDIX 2: Recommended preoperative management of patients with established OSA diagnosis

Established OSA patients

Severity of OSA

Mild

Have any changes occurred since last review in the Sleep Clinic?

NO

YES

Consider arranging a Sleep Medicine re-assessment

Postpone surgery*

Refer to Sleep Medicine

Moderate/severe

Patient compliant with treatment and under regular review

NO

YES

Recent change in OSA status? (e.g. increased sleepiness or worsening of other symptoms)

YES

NO

Refer to Sleep Medicine

Proceed with surgery**

* Certain combinations of risk factors appear to confer an increased risk for OSA. This is particularly pertinent in the 'area of uncertainty' with male gender and BMI ≥ 35 appearing to be particularly pertinent. We therefore recommend a lower threshold for consideration of further assessment where these factors are present in combination with a total score of 3 – 4.

** If surgery is urgent then proceed, but treat as if established OSA diagnosis

* If surgery is urgent then proceed, but treat as if established OSA diagnosis

** Recommended that patients use treatment appliance e.g. CPAP in perioperative period
A Clinical Approach to the Role of Lung Function Testing in Pre-Operative Evaluation
Brendan Patrick Madden¹ and Nordita Ramos-Bascon²

¹ Professor of Cardiothoracic Medicine, St Georges University of London NHS Foundation Trust, London, UK
² Cardiothoracic Clinical Nurse Specialist, St Georges University of London NHS Foundation Trust, London, UK

Summary and Key Recommendations

- Lung function tests are an essential aspect of pre-operative evaluation and all pre-assessment units should have easy access to simple spirometry as well as the ability to refer patients for formal lung function testing.
- The FEV₁/FVC ratio distinguishes between a predominantly obstructive and predominantly restrictive lung pathology.
- The FEV₁ as a percentage of predicted is a measure of the severity of airflow obstruction.
- Patients with severe airflow obstruction or restrictive lung disease are at risk of complications from mechanical ventilation due to high inflation pressures.
- Flow volume curves can reveal reduced small airway calibre and both extra and intra thoracic airway obstruction.
- Measurement of diffusion capacity (gas transfer) gives important information regarding the integrity and size of the alveola/blood membrane.
- Unexplained dyspnea or reduction in gas exchange should prompt consideration of underlying pulmonary embolism or of pulmonary hypertension.
- Prompt referral to appropriate specialists for pre-operative diagnosis and optimisation is indicated if significant abnormalities are identified.

INTRODUCTION
Lung function tests have an established role in assessing and managing patients with diverse cardiorespiratory pathologies. They provide important information regarding:

1. Diagnosis
2. Monitoring therapeutic response
3. Documenting disease cause
4. Pre-operative assessment
5. Disability evaluation
6. Prognosis

The indications for lung function testing are listed in Table 1 and contraindications are listed in Table 2.

Table 1. Indications for performing lung function tests

<table>
<thead>
<tr>
<th>1. Investigations of patients with symptoms/signs/investigations that suggest pulmonary disease e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cough</td>
</tr>
<tr>
<td>• Wheeze</td>
</tr>
<tr>
<td>• Breathlessness</td>
</tr>
<tr>
<td>• Crackles</td>
</tr>
<tr>
<td>• Abnormal chest x-ray</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Monitoring patients with known pulmonary disease for progression or response to treatment e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Interstitial fibrosis</td>
</tr>
<tr>
<td>• COPD</td>
</tr>
<tr>
<td>• Asthma</td>
</tr>
<tr>
<td>• Pulmonary vascular disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Investigations of patients with disease that may have a respiratory complication e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Connective tissue disorders</td>
</tr>
<tr>
<td>• Neuromuscular diseases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Perioperative evaluation prior to e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Lung resection</td>
</tr>
<tr>
<td>• Abdominal surgery</td>
</tr>
<tr>
<td>• Cardiothoracic surgery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Evaluation of patients at risk of lung disease e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exposure to pulmonary toxins such as radiation, or environmental or occupational exposure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Surveillance following lung transplantation to assess for</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute rejection</td>
</tr>
<tr>
<td>• Infection</td>
</tr>
<tr>
<td>• Obliterative bronchiolitis</td>
</tr>
</tbody>
</table>
Static lung volumes (Figure 2) are measured with specialised equipment in the lung function laboratory using body plethysmography (with the patient sitting inside an airtight box using an application of Boyle’s Law) and by helium dilution. The latter employs the law of conservation of mass. Functional residual capacity (FRC) is the volume of air in the lungs following normal expiration. Residual volume (RV) is the amount of air remaining in the lungs after a maximal inspiration (normally 500mls). Total lung capacity (TLC) is the total volume of air in the lungs after a maximal inspiration. It is the sum of RV and vital capacity.

The measured lung function test results are presented as absolute values but importantly also as percentage predicted correlated with age and sex matched population controls.

If patients have FEV1, FVC or PEFR in the region of 30% predicted and if these values are not significantly reversible, then they have severe impairment of respiratory function which in theory would render them potential candidates for lung transplantation should they fulfil lung transplant inclusion criteria. This needs to be borne in mind when considering elective surgical intervention. In general, if patients have severe airflow obstruction, they will not only tend to trap air (i.e. have a high RV) should they require mechanical ventilatory support, but in addition, high inflation pressures will be required. This increases the potential risk of lung injury from barotrauma, which includes pneumothorax, and acute lung injury and infection. In addition, the increased intrathoracic pressure reduces venous return to the heart and as a consequence leads to reduced cardiac output which can facilitate the development of multiple organ dysfunction. RV can be expressed as a percentage of TLC and values in excess of 140% of normal RV contribution to TLC significantly increases the risk of these complications occurring.

Similarly, patients who have significant restrictive physiology will require high perioperative inflation pressures should mechanical ventilatory support be required which can also cause significant perioperative complications. Those with restrictive lung disease will typically have low capability for gas transfer and therefore will also be poorly tolerant of atelectasis, pneumothorax, perioperative infection, acute lung injury or haemodynamic compromise. In addition, patients with restrictive and obstructive lung disease may have associated significant pulmonary hypertension, which may warrant further assessment and therapeutic intervention prior to surgery.

In the past, patients who had smoking-associated lung disease with typical heterogeneous emphysema with predominant upper zone involvement and who had significant elevation in RV

**Table 2. Contraindications to performing lung function tests**

| Myocardial infarction within the last month |
| Stable aneurysm |
| Recent thoraco-abdominal surgery |
| Recent ophthalmic surgery |
| Thoracic or abdominal aneurysms* |
| Current pneumothorax |

*Thoracic and abdominal aortic aneurysms are considered relative contraindications and should be discussed on an individual clinical basis.

The simplest investigations to perform are spirometric measurements of forced expiratory volume in one second (FEV1) (Figure 1), forced vital capacity (FVC) and peak expiratory flow rate (PEFR). These measurements can be performed at the bedside with minimal equipment and provide important information. The ratio of FEV1/FVC is in the region of 70%. If a disease causes a preferential reduction in FEV1, it is termed obstructive. Overall, the ratio will fall and the degree of that obstruction will be reflected in the calculated figure. Examples include asthma and smoking-related lung disease. The severity of chronic obstructive pulmonary disease (COPD) is graded depending on the degree of airflow obstruction (Table 3).

**Table 3. Severity of airflow obstruction in COPD**

<table>
<thead>
<tr>
<th>FEV1 % predicted</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;80%</td>
<td>Mild</td>
</tr>
<tr>
<td>50-79%</td>
<td>Moderate</td>
</tr>
<tr>
<td>30-49%</td>
<td>Severe</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>Very severe</td>
</tr>
</tbody>
</table>

In patients with restrictive physiology, the FVC falls to a greater extent than the FEV1 and the ratio therefore increases. Examples include interstitial lung disease and sarcoidosis. In these conditions, airflow is usually normal.
Evidence-based Guidelines for Preoperative Assessment Units

The Preoperative Association

The shape of the flow volume curve is very important (Figure 3). Following inspiration, there is a rapid rise in the expiratory arm of the curve to the peak expiratory flow rate. The patient continues to exhale to forced vital capacity. In addition to the morphology of the curve, it is important to look at maximal expiratory flow rate (MEFR) at 25%, 50% and 75% of expiration to forced vital capacity. Flow rate at these levels is indicative of small airflow calibre and therefore is an important measurement of small airway patency which may require therapeutic intervention. Patients can have relatively normal FEV1, FVC and PEFR but MEFR may be significantly reduced.

Clinical Examples

1. Restrictive Lung Disease

A 51-year-old non-smoking male patient has a proportionate reduction in FEV1 and FVC (68% and 65% predicted respectively). PEFR is normal at 99% and the FEV1/FVC ratio is increased at 91% indicating restrictive lung disease with preserved airflow function relative to the restrictive pathology. The TLCO and KCO are proportionately and markedly reduced (Figure 4). The flow volume curve showed that the vital capacity was significantly reduced at 2.2 litres (Figure 5). Following respiratory referral, this patient had a thoracic CT scan (Figure 6) which showed evidence of pulmonary fibrosis with ground glass change, honeycombing and traction bronchiectasis. Unfortunately, he did not respond to immunosuppressant therapies and therefore it was decided that he was not fit for proposed surgical intervention. This was on the grounds that he would be poorly tolerant of mechanical ventilatory support, at high risk of ventilator-associated complications including pneumonia, that his respiratory function could deteriorate rapidly following surgery and that furthermore the restriction in his exercise capacity as a consequence of his very reduced gas transfer capabilities would have been a significant postoperative limiting factor to his rehabilitation.

<table>
<thead>
<tr>
<th>Predicted Range</th>
<th>Result</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>2.35-3.60</td>
<td>2.03</td>
</tr>
<tr>
<td>FVC</td>
<td>2.70-4.11</td>
<td>2.23</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>84%</td>
<td>91%</td>
</tr>
<tr>
<td>PEF</td>
<td>346-523</td>
<td>490</td>
</tr>
<tr>
<td>RV</td>
<td>0.70-1.85</td>
<td>1.38</td>
</tr>
<tr>
<td>TLC</td>
<td>3.67-5.63</td>
<td>3.66</td>
</tr>
<tr>
<td>RV/TLC%</td>
<td>18-37</td>
<td>37</td>
</tr>
<tr>
<td>TLCO</td>
<td>7.65-11.48</td>
<td>3.02</td>
</tr>
<tr>
<td>VA</td>
<td>3.34-5.13</td>
<td>3.49</td>
</tr>
<tr>
<td>KCO</td>
<td>1.77-2.43</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Figure 4

The measurement of diffusion capacity (DLCO also known as transfer factor) gives important information regarding the integrity and size of the alveolar blood membrane which is determined by the surface area and integrity of the alveolar membrane and the pulmonary vascular bed. Normally the value is corrected for the patient’s haemoglobin (DLCOc). DLCOc is measured using carbon monoxide, which is soluble and binds to haemoglobin with its uptake limited by diffusion only. It is measured by a single breath technique.

DLCOc is determined by the surface area of the alveolar area and as such, it is impaired in conditions where the surface area is reduced e.g. pulmonary fibrosis, emphysema or pulmonary emboli. The transfer coefficient (KCO) is DLCOc corrected for alveolar volume. In patients with a pneumonectomy, DLCOc may be reduced due to the loss of approximately half of the surface area of alveolar membrane but KCO will remain normal if the remaining lung is normal with normal function of the alveolar blood membrane. Similarly, variation can be seen in diseases that affect the lungs in a heterogeneous manner e.g. COPD or alpha1 antitrypsin emphysema. In COPD, the upper lobes tend to be preferentially damaged whereas in alpha 1 antitrypsin deficiency the lower lobes are predominantly involved. DLCOc will be lower than KCO. Pulmonary emboli should be considered in patients with an isolated reduction in DLCOc without any other obvious respiratory cause.

In patients with pulmonary fibrosis, the condition is usually homogenous and affects both lungs similarly. The DLCOc and KCOc are normally equally reduced.

Flow volume curves

The flow volume curve comprises of an inspiratory phase to maximal capacity followed by an expiratory phase to forced vital capacity. This procedure is performed in a way that often puts patients at a level of anxiety that can interfere with the results. Therefore, following an initial inspiration, a slow vital capacity (SVC) is also performed wherein the patient is asked to exhale slowly to a maximal expiratory volume.

(greater than 180% predicted) were considered for lung volume reduction surgery. In this procedure, non-anatomic stapling or resection of apical bullous disease was performed with a view to decompressing the middle and lower zones of each lung, to improve respiratory mechanics, airflow and gas exchange. Although this surgery is not frequently performed now, endobronchial valve deployment may be useful for selected patients with emphysema. Pulmonary rehabilitation remains an important aspect of treatment. Patients who have high residual volumes with a significant dead space present a major concern for perioperative mechanical ventilatory support.
2. Obstructive Lung disease
This was a 74-year-old male 40 pack-year cigarette smoker, who had an FEV1, FVC and PEFR are 18%, 41% and 21% predicted respectively with as FEV1/FVC ratio of 35%. This patient has severe airflow obstruction (Figure 7) associated with smoking-related lung disease. The residual volume (RV) is 269% predicted. As the emphysema was heterogeneous with more marked upper zone involvement, the overall area of gas transfer is reduced at 46%; however, the KCO was higher at 63% predicted in the face of VA of 77% predicted. This patient would be poorly tolerant of endobronchial intervention and mechanical ventilatory support, and would be likely to develop significant consequences of barotrauma such as acute lung injury, pneumothorax and impaired haemodynamic performance. Furthermore, if mechanical ventilation was necessary, the likelihood of being weaned successfully post-operatively would be low.

A flow volume curve from this patient is shown in Figure 8 and the thoracic CT scan in Figure 9. As you can see in figure 8, the flow volume curve falls off quickly during forced expiration. This is often referred to as ‘scalloping’ and occurs because the small airways tend to collapse as a consequence of damage to the surrounding tissues from the emphysematous process and the lack of maintenance of radial support. There may also be associated small airway inflammatory changes, which intrinsically reduces airway lumen. In addition, there may be large airway malacia, which compounds the problem. The Thoracic CT scan shows bilateral emphysematous disease.

3. Reversible airflow reduction
In a 26-year-old female non-smoker respiratory function tests showed airflow obstruction with FEV1, FVC, FEV1/FVC ratio and PEFR of 57%, 87%, 56% and 69% predicted respectively (Figure 10). Gas transfer is not reduced. This was an airflow problem with no parenchymal lung pathology. The RV was increased at 143% predicted. An important lesson here is that even though the patient’s actual results for FEV1, FVC and PEFR (2.38L, 4.28L at 400L/min respectively) are reasonable, it can be shown that following a bronchodilator challenge, there was a significant improvement in FEV1 (2.38 to 3.33L/sec, 55% improvement). This is important as it suggests that the patient needs to be optimised prior to surgical intervention and furthermore at the time of anaesthesia, as this patient’s airway function was not stable, she may acutely develop bronchoconstriction and present as a medical emergency. Following optimisation which included broncho-modulation, the patient received successful surgical intervention without perioperative complication.

Figure 7

<table>
<thead>
<tr>
<th>Predicted Range</th>
<th>Result</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>2.82-4.49</td>
<td>0.65</td>
</tr>
<tr>
<td>FVC</td>
<td>3.60-5.60</td>
<td>1.88</td>
</tr>
<tr>
<td>FEV1/FVC %</td>
<td>77%</td>
<td>35%</td>
</tr>
<tr>
<td>PEFR</td>
<td>411-649</td>
<td>60</td>
</tr>
<tr>
<td>VC</td>
<td>3.60-5.60</td>
<td>2.22</td>
</tr>
<tr>
<td>FRC</td>
<td>2.63-4.60</td>
<td>6.50</td>
</tr>
<tr>
<td>RV</td>
<td>1.67-3.01</td>
<td>6.28</td>
</tr>
<tr>
<td>TLC</td>
<td>6.15-8.45</td>
<td>8.50</td>
</tr>
<tr>
<td>RV/TLC%</td>
<td>26-44</td>
<td>74</td>
</tr>
<tr>
<td>TLCO</td>
<td>8.03-12.65</td>
<td>4.75</td>
</tr>
<tr>
<td>VA</td>
<td>5.60-7.69</td>
<td>5.13</td>
</tr>
<tr>
<td>KCO</td>
<td>1.04-1.93</td>
<td>0.93</td>
</tr>
</tbody>
</table>

4. Extra-thoracic large airway obstruction
A 28-year-old female HIV positive from Angola who subsequently developed pneumocystis carinii pneumonia. She was prone to keloid formation. She was intubated and had a tracheostomy fashioned. Following six weeks of mechanical ventilatory support, she was successfully weaned and the tracheostomy was removed. After decannulation, she developed significant airflow obstruction and this flow volume curve shows a symmetrical appearance of the inspiratory and expiratory phases, which is compatible with extra-thoracic large airway obstruction (Figure 11). She had a CT trachea with reconstruction (Figure 12) which showed a significant tracheal stenosis. She was successfully treated at rigid and fibreoptic bronchoscopy with laser fulguration.

Figure 10

Figure 11

Figure 12

5. Intra-thoracic large airway obstruction
The flow volume curve (Figure 13) shows a normal inspiratory phase with compression of the expiratory phase. This patient (a 76-year-old male) had intra-thoracic large airway obstruction due to a tumour of the right main bronchus (Figure 14). Following biopsy, the tumour was cleared using laser therapy and airway patency was restored with a right main bronchial stent. Due to proximity to the carina, he did not have a pneumonectomy.
Vascular issues

1. Pulmonary Embolism

In patients with unexplained dyspnoea with no obvious parenchymal or airflow respiratory disease, one needs to consider vascular conditions. These include pulmonary embolism diagnosed by ventilation/perfusion (VQ) scanning or by computerised tomographic pulmonary angiography (CTPA). Pulmonary embolisation is an important cause of reduction of gas transfer capabilities and of pulmonary hypertension. Once diagnosed, it is essential to investigate for an underlying cause. Intrapulmonary thrombotic elements have been frequently encountered in patients with Covid-19 infection who often have pulmonary emboli or in-situ thrombosis affecting segmental and sub-segmental peripheral vessels.

In VQ scanning, the ventilatory phase is usually normal because there is no significant airflow pathology. However, the perfusion to areas of the lung will be compromised as a result of the thrombotic process and therefore a ventilation/perfusion inequality will be observed (Figure 16).

On CTPA, thrombotic elements are visible. They may require thrombolysis if associated with haemodynamic compromise and require anticoagulation. Figures 17 shows CTPA with a massive central pulmonary embolism. The patient received successful thrombolysis. Phosphodiesterase type 5 inhibitors (e.g. Sildenafil) to maximise pulmonary perfusion and decrease pulmonary vascular resistance (PVR) may be additionally prescribed if there is significant pulmonary hypertension.
2. Pulmonary Hypertension

Pulmonary hypertension is defined in patients who have a mean of pulmonary artery pressure (PAP) in excess of 25mmHg at rest. In health, the normal mean PAP is 12 +/-2mmHg and the normal left atrial filling pressure or pulmonary capillary wedge pressure (PCWP) is 6 +/- 2mmHg and cardiac output (CO) is 5L/min. Using an adaptation of Ohm's Law of electrical circuitry, the PVR is calculated as follows:

\[ PVR = \frac{(\text{mean PAP}) - (\text{mean PCWP})}{\text{CO}} \]

In health, this is normally <1.5mmHg/L/min (1mmHg/L/min is known as a Wood unit). In patients with pulmonary hypertension, the PVR can be dramatically increased and this is seen in Figure 18 in a patient with dilated proximal pulmonary arteries and poor peripheral perfusion (pruning).

Pulmonary hypertension can be characterised into five groups. Group 1 includes disease processes that share the common histological presentation of plexogenic pulmonary arteriopathy. Examples are idiopathic and familial pulmonary hypertension, pulmonary hypertension associated with Eisenmenger syndrome, pulmonary hypertension associated with connective tissue disease, hepatic cirrhosis, HIV infection and Schistomiasis. Group 2 conditions lead to pulmonary hypertension secondary to left atrial hypertension e.g. left heart failure while Group 3 diseases produce pulmonary hypertension associated with chronic pulmonary thromboembolism while those in Group 5 represent a heterogeneous group which includes patients with renal failure requiring haemodialysis.

In general, patients in Groups 1, 4 and selected patients in group 5 may be candidates for advanced pulmonary vasodilator therapy, which includes phosphodiesterase type 5 inhibitors (e.g. Sildenafil), endothelin receptor antagonists (e.g. Macitentan) and prostaglandin therapy. Some patients may be candidates for lung transplantation and for selected patients with chronic thromboembolic pulmonary hypertension, pulmonary thromboendarterectomy may be an option. It should be appreciated that advanced pulmonary vasodilator therapy is usually prescribed for appropriate patients whose left atrial filling pressure is <15mmHg. This is because the enhanced venous return through the lung circulation attendant on pulmonary vasodilator therapy can potentiate acute left heart failure in a patient whose PCWP exceeds 15mmHg.

Echocardiography provides important information regarding the size and the function of the right ventricle, the degree of tricuspid regurgitation, the systolic excursion of the tricuspid valve annular plane and an estimate of pulmonary artery systolic pressure. It may also show evidence of underlying structural heart disease e.g. an atrial septal defect or valvular pathology. Confirmation of diagnosis is obtained at right heart catheterisation. Unlike echocardiographic evaluation, right heart catheterisation (Figures 19 and 20) provides direct measurements of mean PAP, mean PCWP and mean CO. It is also possible to directly measure oxygen saturations at different levels if intracardiac shunting is suspected. PVR is a key measurement. If patients have advanced pulmonary hypertension, it is possible that the echocardiographic estimated calculation of pulmonary artery systolic pressure will be a false representation of the severity of their pulmonary hypertension because right ventricular cardiac output progressively falls with time as the PVR increases. A relatively low PASP on echocardiography could provide false reassurance that pulmonary hypertension is not as severe as it actually is. Such reassurance could be catastrophic at the time of anaesthetic induction. If the systemic vascular resistance falls significantly, venous return to the right atrium is reduced. However, the PVR remains elevated or indeed in some patients can increase further as a consequence of vasoconstriction. As a result, there is reduced perfusion across the pulmonary circulation and reduced venous return to the left atrium. Such a ‘pulmonary hypertensive crisis’ can cause profound hypotension or death as a consequence of cardiac arrest.

It is most important that should patients have evidence of pulmonary hypertension that they are referred for further investigation, diagnosis and treatment prior to surgical intervention. If patients have known pulmonary hypertension, there should be early discussion with the pulmonary hypertension centre to develop a coordinated treatment approach. For example, if patients will be unable to take specific medication orally post-operatively, then consideration would have to be given to alternative routes which may include the intravenous or nebulised approach. Additionally, should patients become pregnant, some advanced pulmonary vasodilator therapy (e.g. endothelin receptor antagonists) are contraindicated.

Patients who have significant pulmonary hypertension will often be poorly tolerant of laparoscopic surgical intervention and an open surgical approach is often preferred. This is because the gas insufflation in the abdomen causes compression of the inferior vena cave which will reduce venous return to the right atrium and in turn lead to significant reduction in left atrial filling in the presence of an increased PVR.

Information from right heart catheterisation is presented from a 32-year-old female patient who was subsequently diagnosed with idiopathic pulmonary arterial hypertension (Group 1). She initially presented with dyspnoea climbing stairs following the birth of her first child. It can be seen that she has significant pulmonary hypertension with an estimated PVR exceeding 12 wood units. Of note is that is her PVR has risen significantly and her CO has reduced. This patient needed urgent dual advanced pulmonary vasodilator therapy, which led to significant improvement in her pulmonary haemodynamics.

<table>
<thead>
<tr>
<th>Right Heart Catheterisation readings</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA: 10mmHg</td>
</tr>
<tr>
<td>RV: 62/15mmHg</td>
</tr>
<tr>
<td>PA: 66/38mmHg - mean PA 51mmHg</td>
</tr>
<tr>
<td>PCWP: 11mmHg</td>
</tr>
<tr>
<td>CO: 3.23 L/min</td>
</tr>
<tr>
<td>PVR: 12.38 Woods units</td>
</tr>
</tbody>
</table>
Summary

Lung function tests are an essential aspect of pre-operative evaluation. Attention should be given not only to actual and predicted values of airflow, volumes and gas transfer, but also considered in conjunction with clinical presentation and arterial blood gas analysis. Unexplained dyspnoea or reduction in gas exchange should prompt consideration of underlying pulmonary embolism or pulmonary hypertension. Prompt referral to appropriate specialists for diagnosis and optimisation is indicated if significant abnormalities are identified and a therapeutic strategy should then be developed within the confines of a multidisciplinary team (MDT). It is also important to fully consider prognosis based on clinical presentation and response or indeed lack of responsiveness to optimisation. If the patient has a significant reduction in actuarial survival based on their cardiorespiratory disease, this would impact on the consent procedure. Equally, if it is likely that the patient will develop additional lung injury as a consequence of mechanical ventilatory support or indeed may require prolonged post-operative weaning via a tracheostomy with all the potential attendant complications, this too should be considered in detail pre-operatively.

With the evolution of the speciality of pre-operative medical assessment, we should broaden the concept of lung function testing in assessing cardiorespiratory function. These tests are a dynamic assessment and may mandate further imaging, invasive studies and referral to specialist colleagues. Results should be discussed within the confines of an MDT as necessary to advise on pre-operative optimisation to ensure best outcome.

Further Reading

Introduction

In 2013-14, more than 70,500 people had a pacemaker fitted in England, and more than 10,000 had an implantable cardioverter defibrillator (ICD) fitted. As the population gets older; this number continues to rise. The blanket term Cardiac Implantable Electronic Devices (CIEDs) is now commonly adopted by healthcare professionals to describe pacemakers, ICDs, and implantable loop recorders (ILRs).

Most pacemakers are inserted for the treatment of persistent, symptomatic bradycardia, and some patients have no underlying rhythm and are therefore pacemaker-dependent and will become asystolic if the pacemaker stops working. ICDs are inserted for the treatment of ventricular arrhythmias (VT/VF), while CRT (cardiac resynchronisation therapy) devices are used to optimize ventricular activation and improve cardiac function in heart failure.

Many of these people will need some form of general surgery, either in a planned elective procedure or as an emergency. In either setting, it is vitally important that appropriate care be provided so that the techniques used in surgery, particularly diathermy / electrocautery, do not cause harm to the patient or their device.

