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Editorial

Patient optimisation before surgery: a clear and present challenge in peri-operative care

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It is 2025 and Mrs Smith has just seen her family doctor, who is concerned that she has a colorectal cancer and may need chemotherapy and surgery. Vital data that will allow accurate early assessment of the relative benefits and harms of treatment are electronically communicated to her peri-operative care team. Planning for the evaluation and optimisation of physical and psychological function commences in parallel with the evaluation of treatment options for the tumour. With the facts, Mrs Smith is empowered to be fully involved in shared decision-making and an individualised pathway is mapped out early in her pre-operative journey. The peri-operative care team works closely with her to enable physiological and mental preparation for the chosen treatments. Diet, physical exercise, psychology and co-existing conditions are all optimised. Mrs Smith feels a level of control that minimises her anxiety. She uses an individualised 'electronic health navigator' to guide her nutrition, exercise and psychology programme. All this occurs in parallel with the investigations and chemoradiotherapy for the cancer. Following surgery, Mrs Smith is prepared for the expectation that she will drink, eat and mobilise the same day, and is discharged from hospital only 2 days after her operation. Her 'electronic health navigator' guides her recovery phase, and 6 weeks later she returns to her baseline level of function, both physically and mentally.

Although each of the elements of care described in this vignette have been implemented in isolation, very few hospitals are close to the effective integration of all of these components, and reliable consistent global delivery of this 'ideal pathway' will take time, ambition and an openness to change traditional ways of working.

Towards the end of the 20th century, patients were referred by their general practitioner to a consultant surgeon, listed for surgery and then admitted the day before surgery to allow the 'houseman' to perform investigations and to be seen by the consultant anaesthetist. Consent for surgery was obtained by whichever member of the surgical team was available, typically the most junior doctor, and often on the morning of surgery. Many operations in high-risk patients were cancelled on the day of surgery due to lack of fitness/preparation; many others proceeded without adequate risk assessment, discussion or modification. Many patients suffered complications, including death, following surgery. To try to reduce the risk of mortality and morbidity, a handful of patients were sent to the limited number of intensive care beds available for postoperative care. Augmented postoperative care outside intensive care was uncommon – most patients went straight to the general ward following a short stay in recovery.

In 1987, Shoemaker demonstrated that high-risk surgical patients could be optimised in critical care in the immediate pre-operative period [1]. Even though this novel concept was not widely adopted, it demonstrated that pre-operative strategies could be implemented that would improve surgical outcome. In 1993, Older provided us with

evidence that poor physical fitness, as demonstrated by cardiopulmonary exercise testing, was associated with adverse outcomes following surgery [2]: more than 40 research publications [cited in 2–4], culminating in the recent METS study [5], have reinforced this observation. Around the same time, Kehlet et al. were developing the concept of enhanced recovery after surgery, which has subsequently transformed surgical care worldwide, most notably in a national implementation project in the UK [6]. Enhanced recovery has led to standardisation and streamlining of immediate peri-operative processes with enormous patient benefit. Peri-operative medicine has built on this and is now widely understood to encompass the patient-centred, multidisciplinary and integrated medical care of patients from the moment of contemplation of surgery until full recovery [7]; it embraces collaborative decision-making, prehabilitation, proactive management of comorbidities and individualised postoperative care. Peri-operative care has come of age.

In 2001, the Association of Anaesthetists published its first 'glossy' on the role of the anaesthetist in pre-operative assessment [8]. The content encompassed: identifying potential anaesthetic difficulties and pre-existing medical conditions; improving safety by assessing and quantifying risk; planning of peri-operative care; and providing an opportunity for explanation, discussion and reassurance. The concept of optimising outcome through pre-operative interventions was mentioned, albeit only as a potential opportunity. Updated Association of Anaesthetists guidance published in 2010 highlighted the importance of informed consent as well as management of comorbidities and discharge planning [9]. In the meantime, the parallel development of enhanced recovery was breaking down barriers and eroding the 'silo mentality', bringing teams together to plan and deliver coordinated peri-operative care, with the main focus being on in-hospital care. By 2015, the Royal College of Anaesthetists had embraced peri-operative medicine and committed to developing a collaborative programme for the delivery of peri-operative care across the UK [10]. Although each of these developments has contributed to improving the care of patients around the time of surgery, it is only relatively recently that working with patients pre-operatively, with the aim of enhancing their physical, physiological and psychological resilience to the pathological challenges of surgery, has been considered within the remit of anaesthetists and peri-operative physicians. Intervening to improve immediate peri-operative outcomes, as well as potentially achieve longer term behavioural change, opens new opportunities for anaesthetists to improve public/population health outcomes and improve value. This supplement brings together contributions from expert authors from around the world to provide a 'state of the art' summary of prehabilitation in relation to surgery and the role of anaesthetists in improving patient care through this means.

Carlisle has discussed risk, but has given it a slant that is from the patient's perspective [11]. His arguments demonstrate that it is necessary to look at the extra burden of risk to that patient at that particular age of their life, rather than just looking at population outcome. The review by Sturgess et al. on shared decision-making explores the changing world of consent before surgery [12]. This international team of authors discuss the landmark cases that have ingrained shared decision-making into medical practice and demonstrate its need to protect and promote patient autonomy.

The research literature demonstrates that poor functional fitness has an impact on postoperative outcome; pre-operative optimisation aims to overcome this burden. Pre-operative optimisation of the high-risk elective surgical patient includes both lifestyle modification and medical optimisation of comorbidity. Prehabilitation is the term adopted by the McGill group to describe the identification of impairments of the patient who is being considered for major surgery, and then provide interventions that promote physical, metabolic and psychological health to reduce the incidence and/or severity of these impairments [13]. Prehabilitation has until recently only included physical fitness training, improving nutritional status and psychological robustness. However, it is being increasingly recognised that lifestyle modifications also extend to smoking cessation [14]. Furthermore, many of these interventions, as well as improving surgical outcome, may also improve the general health of the patient. The time before surgery is seen as a 'teachable moment' [15], as patients are more amenable to lifestyle modifications if they can see and gain the immediate benefit of their lifestyle changes. This supplement therefore has contributions covering multi-modal prehabilitation; as well as pre-operative optimisation of physical, [13] respiratory function, [14] nutritional, [16] and psychological status [17].

As well as optimising pyscho-social factors before elective surgery, patients with comorbidity need their existing diseases to be optimised. For some patients this may include screening for undiagnosed disorders. There is now irrefutable evidence that patients with undiagnosed/undertreated diabetes and undiagnosed/undertreated anaemia have worse outcomes and there is now a growing body of evidence to support the identification and

treatment of these two common conditions [18, 19]. This too is discussed in the relevant reviews in this supplement.

The review by Lee et al. discusses the advances in optimisation of the patient with cardiac disease and provides an excellent summary of the current peri-operative management of diagnosed and undiagnosed hypertension, chronic heart failure and implantable devices [20].

The elderly patient presenting for surgery is becoming more common. Not only do older people have co-existing morbidity, they often have multimorbidity with accompanying polypharmacy. In addition they may be frail, which is a recognised risk factor for a worse surgical outcome. Frailty as a distinct disease entity was only defined in 2001. The review by Chan et al. highlights the collaborative interventions that can, and should, be implemented to improve outcome in elderly patients, and reduce the risk of problems from malnutrition and cognitive impairment [21]. The authors also rightly highlight the need for patient-accessible, individualised risk assessment, and further support the approach and advice of Carlisle and Sturgess et al. [11, 12].

The first 10 reviews of this supplement discuss the medical and psychosocial interventions and optimisations that can be implemented pre-operatively, and clearly document the evolution of the pre-operative assessment clinic with a narrow remit into the collaborative pre-operative clinic practising holistic peri-operative medicine. However, for these interventions to be introduced in a timely manner it is necessary to rethink the classical patient pathway, and thus the review on how the patient pathway can be re-engineered to facilitate timely intervention [22]. As well as the need to update the elective care surgical pathway, there is the need to re-engineer the pathway for the emergency surgical patient. The article by Poulton et al. discusses this, as well as the need and the mechanisms available to optimise the pathology and comorbidity of the emergency patient effectively within the limited time available [23].

The interventions proposed by the authors of this supplement are evidence-based and are achievable in most healthcare systems. They are standards of care that these authors would wish for themselves, their family and their patients. So why is the delivery of these interventions so sporadic and variable? The evidence base, while still very new and of modest depth, is developing very rapidly. Resource limitation in the aftermath of the global financial crisis can not only make change challenging but also offers opportunities if improved value can be demonstrated. Professional conservatism rightly resists fads, but may delay implementation of beneficial innovations. Variation in the implementation of effective care is increasingly being challenged, most notably through programmes such as the *'Getting it Right First Time'* initiative in the UK. The minimisation of unwarranted variation through a culture of continuous improvement is a critical driver for the ongoing delivery of improving peri-operative care for patients.

Peri-operative medicine is first and foremost about improving the care of patients to maximise quality and quality of life. Pre-operative patient optimisation is the vital component that empowers patients and doctors to achieve this goal. Who would argue with an approach that allows us to contribute at one and the same time to enhanced surgical outcomes, better value for money and improved public health?

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Review Article

Risk prediction models for major surgery: composing a new tune

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Summary

In this paper I explain why I think that most of the models that predict postoperative mortality should not be used when we're talking to patients about postoperative survival. Available models are isolated in time (from survival in the present) and space (from survival outside hospital). We know a lot about survival outside hospitals, with sufficient detail that we can discriminate between a man born in 1975 vs. 1976, or a woman aged 64 years vs. 65 years. We can use survival outside hospitals to inform what we do in hospital. I use my own survival to contrast with the survival of people older or younger than me. I will use my survival to illustrate how I might expect my mortality hazard to temporarily change when I have a scheduled operation (total hip replacement) and when I'm unwell and have an operation (for a fractured femoral neck). People live longer and longer and we operate on people older and older. We are also intervening earlier in progressive diseases, knowing that people are living long enough to experience harm from their progression. There is an evolving conflict between operating on older people and operating on younger people. Who has most to gain from the operation and who has most to gain from peri-operative critical care? Do we prioritise on reducing death now, in patients with relatively short life expectancies, or do we invest in the long-term survival of patients with relatively low rates of dying now? This conundrum is not informed by current risk models, with their focus on one to three postoperative months: we need to know survival outside hospital to gauge the value of what we do in hospital.

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'Indicate precisely what you mean to say'[1]

It is time to face the music. Any peri-operative risk prediction model that reports odds ratios, risk ratios or their coefficients is unfit to inform pre-operative discussions with patients. Peri-operative models were developed to 'audit surgical practice': they cannot tell patients how the probabilities of outcomes change during the months and years that follow an operation, or the months and years after deciding not to have an operation. They are the wrong tools for the pre-operative assessment consultation.

I am 51 years old. I was born in March 1967, a year when '*A Whiter Shade of Pale*' by Procol Harum topped the charts and the band Fleetwood Mac formed. Ten years later Fleetwood Mac released the chart-topping album '*Rumours*' and I was safe, safer than I have ever been. In 1977, my 1967 male cohort enjoyed its lowest mortality hazard (the risk of an individual dying during a particular period) ever; 28 per 100,000 per year. In the years since '*The Chain*' was released my rate of dying has accelerated, with my mortality hazard doubling every 12 years: 56 per 100,000, aged 22 in 1989 ('*The Seeds of Love*', Tears for Fears); 117 per 100,000, aged 34 in 2001 ('*White Ladder*', David Gray); 236 per 100,000, aged 46 in 2013 ('*Jake Bugg*',

[1] *'When I'm Sixty Four'*, The Beatles, 1967.

Jake Bugg) and, now, aged 51 with a mortality hazard 328 per 100,000, music is just not what it was (*'The Greatest Showman'*, original motion picture soundtrack) (Fig. 1) [1]. The doubling of my mortality hazard every 12 years is described as a hazard ratio of two. The annual mortality hazard ratio is 1.06, that is, ageing by 1 year causes a relative increase in mortality hazard of 6%. Multiply 1.06 by itself 11 times (1.06 exponent 12) gives a value of 2.01, the hazard ratio for a span of 12 years. The hazard ratios for (any) month, week and day are 1.0048 (0.48%), 1.0011 (0.11%) and 1.00016 (0.016%), respectively. By 2054, I will have accumulated – since birth – half a chance of achieving terminal velocity: half the boys who 'skipped the light fandango' will be dead and half will be alive, aged 87.

You will not share my musical heritage if you were not born in 1967, but your birth cohort does have one thing in common with 'the class of 1967', which is that your cohort has the same pattern of mortality hazard, falling from birth to a nadir between 10 years and 15 years of age, followed by the same pitiless escalation of hazard. On a cheerier note – at least to those born after me – mortality hazards have fallen year-on-year for all ages: I can scare my daughter (and myself) with her mortality hazard at 10 years of age of 6 per 100,000 this year (2019), one-fifth of my mortality hazard at the same age in 1977. Had my daughter been a boy his mortality hazard would be 8 per 100,000, and had I been a girl my mortality hazard would have increased from 21 per 100,000 aged 10 in 1977 to 221 per 100,000 now. The increasing mortality hazard after the age of 10 is a combination of external causes, such as injury and poisoning, as well as internal causes, such as atherosclerosis and cancer [2]. The external causes dominate up to the age of 50, but with increasingly chronic characteristics, for instance acute alcohol poisoning being replaced by liver cirrhosis. Most of our deaths chronicle cellular 'wear and tear', the accumulation of genotypic and phenotypic defects that cause cancer (exemplified by breast cancer in middle-aged women), atherosclerosis, the dominant cause of death in men, and dementia, the dominant cause of death after 80 years of age. Our increasing internal fragility is accompanied by an increasing vulnerability to our environment, for instance viral and bacterial infections, as well as trauma, whether accidental or intentional. Scheduled operations are equivalent to road traffic collisions – of varying severities – and emergency operations are their equivalent while septic, conferring a fivefold mortality on top of the hazard of scheduled surgery (personal observation).

I have never had an operation. My first operation is likely to be the replacement of my left hip joint, having been diagnosed with Legg–Calvé–Perthes disease when I was a limping 7 year-old in 1974 (*'The Dark Side of the Moon'*, Pink Floyd). Let us suppose that I survive to when my symptoms persuade me to elect hip replacement – say at 70 years of age in 2037. My (male) cohort's mortality hazard will be 944 per 100,000 per year, or 80 per 100,000 per month (0.08%). Scheduled hip joint replacement, like any other operation, temporarily increases mortality, which subsides towards the pre-operative hazard within one or two months after most operations. In 2037, we will expect 160 per 100,000 men (0.16%) aged 70 years to die in the month after hip replacement, surgery having temporarily doubled mortality. When the day comes for my hip replacement in 2037 I will hobble into the hospital with my – literally – vital statistics; the mortality hazard of a man born in 1967. But which man? My cohort's monthly mortality hazard of 80 per 100,000 is an average figure. There are measurable factors that influence this, for better or worse. I am a privileged, healthy and relatively wealthy man, factors that make my current monthly mortality hazard of around 20 per 100,000 less than that of most other men from 1967. If I maintain my relative health and wealth my pre-operative monthly mortality in 2037 will be 44 per 100,000, increasing to 88 per 100,000 (0.088%) in the first postoperative month. This compares with 300 deaths per 100,000 (0.3%) in the month after hip replacements for men aged 70 years now, in 2019.

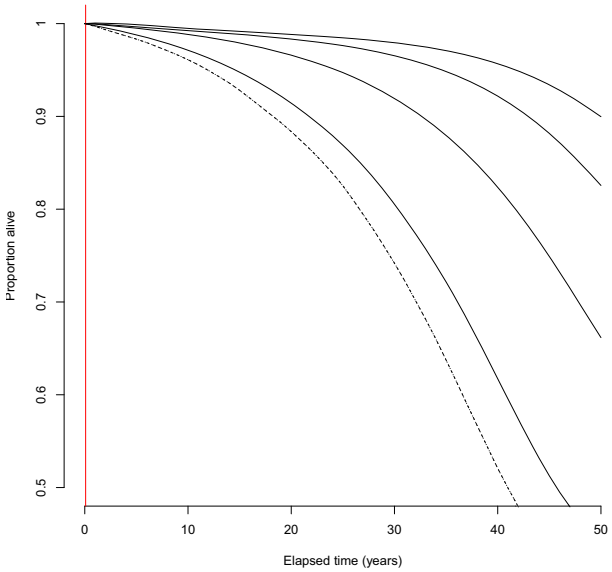

Figure 1 Survival curves for my male cohort, born 1967, when we were aged 10 years, 22 years, 34 years and 46 years (——) and now, in 2019, aged 51 years (·····). The vertical red line indicates ageing during 1 month of elapsed time, a brief period that has little power to detect the differences in survival.

It is better to have one's operation electively; 1500 deaths per 100,000 (1.5%) would be expected for 70-year-old men in the first month after arthroplasty for fractured neck of femur in 2019, five-fold the rate for an equivalent scheduled operation.

By 2037, men born in 1967 will have accumulated sufficient wear and tear that 10% of us will be labelled with pathological cardiovascular phenotypes: myocardial infarction; stroke; peripheral arterial disease; and heart failure. The ravages of time on blood results and physical fitness will reduce eGFR, haemoglobin concentration, albumin concentration, peak oxygen consumption and gas exchange. The average values of these variables are already accommodated within the mortality for my cohort: in effect, the 'average 70-year-old man' will have had 1/10th of a major cardiovascular event and he will possess the average blood results and fitness for his age. Age is a marvellous and powerful descriptor of mortality hazard, for it chronicles the overt phenotypic changes and, more importantly, the covert changes, 'wrinkles on the inside'. When we are tempted to add some variable to predict peri-operative outcome, it should always be normalised to the year, age and sex of the cohort (see below).

Peri-operative scoring systems do not report hazard ratios. Instead they report odds ratios (or their coefficients). I imagine you might say 'So what?', but a better question would be 'So why?' The cardiologists, surgeons and anaesthetists who have developed peri-operative scoring systems have not used Big Demographic Data from the populations of nations. It is as if patients who have surgery are alien; alien from people, like me, who have never had an operation and alien from themselves, after the peri-operative period is done. The alienation of peri-operative researchers from what goes on outside surgical wards has flawed their products, generating problems we are appreciating only now that pre-operative assessment clinics and shared decision-making have become popular. The myopic gaze of peri-operative scoring systems focuses on events 30 days or 90 days after surgery, periods so short that deaths on the first and ninetieth day are treated as equivalent: survival is a binary affair of being alive or dead at the end of follow-up, which is why the associations of peri-operative factors with outcome are expressed as odds ratios. Peri-operative myopia blurs the estimation of how a factor and outcome are associated; discrimination is relatively poor. The derivation populations for peri-operative scoring systems are small, numbering between 5000 and 70,000 patients, observed for 5–90 postoperative days, as opposed to the populations of nations observed for decades. Events are necessarily rare in the brief glimpses of people's lives afforded by peri-operative studies. Mortality in the month after repair of fractured neck of femur is about 5%, a rate higher than most peri-operative populations: in a derivation cohort, 316 out of 6317 patients died within 1 month of surgery [3]. Compare this with the 1.5 million deaths, recorded over 3 years, that contribute to the UK Office for National Statistics life tables. It is no surprise that peri-operative models cannot discriminate between people of different ages: instead, patients are grouped into epochs, for instance < 65 years, 65–79 years and > 79 years.

