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article Title

Perioperative risk - Stratification and modification

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Key words

* Perioperative medicine
* Perioperative care
* Risk stratification
* Risk prediction
* Prehabilitation
* Shared decision making
* Comorbidity
* Multimorbidity

Key Points

* Identifying patients at high risk of post-operative morbidity using individualized risk assessment is essential to help inform decision-making, facilitate preparation for surgery, and guide post-operative care.
* Empowering patients through collaborative shared decision making improves their understanding of treatment options, adherence to therapy, and reduces decision regret.
* Risk can be mitigated by using appropriate interventions to address pre-operative multimorbidity, including diabetes, anaemia, and cardio-respiratory disease.
* The complex interaction between physical, nutritional, and psychological health may be best addressed using multi-modal prehabilitation.
* Future advances in risk stratification and modification are likely to involve the integration of clinical judgement with data from wearable devices, machine learning, and artificial intelligence.

Synopsis

This chapter discusses the important topic of perioperative risk stratification and the interventions which can be used in the perioperative period for risk modification. It begins with a brief overview of the commonly used scoring systems, risk prediction models, and assessments of functional capacity, and discusses some of the evidence behind each. It then moves on to examine how perioperative risk can be modified through the use of shared decision making, management of multimorbidity, and prehabilitation programs, before considering what the future of risk stratification and modification may hold.

**Perioperative risk - Stratification and modification**

L Matthews, D Levett, MPW Grocott

# Introduction

Personalised risk assessment can be a defining step in a patient’s perioperative journey. It lays the foundations for shared decision making and is key to outlining the road map with which patients and clinicians can work collaboratively to navigate the route from the anticipation of surgery to recovery thereafter. It facilitates preparation for surgery, choice of procedure (or alternative), informed consent, and guides the use of post-operative enhanced and critical care facilities and the pathway to recovery.

Risk assessment is pivotal to identifying those patients at higher risk of complications and death as a result of modifiable co-morbidities or behaviours (e.g. smoking, inactivity). Whilst the increased financial cost of post-operative complications is well documented, the clear association between complications and reduced long-term survival is less well recognised and has significant implications.1,2 Perioperative morbidity casts a long shadow, and it is imperative that clinicians exploit the early part of the perioperative pathway to identify and modify key risk factors in order to maximise patient resilience prior to surgery and thereby minimise post-operative harm.3,4

In first part of this chapter we discuss how risk can be assessed using prediction models, clinical judgement, and assessments of functional capacity. In the second part we examine how risk can be modified through shared decision making, managing multimorbidity, and prehabilitation, before finally looking at what the future may bring.

# Risk stratification – Scores and models

Risk stratification tools can be classified as those that use a cumulative scoring system to stratify risk and those that use risk prediction models. Both are normally developed using multivariable analysis of risk factors for the outcome of interest, in this case perioperative morbidity and death. Risk scores are simple to use, but do not provide a numerical estimate of individual patient risk. Prediction models are more complicated in their execution, but do provide an individualised risk estimate.5

The Anesthesiologists Physical Status (ASA-PS) is the best example of a commonly used scoring system. The Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM), Surgical Outcome Risk Tool (SORT) calculator, and the American College of Surgeons National Service Quality Improvement Program (ACS NSQIP) calculator are all examples of prediction models. Scores and models can be further divided into those that give an assessment of overall surgical risk, for example SORT, and those that estimate risk of an adverse outcome for a particular organ system, such as the Revised Cardiac Risk Index (RCRI).

## Assessment of overall perioperative risk

### American Society of Anesthesiologists Physical Status

The ASA-PS classification was originally described in 1941 and was developed to recognise the importance of a patient’s physical state to operative risk.6 It was adopted into practice in 1962 and has evolved into the current iteration which subjectively classifies a patient’s physical status from I to V, on a scale of increasing severity of disease. An ASA classification of I denotes a “normal healthy patient”, whereas an ASA V patient would “not be expected to survive without the operation”. The suffix “E” is added in the setting of emergency surgery and there is an additional ASA VI classification in the context of organ donation. (Table 1) It is simple to use and intuitive, with a higher value being associated with a higher likelihood of post-operative morbidity and mortality across multiple surgical specialties. In a meta-analysis of over 165,000 patients ASA-PS was found to have a sensitivity comparable to other commonly used scores, such as Lee’s RCRI and POSSUM, for predicting post-operative mortality.7