Cardiac Implantable Electronic Devices

Pacemakers and defibrillators are designed to sense intra-cardiac electrical signals and deliver therapy according to need. However, diathermy/electrocautery (and other sources of electromagnetic interference (EMI)) can be misinterpreted by CIEDs as intrinsic cardiac activity and result in inappropriate inhibition of pacing and potentially asystole in a pacing dependent patient. EMI may also result in the induction of fixed rate pacing, or software reset. However, most EMI is usually transient in its effect, with resumption of normal device function upon withdrawal of the interference. Permanent device effects are uncommon and encountered usually in the setting of powerful magnetic fields only (eg. gamma radiation or very strong magnetic fields).

ICDs are implanted in patients who are at risk of life-threatening ventricular arrhythmia, most commonly those with poor ventricular function as a consequence of coronary artery disease, but also in patients with dilated or hypertrophic cardiomyopathy, channelopathies eg. Brugada and long QT syndromes. If an ICD senses external electrical activity, it may interpret this as VT or VF, and deliver inappropriate anti-tachycardia pacing and/or DC shock therapy, which if delivered to a heart in an otherwise stable rhythm may cause cardiac arrest.

Implantable loop recorders are diagnostic devices which permit long term monitoring of cardiac rhythm in suspected intermittent arrhythmia. Whilst they do not represent any additional risk during surgery, EMI from diathermy will be stored as episodes of tachycardia and where possible it would be desirable to interrogate the device before surgery and clear the stored memory after.

Magnets and Cardiac Implantable Electronic devices

Placing a magnet over an unknown device is not recommended. Pacemakers react in different ways to magnets being placed over them, depending on their manufacturer’s settings. Almost all will revert to an asynchronous fixed pacing mode at a rate set by the manufacturer. Asynchronous fixed pacing can cause life threatening arrhythmias if a mis-timed stimulus causes a premature ventricular complex to occur at the critical time during the T wave of the preceding beat. This so-called R-on-T phenomenon, may trigger polymorphic VT or VF.

In general, a magnet placed over an ICD will suspend anti-tachycardia therapy (ATP) and defibrillation, for the duration of the placement of the magnet. Any pacing function will be unaffected. Alternative
means for defibrillation must therefore be available, so it’s essential to place external pads on the
patient before surgery begins if these could not be placed easily during surgery. Care must be taken as
if the magnet slips; the ICD will usually revert to its original settings. It is essential a magnet is readily
available in theatre complex for management of patients with implantable electronic devices.

Classification of Pacemakers and ICDs

Pacemakers may be single chamber, dual chamber or biventricular, depending on where they sense
native cardiac impulses, where they direct their pacing impulses, and how many leads are present. They
are commonly described according to the NBG Pacemaker Code illustrated below. E.g. VVI pacemaker
paces the Ventricle, senses the Ventricle, and inhibits pacing when native ventricular activity is sensed.
Rate modulation refers to the ability of the pacemaker to adapt to different physiological states e.g.
increased heart rate during exercise, or the ability to sense and respond to changes in acid-base status.
Multisite pacing is an indication that the pacemaker can stimulate at multiple sites within the same
anatomical area e.g. multiple sites within the atria. Most pacemakers are either VVI or DDDR (leads in
both right atrium and ventricle, triggered and inhibited + rate modulation)

<table>
<thead>
<tr>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
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</thead>
<tbody>
<tr>
<td>Chamber(s) paced</td>
<td>Chamber(s) sensed</td>
<td>Response to sensing</td>
<td>Rate Modulation</td>
<td>Multisite pacing</td>
</tr>
<tr>
<td>0 = None</td>
<td>0 = None</td>
<td>0 = None</td>
<td>0 = None</td>
<td>0 = None</td>
</tr>
<tr>
<td>A = Atrium</td>
<td>A = Atrium</td>
<td>T = Triggered</td>
<td>R = Rate modulation</td>
<td>A = Atrium</td>
</tr>
<tr>
<td>V = Ventricle</td>
<td>V = Ventricle</td>
<td>I = Inhibited</td>
<td>V = Ventricle</td>
<td></td>
</tr>
<tr>
<td>D = Dual (A+V)</td>
<td>D = Dual (A+V)</td>
<td>D = Dual (V+I)</td>
<td>D = Dual (A+V)</td>
<td></td>
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</tbody>
</table>

Fig 1: The North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and

Pre-operative Management

Patients with any CIED need to be identified at pre-operative assessment screening. Often the
patient has a registration card, and the type of device, manufacturer and model number should be
noted. The reason for the implant (e.g. low ejection fraction) needs to be verified and documented
as part of the pre-admission process.

The cardiology department should be contacted for advice, following a local protocol. Most patients
will not need their device interrogated by a cardiac technician prior to surgery if their pacemaker
was checked within the previous year, and ICDs within the previous six months (without any shocks
being delivered in this interim).

It is important to determine:

- Type of device and manufacturer (Pacemaker / ICD / ILR)?
- Implanting hospital, follow-up hospital?
- Date of last follow-up?
- Reason for insertion of CIED?
- If the patient is pacemaker dependant i.e. at risk of asystole in the event of pacing inhibitions?
- If the battery is near depletion? This will determine the asynchronous rate and may result in the
device not functioning at all if affected by diathermy and the battery is low.

- Device location? CIEDs are usually implanted in the left or right pre-pectoral region; however,
some devices may be located in left lateral chest wall and very rarely the abdomen.
- What effect placing a magnet over the CIED will produce?
- What settings are programmed for an ICD to detect and treat VT/VF?

If the patient has an ICD, a cardiac technician should be requested to turn the defibrillation setting
off immediately prior to surgery, and back on immediately afterwards. If the cardiology department
cannot provide this service or it is outside normal hours, advice should be sought as to whether
placing a magnet over the device is an appropriate alternative. Any anti-arrhythmic or beta-blocker
therapy should be continued peri-operatively, and not withheld. This may necessitate giving small
intravenous doses post-operatively if the patient is nil by mouth.

Intra-operative Management (Elective Surgery)

- There must be an external defibrillator with external pacing capability within the operating room,
and if the patient is pacemaker-dependant, we recommend placing the pads on the chest prior to
surgery.
- Be aware that shivering, large tidal volumes and succinylcholine induced fasciculations may be
interpreted by a pacemaker in demand mode or an ICD, as intrinsic cardiac activity, and severe
bradycardia, asystole or defibrillation may ensue.
- Make sure the ECG monitor is in non-paced mode (so that pacing spikes are not interpreted as
complexes in the event of asystole).
- Place the defibrillator plate as far from the device as possible and avoid the device being between
the operation site and plate e.g. if the device is in the in upper left chest, place plate on right
thigh for surgery below the chest.
- Do NOT place a ring magnet over the device, unless advised to do so by a Cardiac Physiologist /
Cardiologist who knows the details of that patient’s device and programming.
- Monopolar diathermy should not be used near a pacemaker generator or ICD (eg ipsilateral upper
anterior chest wall, shoulder or neck area) due to high risk of EMI and attendant risks already
described.

If diathermy must be used:

- Use bipolar diathermy where possible, to minimise electrical interference.
- If monopolar diathermy is essential, use away from the device, and in short bursts, 1 second or less,
with ECG monitoring to observe the effect on the rhythm. Pure cut is better than blend or
coagulation.
- Between each 1 second burst of diathermy there should be a 3 second delay to allow recovery
from any asystole that occurs during the delivery of diathermy.
- If a serious arrhythmia develops during diathermy, treat the arrhythmia as usual, stop using
diathermy, complete the operation as safely as possible and contact a device physiologist as soon
as possible.
- In the event that the patient becomes asystolic, has a ventricular arrhythmia, or any pulseless
electrical activity during a surgical procedure, resuscitation and medical intervention should take
place without delay in the usual manner of managing a cardiac arrest – irrespective of the
patient’s device.

Emergency Surgery (out of normal hours)

- If cardiological advice is not available, a magnet will usually cause a suspension of the shock
function in an ICD. The magnet needs to be secured over the device with tape for the duration of
the procedure.
• In a patient with an ICD which has not had the shock mode switched off, there must be a 10 second delay between each 1 second burst of diathermy to reduce the possibility of triggering an inappropriate shock.

Postoperative Management

• A 12-lead ECG should be performed as soon after surgery as practical. If the heart rate is below 50bpm on the 12-lead ECG there may be a problem with the device and a device physiologist should be contacted as soon as possible.
• The device technician must be called when the patient with an ICD enters recovery in order to switch the shock mode back on.
• A pacemaker / ICD check should be performed post-operatively prior to discharge if the patient has experienced arrhythmias intra-operatively, if a magnet was placed over the CIED, or if it is thought that diathermy may have damaged the CIED or leads. If the pacemaker was not interfered with prior to, or during surgery, and no adverse cardiac events occurred, the pacemaker can be interrogated at it's next routine interval.

Wireless pacemakers

The first wireless pacemaker (which is the size of a large vitamin tablet - Micra Transcatheter Pacing System 2.6mm x 6.7mm) was approved by the FDA in April 2016. The first one fitted outside of a clinical trial was implanted at the James Cook University Hospital in the same month. It is usually implanted in the right ventricle where it can deliver ventricular pacing. The usual battery life is approximately 12 years. Patients presenting for surgery with these devices in situ should be treated as per the guidelines above. The only difference is placing a magnet over the Medtronic Micra™ Transcatheter Pacing System (TPS) will not result in the pacemaker reverting to asynchronous mode. Thus patients who are pacemaker dependant will be at risk of asystole if the pacemaker interprets extrinsic electrical interference as intrinsic cardiac activity.

Guidelines for the Preoperative use of Echocardiography

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Summary and Key Recommendations

• TTE is most commonly requested to assess left ventricular function and valvular pathology.
• There is no place for routine TTE in preoperative cardiac risk assessment.
• Preoperative TTE is warranted if there are new clinical signs of cardiac failure.
• Repeat TTE is not required in chronic stable cardiac failure.
• Ejection fraction is poorly correlated with postoperative outcome.
• Aortic stenosis is a significant risk factor which is often asymptomatic.
• Preoperative TTE is indicated in a new finding of systolic murmur in those aged over 60 and in any patient if in addition the ECG is abnormal or there are cardiac symptoms.
• Preoperative TTE is indicated in the assessment of known moderate or severe aortic stenosis if the valve has not been imaged within the last 1-2 years.
• Preoperative TTE is indicated in the diagnosis and assessment of pulmonary hypertension.
• Bedside focussed TTE shows promise in addressing availability when surgery is urgent.

References
1. MHRA 2006. Guidelines for the Perioperative management of patients with implantable pacemakers or implantable cardioverter / defibrillators, where the use of surgical diathermy is anticipated.
2. BHRS 2019. British Heart Rhythm Society guidelines for the management of patients with cardiac implantable electronic devices (CIEDs) around the time of surgery.
Introduction

Perioperative cardiac complications are a significant cause of morbidity and mortality in patients undergoing elective non-cardiac surgery. Consequently, such patients should be appropriately investigated to minimise their risk of complications and to improve shared decision making. Transthoracic echocardiography (TTE) is one such investigation which is usually easily available in the elective situation, is painless and has no apparent side effects.

Unfortunately there is little published guidance about which patients should (and which should not) have a TTE before elective non-cardiac surgery. The 2016 NICE guidelines on preoperative testing gives broad indications [1] and international guidelines give advice from a cardiologists viewpoint, rather than that of a focussed preoperative healthcare professional [2,3,4,5].

This article will focus primarily on the use of static transthoracic echocardiography in the preoperative assessment of patients undergoing non-cardiac elective surgery. Transoesophageal, 3D and stress echocardiography will not be discussed, nor shall special indications such as its use prior to solid organ transplantation.

What is a Transthoracic Echocardiogram (TTE)?

A TTE is a non-invasive imaging investigation of the heart and major blood vessels. It employs the use of ultrasound to image the cardiac structures in real time, so that dynamic images and measurements can be obtained. Doppler ultrasound is also used to measure blood flow and tissue movements. For TTEs performed in the UK, a standardised investigation procedure has been devised [5]. Recently, standards have also been developed for shorter, more focussed examinations in emergency situations [6]. In the elective preoperative setting, the commonest indications for requesting a TTE are to assess left ventricular function and to investigate the presence and severity of valvular heart disease.

What information does TTE provide and what are the indications for requesting a TTE?

1.1 Left Ventricular Function

Heart failure has long been identified as being a significant risk for non-cardiac surgical patients and is a feature of the most widely known risk scoring system, the revised cardiac risk index [7]. It has also been demonstrated as major risk factor in more recent studies [8,46]. It is therefore essential that the condition is recognised and controlled before proceeding to surgery. Even stable heart failure is a recognised risk factor for post-operative complications.

Left heart failure typically presents with increasing shortness of breath, worsened by physical activity. The patient may describe breathlessness on lying flat (orthopnoea) with severe episodes occurring during the night (paroxysmal nocturnal dyspnoea). Clinical examination may reveal a 3rd heart sound, and in more severe cases bilateral basal crepitations. Secondary right heart failure may also be present, giving rise to an elevated jugular venous pressure and lower limb oedema. Unfortunately, clinical symptoms and signs are neither sensitive nor specific for diagnosing chronic heart failure, and further investigation is warranted [9].

TTE can provide information as to both the cause and severity of myocardial dysfunction. The presence of regional wall motion abnormalities (RWMAs) would point to a likely ischaemic cause [10], which may influence further management and risk profile. Measurement of left ventricular dimensions in systole and diastole can also estimate the ejection fraction (EF). This is defined as the stroke volume divided by the LV end-diastolic volume X 100, with a normal value of >55%.

However, a significant number of patients with heart failure, particular in the older population, have a normal ejection fraction [11], so this reading alone can lead to false re-assurance. This is termed diastolic heart failure (i.e. impaired relaxation of the ventricle in diastole) and is becoming increasingly apparent as a common and significant predictor of adverse outcomes [12]. In one study, around 60% of surgical patients over the age of 65 had evidence of diastolic dysfunction on TTE despite a normal ejection fraction [13], and such patients have an increased incidence of post-operative cardiac complications and longer term mortality risk [14,15,47].

TTE can be used to assess the presence and severity of diastolic dysfunction in the preoperative setting using a variety of imaging techniques [16]. These include left ventricular inflow measured at the mitral leaflets and myocardial tissue movement at the base of the septum [17]. These allow the echocardiographer to define the severity of the dysfunction, with the terms mild, moderate and severe often interchangeable with grades 1, 2 and 3 respectively [3,19].

1.2 Preoperative TTE in heart failure

A TTE is recommended for patients in whom heart failure is suspected on clinical grounds but this applies all patients, irrespective of whether they are due for surgery. So who warrants a TTE preoperatively? If a member of the preoperative team suspects a new diagnosis of heart failure, then the NICE guidelines recommend measuring B-type Natriuretic Peptide (BNP) [9], a position echoed by guidelines from Canada [48]. If this is elevated or the patient is known to have had a previous myocardial infarction, then immediate referral to a specialist multidisciplinary heart failure team should be arranged. This may be better organised by primary care if surgery is not urgent, but a direct referral to cardiology may be required if surgery cannot be significantly delayed. Local referral rules will dictate practice.

For patients with an established diagnosis presenting for elective surgery, it is reasonable not to repeat a TTE if their symptoms are stable [18]. If they have deteriorated or they are unstable, an echocardiogram may be indicated but usually this should only be requested after discussion with the clinician who normally monitors the patient's cardiac function, who will also be able to advise on any changes in therapy required [9]. It is likely that in the near future, both BNP and cardiopulmonary exercise testing may be of increasing relevance in the perioperative assessment of heart failure [19,20,21].

2.1 Aortic Stenosis

Aortic stenosis (AS) is a significant concern in the perioperative setting. 4% of people over 75 will have significant AS and several published series have characterised AS as a high-risk index for peri-operative complications [22,23,44]. The grading of AS can be conflicting as it is dependent on which echo measurement is chosen as the most important factor. Minners et al. [24] in a large review of echocardiograms showed that 30% of patients with severe AS by aortic valve area (AVA) had non-severe stenosis by mean gradient and 25% had non-severe by peak velocity. ACC/AHA Guidelines 2020 [25] classify asymptomatic AS as severe if either peak velocity is >4m/s or mean gradient >40mmHg. AVA although typically will be ≤1.0cm², is not required to define severe AS. The guidelines further subdivide AS into whether the subject is symptomatic or not. For reference the table illustrates commonly used values to grade AS.
### Degree of Stenosis

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Peak Velocity (m/s)</th>
<th>Mean Pressure Drop (BH)</th>
<th>Peak Pressure Drop (mmHg)</th>
<th>Valve Area (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.4-2.2</td>
<td>-</td>
<td>8-20</td>
<td>&gt;3</td>
</tr>
<tr>
<td>Trivial</td>
<td>2.2-2.5</td>
<td>-</td>
<td>20-25</td>
<td>1.8-3.0</td>
</tr>
<tr>
<td>Mild</td>
<td>2.5-3.2</td>
<td>12-25</td>
<td>25-40</td>
<td>1.2-1.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.2-4.2</td>
<td>25-40</td>
<td>40-70</td>
<td>0.8-1.2</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;4.2</td>
<td>40-50</td>
<td>&gt;70</td>
<td>0.6-0.8</td>
</tr>
<tr>
<td>Critical</td>
<td>&gt;50</td>
<td>-</td>
<td>-</td>
<td>0.6</td>
</tr>
</tbody>
</table>

AS is often asymptomatic in its mild and moderate stages, and even severe cases may be symptom free [26]. If symptomatic, the patient may complain of exertional chest pain, syncope/presyncope or dyspnoea. The classical clinical sign is the presence of an ejection systolic murmur, loudest at the left sternal edge or in the right second intercostal space, radiating into the carotid region. Often an ECG will demonstrate left ventricular hypertrophy, although this is not seen in 15% of severe cases [27]. Nevertheless, clinical examination alone is poor at accurately diagnosing aortic stenosis, let alone assessing its severity [43]. In a series of 83 patients who had a murmur detected by auscultation in the preoperative clinic, only 27 (32%) had AS subsequently found at TTE and 25 (30%) had no valvular abnormality [28].

In addition to confirming whether aortic stenosis is present, TTE can provide information as to the cause and severity of the condition. 2D and M-mode imaging can determine the excursion of the valve leaflets and any thickening or abnormalities such as a bicuspid valve structure. Doppler imaging can measure blood flow across the valve, and from this peak and mean pressure gradients are derived. By measuring the diameter of the left ventricular outflow tract and the velocities through it, an estimation of the valve area can be derived. However, TTE usually under-estimates outflow tract diameter and thereby over-estimates the severity of AS based on AVA. Moreover, if there is a degree of left ventricular impairment, the gradient may underestimate the degree of stenosis.

#### 2.2 Who needs a pre-operative echocardiogram?

The 2006 ACC/AHA guidelines recommend any patient with a Grade 3 murmur or above (a loud murmur, easily audible with a stethoscope) should proceed to echocardiography, and any patient with a Grade 2 murmur (faint) with symptoms or an abnormal ECG should also undergo TTE [24]. However, systolic murmurs in patients under 40 are very unlikely to be pathological unless there is a history of heart disease and even in the 40-60 age group, significant AS is unlikely without additional symptoms or comorbidities [28]. These authors therefore considered TTE not necessary in patients under 60 who have no symptoms and a normal ECG and this is in line with the new NICE guidelines on routine preoperative tests for elective surgery [1] which just advises considering TTE “if there is a heart murmur and any cardiac symptom”. Symptoms or an abnormal ECG (e.g. LVH or AF) in conjunction with a murmur would mandate preoperative TTE.

Aortic stenosis is a progressive condition, and a number of patients presenting for elective surgery will be under regular review by a cardiologist. On average, peak pressure gradients increase by 7mmHg per year and valve area decreases by 0.1cm² per year. Therefore any patient previously diagnosed with moderately severe stenosis should have a repeat echocardiogram on a 1-2 yearly basis [10,24], and the development of any symptoms should prompt urgent referral. Patients with mild disease should also be considered for repeat TTE every 3-5 years [24]. Any patient with severe or critical stenosis undergoing elective non-cardiac surgery should be referred to a cardiologist, as valve replacement may be considered before surgery [4].

#### 2.3 Assessment of perioperative risk

Kertai et al [22] found that AS increased the overall risk of death or non-fatal MI by a factor of 5 after adjusting for clinical factors. Risk increased with AS severity with severe AS associated with 3 times the risk of these outcomes over moderate AS. However, a recent publication by Samarendra and Mangione [28] critically examined the relationship between echo findings and surgical risk. They concluded that patients should only be labelled as high risk (for non-cardiac surgery) if the aortic valve area (AVA) is <0.8cm² and mean gradient is >45-50 mmHg. Asymptomatic patients with AVA >0.8cm², mean gradient <45-50mmHg and preserved LV function should not be labelled as high risk [29]. Certainly the cardiac risk during non-cardiac surgery appears to have declined in recent years according to a recent report with mortality rates similar to controls without AS.[30]

Urgent surgery often presents a challenge in obtaining TTE, but a recent report showed that bedside focussed TTE identified AS in 14% of patients aged over 65 with a fractured neck of femur where it was not suspected clinically [31]. TTE was associated with a lower postoperative mortality and the place of routine focussed TTE in this patient group is currently being debated.

In summary, aortic stenosis is a significant risk factor in the perioperative period but only if severe or symptomatic. Indeed the 2014 ESC/ESSA guidelines on cardiovascular assessment in non-cardiac surgery states “In asymptomatic patients, non-cardiac surgery of low to intermediate risk can be performed safely” [4]. However, it is important that the patient’s primary care physician is involved as surveillance of the valve disease is likely to be needed.

#### 3. Other Conditions

A TTE may also be of use in a number of other conditions, such as aortic regurgitation, mitral regurgitation or stenosis or pulmonary hypertension. However, unlike aortic stenosis which can be severe and asymptomatic, patients with severe degrees of these conditions will usually be symptomatic and would warrant a TTE for investigation of dyspnoea as per the NICE guidelines for heart failure. Pulmonary hypertension is a particularly significant risk factor for adverse outcomes, both intra and postoperatively, and should be identified by TTE if suspected on clinical grounds [32]. Patients with long-standing obstructive sleep apnoea (especially if hypo-ventilating due to obesity), severe chronic obstructive pulmonary disease (COPD) and post pulmonary embolus are three groups which can develop pulmonary hypertension and this possibility should be borne in mind in the preoperative setting. In general however, provided the patient’s symptoms are stable, then routine repeat TTE is unlikely to provide much more information [33].

#### 4. What is the utility of TTE in risk assessment and does it alter outcomes?

As described previously it is clear that, with appropriate patient selection, a TTE can be an extremely important investigation. To improve its usefulness, it must be used and requested only after an appropriate history and clinical examination has been performed. However, there is conflicting evidence as to whether a more liberal use of TTE is beneficial. An intriguing retrospective cohort study from Toronto in 2011 found that a preoperative TTE was associated with increased 30 day mortality in those at low or intermediate risk [34]. Several hypotheses were put forward to explain this finding and it is always pertinent to bear in mind the potential harm from an investigation if it results in inappropriate treatment.

Halm et al [35] found no evidence to support the routine use of preoperative echocardiography for assessing cardiac risk, adding that TTE “provided no significant prognostic information in addition to that predicted by the cardiac risk indices”. By contrast, Rohde et al [36] evaluated the place of preoperative TTE in predicting cardiac complications in 570 patients undergoing major non-cardiac...
surgery. Systolic dysfunction was significantly associated with major cardiac complications (OR 2.4) including MI and pulmonary oedema and prediction models which included TTE variables were significantly better than clinical variables alone.

The 2014 ESC/ESA guidelines [4] state that routine TTE is not recommended for the preoperative evaluation of ventricular function and that LV function assessment has limited predictive value for postoperative outcomes. One explanation for this is that exercise performance, either self-reported or at cardiopulmonary exercise testing [37,38], shows little correlation with ejection fraction at rest. TTE is usually performed in a resting situation, and as such does not provide much insight into myocardial performance under stress (e.g. after surgery).

More recently there have been a number of publications looking at a simplified TTE, often performed at the bedside. Although a number of studies and correspondence have focussed on hip fractures in the elderly [31,39,40,41], one study has looked at TTE in the preoperative clinic [42]. In this study, a change in anaesthetic plan was made in 54 out of 100 patients; 62% of patients with suspected cardiac disease had their anaesthetic plan changed (23% had treatment increased, 39% decreased), whilst only 25% without suspected disease but over 65 years of age had a change (10% increased, 15% decreased).

Summary

TTE is a useful preoperative investigation but it is of proven benefit in only certain conditions which require a full history and examination to suspect – specifically aortic stenosis and cardiac failure. It is therefore reasonable to request a TTE in the following circumstances:

1) Where undiagnosed cardiac failure is suspected (usually secondary to left ventricular impairment, although valvular pathologies may cause similar symptoms) or there has been a clinical deterioration in known cardiac failure

2) To exclude aortic stenosis if an undiagnosed systolic murmur is detected in patients over 60 and in any patient if in addition with an abnormal ECG or cardiac failure

3) To assess progression of disease in patients with known aortic stenosis when coming for surgery without an echo or when it was done more than 1 year ago if moderate or severe or more than 2-3 years ago if mild. All patients with known aortic stenosis should be referred to cardiologists if they become symptomatic or the echo findings suggest a severe or critical category.

4) When pulmonary hypertension is suspected or previously diagnosed in order to assess progression of pulmonary pressures, bearing in mind that TTE can only estimate PAP from a tricuspid regurgitant jet. Accurate measurements of PAP require right heart catheterisation.

Although these recommendations are similar to those made by another author [33], it must be realised that individual patients do not always fall easily into diagnostic groups, and that a pragmatic approach, based on a full history and clinical examination, should be used in all cases.