Studies that observe survival for years, postoperative or otherwise, have enough power to discriminate different mortality hazards, and they usually report hazard ratios between 1.075 and 1.11 for patients 1 year older than other patients. These hazard ratios are larger than 1.06, the annual hazard ratio that rules our increasing mortality. The differences seem inconsequential, but over 24 years, during which my mortality hazard should quadruple, hazard ratios of 1.075 and 1.11 would multiply my mortality hazard by 5.7 and 12.2, respectively. What are these hazard ratios measuring? Recall that my daughter's annual mortality hazard is one-fifth the mortality hazard I had aged 10 years, partly because mortality hazards are less for girls and women, but mainly because life has become safer to the relative tune of 2% per annum for the last few decades (although that might be changing). A study of people recruited in a single year will report a mortality hazard ratio of 1.08 for patients 1 year older, that is, 1.06×1.02, because there is risk from being 1 year older (1.06) and risk from being born 1 year earlier (1.02). The hazard ratio reported by a study will depend upon when people of different ages were recruited: for instance, the mortality hazard ratio of a man aged 75 years, recruited at the beginning of a study, vs. a man aged 74 years recruited 5 years later, would be 1.15 (i.e. $1.06 \times 1.02 \times 1.02 \times 1.02 \times 1.02$), rather than 1.08.

My preoccupation with hazard ratios might not excite you as much as the bass riff from *The Chain*, but the consequences of their misinterpretation may be profound. One of the most common errors is to misattribute reductions in postoperative mortality to changes in peri-operative care, rather than changes in the patients. For example, the authors of a paper published in the *New England Journal of Medicine* reported survival after repair of intact abdominal aortic aneurysm from 2001 to 2008 in 79,932 patients: '*The decline in perioperative mortality probably represents operators' increased familiarity with the procedure.*' and '*It is unlikely, however, that this reduction in peri-operative mortality is driven by improved*

patient selection, because most patients are now treated with the use of endovascular repair, and mortality after open repair was reduced over this period as well.' [4]. And yet, the 4-year survival curves in their Fig. 1b, contrasting better survival in patients who had surgery 2005–2008 vs. 2001–2004, are exactly matched by patient characteristics coming into hospital, without recourse to doctors or hospitals doing anything better [5]. I admit that it is easy to make such a mistake; for several years I unnecessarily alarmed audiences whose mortality hazards doubled every 12 years by incorrectly saying the hazard doubled every 7 years (calculated with an annual hazard ratio of 1.1 instead of 1.06)!

The conflation of the hazard from one variable with the hazard from another variable is not confined to age and time. There are a host of age-related changes to which authors may assign the wrong hazard because the hazard of age has been incorrectly assigned to those covariates in multivariable analyses. For instance, physical fitness declines with age: between the age of 20 years and 90 years a man's peak oxygen consumption declines from around 58 $ml.kg^{-1}.min^{-1}$ to 13 $ml.kg^{-1}.min^{-1}$ (0.64 $ml.kg^{-1}.min^{-1}.year^{-1}$), while gas exchange deteriorates, with the ventilatory equivalent for carbon dioxide increasing from 23 to 32 (0.13.yr^{-1}). At a given age more fit men have a lower mortality hazard than less fit – but otherwise equivalent – men, with a hazard ratio of 1.04 for each decrement of 0.64 ml $O_2.kg^{-1}.min^{-1}$ and a hazard ratio of 1.05 for each unit increment in ventilatory equivalent (the caveat is that these values might be a by-product of the problem discussed in this paragraph) [6, 7]. For instance, consider two similar men aged 51 years, one more fit than the other: 'fit' John, with a peak oxygen consumption of 47 $ml.kg^{-1}.min^{-1}$ and ventilatory equivalents of 27; and 'unfit' Bernard, with a peak oxygen consumption of 15 $ml.kg^{-1}.min^{-1}$ and ventilatory equivalents of 35. Bernard has a higher mortality hazard than John, due to a lower peak oxygen consumption (1.04 exponent 32 = 3.58) and higher ventilatory equivalent (1.05 exponent eight = 1.56). The product of 3.58 × 1.56, which is 5.30, is how many times more Bernard's mortality hazard is than John's mortality hazard. Following the same logic, the reduction in peak oxygen consumption between the ages of 20 years and 90 years incurs a mortality hazard ratio of 6.02 and the reduction in gas exchange incurs a mortality hazard ratio of 1.56, the product of which is 9.39: the reduction in fitness over 70 years incurs almost a 10-fold increase in mortality hazard. How does this compare with the overall increase in mortality hazard during 70 years of life? The annual hazard ratio is 1.06, which over 70 years accumulates a hazard ratio of 59, that is, fitness 'accounts' for 1/6 of the mortality associated with ageing. The mortality hazard ratio associated with being less fit at a given age is different to the hazard ratio associated with the same reduction in fitness due to ageing, that is, ageing is not just being less fit (surprise). In multivariate analyses, age will 'explain' changes in survival with ageing, while fitness will 'explain' changes in survival with ageing and fitness. Fitness will trump age mathematically to an extent that might completely remove age as an independent 'predictive' variable, even though fitness can explain only one-sixth of the increase in mortality that accompanies ageing. This problem is exacerbated by the sampling of multiple birth cohorts in cross-sectional studies, as 'age' will be a composite of the hazard of ageing and the hazard of having been born in a preceding year (Fig. 2).

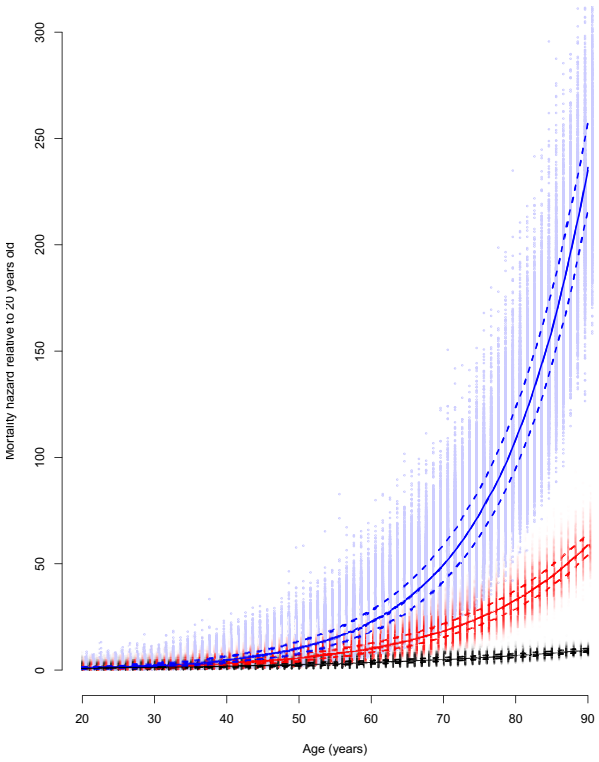

Figure 2 Increasing longitudinal mortality hazard as a person ages from 20 years old to 90 years old and the cohort declines from 341,000, aged 20 years, to 130,000, aged 90 years (red and black symbols). The red symbols indicate the 59-fold increase in mortality hazard over 70 years: median (—); interquartile range (- - - -); and all values (○). The black symbols indicate the nine-fold increase in mortality hazard associated with decreased physical fitness. Most peri-operative mortality models compare survival in a cross-sectional cohort, with 90 year-old individuals being born 70 years before 20 year-old individuals, with higher mortality hazards being associated with historical cohorts as well as older age (blue symbols).

The function of all organs and systems wane with age and all their measurements are prone to the conflation of their prognostic value at a given age and the prognostic value of ageing. Almost every variable you see listed in prognostic tables may have their hazard ratios (or odds ratios) distorted by their covariance with age and with each other, whether the measure be fitness, cognition, renal function, muscle volume, immunocompetence or concentrations of albumin or haemoglobin.

You might say 'This problem doesn't matter because I'm only interested in the performance of the model, that is whether it can order people correctly in a hazard scale (discrimination, horizontal axis) and scale the hazard correctly (calibration, vertical axis).' But such nonchalance messes up both research and practice. Interventions that improve general survival will also improve peri-operative survival: more exercise; less smoking; less alcohol consumption; a balanced diet; and some pills but not others. The sample sizes for randomised controlled peri-operative trials, designed to test such interventions, will be based on observational data (probably limited to peri-operative cohorts, although as I have discussed I think that large studies in the general population are more useful). These trials will recruit too few patients if the associations of mortality (and other outcomes) with birth cohort and age are mistaken as associations with fitness or anaemia, etc. Standard peri-operative models, such as APACHE, POSSUM, NHFS, EuroSCORE and SORT, do not incorporate the steady reduction in population mortality, which is why they increasingly overestimate mortality with time, and predictably they are revised as sequential iterations, from 'Mark B' to 'Mark Z' [3, 8–19]. The 'new' model is out-of-date as soon as it is published. Perhaps discrimination (the odds ratio or hazard ratio), which is not affected much by the passage of time, is valued more than calibration (the odds or the hazard): all iterations correctly predict that older, sicker adults are more likely to die (true since the Stone Age), but the predicted mortalities are incorrect. Preserved discrimination might result in patients most likely to die being assigned postoperative critical care, but miscalibration will misinform consent and it will generate the hubris of an observed mortality less than predicted, 'Whatever it is we're doing, it's clearly working!'

Living longer is an inflationary pressure: it changes how models perform, unless they accommodate the inflation, and it should change what we do. Patients live longer after surgery than in the past. The benefit of prophylactic treatment for a disease that is likely to compromise survival or quality of life increases with each passing year, as people live longer, whether the disease is hypertension, smoking, colorectal cancer, osteoarthritis or abdominal aortic aneurysm. Survival inflation affects two thresholds at which the balance of benefit and harm tips towards treatment. The age threshold is increased – we will be operating on older people. The pathology threshold is decreased – we will be operating on people with milder disease, if we can confidently anticipate its progression, and if the intervention is effective and durable. These two thresholds are potentially at odds with each other, because milder forms of a progressive pathology occur in younger people. How carefully should we look after patients with a low rate of peri-operative mortality, but with a long median life expectancy, for instance a 62-year-old woman having a hemicolectomy with a 330 per 100,000 (0.3%) chance of dying in the first postoperative month and a 27-year median postoperative life expectancy? Or a 63-year-old man with a 48-mm-diameter abdominal aortic aneurysm, with a 670 per 100,000 (0.7%) chance of dying in the first month after endovascular repair and a median postoperative life expectancy of 17 years (but 9 years without repair)? How should we invest in their peri-operative care, compared with patients who have a 3-year median life expectancy and a 10,000 per 100,000 (10%) chance of dying in the first postoperative month? I am worried that we will be so busy looking after the dying that we will forget to look after the living. Traditional peri-operative mortality models cannot comment on this conundrum, but models of survival could help us balance how we invest our resources; who we operate on and how.

'Yours sincerely, wasting away'[1]

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Review Article

Optimisation of pre-operative anaemia in patients before elective major surgery – why, who, when and how?

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Summary

Anaemia in surgical patients is a common and serious problem; around 40% of patients presenting for major surgery are anaemic. Patients with pre-operative anaemia have significantly higher rates of morbidity and mortality and are likely to be transfused red cells. In addition, red cell transfusions are independently associated with worse outcomes. Pre-optimisation of anaemia in surgical patients leads to higher pre-operative haemoglobin concentrations and less need for transfusion. Patients undergoing major surgery (defined as blood loss > 500 ml expected or possible) should be optimised if their haemoglobin concentration is less than 130 $g.l^{-1}$ on screening. Detection of anaemia should follow listing for surgery as soon as possible to allow enough time for optimisation. The most common cause of pre-operative anaemia is iron deficiency, which can be treated with iron therapy. Iron clinics should be set up in either primary or secondary care to allow for optimal treatment. In this review, we present literature supporting the optimisation of pre-operative anaemia and propose a treatment algorithm.

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Introduction

The World Health Organization (WHO) states that every reasonable measure should be taken to optimise the surgical patient's own blood volume using a patient blood management (PBM) approach [1]. Multiple guidelines have been developed to support hospitals in the implementation of patient blood management, including the management and optimisation of pre-operative anaemia [2–6] and cell salvage [7]. Patient blood management has been shown to improve outcomes and reduce healthcare costs in a number of studies. In total knee and hip arthroplasty [8–10] and cardiac surgery [11], implementation of patient blood management has been shown to lead to a reduction in transfusion, hospital stay, morbidity and re-admission to hospital. One prospective multi-centre study evaluated the safety of a hospital-wide implementation of patient blood management; 54,513 patients before patient blood management implementation were compared with 75,206 patients after patient blood management implementation, and patient blood management was shown to be non-inferior. Furthermore, acute renal failure and transfusion were reduced, the mean (SD) number of units transfused per patient being reduced from 1.21 (0.05) to 1.00 (0.05), a 17% relative reduction in the number of units of red cells transfused, $p < 0.001$) [12]. A large Australian study provided data on the implementation of patient blood management in four tertiary hospitals in 605,046 patients. A 5-year programme of implementation was initiated and the final year was compared with the baseline year with regard to red cell transfusion, haemoglobin concentration on admission, mortality and costs. The number of red cell transfusions decreased by 41% (RR (95%CI) 0.59 (0.58–0.60); $p < 0.001$) and fewer elective surgical patients were anaemic on admission (20.8% vs. 14.4%, $p = 0.001$).

Mortality decreased, with the adjusted odds ratio (95%CI) for death being 0.72 (0.67–0.77), $p < 0.001$, and costs were reduced by an estimated 100 million Australian dollars over 5 years [13].

Surgical patients with anaemia are at increased risk for morbidity and mortality and are likely to be transfused with red cells [14–17]. Red cell transfusion itself also increases morbidity and mortality [16–18]. Therefore, detection and treatment of pre-operative anaemia as part of patient blood management is crucial. In this review we discuss the practical management of pre-operative anaemia in surgical patients, targeting those undergoing major surgery where more than 500 ml blood loss is expected [5].

Why?

A significant proportion of patients are anaemic pre-operatively. An average of 39.1% of major surgical patients have pre-operative anaemia [16], the pre-valence ranging between 20 and 45% depending on the type of major surgery [19]. An increasing body of evidence has shown increased morbidity and mortality in patients with anaemia in most surgical specialties. Musallam et al. studied the prevalence and outcomes of anaemia in the dataset of the American College of Surgeons' National Surgical Quality Improvement Program (ACS NSQIP), a prospective validated outcomes registry from 211 hospitals worldwide including a wide variety of major surgical disciplines. A total of 227,425 patients were included and an increased risk of 30-day mortality and morbidity was found in patients with anaemia compared with non-anaemic patients [14]. The European Surgical Outcomes Study (EuSOS) dataset of 46,539 patients showed similar results for patients with pre-operative anaemia who underwent major surgery. Patients with moderate or severe pre-operative anaemia had higher in-hospital mortality, prolonged hospital stay and more intensive care admissions [15]. A recent meta-analysis included 24 observational studies (949,445 patients) which compared outcomes after major surgery, including cardiac surgery, in patients with and without pre-operative anaemia. Patients with pre-operative anaemia were at increased risk of major adverse outcomes including mortality, the OR (95% CI) being 2.90 (2.30–3.68); acute kidney injury, 3.75 (2.95–4.76); and infection 1.93 (1.17–3.18) [16]. In addition, the severity of pre-operative anaemia has also been shown to affect outcome. In cardiac surgery, haemoglobin concentration is linked to increased risk for red cell transfusion and morbidity and mortality. Any haemoglobin < 130 $g.l^{-1}$ is associated with worse outcomes, and a 10 $g.l^{-1}$ decrease in haemoglobin is associated with a 43% (95%CI 40–46%) increased risk for red cell transfusion and a 16% (10–22%) increase in mortality [17].

In surgical patients, red cell transfusion is associated with an independent increase in worse outcomes. A large study used propensity matching within the dataset of the ACS NSQIP to compare the effect of red cell transfusion. Higher rates of morbidity and mortality were found in patients receiving one unit of red cells compared with patients who were not transfused [18].

At present, the evidence that active management of pre-operative anaemia reduces peri-operative morbidity and mortality is limited; however, a number of major randomised controlled trials (RCT) are in progress [20–24]. To date, no large high-quality trials have been published comparing treatment of pre-operative anaemia with standard care/placebo, leaving us with only indirect evidence. Many studies have shown an increase in haemoglobin and a decrease in red cell transfusion when iron deficiency anaemia is treated with iron therapy [2]; the effect on other patient outcomes is awaited.

Iron deficiency anaemia is the most common type of anaemia both worldwide [25] and in the surgical population [26]. In a study of 3342 patients (44.5% of whom were women) scheduled for orthopaedic surgery, cardiac surgery, colorectal cancer resection, radical prostatectomy and gynaecological surgery, 36% of patients were anaemic and of those 62% had absolute iron deficiency anaemia and 10% had anaemia with iron sequestration [27].

The National Institute for Health and Care Excellence (NICE) recently published standards which state that patients undergoing major surgery and who have pre-operative anaemia and iron deficiency should be offered iron therapy [2]. In the general population, evidence indicates a favourable effect of iron therapy in patients with iron deficiency anaemia without chronic kidney disease. The haemoglobin concentration increases in patients receiving either intravenous (i.v.) or oral iron (mean differences 3–30 $g.l^{-1}$ i.v. and 3–31 $g.l^{-1}$ oral respectively, both vs. inactive control) and fewer iron-treated patients receive red cell transfusion compared with inactive control [28]. The NICE guidelines on transfusion included five RCTs comparing i.v. iron with placebo [29–33] and two RCTs comparing oral iron with placebo [34, 35] in different types of surgery. Fewer anaemic patients were found to require red cell transfusion after treatment with iron [2]. Since then, more studies have been published supporting these conclusions [36–39]. No clear differences in other outcomes have been found so far. However, with the current evidence, a treatment impact of pre-operative

anaemia on clinical outcomes cannot be excluded and appropriate treatment of patients with pre-operative anaemia is indicated.

Who?

All patients for elective surgery in whom blood loss is expected to be > 500 ml should have their haemoglobin checked pre-operatively and be investigated if they are found to be anaemic. In the general population, anaemia is defined as a haemoglobin < 130 $g.l^{-1}$ in men and < 120 $g.l^{-1}$ in women by the WHO [40]. We have proposed that the cut-off value/trigger be changed to a haemoglobin > 130 $g.l^{-1}$ for both men and women. Women with haemoglobin levels between 120 and 129 $g.l^{-1}$ are not considered to be anaemic according to the WHO definition, leaving them at a potential disadvantage when undergoing major surgery [41]. These women will not undergo further investigation or treatment of their reduced haemoglobin, even though they are more likely to need peri-operative red cell transfusion due to their lower circulating volume, despite losing similar amounts of blood during surgery as men [42, 43]. A large multi-centre cardiac surgery study showed that, regardless of sex, lower haemoglobin was associated with increased transfusion requirements, prolonged hospital stay and higher mortality. Any reduction below 130 $g.l^{-1}$ was associated in a linear manner with worse outcomes [17]. Furthermore, women with haemoglobin levels between 120 and 129 $g.l^{-1}$ undergoing cardiac surgery are more likely to be transfused, and are transfused more units of red cells and stay longer in hospital [44]. Therefore, we propose a change in the trigger for the treatment of anaemia in women undergoing major surgery to haemoglobin < 130 $g.l^{-1}$ for both sexes [45].

Oncology

Red cell transfusion is associated with a negative impact on survival and tumour recurrence in patients undergoing oncological surgery. Cancer-related anaemia is common (39–54% of cancer patients) and is influenced by multiple factors; this includes a specific process in cancer-related anaemia which is a cytokine-mediated process leading to impaired iron utilisation through hepcidin upregulation, suppressed erythroid maturation and reduced erythropoietin production [46, 47]. Anaemia may shorten survival time in cancer patients [48] and worsen local tumour control [49]. In addition, meta-analyses in different types of cancer show that red cell transfusions increase the risk of tumour recurrence and decrease survival rates [50–56]. Pre-operative anaemia in patients for colorectal cancer surgery is common (30–67%) and is a cause for concern [49]. The mechanism for development of anaemia is often through ongoing tumour-induced blood loss and/or the mechanism mentioned above where increased cytokine activity induces decreased iron uptake and utilisation through hepcidin upregulation, also known as anaemia of chronic disease or anaemia of inflammation [57]. Anaemia also leads to tumour hypoxia in patients with cancer, which means that chemotherapy and radiotherapy have less impact, because oxygen is essential for the cytotoxic effects of these treatments [58–60]. A recent systematic review found that anaemic patients with rectal cancer have a worse overall survival and disease-free survival; results patients with colon cancer did not show worse overall for disease-free survival [52]. Transfusion of red cells is associated with increased all-cause mortality and cancer-related mortality [61] as well as increased recurrence of colorectal cancer [62]. Whether the relationship between anaemia, red cell transfusions and morbidity/mortality is the cause is unknown. Several studies investigating the effect of treatment of pre-operative anaemia have been published showing an increase in pre-operative haemoglobin after i.v. iron treatment [37, 63]. To date, no studies have been published investigating treatment of pre-operative anaemia on clinical outcomes in this group of patients.