Despite its ease of use and reasonable predictive characteristics, ASA-PS has a number of limitations. It does not take into account the planned surgery, objective observations, nor attempts to improve modifiable co-morbidities, and has been shown to be a poor predictor of risk of complications for individual patients.8 This makes it less useful than other tools, for example the SORT and American College of Surgeons National Service Quality Improvement Program (ACS NSQIP) calculators, for personalised risk discussions during a shared decision making consultation. Furthermore, a high level of inter-observer variability is observed due to the subjective nature of the classification.9,10

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| --- | --- |
| ASA-PS Classification | Definition |
| I | A normal healthy patient |
| II | A patient with mild systemic disease |
| III | A patient with severe systemic disease |
| IV | A patient with severe systemic disease that is a constant threat to life |
| V | A moribund patient who is not expected to survive without the operation |
| VI | A brain-dead patient whose organs are being removed for donor purposes |

Table 1. ASA-PS classification definitions

### Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM)

The POSSUM was developed in 1991 using multivariable analysis to establish 12 physiological and six surgical variables that best predicted 30-day morbidity and mortality following elective and emergency surgery.11 (Table 2) The model was updated in 1998 by Prytherch and colleagues because of concerns that the initial model over-estimated post-operative mortality. The adapted model, called the Portsmouth-Possum (P-POSSUM), predicts post-operative survival more accurately than the original model.12 However, the P-POSSUM does not provide an estimate of morbidity.

Variations of the POSSUM model are available for the prediction of post-operative mortality in both colorectal (CR-POSSUM) and oesophago-gastric (O-POSSUM) surgery.13,14 These comprise 10 and 16 variables, respectively, many of which are common to the original POSSUM. Although reasonably accurate, both P-POSSUM and its subsequent variations have been shown to consistently over-predict post-operative mortality.15,16,17 Furthermore, whilst P-POSSUM may be used to generate an individualised assessment of risk of mortality, error is introduced by the requirement to make assumptions about likely operative findings, and then revise them post hoc.

|  |  |
| --- | --- |
| Physiological parameters | Operative parameters |
| Age | Haemoglobin | Operative type |
| Cardiac disease | White cell count | Number of procedures |
| Respiratory disease | Urea | Blood loss |
| ECG findings | Sodium | Peritoneal contamination |
| Systolic blood pressure | Potassium | Malignancy |
| Heart rate | Glasgow coma score | Urgency of surgery |

Table 2. P-POSSUM physiological and operative parameters

### The Surgical Outcome Risk Tool

The first iteration of the SORT calculator was developed in 2014 using data from patients having surgery in the United Kingdom (UK), and estimated the risk of in-hospital mortality following elective surgery using information about the planned procedure and six pre-operative variables (ASA-PS classification, urgency of surgery, high-risk surgical specialty, surgical severity, cancer and age).18 It is validated for use in non-neurological and non-cardiac surgery.

Unlike other risk prediction models, such as P-POSSUM, it does not require any pre-operative investigations and is therefore easier to use early in the perioperative pathway to support shared decision making and plan post-operative care. It is accurate across a wide range of surgical specialties and was recently reported to be a better predictor of 30-day post-operative mortality than P-POSSUM in a large, international, observational study.19 The discrimination of SORT appears to be improved by the addition of clinical judgment, resulting in the inclusion of a clinical risk assessment in version 2 of the SORT calculator. Both are available at <http://www.sortsurgery.com/>. Version 2 of the calculator is recommended for use when the opinion of an experienced clinician or multi-disciplinary team is available. If this is not possible then use of SORT version 1 is recommended.20 (Table3)

|  |
| --- |
| Surgical Outcome Risk Tool variables |
| Planned surgical procedure |
| Severity of planned procedure (Minor/Intermediate/Major/Complex) |
| ASA-PS |
| Urgency of surgery |
| Thoracic, Gastrointestinal or Vascular surgery |
| Cancer |
| Age |
| Clinical risk assessment (SORT version 2 only) |

Table 3.Surgical Outcome Risk Tool variables

### American College of Surgeons National Service Quality Improvement Program Surgical Risk Calculator

The ACS NSQIP Surgical Risk Calculator uses 20 patient specific variables in addition to the “Current Procedural Terminology” (a billing code for the operative procedure) to estimate the risk of 18 different post-operative outcomes within 30 days of surgery. These include death, complications, return to theatre and discharge to nursing or rehabilitation facilities. It is available at https://riskcalculator.facs.org/RiskCalculator/index.jsp.

NSQIP was first described in 1998 and the ACS surgical risk calculator was launched in 2013.21 It was developed and validated using data from over 1.4 million patients from 393 hospitals in the United States, the first version predicted nine adverse outcomes.22,23 The most recent version uses data collected from over 5 million procedures and 874 hospitals across North America. Similar to SORT, the ACS NSQIP calculator also has the option to include clinical judgement, in this case the “surgeon adjustment of risks”. This adjusts the predicted risk using the standard deviation of the risk of the planned procedure, depending on perceived risk.