References

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Guidelines for the Pre-operative Assessment and Peri-operative Management of the Patient at Risk of Acute Kidney Injury including Patients with Renal Impairment

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Summary and Key Recommendations

- Avoidance of acute kidney injury (AKI) should translate into a reduction in perioperative morbidity and mortality as well as resulting in significant economic savings. Therefore, it should be considered as standard care of the pre-operative management for every patient.
- Perioperative AKI should be defined by the KDIGO criteria.
- Determine the risk of perioperative AKI by selecting an appropriate scoring system such as the “any-stage AKI score”.
- In the preoperative period there is no need to stop statins, ACE inhibitors or A2RBs unless additional factors predisposing to AKI are likely e.g. the use of other nephrotoxins.
- Consider using peri and post-operative goal-directed fluid therapy and avoid systolic hypotension.
- Assess for risk factors for AKI including CKD and optimise where possible.
- In the event of post-operative AKI developing ensure a timely nephrology referral where the aetiology is not clear.
- Consider the use of biomarkers for AKI if available.
Introduction

The development of Acute Kidney Injury (AKI) is a predictor of immediate and long-term adverse outcomes with perioperative patients, particularly those undergoing cardiac or vascular procedures at high risk of developing AKI [1, 2]. AKI is associated with significant economic cost, morbidity and mortality with even minor AKI having significant long-term sequelae [3]. Early intervention is essential to prevent post-operative AKI with the peri-operative period offering an opportunity to assess for the potential development of post-operative AKI [PO-AKI] which may occur in up to 20-40% of patients. Furthermore, the peri-operative period allows for deployment of management strategies that may reduce the incidence and severity of AKI [4].

AKI Definition

Previously acute renal failure [ARF] was determined by non-specified increases in serum creatinine [sCr], although the creatinine rise is delayed by approximately 24 to 48 hours after surgical insult making early diagnosis difficult [5]. In 2004, the Acute Dialysis Quality Initiative Consensus Group [ADQI] created a definition for AKI the RIFLE criteria which allowed for a standardised method to characterise AKI, enabling improved reporting in studies for AKI outcomes and diagnosis. However, as the RIFLE criteria underestimated the effect of small creatinine changes on mortality the Acute Kidney Injury Network [AKIN] amended the RIFLE criteria to consider this. AKI is currently defined by a rapid deterioration [hours to days] in kidney function and defined using the KDIGO classification as stages 1 to 3 as determined by changes in serum creatinine and/or urine output [Table 1] [6]. However, serum creatinine and urine output measurements have limitations due to the delay in peak levels and lack of specificity. More recently novel biomarkers have been shown to identify AKI earlier with increased sensitivity to AKI, which might lead to earlier detection and diagnosis [5].

Predictive Scoring Systems

Risk prediction models employ combinations of independent predictors and assign a relative weighting to predict a clinical outcome [7]. Risk prediction models for surgical patients are potentially attractive in that in most cases the patient baseline data is known, importantly for AKI models this includes baseline renal function, the time of insult is known, and the patients are monitored closely post-operatively. The use of an easily applied scoring system applicable to any patient due for major surgery would allow for rapid and early identification of individuals at increased risk of AKI. A systematic review on risk prediction models for major non cardiac surgery found that only one was in general surgical patients and of the models described none were externally validated and lacked any impact analyses [8].

1 General Surgery Scoring Systems

A cohort of 4544 patients [UK and Ireland] undergoing major abdominal surgery were assessed for a primary outcome of the incidence of AKI within 7 days. Six variables were identified and as a result the percentage risk of developing AKI is calculated based on these which include age, gender, ASA grade, Baseline eGFR, planned laparoscopic surgery, pre-op ACEi/ARB. The authors created an online tool to aid swift pre-operative assessment. A further study on 455 ICU patients, including surgical patients developed a prediction model based on 5 variables which included two novel markers [TIMP-2 and IGFBP7] which improved performance and speed of diagnosis [9].

2 Cardiac Surgery Scoring Systems

Several cardiac surgical scoring systems exist. These include the Mehta Score derived from the Society of Thoracic Surgeons National Cardiac Surgery database which identified a cohort of 450,000 patients undergoing CABG +/- valvular surgery [10]. The Cleveland Clinic Score was developed from a cohort of over 30,000 patients during a nine-year study period ending in 2002. Based on 13 variables it offers discriminatory value to predict post-operative RRT and severe AKI [11]. In 2014 a pre-operative assessment for cardiac surgery, the any-stage AKI risk prediction model was developed with a total of 14 variables, to predict any-stage of AKI [12].

Risk Factors

Table 2 outlines the major patient related and procedure related risk factors for PO-AKI.

Pre-operative Risk Factors

1. Chronic Kidney Disease [CKD] and Proteinuria

Reduced Glomerular Filtration Rate [GFR] and chronic kidney disease [CKD] are known independent risk factors for AKI [13]. More recently, proteinuria has also been shown as an independent risk factor for AKI with the albumin to creatinine ratio [ACR] directly correlating with AKI risk [14]. Of note, those with a normal eGFR but significant proteinuria, [identified with a urine dipstick] had an increased severity of AKI compared to those with a normal eGFR in the absence of proteinuria.

2. Serum Albumin

A serum albumin level of <4g/dL has been shown to be an independent variable for AKI and in those with no pre-existing CKD there is strong association for the prediction of requiring post-operative renal replacement therapy [15, 16].

3. Uric Acid

Raised uric acid levels pre-operatively is predictive of AKI in patients undergoing cardiac surgery. Concentrations exceeding 6.5 mg/dL are associated with an 8-fold increase with the development of an AKI post-operatively and a concentration >7.0 mg/dL corresponds to a 40-fold increase [17]. Hyperuricaemia is associated with both an increased ICU length of stay and ventilator days as well as post-operative AKI [20]. Although hyperuricaemia may lead to tubular precipitation of uric acid crystals in the renal tubules and this may cause AKI but more recently there is speculation that AKI may develop via crystal-independent mechanisms involving both renal perfusion and pro-inflammatory pathways [18].

4. Anaemia

A low haemaglobin concentration is a known independent risk factor for AKI [15, 19]. However pre-operative anaemia with transfusion has an increased risk when compared to normo-anaemic patients requiring transfusion intra-operatively to developing AKI in cardiac surgery [20]. Therefore alternative strategies such as use of erythropoietin or iron transfusion should be considered pre-operatively.

5. Left Ventricular Dysfunction [LVD]

An ejection fraction of <55% is an independent risk factor for developing AKI as well as an increased risk of cardiovascular mortality [21].

Biomarkers

The potential use of biomarkers rather than serum creatinine for the early detection of renal injury which would peak rapidly after renal injury and be specific for renal damage may change future practice when diagnosing AKI. Various candidate molecules have been considered as alternatives to serum creatinine given the limitations with creatinine as a measure of GFR. Firstly, GFR must decline by 50% before a significant rise in serum creatinine occurs. Secondly, creatinine production is affected by several factors such as: muscle mass, protein intake and catabolism, volume of distribution, gender and sepsis.

Many biomarkers have been studied in a variety of settings with variable performance. Unsurprisingly cardiac surgery has been an area of most interest with relatively few studies in general surgical patients. Cystatin C is a small, charged molecule that is a more accurate determinate of filtration than
serum creatinine with some evidence that at 6 hours post surgery AKI could be diagnosed before rises in serum creatinine [22]. More recently, the combination of Cystatin-C with the RIFLE criteria resulted in greater discriminatory power for detecting AKI [23].

Neutrophil Gelatinase-Associated Lipocalin (NGAL) has been validated for the detection of post-operative AKI in both paediatric cardiac surgery and after liver transplantation [24]. NGAL is a protein produced in the renal tubules in response to ischemic or nephrotic insult. Furthermore, it is secreted in the urine and peak levels occur typically within 1 to 3 hours of surgery, urinary NGAL therefore allows for rapid diagnosis of AKI, and has the potential to predict the development of AKI.

Fatty Acid Binding Protein (FABP) is an intracellular transport protein which has also been validated in patients undergoing cardiac surgery [25], Insulin Like Growth Factor Binding Protein 7 (IGFBP7) and Tissue inhibitor of Metalloproteinase-2 (TIMP-2) are released in the early stage of tubular stress and are expressed during cell cycle arrest, a physiological protective strategy to avoid replication of damaged DNA [26]. Dickkopf-3 (DKK3) is a stress-induced, renal tubular epithelial derived glycoprotein, secreted into the urine. Increased urinary DKK3 levels are associated with a high risk for AKI and the subsequent loss of kidney function after cardiac surgery [27]. Proenkephalin A (PENK) is an endogenous opioid polypeptide and has been shown to be a highly specific biomarker for renal function and associated with AKI in multiorgan failure, specifically in sepsis [28].

Potential peri-operative management

The peri-operative period should include optimization of organ perfusion and post-operative enhancement of the surgical patient.

1. Fluid Balance and Haemodynamic Optimisation

Goal directed fluid therapy is one of the most effective strategies for reducing PO-AKI in patients undergoing cardiac surgery [29]. Of note, a positive fluid balance in the post-operative period has been shown to increase the risk of AKI which may reflect injudicious use of fluids rather than a need for volume replacement [30].

2. Dexmedetomidine

Dexmedetomidine, a selective α2-adrenergic receptor agonist. Dexmedetomidine reduced the incidence of AKI in patients undergoing heart valve surgery and has been suggested to increase renal blood flow together with anti-inflammatory and anti-oxidative properties [31]. However, meta-analysis failed to show an impact on end points such as length of days on mechanical ventilation, and duration on the ICU or in hospital [32]. Decreasing duration and exposure to nephrotoxic drugs in the peri-operative period can reduce the risk of developing AKI as demonstrated in paediatric patients at risk of AKI [33].

3. Remote Ischaemic Pre-conditioning

Remote ischaemic pre-conditioning involves applications of brief intervals of ischaemia and reperfusion to a distant limb, which is thought to result in an adaptive mechanism of protection in distant organs. A blood pressure cuff is applied to the arm and inflated to 200-300mmHg for several minutes and released. This is thought to activate anti-inflammatory, neuronal and humoral pathways. There are studies with conflicting evidence despite initial promising results and as a result future clarification with more studies is required. Whilst there have been promising results in cardiac surgery, including reduction in rate of AKI and RRT and developing CKD, other studies have been unable to establish a link in reduction in rates of AKI. Further research is required to determine whether there is any clinical value.

Conclusions

AKI has serious implications for surgical patients including an increase in both mortality and morbidity. Avoidance of AKI should translate into improved outcomes including economic savings. It should therefore be considered an integral part of the pre-operative management for every patient. Assessing individual risk of peri-operative AKI with use of predictive scoring systems may identify patients at risk early as part of an individualised risk assessment.

Pre-operative assessment in those deemed at high risk either through patient factors or the proposed surgical exposure should be performed and optimization of any reversible risk factors should include serum haemoglobin, serum albumin, the presence of proteinuria and an assessment of left ventricular function. The use of biomarkers post-operatively can also be considered and this aspect of management may well change considerably with further research. Goal directed fluid therapy, avoidance of hypotension, RRT and early nephrology referral in the event of a serious AKI should be considered.

Table 1. Classification of AKI

<table>
<thead>
<tr>
<th>KDIGO Classification</th>
<th>Urine Output Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>Creatinine Criteria</td>
</tr>
<tr>
<td>1</td>
<td>Increase Cr x1.5-1.9 within 7 days or an increase Cr &gt; 0.3mg/dl within 48Hr</td>
</tr>
<tr>
<td>2</td>
<td>Increase Cr x2.0-2.9</td>
</tr>
<tr>
<td>3</td>
<td>Increase Cr &gt;3.0 from baseline OR Serum Cr ≥4mg/dl or initiation of RRT or GFR decrease to &lt;35ml/min [1.73m²] in patients &lt;18 yr old</td>
</tr>
</tbody>
</table>

Table 2. Risk Factors For PO-AKI

<table>
<thead>
<tr>
<th>Patient Risk Factors</th>
<th>Procedure Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Use of intravenous contrast</td>
</tr>
<tr>
<td>BMI &gt; 35kg/m²</td>
<td>Pre-operative blood transfusions</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Epidural anaesthesia in liver resections.</td>
</tr>
<tr>
<td>Left Ventricular Dysfunction</td>
<td>Intra-operative blood transfusions</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Large colloid infusion</td>
</tr>
<tr>
<td>Cerebrovascular Accident</td>
<td>Intraoperative hemodynamic instability</td>
</tr>
<tr>
<td>Complexity of impending surgery</td>
<td>Use of diuretics and vasopressors</td>
</tr>
<tr>
<td>Reduced estimated GFR</td>
<td></td>
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</tbody>
</table>
Figure 1: Suggested Pre-op Assessment Process for Major Surgery

- Use of a Scoring System (Any stage AKI) & Measure Hb, Albumin, LVEF, Proteinuria
- High Risk - reconsider planned surgery
  - Low or Moderate Risk - Proceed
  - Predictive Biomarkers; Ideally TIMP-2 and IGFBP7 if available.
  - Measure baseline serum Creatinine
- Optimise - Hb, stop potential Nephrotoxins
- Proceed to Surgery
- Post-op monitoring for AKI 2/3 with early RRT and nephrology referral if it occurs

References


Guidelines for the Management of Antiplatelet Therapy in the Perioperative Period
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Summary and Key Recommendations

- The risk for perioperative cardiac events is increasing as the prevalence of ischaemic heart disease and coronary stents rises in the surgical patient population.
- The presence of coronary artery stents makes the perioperative management of antiplatelet therapy essential.
- Preoperative discontinuation of aspirin taken for secondary prevention is associated with increased risk of adverse cardiac events. This risk is highest for patients with coronary stents.
- Most routine operations can be undertaken without interrupting aspirin unless there is a risk of bleeding into an enclosed space. This also applies to dipyridamole.
- When clopidogrel is used as monotherapy, and discontinuation considered essential, low-dose aspirin should be substituted (unless contra-indicated).
- In situations of high thrombotic risk, when the patient is on dual antiplatelet therapy, elective surgery should generally be delayed until clopidogrel can be safely stopped.
- When surgery cannot be delayed and thrombotic risk is high, the continuation of both aspirin and clopidogrel should be a discussion between surgeon, anesthetist, and cardiologist.
- At present there is a lack of evidence about the bleeding risks with newer antiplatelet agents (prasugrel, ticagrelor, cangrelor).
- Recent advances in stent technology support a shorter period of DAPT (Dual Antiplatelet Therapy) coverage.
Introduction

Patients presenting for operations are commonly on antiplatelet medication. It is estimated that 4-10% of patients with coronary stents will present for non-cardiac surgery within the subsequent year. The higher overall morbidity of this elective surgical population increases the risk of perioperative myocardial events. There is evidence that the traditional approach of stopping these drugs before surgery puts these patients at a greater risk of perioperative ischaemic cardiovascular events, a point which is particularly true in patients with coronary stents. Conversely, there are suggestions that the increased intraoperative bleeding of patients on antiplatelet drugs is in most instances manageable [1,2]. This poses an important challenge: the need to balance the risk of intra-operative bleeding of patients on antiplatelet agents against the risk of adverse cardiovascular events when stopping these agents. An evidence-based approach is necessary for the optimal management of perioperative antiplatelet medication therapy, but given the lack of definitive trial based evidence, most literature is recommendation based on expert consensus opinion.

1. Antiplatelet agents

1.1 Acetylsalicylic acid (Aspirin)

Aspirin acetylates the enzyme cyclooxygenase 1 (COX-1) and to a smaller degree, COX-2. COX-1 is part of the arachidonic acid pathway towards the production of Thromboxane A₂ (TXA₂). The latter is mainly produced in platelets and leads to platelet aggregation as well as vasoconstriction, so the inhibition of COX-1 results in reduced levels of TXA₂ and consequently reduced platelet aggregation [3]. The blocking of COX-1 by aspirin is irreversible, and platelet function can only recover through synthesis of new platelets. Platelets have a lifespan of approximately 10 days but not 100% need to be functional for effective aggregation, so platelet function is partially restored 4 to 5 days after stopping the drug [4].

Aspirin at low doses has been shown to reduce the risk of myocardial infarction and death in patients with ischaemic heart disease [5,6], the risk of stroke in cerebrovascular disease [7] and the risk of stroke after carotid endarterectomy [8]. Its major side effects are increased bleeding and gastrointestinal complications. Although gastrointestinal effects are dose dependent, even at low doses aspirin increases the risk of gastrointestinal bleeding 2 to 3 fold [3].

It is worth noting the phenomenon of aspirin ‘resistance’, whereby platelets continue to exhibit high reactivity despite treatment. It is not fully understood but thought to be multifactorial, and estimates of its incidence vary depending on the laboratory assay used to quantify platelet function. A meta-analysis in 2007 reported a 27% incidence for clinical aspirin resistance, with these patients being at higher risk of cardiovascular complications [9].

Indications: Aspirin is the most commonly used antiplatelet drug. It is used for secondary prevention in coronary artery disease, after coronary stent implantation and after coronary artery bypass grafting. It is also used in secondary prevention of cerebro-vascular and peripheral vascular disease as well as after carotid endarterectomy or stenting [3,10]. Regular use of aspirin has been found to reduce the incidence of developing colorectal, oesophageal and breast cancer and also a reduced risk of metastasis from colorectal cancer.

1.2 Thienopyridines (Clopidogrel, Prasugrel)

Both are prodrugs that undergo metabolic activation by p450-dependent hepatic enzymes. The active metabolites inhibit the platelet P2Y₁₂-receptor, which in turn blocks ADP - mediated platelet aggregation (ADP: adenosinediphosphate). This process is irreversible, so despite the short half-life of thienopyridines, the antiplatelet effect of these drugs disappears only when enough new platelets have been synthesized. In the case of clopidogrel, platelet function does not return to normal until 7 to 10 days after cessation of therapy [3].

Clopidogrel has been shown to reduce endpoints such as vascular death, myocardial infarction and ischaemic stroke in patients with recent ischaemic events when compared to aspirin [11]. While there is clear evidence of the added benefit of dual antiplatelet therapy with aspirin and clopidogrel in acute coronary syndromes, the situation is less clear in patients with stable angina or previous ischaemic stroke [3,12,13]. Current NICE guidelines recommend monotherapy with clopidogrel for ischaemic stroke and aspirin alone for stable angina. [58]

The main side effect of clopidogrel is bleeding. Dual antiplatelet treatment compared to monotherapy with aspirin increases the risk of minor bleeds in most of the studies mentioned above. A few trials report an increase in major bleeds, e.g. the CURE trial, with a 2.7% rise with aspirin monotherapy to 3.7% with combination therapy [12], whereas other trials show a remarkably good safety profile of dual therapy without excess major bleeds [13]. Analogous to aspirin there is the problem of clopidogrel ‘resistance’: about one-third of patients exhibit a degree of clopidogrel resistance with an associated higher risk for adverse cardiac and vascular events despite treatment [3].

Indications: Clopidogrel is the main thienopyridine in use. It is used on its own in cases of aspirin-contra-indications or intolerance and increasingly as preferred monotherapy after transient ischaemic attack (TIA) or cerebrovascular accident (CVA). More commonly, clopidogrel is used in combination with aspirin in higher risk cases, such as secondary prevention of high risk coronary artery disease, in acute coronary syndromes (ST-elevation and non-ST-elevation myocardial infarction) and after coronary stent implantation [10]. It is worth noting that aggressive antiplatelet therapy is necessary in the early stages after coronary stent implantation as there is a high risk of acute stent thrombosis prior to endothelialization of the stent.

Current recommendations for stable coronary disease treated with bare metal stents (BMS) is to continue antiplatelet treatment with acetylsalicylic acid and clopidogrel for one month and for 12 months in patients with acute coronary syndrome and then lifelong continuation with aspirin alone [14]. Drug eluting stents (DES) are designed to inhibit fibroblastic proliferation and reduce late in-stent re-stenosis. This also delays early stent endothelialisation so the risk for early stent thrombosis persists for longer when compared to bare metal stents and hence the recommendation is to continue dual antiplatelet therapy for 6 months in stable coronary artery disease and 12 months in acute coronary syndrome. [14] Improved stent technology and drug elution with the second and third generation DES stents do not necessitate antiplatelet therapy beyond 6 months (with some differences between American and European guidelines). [48, 59]

Prasugrel is a newer thienopyridine with more potent, more consistent and a quicker onset of platelet inhibition compared to clopidogrel [15]. Its pharmacodynamics are similar to clopidogrel, with irreversible platelet inhibition but it exhibits much less inter-patient variability and recovery of platelet function also takes much longer as compared to clopidogrel. It is currently used mainly in the acute setting as an adjunct to percutaneous coronary intervention but might well become more common in long-term antiplatelet therapy. Other indications include therapy in diabetic patients and also in patients who have had stent thrombosis while on clopidogrel. It is contraindicated in patients who have a high risk of bleeding (Elderly>75 yrs, Low BMI, Hepatic and renal impairment, GI bleed)

1.3 Ticagrelor

Ticagrelor is an agent of the new cyclopentyltriazolopyrimidine class that, like the thienopyridines, blocks the P2Y₁₂-receptor, but in a reversible fashion and at a different binding site. Its anti-platelet
effect is more potent and faster in onset than clopidogrel. It displays a lower incidence of resistance hence the platelet inhibition is more consistent. Platelet inhibition is not discernible five days after discontinuation of the drug [10]. In a large study of secondary prevention in patients with acute coronary syndrome, ticagrelor was superior to clopidogrel in reducing death from vascular causes and myocardial infarction [16], but at present it is unclear whether ticagrelor causes more bleeding complications than clopidogrel. It is currently the drug of choice, along with aspirin, for patients post acute coronary symptoms and post PCI [59].

1.4 Dipyridamole

Dipyridamole increases intraplatelet concentrations of cyclic adenosine monophosphate (cyclic AMP), which in turn inhibits platelet aggregation and leads to vasodilation. There is evidence that the combination therapy of aspirin and dipyridamole is more effective than aspirin alone in secondary prevention of ischaemic stroke [17, 18] but no benefit could be shown in coronary artery disease [18]. After stopping dipyridamole platelet aggregation recovers quickly, so when used alone it can be stopped one day prior to interventions.

Indication: Dipyridamole is recommended in combination with aspirin for the secondary prevention of ischaemic stroke [19]. Its use has been declining with the advent of the thienopyridines.

1.5 Cilostazol

Cilostazol is a phosphodiesterase type III inhibitor that suppresses platelet aggregation reversibly, with self-limiting effects based on its half-life of 10 hours [42]. It is a vasodilator indicated for the improvement of walking distances in patients with intermittent claudication for whom lifestyle modifications and other appropriate interventions have failed to improve their symptoms [45, 46]. However in the UK current recommendations are for clopidogrel rather than cilostazol.

1.6 Glycoprotein IIb/IIIa receptor antagonists (Tirofiban, Abciximab)

The final step of platelet aggregation is the activation of Glycoprotein IIb/IIIa receptors which bind substrates such as fibrinogen leading to the interlinking of adjacent platelets. Blocking Gp IIb/IIIa receptors is therefore a very powerful way of inhibiting platelet aggregation. After a bolus dose of abciximab platelet aggregation returns to at least 50% of baseline within 24 hours [3]. Tirofiban has a half-life of 2 hours, is therefore given as a bolus followed by an infusion and platelet function recovers to 50% of baseline within 4 hours of stopping [3]. These drugs require intravenous administration and need specialist supervision. Current indications are as an adjunct to PCI or after an acute MI while awaiting PCI and also have been used as bridging therapy in high risk patients undergoing urgent surgery soon after a cardiovascular intervention, [56].

Side effects of Gp IIb/IIIa blockade are major bleeding (increase from 2.7% to 4.1% [20]) and thrombocytopenia (1-2% of cases of abciximab treatment [3]). As Glycoprotein IIb/IIIa receptor antagonists are used only in the acute context of acute coronary syndromes, they are not encountered in the perioperative setting of elective operations.

NICE guidelines on antiplatelet medication (Concise summary: last revised August 2020)

Primary prevention

Current NICE guidance does not recommend routine primary prevention for cardiovascular disease. Primary prevention with aspirin may be considered for patients with controlled hypertension who have a high cardiovascular risk (>20% in 10 yrs ) or who have diminished renal function.
2. Risk of cardiovascular events

2.1 Cardiovascular events in the perioperative period

The risk of thromboembolic events is increased in the perioperative period due to several factors. Firstly, an acute phase response promotes increased platelet adhesiveness and decreased fibrinolysis, leading to a hyper-coagulant state. Secondly, the stress response of surgery leads to increased sympathetic tone, vasoconstriction and higher shear stress on arterial plaques. Dehydration due to fasting raises blood viscosity, both increasing the risk of vascular ischaemic events. Thirdly, there is a rebound phenomenon after stopping antiplatelet drugs with increased platelet adhesiveness in the period of decreasing drug effect [21].

2.2 Discontinuation of antiplatelet therapy

The rebound phenomenon after discontinuation of antiplatelet agents has been mentioned above. To what extent this increases the risk for cardiovascular events depends on the agent used and the indication for antiplatelet therapy, so risk needs to be discussed in that context.

2.2.1 Aspirin for prevention of perioperative myocardial infarction

Two randomised, double-blinded, placebo-controlled trials investigated the risk of major perioperative cardiac events in patients on aspirin undergoing intermediate to high-risk non-cardiac surgery. One showed a relative risk reduction for such events of 80% with preoperative aspirin [22], while the other trial did not show any difference in the incidence of thrombotic events between groups taking or not taking aspirin in the preoperative period [23]. These results are contradictory but upon closer inspection both trials missed the recruitment target to fulfill their own power calculations and there were small but distinct differences in the management of the study drug. In the negative trial, aspirin was more likely to be recommenced earlier in the postoperative period and could have thus provided more cardio-protection, as the majority of adverse events happened within the first three postoperative days in both trials.

The POISE-2 trial was a large, multicenter, randomised controlled trial (RCT) that looked at the effects of aspirin and clonidine, both vs placebo on perioperative mortality and myocardial infarction in patients ‘at risk’. The trial found no difference in peri-operative cardiac outcomes but did find an increase in major bleeds between the aspirin group and the placebo (4.6% vs 3.8%). However only 23% of patients had known coronary artery disease and the trial excluded patients with stents who had not completed the full course of DAPT [25]. By contrast, when a subset of patients with previous PCI were analysed separately, aspirin was found to reduce the relative risk of death and non-fatal myocardial infarction with a hazard ratio of 0.5 (p=0.0360) [26].

The European Society of Cardiology guidelines from 2017 recommend continuing aspirin perioperatively if bleeding risk allows (class IB evidence) [48].

2.2.2 Aspirin / Clopidogrel in patients with coronary stents

Premature cessation of DAPT is one of the strongest predictors of stent thrombosis with catastrophic results [28] and this was highlighted in an early small observational study [29]. A total of 27 patients were operated on within three weeks of percutaneous coronary intervention. 6 out of 7 patients in whom thienopyridine treatment was stopped died in the postoperative period, but there was only one death in the 20 patients in whom it was continued.