Up to 50% of patients with gynaecological malignancies have anaemia. The most common causes in this patient group are: blood loss from the tumour; renal dysfunction secondary to platinum-based chemotherapy and marrow dysfunction from chemotherapy and/or radiotherapy [46]. Many patients have iron deficiency anaemia [64]. Several studies have shown that a preventive strategy of administering i.v. iron during chemotherapy increases haemoglobin concentration and reduces transfusion [65–67].

Orthopaedics

Orthopaedic surgery is one of the most appropriate clinical fields for optimisation of pre-operative anaemia [68]. Orthopaedic surgery is a field where blood loss is likely, especially during major joint replacements [42]. The prevalence of pre-operative anaemia is 15–40% [69]. An ageing population requires more hip and knee arthroplasties and even more revision procedures, which are accompanied by more blood loss and higher transfusion requirements [70]. The majority of surgery is elective and postponing surgery for optimisation of pre-operative anaemia is warranted. Several studies have shown improved haemoglobin and decreased need for red cell transfusions with treatment of pre-operative anaemia [38, 39, 71] and the implementation of a patient blood management programme [8, 9]. Therefore, patients

scheduled for major elective orthopaedic surgery should be optimised if they have pre-operative anaemia.

Cardiac surgery

Patients undergoing cardiac surgery are at particular risk of the consequences of pre-operative anaemia due to risk of peri-operative blood loss, their underlying cardiac condition and the haemodilution associated with cardiopulmonary bypass. In the UK, 23–45% of cardiac surgical patients have pre-operative anaemia [17]. Pre-operative anaemia is associated with worse outcomes [17, 72–75] and haemoglobin concentration is also independently associated with an increased risk of transfusion and mortality [17]. Furthermore, red cell transfusion is independently associated with a worse outcome [76] and optimisation of pre-operative anaemia leads to higher haemoglobin [77]. Whether treatment leads to prevention of worse outcomes is uncertain at this point, but two large trials are underway [21, 22]. Until then, it seems reasonable to start treatment of pre-operative anaemia in the cardiac surgical population because the potential for improvement is large.

Obstetrics

Lastly, pregnant women are of particular interest because anaemia is highly prevalent and a surgical intervention with concomitant blood loss (caesarean section or postpartum haemorrhage) is likely to result in transfusion if the woman is anaemic [78]. During pregnancy, physiological changes lead to a greater increase in plasma volume relative to the increase in haemoglobin mass, leading to a lower haemoglobin concentration. The definition for anaemia in pregnant women therefore differs from non-pregnant women, being haemoglobin < 110 g.l^{-1}, haemoglobin < 105 g.l^{-1} during the second and third trimesters, respectively and < 100 g.l^{-1} postpartum. Up to 30–40% of pregnant women have iron deficiency anaemia. Iron deficiency anaemia is associated with maternal and fetal morbidity. Systems for rapid investigation and treatment of anaemia in pregnancy should be available. Initial treatment is usually oral iron supplements [79]. However, if anaemia persists and oral iron is ineffective or not tolerated, i.v. iron administration is indicated.

When?

Detection of pre-operative anaemia should be carried out as soon as possible, at least 14 days before elective surgery [80] and preferably more than 30 days before surgery [68]. Patients at risk for moderate-to-high blood loss (> 500 ml) and > 10% chance of receiving red cell transfusion should be included for investigation of anaemia [5]. Laboratory investigations for the detection and diagnosis of anaemia should be performed directly after the decision to perform surgery. These laboratory investigations can be carried out in primary care or in the surgical outpatient clinic. Waiting until the pre-operative assessment/clinic is too late and causes an unnecessary delay. If anaemia is detected and treated in primary care, good communication between the general practitioner and the surgical team is essential to facilitate a timely and efficient approach. In the UK, patients have a median (IQR) period of 43 (16–94) days between listing and elective procedure and a median of 21 (IQR 10–49) days between pre-operative assessment and surgery. Patients undergoing elective orthopaedic surgery have the longest wait before surgery, and patients undergoing colorectal surgery the shortest, with a median of 15 days. Only 4% of patients undergo their procedure before the initial planned date [81]. Postponement of major, non-urgent surgery should be considered to allow the diagnosis and treatment of pre-operative anaemia [5].

A quick way to screen for anaemia is to use point-of-care testing with haemoglobin evaluation [82]. If anaemia (haemoglobin < 130 g.l^{-1}) is suggested using point-of-care testing, laboratory testing should follow; further evaluation should include full blood count, serum ferritin, transferrin saturation, vitamin B_{12} and folate, a marker of inflammation (e.g. serum C-reactive protein) and a marker of renal function (e.g. serum creatinine) [5].

How?

Iron deficiency anaemia has a complex origin, including nutritional deficiency and chronic inflammatory state resulting in absolute iron deficiency, functional iron deficiency or iron sequestration [83]. Absolute iron deficiency is a state where iron stores are severely decreased, resulting in anaemia. Functional iron deficiency, on the other hand, refers to insufficient iron mobilisation despite normal or elevated iron stores. Inflammation plays an important role in iron sequestration, where upregulation of hepcidin causes inhibition of intestinal iron absorption and increases iron sequestration in liver and macrophages, also known as anaemia of chronic disease. In Fig. 1, we propose a treatment algorithm for different types of anaemia from diagnosis to surgery based on a recent international consensus statement [5].

Treatment of iron deficiency anaemia should be carried out with iron supplementation, and there is good evidence that this results in higher haemoglobin concentrations, lower transfusion rates and better quality of life [2, 28, 84, 85]. When the interval between investigation and surgery

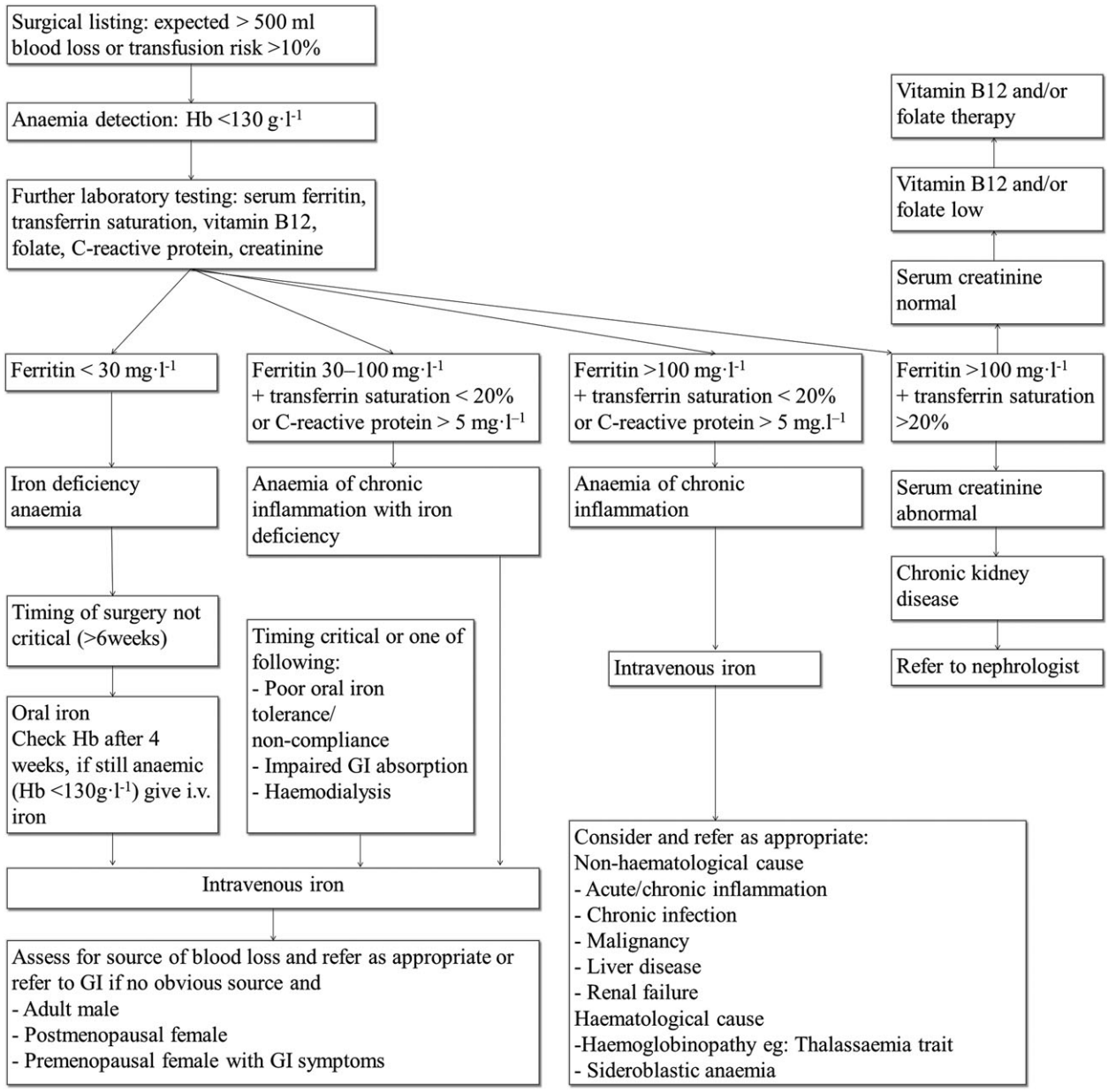

Figure 1 Treatment algorithm for pre-operative anaemia.

is sufficient (> 6 weeks), oral iron treatment may be considered [5]. Oral iron is cheap and both oral and i.v. iron increase haemoglobin concentration, whereas decreasing the need for red cell transfusion. Oral iron should be in the form of 40–60 mg elemental iron (one tablet or sachet) daily or 80–100 mg every other day [5]. A longer period of treatment is required for oral iron compared with i.v. iron and more side-effects occur [84]. Gastro-intestinal side-effects might lead to poor compliance with oral iron treatment. In practice, monitoring of efficacy for oral iron is recommended after 4 weeks of treatment. Intravenous iron is indicated if oral iron is poorly tolerated, is ineffective (no increase in haemoglobin after 4 weeks), if there is insufficient time until surgery (< 6 weeks), or in case of functional iron deficiency [2, 5, 86].

Intravenous iron is a relatively safe treatment [87, 88]. A large systematic review was published in 2015 reviewing 103 trials comparing i.v. iron with placebo, no iron, oral iron or intramuscular iron. The trials were searched for the outcome of severe adverse events, such as infections and infusion, cardiovascular, neurological, respiratory, gastro-intestinal, thromboembolic and constitutional severe reactions. A total of 10,390 out of 19,253 patients received i.v. iron treatment. There was no increased risk of severe

adverse effects with i.v. iron, the relative risk (95%CI) being 1.04 (0.93–1.17). The one concern that was identified was a possible association between i.v. iron and infection, with a relative risk (95%CI) of 2.47 (1.43–4.28). However, only one type of i.v. iron preparation (ferric gluconate) had a significant increased risk when analysed separately. No death or case of anaphylaxis was reported by any trial [87]. Anaphylaxis as a complication of i.v. iron therapy has only been reported in spontaneous postmarketing reports and the total number of life-threatening and fatal events reported is very low. Provided that adequate measures are taken, the benefits of i.v. iron significantly outweigh the risks [89].

Iron clinics may be set up either in primary or secondary care to provide i.v. iron for patients with pre-operative anaemia. However, patients need to be monitored (oxygen saturation, heart rate and non-invasive blood pressure) during iron infusion (which can normally be administered in 15–30 min) and for 30 min afterwards; resuscitation equipment and trained personnel should also be available. This often means a secondary care environment is chosen, as such monitoring facilities are not common in primary care in the UK. However, some primary care commissioners have set up local services, including a mobile i.v. iron service in Norfolk (http://www.norfolkcommunityhealthandcare.nhs.uk/The-care-we-offer/Service-search/intravenous-therapy.htm).

Routine use of erythropoietin is not recommended; it is not licensed for this indication in the UK. Although erythropoietin reduces the number of transfused patients, number of red cell transfusions, and the length of hospital stay, it potentially increases the risk of thrombosis and mortality [90]. The risks of erythropoietin therapy appear to outweigh the benefits, but erythropoietin should only be considered in patients with pre-operative anaemia who refuse red cell transfusions (Jehovah's Witnesses [91]) or if the appropriate blood type for transfusion is not available [2].

The efficacy and safety in diagnosing and treating pre-operative anaemia should be evaluated yearly by collecting and presenting appropriate data. We recommend the following data should be collected: proportion of patients having surgery with treatable anaemia uncorrected; proportion of patients having surgery with treatable anaemia corrected; transfusion rate for surgical patients (pre-operative, intra-operative, postoperative); cancellation rate (due to anaemia); i.v. iron infusion reactions; transfusion reactions; length of hospital stay; readmission rate within 30 days and patient experience.

The future

The increased risk of morbidity/mortality due to anaemia before major surgery is well established [14–16] and awareness for pre-operative anaemia has been created through guidelines underlining the importance of optimisation through patient blood management [2–6]. It seems rational to optimise haemoglobin concentration in patients with pre-operative anaemia before undergoing major surgery. There is good evidence that iron therapy in the pre-operative period increases haemoglobin concentration and reduces transfusion. However, to date, no definitive trials have been published that show an impact on morbidity and/or mortality. Despite this, many national bodies recommend active treatment of iron deficiency anaemia with iron, and it has been a NICE quality standard of care in the UK National Health Service since 2017 [80]. The outcomes of ongoing major randomised controlled trials are keenly awaited.

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Review Article

Pre-operative nutrition and the elective surgical patient: why, how and what?

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Summary

Pre-operative nutrition therapy is increasingly recognised as an essential component of surgical care. The present review has been formatted using Simon Sinek's Golden Circle approach to explain 'why' avoiding pre-operative malnutrition and supporting protein anabolism are important goals for the elective surgical patient, 'how' peri-operative malnutrition develops leading in part to a requirement for pre-operative anabolic preparation, and 'what' can be done to avoid pre-operative malnutrition and support anabolism for optimal recovery.

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Introduction

In the peri-operative period, the primary nutrition goals are to evaluate the patient for pre-existing malnutrition, treat malnutrition to optimise surgical readiness, minimise starvation, prevent postoperative malnutrition, and support anabolism for recovery [1]. Although additional nutritional considerations will be required for surgical subspecialities and to provide personalised patient care, these basic nutrition principles hold true for all cases. Our paper uses Simon Sinek's Golden Circle approach [2] to apply these basic surgical nutrition principles to the pre-operative period, largely focusing on elective abdominal surgery.

Surgical stress response

An understanding of the surgical stress response is essential to understanding the role nutrition plays in promoting optimal surgical recovery. Surgical trauma induces a state of metabolic activation (the surgical stress response) that parallels the extent of injury, and which is characterised by hormonal, haematological, metabolic and immunological changes [1, 2]. The surgical stress response is clinically manifested as salt and water retention to maintain plasma volume; increased cardiac output and oxygen consumption to maintain systemic delivery of nutrient and oxygen-rich blood; and mobilisation of energy reserves (glycogen, adipose, lean body mass) to maintain energy processes, repair tissues and synthesise proteins involved in the immune response [2].

Nutritionally-relevant clinical consequences of the surgical stress response include hyperglycaemia and whole-body protein catabolism [1, 2]. Catabolism manifests clinically as the wasting of lean tissue, including muscle, and largely occurs due to a reprioritisation; lean mass is mobilised, releasing amino acids into circulation for preferential uptake by the liver to allow the synthesis of acute phase reactants, and the production of glucose from non-carbohydrate sources via gluconeogenesis. Hyperglycaemia is the result of peripheral and central insulin resistance. Peripheral insulin resistance refers to impaired insulin-mediated glucose uptake, whereas

central insulin resistance refers to the inability of insulin to suppress glucose production from the liver [2].

Adequate pre-operative physiological reserve, commonly defined as the capacity for organs to function before exhaustion, is required to meet the functional demands of the surgical stress response, including increased cardiac output and delivery of oxygen [2, 3]. Likewise, pre-operative energy reserves, such as lean body mass, are required to support the stress-induced mobilisation of reserves so that physiological integrity and strength is not compromised [3, 4]. Surgical patients with low reserve, including malnourished, frail and sarcopaenic (muscle-depleted) patients, are vulnerable, with diminished capacity to respond to the added demands of a surgical insult [5, 6].

Malnutrition

There is no universally accepted definition for malnutrition; however, commonalities among definitions include an 'unbalanced nutritional state' that leads to 'alterations in body composition' and 'diminished function' [7]. An unbalanced nutritional state refers to both over- and undernutrition [8]. Patients who suffer from overnutrition consume excess energy, and patients who suffer from undernutrition consume too few nutrients, including energy and protein [8]. The 'body composition' term refers to anthropometric changes in total body and lean mass [1], whereas 'function', which most commonly refers to physical function, also encompasses cognitive and immune function [9].

In the Western world, undernutrition is seldom the exclusive result of a deficient nutrient intake, and thus definitions for malnutrition often additionally include an aetiology-based diagnosis for malnutrition [9]. A definition of malnutrition for the undernourished surgical patient might thus be '*a nutritional state in which nutrient intake does not match nutrient needs – due to underlying disease (s), the surgical stress response, chronic or acute inflammation, intestinal malabsorption (e.g. diarrhoea) and/or patient-related factors (e.g. socio-economic status) – leading to losses in lean tissue and diminished function*'.

Although it is important to be aware that malnutrition and undernutrition are not synonymous, the remainder of this article is restricted to malnutrition in the undernourished state.

Why avoid pre-operative malnutrition?

Nearly 50% of patients admitted to hospital are malnourished or at risk of malnutrition [10]. If malnutrition persists unabated, clinical problems ensue, including functional impairment, decreased immune defence, delayed wound healing and organ dysfunction [11]. Prospective cohort studies from around the world suggest that malnourished hospitalised and surgical patients have significantly worse clinical outcomes, including as much as fourfold greater risk of mortality [12–15]; greater odds of complications [12, 16–19]; more frequent re-admissions [10, 12, 14, 20]; prolonged hospitalisations [10, 12, 14, 16, 19]; and increased healthcare costs [12, 21].

Experimental evidence indicates that malnutrition is a modifiable risk factor for surgery. A meta-analysis of 15 randomised controlled trials (RCTs), including 3831 malnourished patients undergoing a variety of surgical procedures, identified that peri-operative nutritional support was significantly more effective than the control at decreasing the incidence of infectious complications, with a risk ratio (RR; 95%CI) of 0.6 (0.5–0.7; $p < 0.01$); non-infectious complications 0.7 (0.6–0.9; $p < 0.01$); and shortening the length of hospital stay by approximately 2 days (95%CI −5.1 to −0.2; $p < 0.05$) [22]. A Cochrane review of 13 RCTs, including 548 patients, of pre-operative nutritional therapy in gastro-intestinal surgery found that pre-operative immune-enhancing nutrition compared with no or standard nutrition significantly reduced total postoperative complications, RR (95%CI) 0.7 (0.5–0.8; $p = 0.0006$) [23]. The review also included 260 predominantly malnourished patients, in whom parenteral nutrition compared with no nutrition was also beneficial at reducing major complications, RR (95%CI) 0.6 (0.5–0.9; $p = 0.005$) [23]. Collectively, these studies indicate that both nutritional deficiencies and nutritional repletion have an impact on surgical recovery.