## Cardiac specific risk prediction models

Cardiac events account for a significant proportion of deaths following non-cardiac surgery. Historically, the term Major Adverse Cardiac Events (MACE) has been used to describe a range of post-operative cardiac complications associated with increased morbidity and death. More recently, the term Myocardial Injury after Non-cardiac Surgery (MINS) has evolved to describe post-operative troponin elevations associated with increased 30-day mortality.24

The purpose of perioperative cardiac risk assessment is to identify those at risk of MACE and MINS in order to inform patient choice, surgical options, and decide if additional investigations and interventions are warranted to reduce post-operative morbidity. The risk of a particular procedure is defined as low (<1%), intermediate (1-5%) or high (>5%) with regards to the risk of myocardial infarction (MI) or cardiac death within 30 days of surgery).25 (Table 4) This information is combined with patient specific variables in the commonly used cardiac risk prediction models.

|  |  |  |
| --- | --- | --- |
| Low risk (<1%) | Intermediate risk (1-5%) | High risk (>5%) |
| Superficial surgeryDental surgeryEyeMinor gynaecology, urology and orthopaedic | Symptomatic carotidEndovascular aneurysm repairHead and neckMajor gynaecology and urology | Aortic and major vascularMajor hepato-biliaryOesophagectomyRepair of perforated bowelPneumonectomy |

Table 4. Procedural risk of myocardial infarction or cardiac death within 30 days

### The Revised Cardiac Risk Index

A number of tools have been developed over the last 35 years for the assessment of cardiac risk in non-cardiac surgery, most notably those by Goldman,26 Detsky,27 and Lee and colleagues.28 Lee’s RCRI is the most contemporary of these, published in 1999, and is a modification of the earlier work by Goldman et al. It was developed and validated in patients aged over 50 undergoing major non-cardiac surgery, and uses six variables to predict post-operative MI, pulmonary oedema, ventricular fibrillation, cardiac arrest, and complete heart block. (Table 5) It is a cumulative score, with each additional point conferring additional risk of a major cardiac event. For example, an RCRI score of 1 is associated with a 6% risk of MI, cardiac arrest or death, whereas a score of 3 or more increases this to 15%.29

Since its’s initial development the RCRI has been criticised for under-estimating the risk of post-operative cardiac morbidity in non-cardiac surgery.29,30 However, this is likely in part due to the evolution of the definitions of MACE and changes in the cardiac biomarkers used to assess cardiac injury. Lee’s 1999 paper used Creatinine Kinase Muscle and Brain isoenzyme as a biomarker for myocardial injury whereas more recent studies use troponin, resulting in increased diagnosis of post-operative myocardial injury, albeit likely of less certain clinical significance.

### The Myocardial infarction or Cardiac Arrest model

More recently, Gupta et al. described the Myocardial Infarction or Cardiac Arrest (MICA) model. It was developed using data from over 200,000 patients from the 2007 NSQIP database, and subsequently validated in over 250,000 patients from the 2008 database.31 It is available at <http://www.surgicalriskcalculator.com/miorcardiacarrest>.

The MICA uses five variables to predict intra- or post-operative MI or cardiac arrest within 30 days of surgery and demonstrates a high degree of discrimination (AUROC 0.874) (Table 5). Although superior to the RCRI for this particular outcome (AUROC 0.747), the RCRI gives additional estimates for the risk of pulmonary oedema, ventricular fibrillation and heart block. Depending on the particular outcome of interest, both are therefore recommended for use by the European Society of Cardiology.32 A comparison of the two is described in Table 5.

|  |  |
| --- | --- |
| Lee’s Revised Cardiac Risk Index | Myocardial Infarction or Cardiac Arrest model |
| Type of surgery | Type of surgery |
| History of ischaemic heart disease | Dependent functional status |
| History of congestive heart failure | ASA-PS classification |
| History of cerebrovascular disease | Age |
| Creatinine >170μmol/L | Creatinine > 133μmol/L |
| Insulin therapy | - |

Table 5. Comparison of the Revised Cardiac Risk Index and the Myocardial Infarction or Cardiac Arrest model

## Assessment of functional capacity

Functional capacity is a term used to describe the ability of an individual to perform activities of daily living during sustained aerobic metabolism.33 This ability is determined by the integrated working of the pulmonary, cardiovascular, musculoskeletal and metabolic systems. By combining an objective assessment of functional capacity with information about co-morbidities and the planned surgical procedure a more individualised assessment of risk can be achieved.