There are several reasons why the thrombotic risk is increased after coronary intervention: in the immediate aftermath any dilated coronary lesion is unstable because dilatation disrupts the plaque and its endothelial covering. Furthermore, any deployed stent represents a foreign surface with increased thrombogenicity prior to endothelialization. With drug eluting stents (DES), this process is delayed, therefore the risk of stent thrombosis is higher and persists for longer. However, Compared with 1st generation DES, newer generation DES are associated with lower risk of stent thrombosis and require a shorter duration of DAPT [48].

The Danish registry study in 2016 [24] and a number of other recent studies have pointed to time since stent insertion and other comorbidities rather than interruption of antiplatelets per se as being the more important determinant of postoperative major cardiac and cerebral events (MACCE) [30,31,43,44]. Howell et al in a prospective observational study found no evidence of a protective effect of DAPT from perioperative MACE in patients with stents having noncardiac surgery [43]. Furthermore a study that looked at the effectiveness of platelet inhibition by platelet mapping assays perioperatively found that the incidence of cardiac events was high in spite of adequate antiplatelet cover and the authors postulated that time from PCI to surgery and supply-demand of blood flow in the immediate postoperative period was more relevant [44].

2.2.3 Antiplatelet therapy for other indications

In cerebrovascular disease, a small case-control study postulated more than a 3-fold risk for ischaemic events in aspirin withdrawal [32] and current guidelines support antiplatelet therapy for 3-6 months following a stroke or TIA and long term cover with DAPT after carotid endarterectomy and carotid or vertebral stenting [51]. A meta-analysis on risks of perioperative aspirin discontinuation acknowledges the lack of prospective studies and is therefore careful with bold statements and risk estimates. An interesting observation is the mean time-interval between aspirin withdrawal and adverse events: it was shortest for acute coronary syndromes (mean of 8.5 days), followed by 14.3 days for acute cerebral events and 25.8 days for acute peripheral arterial syndromes [1]. This could be interpreted as confirming the notion that coronary ischemia is the most likely and most important adverse consequence of a short interruption of antiplatelet therapy in the perioperative phase.

Current NICE guidelines support monotherapy with clopidogrel or aspirin or modified release dipyridamole in patients with peripheral arterial disease along with risk reduction with exercise smoking cessation and statins. Secondary to interventions such as angioplasty / stents or surgical revascularization, monotherapy or DAPT is continued for 6-12 months [50]. No data are currently available for risk associated with dipyridamole or clopidogrel discontinuation in the above indications.

2.3 Cardiovascular risk stratification depending on morbidity and time intervals

Another approach to classifying thrombotic risk focuses on the exact type of cardiovascular morbidity and importantly also on the time delay since the occurrence of cardiovascular events [61].
Table 2: Risk for thrombotic events depending on morbidity

| High risk for thrombotic events: (>5%*) | - Recent (< 6 weeks) myocardial infarction, coronary artery bypass graft, CVA
- coronary interventions
- BMS (bare metal stent) <4 weeks old
- DES (drug eluting stent) <6 months old
- Balloon angioplasty <2 weeks
- Complex PCI (long, multiple or overlapping stents, Left main stem stent, bifurcations) <12 months
- <6 months after PCI for MI |
| Intermediate risk for thrombotic events: (1-5%)* | - MI, CABG, stroke within 6 – 24 weeks
- 2-4 weeks after balloon angioplasty
- >1 month and <6 months after PCI with BMS
- >6 months and <12 months after PCI with DES
- >12 months after complex PCI (multiple stents, overlapping stents, LAD lesion, bifurcation, long stents)
- heart failure, diabetes |
| Low risk for thrombotic events: (<1%*) | - >6 months after MI, CABG, stroke, bare metal stent (BMS)
- >4 weeks after balloon angioplasty
- >6 months after PCI with BMS
- >12 months after PCI with DES |

*30-day ischaemic event rates of cardiovascular death and MI; BMS-bare metal stent; PCI- Percutaneous coronary intervention; DES – drug eluting stent; ST – stent thrombosis

3. Risk of intra-operative bleeding under antiplatelet therapy

3.1 Acetylsalicylic acid

Two randomized, controlled, prospective trials investigating perioperative bleeding and thrombotic risks in patients on aspirin or placebo undergoing non-cardiac surgery have been published [22,23]. Both were not powered to detect a difference in bleeding events, so their negative findings in that aspect have to be interpreted with caution. However, in light of the fact that all other available studies are either from cardiac surgery or represent retrospective or non-randomized data, their results should not be dismissed entirely. In the first trial, a total of 220 patients at risk of cardiovascular events were randomized to either aspirin or placebo with all bleeding outcomes (amount of bleeding, surgeon’s assessment of bleeding tendency, transfusion requirements) being non-significant between the groups [22].

The second trial investigated 291 patients assigned to either aspirin or placebo and found no significant difference in ‘major bleeding’ or ‘bleeding’ events [23]. All other studies in non-cardiac surgery are non-randomized, small and in part also of limited quality. A meta-analysis of available data arrived at an increase of bleeding rate by a factor of 1.5 in patients on aspirin [1]. This increase in bleeding, however, did not seem to cause higher morbidity or mortality, with a few notable exceptions.

Most surgery such as dental, minor general, vascular, ophthalmological and dermatological procedures, as well as biopsies and endoscopies seemed safe. The exceptions were in tonsillectomies, where the re-operation rate was significantly increased and in transurethral prostatectomies, where two fatalities were reported as well as a higher transfusion rate. Finally, aspirin increased the risk of intracerebral hematoma following neurosurgery, and it was implicated in bleeding-related fatalities [1]. In orthopaedic surgery the evidence is mixed. One large trial found an increase in local and gastrointestinal bleeding in patients undergoing hip arthroplasty that was not reproduced in other trials of major orthopaedic operations [34]. As mentioned already, continuation of aspirin was also found to increase the risk of major bleeding in the POISE-2 trial [25].

3.2 Clopidogrel / dual therapy

Almost all evidence regarding clopidogrel monotherapy has been generated in cardiac surgery. A meta-analysis of coronary artery bypass surgery trials showed that clopidogrel taken until the operation significantly increased blood loss, transfusions, surgical re-exploration and length of hospital stay while not significantly affecting mortality [35]. A small retrospective analysis of non-elective orthopedic surgery performed under clopidogrel found no serious complications or increased transfusion requirements compared to matched control [36].

In dual antiplatelet therapy, one study investigating various non-coronary surgical procedures after stent insertion found only a small increase of transfusion rates from 39% (no antiplatelet therapy) to 43% (dual therapy) [37]. In contrast, another study looking at a similar patient group found a much higher difference between single and dual antiplatelet therapy: the risk of severe bleeding increased from 4 to 21% [38]. Both studies were small reflecting the paucity of the evidence-base in non-cardiac surgery. A recent review estimated the increase of blood loss with aspirin to be 20% and with dual treatment 50% across non-cardiac surgery, but found no clear increase in mortality or morbidity except in neurosurgery [39]. More recently the investigators on the OBTAiN clinical trial showed an increased risk of bleeding with dual antiplatelet therapy with no evidence of a protective effect on perioperative MACE in patients who have undergone previous PCI [43].

A recent study found that dual therapy with aspirin and clopidogrel was not associated with an increase in bleeding complications or transfusion requirements in patients undergoing peripheral arterial surgery [49]. In addition a recent meta-analysis (2938 patients) has shown that patients on clopidogrel with hip fractures can be managed as per usual protocols (Early surgery and continuation of clopidogrel) [57].

There are insufficient data to draw any conclusions about perioperative bleeding risk with dipyridamole.

3.3 Risk stratification for intraoperative bleeding depending on type of surgery

Independent of antiplatelet medication, the risk of hemorrhage of surgery can be classified depending on the type and location of surgery [2]. It is important to note that both the risk of hemorrhage and the potential consequences determine the grading:
4. Regional Anesthesia and anti-platelet drugs

Neuraxial anaesthesia is often considered in patients taking antiplatelet agents for coronary stent protection and the decision to use such a technique must be based on careful assessment of the overall balance of risk and benefit for each individual. Regarding the time frame between stopping antiplatelet agents and neuraxial blockade, the following guidelines have been published by the Association of Anaesthetists [62] and the American Society of Regional Anaesthetists.[47].

5. Practical approach to perioperative antiplatelet treatment in non-cardiac surgery

The perioperative management of antiplatelet therapy must always balance the thrombotic risks of stopping with the bleeding risks of continuing the drugs. The basic questions prior to surgery that provide the necessary information for decision making are outlined below:

- what is the nature of the operation?
- how necessary / urgent is it?
- what is the indication for antiplatelet therapy?
- how high is the thrombotic risk?
- what is the risk for bleeding?
- what are the potential consequences of bleeding?
- if discontinued, when to recommence antiplatelet therapy?

Several US and European professional bodies have published guidelines [41,42,43,52,54,56,59,60]. There is general consensus on the main principles of managing antiplatelet therapy perioperatively: a simplified approach that covers most straightforward cases is outlined in the algorithm in figure 1. It should be emphasized that these guidelines do not cover cardiac surgery. Borderline situations need further consideration, for instance of the precise bleeding risk of surgery as detailed in chapter 3.3, and of the precise thrombotic risk (see chapter 2.3).

In patients who have coronary stents, not only the type of stent (BMS versus DES) but the time since insertion and complexity of the stent needs to be considered in addition to patient co-morbidities such as systolic dysfunction, renal dysfunction and diabetes. [44]. As details of the stent per se may not be apparent at pre-assessment, a pragmatic policy would be to discuss each case individually between surgeon, cardiologist and anaesthetist for stents placed within the preceding year.

An overview of this decision-making process depending on thrombotic vs hemorrhagic risk is given in Table 5 below.

Transurethral prostate resection is an example of a practical dilemma: reports of two fatal hemorrhages associated with aspirin treatment [1], should lead to careful consideration of whether to continue or withhold aspirin therapy [42]. In practice however, surgeons are divided in their approach and local agreements are necessary to avoid unnecessary cancellations.

Elective surgery and patients with stents:
Elective surgery should be deferred in patients with drug eluting stents for at least 6 months and with bare metal stents for at least 1 month. After balloon angioplasty elective surgery should be deferred for at least 2 weeks. Aside from the timing of surgery relative to PCI, patient co-morbidities and indication for PCI (stable heart disease vs acute coronary symptom) are also important factors to take into consideration.

Recent stenting and urgent surgery
In patients presenting for surgery on dual antiplatelet therapy after recent coronary stenting, the key question is whether it is feasible to delay the operation. If these delays are not acceptable, operating under dual therapy is recommended [42]. If the bleeding risk is deemed high then an individualized risk-benefit analysis needs to be made, aspirin should be continued and such surgeries should be performed in centers that have access to cardiac catheterization facilities 24/7. Bridging therapy with IV antiplatelets (Tirofiban, cangrelor, eptifibatide) may be necessary. [59].

Unplanned / emergency surgery in patients on dual therapy:
Both aspirin and clopidogrel have short half-lives, and plasma levels of active drug are low only...
Stopping and restarting antiplatelet agents

If antiplatelet therapy is discontinued, it should be for the shortest time possible. Inter-individual variation in sensitivity to ADP receptor antagonism may allow some patients to have a shorter period of discontinuation. Assessment of platelet function may help identify such patients. Corredor et al have reviewed the utility of platelet function testing in cardiac surgery and found the most robust evidence was for thrombo-elastography to be incorporated into a blood management algorithm to reduce transfusion [53].

Post operatively, early reinstitution is important after ensuring hemostasis. There is scant evidence to support bridging therapy during the period of antiplatelet withdrawal: heparin does not replace the antiplatelet effects and should not be used and there is minimal data regarding short-acting antiplatelet drugs such as Glycoprotein IIb/IIIa inhibitors (tirofiban, eptifibatide). However, such a strategy is likely to be associated with higher risk of bleeding [54].

In the case of clopidogrel, restarting with a loading dose should be considered (e.g. 300 mg given as soon as possible post-operatively) [52]. The second thienopyridine, prasugrel, although more potent than clopidogrel, displays similar pharmacodynamic properties and should be treated in the same way as clopidogrel. For the reversible P2Y12-inhibitor ticagrelor, similar considerations apply as for clopidogrel, bearing in mind the greater potency of the drug with regards to bleeding. Dipyrimadole has a reversible effect with a short half-life. It is usually given in combination with aspirin and similar principles to stopping aspirin would apply in combination therapy.

Finally, the current paucity of reliable, high quality evidence and the development of several new platelet inhibitors make this a situation in flux where alterations to current practice can be expected as new evidence becomes available.

Table 5: Overview of decision-making process for perioperative management of DAPT

<table>
<thead>
<tr>
<th>HEMORRHAGIC RISK</th>
<th>THROMBOTIC RISK</th>
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<tr>
<td>Low risk</td>
<td></td>
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<tr>
<td>Continue aspirin,</td>
<td>Postpone elective</td>
</tr>
<tr>
<td>discontinue</td>
<td>surgery, if</td>
</tr>
<tr>
<td>clopidogrel</td>
<td>surgery cannot</td>
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<tr>
<td>and resume within</td>
<td>be deferred</td>
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<tr>
<td>24-72 hours with</td>
<td>continue aspirin,</td>
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<tr>
<td>a loading dose</td>
<td>stop clopidogrel,</td>
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<td></td>
<td>resume within</td>
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<td></td>
<td>24-72 hours with</td>
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<td></td>
<td>a loading dose</td>
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<tr>
<td>Intermediate risk</td>
<td></td>
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<td>Continue aspirin,</td>
<td>Postpone elective</td>
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<tr>
<td>discontinue</td>
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<td>clopidogrel and</td>
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Stopping and restarting antiplatelet agents

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Finally, the current paucity of reliable, high quality evidence and the development of several new platelet inhibitors make this a situation in flux where alterations to current practice can be expected as new evidence becomes available.
References


Summary and Key Recommendations

- The use of herbal/traditional/complementary remedies amongst patients is variable and probably underreported.
- Patients should be asked specifically about their use of herbs, vitamins, supplements, or other natural or alternative products.
- Although regulation has been improved, there remain concerns over the efficacy, pharmacodynamics and pharmacokinetics of these agents.
- There is insufficient data on many of these herbal remedies to provide robust scientific recommendations on when to stop them before surgery. However a pragmatic recommendation of 7 days will be sufficient for the commonly used remedies.
- Cannabinoids and marijuana should be discontinued 72 hrs before general anaesthesia.
- It is recommended that departments provide consistent advice on the perioperative management of herbal remedies and that this is regularly reviewed.
INTRODUCTION

Herbal and traditional remedies have been used for centuries in various forms throughout the world, with considerable geographical and cultural variation. Many of the prescription drugs in current use have been derived from plant products. The World Health Organisation estimates that up to 80% of the world’s population still rely on herbal and traditional remedies [1]. Reported prevalence rates for herbal medicine usage in Europe range from 5.9% to 48.3% [2].

Such remedies are used to treat a wide variety of conditions, which often have a chronic course. Of relevance to anaesthesia and surgery are those remedies used to treat chronic pain, post-op nausea and vomiting and anxiety [3]. There is a common misconception that these agents are safe because they are ‘natural’ [4].

The term ‘herbal and traditional remedies’ is non-specific and other terms e.g. complementary medicine or alternative remedies are used interchangeably. Broadly speaking, herbal medicines are those with active ingredients made from plant components, such as leaves, roots or flowers. In the UK, according to the Human Medicines Regulation 2012 [5], a product is a herbal medicine if the active ingredients are herbal substances and/or herbal preparations only. For the purposes of this guideline, the term ‘herbal remedies’ will also include over-the-counter health-promoting supplements derived from plants.

Peri-operative Usage

The unquantifiable concerns amongst healthcare professionals regarding such remedies stem from several issues [6, 7]:

- Many patients do not consider these products to be drugs or medication and often do not disclose their use to healthcare providers. A recent study showed that only 23% of preoperative surgical patients discontinue their herbal medication regimens prior to surgery [8]
- They may interact with prescribed and administered conventional medication [9]
- They may have side effects or cause adverse reactions
- Not all herbal remedies are regulated. Specifically customised preparations for individuals do not need a licence; those manufactured outside the UK may not be subject to regulation
- Evidence for the effectiveness of herbal remedies is generally limited

Despite growing knowledge about herbal remedies and drug interactions, most of these concerns have arisen based on theoretical data rather than clinical evidence from patients. Pharmacokinetic information about these agents is often lacking and hence, it might not be possible to provide robust advice on when to stop these agents prior to anaesthesia and surgery. Pragmatically therefore, patients should be advised to discontinue all non-essential herbal remedies for one week prior to elective surgery. Some products may not need to be discontinued this far in advance, or even at all, however there is usually insufficient information about pharmacological effects and half-life of the constituents of such remedies to tailor the advice for the patient [10].

REGULATIONS

In the UK, the majority of herbal remedies are exempt from the licensing requirements set out in the Medicines Act 1968. In the US, herbal products are classified as dietary supplements by the Food and Drug Administration (FDA) under the Dietary Supplemental Health and Education Act of 1994, and are not subjected to rigorous testing. Few instructions exist regarding proper usage, dose requirements, side effects, toxicity and drug interactions.

The lack of compulsory post-marketing surveillance means that the incidence, nature and scale of adverse effects in the UK are unknown. Hence, herbal remedies available over-the-counter can be of variable quality and content; heavy metals including mercury, lead, thallium, cadmium, copper, iron, manganese, nickel, zinc and arsenic have all been found in herbal remedies, despite their purported natural origins [11]. This makes it difficult to interpret any reactions in the patient or to determine if the herbal remedies are responsible.

In order to improve the regulation of herbal remedies, the Traditional Herbal Registration (THR) was introduced. Qualification for a THR requires the submission of scientific evidence relating to the safety, quality and traditional use of the product. THR-registered products would generally have been in use for treatment of the stated condition for a minimum of 30 years, 15 years of which must have been in the European Union [12]. A list of herbal remedies granted a THR status in the UK is available online [13].

As for any other medication, side effects or adverse reactions (including suspected reactions) to a herbal remedy should be reported using the Yellow Card Scheme run by the Medicines and Healthcare products Regulatory Agency (MHRA).

At international level, the International Regulatory Cooperation for Herbal Medicines (IRCH) is a global network of regulatory authorities responsible for the regulation of herbal medicines, established in 2006 under the umbrella of the World Health Organisation. Its mission is to protect and promote public health and safety through improved regulation for herbal medicines.

COMMON HERBAL REMEDIES

The market for herbal remedies is constantly evolving, with new products regularly added to those already available to the general public either over-the-counter, face-to-face via a practitioner or on the internet. This is a non-exhaustive list of the most commonly used herbal remedies that could affect the user in the peri-operative period. A summary is provided in Appendix 1.

Echinacea

- Popular ‘health supplement’ primarily used to prevent or treat common cold
- Some evidence that it may decrease severity and duration of upper respiratory tract infections, though not as prophylaxis. Likely due to its immunomodulatory effects through cytokine signalling
- Side effects: gastrointestinal disturbance, headache, dizziness
- Risk of hepatic dysfunction / failure in chronic usage, thereby enhancing hepatotoxic effects of drugs such as amiodarone, methotrexate and halothane
- Immunostimulatory in the short term, but potent immunosuppressant in longer term. Should be avoided in patients requiring peri-operative immunosuppression (such as transplant candidates)
- Peri-operative period:
  - Pharmacokinetic data is lacking; no available recommendations regarding their use peri-operatively

Ephedra (Ma Huang)

- Marketed as a CNS stimulant, weight loss supplement and for treatment of asthma
- Contains the alkaloids ephedrine (predominant compound), pseudoephedrine, methylephedrine and nor-pseudo-ephedrine
- Sympathomimetic with direct agonist effect on - and - adrenergic receptors, indirectly increases presynaptic noradrenaline release
- Side effects: palpitations, hypertension, tachycardia, cerebrovascular accident and seizures. Chronic use associated with cardiomyopathy. Other adverse effects reported include myocardial infarction, fatal arrhythmias, acute hepatitis and psychosis
• Peri-operative period:
  • Combination with sympathomimetic drugs can cause life-threatening arrhythmias, hypertension and hyperthermia
  • Long-term use of ephedra may deplete endogenous catecholamine stores leading to further cardiovascular instability intra-operatively and tachyphylaxis to other sympathomimetic drugs; direct-acting sympathomimetic agents may be preferable in this situation
  • Fatal arrhythmias reported in ephedra users exposed to halothane anaesthesia
  • Pharmacokinetic data suggests discontinuation for at least 24 hours before surgery

Garlic (Allium sativum)
• Common culinary ingredient, marketed as health supplement with claims to benefit those with cardiovascular disease, diabetes and even tumours
• Contains cysteine, which decreases thromboxane formation and alters arachidonic acid metabolism. Dose-dependent inhibition of platelet aggregation
• Side effects: nausea, hypotension and allergic reactions. Several case reports of garlic causing bleeding problems
• Peri-operative period:
  • Garlic can potentiate the anti-platelet effects of aspirin and NSAIDs; this effect may be irreversible
  • Discontinue for at least 7 days before surgery (if possible)

Ginger (Zingiber officinale)
• Another common culinary ingredient, marketed as an anti-inflammatory and anti-emetic
• Directly stimulates gastro-intestinal tract, also postulated to inhibit peripheral and central serotonergic pathways. A systematic review of randomised controlled trials showed no significant difference in incidence of post-operative nausea and vomiting between the ginger and placebo groups
• Peri-operative period:
  • Potent inhibitor of thromboxane synthetase enzyme, may prolong bleeding time
  • Risk assessment for bleeding is prudent, particularly if used alongside NSAIDs and warfarin

Ginkgo biloba
• Promoted as health supplement for cognitive performance and dementia prevention
• Believed to protect vascular walls and neurons by scavenging free radicals and inhibiting platelet-activating factor. Ginkgo extracts contain several flavonoids, terpenoids and organic acids
• Approved for use in Germany for treatment of dementia after a large multi-centre, randomised controlled trial showed improved cognitive performance in patients with dementia
• Treatment of peripheral vascular disease by decreasing blood viscosity and improving blood flow
• Side effects: gastrointestinal upset and headaches
• Peri-operative period:
  • As a potent inhibitor of platelet activation, ginkgo should be avoided in combination with NSAIDs, aspirin and warfarin
  • Several reports of intracranial haemorrhage in patients using ginkgo
  • Pharmacokinetic data suggests discontinuation for 36 hours before surgery

Ginseng (Panax ginseng)
• Originally used in Traditional Chinese Medicine and considered a rare and highly-priced health supplement, now cultivated for worldwide distribution as food products and in the form of supplements containing varying levels of active components (ginsenosides)
• Marketed for immune system benefits, mood enhancement and aphrodisiac effects
• Pharmacological profile incompletely understood due to heterogeneous and sometimes opposing effects of its constituents
• Mild sympathomimetic effect and may interact with the monoamine oxidase enzyme
• Neuroprotective effect believed to be due to the inhibition of sodium channels in the CNS
• Some degree of hypoglycaemic activity and interference with platelet aggregation
• Side effects: irritability, insomnia and gastro-intestinal disturbance. Predisposition to gynaecomastia and vaginal bleeding (weak oestrogenic effect)
• Peri-operative period:
  • May increase bleeding risk - use with caution in combination with NSAIDs and warfarin
  • Tremor and mania have been reported with the combination of ginseng and monoamine oxidase inhibitors (MAOI); this combination should be avoided
  • Intra-operative monitoring of blood sugar is recommended especially for patients already on hypoglycaemic agents
  • Pharmacokinetic data from animal studies demonstrate potentially irreversible inhibition of platelet activity
  • Discontinue at least 7 days before surgery

Kava (Piper methysticum)
• Derived from the dried root of the pepper plant family
• Used as an anxiolytic and sedative, with effects mediated by potentiation of GABA transmission.
• Potentiates the effects of barbiturates and benzodiazepines
• Side effects: hepatotoxicity, skin changes, extrapyramidal-like dystonic reactions
• Peri-operative period:
  • May reduce the requirements for anaesthetic agents and potentiate their sedative effects
  • Discontinue for at least 24 hours before surgery

St John’s Wort (Hypericum perforatum)
• Widely used in Western societies as a natural antidepressant and for other mood disorders
• Believed to act via inhibition of serotonin, noradrenaline and dopamine re-uptake by neurones; efficacy found to be equivalent to tricyclic antidepressants in the treatment of mild to moderately severe depressive disorders
• Peri-operative period:
  • Side effects: gastrointestinal disturbance, fatigue, dizziness, confusion, headache and photosensitivity
  • Numerous important interactions between conventional drugs and St John’s Wort
• Risk of a serotonergic syndrome characterised by muscle rigidity, autonomic dysfunction and altered mental state when used in combination with drugs which also increase plasma serotonin levels. Requires same precautionary measures as for patients on conventional MAOI
• Potent inducer of hepatic cytochrome P450 CYP3A4 isofrom; may significantly increase metabolism of many concomitantly administered drugs e.g. alfentanil, midazolam and lignocaine
• Induces the P450 2C9 isofrom, reducing the effect of warfarin and NSAIDs
• The sedative properties of St John’s Wort may potentiate or prolong effects of anaesthetic agents
• Pharmacokinetic data suggests discontinuation for at least 5 days prior to surgery, especially in patients awaiting organ transplant and hence requiring immunosuppression, as well as those who may require oral anticoagulation

Valerian (Valeriana officinalis)
• Used as an anxiolytic and sedative
• Produces dose-dependent sedation with some hypnotic effects, believed to be via inhibition of GABA breakdown and re-uptake
• Side effects: tremor, headache, hepatic dysfunction and cardiac disturbances
• Peri-operative period:
• Caution in patients who may be physically dependent on Valerian - risk of benzodiazepine-like withdrawal. Tapering the dose prior to elective surgery may be prudent (if possible)

CANNABIS AND MEDICAL MARIJUANA [14, 15]

Cannabinoids are derived from the Cannabis plant and their medicinal use in the UK has undergone recent policy changes (2018). In addition to recreational smoking, other cannabis-derived products have become mainstream in recent years (including vape oil, edible and cosmetic products). Research into its effects on humans has been limited by its classification; animal studies cannot be easily extrapolated due to interspecies differences.

Exogenous cannabinoids can be plant-derived (phytocannabinoids) or synthetic. Over a hundred phytocannabinoids exist, with varying effects on endogenous cannabinoid receptors, but only delta-9-tetrahydrocannabinol (THC) and Cannabidiol (CBD) are medically-relevant.