How does malnutrition develop?

Malnutrition is a nutritional state in which nutrient intake (from food, supplements, nutrition support) does not match nutrient needs, with multifactorial origins (Fig. 1) [8]. Impaired intake is considered the most important aetiological factor in the development of malnutrition [24], and can be its sole cause. Malnutrition may be related to disease and inflammatory processes altering nutrient requirements, rendering a previously adequate intake inadequate; disease- and treatment-related symptoms may also impede intake (referred to as nutrition-impact symptoms, for example, loss of appetite [25, 26]).

Before surgery, the onset of malnutrition might stem from a combination of the following: mechanical obstruction (e.g. tumour-related bowel obstruction); gastro-intestinal abnormalities (e.g. malabsorption); drug or treatment-related side-effects (e.g. nausea, intestinal failure from radiotherapy damage); metabolic abnormalities as a

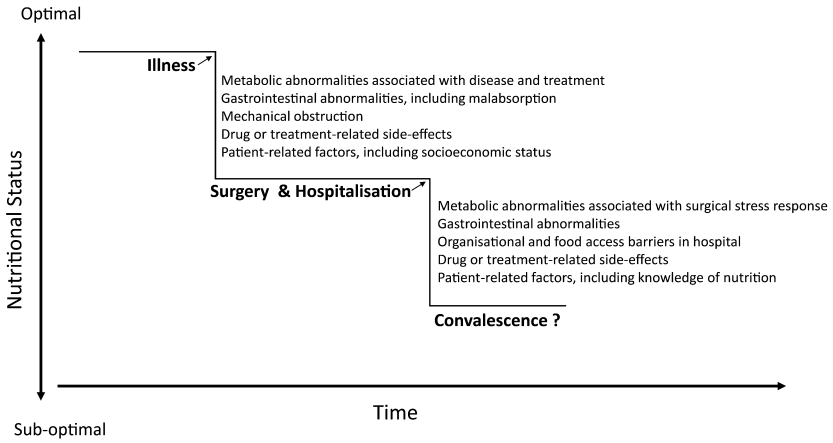

Figure 1 Diagram of potential deterioration in nutritional status over the peri-operative period. There are several peri-operative stages at which nutritional status could be compromised. The onset of disease and disease treatments may introduce metabolic abnormalities, including inflammation, that alter nutrition needs. Patients may find it difficult to meet their nutrient needs through food intake due to tumour-related obstruction, malabsorption and the onset of nutrition-impact symptoms (e.g. loss of appetite). Patient-related factors, including socio-economic status, additionally have an impact on food intake. Furthermore, malnutrition often goes undiagnosed, leaving the patient to face the surgical stress response in a suboptimal nutritional state, with diminished physiological reserves to respond to the demands of this stress response. In hospital, several barriers to adequate food intake exist, such as missed or interrupted meals, that have further impact on nutritional status. Patients are often discharged home without nutritional follow-up, they suffer further nutrition-impact symptoms from their pain medication and/or additional treatments, while relying on their own knowledge of food and nutrition to begin the process of convalescence.

result of primary and comorbid diseases (e.g. tumour-induced insulin resistance can mobilise endogenous energy sources such as amino acids); and several patient-related factors that have an impact on food intake (e.g. socio-economic status, social isolation, nutritional knowledge) [24, 25].

After surgery, patients are also faced with several additional barriers to adequate food intake, including the surgical stress response and organisational barriers in hospital (e.g. missed meals or tube feeds withheld due to scheduled clinical investigations). The Canadian Malnutrition Task Force (CMTF), a prospective study involving 18 acute care hospitals across Canada, identified that nearly 50% of hospitalised patients felt 'too sick' to eat, a third of patients had difficulty opening food packages, two-thirds were not given hospital food when meals were missed, and nearly half did not get help when needed [26]. In fact, even patients provided with standardised enhanced recovery after surgery (ERAS) nutrition care did not meet minimally adequate requirements for protein [27, 28], and required nutritional education to correct misconceptions that impeded adequate nutrition in hospital [29]. The CMTF also identified that most patients did not improve their nutritional status during hospitalisation, and that half of the patients who remained in hospital > 7 days were identified as malnourished at discharge. Furthermore, 75% of malnourished patients did not receive care from a dietician during their hospital stay, and only 11% received dietetic care post-discharge [30–33].

What can be done to avoid malnutrition?

Nutritional management should begin pre-operatively to optimise nutritional status in preparation for the metabolic demands of surgical injury. Nutritional management should continue postoperatively to maintain nutritional status for supporting wound healing, improving the immune response and facilitate functional recovery [1, 2].

Surgical nutrition guidelines, such as the European Society for Clinical Nutrition and Metabolism [1], American Society of Parenteral Enteral Nutrition [34] and the American Society for Enhanced Recovery with Peri-operative Quality Initiative [35] all provide details on selecting nutrition screening tools, malnutrition assessment tools, and treatment for malnourished and at-risk patients. Nearly all guidelines suggest systematic, routine screening for malnutrition and subsequent nutrition assessment with a validated malnutrition assessment tool or a comprehensive nutrition assessment by a registered dietician if the nutrition screen is positive. A comprehensive nutrition assessment involves understanding the personal cause(s) of malnutrition and correcting barriers to adequate food intake. Patients identified as malnourished, or at risk, require individualised treatment plans that may include therapeutic diets (e.g. high protein), fortified foods, high

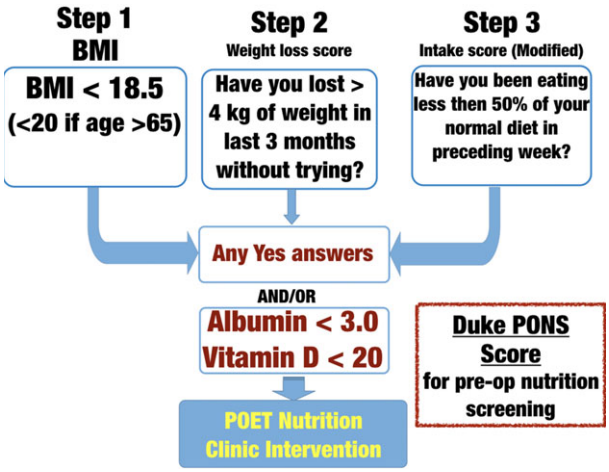

Figure 2 Duke University Pre-Operative Nutrition Score (PONS; adapted from reference [35]). PONS utilises data-driven questions from the validated Malnutrition Universal Screening Tool [37] to assess for malnutrition risk in peri-operative patients. Any score ≥ 1 signifies malnutrition risk, and the patient should receive pre-operative nutrition therapy before undergoing surgery.

protein oral nutrition supplements, enteral nutrition and/or parenteral nutrition [36].

Examples of an existing tool, the Peri-operative Malnutrition Score [35, 37], used to identify malnutrition risk, and a nutrition optimisation programme for patients at risk of peri-operative malnutrition at Duke University, the Peri-Operative Enhancement Team clinic, are shown in Figs. 2 and 3.

Protein anabolism

Body proteins are constantly synthesised and degraded to maintain a neutral whole-body protein balance in normal, healthy adults [38]. The extent to which body proteins are broken down, releasing amino acids into circulation for reuse, is considerable; however, this recycling is not 100% efficient and, in particular, nine amino acids, referred to as essential or indispensable amino acids, cannot be synthesised de novo by adults, necessitating a daily requirement to ingest dietary protein [38]. When protein ingestion does not meet metabolic demands, catabolism (body protein breakdown) ensues to meet needs. When whole-body protein synthesis outweighs protein breakdown, anabolism is favoured [38].

Why support protein anabolism before surgery?

Maintaining lean mass, including muscle mass (the largest 'reservoir' of amino acids), is essential to support wound healing, immunity and autonomy [11, 39, 40]. Muscle-depleted patients (i.e. sarcopaenic patients) have limited reserve to respond to the surgical stress response [41, 42], increasing their odds of developing complications [6, 43], an increased length of hospital stay [43], and contributing to poor survival [6, 43, 44]. Computed tomography studies are beginning to define pre-operative body composition profiles, including low muscle mass, that predict surgical outcomes. Multivariable analysis of 805 colorectal cancer patients identified that low muscle mass before surgery was an independent predictor of overall survival; however, it was the presence of myosteatosis (fatty infiltration, an indicator of muscle quality), that was associated with prolonged hospital stay. The authors also identified that, in particular, obese patients with low muscle mass were more likely to suffer from 30-day morbidity and mortality rates [6]. These findings suggest that specific body composition profiles predict different surgical risks.

Experimental evidence supports the idea that prehabilitation, an anabolic intervention comprising exercise, nutrition, and psychological preparation in the waiting period before surgery, promotes a better surgical outcome [45, 46]. Much like training for a marathon, surgical prehabilitation employs multi-modal interventions in the pre-surgical period to fortify physiological reserve, and thus prepares patients emotionally and physically to withstand surgical insult [41]. Randomised controlled trials indicate multi-modal prehabilitation successfully improves a variety of surgical outcomes in abdominal surgery patients, including earlier return to baseline function [45–47]. A recent meta-analysis of nine prospective cohort and RCT studies of nutrition prehabilitation, with or without exercise, in colorectal surgery identified that receipt of any prehabilitation significantly reduced days spent in hospital compared with controls by 2 days (95%CI −3.5 to −0.9 days) [48]. Moreover, frail patients appear to gain the greatest benefits from prehabilitation treatment [45, 49]. As examples, colorectal cancer patients with poor baseline functional capacity experience more meaningful gains in pre- and postoperative function compared with patients with good baseline functional capacity [49]; and patients aged over 70 years with functional limitations (ASA physical status 3–4) suffer fewer postoperative complications after abdominal surgery if treated with personalised multi-modal prehabilitation, when compared with control patients [45].

How come surgical patients require pre-operative anabolic preparation?

Patients with illness, including surgical injury, inflammation and malignant disease, often present with an elevated turnover of body proteins, necessitating a greater total protein intake to attenuate the catabolism of body tissues to

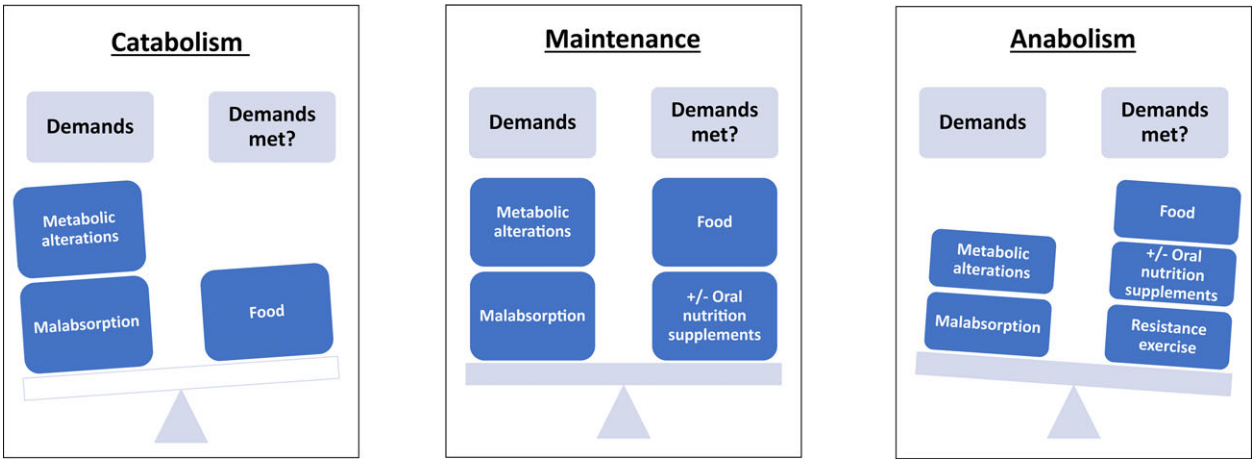

Figure 4 Diagram of the balance between peri-operative metabolic supply and demand. Patients with illness, including surgical injury, acute or chronic inflammation and cancer, often have greater needs for dietary protein. Elevated protein needs are the result of metabolic alterations associated with illness and illness-related treatments. When protein ingestion from food does not meet metabolic demands, body tissue is catabolised to meet needs. By meeting metabolic demands and maintaining homeostasis, largely through food intake, the patient avoids excessive catabolism and consequent losses of body protein and strength. Patients can achieve anabolism and build body tissue before surgery through adequate food/nutrient intake, adequate protein intake (from food and/or supplements), and resistance exercise.

occasions, so that each participant served as his own control, after an intense bout of leg-based resistance exercise. The authors found that muscle protein synthesis was maximally stimulated at 20 g [60].

Based on evidence of this ceiling effect in muscle, an 'equal distribution hypothesis' has been proposed [64]. This recommends that protein intake should be spread across all meals [63] and when eating after exercise [58], aiming for an amount of 20–35 g [59, 64]. It also suggests that the anabolic response is increased with habitual repetition. A 7-day crossover feeding study in healthy adult men by Mamerow et al. [65] supports this hypothesis. The authors found that 24 h mixed muscle protein synthesis was approximately 25% greater in response to an even distribution of protein (i.e. 30 g with meals) rather than a skewed protein distribution, despite diets being iso-energetic and isonitrogenous.

There are some criticisms of the 'equal distribution hypothesis'. An editorial stated that it is premature to conclude that an acute anabolic response accurately predicts the anabolic response over the long-term [66]. Also, laboratory settings do not reflect real life eating patterns; in reality, our meals are often composed of mixed macronutrients rather than protein alone. The macronutrient composition of meal intake may influence protein synthesis [59]. Finally, because the hypothesis is based on studies of muscle protein synthesis, which do not account for whole-body protein needs, some authors believe the total anabolic response may be underestimated [67].

Most often, 'high-quality' proteins are reported to exert the greatest effect on muscle protein synthesis [56]. According to a recent report by the Food and Agriculture Organization (FAO) of the United Nations, protein quality should be assessed based on the availability of essential amino acids after digestion in comparison with amino acid requirements [68]. The FAO has adopted the digestible indispensable amino acid score to quantify protein quality. Using this scoring system, animal proteins tend to constitute high-quality proteins, with milk proteins among the highest quality [68].

If we extrapolate all these findings from healthy populations, while recognising that they need to be confirmed in surgical settings, a protein-centred approach to meal planning that includes high-quality proteins and a relatively even daily distribution of protein intake might effectively maximise protein synthesis. This would require a change in eating habits; for instance, North Americans tend to consume > 60% of their daily protein at their evening meal [69], and thus would not achieve the 'muscle full effect' at their earlier meals. While the 'equal distribution hypothesis' is intriguing, whole-body protein needs should not be forgotten, and these might require > 35 g protein intake with meals. Optimal total daily protein intakes for surgery are currently not well defined, although several guidelines suggest that surgical patients should consume at least 1.2–2.0 g protein.kg^{-1}.day^{-1} [1, 35].

Additional nutrients, such as omega-3 fatty acids and vitamin D, may also complement or augment the protein anabolic response. Smith et al. [70] randomly assigned 16 healthy, older adults to receive either omega-3 fatty acids or corn oil for 8 weeks. Corn oil supplementation had no effect on muscle protein synthesis rate, whereas omega-3 fatty acid supplementation was found to augment muscle protein synthesis. Likewise, a meta-analysis of 13 RCTs of supplemental vitamin D in adults aged > 60 years, compared with placebo or standard treatment on muscle function, found that supplementation with at least 800 IU of vitamin D decreased postural sway, reduced time to complete the Timed Up and Go Test, and marginally increased lower extremity strength [71]. These findings might also be applicable in clinical settings.

In conclusion, avoiding malnutrition and supporting anabolism are basic surgical nutritional goals. Before surgery, these goals can be met through nutrition screening and assessment to diagnose, treat and prevent malnutrition. Pre-operative nutritional interventions, such as nutritional prehabilitation with exercise cotherapy, function to optimise overall nutritional status and support protein anabolism before surgery, conditioning stronger patients for an earlier surgical recovery.

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Review Article

Pre-operative cardiac optimisation: a directed review

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Summary

Cardiac events remain the leading cause of peri-operative morbidity and mortality, and patients undergoing major surgery are exposed to significant risks which may be preventable and modifiable. Proper assessment and management of various cardiac conditions in the peri-operative period by anaesthetists can markedly improve patient safety, especially in high-risk patient populations. This involves understanding and applying current evidence-based practice and international guidelines on the main aspects of cardiac optimisation, including management of patients with hypertension, chronic heart failure, valvular heart diseases and cardiac implantable electronic devices. Peri-operative management of antihypertensive drugs in keeping with the current best evidence is discussed. Pre-operative cardiac risk assessment and cardiac biomarkers can be used to help predict and quantify peri-operative adverse cardiac events. There is an increasing need for anaesthetist-led services, including focused transthoracic echocardiography and management of implantable cardiac electronic devices. Anaesthetists should be encouraged to play a proactive role in pre-operative risk stratification and make timely multidisciplinary referrals if necessary. A personalised approach to pre-operative cardiac optimisation enables a safer peri-operative journey for at-risk patients undergoing major surgery.

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Introduction

It is estimated that around 200 million major operations are performed every year worldwide [1]. Overall complication rates vary among different countries but are probably around 10% [2], with cardiac complications now one of the leading causes of all morbidity and mortality [3, 4], accounting for 40% of postoperative mortality in one study utilising troponin levels [3]. Major adverse cardiac events comprise: acute myocardial ischaemia or infarction; angina; congestive heart failure; atrioventricular block; arrhythmias; and cardiac arrest [5]. This has a significant impact on immediate and long-term prognosis, and adds to the burden on the healthcare system by increasing the utilisation of intensive care facilities, drugs and equipment and prolonging the length of hospital stay [6, 7].

Thorough assessment of cardiac morbidity is particularly important for high-risk surgical patients. Although many risk scoring systems are available, the most validated one is the revised cardiac risk index, which consists of one procedural and five clinical risk factors

Table 1 Revised cardiac risk index [8].

Risk factor	Points
Cerebrovascular disease	1
Congestive heart failure	1
Creatinine level > 2.0 mg.dl^{-1}	1
Diabetes mellitus requiring insulin	1
Ischaemic cardiac disease	1
Supra-inguinal vascular surgery, intrathoracic surgery or intra-abdominal surgery	1
Risk of major cardiac event	
Points	Percentage risk (95%CI)
0	0.4 (0.05–1.5)%
1	0.9 (0.3–2.1)%
2	6.6 (3.9–10.3)%
≥ 3	≥ 11 (5.8–18.4)%

(Table 1) [8]. A systematic review has proven a linear relationship between the score and the likelihood of peri-operative cardiac complications [9], but it is still debatable as to whether at-risk patients can benefit from such stratification approaches.

Surgical patients present with various cardiac conditions and the peri-operative management strategies are, therefore, diverse. The common ones are addressed below. The level of evidence and the strength of recommendation of particular management options are graded according to a pre-defined scale (Table 2).

Hypertension

Hypertension alone is only a minor independent risk factor for adverse cardiac events in non-cardiac surgery [10], but patients with uncontrolled hypertension tend to have volatile intra-operative blood pressure which can increase risk. In the context of isolated hypertension, delaying or cancelling surgery for additional cardiac testing is usually neither necessary nor desirable. The potential benefit of delaying surgery for optimisation must be weighed against the risks of postponing surgery. Despite the availability of guidelines that recommend elective surgery should not be deferred if the blood pressure is below 180 mmHg systolic and 110 mmHg diastolic [11], cancellation of surgery due to 'suboptimal' peri-operative control of hypertension is still encountered occasionally. The American College of Cardiology (ACC) and American Heart Association (AHA) published an updated guideline in 2017 on the definition of hypertension (Table 3) and recommendations for hypertensive patients undergoing surgical interventions (Table 4) [12].