In this section we discuss the principal methods of perioperative functional capacity assessment. Cardio-pulmonary exercise testing (CPET) is considered the gold standard in the perioperative setting, as it mimics the physiological impact of surgery on the pulmonary, cardiovascular, musculoskeletal and metabolic systems. However, CPET requires specific equipment, personnel, and expertise, which may not be available or appropriate for particular patients. In this situation simpler assessments should be used, such as the six minute walk test (6MWT), appreciating that these are unable to accurately assess aerobic capacity.34

### Cardiopulmonary exercise testing

Cardiopulmonary exercise testing is a non-invasive, objective, assessment of a patient’s functional capacity that produces dynamic integrated evaluation of physiology that cannot be obtained by testing organ systems in isolation or at rest.35,36 Consensus guidelines recommend CPET be used to estimate pre-operative risk, inform shared decision-making, and guide post-operative levels of care.37

The earliest description of CPET for perioperative risk prediction in non-cardiothoracic surgery was by Older and colleagues, who demonstrated that an anaerobic threshold (AT) <11 ml.kg−1.min−1 was associated with increased post-operative mortality in patients aged over 60 having major abdominal surgery.38 Since then the use of perioperative CPET has expanded significantly and has been shown to predict post-operative morbidity and mortality in bariatric, colorectal, hepatobiliary, thoracic, upper gastro-intestinal, urology, and vascular cohorts.39,40

The majority of tests are performed using cycle ergometry, a safe procedure with a low complication rate (< 5 per 100,000 tests).41,34 Breath-by-breath expired gas analysis is combined with continuous ECG and SpO2 monitoring during incremental exercise. The measurements taken enable the calculation of key cardio-pulmonary and gas exchange variables, of which the most commonly described in the perioperative literature are the peak oxygen uptake (VO2peak), AT, and the Ventilatory Equivalent for CO2 (VE/VCO2). (Table 6)

The risk thresholds associated with these variables depend on numerous patient, surgical, and healthcare system factors and some have decreased over time as perioperative care has improved.42 The contribution of other CPET variables to risk assessment is increasingly being explored. Examples include the oxygen pulse, an indirect assessment of dynamic stroke volume and oxygen consumption.39

|  |  |
| --- | --- |
| CPET variable | Definition |
| Peak oxygen uptake (VO2peak) | Highest oxygen uptake achieved on a rapid incremental exercise test |
| Anaerobic threshold (AT) | Oxygen uptake above which there is a metabolic transition to increased glycolysis and lactate begins to rise with an associated metabolic acidosis |
| Ventilatory equivalent for carbon dioxide (VE/VCO2) | The ratio of minute ventilation to carbon dioxide production, reported at the anaerobic threshold or as the gradient of the VE/VCO2 slope |

Table 6. Definition of commonly reported CPET variables

Cardio-pulmonary exercise testing as a predictor of perioperative risk was recently assessed in the Measurement of Exercise Tolerance before Surgery (METS) study, described in more detail in the “Clinical Judgement” section below.43 Although CPET was not predictive of the death or MI within 30 days of surgery, it was the only method that predicted complications after surgery. Of note, the METS participants had a higher mean VO2peak compared to non-selected studies, which may suggest a bias towards healthier participants and limit generalisability to higher risk populations.44

### Alternative assessments of functional capacity

Where CPET is unavailable simpler functional capacity assessment should be considered. The 6MWT is the most commonly used walking test amongst those that assess cardio-pulmonary function.45 It measures the distance that a patient can quickly walk on a flat, hard, surface in six minutes.46 Evidence for its use is mixed with some studies demonstrating differences in outcomes and others not.47 It appears to be an adequate discriminator between a high and low AT, and in a secondary analysis of a sub-group of the METS cohort Ramos et al. found the 6MWT to moderately correlate with CPET variables.48,49

Other options include the incremental shuttle walk test (ISWT) and the timed up and go (TUG) test. The ISWT is a maximal exercise test controlled by a series of pre-recorded signals, and was found to be a better predictor of post-operative outcomes than the 6MWT in patients having abdominal surgery in a review by Moran et al.47,50 Participants must cover 10 metres between signals, the interval between which decreases as the test proceeds. The test is finished when the participant fails to keep up with the signals. The ISWT shows a strong relationship with VO2peak in general surgical patients and good discriminatory ability between patients with a high or low AT.51 The TUG test was originally designed to assess mobility in frail older people.52 It assesses the time taken to out of a chair, walk three meters, and return to the seated position. It is associated with major post-operative complications in cancer surgery.53

## Clinical judgement

Subjective assessment of perioperative risk remains a contentious area. In recent years two large studies have assessed subjective clinical judgement compared to risk stratification tools and objective assessments of functional capacity.