THC
• Most potent phytocannabinoid, responsible for intoxicating effects of recreational marijuana
• Binds tightly to CB1 receptors in the brain, inhibits neurotransmitter release and produces an exaggerated mood response and euphoria
• Products containing THC for medical purposes are regulated in the UK and require a prescription, with prescribing restrictions on some e.g. named patient basis, prescriber on specialist register

CBD
• Does not have intoxicating effects, cognitive alterations or withdrawal effects of THC; minimal risk of misuse or dependence [16]
• Binds loosely to CB1 receptors, modulates neurotransmission (believed to reduce seizure activity, anxiety and depression) and up-regulates CB receptors (increasing sensitivity to natural endocannabinoids, hence improving pain tolerance and mood)
• Modulates other neurotransmitter receptors including serotonin and opioid receptors, with effects on mood and pain tolerance respectively
• THC-free CBD extract is available for management of pain, anxiety or insomnia etc. Any other CBD products sold in shops or on the internet are legally controlled to contain no more than 0.2% THC in the EU, although declared contents may be inaccurate, as with other herbal remedies

Synthetic cannabinoids
These are entirely laboratory-derived and will not be considered here other than a brief mention that these can be used for medicinal (e.g. nabilone and dronabinol mimic the action of THC and are both potent anti-emetics) and recreational purposes (e.g. Spice).

Effects of cannabinoids
• Central nervous system - anxiety / anxiolysis, paranoia, psychosis, headache
• Cardiovascular - tachycardia, vasodilation, orthostasis, risk of myocardial infarction
• Respiratory - bronchodilation, hyperactivity, airway oedema
• Clotting - conflicting evidence supporting both pro- and anti-thrombotic effects

Due to the nature of recreational use, possibly in conjunction with alcohol, it may not be possible to elicit a detailed history or discontinue usage in patients undergoing emergency surgery. The pharmacokinetics of cannabinoids are difficult to predict and will depend on THC concentration, rate of delivery, hepatic metabolism (into psychoactive and non-psychoactive metabolites) etc.

Issues relevant to the peri-operative period include:
• Interactions reported with multiple drugs including cross tolerance with opioids, excessive CNS depression with barbiturates, benzodiazepines, reduced effectiveness of propofol
• Potentiation of non-depolarising muscle relaxants, norepinephrine, augmentation of drugs causing cardiorespiratory depression, more pronounced response to inhaled anaesthetic agents
• Systematic review did not find sufficient evidence for association between marijuana and cardiovascular outcomes including myocardial infarct and cerebrovascular infarct [17]. However, it would be prudent to avoid drugs that affect heart rate in a patient with recent marijuana use, in view of the tachycardia it causes
• No clear guidance available on discontinuation before elective surgery. Marijuana use should ideally be stopped 72 hours before general anaesthetic, to reduce the risk of airway hyperresponsiveness following airway instrumentation [18]
• Increased risk of aspiration due to delayed gastric emptying [19]
• Potential withdrawal syndrome in post-operative period, presenting with sweats, fever, chills, aggression, abdominal cramps, sleep disturbance
• Pain control issues - may require more analgesia

AVAILABLE GUIDELINES

In the UK, there remains considerable variation in adherence to available guidelines and more importantly, there is no coherence in the advice being offered to patients in the peri-operative period [20, 21]. UK professional organisations such as the Royal College of Anaesthetists and Association of Anaesthetists of Great Britain and Ireland do not provide specific advice beyond generic peri-operative recommendations. The British Society of Day Surgery has published more specific and detailed guidelines on the management of herbal remedies [24].

The 2003 American Society of Anaesthesiologists recommended that patients cease herbal medications 2 weeks before surgery [22] but the more recent American Society of Regional Anaesthesia recommends one week as being appropriate before interventional spinal or pain procedures. However tests of platelet function are recommended if large doses of garlic are taken daily or with comcomitant aspirin, NSAID or antidepressant use [23]

The use of herbal remedies and their development is constantly evolving; sources of information for anaesthetists should be readily available for reference (see Appendix 2). In addition, all potential side effects encountered must be reported to the relevant bodies.

CONCLUSIONS

The lack of disclosure by patients regarding their use of herbal remedies may be due to a combination of ignorance (‘natural’ is often assumed to be safe) and fear of prejudice from the medical community. Herbal remedies can also be taken in combined preparations; patients may be oblivious to their actual content. Hence, it is imperative that anaesthetists specifically ask about their use preoperatively, with the assurance that information divulged will only be for the purposes of providing the best care for the patient.

There is currently no clear data regarding specific adverse interactions between herbal remedies and drugs used in anaesthesia. The pharmacodynamic and pharmacokinetic properties of many of these remedies are yet to be conclusively ascertained.


Ephedra/Ma Huang

Garlic (Allium sativum)

Ginseng (Panax ginseng)

Green tea (Camellia sinensis)

Guaraná (Paulinia cupana)

Kava (Piper methysticum)

References


Appendix 1 (selected herbal remedies adapted from [24, 25, 26, 27])

<table>
<thead>
<tr>
<th>Herbal medicine</th>
<th>Use</th>
<th>Pharmacological effects</th>
<th>Perioperative consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloe vera (Aloe barbadensis miller)</td>
<td>Joint health</td>
<td>Reduction of prostaglandin synthesis</td>
<td>Hypoglycaemia Risk of bleeding Hepatotoxicity</td>
</tr>
<tr>
<td>Cranberry (Vaccinium oxyccoccus)</td>
<td>Antibacterial Urinary tract infection</td>
<td>Inhibits metabolism of warfarin Immunomodulating</td>
<td>Risk of bleeding</td>
</tr>
<tr>
<td>Devil’s Claw (Harpagophyllum procumbens)</td>
<td>Joint health</td>
<td>Induction of cytochrome P450 enzyme</td>
<td>Hypoglycaemia Hypotension</td>
</tr>
<tr>
<td>Echinacea purpurea</td>
<td>Promotes general wellbeing</td>
<td>Activation of cell-mediated immunity</td>
<td>Immune suppression Hepatotoxicity</td>
</tr>
<tr>
<td>Eurycoma longifolia</td>
<td>Weight loss Mood enhancer Asthma</td>
<td>Sympathomimetic (direct and indirect)</td>
<td>Risk of myocardial ischaemia, stroke and hypertension Haemodynamic instability Arrhythmias</td>
</tr>
<tr>
<td>Garlic (Allium sativum)</td>
<td>Cardiac health Cardiovascular wellbeing</td>
<td>Inhibition of platelet aggregation</td>
<td>Blood pressure changes Increased risk of bleeding Nausea</td>
</tr>
<tr>
<td>Ginger (Zingiber officinale)</td>
<td>Culinary ingredient</td>
<td>Inhibit serotonergic pathways</td>
<td>Sedative effects Risk of bleeding</td>
</tr>
<tr>
<td>Ginseng (Panax ginseng)</td>
<td>Immune system benefits</td>
<td>Mild sympathomimetic</td>
<td>Impaired wound healing Antplatelet effect Headaches</td>
</tr>
<tr>
<td>Guarana (Paulinia cupana)</td>
<td>Weight loss Stimulant</td>
<td>Inhibits Na channels in the CNS</td>
<td>Cardiovacular instability Impaired wound healing Immunomodulating Increased risk of infection</td>
</tr>
<tr>
<td>Green tea (Camellia sinensis)</td>
<td>Neurodegenerative diseases Anti-cancer</td>
<td>CNS stimulant Antioxidant Source of Vitamin K</td>
<td>Antplatelet effect Stimulant Risk of bleeding</td>
</tr>
<tr>
<td>Kava (Piper methysticum)</td>
<td>Anxiolytic Sedative</td>
<td>Potentiation of GABA transmission Dopamine antagonist</td>
<td>Sedative effects Hepatotoxicity Dermatological changes</td>
</tr>
</tbody>
</table>
Summary and Key Recommendations

Over the past 2 decades, new drug development for autoimmune inflammatory diseases including rheumatoid arthritis and related conditions, psoriasis and inflammatory bowel disease has been rapid. Many of these drugs, in particular biologic and targeted synthetic DMARDs, are associated with an increased risk of infection although whether this extends to post-operative infections including prosthetic joint infections is less clear. Data to support evidence-based decision making regarding the peri-operative management of DMARDs are limited and largely of low quality.

- It is advised to ensure a full drug history, including hospital prescribed injections and infusions, is taken from all patients as most new biologic DMARDs will not appear on GP prescription records. This should include all drugs received in the past 6 months where possible.
- It is currently recommended that patients can continue conventional DMARDs throughout surgery but should pause all biologic DMARDs at least 1 dosing interval prior to surgery. For some drugs this can be up to 3-6 months although most are dosed more frequently.
- Patients receiving new JAK inhibitors, a daily targeted synthetic DMARD, should hold this medication at least 1 week prior to surgery.
- Biologic DMARDs and JAK inhibitors can be restarted a minimum of 14 days after surgery once it is confirmed that there are no issues with wound healing and staples and sutures have been removed. They should NOT be administered in the setting of infection.

### Appendix 2: List of useful sites

- **HerbMed**
  www.herbmed.org

- **Medicines Complete**
  https://about.medicinescomplete.com/

- **National Centre for Complementary and Alternative Medicine**
  http://nccam.nih.gov

- **Natural medicines comprehensive database**
  http://naturaldatabase.therapeuticresearch.com

- **The handbook of perioperative medicines**
  https://www.ukcpa-periophandbook.co.uk/

- **Toxbase**
  www.toxbase.org

- **WebMD Vitamins and Supplements Center**
  https://www.webmd.com/vitamins/index
INTRODUCTION

1. Introduction

Disease modifying anti-rheumatic drugs (DMARDS) are now the standard of care for many autoimmune inflammatory diseases such as rheumatoid arthritis [RA] and other inflammatory arthritides, connective tissue diseases including systemic lupus erythematosus [SLE], psoriasis and inflammatory bowel disease. Most patients with inflammatory arthritis will start DMARDS soon after diagnosis and will likely remain on these for the rest of their lives. Therefore, it is probable that patients with these conditions who require surgery will be receiving these drugs at the time surgery is planned. Many DMARDS are immunosuppressive and thus there is a concern whether continued DMARDs through the peri-operative period may increase the risk of post-operative infections, and particularly for patients undergoing orthopaedic procedures, prosthetic joint infections.

The aim of this chapter is to review the use of common DMARDS in the peri-operative period. Most of the evidence about DMARD use and surgical risk is based on studies in patients with RA undergoing elective orthopaedic procedures, the most common procedure in this patient group, and will be the focus of this chapter. It is not certain but is likely that the evidence from elective orthopaedic surgery can also be applied to other elective procedures and other conditions. The evidence in this chapter is not meant to represent specific treatment guidelines but will reference clinical guidelines where these exist. In all patients, individualised risk and decision making should take preference over strict guidelines. Management of DMARDs in non-planned or urgent surgeries will be discussed briefly towards the end of the chapter.

2. What are DMARDs?

The goal of treating RA is remission or low disease activity and DMARDs play an integral role in this treatment. DMARDs themselves represent a heterogeneous group of medications which have the common feature of having been shown in clinical trials to slow or stop radiological damage. Successful treatment results in reduction in symptoms and joint inflammation as well as inhibition of bone and joint damage. In recent years, a treat-to-target approach, with the target being remission, has been adopted by the rheumatology community, whereby DMARDs are started as soon as possible after disease onset and escalated until disease control is achieved [1]. Once disease control is achieved, the DMARD is either maintained or in some patients, the dose may be tapered, but rarely discontinued unless adverse effects are experienced. DMARDs are now classed into 3 broad sub-categories: conventional synthetic [cs], biological [b] and targeted synthetic (ts) DMARDS (Table 1).

Conventional synthetic DMARDs include the commonly used drugs methotrexate (MTX), sulfasalazine, hydroxychloroquine and leflunomide. Methotrexate is recommended as the first line treatment for RA by the European League Against Rheumatism (EULAR) [1] and is one of the recommended first line treatments by the National Institute for Health and Care Excellence (NICE) [2]. Other drugs in this category used more often in other autoimmune inflammatory diseases included ciclosporin (psoriasis), 5-ASA/mesalamine (inflammatory bowel disease) and mycophenolate mofetil and azathioprine (connective tissue diseases). The mechanism of action of these drugs in RA and related conditions is not always known, with many being repurposed from other conditions, but all are thought to be immunomodulatory and immunosuppressive to variable degrees.

In the early 2000s, the management of autoimmune inflammatory diseases such as RA underwent a revolution with the introduction of bDMARDs. Unlike csDMARDs, most bDMARDs have been developed specifically for RA and other autoimmune inflammatory diseases. They are protein-based compounds, largely monoclonal antibodies or recombinant receptor proteins, with specific cellular (such as CD20 on B-cells) or cytokine targets (such as tumour necrosis factor [TNF] and interleukin [IL-6]). They must be administered by subcutaneous or intravenous routes.

The first of these was infliximab, an anti-tumour necrosis factor (TNF) monoclonal antibody. Over the past 20 years we have seen an exponential growth in bDMARDs across indications, with >20 new biologic drugs targeted against several different cytokine and cell types (Table 1). The majority of these are licensed for rheumatoid arthritis, but over the last few years we have seen biologics specifically developed for ankylosing spondylitis [e.g. anti-IL17], psoriasis (e.g. anti-IL17, anti-IL12/23) including psoriatic arthritis, inflammatory bowel disease [e.g. anti-CD47 integrin] and SLE [e.g. anti-B-lymphocyte stimulator (BLyS)]. Unlike most csDMARDs, bDMARDs are classed as high-cost drugs and their use is regulated in the UK by NICE [3].

Table 1 Common Disease Modifying Anti-Rheumatic Drugs Used in the Management of Rheumatoid Arthritis and Other Autoimmune Inflammatory Diseases*

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Usual maintenance dose, route</th>
</tr>
</thead>
<tbody>
<tr>
<td>csDMARDs</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>15-25 mg weekly, PO or SC</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>200-400 kg daily, PO</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>2 g daily, PO</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>20 mg daily, PO</td>
</tr>
<tr>
<td>bDMARDs</td>
<td></td>
</tr>
<tr>
<td>Tumour necrosis factor inhibitors</td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>40 mg weekly, SC</td>
</tr>
<tr>
<td>Etanercept</td>
<td>50 mg weekly, SC</td>
</tr>
<tr>
<td>Infliximab</td>
<td>3 mg/kg 8 weekly, IV</td>
</tr>
<tr>
<td>Certolizumab-pegol</td>
<td>200 mg every 2 weeks, SC</td>
</tr>
<tr>
<td>Golimumab</td>
<td>50 mg once monthly, SC</td>
</tr>
<tr>
<td>Anti-B cell therapies</td>
<td></td>
</tr>
<tr>
<td>Rituximab [anti-CD20]</td>
<td>2*1000mg 2 weeks apart, every 6+ months</td>
</tr>
<tr>
<td>Belimumab [anti-BlyS]</td>
<td>Weight based dose once monthly, IV or 200mg once monthly, SC</td>
</tr>
<tr>
<td>Anti-IL17</td>
<td></td>
</tr>
<tr>
<td>Secukinumab</td>
<td>150-300mg monthly, SC</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>80 mg every 4 weeks, SC</td>
</tr>
<tr>
<td>Brodalumab</td>
<td>210 mg every 2 weeks, SC</td>
</tr>
<tr>
<td>Anti-IL12/23</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>45 mg every 12 weeks, SC</td>
</tr>
<tr>
<td>Anti-IL23</td>
<td></td>
</tr>
<tr>
<td>Gusekumab</td>
<td>100 mg every 8 weeks, SC</td>
</tr>
<tr>
<td>Anti-IL6</td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>162 mg once weekly, SC or 8 mg/kg once monthly, IV</td>
</tr>
<tr>
<td>Sarilumab</td>
<td>200 mg every 2 weeks, SC</td>
</tr>
<tr>
<td>Anti-CD84</td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>125 mg once weekly, SC or weight based dose once monthly IV</td>
</tr>
<tr>
<td>Anti-CD47 integrin</td>
<td></td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>108 mg every 2 weeks, SC or 300mg every 8 weeks, IV</td>
</tr>
<tr>
<td>tsDMARDs</td>
<td></td>
</tr>
<tr>
<td>Baricitinib</td>
<td>2-4 mg daily, PO</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>5 mg BD, PO</td>
</tr>
<tr>
<td>Ruxolitinib</td>
<td>5mg-20mg daily P</td>
</tr>
</tbody>
</table>
Most recently, tDMARDS, have been approved, initially for RA but also now used in psoriatic arthritis and inflammatory bowel disease. Unlike bDMARDS, tDMARDS are targeted oral medications. The current licensed therapies, baricitinib and tofacitinib, inhibit janus kinase [JAK inhibitors] and differ from bDMARDS in their daily oral formulation. Like bDMARDS, they are high-cost drugs and their use is regulated by NICE.

In 2018, NICE published updated guidelines for the management of RA [2]. These state that all patients with new RA should be treated initially with csDMARDs. Although there is a range of medications in this category, the majority of patients are started on MTX with a smaller proportion started on sulphasalazine [4]. Some patient, particularly those deemed to have risk factors for more severe disease, are started on a combination of csDMARDs, usually MTX plus hydroxychloroquine or less commonly MTX plus sulfasalazine. If the first csDMARD [or combination] is not effective or not tolerated, a second csDMARD will be substituted or added. For patients whose disease has not been brought under control with two csDMARDS, most will move onto a bDMARD. Biologic DMARDS are often used in combination with csDMARDS but never in combination with another bDMARD or tDMARD, due to a concern about heightened infection risk [5]. Patients who do not respond to their first b/tsDMARD will tend to cycle through these two classes of DMARDS until disease control can be optimised.

Currently the majority of DMARDS are initiated by hospital specialists. Some csDMARDS, such as MTX, maybe be prescribed subsequently in primary care under a shared care agreement with the hospital but b/tsDMARDS are exclusively prescribed by hospital doctors and as such will not usually appear on GP records in the UK or on repeat prescription lists; therefore all patients with an autoimmune inflammatory disease should be asked specifically for a full list of their medications from all sources. A special note should be made for the drug, rituximab. An anti-CD20 monoclonal antibody administered by intravenous infusion, this treatment temporarily but profoundly depletes a patient’s B-cells. The B-cell depletion is rapid, but the length of depletion is variable. The drug is usually administered at intervals no less frequent than 6-monthly, although some patients can go as long as a year before further rituximab is required due to prolonged effects. As the gap between infusions can be long in some patients, they may not consider it as one of their regular medications and should be directly asked.

In addition to DMARDS, it has been estimated that over 50% of patients with RA will also receive treatment with glucocorticoids [6]. Although the edict to try and minimise exposure to steroids remains true for RA, many patients will receive intermittent courses of steroids, often administered intramuscularly or intra-articularly for management of early disease activity until the effects of csDMARDS are realised or for treatment of disease flare.

3. Peri-operative risk of DMARDS

The main risks of joint arthroplasty include bleeding and infection, including surgical site infections [SSI] and other immediate post-operative complications such as catheter-related urinary tract infections; however the most feared risk is prosthetic joint infections, primarily due to Staphylococcus aureus. Although the absolute risk of prosthetic joint infection following joint arthroplasty is low, estimated to affect <2% of joint replacements [7], numerically this still represents a significant burden for the health care system. The impact of prosthetic joint infections is profound and infected prosthetics often require removal of the hardware, prolonged IV antibiotics, resulting in significant functional decline and high mortality. It also comes at an incredible expense to the health system. The risk of prosthetic joint infections is estimated to be significantly higher among patients with RA compared to those undergoing the procedure for the more common osteoarthritis [7,8].

Patients with rheumatoid arthritis already have an increased risk of infection more generally, including native joint infections [9]. Infection has long been recognised as an important cause of morbidity and mortality in RA where it has been shown that even prior to the advent of biologic DMARDS, patients with RA had a 2-fold increase in a risk of hospitalised infection and a 22-fold increased risk of septic arthritis. The introduction of biDMARDS has increased this risk further, with many large national drug registries showing a small but further increased risk of serious infection with bDMARDS [10,11], including joint infections [12]. The risk appears to be highest in the first 6 months of therapy but decreases as inflammation comes under control. Following ineffectiveness, infection is the leading cause for TNFi discontinuation [13]. The reasons for this increased infection risk are complex and not solely related to DMARD treatment. Other risk factors include active inflammation, poor mobility, comorbidities including more frequent pulmonary disease and the widespread use of glucocorticoids [14].

Given that there is a known association between DMARDS and infection even outside of the peri-operative period, careful management of DMARDS around the time of surgery to minimise this risk further is therefore critical; however, stopping DMARDS prior to surgery increases the risk of disease flare and subsequent further glucocorticoid use, both of which will also increase the risk of infection in the peri-operative period and interfere with rehabilitation following joint replacement. Thus, any decision around management of DMARDS in the peri-operative period is a careful balance between reducing the risk of post-operative infection but also preventing a disease flare.

Understanding the role DMARDS play in the risk of prosthetic joint infections and other surgical complications has been challenging due to the absence of high-quality controlled trials. Most of the evidence to help guide treatment decisions have been based on case series or observational research. These study designs suffer from bias and confounding, such that patients deemed to be higher risk for infections may be asked to discontinue their treatment preferentially to others. The complexity or nature of the surgery may also influence treatment decisions. Both factors will also be risk factors for adverse surgical outcomes and thus any conclusions may be confounded.

There is also a challenge of measurement error and exposure misclassification using large observational datasets, an increasingly common approach, which may not accurately capture short pauses in therapies. Patients who are no longer receiving DMARD treatment may differ significantly from those whose disease is under control on treatment but who temporarily pause treatment prior to surgery. Therefore, identifying appropriate and relevant comparison groups is also challenging. The next section explores data related to individual DMARDS and peri-operative risk.

3.1 Conventional Synthetic DMARDS

a. Methotrexate

Methotrexate remains the best studied csDMARD. The best evidence regarding MTX and surgical risk comes from a 2001 unblinded clinical trial [15] which randomised 88 patients receiving MTX to continue their therapy and 72 patients to discontinue MTX 2 weeks prior to surgery, restarting it 2 weeks later. Overall, adverse outcomes were uncommon in both groups but a combined outcome of infectious and surgical complications was less common among the group who continued their MTX compared to those who stopped [2 versus 15%, p<0.003]; however, 8% if patients who stopped their MTX flared in the 6-week post-op period compared to no patients who continued their MTX [p=0.04]. The conclusions of this trial were that patients should continue their MTX through the peri-operative period.
Results from other studies have been mixed, although overall, the quality of these studies has been low. A small unblinded study which randomized 64 patients [1:1] to either continue or interrupt MTX 1 week prior to orthopaedic surgery observed no post-operative infections in either group [16]. It should be noted that the average dose of MTX in this study was 10mg/week which is much lower than current doses, which range from 15-25mg/week.

A 1996 case series observed 32 patients [13 of whom were assigned to interrupt their MTX 1 week prior to surgery and 19 who were not] and found a higher rate of infections among patients who continued their MTX, including 2 infected prostheses, 1 infected joint fusion, and 1 deep wound infection compared to no infections among those who interrupted their therapy \[p=0.03\] \[17\]. This compares to a 2006 Japanese study which looked at outcomes in 48 patients (77 procedures) who continued their MTX prior to surgery and 12 (21 procedures) who discontinued MTX at least 1 week prior to surgery with no difference in rates of infection but higher rates of post-operative flare and poorer wound healing among those who stopped \[18\].

b. Non-Methotrexate csDMARDs

Unfortunately, the information we have regarding other csDMARDs is very limited. An observational study found no difference in short term outcomes among 41 patients who continued leflunomide compared to 41 patients who had stopped leflunomide at least 4 weeks prior to surgery. Notably there were no serious or deep infections in either group. For other commonly used drugs in this class, particularly hydroxyclooroquine and sulphasalazine, there are very limited data although these drugs are not felt to have significant immunosuppressive effect. A 1996 retrospective study of 204 patients undergoing various orthopaedic procedures did not identify any csDMARD as a risk factor for early wound complications in a multivariable model \[20\].

Based on these very limited data, both the 2017 American College of Rheumatology [ACR]/American Association of Hip and Knee Surgeons (AAHKS) Guidelines for the Peri-operative Management of DMARDs in patients undergoing elective knee and hip surgery [21] and the 2017 British Society for Rheumatology [BSR] guidelines for the prescription and monitoring of csDMARDs [22] state that csDMARDs can be continued over the perioperative period. It should be noted however that due to the prolonged clinical effects of many csDMARDs, the likelihood of a flare in the very short term is overall very low, such that missing a few days of treatment is unlikely to have a major effect in most patients. For example, omitting the dose on the morning of surgery in a fasting patient should not have any detrimental effects on disease activity and therefore, decisions should be made on a case by case basis.

Special attention should be paid in those patients receiving methotrexate who do develop infection due to the known drug interaction between MTX and trimethoprim [23], which increases the risk of pancytopenia. For all csDMARDs, it is advised that they are temporarily discontinued in all patients receiving any antibiotics until the course of antibiotics is complete \[22\].

3.2 Biologic and Targeted Synthetic DMARDs

There have been more publications regarding the safety of peri-operative outcomes in patients receiving bDMARDs, but there have been no randomised trials on this topic. As such, all guidance is based on observational data and expert opinion.

a. TNF Inhibitors

Like csDMARDs, most data on bDMARDs in the peri-operative period have focused on orthopaedic procedures with most studies focusing on TNF inhibitors, the oldest and most used bDMARD. Again, balancing between the risk of post-operative infections and disease flare remains an important issue, especially as the effects of bDMARDs are quicker than most csDMARDs and flare of disease after drug discontinuation may occur sooner. A 2020 systematic review of studies looking at TNF inhibitor discontinuation found that 62% of patients who were previously in remission will flare once the treatment has stopped \[24\] although the timing of this can be highly variable. A small observational study of 31 patients with RA undergoing elective foot or ankle surgery who were all advised to continue their usual DMARDs found no difference in the rates of infectious complications between the 15 patients who were receiving TNF inhibitors compared to the 16 who were not \[25\]. Den Broeder et al undertook a large retrospective analysis of outcomes, with a focus on SSI, following 1219 elective orthopaedic procedures in patients with RA \[26\]. They compared outcomes between those who had not received TNF inhibitors, those who had stopped TNF inhibitors at least 4 half-lives prior to surgery and those who received the drug within this window. They found no difference in the risk of SSI (Odds Ratio OR 1.5 [95% Confidence interval CI] 0.4, 5.2) between those who had received TNF inhibitors and had either stopped or continued their drug. The strongest risk factor for SSI was a history of previous SSI or skin infection. It should be noted however that a local protocol to advise patients to stop their TNF inhibitor 2 weeks prior to surgery was in place although practice varied and adherence to this protocol was not recorded.