Treatment of pre-operative hypertension can be complicated, and the condition is further compounded by the phenomena known as 'masked hypertension' and 'white coat hypertension' [13, 14]. White coat hypertension is an elevated blood pressure in the clinical setting with a normal pressure at home. Masked hypertension is defined as a normal blood pressure in the clinic, but an elevated blood pressure out of the clinic. It may occur in as much as 10% of the general population, and is important because it is not diagnosed by routine medical examinations, but carries an adverse prognosis, both in terms of increased target organ damage and cardiovascular events. Patients are frequently relatively young and male, with stress or increased physical activity during the daytime, and are often smokers or have excessive alcohol consumption. Masked hypertension has also been described in treated hypertensive patients and in

Table 2 Definitions of class of recommendation and level of evidence.

Class of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful	Is not recommended
Level of evidence	**Definition**	
Level A	Data derived from multiple randomised clinical trials or meta-analyses	
Level B	Data derived from a single randomised clinical trial or large non-randomised studies	
Level C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries	

Table 3 Definition of hypertension in adults [12].

Category	Systolic blood pressure		Diastolic blood pressure
Normal	< 120 mmHg	and	< 80 mmHg
Elevated	120–129 mmHg	and	< 80 mmHg
Hypertension			
Stage 1	130–139 mmHg	or	80–89 mmHg
Stage 2	≥ 140 mmHg	or	≥ 90 mmHg

An individual with systolic blood pressure and diastolic blood pressure in two different categories should be assigned to the higher category.

children, in whom it may be a precursor of sustained hypertension. It may be suspected in individuals who have a history of occasional high blood pressure readings, but who are apparently normotensive when checked in the clinic.

There is a wide range of medications available to reduce blood pressure to the desired target before surgery. Hypertensive subjects have more arterial pressure lability intra-operatively, although this has not been shown to be associated with increased 30-day mortality [15]. Anaesthetists can monitor intra-operative haemodynamic fluctuation either directly or indirectly and have a range of drugs at their disposal to maintain blood pressure within an acceptable range. Anaesthetic drugs will also affect blood pressure but should only be used to maintain an optimum depth of anaesthesia, not to control blood pressure. Therefore, it is the treatment of cardiovascular risk, not hypertension per se, that is important.

Table 4 Recommendations for hypertensive patients undergoing surgical interventions [12].

Pre-operative	
1	In patients with hypertension undergoing major surgery who have been on beta-blockers chronically, beta-blockers should be continued. (Class I, level B evidence)
2	In patients with hypertension undergoing planned elective major surgery, it is reasonable to continue medical therapy for hypertension until surgery. (Class IIa, level C evidence)
3	In patients with hypertension undergoing major surgery, discontinuation of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers peri-operatively may be considered. (Class IIb, level B evidence)
4	In patients with planned elective major surgery and SBP of ≥ 180 mmHg or DBP of ≥ 110 mmHg, deferring surgery may be considered. (Class IIb, level C evidence)
5	For patients undergoing surgery, abrupt pre-operative discontinuation of beta-blockers or clonidine is potentially harmful. (Class III, level B evidence)
6	Beta-blockers should not be started on the day of surgery in beta-blocker naïve patients. (Class III, level B evidence)
Intra-operative	
7	Patients with intra-operative hypertension should be managed with intravenous medications until such time as oral medications can be resumed. (Class I, level C evidence)

Class, recommendation class; level, level of evidence (see Table 2); DBP, diastolic blood pressure; SBP, systolic blood pressure.

Nowadays, anaesthetists have more opportunity to assess and optimise hypertension in the outpatient assessment clinic before surgery. Firstly, the patient's baseline blood pressure should be determined, either by checking their self-monitoring record, or the record from their primary care physician [11]. If long-standing hypertension is suspected, there should be an assessment of possible end-organ damage including left ventricular hypertrophy, diastolic dysfunction, atherosclerotic coronary artery disease, heart failure, glomerular injury, renal tubular ischaemia and end-stage renal failure [16].

For patients with systolic blood pressure < 180 mmHg and diastolic blood pressure < 110 mmHg, antihypertensives should be continued in the peri-operative period [11]. In patients with planned elective major surgery and a documented systolic pressure of ≥ 180 mmHg or diastolic pressure of ≥ 110 mmHg, surgery should be postponed [12], and blood pressure-lowering treatment should be discussed and commenced by following the National Institute for Health and Care Excellence/British Heart Society CG127 algorithm [11]. In particular, patients with diastolic pressure ≥ 110 mmHg immediately before surgery have been shown to have increased risk of complications including myocardial infarction and renal failure [17].

Earlier clinical trials alluded to a possible beneficial effect of beta-blockers in prevention of peri-operative cardiac risks [18, 19]. However, the peri-operative ischemic evaluation (POISE) trial and a subsequent meta-analysis showed that although initiation of beta-blockers one day or less in patients before non-cardiac surgery will decrease rates of nonfatal myocardial infarction, it paradoxically increases the risk of stroke, hypotension, bradycardia and death [20, 21]. The POISE trial was criticised for not using a titrated dose of beta-blocker, because initiating and titrating beta-blockers to heart rate weeks before surgery

Table 5 Recommendation for peri-operative beta-blocker therapy [23, 24].

ESC/ESA guideline 2014 [23]	ACC/AHA guideline 2014 [24]
Class I	Class I
Peri-operative continuation of beta-blockers is recommended in patients currently receiving this medication (Class I, level B†)	Peri-operative continuation of beta-blockers is recommended in patients currently receiving this medication (Class I, level B)
Class II	Class II
Pre-operative initiation of beta-blockers may be considered 1 In patients scheduled for high-risk surgery and who have ≥ 2 clinical risk factors or ASA status ≥ 3 (Class IIb, level B) 2 In patients who have known IHD or myocardial ischaemia (Class IIb, level B) When oral beta-blockade is initiated in patients who undergo non-cardiac surgery, the use of atenolol or bisoprolol as a first choice may be considered (Class IIb, level B)	Guide management of beta-blockers after surgery by clinical circumstances (Class IIa, level B) It may be reasonable to begin beta-blockers 1 In patients with intermediate- or high-risk pre-operative tests (Class IIb, level C) 2 In patients with > 3 revised cardiac risk index factors (Class IIb, level B) 3 Long enough in advance to assess safety and tolerability, preferably > 1 day before surgery (Class IIb, level B) Initiating beta-blockers in the peri-operative setting as an approach to reduce peri-operative risk is of uncertain benefit in those with a long-term indication but no other revised cardiac risk index risk factors (Class IIb, level B)
Class III	Class III
Beta-blockers not recommended 1 Peri-operative high dose beta-blockers without titration (Class III, level B) 2 Patients scheduled for low-risk surgery (Class III, level B)	Beta-blockers should not be started on the day of surgery (Class III, level B)

Class, recommendation class; level, level of evidence; ESC, European Society of Cardiology; ESA, European Society of Anaesthesiology; ACC, American College of Cardiology; AHA, American Heart Association.

has been advocated as there is significant pharmacogenetic variability in response [22]. Table 5 summarises the current recommendations for peri-operative beta-blocker therapy [23, 24]. However, this strategy is limited by the timing of assessment before surgery [25]. Step-wise titration of beta-blockers in the pre-anaesthetic clinic allows optimisation of blood pressure and heart rate control, which may reduce peri-operative adverse cardiac events without increasing other risks [26]. Patients on chronic treatment with beta-blockers for ischaemic heart disease, arrhythmias or hypertension should be maintained on this medication throughout the peri-operative period (Class I recommendation) [23, 24].

There is some controversy over whether it is appropriate to continue angiotensin-converting enzyme inhibitors/angiotensin-II receptor blockers in the peri-operative period. There is an increased risk of intra-operative hypotension when they are continued [27, 28] and clinically-significant hypotension is independently associated with increased myocardial infarction, stroke and death, leading to the recommendation towards withholding them at least 24 h before major surgery [12, 21, 29, 30]. However, other studies show conflicting results with no sufficient available evidence to recommend discontinuing the drugs on the day of surgery [31–33]. Anaesthetists should be aware of the potential risk of intra-operative hypotension in patients receiving the drugs and be prepared to manage it [33]. In patients on chronic treatment, it is reasonable to continue them under supervision (Class IIa recommendation) [23, 24]. Likewise, if the drugs are discontinued before surgery for fear of intra-operative hypotension, it is reasonable to resume them after surgery as soon as possible (Class IIa recommendation) [23, 24].

Calcium channel blockers should be continued. There is little evidence to support their initiation pre-operatively for cardioprotection and, in a meta-analysis of studies investigating this, most of the benefits shown were attributed to diltiazem [34].

Alpha-2 agonists reduce central sympathetic activity and peripheral noradrenaline release, which can attenuate the adrenergic stress response to surgery, and the reduction in heart rate can improve myocardial oxygen balance. A meta-analysis had suggested that alpha-2 agonists reduce mortality and myocardial infarction after vascular surgery [35] but another meta-analysis, restricted to dexmedetomidine, did not show a significant improvement in cardiac outcomes, although hypotension and bradycardia were increased [36]. The more definitive POISE-2 trial suggests that alpha-2 agonists should

probably not be used for 'cardioprotection' in non-cardiac surgery [37], and this opinion is reflected in the most recent guidelines from North American and European bodies (Class III recommendation) [23, 24].

Nitrates are known to attentuate myocardial ischaemia. However, a 2016 Cochrane systematic review found no role for any preparation of nitrate in the prevention of peri-operative cardiac events, although only 3 trials recruiting a total of 149 patients, reported the all-cause mortality at 30 days [38]. To date, prophylactic use of nitrates is not recommended, as they may pose a significant risk with pre-load reduction [23]. A general approach for peri-operative management in the high-risk population would be to advise the patient to continue usual doses as needed, especially in case of symptom control in angina pectoris. No guidelines have been published concerning this topic.

At present, the recommended frequency of blood pressure monitoring varies hugely among different international guidelines, ranging from every primary care visit to every 5 years [39–41]. A specialist-led pre-operative assessment clinic [42] provides opportunity to stratify patients based on risks, to make timely referrals and prescribe medications according to latest ACC/ESC guidelines [23, 24]. The referring physician should be informed for patients with newly diagnosed hypertension.

Chronic heart failure

Heart failure is a global problem, with at least 26 million people affected [43, 44]. The prevalence of heart failure is also increasing as the population ages, and more patients with congestive heart failure will present for surgery [45]. Ejection fraction is the stroke volume divided by the end-diastolic volume and can be used in classification. Current terminology distinguishes: heart failure with preserved ejection fraction; heart failure with mid-range ejection fraction; and heart failure with reduced ejection fraction, based on the ejection fraction, natriuretic peptide levels and the presence of structural heart disease and diastolic dysfunction [46] (Table 6).

When assessing these patients, a detailed history and clinical examination are crucial to determine the cause and quantify its severity (Tables 7 and 8). Patients with current or previous history of heart failure are well known to have more peri-operative complications and this is an independent prognostic variable for all cardiac risk scores [8]. The revised cardiac risk index is the most validated clinical risk score and has been used as a tool to assess the risk of cardiac complications after non-cardiac surgery [8]. A 12-lead ECG should be done to look for myocardial ischaemia and arrhythmia. There is a consensus among international guidelines [23, 24, 47–49] that patients with active cardiovascular signs or symptoms should have an ECG, especially those undergoing high-risk surgery (Table 9). A pre-operative ECG is recommended for patients who have risk factor(s) and are scheduled for intermediate or high-risk surgery (Class I, level C evidence; it may also be considered for patients who have risk factor(s) identified by revised cardiac risk index and are scheduled for low-risk surgery (Class IIb, level C evidence) [23].

There is no high-quality evidence on the use of routine pre-operative chest radiography and it is not mandatory in patients with stable chronic heart failure [47]. Resting echocardiography is also not routinely recommended in patients with chronic and stable heart failure [50]. However, patients with signs and symptoms of worsening heart failure require investigations to assess the severity of systolic or diastolic dysfunction which will guide peri-operative management. In patients with acutely decompensated heart failure (New York Heart Association class IV), surgery should be postponed, if possible, and the opinion of a cardiologist sought for titration of heart failure medication [24]. Cardiac biomarkers have been used to predict the risk

Table 6 Diagnosis of heart failure [46].

Type of HF	HFrEF	HFmrEF	HFpEF
Criteria			
1	Symptoms ± signs[a]	Symptoms ± signs[a]	Symptoms ± signs[a]
2	LVEF < 40%	LVEF 40–49%	LVEF > 50%
3	–	1 Elevated levels of natriuretic peptides; 2 At least one additional criterion: a A relevant structural heart disease (LVH and/or LAE) Diastolic dysfunction	1 Elevated levels of natriuretic peptides; 2 At least one additional criterion: a A relevant structural heart disease (LVH and/or LAE) Diastolic dysfunction

HF, heart failure; HFrEF, heart failure with a reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with a preserved ejection fraction; LAE, left atrial enlargement; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction.
[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

Table 7 Modified Framingham criteria for congestive heart failure [108].

Major criteria	Minor criteria
Paroxysmal nocturnal dyspnoea or orthopnoea	Bilateral ankle oedema
Central venous pressure > 16 cmH_2O	Nocturnal cough
Pulmonary rales	Dyspnoea on exertion
Cardiomegaly	Hepatomegaly
Acute pulmonary oedema	Pleural effusion
Third heart sound gallop	Tachycardia (heart rate ≥ 120 beats/min)
Weight loss > 4.5 kg in 5 days in response to treatment	Weight loss > 4.5 kg in 5 days in response to treatment

The diagnosis of heart failure requires that either two major or one major and two minor criteria are met.

Table 8 New York Heart Association (NYHA) Functional Classification [109].

NYHA functional classification	
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea
Class II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation or dyspnoea
Class III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary physical activity results in fatigue, palpitation or dyspnoea
Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased

Table 9 Cardiac risk stratification for non-cardiac surgical procedures [110].

Risk of procedure	Examples
High (> 5%)	Aortic and major vascular surgery, peripheral vascular surgery
Intermediate (1–5%)	Intraperitoneal and intrathoracic surgery, carotid endarterectomy, head and neck surgery, orthopaedic surgery, prostate surgery
Low (< 1%)	Endoscopic procedures, superficial procedures, cataract surgery, breast surgery, ambulatory surgery

'Cardiac risk' denotes combined incidence of cardiac death and nonfatal myocardial infarction.

of post operative major adverse cardiac events. Myofibrillar proteins, such as troponin T and troponin I, and natriuretic peptides such as brain natriuretic peptide (BNP) and N-terminal fragment of proBNP (NT-proBNP), are released into the circulation as a result of myocyte injury and stress. Several studies have investigated the prognostic values of BNP and NT-proBNP to predict major cardiovascular events after non-cardiac surgery [51–58]. The European Society of Cardiology and European Society of Anaesthesiology guidelines for pre-operative cardiac risk assessment have recommended the measurement of natriuretic peptides in high-risk patients (Class IIa, level B evidence) [59]. Post-operative raised levels of BNP or NT-proBNP compared with pre-operative levels has been shown to be associated with increased adverse cardiac events [60]. However, it is not clear how to tailor the peri-operative management to improve outcomes in patients with raised plasma BNP or NT-proBNP. Apart from natriuretic peptides, a raised postoperative troponin level has also been shown to be a very strong predictor of 30-day mortality and long-term outcomes for patients undergoing non-cardiac surgery [3, 61]. Post operative myocardial infarction is notoriously difficult to diagnose, as most patients have no symptoms and such myocardial injury could only be detected by serial serum troponin monitoring [3]. Therefore, it is recommended for at-risk patients to have their troponin levels monitored in the first few postoperative days, although further studies are required to define how cardiac optimisation should be performed in the most vulnerable group.

There is a growing body of evidence supporting outcome improvements in patients with better overall physical condition. Guidelines for the diagnosis and treatment of acute and chronic heart failure recommend supervised aerobic exercises to improve functional status and reduce the risk of hospital admission [46]. The evidence comes mostly from patients with heart failure and a reduced ejection fraction. The HF-ACTION trial is the largest multi-centre, randomised controlled trial so far to look at the efficacy and safety of aerobic exercise training among patients with heart failure; it enrolled more than 2000 patients [62]. For the primary composite end-point of all-cause mortality or all-cause hospitalisation, there was no significant difference between supervised exercise training and usual care (education and recommendation of regular exercise). However, after adjustment for prognostic baseline variables, there was a significant but modest reduction in all-cause mortality or all-cause hospitalisation in the exercise training group [62]. Other studies have shown improvements in functional status and quality of life after exercise training in patients with heart failure with reduced ejection fraction [63, 64]. In addition, it has been demonstrated that exercise training improves peak oxygen

uptake in patients with heart failure [64–66]. Apart from that, it improves cardiac structure and function, with significant improvements in left ventricular ejection fraction, end-diastolic and end-systolic volumes observed in patients receiving aerobic exercise training [67].

The clinical significance of cardiac rehabilitation is well described, especially in patients with heart failure. However, there is limited research about the use of pre-operative rehabilitation, also known as pre-habilitation, in this patient group. Preliminary evidence shows that pre-operative supervised exercise training enhances postoperative outcome in terms of shorter hospital stay and fewer postoperative complications [68, 69]. A systematic review has shown that pre-operative aerobic exercise training is effective in improving physical fitness in patients planned for intra-abdominal and intrathoracic surgery [70]. Pre-habilitation may well have a useful role but further large-scale studies will be needed to determine the best type of training to be prescribed for surgical patients with underlying heart failure. First of all, at-risk patients should be identified, and functional capacity and frailty are components of pre-operative evaluation. Biccard [71] provides evidence for predicting peri-operative complications associated with major non-cardiac surgery using stair-climbing capacity (four metabolic equivalents). Type of exercise and its duration is, as yet, undefined. It would be reasonable to initiate pre-habilitation during the waiting period for elective surgery, as patients tend to have little physical activity while waiting [72–74]. The PREHAB study [75], which hypothesises that an interdisciplinary pre-operative programme composed of an 8-week comprehensive exercise therapy and education programme will improve postoperative clinical outcome of frail elderly patients awaiting elective cardiac surgery, is still ongoing and results are expected to be released this year.

Cardiac murmurs

Systolic cardiac murmurs are common. In a study on an unselected cohort of elderly patients with fractured neck of femur, 30% had mild aortic stenosis or aortic sclerosis and 8% were found to have either moderate or severe aortic stenosis [76]. Yet, clinical examination alone is neither sensitive nor specific for evaluating undifferentiated murmurs, and valvular lesions are often missed with auscultation [77, 78]. In particular, it is unreliable in diagnosing combined disease in the aortic and mitral valves with a sensitivity of 55%, even in experienced hands [77]. The ability to detect diastolic heart murmurs is even worse, especially in the presence of a systolic murmur, with a sensitivity of only 20–40% [77, 79].

Previously undetected cardiac murmurs are commonly found during pre-operative assessment [80, 81] and are among the most common reasons for referral to a cardiologist [82]. A comprehensive history and physical examination remains the cornerstone of assessment. Recently, especially with cheaper and more portable ultrasound devices, there has been an expansion of echocardiography use in the peri-operative period among anaesthetists [83–86]. This, however, also has created challenges. Ideally, operations should be postponed while waiting for formal echocardiography, which may be undesirable, especially in emergencies. In a patient presenting with an otherwise asymptomatic cardiac murmur, although it would be useful to have transthoracic echocardiography to exclude cardiac pathology, such expertise may not always be readily accessible. Fortunately, training in, and utilisation of, pre-operative focused transthoracic echocardiography is becoming more available to anaesthetists [87, 88]. The examination is non-invasive and can be completed within 10 min in an outpatient setting. It allows the detection of significant valvular lesions, assessment of left and right ventricular function and detection of pericardial effusion [84]. It has been shown that even relatively junior anaesthetists can diagnose aortic stenosis, and assess its severity, after limited training [89].