In the 2018 METS study Wijeysundera and colleagues compared four methods of functional capacity assessment in the prediction of a composite primary outcome of death or MI within 30 days of surgery.43 These methods evaluated were: (i) subjective assessment of metabolic equivalents; (ii) CPET; (iii) Duke Activity Status Index (DASI) questionnaire; and (iv) serum NT pro-BNP (BNP). METS was conducted in 25 hospitals in Canada, UK, and Australasia, and enrolled patients aged 40 and over having elective non-cardiac surgery. 1,401 participants were included in the final analysis and at 30 days 0.4% had died and 2% had had an MI. The DASI questionnaire and BNP were both associated with the primary outcome. CPET was not, but was uniquely associated with complications. Subjective assessment was associated with neither and the authors concluded that it should not be used to assess functional capacity in clinical practice.

In SNAP-2: EpiCCS (SNAP-2), published in 2020, Wong and colleagues compared three risk assessment models (P-POSSUM, SORT, and the Surgical Risk Scale) with subjective assessment and investigated whether these models improved risk prediction.19 SNAP-2 was conducted in 274 hospitals in the UK and Australasia and included patients aged 18 and over whose procedure required an anaesthetist. Clinicians were asked to estimate the risk of 30 day post-operative mortality and to detail how they came to this estimate. 21,325 cases were included for analysis and a 30-day mortality of 1.4% was observed. Nearly 80% of clinicians reported using subjective assessment alone to inform their risk assessment. Of the three risk assessment models the SORT calculator performed best (AUROC 0.90). Subjective assessment alone demonstrated good discrimination (AUROC 0.89). The model providing the best discrimination was a combination of SORT and subjective assessment (AUROC 0.92). The authors concluded that combining subjective and objective risk assessment provided a more accurate estimate of 30-day postoperative mortality than subjective assessment alone.

Both publications were multicentre, international, studies run in high-income countries with comparable healthcare systems. Both described the observed mortality to be similar to previously published large cohort studies. However, they differ is in what was “subjectively assessed”. In the METS study clinicians were asked to assess functional capacity in metabolic equivalents, graded as poor (<4), moderate (4–10), or good (>10). This assessment was then used in the analysis of the primary outcome. In SNAP-2 clinicians were asked to estimate the percentage risk of death in six pre-defined categories ranging from <1% to >50% as part of their completion of the case report form. In relation to the perioperative utility of clinical judgement, the conclusion that should perhaps be drawn is that clinicians appear good at subjectively assessing the risk of post-operative mortality, but not functional capacity. However, it is notable that other studies of clinical judgement have not been as supportive of this approach.

# Modification of perioperative risk

Having assessed the risk of morbidity it is incumbent on clinicians to mitigate that risk where possible. This begins by ensuring patients have made an informed decision about the options available to them, which can be achieved through shared decision making. The impact of multimorbidity, including diabetes, anaemia, and cardio-respiratory disease should also be addressed and appropriate interventions put in place. Finally, resilience to the insult of surgery may be maximised through the use of multi-modal prehabilitation.

## Shared decision making

Reducing the risk of poor outcome is not simply about prescribing a new anti-hypertensive or advising a patient to exercise more. Approximately one in seven patients report decision regret following surgery and there is a moral obligation to ensure patients are aware of the material risks of the planned operation before proceeding.54 The process by which patients and clinicians work collaboratively to make evidence-based decisions centred on the patient’s preferences and values is termed shared decision making (SDM).55 Empowering patients in decisions about their care improves their understanding of the available treatments, adherence to therapy, and results in less decision regret.56 A central part of the SDM process is helping the patient weigh up the risks and benefits of each available treatment option, including that of not having surgery. This can be supported by the patient asking four “BRAN” questions of healthcare professionals: (i) What are the Benefits?; (ii) What are the Risks?; (iii) What are the Alternatives?; (iv) What happens if I do Nothing?56

One commonly used SDM method is the three-stage model.57 The first step in this approach is the “Team talk”, where patients and clinicians work together to discuss choices and explore goals. This is followed by the “Option talk”, where alternative treatment options are compared, before moving on to a “Decision talk” where the informed patient arrives at a final choice. This process is iterative and under-pinned by collaborative deliberation.58 Whichever model is used, clear communication of risk is key and this is can be achieved with the use of decision aids. These provide easy to interpret depictions of the, sometimes nebulous, concept of individual risk and help patients consider their own personal preferences and values.59,60 In a 2017 Cochrane review the use of decision aids was found to reduce the number of people choosing major elective invasive surgery, in favour of more conservative options (RR 0.86; 95% CI 0.75 - 1.00).61