Infliximab is a TNF inhibitor which is given by intravenous infusion every 8 weeks and as such, rates of doses are recorded accurately in administrative databases. George et al \[27\] undertook an analysis which studied the association between the timing of the most recent infusion of infliximab and the date of orthopaedic surgery, with the reference group being those who received their last dose between 8-12 weeks prior to date of procedure. They found no difference in the rates of serious infection within 30 days or prosthetic joint infection over 1 year between the reference group and other groups who had received the drug either within 4 weeks, 4-8 weeks, 12-16 weeks or >16 weeks prior to surgery. Although this study did allow for patient differences in their statistical model, infliximab is now one of the less commonly used TNFi in rheumatology, with patients [and hospitals] favouring self-injection at home.

Despite these reassuring studies, not all studies have been consistent in these findings. A 2016 meta-analysis of 5 observational studies looking at the risk of TNF inhibitors and post-operative complications included 2743 patients, of whom approximately 50% of patients continued their TNF inhibitors throughout the operative period \[28\]. It found that SSI infections were less common among patients who discontinued their therapy \[3% versus 6%, OR 0.6 [95% CI 0.4-0.9]\] but with a higher rate of flares among patients who discontinued compared to those who continued \[20\% versus 3%, OR 0.5 [95% CI 1.1-24.8]\]. This analysis did not look specifically at prosthetic joint infections.

b. Non-TNF Inhibiting bDMARDs

Data regarding the peri-operative risk of non-TNF inhibitors is very limited. A large analysis by George et al \[29\] compared the risk of serious infection within 30 days and prosthetic joint infections within 1 year among 10923 procedures in 9911 patients receiving various bDMARDs. They found that compared to abatacept, an anti-CTLA4 receptor antagonist, the risks were similar with TNF Inhibitors, tocilizumab and rituximab, although the sample size of patients receiving the latter 2 drugs was small.

The French AIR Rituximab registry \[30\] reported on surgical outcomes among 133 patients who had undergone 140 surgical procedures, including 94 orthopaedic procedures, following rituximab. Overall, complications were rare with 9 patients experiencing 12 complications, including 8 SSI. The mean time between the most recent rituximab infusion and the date of surgery was 6.4 months \[interquartile range 4.3– 8.7 months\] and there was no difference between patients with and without complications.

The retrospective observational 2013 Tocilizumab in the Peri-operative Period (ToPP) study reported on 166 procedures \[31\]. Overall post-operative infections, delayed wound healing and flares were
Tocilizumab is a powerful suppressor of the acute phase response which may persist beyond the usual dosing period. A small study by Hirao et al which compared 22 patients receiving tocilizumab and 22 patients receiving csDMARDs found that on post-operative days 1, 2, and 3, patients receiving tocilizumab had a lower mean daily temperature compared to those receiving csDMARDs only [33]. No increase in CRP was observed in patients receiving tocilizumab. Thus, the acute phase response in the setting of infection in the post-operative period may be suppressed in patients receiving tocilizumab and thus close monitoring and high suspicion for infection is warranted.

4. Guidance on the use of b/ts DMARDs in the Peri-operative Period

In the absence of high-quality research in this area and with the mixed findings across studies, coupled with the known general increased risk of infection in relation to b/ts DMARDs, both the 2017 ACR/AARHS [21] and the 2019 BSR bDMARD Safety Guidelines [36] recommend that patients receiving b/tsDMARDs stop their b/tsDMARD therapy prior to surgery. This was based on consensus and expert opinion, including the opinion of patients who, as stated in the ACR/AARHS Guidelines, weighed the risk of infection as more concerning than the risk of disease flare.

The safest length of time that a patient should stop their drugs prior to surgery to manage the balance between infection risk and disease flare is unknown and has varied in past guidelines to include specific dosing intervals as well as multiples of drug half-lives. Both guidelines now state that patients should stop their b/tsDMARD at least 1 dosing interval prior to surgery, with the principle being that the effect of the drug will be at its nadir at the end of the dosing cycle. For rituximab this means surgery should be planned for 6 months after the last dose.

In cases of doubt, consultation with the patient’s rheumatologist is warranted, as it is possible to check a patient’s CD19 lymphocyte counts which can indicate if B-cell reconstitution has occurred post-rituximab. The BSR guidelines highlight 2 exceptions to this general b/tsDMARD guideline: for higher risk procedures [not defined], the BSR guidelines state that a longer period of time, such as 3-5 half-lives of the drug, should be considered. For some drugs, however, this may be a very long period and therefore, may be difficult to implement in practice. They also suggest a slightly longer interval for subcutaneous tocilizumab of 2 weeks compared to the usual dosing interval of 1 week due to the observed suppression of fever and CRP following treatment [33]. The safest dosing gap for patients receiving csDMARDs is unknown. Currently available therapies are daily oral doses and both ACR/AARHS and the BSR guidelines recommend patients interrupt their therapy for at least 1 week.

There is no evidence to guide the optimal time to restart DMARDs following surgery. In all cases, it is suggested that treatment should be resumed a minimum of 14 days after surgery once it is confirmed that there is no issues with wound healing, SSI or systemic infection and staples and sutures have been removed.

Attention should be paid to recent use of glucocorticoids and where possible, ensuring the patient is on as low a dose as possible is warranted. A 2019 study [29] found that compared to patients who have not received steroids within 90 days of surgery, patients receiving 10 mg or more per day had higher incidence of hospitalised infection and higher incidence of prosthetic joint infection. This was not a randomised study and it is known that patients receiving chronic glucocorticoids may also have more severe underlying disease. Chronic steroid use will also impair wound healing, increase the viability of skin and superficial blood vessels, and increase the risk of diabetes, osteoporosis and fracture.

5. Peri-operative use of DMARDS in patients undergoing unplanned surgery

In the case of patients undergoing urgent or unplanned surgery, it will not be possible to interrupt DMARD or glucocorticoid therapy prior to surgery. In these cases, it is crucial to ascertain an accurate drug history and for patients receiving b/ts DMARDS, discontinuation of these therapies in the post-operative period until effective wound healing is observed [minimum 14 days] would be recommended in line with guidelines for elective surgery. Careful attention to post-operative infections is warranted.

6. Consultation with the DMARD prescriber

Optimally, there should be a dialogue between the rheumatologist or other hospital doctor who has prescribed the DMARD and the surgical team. Although guidelines exist for management of DMARDS in the peri-operative period, individual risk assessment based on the patient and the procedure should take place. For some patients with severe underlying rheumatic diseases, such as SLE or vasculitis, the risk of organ-threatening damage when DMARDs are discontinued may outweigh the risk of post-operative complications and therefore, personalised treatment protocols may need to be put in place [21].

7. Conclusions

Unfortunately, despite the widespread use of DMARDS in the management of rheumatic diseases and other inflammatory conditions, information to inform their use in the peri-operative period is of generally poor quality. Guidelines based on expert opinion and observational data suggest that csDMARDs can be continued through the peri-operative period but that b/tsDMARDs should be discontinued at least one dosing interval prior to surgery. In all cases, an individualised risk assessment should take place based on the patient and the planned procedure and where possible, consultation with the DMARD prescriber is indicated.
References


3. National Institute for Health and Care Excellence. Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs: only have failed [Internet]. 2016 [cited 2020 Sep 1]. Available from: https://www.nice.org.uk.guidance/ta375


Appendix: Supplementary biological agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type</th>
<th>Dose</th>
<th>Duration</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Ibrutinib</td>
<td>Tyrosine kinase inhibitor</td>
<td>420mg od</td>
<td>1 week</td>
<td>Withhold for 1 week prior</td>
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<tr>
<td>Ixazomib</td>
<td>Proteosome inhibitor</td>
<td>2.3mg - 4mg weekly</td>
<td>Time surgery 1 week after dose</td>
<td>Withhold for 1 week prior</td>
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<tr>
<td>Ibatinib</td>
<td>Tyrosine kinase inhibitor</td>
<td>400mg od</td>
<td>1 week</td>
<td>Withhold for 1 week prior</td>
</tr>
<tr>
<td>Ruxolitinib</td>
<td>JAK 1 &amp; 2 inhibitor</td>
<td>5mg-20mg od</td>
<td>1 week</td>
<td>Withhold for 1 week prior</td>
</tr>
</tbody>
</table>
Evidence-based Guidelines for Preoperative Assessment Units

Preoperative Alcohol Consumption - Guidelines for Assessment and Management
Lyn Owens
Nurse Consultant - Strategic Lead Alcohol Care Team, Hepatology. Liverpool University Hospitals NHS Foundation Trust

Summary and Key Recommendations

- “Make every contact count” Use the preoperative assessment clinic as an opportunity to identify patients at risk due to their drinking.
- Alcohol presents hidden harms to individuals that both patient and clinician may be unaware of.
- Alcohol consumption prior to surgery has been shown to increase risk of a number of often life threatening post-operative complications.
- Use alcohol assessment to identify preoperative interventions to improve postoperative outcomes.
- Plan surgery to coincide with achievement of alcohol treatment goals.
- Provide support for alcohol reduction or cessation: utilising local services and protocols.

INTRODUCTION

The following guideline will provide a synopsis of evidence for alcohol-related harms and risks for patients planning to undergo a surgical procedure. Guidance on how to detect patients at risk due to alcohol consumption will be presented alongside evidence-based guidance on how to optimise care and reduce post-operative complications.

Across the western world, the incidence of hazardous drinking in elective surgical settings has been estimated at between 7 and 49% and in emergency surgical patients between 14 and 38%. [1]

Less than 10% of drinkers report having discussed their alcohol consumption with a healthcare professional [2]. This is disappointing, as opportunities are being missed, and we know that early identification of Alcohol Use Disorders (AUD) leading to an intervention has been shown to be highly cost effective with one review concluding that “The public sector saves £5 for every £1 spent on treatment” [3]. Furthermore, of those patients who have been identified as having an AUD only 1 in 6 receive any form of treatment [4].

Alcohol consumption prior to surgery has been shown to increase risk of a number of often life threatening post-operative complications. Given that the risk of poor outcomes increases with alcohol consumption, it seems imperative to determining the susceptibility through screening for AUDs [5]. Preoperative assessment clinics are an ideal environment to opportunistically identify patients with AUDs, plan appropriate interventions and prevent future harms.

Alcohol-related risks in the surgical patient

Infection. Alcohol-induced dysregulation of the immune system renders the patient susceptible to a vast array of infectious pathogens [6] and has been shown to be an independent predictor of superficial surgical site infection, wound disruption and pneumonia [7]. Indeed, drinking in excess of just 2 units per day can produce a reduction in immune capacity [1], making wound infection more likely [8].

Subclinical cardiac insufficiency and arrhythmias are also features of patients with AUDs undergoing surgery [9], and are important risk factors for development of postoperative cardiac complications. Importantly, preoperative abstinence significantly reduces the incidence of postoperative arrhythmias [8] [10].

Bleeding. Alcohol has a direct effect on blood coagulation and fibrinolysis. Drinking 2 drinks per day can increase the risk of post-operative bleed [11].

Peri and post-operative Acute Alcohol Withdrawal (AAW). Symptoms of AAW will develop in alcohol-dependent patients between 6 and 24 hours from their last drink. This is an important consideration when abstinence is enforced by illness or injury requiring surgery [12]. In a large Australian study, it has been reported that up to 8% of surgical admissions with an AUD had seizures or hallucinations during their admission [13], a further study of surgical inpatients reported a 16% incidence of post-operative AAW, the incidence raising to 31% in trauma patients [14].

Thiamine deficiency leads to delays in both wound healing and functional recovery [15]. Length of stay (LOS). Any surgical complication will result in increased LOS in hospital, and a threefold increased risk of death [16] [7].
Screening for Alcohol Use Disorders

Whilst society for the most part accepts alcohol consumption; it simultaneously stigmatises alcohol-related problems. This means that patients who are not obviously drunk on a regular basis, but who may nevertheless be drinking more than they should, often miss out on treatment and advice that would help them through the process of surgery.

It is important that you familiarise yourself with the Chief Medical Officers of England low risk drinking guideline for both men and women which states:

- To keep health risks from alcohol to a low level it is safest not to drink more than 14 units a week on a regular basis.
- If you regularly drink as much as 14 units per week, it’s best to spread your drinking evenly over three or more days. If you have one or two heavy drinking episodes a week, you increase your risk of long-term illness and injury.
- The risk of developing a range of health problems (including cancers of the mouth, throat and breast) increases the more you drink on a regular basis.
- If you wish to cut down the amount you drink, a good way to help achieve this is to have several drink-free days a week.

1. Risk categorisation according to units consumed.

National Institute for Health and Care Excellence (NICE) define harms as follows [17]:

Harmful drinking (high-risk drinking)
- A pattern of alcohol consumption that is causing mental or physical damage (ICD-10, DSM-V).
- Drinking 35 units a week or more for women. Drinking 50 units a week or more for men.

Hazardous drinking (increasing risk drinking)
- A pattern of alcohol consumption that increases someone’s risk of harm. Some would limit this definition to the physical or mental health consequences (as in harmful use). Others would include the social consequences. The term is currently used by the World Health Organization to describe this pattern of alcohol consumption. It is not a diagnostic term.
- Drinking more than 14 units a week, but less than 35 units a week for women. Drinking more than 14 units a week, but less than 50 units for men (Health Survey for England 2015: Adult alcohol consumption).

Higher-risk drinking
- Regularly consuming over 50 alcohol units per week (adult men) or over 35 units per week (adult women).

2. Alcohol Use Disorder Identification Tool (See appendix)

AUDIT has been validated in hospital and community settings, and has 92% -94% sensitivity and specificity of 94%-96% using the ≥8/40 threshold, with overall accuracy of 94.4% [18, 19]. AUDIT scores of 5 or more up to a year before surgery have been associated with increased postoperative complications. The higher the AUDIT score the greater the risk [20].

Patients found to be scoring 8 or more on a full AUDIT questionnaire should be offered support and motivational advice on reducing their alcohol consumption. On follow-up appointment, following delivery of brief advice, if the patient hasn’t managed to cut down their drinking further assessment to consider the possibility of alcohol dependence should be undertaken [17]. Furthermore, as part of a screening process AUDIT is a sensitive tool to identify potential dependence in outpatient treatment settings [21], with those scoring >16 requiring further assessment.

Screening for alcohol dependence and associated risk of AAW, and the need for medically assisted withdrawal should be integrated in the preoperative and emergency assessment [22-24].

3. Severity of Alcohol Dependence Questionnaire (SADQ)

SADQ is a quick, reliable, and valid instrument of 20-items designed to measure severity of dependence on alcohol and can be self-administered. The questionnaire focuses upon the experience of withdrawal symptoms [25]. From a clinical perspective NICE recommend subdividing dependence into categories of mild, moderate and severe. “People with mild dependence (those scoring 15 or less) usually do not need assisted alcohol withdrawal. People with moderate dependence (with a SADQ score of between 15 and 30) usually need assisted alcohol withdrawal, which can typically be managed in a community setting unless there are other risks. People who are severely alcohol dependent (with a SADQ score of more than 30) will need assisted alcohol withdrawal, typically in an inpatient or residential setting”[17].

The principles of AAW therapy are to provide an appropriate protocol based benzodiazepine [17] guided by repeated reassessment with validated tools. This approach has been shown to reduce LOS and morbidity [26].

4. Biochemical markers

The use of biochemical markers may seem attractive however, they have not been shown to be superior to screening tools for identification in the surgical setting. This is due to the introduction of uncertainties and variances, leading to problems in interpreting both positive and negative test results [1, 27, 28]. In general populations questionnaires are superior for screening purposes [29] but biochemical markers may supply additional information. Moreover evidence from studies conducted in secondary care settings have shown that biofeedback in the form of including biomarker results as part of a brief intervention (FRAMES[35]) may help motivate patients with an AUD to change their drinking behaviour. A pilot study has shown that 90% of patients reported that biofeedback of information about their liver damage (assessed with non-invasive fibrosis tests) helped them reduce their alcohol consumption [36].

CDT Studies show that CDT is much better at detecting chronically heavy drinkers than hazardous drinkers [30] CDT also performed better in detecting patients with alcohol dependence than in detecting patients with high alcohol consumption irrespective of dependence [31].

GGT As other medical conditions and several medications may cause an elevation of GGT besides alcohol use, in non-healthy populations the specificity to detect chronic heavy drinking may be reduced [32].

MCV The sensitivity of MCV to detect heavy drinking is about 40–50%, but its specificity is high (80–90%) and very few abstainers and social drinkers will have elevated MCV [27].

Combining biochemical markers enhances detection of problem drinking in men but not in women [32].

AST/ALT Ratio Most patients with high alcohol consumption but without severe liver disease do not have an AST/ALT ratio above 1. High AST/ALT ratio suggests advanced alcoholic liver disease, [33] and does not appear to be useful in identifying AUDs [34].
What to do in the preoperative assessment clinic

1. Aims of Treatment
   Prevent postoperative complications that may lead to increased mortality, effect patient well-being, delay recovery, increase length of hospital stay, prevent unrecognised post-operative withdrawal symptoms.
   • Stratification of patient risk to identify appropriate treatment plans.
   • Plan surgery to coincide with achievement of alcohol treatment goals.
   • Provide support for alcohol reduction or cessation: utilising local services and protocols.

2. You are now ready to have a conversation with your patient about their drinking
   If the patient drinks alcohol administer the AUDIT questionnaire [19].
   • Begin the AUDIT by saying “Now I am going to ask you some questions about your use of alcoholic drinks during this past year.”
   • Read the questions as written. Record answers carefully.
   • Explain what is meant by “alcoholic drinks or units” by using examples of beer, wine, vodka, etc. (Figure 1)
   • Record the score.

   Use the AUDIT tool scoring system to categorise risk and determine the most appropriate intervention. (Table 1 & Appendix)

Table 1. AUDIT score, interpretation, and action

<table>
<thead>
<tr>
<th>AUDIT Score</th>
<th>Risk category</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>0 to 7</td>
<td>indicates low risk</td>
<td>Give brief advice to reduce risk for alcohol harm</td>
</tr>
<tr>
<td>8 to 15</td>
<td>indicates increasing risk</td>
<td>Provide brief intervention (structured approach)</td>
</tr>
<tr>
<td>16 to 19</td>
<td>indicates higher risk</td>
<td>Provide brief intervention (structured approach)</td>
</tr>
<tr>
<td>20 or more</td>
<td>Indicates possible dependence</td>
<td>Consider referral to specialist alcohol harm assessment.</td>
</tr>
</tbody>
</table>

3. How to deliver brief advice.
   This is a simple process of helping the patient understand risk categories for alcohol consumption and provide feedback on their individual risk.

4. How to deliver a brief intervention (non-dependent patients)
   Now that you know what your patient is drinking at increasing risk, you can identify any problems the patient may be experiencing and use this to inform the conversation about change.
   Brief intervention effectiveness is enhanced when it is delivered in a structured way. The components of a brief intervention can be guided using the FRAMES approach [35].

   **FRAMES**
   - **Feedback**: talk to your patient about the potential risk of their drinking on their surgery and post-operative recovery.
   - **Responsibility**: be clear that changes can only happen if the patient agrees.
   - **Advice**: help the patient with information and strategies to change, e.g. reduce drinking by reducing the strength of their drinks and having drink free days.
   - **Menu**: help the patient explore options that best suit their life situation.
   - **Empathy**: always use an approach that is warm, reflective and understanding.
   - **Self-efficacy**: help the patient believe in their ability to change and your confidence in that ability.

5. How to manage the alcohol dependent patient
   It is important that any patient with potential dependence undergoes an assessment by a specialist. This will very much depend upon local availability. However, many hospitals now have Alcohol Care Teams and these should be utilised where available, alternatively referral to specialist community teams will be needed.
   The aim of specialist assessment in the preoperative patient is to provide timely access to alcohol withdrawal management and safely achieve abstinence prior to surgery.

Conclusions
   Preoperative clinics may be the ideal environment in which to identify alcohol as a risk factor for peri and post-operative complications. This guideline proposes tools to be used to facilitate the accuracy of that assessment and facilitate appropriate and effective timely interventions.
Summary and Key Recommendations

- Risk prediction tools should be used to guide multi-disciplinary decision-making, the allocation of appropriate resources and communication with patients and their families.
- The ideal risk prediction tool incorporates information on patient health and fitness, and surgical magnitude and urgency.
- Evidence from national audits suggests that formal assessment and documentation of risk is poorly and infrequently performed by clinicians in the pre-operative setting. Where risks are documented patients are more likely to receive care that meets standards.
- There are a number of tools available to assist the clinician in pre-operative risk assessment. These can be divided into risk prediction scores (providing a numerical scale of risk) and models (providing a percentage estimate of risk).
- No tool is without limitations and all should be used alongside clinical judgment. Inter-hospital variation of the structure and process of care delivery may account for some performance limitation.
- The SORT is easy to use requiring readily available preoperative data and has better calibration and discrimination than P-POSSUM and SRS. A version of the SORT which incorporates clinical judgement could be used by MDTs and/or experienced perioperative clinicians, and the original SORT by other colleagues.
- Further research should focus on the clinical effectiveness of risk prediction tool implementation (i.e. does using risk assessment tools actually improve patient outcomes) and on predicting other patient-centred outcomes such as longer-term survival and health related quality of life.
INTRODUCTION

Over 310 million surgical procedures are performed worldwide each year, representing a significant healthcare and economic burden.[1] The annual number of surgical procedures performed by the NHS is estimated at almost 8 million with numbers expected to continue to increase year-on-year.[2] Post-procedural short-term mortality rates of up to 3.1% have been reported.[2] and estimates of major post-operative morbidity in the UK are approximately 15%.[3,4] The impact of post-operative morbidity should not be underestimated, as it has been found to be associated with an increased risk of death for some years after surgery.[3] In Khuri’s seminal analysis of over 100,000 surgical procedures, the most important obstacle to survival in these patients was the occurrence of a complication in the 30 days immediately post-operatively, which reduced median survival by 69%.[5] Over recent years a variation in post-operative morbidity and mortality between UK hospitals has consistently been reported by national and local audit programmes. This variation suggests that structures and processes aimed at improving post-operative outcomes are delivered more effectively in some hospitals than others, thus indicating the opportunity to improve outcomes by improving standards of care.

As well as there being a legal requirement within the UK to perform an individualised risk assessment of a patient's risk of adverse outcomes,[7] the identification of high risk patients is of importance when considering patients perioperative pathway and identifying steps to minimise their risk of adverse outcomes. This chapter details the recommendations over use of risk prediction tools and some principles for selecting and using these tools.

Recommendations from National Reports.

The 2011 NCEPOD report entitled ‘Knowing the Risk’, [8] studied the care provided for over 15,000 adult patients admitted for elective or emergency non-cardiac surgery over consecutive days, highlighting multiple areas where care was substandard. The report particularly stressed that risk was not well identified or acted upon by clinicians. ASA-PS grade was noted to be a poor predictor of risk on its own, with many patients who were thought by their anaesthetist to be high-risk, having an ASA-PS score of I or II. Of the cohort that anaesthetists had defined as high risk, only 20% were admitted to the intensive care unit (ICU) immediately post-operatively and nearly half of those who died were never admitted to the ICU. The highest mortality rate was found among those patients who were admitted to ICU after first being admitted to a ward immediately post-operatively. The authors found that there was a lack of consensus, even among their advisors, as to what constitutes perioperative risk.

As a result, the principle recommendation of the report was the adoption of a national pre-operative risk scoring system.

“Our Advisors are in no doubt that we need a UK-wide system that allows rapid and easy identification of patients who are at high risk, and that these people should be recognised as such and managed appropriately. That to me is the most striking take-home message of this Report.”

Mr Bertie Leigh, Chairman of NCEPOD.

The 2010 report by the Royal College of Surgeons entitled ‘The Higher Risk Surgical Patient’, made similar recommendations for the care of high-risk, non-elective surgical patients. It advised that each patient should have their risk of death calculated and documented pre and post-operative.[9] This risk score should then be used to decide whether the planned surgery is the most appropriate action for that patient. If surgery is deemed appropriate, the perceived risk should be used to determine the appropriate allocation of resources. The updated version of this report from 2018 aligns with the NCEPOD recommendation that patients with a predicted risk of mortality >5% should be admitted to a critical care unit after surgery.[10]

National audit programmes continue to highlight the importance of perioperative risk scoring. One of the main recommendations of the first National Emergency Laparotomy Audit (NELA) report published in 2015 [11] was that pre and post-operative risk scoring should be performed and documented for all patients in order to prioritise care and aid in the allocation of resources. Similarly, the most recent Perioperative Quality Improvement Programme (POQIP) Annual Report emphasises the need for individualised risk assessments and their important contribution to decisions in determining patients post-operative pathway of care.[4] It is notable that in the 10 years since the NCEPOD report was published, we have made some, but not complete progress, towards the ambition of universal individualized documented risk assessment and appropriate actions taken thereafter – recent reports from both NELA and POQIP indicate that there is still room for improvement.

How can we identify patients with a high peri-operative risk?

One approach would be to focus efforts on high-risk populations, for example, patients presenting for emergency surgery. Data from the national hip fracture audit and from the National Emergency Laparotomy Audit (NELA) demonstrates that these groups of patients are high-risk.[11,12] The most recent data from NELA suggest an overall mortality of 9.6%, which remains up to five times higher than mortality in high-risk elective surgery. [6,13,14]

However, limitations to focusing solely on the sub-populations of patients who present for high-risk procedures can be demonstrated by considering the ‘Prevention Paradox’. Whilst it is widely known that emergency surgery may carry a higher percentage risk of death for individual patients, the majority of surgical procedures that are performed are elective and it is in this elective group of patients that the highest numbers of deaths actually occur. Determinants of peri-operative risk include patient-level (age, fitness and co-morbidities), surgical-level (complexity and urgency of surgery) and system-related risk factors;[15,16] Basing risk assessment on specific types of surgery for example, emergency or major and complex surgery, may fail to capture a large number of patients who would also be considered high risk on the basis of their fitness or past medical history. An alternative approach is to focus on the individual risk scoring of all surgical patients. There are a variety of risk stratification tools available to help clinicians calculate individual risk and therefore identify those who fall into the highest risk categories.