There is now widespread use of echocardiography in patient assessment and management [90], and recent studies on the impact of focused transthoracic echo in pre-operative assessment [91, 92]. Having said that, focused echocardiography cannot replace clinical assessment and physical examination, nor does it replace a formal echocardiogram. Despite an improvement in diagnostic accuracy, evidence showing a scientifically robust positive clinical outcome is lacking. A retrospective cohort involving more than 250,000 patients with elective, intermediate- to high-risk, non-cardiac surgery showed pre-operative echocardiography was not associated with improved survival or shorter hospital stay, which casts doubt on the value of pre-operative echocardiography for improving peri-operative care and outcomes [93]. However, pre-operative consultation by physicians is also common practice, and yet patient outcome improvement is not apparent. On the other hand, pre-operative medical consultation may paradoxically result in increased short and long-term mortality, prolonged hospital stay, increased pre-operative testing and increased pharmacological intervention [94]. Consequently, we encourage anaesthetists to play a more proactive role in pre-operative management.

Recent studies demonstrate the impact of focused echocardiography in enhancing peri-operative management and the predictive value of peri-operative cardiac events [91, 92, 95–97]. Nonetheless, anaesthetist-led focused echocardiography is not a substitute for detailed assessment by a cardiologist. Theoretically, a reduction in unnecessary medical consultations can help reduce the burden on the whole healthcare system and reinvest resources in improving patient care; however, the overall efficacy and cost-effectiveness of this anaesthetist-led service is still lacking and needs further evaluation in large-scale clinical trials [98].

Patients with a cardiac implantable electronic device

The use of implantable electronic cardiac devices, which include pacemakers, implanted cardioverter-defibrillators, cardiac resynchronisation devices and implantable cardiac monitors, is increasingly common [99, 100]. The use of cardiac implantable electronic devices has provided significant benefit, yet also creates considerable challenges to healthcare personnel. Of particular note, the majority of patients with the devices fall into a high-risk stratification group relative to their physical status. For instance, patients with advanced biventricular failure may receive cardiac resynchronisation therapy; both of these will make the peri-operative management challenging [101].

Cardiac implantable electronic devices are problematic intra-operatively because their functions can be hindered by electromagnetic interference. There are multiple sources of such radiation in the operating theatre including electrocautery, evoked potential monitors, nerve stimulators, radiofrequency ablation, extracorporeal shock wave lithotripsy and electroconvulsive therapy [102]. Different devices will behave differently when there is excessive electromagnetic interference, which may cause rate interference, pulse generator damage, lead tissue damage and switching to inappropriate electrical reset mode. For patients with an implanted pacemaker, interference can result in oversensing [103] which will, in turn, lead to inappropriate inhibition and then serious bradycardia or asystole. With implantable cardioverter-defibrillators, electromagnetic interference can lead to inappropriate delivery of a defibrillator shock. Mechanical interference can also affect the normal function of the pacemaker, for example, when a guidewire is advanced during insertion of a central venous catheter and results in ventricular oversensing [103]. When assessing these devices, a thorough cardiovascular history and activity tolerance should be obtained to determine the indication for implantation and look for signs and symptoms suggestive of malfunction such as dizziness, syncope and deteriorating functional status. The time when the device was last checked and the specific recommendation from a cardiologist should be carefully documented. It is recommended by the Heart Rhythm Society that device interrogation should be arranged for a pacemaker within 12 months, an implantable cardioverter-defibrillator within 6 months and a cardiac resynchronisation therapy device within 3–6 months before surgery [103, 104]. Review of the electrocardiograph or consultation with the cardiology team can determine whether the patient is device dependent, and information such as the type and site of the procedure, patient positioning and anticipated sources of intra-operative electromagnetic interference should be obtained [105].

In all circumstances, close communication is required with the surgeon and cardiologist, particularly if reprogramming is expected before and after surgery. Anaesthetists have the potential, and opportunity, to offer structured peri-operative management of implanted cardiac devices before surgery. A pilot anaesthetic device service, led by anaesthetists in the US, has been reported. These doctors were trained to provide basic management of cardiac implantable electronic devices, including interrogation and reprogramming, in the pre-operative holding areas and recovery area and the programme was shown to be safe with specialist support if necessary [106]. It has been postulated that, in collaboration with the electrophysiology and cardiology services, anaesthetists could be more proactive in managing these patients and, thereby, reducing interdepartmental consultations and patient waiting time before surgery [99, 106].

For patients who are pacemaker-dependent with a high chance of electromagnetic interference, temporary reprogramming to asynchronous (non-sensing) mode will usually be required. Similarly, for those with implantable cardioverter-defibrillators, the device should be reprogrammed to suspend the anti-tachycardia function and prevent delivery of an unwanted shock. Devices with advanced functions (i.e. rate response function, sleep/rest mode) should have these functions turned off [105].

In general, no device reprogramming is required for surgery below the umbilicus [103]. When reprogramming is required, it is usually performed by trained personnel with a device-specific programming machine. Classic teaching describes placing a magnet onto the device for temporary suspension of the function of cardiac implantable electronic devices, however, this approach is seldom employed nowadays. The responses of the different devices to the

Table 10 Recommendations for management of cardiac implantable electronic devices (adapted from [107]).

Procedure	Intra-operative pacemaker monitoring	Pacemaker reprogramming	Postoperative pacemaker check	Implantable cardioverter-defibrillator deactivation/ re-activation
Surgery below umbilicus or upper limb distal to elbow	+	–	–	+
Surgery above umbilicus or upper limb proximal to elbow	+	±[a]	±[a]	+
Cardiac surgery	+	+	+	+
Ophthalmic surgery (if unipolar diathermy anticipated)	+	±[a]	±[a]	+
Endoscopy procedure	+	±[a]	±[a]	+
Dental surgery (only if diathermy use is anticipated)	±	±[a]	±[a]	+
Lithotripsy	+	±[b]	±[b]	+[c]
Electroconvulsive therapy	+	±[b]	±[b]	+[c]
Nerve conduction studies	+	±[a]	±[a]	±

[a] ±: Consider reprogramming if patient is pacemaker dependent; postoperative pacemaker check required if reprogrammed.
[b] ±: Consider reprogramming if patient is pacemaker dependent; interrogate pacemaker within 1 month after procedure.
[c] +: Deactivate implantable cardioverter-defibrillators peri-operatively and reactivate postoperatively, carry out checks after procedure.

magnet vary and are, thus, unpredictable, but it is also challenging to keep it in the optimal position particularly, when the surgery is performed in the lateral or prone position. In circumstances when placing a magnet is required, it is crucial to clarify with the cardiologist what will be the exact response of the cardiac implantable electronic device [104]. The British Society of Heart Rhythm has published a guide on the actions required for device management during different clinical scenarios (Table 10) [107]. These scenarios can be diverse and there is a paucity of evidence for peri-operative management of these devices for every specific procedure. As mentioned above, it is still advisable to discuss with the parent team for patients either with a complex device implanted or those with complicated cardiac conditions.

Conclusion

Many of the conditions mentioned above can be optimised before surgery and, therefore, to some extent can be regarded as modifiable risk factors. Anaesthetists can play an important role both in stratifying the risks and in initiating or titrating management, as well as liaising with other specialists where appropriate. Ultimately, the objective of pre-operative cardiac optimisation is to identify and modify these conditions well in advance to avoid cancellation or postponement of surgery and reduce the likelihood of peri-operative complications.

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Review Article

Shared decision-making in peri-operative medicine: a narrative review

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Summary

This review on shared decision-making comes at a time when international healthcare policy, domestic law and patient expectation demand a bringing-together of the patient's values and preferences with the physician's expertise to determine the best bespoke care package for the individual. Despite robust guidance in terms of consent, the anaesthetic community have lagged behind in terms of embracing the patient-focused rather than doctor-focused aspects of shared decision-making. For many, confusion has arisen due to a conflation of informed consent, risk assessment, decision aids and shared decision-making. Although they may well be linked, they are discrete entities. The obstacles to delivering shared decision-making are many. Lack of time is the most widely cited barrier from the perspective of physicians across specialties, with little time available to the anaesthetist at the day-of-surgery pre-operative visit. A more natural place to start the process may be the pre-operative assessment clinic, especially for the 'high-risk' patient. Yet shared decision-making is for all, even the 'low-risk' patient. Another barrier is the flow and the focus of the typical anaesthetic consultation; the truncated format presents the danger of a cursory, 'time-efficient' and mechanical process as the anaesthetist assesses risk and determines the safest anaesthetic. As patients have already decided to proceed with therapy or investigation and may be more concerned about the surgery than the anaesthesia, it is often assumed they will accept whatever anaesthetic is offered and defer to the clinician's expertise – without discussion. Furthermore, shared decision-making does not stop at time of anaesthesia for the peri-operative physician. It continues until discharge and requires the anaesthetist to engage in shared decision-making for prescribing and deprescribing peri-operative medicines.

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Introduction

Shared decision-making aims to bring together the patient's values and preferences with the physician's expertise to determine the best bespoke care package for the individual [1]. Its increasing prominence is due to a confluence of forces: quality improvement initiatives; the impact of patient advocacy groups; changes in healthcare policy; the need to distribute limited resources fairly and wisely; and a desire to understand complaints and claims and thereby reduce medicolegal payouts. Along with the development of biopsychosocial models of health, the differentiation of illness from disease and a focus on patient-defined outcomes, shared decision-making is one component of a broader shift towards 'patient-centred

care' – indeed, it has been called the 'pinnacle' of this movement [2].

The concept of shared decision-making has been prominent in the literature for approximately three decades. The 1980s and 1990s saw the publication of highly influential work [3–6] that argued for a move beyond the basic principle of 'informed consent' to a more deliberative interaction featuring robust discussion between doctor and patient about the best way to shape care in alignment with the latter's values and preferences. Commentary, descriptive and interventional research, and policy and institutional initiatives have continued since (Table 1). For example, the Institute for Healthcare Improvement reinforced the importance of patient experience, satisfaction and involvement by including it in its *Triple Aim Framework* [7]. In 2011, Collins and Coulter [8] tried to set the pace in the UK with the headline title '*Making shared decision-making a reality*', and now, in 2019, we are making tentative steps towards the shared decision-making ideal in the peri-operative space [1, 9, 10]. It is apparent from the very gradual pace of shared decision-making work that the ideal is proving harder to deliver than anticipated, for reasons that we will discuss at length below.

Despite these difficulties, achievement of processes that more robustly involve patients in peri-operative decisions remains an important goal. National surveys of inpatient experiences performed in the UK by the Care Quality Commission demonstrate the importance of involving patients in decisions about their care [12, 13], and some improvements have been made: between 2009, 2013 and 2017 there was an increase from 75% to 78% to 81% of patients responding that their questions relating to their operation were answered in a way they could 'completely' understand. Whether this finding can be extended to anaesthesia remains to be found. In addition to involvement, the evidence supports the need for patients to be offered choices and to have their opinion heard [14], something that is written into the NHS Constitution [15] as part of a patient's rights, and in the GMC's 'Good Medical Practice' guidance for doctors practising in the UK [16].

Table 1 Key publications in the evolution of shared decision-making in peri-operative medicine.

1984: Katz. The Silent World of Doctor and Patient [3].
1992: Emanuel & Emanuel. Four models of the physician-patient relationship [4]
1993: Gerteis et al. Through the Patient's Eyes 1993[5]
1997: Charles et al. Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango) [6]
2008: Berwick et al. The Triple Aim: health, care and cost. Cited in [7].
2011: Coulter & Collins. Making shared decision-making a reality. No decision about me without me [8]
2012: Barry, Edgman-Levitan. Shared decision-making – the pinnacle of patient centred care [2]
2017: The SHARE approach. Agency for Healthcare Research and Quality, Rockville, MD [11]
2017: Yentis et al. AAGBI: Consent for Anaesthesia 2017 [9]
2017: Royal College of Surgeons. Consent: Supported Decision-Making [10]
2018: Peri-operative Quality Improvement Programme. 5 National Improvement Opportunities 2018–2019 [1]

Evolution of English law from 'consent' to shared decision-making

It is worth first describing the legal background to the development of shared decision-making as a concept and practice in the UK. In Britain, a recent landmark case, (Montgomery (Appellant) v Lanarkshire Health Board (Respondant) [2015] UKSC 11 on appeal from [2013] CSIH 3) [17], changed the landscape for doctors by highlighting the pivotal role of the partnership between healthcare provider and patient and relegating paternalism to the past. The case involved a woman with gestational diabetes and her choice of delivery options; a lower segment caesarean section was not offered, and shoulder dystocia occurred at the time of vaginal delivery, with subsequent injury to the baby. The Law Lords supported Mrs Montgomery and set a new direction in consent, moving away from the Bolam test [18]: being able to demonstrate that you (the medical professional) acted in a way that a responsible body of medical professionals in your field would deem reasonable is no longer a viable defence.

Dependence on the Bolam test had actually been questioned before Montgomery with the Bolitho test [19] (Bolitho (Deceased) v City and Hackney HA [1997] 3 WLR 1151), when on appeal the Law Lords placed two caveats onto the 'reasonable professional opinion' Bolam test: consideration must have been given first to both the risks and benefits of the treatment given, and second to the logic upon which that consideration was made – in other words, the decision needed to stand up to interrogation of reason rather than rely on the opinion of learned men. The shift towards shared decision-making has included a number of cases, yet in essence we have travelled from what a body of professionals deem reasonable (Bolam), to whether the practice is justifiable or stands up to an assessment of logic (Bolitho), to what a reasonable patient would want or need to know (Montgomery).

A number of comments in the Montgomery judgement are salient with regard to consent and shared decision-making. When it comes to consent, Lords Reed and Kerr stated, '*The doctor's duty is not fulfilled by bombarding the patient with technical information which she cannot reasonably be expected to grasp, let alone by routinely demanding her signature on a consent form*'. Moving the medical profession towards shared decision-making, the Law Lords highlighted that '*the assessment of whether a risk is material or not cannot be reduced to percentages. The significance of a given risk is likely to reflect a variety of factors besides its magnitude*', making it essential for the clinician to find out more about the patient's values and preferences to try and determine what may or may not present a material risk. A dialogue with the patient, '*even (among) those doctors who have less skill or inclination for communication*' forms the backbone of shared decision-making; yet this can present an almost insurmountable obstacle in systems of modern healthcare delivery where demand, numbers of patients and expectations outstrip resources in terms of time and money.

Challenges of the peri-operative context

The obstacles to carrying out shared decision-making become quickly apparent when we turn our attention to the peri-operative setting. The UK anaesthesia community have in many ways been ahead of the UK law in relation to consent [9], but they have lagged behind in terms of embracing the more patient-focused rather than doctor-focused aspects of shared decision-making. Although surgical outpatients have ranked aspects of care related to information and communication as their highest anaesthesia-related priorities [20], the pre-operative context presents several specific challenges to a fleshed-out and patient-centred decision-making process. One unsurprising obstacle is time. Lack of time is the most widely cited barrier to implementing shared decision-making from the perspective of physicians across specialties [21]. In their document, '*Consent: Supported Decision-Making*' [10], the Royal College of Surgeons recognised that 'time pressures can leave little opportunity to discuss diagnoses or treatment options' (p. 18) and that 'complying with the standard may involve setting aside more time'. Their firm suggestion was to plan for this increase in clinic time commitment, recommending that surgeons discuss this need with the Medical Director in their hospital [10].

The issue of time is a particular problem for the anaesthetist, who has very little of it on the morning of surgery. The natural place to start shared decision-making in anaesthetic practice is thus the pre-operative assessment clinic, and this concept has received widespread support [9, 22–24]. The argument is easily won in the high-risk patient, where understandable decisional conflict can be better addressed over more than one visit, giving plenty of time to reflect on the significance of choices or discuss with family members. Yet shared decision-making is for all, including the routine, low-risk, elective patient for minor surgery, because there will always be risk, and there will always be patient and clinician preferences. Anaesthesia consultations carried out directly before surgery do not follow the familiar regimented stages of conventional outpatient consultations [25]: opening overtures; discovery of the patient's reason for attendance; verbal/physical examination; diagnosis; discussion of treatment or further diagnostic procedures; and termination of consultation. Instead, their truncated format presents the danger of a cursory and mechanical consent process for low-risk patients. Sir Ian Kennedy, in a review of a UK hospital's response to a breast surgeon found guilty of performing operations that did not align with his descriptions of said operations to patients, eloquently describes the tendency of consent to slip into an empty administrative routine to be completed as quickly as possible [26] (Point 6.12, p. 52):

> *"Further light is cast on the failure to grasp the importance of consent by the practice, which I still encountered in 2013, of clinicians talking of 'consenting' patients. The objections to this awful phrase are not merely linguistic. They go to the heart of a proper understanding of the relationship between patients and clinicians. Consent is a device designed to signal to clinicians that patients are in charge of their own bodies and that clinicians need to ask permission (consent) before doing things to them. If, however, the prevailing culture is one in which the patient is seen as the recipient of whatever is on offer, then consent can come to be seen as some perfunctory exercise to make sure some difficult-to-understand-why hurdle is jumped over. Hence, the patient is 'consented' and the clinician can then get on with things, having had to pause as briefly as possible to tick the consent box."*

Professor Kennedy's account hints at a second difficulty inherent to decision-making in anaesthesia: the position of the anaesthetist within the peri-operative pathway. The surgical patient, by the time he or she speaks with an anaesthetist, has already agreed to a plan for investigation or treatment. Anaesthesia consultations are not done to decide whether the patient will have anaesthesia [27]; the

patient is already somewhat positioned as the *'recipient of whatever is on offer'* to use Kennedy's phrase, because he or she has already agreed to an overarching course of care. The patient's and the anaesthetist's assessment and understanding of the risks associated with anaesthesia occur only against the backdrop of a preceding decision, made by the patient and another physician, to undergo the procedure at hand. This inflects the pre-operative consultation in complex ways that must be clarified by further empirical study. It may be the case, for example, that patients have a greater tendency to defer to physicians about anaesthetic decisions because they have already decided on the procedure [28]. It may also be true that anaesthetists do not typically bring up process elements like choice of airway device, medication and route of administration because they view such process elements as matters of 'clinical judgement,' part of the procedural package to which the patient has already consented. However, they commonly initiate discussions about procedural elements such as the choice of regional vs. general anaesthesia [29] even though the 'process' elements can affect peri-operative risk to a similar degree.

Anaesthesia is a highly task-focused specialty. The anaesthetist is presented with a patient, who has a set of comorbidities, and a plan for undergoing a procedure. For the high-risk patient, the task is to assess the risk of morbidity and mortality for that patient's pathology and physiological state according to the anaesthetic and surgical techniques available. In the rush to optimise the patient to ensure the best outcome, some have suggested that anaesthetists should ask the primary care physician to send haemoglobin, electrolytes and glycated haemoglobin results at time of referral. But due to the 'downstream' position of the anaesthetist in the peri-operative pathway, such a strategy is not ideal from the standpoint of shared decision-making. Has the patient been referred by the primary care physician for surgery, or simply for a surgeon's opinion? Is the role of the surgeon to only discuss the knee replacement (for instance), or might they have more options to consider, at which point the patient may need time to decide about or even to refuse surgical intervention, once they have been through a shared decision-making process? One could argue that taking tests in anticipation of surgery (before a decision has been made) is a form of coercion, and it may give rise to unanticipated results that require further investigation that the patient may or may not want. Directing attention to the role of the anaesthetist in the entire peri-operative pathway highlights the fact that decision-making is not a discrete event but a temporally unfolding *process* [30]. This process begins well before the anaesthetist becomes involved, and it does not stop when the patient leaves the recovery room: as peri-operative physicians, anaesthetists have an important role to play in ensuring that excellent recovery is a reality [31], and that take-home analgesics are prescribed and deprescribed in a responsible fashion [32].