Shared decision making shifts the focus from historical paternalism to putting the patient at the centre of decisions about their care. It’s significance is highlighted by its position as a central pillar in the long term plans of large healthcare systems, such as the UK National Health Service.62 Although not a novel idea in healthcare, first described in the early 1980’s, the literature regarding perioperative SDM is currently limited to a handful of studies. Research programmes, such as Optimising Shared decision makIng for high RIsk major Surgery (OSIRIS)63 are underway and should help inform future SDM practice.64

## Multimorbidity

Multimorbidity is defined as the presence of two or more chronic conditions.65 Prevalence increases with age and it is associated with perioperative morbidity and death. A comprehensive review of all conditions is beyond the scope of this chapter. This section therefore focuses on those which are commonly encountered and may be amenable to intervention in the perioperative period.

### Diabetes

More than half a billion of the world’s population are diabetic. In Europe over a third of people with diabetes are unaware of their condition, and in the UK diabetic patients account for 15% of all surgeries undertaken.66,67 It is a chronic, multisystem, disease associated with increased post-operative length of stay, complications, and death.68,69,70 Outcomes are worse for patients in patients for whom the condition is unrecognised prior to surgery, highlighting the importance of addressing this modifiable condition across the continuum of primary and secondary care.71,72

World Health Organisation (WHO) guidance recommends the use of one of four diagnostic tests to diagnose diabetes. These are fasting plasma glucose; the oral glucose tolerance test; random glucose in a person with signs and symptoms; and HbA1c.73 HbA1c is the average erythrocyte glycation over three months and the most commonly used test in recent perioperative guidance, with a level ≥ 48mmol/mol being diagnostic for diabetes.73 Despite the increased risk of harm from undiagnosed diabetes routine pre-operative screening is not currently recommended, which some argue is a missed opportunity to improve outcomes.74,75 For a detailed review of management the reader is directed towards guidelines recently published by the UK Centre for Perioperative Care.76

There is limited literature exploring pre-operative diabetic interventions, in part because most would consider the possibility of randomising a known diabetic patient to no treatment unethical. Given the strength of observational data, most guidelines promote the pre-operative optimisation of HbA1c.77 Current National Institute for Health and Care Excellence guidance recommends that a known diabetic patient should have their HbA1c checked within three months of surgery and commence treatment if it is ≥ 58mmol/mol.74,78 In the UK an HbA1c ≥ 69mmol/mol should prompt specialist referral for optimisation and consideration of surgical delay.76 Similar practice is observed internationally, though precise HbA1c thresholds vary.77

### Anaemia

Approximately 40% of patients having major surgery are anaemic.79 Perioperative anaemia is associated with increased morbidity and mortality, possibly through the risk of allogeneic blood transfusion.80,81 The WHO currently recommend haemoglobin thresholds of < 130g/L in men and < 120g/L in women be used to define anaemia.79,82 The use of these values has faced criticism for putting women at greater risk during major surgery, as they may be more likely to require blood transfusion due to a smaller circulating blood volume.83,84

Patients having major surgery should have a haemoglobin checked at least 14 days pre-operatively and if < 130g/L further investigations should be undertaken to establish cause. These include full blood count, haematinics, transferrin saturation, CRP, and renal function.85,86 In the majority of cases the cause is iron deficiency and, if so, international guidelines currently recommend iron therapy.86,87 Iron can be given orally or intravenously, however if the time between diagnosing anaemia and surgery is less than six weeks intra-venous preparations may be preferred due to the slower onset of oral iron.

The iron therapy literature has evolved since these guidelines were published. Although early observational studies appeared to suggest a benefit in reducing transfusion rates, a 2019 Cochrane review not find a significant benefit for the use of iron compared to placebo for the reduction of blood transfusion (RR 1.21, 95% CI 0.87-1.70).88 More recently, the Preoperative intravenous iron to treat anaemia before major abdominal surgery trial (PREVENTT) found no difference in blood transfusion or death in 487 patients undergoing major elective abdominal surgery randomised to either intravenous iron or placebo.89 However, some have questioned the generalisability of PREVENTT as routine iron studies were not stipulated in the trial design prior to receiving treatment.