How do we evaluate a risk prediction model?

1. Performance

The performance of a risk assessment tool should be assessed by testing it for both discrimination and calibration.[17]

Discrimination

This is the ability of a tool to successfully identify who will have the outcome of interest and who will not. To demonstrate this, Receiver operating characteristic (ROC) curves are made by plotting the relationship between sensitivity and 1-specificity. The frequency with which the prediction tool predicts an outcome that goes on to actually occur, is measured by the area under the ROC curve (AUROC).[18] Perfect discrimination has an AUROC of 1.0, no discrimination has an AUROC of 0.5. A good discriminator is considered to have an AUROC of greater than 0.9, and a poor discriminator, less than 0.7.[19]

Calibration

This is the comparison between the predicted outcome, as defined by the risk prediction tool, and the actual outcome. In other words it is the ratio of observed events to expected events. This relationship can be mapped on a calibration plot, with x=y indicating a perfectly calibrated model.
2. Generalisability

If the model is found to retain good levels of calibration and discrimination in different datasets to the one used to create the tool, it is considered to be generalisable. To truly test this, the tool must undergo a process of external validation, where it is tested against a group of patients which is independent of the original development cohort. Internal validation can give valuable insights into a model’s performance but is not a true test of generalisability and is often an over-estimation of a model’s predictive ability.

3. Utility

This relates to ease of use. An ideal tool would be simple and quick to use, easy to access, usable at the bedside and would not require expert knowledge or expensive equipment. A tool with optimal utility in the pre-operative setting would only require the input of readily available, pre-operative data.

4. Clinical effectiveness

The question of whether the tool is clinically effective is an important one. An effective risk prediction tool would offer information that could be used by the clinician to appropriately alter the patient journey and subsequently improve patient outcome.

RISK PREDICTION TOOLS

There are a variety of tools available to allow the clinician to make an estimate of perioperative risk for an individual patient. These can be divided into risk scoring systems and risk prediction models. Both systems are usually developed using multivariable analysis to identify risk factors for a specific outcome. Risk scores add a weighting to each risk factor depending on the strength of the regression co-efficient and then calculate a total score for each patient.[20] The patient can be placed on a scale in which they are compared to other patients but cannot be provided with their own individual risk of an outcome occurring. In comparison, a complex risk prediction model can offer this. By entering patient information into the model, an individual probability of a particular outcome can be obtained.

1. Risk Scores

1.1 ASA-PS

The American Society of Anaesthesiologists Physical Status score (ASA-PS) is probably the most commonly used risk score by anaesthetists. The ASA-PS score allows clinicians to place a patient’s physical status into one of five categories depending on their co-morbid state and perceived functional status. Originally reported in 1941 and including six categories at that stage, it was designed to serve as a score to enhance statistical records only and not to prognosticate risk.[21] Following discussion of the many variables that contribute to a patient’s prognosis after surgery, the author of the original report concludes “No attempt should be made to prognosticate the effect of a surgical procedure upon a patient of a given “Physical State”.

The ASA-PS has many attributes. It is familiar to all anaesthetists and has good interdisciplinary understanding. It is simple, easy to use and a high ASA score has been shown to correlate with poor outcome.[22,23] Its validity as an assessment of functional capacity has been demonstrated, which may go some way to explaining this predictive ability.[24] However, there are a number of limitations to its use as a sole risk-scoring tool. As an inherently subjective score, inter-rater reliability can be poor, and training is required to support clinical use.[25-27] It crudely differentiates between high and low risk patients, with the population mortality of ASA 3 patients estimated at 3% and ASA 4 patients around 16%.[28] It cannot therefore be used for an individualized risk assessment for a specific patient. Crucially, it does not consider the severity or urgency of the proposed surgery – an ASA 4 patient having a minor procedure under local anaesthetic is unlikely to have a poor outcome as a result of the surgery.

1.2 The Charlson Co-morbidity Index

The Charlson Index was first published in 1987 and was designed to classify co-morbid disease to enable prediction of mortality in medical patients.[29] Whilst perhaps not frequently used by the perioperative practitioner in risk assessment of individuals prior to surgery, it remains relevant as the method used to risk-adjust Hospital Episode Statistics data. Co-morbid diseases are weighted according to the strength of their association with one-year mortality and the number of co-morbidities per patient is taken into account. The sum of these weighted scores gives a patient an overall score of risk. When compared to other risk scoring tools in the surgical setting, it has been found to be a poor predictor of short-term mortality.[30]

1.3 RCRI

Lee’s revised cardiac risk index, published in 1999 is a validated and well-established tool for estimating perioperative risk of major adverse cardiac events (MACE).[31] It does not provide an estimation of mortality or other organ specific morbidity. The authors, through a large observation study identified six independent predictors of risk, one of which was the severity of anticipated surgical insult. Patients with two or more risk factors are considered high risk of MACE. A recent systematic review found that the Lee Revised Cardiac Risk Index was, the only index they identified which, had been both internally and externally validated and that despite its age it remains one of the most useful perioperative cardiac risk prediction indices.[32]

2. Risk Prediction Models

2.1 POSSUM tools

The original Physiological and Operative Severity Scoring for the enumeration of Mortality and morbidity (POSSUM) was developed to compare mortality and morbidity across a wide range of surgical procedures. This risk-adjusted scoring system used 18 variables (12 physiological and 6 operative) and calculated the risk of morbidity and mortality for each surgical patient. It was found to over-predict adverse outcomes, especially for low risk patients and therefore its use was cautioned against.[33]

As a response to this, a group in Portsmouth used the same variables but introduced modifications to the mathematical model (for the prediction of mortality only) and this is known as the P-POSSUM score.[33,34] The P-POSSUM score is currently widely used and has been validated in several countries and in many heterogeneous and surgery specific cohorts.[35-38] Despite this however, there are a number of limitations to this model.

First, it requires intra-operative data such as intra-operative blood loss and presence of intra-peritoneal soiling before a risk can be generated, and therefore guesswork is required to use it in the preoperative setting. Second, P-POSSUM requires the input of 18 variables and as such may not be considered user-friendly by the clinician. Third, several of the variables are subjective such as interpretation of a chest x-ray, which therefore risks measurement error.
A number of surgery specific POSSUM models (e.g. CR-POSSUM for colorectal surgery, O-POSSUM for oesophageal surgery, V-POSSUM for vascular surgery) have been more recently developed but different studies have shown varying degrees of utility with regard to their suitability as a tool to predict post-operative risk. For example, Hong et al concluded that P-/O- POSSUM were better predictors of mortality in gastric cancer patients than POSSUM [39] but Eichelmann et al found that O-POSSUM failed to predict mortality and POSSUM was superior.[40]

2.2 NSQIP

The American College of Surgeons National Surgical Quality Improvement Programme (ACS-NSQIP) Surgical risk calculator is a multivariable model to predict a range of outcomes within 30 days of surgery inclusive of morbidity, serious morbidity and mortality. The universal model [41] was published in 2013 following the publication of previous surgery specific models.[42] Data from 393 hospitals incorporating over one million patients were used to construct the model. It is necessary to input the type of surgery and 21 patient specific variables in order for the model to calculate individualised risk predictions for specific post-operative complications and for overall post-operative mortality.

In 2016, the model was updated to include three additional outcomes (serious morbidity, return to operating room, discharge destination) and was recalibrated. The initial model performed well with AUROC for mortality of 0.94 and an AUROC for morbidity of 0.82 [41] but there was a slight tendency for risk to be overestimated for low- and high- risk patients and underestimated for mid-risk patients. Following recalibration the authors report the elimination of this distortion and the tool now providing accurate estimates of surgical risk.[43]

There are a few limitations when considering its overall performance. First, it is a web-based model and as such requires availability of the necessary IT resources. It is significantly more complex than some other risk prediction tools requiring the input of 21 variables, which may be considered time consuming for the busy perioperative clinician. Second, it requires the input of subjective variables such as ASA scoring leaving it open to inter-rater variability.[44] Third, although the calculator takes 21 pre-operative risk factors into account, the authors consider that there may be other factors a surgeon would consider to have an influence on risk. To allow room for this clinical judgment, the tool incorporates a ‘surgeon adjustment score’. This allows the surgeon to adjust the degree of calculated risk within the confidence interval for that particular predicted risk, according to their clinical acumen. This is another area where the model may introduce inaccuracy. Finally, the model has not been validated outside NSQIP hospitals, which account for 10% of all hospitals in the United States. This raises questions regarding its generalisability to different countries and institution types.

2.3 Surgical Outcome Risk Tool (SORT)

The SORT was developed in the UK in response to the 2011 NCEPOD report ‘Knowing the Risk’, which called for a national system to identify high-risk patients pre-operatively.[29] The authors used data from this large, prospective, multi-centre, observational cohort study to derive this risk prediction model. Data from over 11,000 patients were used to derive the model and data from a further 5,000 patients were used to internally validate it.

SORT predicts 30-day mortality in adults undergoing non-cardiac and non-neurological inpatient surgery. It is a simple to use model requiring the input of only 6 pre-operative variables along with the planned procedure and as such, may be considered the plain ‘go to’ model compared to some other risk prediction models. The six variables are: (i) ASA-PS (ii) urgency of surgery (iii) surgical specialty (iv) severity of surgery (v) cancer and (vi) age. No blood, imaging or intra-operative results are required which allows risk prediction by clinicians early in the preoperative assessment phase.[29]

Data were generated from a range of surgical specialties and emergency and elective cases across a range of UK hospitals. Internal validation demonstrated the SORT to be more accurate than the ASA-PS and the SRS.[29] Recent work by Wong et al. has demonstrated better external validation of SORT than P-POSSUM or SRS and good to excellent discrimination of SORT with an AUROC of 0.9.[45] While a morbidity model has also been developed [46] this has yet to be externally validated in a large heterogeneous dataset.

2.4 National emergency laparotomy audit (NELA) calculator

The NELA risk prediction tool was developed using data from over 38,000 patients entered into the NELA between 2014 and 2016. It estimates risk of death within 30 days of emergency abdominal surgery. P-POSSUM was originally used to predict mortality for NELA patients but was found to overestimate mortality for patients whose predicted risk fell into the >15% cohort (i.e. a significant proportion of patients undergoing emergency laparotomy).[47] The NELA-specific risk calculator was found to be more accurate than P-POSSUM in the NELA cohort of patients.[48]

A NELA smartphone app has been developed on which both P-POSSUM and NELA calculators are available facilitating its use by busy clinicians. Its main advantage is its specificity for emergency laparotomies. Its limitations include the requirement of an extensive data set similar to P-POSSUM including intra-operative findings and it does not generate a morbidity risk. In contrast to the P-POSSUM score, the NELA calculator includes ASA scoring which gives rise to inter-rater variability.

2.5 Combining subjective and objective risk assessment measures

Clinicians frequently rely on their own clinical acumen based on previous knowledge and experience to make an assessment of a patient’s perioperative risk. The ability of clinicians to predict post-operative outcomes compared with predictive risk tools to date have produced mixed findings. Several studies have demonstrated the ability of clinicians to define and predict risk is inconsistent.[8, 49] Yet one study specific to major hepatobiliary and gastrointestinal surgery found that a surgeons ‘gut feeling’ was more accurate in the prediction of morbidity than P-POSSUM.[50] These findings suggest that clinical judgment is important but alone it is not enough to accurately predict outcomes post-operatively.

Recent work compared the accuracy of three objective surgical risk tools (P-POSSUM, SRS and SORT) with subjective clinical assessment in predicting 30-day mortality in almost 300 hospitals in the UK, Australia and New Zealand.[45] This prospective observational study included of over 22,000 adult patients undergoing surgery requiring at least a one night stay in hospital. The study found that all objective surgical risks tools over-predicted risk but the SORT was found to have the best calibration and discrimination of the objective tools. Further findings were that subjective assessment was as accurate as SORT for predicting death in hospital within 30 days of surgery and the combination of a subjective assessment with a risk model improved perioperative risk estimation further.

The SORT-clinician judgment model appears to be a very promising tool, which would aid with clinical decision-making, allocation of resources and communication with patients and their families. It is important to recognize that the ‘clinician judgment’ estimate was provided by the perioperative team, and therefore will have been the estimate of an experienced multidisciplinary team. It may therefore be worth considering using the combined objective-subjective estimate when senior or MDT colleagues are available to provide the subjective perspective, and reverting to the objective SORT model alone, when less colleagues less experienced in perioperative risk and outcome are undertaking risk assessment.

Evidence-based Guidelines for Preoperative Assessment Units

The Preoperative Association
WHY ARE WE NOT USING RISK PREDICTION TOOLS?

Despite the availability of many risk prediction tools, widespread adoption of their use is poor. The NCEPOD report stated that, according to the case notes of the 496 patient's identified as high risk, only 7.5% of patients were given an estimate of mortality pre-operatively.[8] Similarly, a recent study which included over 22,000 patients undergoing surgery, found that clinicians used subjective assessment alone in almost 90% of cases.[45]

There are a number of possible reasons why clinicians may not use risk prediction tools. First, there may be uncertainty about which tool to use and when. The number of tools available and the differing opinions on their use may be overwhelming. Secondly, clinicians may prefer to use their clinical experience and judgment in assessing risk particularly when the accuracy of subjective assessment with objective methods is unclear.[51] Third, there may be concerns regarding the accuracy of risk prediction tools. As demonstrated for the tools explored above, limitations can be found with all risk prediction tools. Even if they are deemed highly discriminative, with AUROC > 0.9, that still means that there is a 10% room for error. Often when a tool is made more generalizable, it sacrifices its power of discrimination and level of calibration. Finally, many tools require the availability of multiple investigations (some of which are not available pre-operatively) that can be time-consuming to input. This in itself may be a barrier to clinicians using risk prediction tools.

WHAT IS THE ‘PERFECT’ RISK PREDICTION TOOL?

There are many reasons why the creation of a perfectly precise, well-calibrated and fully generalizable risk tool poses a huge challenge. Surgical outcome is not just dependent on the patient’s co-morbid state and the nature of the procedure they are having. Hospitals differ in their structural organization and in the processes of care that they deliver. This variation in structure and process is well demonstrated in our national audits and databases.[4,6,8,12]

Emergency surgery poses its own challenges for risk scoring. Patients often present with acute physiological derangement and with limited time for improvement pre-operatively. Again, hospitals differ greatly in the way in which they provide emergency care, for example, the seniority of out of hours staff, the provision of a dedicated emergency theatre or the availability of unplanned ICU care post-operatively.[8,52,53] Such structure and process variation was evident in both the organisational (structure) and patient-level (process) reports of the UK National Emergency Laparotomy Audit.[6]

In view of the difficulties associated with predicting risk in groups of patients presenting for emergency surgery several procedure specific risk calculators have been developed such as the NELA calculator and the Nottingham Hip Fracture Score.[48,54] In general, surgery specific risk models have shown some promise in more accurately predicting risk for sub-groups of patients but continued work is needed. On the other hand, busy clinicians may favour a single risk tool, which is generalizable to all surgery types and patient groups. To this end, the SORT and SORT-clinical judgement models provide good estimates of risk in individual specialty specific cohorts of patients.[45]

There is debate about which outcome measures should be our focus. Most highly validated tools can only accurately give predictions of mortality, whereas perhaps morbidity and likelihood of disability free survival is of greater importance to our patients and for the optimal distribution of healthcare resources.[55] Morbidity is a more common occurrence post-operatively than mortality. However, morbidity prediction models tend to be less accurate than mortality prediction models, when discrimination is assessed in large multi-centre databases. This is likely to be due (at least in part) to the inter-rater variability in measuring and reporting postoperative complications, and the variation in how complications may be defined.
References


References
Introduction

There are two areas of consent that staff in pre-assessment will encounter – consent for a surgical procedure and consent for anaesthesia. These are inextricably linked, with each influencing the other. The purposes of a pre-assessment appointment are closely aligned with the consent process. The appointment is an opportunity for the peri-operative team to identify patient factors (medical or social) which may impact on the risks of surgery or anaesthesia and also to provide the patient with information related to their hospital admission, surgical procedure (including anaesthesia) and recovery. The risks of both surgery and anaesthesia will vary according to patient factors which may be first identified at a pre-assessment appointment. The pre-operative appointment is therefore a key point in the consent process for elective surgery.

This chapter covers information about consent relevant to pre-assessment teams and therefore concentrates on elective and expedited surgery in adults. It does not cover urgent or emergency surgery, or consent for surgery in the obstetric or paediatric population although many of the principles still apply.

There is comprehensive and extensive guidance about consent published by the Department of Health [1], GMC [2], the Association of Anaesthetists [3] and the Royal College of Surgeons [4]. This chapter covers the key principles regarding consent in these guidance documents and is intended to be a practical guide to implementing them. The reader is referred to the nationally published guidance for further information and clarification.

Footnote: The legal frameworks and terminology for decision making and consent vary according to the country with which the surgery is being performed, even across the UK. For example, in England, Wales and Northern Ireland the term “best interests” is used in decision making, whereas Scottish law refers to “benefits” to the patient. The Association of Anaesthetists Guidance summarises the differences in legal frameworks for decision making in its Appendix 1 [3].

What is valid consent?

For consent to be considered valid, the following three conditions must be in place.

1. It must be from a person who has capacity.
2. It must be given voluntarily, with no coercion from others (family, friends or healthcare professionals).
3. It must be informed. This means the patient must be given the information they need about the overall benefits of the procedure, the risks of having the procedure and the alternative options, including doing nothing. This information should be provided in appropriate format(s) for that particular patient, over a time-scale which allows them to consider the options, with consideration to the factors that matter to the patient.

Please note that documentation of consent is not a pre-requisite for it to be valid, although there are some procedures where it is legally required in the UK, such as fertility treatment. Documentation is, of course, important, as it provides evidence of the consent process. It is discussed further below.

Why do we need to gain consent?

Gaining valid consent for performing a procedure is a professional, ethical and legal obligation of any healthcare professional that performs procedures. Modern medicine has moved far away from the paternalistic approach of previous years, and the principles of decision making and consent emphasise the importance of doing this in partnership with patients. Performing an elective procedure without valid consent is against legal and GMC guidance and may result in prosecution (for assault / battery, or more commonly for negligence) and GMC referral.

Summary and Key Recommendations

- Consent should be informed, voluntary and from a person who has capacity.
- Consent is a process and should involve shared decision making principles and / or frameworks.
- Pre-assessment clinics have an important role in the consent process by:
  - Providing patients with key information related to the procedure and anaesthetic, especially written information.
  - Identifying patient specific factors which may impact on the “material risks” to a particular patient.
- Pre-assessment staff should be with familiar with how to recognise if a patient does not have capacity and how to manage this situation in their organisation.
- A consent form for an elective surgical procedure should usually have been signed prior to the patient attending for nurse-led pre-assessment.
- It is not necessary to take separate written consent for anaesthesia which is performed to facilitate a surgical procedure.
Who can give consent?

For adults, only the person having the procedure, or their legally appointed deputy, can consent to a procedure. If the person is unable to consent, due to an impairment of their capacity (temporary or permanent) then a decision about whether to perform a procedure needs to be made by the responsible medical team, after consultation with relevant other parties (see below).

How is capacity defined?

Mental capacity is the ability to make a decision. The starting point for capacity is that it is presumed to be present and this presumption must not be influenced by patient demographics such as age, ethnicity or disability [5].

How is capacity assessed?

In order to demonstrate capacity, a person must be able to do all of the following:

- Understand relevant information relating to the decision, such as what the procedure involves and what its risks and benefits are
- Retain this information
- Use the information to make a decision
- Communicate the decision to others

It is the responsibility of the person taking consent, to take all reasonable steps to help the patient understand the information and to communicate that decision. It is important to remember that patients with capacity may make unwise decisions or ones that others do not understand. (This is most often seen in the context of a refusal for treatment. It is of note that a patient cannot demand a healthcare professional to perform a specific treatment which is not indicated.) This does not mean that they do not have capacity.

Usually, a lack of capacity will have been identified prior to the patient attending a pre-assessment appointment. However, capacity is time and procedure specific, and may fluctuate, so it is possible that a person may have been felt to have capacity in the outpatient setting, but then this be questioned in the pre-assessment setting, or indeed vice versa. If the patient cannot recall the operation they are having and the reason for this, this is a red flag that they do not have capacity.

Who can assess capacity?

Capacity can be assessed by any healthcare professional and organisations often have mental capacity assessment forms to help with the assessment and documentation of this [6].

What to do if you feel a patient does not have capacity

The following steps should be taken if it is felt that a patient does not have capacity in the pre-assessment clinic:

1. Document the reasons for this on appropriate paperwork.
2. Contact the lead clinician to co-ordinate a best interests meeting.
3. Refer the patient to the organisations safeguarding team or equivalent, to assist with the best interests meeting.

What is a best interests meeting?

A best interests meeting is between the healthcare professional(s) proposing a treatment, a patient who does not have capacity and those close to the patient such as their next-of-kin and other relatives / friends / carers. It may also involve other healthcare professionals involved in the patients care. The patient's representatives are involved in order to help establish the patient's "needs, preferences, values and priorities" and not to consent on their behalf. This information enables the healthcare professionals to determine what treatment will be of overall benefit to them.

If the patient does not have any next-of-kin who are able to be consulted (for example if the next-of-kin is too frail or does not wish to be involved), then an Independent Mental Capacity Advocate (IMCA) must be appointed and consulted at the meeting instead [7]. Organisations will have their own referral systems for IMCAs.

What is a legally appointed deputy?

There are two forms of legally appointed deputy for healthcare decisions, a Lasting Power of Attorney (LPA) for Health and Welfare and (less commonly) a Court Appointed Deputy. A LPA is appointed by the Office of the Public Guardian [8]. Both will have documentary evidence, which should be included in the patient's notes and neither has the power to refuse life-sustaining treatment.

Advance directives

A patient may make decisions regarding future medical care in advance of losing capacity. This is known as an advance directive. They may state their wish to refuse routine or life-saving treatments (for example a Jehovah's witness may refuse to receive blood products). A refusal of life-saving treatment must be in writing and witnessed. If a patient expresses that they have an advance directive to pre-assessment staff, they should ensure that this information is highlighted to those who will be involved in their care and a copy of a written directive should be included in the patient's medical notes.

Who should take consent?

Consent should ideally be taken by the person who is going to perform the procedure. The GMC guidance states that it may be delegated to another healthcare professional providing that that person has appropriate qualifications and training and sufficient knowledge of the proposed procedure and its risks and benefits and has skills in shared decision making. It also states that it is the responsibility of the person delegating to ensure these conditions are met, and that the person they delegate to understands and agrees to refer any queries or requests for further information back to an appropriate person.

Pre-assessment nursing staff should not be expected to take consent for either a surgical or anaesthetic procedure. However, as mentioned above, they are a vital part of the consent process, with respect to the provision of information and / or identification of patient factors which may increase the patients' risk. They are also a point in the admission process where the patient can raise any questions and where the need for a further discussion regarding the procedure may be identified. It should be expected and accepted that there will be times when the pre-assessment team refer patients back to the surgeons for further discussion.

A patient may also ask questions related to the surgical procedure at anaesthetist-led appointments. Whilst anaesthetists may be able to answer some of these questions, and this is important to help the patient understand the nature of the procedure, they should only do this within the limits of
their capability. They should refer back to the responsible surgeon if there are questions that they cannot answer.

In the similar way, a surgeon should not take consent for the anaesthetic needed for a procedure. However, they should be able to provide information and mention anaesthetic options. They should then refer the patient to an anaesthetist for more information.

When should consent be taken?

For elective and expedited surgery, consent for the surgical procedure should be taken in advance of being admitted to hospital for the procedure, using the shared decision making principles described below. This allows opportunity for the patient to reflect on the information which has been given to them and to decide if they have any questions.

For high-risk surgical patients, consent for anaesthesia and any associated procedures, should also be taken in advance of being admitted to hospital, for example in a high-risk anaesthetic clinic.

For other patients, it is acceptable to take consent for anaesthesia on the day of surgery, providing that information has been given to the patient in advance of admission, either at the time of booking surgery or at the pre-assessment appointment. It is not acceptable to take consent for anaesthesia or provide new information to an elective patient in the anaesthetic room, immediately before induction of anaesthesia.

What should be discussed?

Valid consent requires that the patient is informed about the nature and purpose of the intended procedure, the risks of harm from the procedure and the alternatives to it. Importantly these must be discussed in relation to the individual patient, accounting for their medical and personal circumstances and the amount of information provided should also be tailored accordingly. If patients wish to involve others in this discussion, this should be accommodated wherever possible and the patient should always be given the opportunity to ask questions.

Shared decision making

The GMC guidance on consent from both 2008 and 2020 emphasizes the importance of involving patients in decision making related to their treatment and I or care, a practice known as Shared Decision Making (SDM). SDM is “the process whereby patients and clinicians work together to make evidenced based decisions centred on patient values and preferences” [9]. The concept is backed by NICE [10], NHS England and HEE [11] and has been evaluated in a Cochrane review [12]. Specifically, SDM should involve establishing what matters to an individual patient, in order that the discussion can be tailored accordingly and relevant information exchanged.

Although this concept is not new, the landmark legal case of Montgomery vs Lanarkshire Health Board, brought the law in line with previous professional guidance, confirming the importance of understanding what matters to an individual patient when taking consent. The judgement in this case stated that it was expected that the person taking consent should explain all “material risks” relevant to that patient. Materiality was defined as “...whether a reasonable person in the patient’s position would be likely to attach significance to the risk, or the doctor should reasonably be aware that the particular patient would be likely to attach significance to it” [13].

Whilst it is expected that SDM conversations will have occurred prior to patients attending pre-assessment appointments, it is nevertheless helpful for pre-assessment staff to understand these principles and how they may be put into practice. SDM is also relevant to anaesthetists performing high-risk anaesthetic clinics, where often further discussion related to surgical and anaesthetic risk occurs. To aid this process, models for SDM have been proposed. One such model describes three different stages to SDM conversations, “team talk”; “option talk” and “decision talk” [14]. Similarly, tools for evaluating the effectiveness of these conversations have also been developed [15].