Patients' preferred decision-making roles

Another issue particularly germane to shared decision-making in the peri-operative context is the extent to which a given patient prefers to participate in a specific anaesthesia-related decision. Considerable individual variation in patient preferences for involvement in decision-making has been shown [33]. Furthermore, decision-making preferences appear to be changing over time: 43% of analyses conducted between 1974 and 1989 found that a majority of patients preferred to participate in decisions, as compared with 71% of analyses in 2000–2007 [34]. Physicians are generally not proficient at estimating the decision-making preferences of their patients [35], an inaccuracy that is borne out in actual consultations, as the patient-involving behaviours of physicians do not vary in association with variations in patients' self-reported decision-making roles [36]. Unfortunately, this inability to determine how, and to what extent, patients would like to be involved in decisions has been demonstrated in studies that have specifically examined anaesthetists [37]. Professor Kennedy offers an account [26] of a couple in the midst of a decision-making process around breast surgery that vividly illustrates the consequences of a provider's failure to match their interactional approach to the inclinations of a patient and her family (Point 6.11, p. 52):

> *"He (Mr Patterson) was incensed to be told by a member of staff dealing with his wife's subsequent complaint, that in deciding whether to have a second operation, 'It is usual practice as part of the consent process for a surgeon to discuss various surgical options with their patient. . .. Ultimately, the decision whether or not to undergo surgery. . . has to be the decision of the patient themselves (sic).' His response, quite rightly in my view, was that 'his wife should not have been put in the position of having to decide on the correct procedure. . .. We were faced with a dilemma we were not qualified to resolve'."*

This reflection also reinforces study findings that confirm the importance patients place on being fully involved without having to necessarily make the final decision [25, 26]. This may frequently be the case in

anaesthesia consultations, where patients may be focused more on wider goals [38] such as the type of surgical procedure they are undergoing, than the granular details of anaesthesia. However, this orientation does not mean that the patient will not value thorough communication with the anaesthetist and this is a dialogue that would be required anyway in order for the physician to ascertain that the patient does not wish to exert strong decision-making power about aspects of anaesthesia.

Implementation of shared decision-making

In recent years, the medical decision-making community has largely shifted from examining the concept of shared decision-making and its potential effects to pushing to implement it in practice [39, 40]. The most common type of intervention used to pursue implementation of shared decision-making has been the decision aid. Cathy Charles, who played a central early role in theorising the shared decision-making model, has made a convincing argument that, in some circles, decision aids and shared decision-making are now treated as synonymous [41]. Outcomes associated with the implementation of decision aids [42] have at times been attributed to the achievement of shared decision-making [43] when in fact no studies have yet shown that the use of a decision aid changes provider–patient interaction into something resembling shared decision-making.

The concept of shared decision-making was based on moving beyond traditional consent – with its primary focus on information provision – to a model that involved the patient in a deliberative discussion with the physician about what may be the best path forward. That decision aids have become the main vehicle for trying to achieve this type of discussion is thus a somewhat strange development, since their focus is on delivering more information to the patient. Shared decision-making as proposed by its founding theorists contains a deliberation stage, following on from information transfer, that is, fundamentally intersubjective, highly dynamic and spontaneous, and powerfully inflected by social norms, affect and asymmetries of authority and expertise. It is not clear that information provision is the main barrier keeping patients from participating in this stage [44], or that more information will always lead this stage to generate a better decision [45].

Shared decision-making's struggle to truly push beyond informed consent is evident in the anaesthetic literature, much of which has narrowly focused on consent: editors and authors have blurred the lines between shared decision-making and consent [46] and articles have frequently concerned themselves with the timing and amount of information given about medical procedures and likely outcomes rather than tackling the more difficult areas of what is important to the patient and what preferences they may have for their care [9, 28, 47, 48]. In the future, it will be vital for peri-operative practitioners and researchers to continue developing and implementing guidelines and interventions that encourage meaningful dialogue between patients and physicians, resulting in a choice of the best treatment modality, and taking patient preferences and values into account. For example, Choosing Wisely [49], a campaign run from the Academy of Royal Colleges in the UK, has a series of MAGIC questions (Table 2) that can help the patient to guide the clinician into a dialogue about their healthcare and treatment options. These questions arose from the health foundation's 'MAking Good decisions In Collaboration' programme, completed in April 2013 [49]. In the United States, the Agency for Healthcare Research and Quality has produced a set of steps to direct the practitioner through the process of shared decision-making called the SHARE approach [11] (Table 3). These strategies, in combination with decision aids, are an important step – although only an initial one – in helping patients and clinicians choose care that is 'supported by evidence, not duplicative, free from harm, truly necessary, and consistent with patients' values' [49].

Shared decision-making is a central component of the international priority of delivering high-quality, truly patient-centred, healthcare. The literature, the law and healthcare policy confirm that shared decision-making is what patients (and doctors – when they are patients) want. It is more than informed consent; it is more than the transfer of information.

Table 2 MAGIC questions for patients to ask their healthcare professionals [49, 50].

Do I really need this test, treatment or procedure?
What are the risks or downsides?
What are the possible side-effects?
Are there simpler safer options?
What will happen if I do nothing?

Table 3 The SHARE approach to shared decision-making: five essential steps for clinicians [11].

Seek your patient's participation
Help your patient explore and compare treatment options
Assess your patients values and preferences
Reach a decision with your patient
Evaluate your patient's decision

Shared decision-making requires a dialogue that takes place over a number of consultations, providing the patient time for pause and thought. The challenges for implementation by healthcare providers in current service-driven environments remain and require an appreciation of the true meaning of the concept of shared decision-making, and the more exacting task of finding the time.

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Review Article

Multi-modal prehabilitation: addressing the why, when, what, how, who and where next?

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Summary

Just as there is growing interest in enhancing recovery after surgery, prehabilitation is becoming a recognised means of preparing the patient physically for their operation and/or subsequent treatment. Exercise training is an important stimulus for improving low cardiovascular fitness and preserving lean muscle mass, which are critical factors in how well the patient recovers from surgery. Despite the usual focus on exercise, it is important to recognise the contribution of nutritional optimisation and psychological wellbeing for both the adherence and the response to the physical training stimulus. This article reviews the importance of a multi-modal approach to prehabilitation in order to maximise its impact in the pre-surgical period, as well as critical future steps in its development and integration in the healthcare system.

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Introduction

In order to improve patient outcome after surgery, there is a shift towards recognising the pre-surgical period as an effective means to optimise the physical status of the patient before the stress of their operation. In the current literature, a wide range of pre-surgical interventions are referred to as prehabilitation. Given the relatively short time span between diagnosis and surgery in which to implement a meaningful programme, there is a need not only to focus on each of the important elements of prehabilitation on their own, but also how they complement and reinforce each other to provide a multifaceted approach for more effective intervention.

Why? The importance of prehabilitation in the surgical context

Over the past decade, there has been a growing realisation that successful surgery is not dependent solely on the operation alone but, rather, on how well the patient is able to return to a physically and psychologically healthy state. The goal of this review is to highlight the importance of a multi-modal proactive approach to patient recovery after surgery.

At three months after major elective abdominal surgery, up to 50% of patients still demonstrate a degree of disability [1]. Since a goal of fast track and enhanced recovery protocols is to shorten the length of hospitalisation, it is important that patients are able to function well physically, and be relatively self-sufficient, once discharged. A main determinant of recovery is surgical morbidity, since complications have a significant impact on the patient's postoperative physical status and overall quality of life. Although not conclusive, there is emerging evidence that prehabilitation plays an important role in patient recovery by diminishing the risk of developing postoperative complications, especially in high-risk populations [2].

Low cardiorespiratory fitness can limit access to curative therapies; indeed, despite a higher incidence of cancer in the elderly, the proportion of patients with a cancer diagnosis who undergo surgery progressively declines with age [3].Through the enhancement of pre-operative functional capacity and adoption of best-evidence practice clinical guidelines, clinicians may have the means to safely and effectively increase the number of candidates eligible for curative-intent surgical resection.

The role of prehabilitation may also play an important role in the preparation of the patient for subsequent cancer treatment, as chemotherapy, radiotherapy and hormonal treatment are all known to have a negative impact on functional capacity [4]. Poor physical and nutritional status have been identified as important reasons for low adherence and responsiveness to neo-adjuvant therapy. Delays in the commencement of adjuvant treatment due to poor physical status are associated with higher mortality rates [5]. In light of these important concerns, there is a growing interest in prehabilitation as a part of a cancer care continuum, for the prevention and/or attenuation of treatment-driven disorders, the improvement in access and adherence to curative therapies, and the enhancement of quality of life.

Following the traditional rehabilitative approach, early studies on interventions intended to improve physical function in the pre-operative period were primarily focussed on orthopaedic, cardiac and cancer patients. The rationale underlying this type of intervention is strong [6], and good quality systematic reviews show a positive impact of pre-operative exercise therapy on physical function, quality of life, postoperative complications and length of hospital stay [7–10]. However, despite this evidence, surgical prehabilitation is not yet a component of routine clinical practice. Alongside logistical and economic considerations, a step towards a better understanding of the clinical impact of prehabilitation, as well as a scientific-based method of implementation, is now due. Indeed, the quality of meta-analysis is often limited by significant heterogeneity of pre-operative interventions, cancer type, surgical techniques and peri-operative management, and usually lacks detailed information about effective doses, duration and adherence. Furthermore, to date, there has been no original comparative research examining which is the most appropriate intervention, for example, unimodal vs. multi-modal; supervised vs. home-based exercise; aerobic vs. resistance exercise, high vs. moderate intensity aerobic exercise; also lacking are guidelines on how individualised care should be conducted.

When? Using the pre-operative period to improve physiological reserve and functional capacity

Surgery represents a major metabolic stress that promotes loss of lean muscle mass, homeostatic instability and the impairment of aerobic capacity. Patients who undergo major surgery stay in the hospital, on average, a total of 7–9 days, with the largest number of bed-days attributable to the postoperative recovery period. Clearly, a rapid return to full physical function after major surgery has the potential to improve outcomes for patients, thus allowing them to return home and resume normal activities earlier. Furthermore, accelerated early recovery also has health economic benefits and potentially more efficient use of available hospital beds.

Although great progress has been made in surgical technologies, anaesthesia, analgesia and peri-operative care, complication rates after major surgery remain above 30% [11]. Furthermore, major surgery is associated with a 40% reduction in physiological reserve. In fact, patients report physical fatigue, reduced appetite, pain, disturbed sleep and a decreased ability to concentrate for up to 4 weeks after discharge [12]. Even after 6–9 weeks, functional capacity may not be fully recovered [13]. When the impact of abdominal surgery is evaluated using measures of functional capacity, only 30% of elderly patients had recovered to pre-operative levels at 8 weeks and 50% at 6 months after surgery [1, 14].

The introduction of fast track and enhanced recovery protocols that target the intra- and postoperative periods have been associated with a 30% risk reduction in postoperative complications, shorter hospital stay by one day and no increase in re-admission rates. Relatively little emphasis, however, has been placed on optimising patient physical function in the pre-operative period. This time frame offers many advantages, as it is not affected by postoperative symptoms and concerns. As there is a waiting period before surgery for most elective procedures, this represents an opportunity to intervene in a targeted fashion to improve postoperative recovery (Fig. 1). Active engagement of the patient in the preparation process may have benefits beyond the physical, and alleviate some of the emotional distress surrounding the anticipation of surgery and the recovery process.

What? The multi-modal approach to prehabilitation

Prehabilitation has been defined as '*a process on the cancer continuum of care that occurs between the time of cancer*

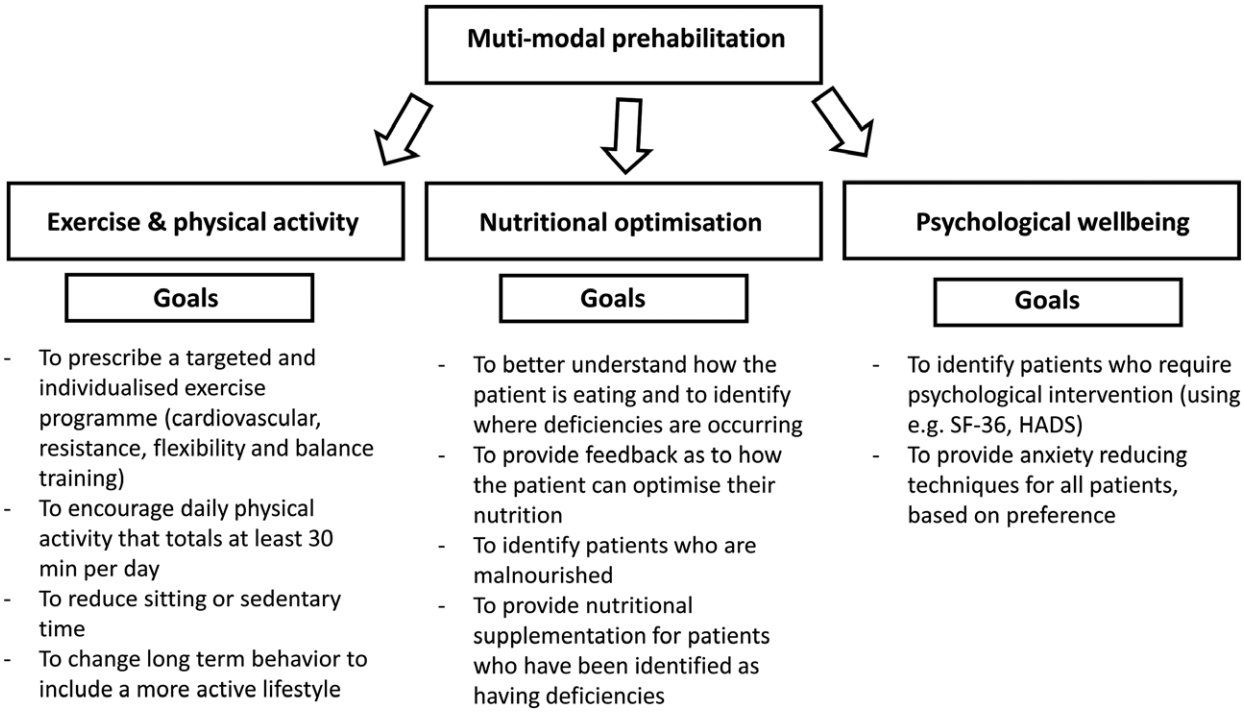

Figure 1 An overview of a multi-modal prehabilitation programme and related goals. SF-36, 36-Item Short Form Health Survey; HADS, Hospital Anxiety and Depression Scale.

diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments' [6]. Importantly, this definition addresses the concept of multi-modality, as it states that physical and psychological factors must be assessed and included as elements of an effective intervention. Multi-modal prehabilitation considers the set of complex interactions between the physical and psychological health of a patient, which must be addressed and individualised to maximise the outcomes of the intervention [15]. When a patient is found to have poor functional capacity by means of assessments such as cardiopulmonary exercise testing or a 6-min walk test, it is understandable to focus on exercise. Recent systematic reviews provide an important framework for guidelines, best evidence and standardisation for effective exercise prescription in the prehabilitation setting [7, 16–18]. Hijaziet al., within the context of their review, advance the discussion of multi-modality by suggesting that nutrition and psychological components should be standard in all prehabilitation programmes [16].

Prehabilitation, although an ideal opportunity to improve patient health status before surgery, also presents multiple challenges for programme delivery: the time frame between diagnosis and surgery is relatively short, and requires an effective intervention in which patient compliance is critical. Furthermore, the physiological conditions of the patient must be optimised in order to maximise the effects of the intervention. For instance, if a patient is malnourished, their response to exercise training may be reduced [19].

Early investigations in prehabilitation have demonstrated the importance of a multi-modal approach. A study that compared a combination of vigorous intensity bicycle exercise and resistance training vs. a sham control of light walking and deep breathing reported not only a low adherence to the bicycle/resistance training protocol (16%), but also that the light walking and breathing intervention had a greater effect on 6-min walk test results both at pre-operative and into the postoperative period [20]. Given the counterintuitive results, the authors hypothesised that, given the demands of the exercise programme, the subjects were physically and perhaps psychologically unprepared for the challenge of the training protocol and might have benefited from a multi-modal approach [19]. Indeed, more

recent studies that have employed multi-modal interventions, including nutritional supplementation (specifically protein), anxiety reduction techniques and a combination exercise protocol (cardiovascular and resistance training), have reported improved functional capacity and higher adherence rates in the pre-operative period, as well as an enhanced postoperative recovery, when compared with unimodal and more traditional rehabilitative approaches [21, 22].

A diagnosis of cancer is distressing to patients and may result in high levels of anxiety and/or depression, with a negative impact on morbidity and mortality [23]. Indeed, patients with colorectal cancer and concurrent depressive symptoms, as determined by the Hospital Anxiety and Depression Scale, have been shown to present with lower functional capacity, and thus present a challenge in the pre-operative clinic (M. Barrett-Bernstein, unpublished observations). In addition to having an impact on physical function, it has been shown in the cardiac rehabilitation setting that anxiety impedes adherence to exercise interventions, thus limiting their effectiveness [24]. In light of the interactions between anxiety/depression, physical function and the ability to participate actively in exercise training programmes, psychological support for those patients that require it remains a high priority for inclusion in prehabilitation programmes.

Considering the relatively short window of opportunity for prehabilitation, it is critical to support the full physical and psychological needs of patients in order to prepare them best for surgery and recovery. As there is a growing movement to standardise clinical implementation of prehabilitation, there is a clear need for further investigation, optimisation of a multi-modal approach and an open discussion between healthcare providers who might best support these initiatives.

How? Implementing multi-modal prehabilitation from the perspective of physical activity and exercise

Firstly, both physical activity and exercise must be clearly defined: physical activity can be understood as any bodily movement produced by skeletal muscles that results in energy expenditure, whereas exercise is a clear subset of physical activity that is planned, structured and repetitive and has, as a final intermediate objective, the improvement or maintenance of physical fitness [25, 26]. A patient may be prescribed specific or local therapeutic strengthening exercises as a part of a short-term, targeted rehabilitative programme intended to correct an impairment or particular deficit [27]. It is important to emphasise that all of these factors are important components of prehabilitation and, taken together, provide a multifaceted intervention to change lifestyle behaviour, improve physical function and enhance recovery.

Current recommendations for the general population include 150 min of moderate or 75 min of vigorous physical activity per week; this can be performed safely by the pre-surgical cancer patient unless there is a specific contraindication. Exercise prescription should specify the 'FITT' principle: frequency (how often?); intensity (how hard?); time (how long?); and type (what kind of exercise has been prescribed?). For exercise prescription purposes, the recommendations are typically based on the guideline of 150 min per week, and broken down into bouts of aerobic training that should occur at least every second day, for approximately 30–45 min in duration, at a moderate level of intensity (e.g. 50–75% of age-predicted maximum heart rate). The exercise itself may be of different types, according to availability of equipment or patient preference. In addition to the aerobic component, resistance exercises should be performed at least twice a week, targeting all major muscle groups. Both flexibility and balance exercises are also encouraged as a part of a comprehensive training programme [28, 29]. Throughout the prehabilitation period, the patient must be assessed regularly in order to verify that the stimulus is adequate, thus avoiding a situation where the exercise is either too strenuous or insufficient. It must be emphasised that the FITT principle of prescription is only a framework, and must be tailored to suit the needs and physiological status of each patient [30]. In light of this, it is important that the exercise be designed and supervised by qualified personnel who can effectively individualise and deliver safe and targeted programmes. Adequate recovery between bouts of exercise must be ensured in order to maximise the benefits of the activity, as well as preventing fatigue and physical maladaptation. Jones et al. provided a review suggesting a comprehensive approach to and rationale for exercise prescription, specific for the population of patients with cancer [30].

Even for the patient who is unable or does not want to embark on an exercise training programme, health benefits can still be acquired by increasing the amount of movement performed on a daily basis. Replacing inactive or sedentary time with physical activity, even in short sessions of ≥ 10 min, is a strategic means to improve health status, especially in previously inactive individuals [31]. Increasing the amount of movement on a daily basis can include many easy to perform and enjoyable activities such as light

intensity walks, stair climbing, gardening, housework, dancing, yoga, swimming or hiking. In the case of prehabilitation, daily physical activity strategies can provide an excellent complement to a programmed exercise prescription. It has been shown previously that prehabilitation offers an excellent opportunity for patients to modify physical activity and exercise behaviour in the pre-surgical period [32].