### Frailty

Frailty is a complex condition with numerous definitions. The British Geriatric Society describe it as a “distinctive health state related to the ageing process in which multiple body systems gradually lose their in-built reserves”.90 It is associated with increased perioperative morbidity, mortality, and length-of-stay.91,92 It is also associated with post-operative functional decline and discharge to institutional care.93,94 Managing frailty was recently identified as one of the three top priorities in Perioperative Medicine. It ranked higher than predicting perioperative risk, management of co-morbidities, and pre-operative exercise therapy.95

The two most commonly described models of frailty are the phenotype model and the deficit accumulation model. The phenotype model describes a combination of three or more of: unintentional weight loss; self-reported exhaustion; weakness; slow walking speed; and low physical activity.96 The deficit accumulation model details 70 different deficits, with the likelihood of being frail increasing as deficits accumulate.97 Both models are time-consuming to assess and, in the case of the phenotype model, require specialist equipment. Simpler alternatives include the Clinical Frailty Scale (CFS) and Edmonton Frail Scale (EFS). The CFS is a nine-point scale grading patients from very fit to terminally ill, and is designed for use in the outpatient setting. The EFS is a 17-point scale assessing 10 different cognitive, functional and medical domains. It is validated for use by non-Geriatricians and takes less than five minutes to complete.98

Those identified as being frail should ideally be referred onto a perioperative team with expertise in comprehensive geriatric assessment (CGA).99The CGA is a multidimensional, holistic, assessment which is considered the gold standard for managing frailty.100 This may involve a clinician with expertise in geriatric medicine. In the last decade there has been a significant increase in geriatric medicine services being integrated into perioperative pathways, with geriatrician-led services becoming more common.101 The Pro-active care of Older People undergoing Surgery is one example of such a service.102 There is observational data to support these shared care models in combination with CGA in reducing complications, length-of-stay, healthcare costs, and enabling a quicker return to function.103,104,105

## Prehabilitation

Prehabilitation is a term which describes the process by which patients improve their physiological, metabolic, and psychological fitness before surgery to withstand the stress of the operation. The overall the aim is to improve resilience to physiological stress and thereby reduce morbidity and accelerate recovery.106 In contrast to the medical management of co-morbidities and multimorbidity which typically involve pharmacological or procedural interventions, prehabilitation is characterised by behavioural changes by the patient, encouraged and supported by healthcare professionals. This is achieved through physical and psychological screening and assessment and then prescription of appropriate interventions. Screening and assessment evaluate baseline functional capacity, nutritional status, and harmful behaviours (smoking, alcohol, drugs) as well as identifying co-morbidities that may be barriers to prehabilitation interventions. Interventions including exercise, dietary modification, and behavioural change support are targeted at improving improve physical and psychological health and thereby maximising resilience.107. In relation to surgery, this approach was originally described by Carli et al. in the elderly surgical population, with promotion of a combination of aerobic exercise, resistance training, and nutritional interventions. It has since been applied across a wide variety of perioperative settings, particularly surgery for cancer where much of the literature currently resides.

Prehabilitation can be a uni-modal or multi-modal intervention. The commonest modes are those that target functional capacity, nutritional health, and psychological wellbeing. Much of the literature focuses on the first of these domains. In a randomised controlled trial in 2018, Barberan-Garcia and colleagues found exercise focused prehabilitation to reduce post-operative complications in high-risk patients having intra-abdominal surgery.108 The proposed mechanism for this reduction was through improved aerobic capacity. Improved functional capacity has also been observed in small trials of prehabilitation in a number of surgical oncology cohorts.109,110,111. However, improved functional capacity may not universally translate into better clinical outcomes. Two recent systematic reviews of patients having surgery for intra-abdominal and gastro-intestinal cancers found that prehabilitation improves functional capacity and reduces length of stay, but did not affect post-operative complications.112,113

The interaction between physical, nutritional, and psychological health is complex, hence a multi-modal approach may be the best way of maximising individual patient benefit.114,115 With regards to nutrition, prehabilitation programmes combining nutrition and exercise interventions have been shown to reduce length of stay in patients having colorectal cancer surgery.116 Furthermore, in a recent systematic review of multi-modal prehabilitation in patients having surgery for lung cancer, only nutritional prehabilitation was found to reduce complications.117 Addressing psychological wellbeing is also important in a multi-modal approach, as anxiety and depression are known to affect post-operative outcomes.118 Interventions rooted in behavioural change science may improve outcomes and there is evidence for the use of psychological interventions in patients having surgery for breast, colon, and prostate cancer.119 To further support a multi-modal approach two recent studies have shown psychological and nutritional interventions, in combination with exercise, to improve treatment adherence, fitness, and post-operative recovery.120,121

One of the main difficulties in drawing strong conclusions from the prehabilitation literature is the heterogeneity of interventions and the cohorts in which they are studied. There does, however, appear to be an overall signal for benefit and prehabilitation has already become a key recommendation for people living with cancer.122 Key questions for perioperative medicine, such as timing, combination, location, and “dosing” of therapies in individual cohorts will hopefully be addressed through a number of randomised controlled trials currently in progress.