Decision making frameworks

Decision making frameworks are designed to assist with the SDM process. One example of a framework is the “BRAN” decision making framework, developed by Choosing Wisely UK which is part of a global initiative, aimed at improving conversations between patients and clinicians [16]. This framework encourages the patient to ask four questions to enable better decision making:

• What are the Benefits?
• What are the Risks?
• What are the Alternatives?
• What if we do Nothing?

A leaflet can be downloaded to help with this conversation [17].

What information should be provided?

At a nurse-led pre-assessment appointment, patients should be provided with written and verbal information about their procedure and the peri-operative care pathway, if this has not been done at an earlier point in the pathway. With respect to the consent process, this should include:

• Information about what the patient can do to prepare for surgery and minimise their peri-operative risks, for example the Fitter, Better, Sooner leaflet from the RCoA [18], information about thromboprophylaxis and post-operative recovery and rehabilitation.
• Information about the admission process, such as fasting, pre-medication, transfer to theatre, ward information
• Information about the side effects and risks of harm of the anaesthetic and analgesic techniques they are likely to be offered. This should be in the form of an evidenced-based patient information leaflet. (This may mean the patient is given information about both general and regional anaesthesia, as well as information about other options for pain relief).
• Information about when they will have opportunity to ask further questions and meet key staff who will be involved in their care.

Many hospitals choose to use national evidence-based patient information leaflets such as those by the RCoA [19], RCS [20], and / or subspecialty or local leaflets as necessary.

What if patients refuse information?

If a patient declines information about the procedure or risks, then it is important to explain to them that this makes it harder to know whether their consent is valid. It is useful to ask if some basic information such as the reason for the proposed procedure and the most serious risks could be mentioned, and also to try to find out why the person does not wish to know the information. As one of the conditions for valid consent is that it must be informed, if a patient attending pre-assessment refuses information, then the responsible clinician should be told. It may be necessary to involve other parties, but this will depend on the procedure being proposed. Documentation of the discussion is vital.
How should consent be documented

The following aspects of the consent process should be documented:

1. The decision making conversation regarding the surgical procedure, including any alternative options offered to the patient as well as the option of doing nothing. This should be documented in the medical notes and also on correspondence with the patient and GP. This is usually done prior to the pre-assessment appointment.

2. The benefits of having the procedure and the potential risks of harm which have been discussed. These should be documented on the consent form, which is then signed and dated by the patient and the healthcare professional.*

3. Any information (verbal / written / electronic) that the patient has been given. This includes patient information leaflets in the pre-assessment clinic.

4. The planned mode of anaesthesia should be included on the consent form for the surgical procedure. This is usually general / regional anaesthesia or local anaesthesia.

5. If the patient is seen in a high-risk anaesthetic clinic, the details of this conversation, including the options for analgesia and anaesthesia which have been discussed, should be documented in the medical notes. Any risks of harm discussed should also be documented.

6. The surgical consent form should be re-signed on the day of surgery, to reflect that the patient has not changed their mind. When patients attend pre-assessment, they can be reminded that they will have this opportunity for further information and questions.

7. Details of the anaesthetic pre-assessment visit, including consent for anaesthesia are usually documented on the anaesthetic chart. Often a tick box system is used to help with this.

*If a patient does not have capacity then a consent form 4 is used (see table).

Guidance states that a patient does not need to provide separate written consent for anaesthesia performed as part of a surgical procedure and therefore a separate consent form specific for the anaesthetic is not required.

<table>
<thead>
<tr>
<th>Type of consent form</th>
<th>When is it used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent form 1</td>
<td>For all adult patients with capacity. (It may also be used for “legally competent” children.)</td>
</tr>
<tr>
<td>Consent form 2</td>
<td>For parental consent for a child or young person.</td>
</tr>
<tr>
<td>Consent form 3</td>
<td>For patient or parental consent for procedures where consciousness is not impaired (i.e. an anaesthetist is not involved in the patient’s care).</td>
</tr>
<tr>
<td>Consent form 4</td>
<td>For an adult patient who does not have capacity. This needs to be signed by two healthcare professionals.</td>
</tr>
</tbody>
</table>

References


6. Examples of mental capacity assessment forms


16. Choosing Wisely UK. https://www.choosingwisely.co.uk/shared-decision-making/


19. RCoA Patient Information Leaflets. https://www.rcseng.ac.uk/patient-information

1. INTRODUCTION

Sedentary behaviour is defined as activity involving an energy expenditure of <1.5 metabolic equivalents (METS), typically lying or sitting. 44% of UK adults do not currently achieve national recommendations for physical activity, with 30-40% spending 6 or more hours sedentary per day [1]. There is a clear association between inactivity and major comorbid disease: sedentary individuals have a two to threefold increased risk of cardiovascular disease and death, diabetes, obesity, malignancies of multiple organ systems and all-cause mortality [2]. This represents a major challenge at both the individual patient and public health level.

Sedentary behaviour is also associated with reduced aerobic fitness levels. This is particularly pertinent as part of the ageing process given that maximal aerobic capacity (VO2 max – a marker of aerobic fitness) naturally declines by approximately 10% per decade beyond 30 years of age [3]. In addition, a progressive loss of lean muscle mass, or sarcopenia, occurs as a common component of the increasingly recognised and linked ‘frailty syndrome’. Collectively, these changes significantly compromise the ability of patients to withstand the physiological insult of major surgery.

Encouragingly, these physiological changes can be offset through regular exercise and are minimised in habitually active individuals. Indeed, the Academy of Medical Royal Colleges have described regular exercise as a cheap, effective and readily accessible ‘miracle cure’ for population health. Interest continues to build in the preoperative optimization of physical fitness, with the aim of improving outcomes following surgery.

In the following guideline, we outline the extent of the threat posed to the surgical patient from sustained physical inactivity. We also provide evidence-based guidance as to how best advise and support patients in enhancing their physical fitness to improve perioperative outcomes.

2. NATIONAL PHYSICAL ACTIVITY RECOMMENDATIONS

The UK Chief Medical Officer’s (CMO) guidance [4] recommends adults to undertake the following amounts of weekly physical activity to safeguard aerobic capacity and protect against loss of lean muscle mass [4]:

- 150 minutes of ‘moderate’ intensity aerobic exercise
- OR
- 75 minutes of ‘vigorous’ intensity aerobic exercise
- AND
- Muscle strengthening activity at least twice per week

Older adults (>65 years of age) should also undertake activities that improve balance at least twice per week.

Activity describes any body movement that contracts muscles to burn more calories. The exact nature and format are not specified, however table 1 provides examples of ‘moderate’ and ‘vigorous’ activities as defined by the World Health Organisation (WHO).

Summary and Key Recommendations

- Prolonged physical inactivity leads to reduced aerobic capacity and loss of muscle mass (sarcopenia). This compromises the body’s ability to withstand the physiological demand of major surgery increasing risk of adverse perioperative outcomes. Inactivity also promotes chronic health conditions that further elevate risk.
- Baseline activity levels, and objectively measured functional capacity, should be assessed prior to major surgery to help guide individual patient management.
- Preoperative exercise training has the potential to offset poor physical fitness resulting from chronic inactivity, or the effect of neoadjuvant cancer therapies, and improve perioperative outcomes.
- Surgery presents a ‘teachable moment’ to facilitate lifestyle change. Enhanced patient motivation in the preoperative period requires structured support to provide the opportunity and capability to make change.
- Combined programmes incorporating aerobic, resistance and inspiratory muscle training may yield the greatest benefits. An ‘exercise prescription’ approach may be most effective.
- Patient and perioperative team education is critical to success and compliance. Consistent messaging across the entire perioperative pathway by all team members is key.
- Provision of preoperative structured exercise training is a collaborative effort between patients, primary care, secondary care and public health services to ensure available resources are appropriately allocated to patients most likely to benefit.
- A ‘menu’ of exercise support options will engage the widest number of surgical patients, one size cannot fit all.
- Exercise can be considered as one component of a multimodal prehabilitation approach to improve patient ‘readiness’ for surgery.
Table 1: WHO classification of aerobic exercise intensity

<table>
<thead>
<tr>
<th>Moderate Level (4-6 METS)</th>
<th>Vigorous Level (6 METS +)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activity</strong></td>
<td><strong>Activity</strong></td>
</tr>
<tr>
<td>Gardening</td>
<td>Heavy shovelling or digging</td>
</tr>
<tr>
<td>General housework and domestic chores</td>
<td>Hiking</td>
</tr>
<tr>
<td>Involvement in children's games and sports</td>
<td>Carrying heavy loads (&gt;20kg)</td>
</tr>
<tr>
<td>Carrying moderate loads (&lt;20kg)</td>
<td>Exercise</td>
</tr>
<tr>
<td>Brisk walking</td>
<td>Running</td>
</tr>
<tr>
<td>Doubles tennis</td>
<td>Competitive sports</td>
</tr>
<tr>
<td>Slow swimming</td>
<td>Walking uphill</td>
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<tr>
<td>Dancing</td>
<td>Fast cycling</td>
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<tr>
<td>Slow cycling</td>
<td>Fast swimming</td>
</tr>
<tr>
<td>Aerobics</td>
<td>Aerobics</td>
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</table>

For individual patients, achieving these targets leads to a reduced incidence and severity of major chronic health conditions (e.g., heart disease, diabetes and cancer) reflected in a 30% reduction in all-cause mortality compared to less active adults. Physical, mental and sleep health are enhanced in active individuals with an associated superior quality of life [4]. Regular physical activity has been shown to be superior to specific pharmacological interventions for chronic health conditions, with greater compliance and a lower associated side-effect profile [5].

The population health challenge is stark. Less than one-third of adults are compliant with these recommendations. A perceived lack of general patient awareness is compounded by some uncertainty amongst perioperative clinicians. Prior work by our team supported by the Preoperative Association reinforces this. A national online survey of 650 primary and secondary healthcare professionals demonstrated that only 51% and 23% respectively were aware of the WHO recommended activity levels. In addition, only one-half of all respondents recommended increased physical activity prior to major surgery. This worrying finding can only be improved through increased awareness and education amongst healthcare professionals managing patients in the lead up to major surgery.

3. PERIOPERATIVE IMPLICATIONS OF PHYSICAL INACTIVITY

Aerobic fitness can be defined as the coordinated capacity of the cardiovascular, respiratory and musculoskeletal systems to boost the delivery and handling of oxygen within the body. Major surgery represents a major stressor and subsequent physiological challenge to the body: the association between physical fitness and the patients’ ability to tolerate surgery is well established across a broad range of surgical procedures [6]. Patients with lower aerobic fitness levels have a significantly increased risk of adverse perioperative outcomes including; major morbidity, mortality, increased hospital length of stay (LOS) and reduced health-related quality of life. This is compounded through the increased risk from associated comorbid disease and frailty (where this exists) [7].

4. PREOPERATIVE ASSESSMENT OF FUNCTIONAL CAPACITY

Accurately defining an individuals’ functional capacity is therefore a key component of comprehensive preoperative assessment. The METS study has confirmed the extremely poor sensitivity and specificity of subjective patient reporting for identifying ‘less fit’ patients [8]. Therefore, an objective assessment is recommended. A number of independently validated testing modalities are employed including:

- Timed stair climbing [9]
- The 6-minute walk test [10]
- The incremental shuttle walk test [11]
- Cardiopulmonary exercise testing (CPET) [12]

Of available options, CPET has the strongest evidence base at the time of writing. Approximately 60% of UK Trusts are now able to access CPET for assessment of patients in the preoperative setting. Whilst further discussion of objective exercise testing, and delineation of risk thresholds for individual testing modalities is beyond the scope of this document, several recently published sources are available [12].

5. EXERCISE PREHABILITATION STRATEGIES

5.1 The rationale for preoperative exercise training

Preoperative exercise may form one component of a ‘prehabilitation’ approach [13], seeking to optimise physical and mental health and wellbeing prior to surgery, whilst minimising the risk and severity of postoperative complications thereby supporting a smooth and complete recovery. Other prehabilitation efforts may be directed (not exclusively) at diet and nutrition, cessation of smoking, alcohol reduction or psychological preparation for surgery. This approach can be considered in a continuum with ‘preoptimization’ of chronic health conditions and postoperative recovery, with pre and rehabilitation running through the entire perioperative journey.

As detailed above, inactive surgical patients stand to gain substantial health benefits from reaching CMO targets for physical activity. For the most inactive and least fit patients, being supported toward this level before surgery may reflect a substantial increase in their objectively measured functional capacity. However, in the majority of cases, a more structured approach may give patients the best chance of achieving meaningful improvements in functional capacity that can influence their outcome. Exercise is closely linked to but distinct from activity, and can be defined as purposeful effort to achieve measurable improvement in a specific domain of physical fitness such as aerobic capacity. This subtle shift in mindset from ‘increasing physical activity’ to ‘structured exercise training’ is key for patients facing highest risk, major surgery, typically associated with shorter preoperative timeframes.

The theory underpinning this concept is shown in Figure 1. A structured programme should lead to an enhanced functional capacity prior to surgery, creating enough physiological reserve to deal with the subsequent surgical stress response. This facilitates a reduction in postoperative morbidity and functional dependence compared to patients remaining inactive prior to surgery.
Dependent

Non-rehabilitated Patient

Routine Recovery

Survival

Postoperative Complications

Figure 1: Proposed protective effect of exercise prehabilitation on perioperative functional status

The green line represents a preoperatively inactive patient who experiences the expected marked reduction in functional status following surgery. During the postrehabilitative phase, the rate and extent of their recovery will be influenced by the incidence of complications. A single perioperative complication delays recovery and may result in a permanent reduction in functional status or a loss of independence. The blue line represents a prehabilitated patient whose fitness has improved prior to surgery. On exposure to the same major physiological insult with surgery they experience a smaller initial drop in functional status alongside a swifter return to independence through a shorter recovery period. Additionally, their enhanced reserve enables a faster recovery and less risk of long-term dependency should a complication still occur.

Improving aerobic fitness and sarcopenia (loss of muscle mass) requires a combined approach consisting of both muscle strength (resistance) and aerobic training. Inspiratory muscle training (IMT) may form a third component of a multimodal preoperative training programme as a specific form of resistance training to build strength and endurance in the muscles of breathing.

5.2 Evidence for preoperative exercise training

The evidence base for preoperative exercise continues to build for patients undergoing major surgery across a range of specialties. Systematic reviews have demonstrated significant reductions in overall, and pulmonary morbidity, alongside improved postoperative functional status following major colorectal, vascular and hepatobiliary surgery [14]. The included trials compared aerobic, resistance and IMT or combination programmes to standard care. A further review suggested greater reductions in complications with combined programmes. Reduced complication rates have also been demonstrated in systematic reviews of exercise prehabilitation prior to oesophagectomy [16] and major cardiac surgery [17].

Despite this growing cross-specialty body of evidence, the authors of the above reviews have consistently acknowledged the heterogeneity between included studies and the relatively small size of included trials. We are aware of four major multicentre exercise prehabilitation trials underway that will address this, significantly enhancing the current evidence base.

5.3 Preoperative exercise training in major cancer surgery

Patients preparing for major cancer surgery face a unique challenge. A study published by West et al [18] demonstrated a 16-19% drop in objectively measured aerobic capacity following preoperative neo-adjuvant chemoradiation therapy (NACRT). Combined with the typically short window between cancer diagnosis and surgery, this substantially increases perioperative risk. Crucially, this fitness drop can be reversed in workable timeframes (4-6 weeks) [18]. Whilst the study was not powered to detect perioperative outcomes, confirming that an appropriately constructed training programme can offset the negative impact of NACRT on patient fitness levels preoperatively is important. A recent collaborative publication on multimodal prehabilitation guidance for people with cancer has been published by the Royal College of Anaesthetists, National Institute of Clinical Excellence and Macmillan Cancer Support [19].

5.4 Trainability, adaptive response and aerobic exercise intensity

Older people enjoy similar relative fitness improvements to younger individuals with aerobic exercise. Indeed an individual's adaptive response to exercise varies significantly, with up to 40% of individuals appearing to get no initial fitness benefit (non-responders) [20]. This phenomenon appears to be dependent on certain genetic and environmental factors, but is independent of age and sex. The number of non-responders diminishes as volume of exercise increases, suggesting that longer duration programmes of higher intensity may be more beneficial [20]. Despite this, significant fitness improvements can be made in as little as 3-4 weeks with most early time-efficient benefits being made in shifting sedentary individuals to low and intermediate levels of fitness.

Short-term benefits in improving fitness are crucial in the context of short preoperative timframes. High Intensity Interval Training (HIIT) has been shown to be superior to moderate continuous training (MCT) in this regard. HIIT is also associated with a greater magnitude of benefit for any given duration of programme [21].

5.5 Safety of Aerobic training

This remains a valid concern given the ‘average' patient undergoing major surgery is 67 years of age with at least 2 comorbidities. However, published studies continue to demonstrate the safety of preoperative interventions across surgical populations with very low adverse event rates. This must also be considered in the context of several thousand maximal effort cardiopulmonary exercise tests now undertaken across the UK with very low adverse event rates reported. Any aerobic training programme (MCT or HIIT) would not be expected to reach these exercise intensities thereby providing additional safety reassurances [12].

Additional robust data available comes from the cardiac rehabilitation setting. Large published data series from Scandinavia have demonstrated an overall risk of 1 serious adverse cardiac event per 23,000 and 130,000 exercise hours for HIIT and MCT respectively [22]. Risk is increased approximately 7-fold during rehabilitation of previous habitually sedentary individuals with cardiac disease. Absolute risk would therefore appear to be low even in the highest risk group of individuals undertaking any form of exercise.
Despite this excellent overall safety profile, there is a need for vigilance in high-risk patient populations. We advocate a risk profile assessment encompassing evaluation of clinical risk factors, physical examination and ideally an objective assessment of physical fitness for individual patients prior to undertaking regular exercise.

6. CLINICAL IMPLEMENTATION

Work by Macdonald et al [23] has confirmed that the preoperative period is a ‘teachable moment’ to facilitate health behaviour change. This study identified high levels of patient motivation to increase activity levels and engage with exercise training before surgery. Patient confidence levels to effect that change were lower, suggesting that structured support is necessary to successfully enhance patient fitness. This is backed by established behavioural science principles, that motivation must be coupled with capability and opportunity to effect change.

Successful implementation and adherence of patients to preoperative exercise programmes can prove challenging. However, a number of exercise prehabilitation programmes are now established in the UK [24-25] reporting high levels of patient engagement, adherence and excellent patient reported outcomes. Without exception, these services have sought to break down the numerous barriers that may prevent patient engagement including, amongst others:

- Available patient time
- Distance from available support
- Travel and parking costs
- Reluctance to undertake additional hospital visits
- Comorbid disease and anxiety around exercise
- Availability of space, equipment and staff time

Overcoming these issues requires an integrated approach involving patients, healthcare professionals and commissioners.

6.1 Patient Selection

Appropriate targeted patient selection is key. Moving from a sedentary to an active lifestyle is likely to benefit any patient approaching surgery. However the characteristics of patients most likely to benefit from more structured preoperative exercise intervention include:

- Planned major/complex surgery (NICE elective surgery grading) – particularly where intra-body cavity surgery is planned e.g. laparotomy, thoracotomy procedures.
- Evidence of sedentary behaviour or low activity level (<150 minutes/week moderate activity)
- Significant co-morbid disease likely to benefit from increased activity/exercise (see introduction)
- Patients at risk of reduced or compromised fitness levels or sarcopenia e.g. those undergoing preoperative chemo-radiotherapy and age > 70 years.

A baseline risk assessment should be undertaken including clinical risk factors relevant to exercise ± an objective fitness assessment if there is any clinical doubt.

Recently, a tiered approach has been advocated to rationalise the exercise ‘offer’ made to patients undergoing surgery and the prudent use of likely limited resources to provide more intensive, structured training support (Figure 2).

6.2. Education

Success is dependent on consistent and repeated messaging by healthcare professionals throughout the perioperative pathway. Results from our national survey (previously described – section 2) starkly bring this in to focus. Addressing this is essential for engagement of patients and carers. Shared-learning and more integrated working across primary and secondary care, is a key goal set out in the NHS England 5-year plan. This is the concept of ‘Making Every Encounter Count’ (MECC).

6.3. Potential exercise interventions and principles for programme design

Table 2 presents a ‘menu’ of possible preoperative options that can be considered and tailored based on patient, clinical and local resource factors. It should be recognised that no approach will be suitable for all patients or all settings.

When designing an exercise programme, a ‘prescribing’ approach is useful. The ‘FITT’ acronym requires the frequency, intensity, time and type of exercise to be specified. The goal of each component should be clear. Improvement of aerobic capacity or the building of lean muscular strength and endurance will require different forms of training. Programmes should incorporate a baseline objective assessment of fitness with a preoperative re-assessment to measure improvement.

A structured review of currently available evidence including suggested protocols and targets for aerobic, resistance and IMT has been previously published to guide perioperative teams [26]. The internationally recognised consensus for exercise reporting template (CERT) [27] is a framework for the academic reporting of exercise interventions and a very practical guide to the elements that must be considered when designing a clinical programme.

Figure 2: A tiered approach to preoperative exercise support (adapted from 13 & 19)
Options for local implementation will very much depend on infrastructure and resources available, it is notable that existing UK exercise prehabilitation services have developed varied models. In particular, we advocate engagement with public health colleagues that may provide access to facilities and staff outside of the hospital setting that can be readily offered to surgical patients. Options may range from exercise prehabilitation leaflets to exercise-on-referral classes in health and leisure facilities. The latter option is likely to be more enjoyable and lead to higher rates of compliance. Of note, several UK prehabilitation programmes have utilised public health trainers, supported by healthcare professionals, to deliver structured exercise training. This builds on the substantial experience of these individuals of working with a range of patients with highly varied chronic conditions and healthcare needs.

6.5 Ensuring Safety

Ensuring patient safety at all times whilst encouraging increased exercise and activity levels is paramount. As well as advocating the importance of screening for any physical or medical conditions that may preclude certain exercise regimes, we suggest the following as good practice:

- All patients should be provided with information pertaining to safe exercise and warning signs that warrant cessation of exercise and the need to seek medical advice. This can be delivered within a patient information leaflet or via online tools.
- Patients participating in structured exercise initiatives should ideally be supervised by a trainer with a Basic Life Support qualification.
- All participating centres should be equipped with appropriate resuscitation equipment e.g. automated defibrillators.

6.6 Preoperative exercise in multimodal prehabilitation

As outlined above, exercise may form one component of a multimodal prehabilitation approach to enhance general health and wellbeing prior to surgery. Multiple unhealthy behaviours are known to cluster in surgical patients [23], particularly those requiring major intervention. There is significant potential for synergy between simultaneous interventions, for example, the benefits of a preoperative exercise programme will be significantly enhanced by nutritional support and cessation of smoking. In addition, engagement with the modification of one unhealthy behaviour may motivate patients to tackle others [28].

7. GENERAL RECOMMENDATIONS

- All efforts should be made to identify habitually inactive patients prior to surgery. As a minimum, patients undergoing surgery should be encouraged to increase physical activity to 150 minutes per week of moderate intensity or 75 minutes per week of vigorous intensity (per CMO guidance).
- Patients with chronic health conditions or those approaching major intervention will likely require structured exercise training support to objectively enhance their fitness prior to surgery.
- Training may focus on aerobic capacity, resistance training or inspiratory muscle training depending on type of surgery. Combined programmes may yield the greatest benefits.
- Programmes require a minimum preoperative duration of 4-6 weeks to optimize effect, particularly in older adults. Although HIIT has been shown to be superior to MCT for enhancing aerobic capacity, we recommend that this is only undertaken following thorough clinical assessment of risk factors and in a monitored supervised environment with appropriate back up facilities.
- Ideally patients should be offered options to ensure compliance and fit with varied needs and preferences.

### Table 2: Menu of preoperative exercise options for patients

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Delivery</th>
<th>Positives and indications</th>
<th>Drawbacks and barriers</th>
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<tbody>
<tr>
<td><strong>Patient information leaflets</strong></td>
<td>This can act as an intervention in itself and signpost other locally available opportunities. Distribution at contact points along the preoperative pathway</td>
<td>Simple, cheap, versatile and able to reach a large number of patients; Can reinforce simple verbal advice from the perioperative team; National resources available at <a href="https://rcoa.ac.uk/patient-information/preparing-surgery-fitter-better-sooner">https://rcoa.ac.uk/patient-information/preparing-surgery-fitter-better-sooner</a></td>
<td>Challenging to monitor compliance or establish impact; Likely to engage only the most motivated of patients without clear signposting and pathways to structured support</td>
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<tr>
<td><strong>Exercise on prescription / Exercise on referral (ERS)</strong></td>
<td>Prescribed according to the ‘FIT’ acronym (frequency, intensity, time and type). Widely commissioned already in UK primary care for health conditions e.g. obesity, diabetes</td>
<td>Flexible, allowing tailoring to individual need and ability; Can incorporate everyday activities; Can be delivered through local gym/health centres; Evidence based for achieving short term increases in physical activity (NICE recommended)</td>
<td>Heavily reliant on patient engagement, motivation and local infrastructure; May involve financial costs for patients; May have limited medium to long-term impact and not all patients achieve intended targets; Not trialled in the preoperative setting</td>
</tr>
<tr>
<td><strong>Group based exercise prehabilitation</strong></td>
<td>A range of venues and formats are currently utilised in the UK</td>
<td>‘Tailored’ support to the preoperative context; Highly motivating and effective for some patients who would not otherwise engage individually. Can be delivered through local gym/health centres or make use of existing cardiac/pulmonary rehabilitation programmes and facilities; Naturally incorporates supervision and monitoring</td>
<td>Many patients are uncomfortable in the group setting; Limited flexibility for busy patients; Requires allocation of facility space and staff time</td>
</tr>
<tr>
<td><strong>Online exercise prehabilitation classes</strong></td>
<td>Sessions can be designed for remote participation led and supervised by staff</td>
<td>Removes travel and cost pressures; Wearable device integration can allow monitoring and interaction with facilitating staff</td>
<td>Reliant on comfortable use of information technology and access to reliable Wi-Fi.</td>
</tr>
<tr>
<td><strong>Digitally facilitated self-managed exercise prehabilitation</strong></td>
<td>Digital platforms can be customised to allow engagement with a ‘home-based’ exercise programme</td>
<td>Home-based support is the preference of approximately 50% of surgical patients; Offers maximum flexibility to patients and the travel/cost advantages of online classes</td>
<td>Requires a degree of IT confidence; Monitoring engagement and adherence can be challenging; Requires clear safety processes prior to enrolment</td>
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References