### Smoking and alcohol cessation

Despite the pathological effects of smoking tobacco being well documented it remains the leading cause of premature death in the UK and USA.123,124 Every patient interaction can be a teachable moment and there is a responsibility for perioperative clinicians to intervene from the perspective of surgical risk, as well as the larger picture of long-term patient and public health.125 There is a clear association between smoking and increased post-operative morbidity.126,127 This risk can be significantly reduced by pre-operative smoking cessation interventions.128 These include behavioural change techniques, nicotine-replacement therapy (NRT), and the nicotine receptor agonist varencicline.

In a 2014 Cochrane review examining interventions for pre-operative smoking cessation high-intensity behavioural interventions were shown to increase abstinence at one-year and were associated with a reduction in post-operative complications (RR 0.42, 95% CI 0.27–0.65).129 There is limited data for the pharmacological interventions, such as NRT and varencicline, having an impact on post-operative morbidity, however they do demonstrate an improvement in smoking cessation rates and should therefore be considered in appropriate patients.130,131

Excess alcohol consumption is also a major cause of premature and preventable death, and causes over 5% of the global burden of disease.132 In the UK the health, social, and economic costs are estimated to be between £21 and £52 billion a year.133 Alcohol misuse is associated with worse outcomes following surgery and efforts should be made to reduce consumption to within “safe” limits.134,135 A 2018 Cochrane review assessing the effectiveness of perioperative alcohol cessation interventions on rates of complications and alcohol consumption found intensive interventions increased the number of people quitting alcohol and reduced post-operative complications.136 The Alcohol Use Disorders Identification Test (AUDIT-C) is a quick screening test which can be used for identifying at-risk drinkers. It is a modification of an original 10 question AUDIT tool developed by the WHO and comprises three questions with a maximum of four points available for each question.137 Scores ≥ 4 in men and ≥ 3 in women suggest alcohol misuse, with higher scores suggesting greater severity of misuse.

# The future: wearable technology, artificial intelligence, and machine learning

It has been over 80 years since the ASA-PS classification was first described.6 Risk stratification has come a long way since 1941 and it is likely that the next advance is going to be greater integration of clinical acumen with information generated by wearable devices and analysed by artificial intelligence (AI). Machine learning is one example of how AI can be used in clinical practice. Machine learning involves programming a computer to behave in a way that would be described as “learning” if undertaken by humans.138 It is a necessary part of predictive analytics and uses large data-sets to develop systems, identify patterns, and make decisions.139 Much of machine learning is built on neural networks, which underpin deep learning algorithms. Neural networks are named such as they are designed to mimic human neuronal signalling.140

Machine learning and neural networks have already shown promise for intra-operative care, such as predicting intra-operative hypotension using arterial waveform analysis and using deep neural networks to predict levels of sedation during total intravenous anaesthesia.141**,**142 But what about risk prediction? Assessment of pre-operative functional capacity may be enriched by the global expansion in wearable technology.143 Data produced from wearables in combination with machine learning has already been applied in predicting outcomes and functional recovery for patients undergoing colorectal, hepato-biliary, and major joint replacement surgery.144,145,146 Furthermore, Jones and colleagues recently demonstrated that data output from wearables were moderately associated with a number of CPET variables, suggesting they could play a larger role in pre-operative functional capacity assessment in the future.147

Artificial intelligence may also enhance risk prediction of poor outcomes, both pre-operatively and in the operating theatre. In 2018 Fritz and colleagues described a neural network model for predicting 30-day post-operative mortality, with an AUROC of 0.867.148The model included pre-operative and intra-operative data, enabling it to give a “real-time” estimate of the risk of post-operative death. An interesting proposition when considering how this might aid decisions around whether or not a patient requires post-operative critical care. In similar work, Hill et al. were able to use machine learning and electronic patient record data to construct an automated score that was a better predictor of in-hospital mortality than some conventional scores, such as the ASA-PS.149 Most recently, machine learning has been applied to answer previously unanticipated perioperative questions, such as predicting the risk of mortality in patients undergoing surgery with concurrent SARS-Cov-2 infection.150

# Conclusion

Personalised risk assessment underpins all elements of perioperative care from shared decision making, prehabilitation, and management of comorbidity/multimorbidity to choice of post-operative care environment and application of enhanced recovery. A variety of increasingly sophisticated approaches have evolved over the last half-century leading to a current position where reasonable estimates of overall, and disease specific, risk can be obtained when clinicians apply the available techniques. Looking forward, developments in data inputs (e.g. wearables) and analysis techniques (e.g. AI) are likely to result in more accurate and specific prediction of risk throughout the perioperative journey.

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