Even in the general population, it is a challenge to embark upon major lifestyle changes, such as exercise [33]. Given that prehabilitation occurs at a very stressful point in time for the cancer patient, it must be emphasised that the patient's own goals, needs and preferences must be reflected in their programme prescription. Barriers should be identified and strategically addressed in order to maximise adherence [34]. As mentioned previously, the time frame for prehabilitation is relatively short, so patient compliance is critical and any approach must take into consideration factors that will favour active participation.

How? Implementing multi-modal prehabilitation from the perspective of nutrition

Malnutrition from either inadequate food intake, and/or metabolic and inflammatory changes that alter nutrient requirements or absorption, leads to wasting and diminished physical function. It is associated with increased morbidity, prolonged hospitalisation and re-admissions, prolonged surgical recovery and poorer quality of life. North American surgical consensus recommendations suggest that nutrition therapy is provided in all at-risk patients to mitigate potential malnutrition-induced complications throughout the peri-operative period [35].

Nutritional care includes sufficient protein to achieve anabolism, and sufficient energy to maintain body weight at times of major stress. The quality of the protein, the density of the protein in the protein food source and the non-protein food source should be taken into account. Non-protein components of diet, fat, carbohydrates and fibres as well as micronutrients need to be integrated [36]. The integration of nutrition and physical activity maintains physiological reserve sufficient to reduce the stress associated with surgery. In order to generate a positive net protein balance in favour of lean body mass accretion, essential amino acids need to be administered to produce a state in which protein synthesis exceeds that of protein breakdown. Taken immediately after resistance exercise, 20–30 g of protein in liquid form is regarded as sufficient to maximally stimulate muscle protein synthesis in healthy individuals [37].

How? Implementing multi-modal prehabilitation from the perspective of psychological wellbeing

In the context of surgery, psychological distress has been shown to have a negative impact on wound healing and postoperative pain relief, and result in prolonged hospitalisation and more functional limitation. Anxiety and depression is very common in patients with a cancer diagnosis; depression in this population has been shown to be associated with low levels of functional capacity, higher levels of pain, non-compliance with medical treatment, diminished immune response and carries an elevated risk of mortality [38]. High rates of anxiety and depression in the population of patients with cancer, as well as the negative effects of psychological distress on mental and physical wellbeing, have led to the investigation of whether pre-operative psychological interventions can reduce psychological distress in this patient population. Evidence supporting the role for 'psychological prehabilitation' before surgery comes from randomised controlled trials in breast, colon and prostate cancer patients [39]. Interventions implemented before surgery, such as relaxation techniques (deep breathing, progressive muscle relaxation and meditation) or guided imagery, have been shown to have a positive effect on pain severity, fatigue and quality of life.

Who? Targeting specific patient groups

Based on the concept that increasing physiological reserve before, rather than after, surgical admission promotes a higher level of functional capacity over the entire peri-operative and recovery period, it would make sense to target those who need particular attention such as the elderly, patients with frailty or those at risk of malnutrition.

The annual percentage of surgical interventions in the last 30 years has almost doubled for men and women aged 75–84 years-old compared with the middle-aged population. Elderly patients tend to have more postoperative complications and a longer convalescence than younger patients; surgical morbidity and mortality increases with advancing age and rises sharply after the age of 75 [40]. Elderly patients tend to spend more time sitting and in bed, with a negative impact on muscle mass and cardiovascular homeostasis, thus leading to poor pre-operative functional and nutritional status. Multi-modal prehabilitation is an attractive care strategy for this population, as it aims to increase functional capacity during the pre-operative period in anticipation of the stress of surgery and the metabolic cost of recovery [41].

Frail patients pose a significant challenge to healthcare providers as they may have chronic diseases such as cancer, dementia or coronary artery disease, thus requiring multiple interventions. Frailty is associated with functional decline and disability, and it would seem logical that this at-risk group could benefit from multi-modal prehabilitation. Structured and personalised prehabilitation programmes that include moderate exercise protocols, combined with nutritional optimisation and adequate psychological support, can improve postoperative outcome in these individuals. This is an important, targeted and rapidly developing area of clinical research.

What next? Future steps and directions in multi-modal prehabilitation

We have reviewed the concept of surgical prehabilitation and introduced the various aspects of intervention that have the intention of enhancing functional capacity and postoperative outcome.

It is evident that prehabilitation must be integrated comprehensively with other elements of an enhanced recovery programme to maximise its effectiveness. A multi-modal approach during the pre-operative period can include medical and pharmacological optimisation, correction of anaemia, alcohol and smoking cessation, as well as exercise and physical activity, nutritional optimisation and anti-anxiety strategies [18]. Such an approach may offer an opportunity to preserve or enhance physiological integrity and optimise surgical recovery. Most of the published studies indicate a positive effect of prehabilitation on postoperative functional capacity and earlier return to daily activities [42]. Nevertheless, there remains a clear need to evaluate the effectiveness of prehabilitation in specific populations using appropriate outcome measures and valid metrics, as well as establishing whether multi-modal interventions can diminish the risk of developing long-term disability in high-risk patients. Finally, the impact of prehabilitation on healthcare utilisation, cancer treatment surgical stress response and postoperative complications needs to be further elucidated.

Multi-modal prehabilitation requires an interdisciplinary approach, as it proposes a shift from the current healthcare paradigm. The challenge is to recognise that the pre-operative period represents an opportune time for preventative intervention, and to fully utilise this period in order to promote more effective clinical care.

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Review Article

Psychological factors, prehabilitation and surgical outcomes: evidence and future directions

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Summary

The pre-operative optimisation of comorbidities is increasingly recognised as an important element of the pre-operative pathway. These efforts have primarily focused on physical comorbidities such as anaemia and the optimisation of exercise and nutrition. However, there is a growing recognition of the importance of psychological morbidity. Increasingly, evidence suggests that psychological factors have an impact on surgical outcomes in both the short and long term. Pre-operative anxiety, depression and low self-efficacy are consistently associated with worse physiological surgical outcomes and postoperative quality of life. This has led to the emergence of psychological prehabilitation and the trimodal approach to prehabilitation, incorporating psychological intervention as well as exercise and nutritional optimisation. However, there is currently insufficient evidence to be sure that pre-operative psychological interventions are of benefit, or which interventions are most effective, because their impact has been mixed. There is an urgent need for high quality, contemporaneous prospective trials with baseline psychological evaluation, well-described interventions and agreement on the most appropriate psychological, quality of life and physiological outcomes measures.

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Introduction

The ageing population and the consequent increase in frail, elective surgical patients with multiple comorbidities present a challenge to the peri-operative team. The risks and benefits of surgery can be difficult to evaluate, and the involvement of the patient in treatment decisions using shared decision-making is important [1].The evaluation and pre-operative optimisation of comorbidities is increasingly recognised as an important element of the pre-operative pathway [2, 3]. Classically, these efforts have focused on physical comorbidities such as diabetes and anaemia, and optimisation of diet and physical activity/exercise. There is, however, a growing recognition of the importance of psychological morbidity. Increasingly, evidence suggests that psychological factors have an impact on both physiological and psychological surgical outcomes in both the short and long term. This has led to the emergence of psychological prehabilitation and the trimodal approach to prehabilitation incorporating psychological intervention, predominantly addressing anxiety and depression and enhancing coping skills, as well as exercise and nutritional optimisation. We will review this evidence and identify important areas for future research.

Psychological factors and surgical outcomes

Psychological factors affect physiological and psychological outcomes postoperatively [4, 5] in a range of surgical contexts including cardiac surgery [6], general surgery [7] and thoracic surgery [8]. A variety of psychological features has been evaluated, including mood-related factors, personality traits, attitudinal factors and coping strategies (Table 1) [9].

Two recent systematic reviews have evaluated the effect of psychological factors on short-term physiological surgical outcomes [4, 9]. Mavros et al. summarised the association between psychological factors and physiological outcomes affecting the site of surgery, namely wound healing and postoperative complications in the first month after surgery. They identified 16 studies including 1473 patients [4]. They found significant heterogeneity in both the psychological factors and the outcomes evaluated. Despite this, almost all studies identified a psychological variable with a statistically significant association with one of the measured outcomes. Some psychological features had a protective effect, whereas others were associated with a negative outcome. The positive and negative psychological factors are summarised in Table 2. Rosenberger et al. evaluated the effect of mood, attitudinal factors, personality and coping mechanisms on complications, pain and analgesic use, functional recovery, length of hospital stay and ratings of physical recovery [9].Twenty-nine studies incorporating a variety of surgical specialities were included. Again, not only was significant heterogeneity reported between studies, but also some important consistent themes emerged. With regard to mood, anxiety predicted short-term operative outcomes, length of stay and patient ratings of recovery, whereas depression particularly predicted long-term pain. Attitudinal factors, particularly self-efficacy, a positive outlook and patient-perceived control were associated with earlier functional recovery. In contrast, global personality measures, such as neuroticism and extraversion, were not strong predictors of short-term physical outcomes. In their entirety, these systematic reviews suggest that psychological factors that are amenable to psychological interventions, such as mood disorders and self-efficacy, are associated with outcome after surgery and may be a target for pre-operative interventions.

Table 1 Pre-operative psychological factors evaluated in studies addressing surgical outcomes.

Mood factors
Anxiety, depression, psychological stress, hostility, perceived stress, anger
Attitudinal factors
Self-efficacy, perceived control, positive expectations, optimism, locus of control and desire for involvement
Personality traits
Neuroticism, extraversion, self-esteem, motivation, ego strength, inadequacy

Table 2 Psychological factors associated with positive and negative short-term surgical outcomes.

Factors associated with favourable outcomes
Self-efficacy, low pain expectation, external locus of control, optimism, religiousness, anger control
Factors associated with unfavourable outcomes
Trait anxiety, state anxiety, depression, intramarital hostility, state anger, psychological distress

Psychological factors and postoperative pain

The relationship between psychological factors and postoperative pain, both acute and chronic, has been extensively investigated [10, 11]. In a qualitative systematic review including 48 trials and 23,037 patients, Ip et al. identified pre-operative factors that predicted acute postoperative pain. Anxiety was one of the four factors found to be reliably associated with postoperative pain, the others being age, type of surgery and pre-operative pain. The relationship between depression and acute postoperative pain has been less consistent [12]. Chronic postsurgical pain occurs in between 10% to 70% of patients having major surgery, and is associated with long-term reduction in quality of life and significant economic implications [11]. Pre-surgical psychological risk factors for chronic postsurgical pain development have consistently been identified. Systematic reviews provide a high level of evidence for the predictive value of pre-surgical depression, psychological vulnerability and chronic stress on the risk of chronic pain after surgery [13]. Pre-operative anxiety and pain catastrophising have also been shown to double the risk of chronic postsurgical pain after surgery [14].

Relatively few studies have evaluated the protective effect of psychological factors on the development of chronic postsurgical pain. Dispositional optimism has been shown to be protective in women undergoing breast cancer surgery [15] and in patients undergoing coronary artery bypass surgery, after controlling for clinical and behavioural covariates [16]. Such studies suggest that having an

optimistic outlook about surgical outcome may reduce the risk of chronic postsurgical pain. The propensity to engage in adaptive health behaviours, as measured by the Patient Activation Measure, has also been shown to be predictive of reduced pain at 6 months after knee arthroplasty [17]. Pain self-efficacy evaluates an individual's confidence to perform activities despite pain; a higher score is associated with better functional recovery after arthroplasty, but not the degree of pain [18]. This literature, although limited in scope, suggests that enhancing self-efficacy and adaptive behaviours in the peri-operative period, and encouraging optimism, may improve outcomes for major surgical patients.

Psychological factors and postoperative quality of life

In addition to the evidence describing the importance of psychological factors on physiological outcomes after surgery, emerging data suggest psychological state before cancer surgery may have an impact on longer term quality of life and wellbeing. For example, Foster et al. conducted a trajectory analysis of the health and wellbeing of colorectal cancer patients over a 2-year period. Baseline measures were acquired before cancer surgery, and patients were followed up at regular intervals up to 2 years after diagnosis. Higher pre-surgical depression and lower self-efficacy to manage illness were significantly associated with poorer trajectories of recovery, even after adjusting for disease and treatment characteristics and the presence of a stoma. This reiterates the findings regarding the importance of self-efficacy for pain as described above, and supports the hypothesis that providing psychological prehabilitation that fosters coping skills might enhance recovery [19].

Psychological interventions to improve surgical outcomes

The evidence discussed thus far suggests that psychological factors that are amenable to change, such as anxiety, depression and poor self-efficacy, have an important impact on surgical outcomes, both physiological and psychological; however, an important question is, do psychological interventions improve outcome? A recent Cochrane review synthesised the evidence of psychological preparation and postoperative outcomes of pain, return to normal activities (behavioural recovery), length of hospital stay and negative effect in adults undergoing elective surgery. They evaluated a broad range of psychological interventions including: procedural information (information about what, when and how processes will happen); sensory information (what the experience will feel like and what other sensations they may have, for example, taste, smell); behavioural instruction (telling patients what they need to do); cognitive intervention (techniques that aim to change how people think); relaxation techniques; hypnosis; and emotion-focused interventions (techniques that aim to help people to manage their feelings). They included 105 studies from all surgical specialities. Small beneficial effects on all outcomes were reported, with no evidence of harm. However, the quality of evidence was low, with a high risk of bias in the majority of studies [20]. It is clear that there is a need for further prospective well-controlled trials to evaluate pre-operative psychological interventions. In particular, baseline evaluation of psychological state, including anxiety and depression and self-efficacy levels, is important, as is the use of standardised physiological and psychological outcomes.

Pre-operative education programmes

Pre-operative education programmes include information about the surgery, pain, pain medication and what to expect in the postoperative period. These 'joint schools' and 'surgery schools' are increasingly incorporated into pre-operative pathways, with multiple aims: reducing anxiety; increasing the patient's understanding of the importance of engagement in postoperative mobilisation, and addressing maladaptive behaviours around diet and physical activity. A systematic review of such interventions concluded that pre-operative education reduces anxiety, postoperative pain and length of stay, and improved satisfaction [21]. Such programmes have been incorporated into routine care for joint arthroplasty [22], and are an integral element of enhanced recovery after surgery pathways that have been demonstrated to improve surgical outcomes [23, 24]. More recently, surgery schools have been incorporated into enhanced recovery programmes, with apparent beneficial effects on outcomes, although it is not clear which elements of the package of care are most effective [25]. Although these programmes tend not to be described as 'psychological interventions', it is clear that there is considerable overlap with the evidence discussed previously. This suggests that numerous benefits may result from telling patients what to expect on the day of surgery and how to prepare, as well as expectations for the immediate postoperative period.

Psychological prehabilitation – a cancer focus

Increasingly, studies investigating the role of psychological prehabilitation are emerging, particularly within the field of

oncology; these have an emphasis on reductions in stress and anxiety. Tsimopoulou et al. [5] synthesised the evidence of pre-operative psychological interventions on postoperative outcomes in cancer patients. They identified seven studies, including 605 patients from six randomised controlled trials. Interventions included the use of relaxation techniques, guided imagery, stress management and psychotherapeutic intervention. Interventions were implemented 1 day to 2 weeks before surgery. There was no evidence of improvement on what the authors describe as 'traditional surgical outcomes'; these included hospital length of stay, complications and analgesia use. However, three of four studies reported improvement in patient-reported outcomes, with reduced depression either pre- or postoperatively. The effects of psychological interventions on postoperative quality of life were mixed, with some suggestion of improvements in physical function aspects of quality of life, but little evidence of improvement in cancer-related domains, such as symptom severity. The authors suggest stress management training may be more effective in improving quality of life than psychotherapeutic approaches; however, as there is considerable variation in outcome measures, such conclusions may be premature. A more recent review of 18 prehabilitation interventions in cancer patients identified some additional studies that included a psychological component [26]. Both reviews note that the included studies tend to be small, at risk of bias and use a variety of outcome measures, making synthesis of the evidence difficult. There was also significant heterogeneity in the timing of data collection for outcomes, ranging from a week before surgery to 3 months after surgery.

The emphasis in the aforementioned reviews has been on unimodal models of prehabilitation; however, it has been acknowledged that prehabilitation programmes should enhance both functional and mental capacity, mirroring existing efforts in rehabilitation by including exercise, nutritional and psychological support [27]. A pilot observational study compared a historical control with a 4-week trimodal prehabilitation programme in 87 colorectal cancer patients [28]. The programme included home-based moderate intensity aerobic and resistance exercise, and nutritional counselling with protein supplementation. The psychological component of this intervention included a 90-min consultation with a trained psychologist who provided techniques to reduce anxiety, including relaxation exercises based on imagery and visualisation, as well as breathing exercises. The participants were given a CD to facilitate performance of the exercises at home. Postoperative functional capacity evaluated by the 6-min walk test was better among those who received the intervention at 4 and 8 weeks follow-up; however, baseline scores were not reported. There was no impact on quality of life as measured by the SF-36, although there was a significant reduction in both the anxiety and depression elements of the hospital anxiety and depression scale. The same research group went on to conduct a randomised controlled trial in 77 colorectal cancer patients using a very similar trimodal programme delivered either before surgery (prehabilitation group) or after surgery (rehabilitation group). Eighty per cent of prehabilitation patients regained their baseline physical function by 8 weeks postoperatively, compared with 40% who received the intervention after surgery. No differences were observed in health-related quality of life (as measured by the SF-36), anxiety or depression (using the Hospital Anxiety and Depression Scale); however, the study was not powered to detect such differences [29].

Clearly there is a need for more and larger trials evaluating the efficacy of psychological prehabilitation, either alone or as part of a multi-modal intervention, to investigate any impact on psychological morbidity.

There is also reason to believe that unimodal exercise prehabilitation may have a positive impact on quality of life. It is well established that exercise alone has beneficial impact on quality of life in cancer patients during and after treatment [30–32]. There is also a suggestion that supervised exercise may have a greater effect than unsupervised [33]. However, data are limited in the prehabilitation setting, as quality of life is measured infrequently in prehabilitation exercise trials. For example, a review of exercise prehabilitation in elderly patients undergoing colorectal cancer surgery [34] identified six studies, but only one measured quality of life [35]. In this small pilot randomised controlled trial of 42 patients, subjects randomly allocated to the intervention group performed supervised exercise training twice a week, and were prescribed a home-based exercise programme for up to 4 weeks before surgery. Adherence to the supervised exercise component was 97%; however, there were no changes over time or differences between groups in postoperative cancer-specific quality of life, as measured by the EORTC-QLQ-Q30 (European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30) [35]. In a review of 21 pre-operative exercise interventions in adult surgical patients, not limited to cancer, only nine examined health-related quality of life, with just one reporting quality of life improvements postoperatively [36].

It should also be considered that quantitative measures may not capture all facets of quality of life that are important to patients, and that they may be affected by exercise prehabilitation. Qualitative methods can capture these personal perspectives of quality of life, providing a more in-depth understanding of the experience and impact of exercise participation for patients. A recent meta-synthesis explored the existing qualitative research examining the impact of physical activity on quality of life in cancer patients [37]. Nine of the 40 studies involved patients undergoing treatment. Physical activity was found to have a positive impact on four dimensions of quality of life, which were physical, psychological, social and spiritual. The review also included studies of patients in the pre-surgical period. Burke et al. [38] found that exercise before surgery in adults with advanced rectal cancer gave patients a direction and purpose and fostered a sense of control, factors that were unlikely to be captured in existing quantitative measures of quality of life. Similarly, in a study of women with breast cancer participating in a 16-week supervised exercise intervention undergoing adjuvant chemotherapy, participants talked about a feeling of empowerment and motivation to focus on their health [39].

The existing evidence base presents significant heterogeneity regarding the impact of prehabilitation programmes on psychological morbidity and quality of life. This is likely to be due to the variability in intervention and participant characteristics, sample size, timing of outcome measurements and choice of outcome measure. It is clear that larger trials examining both uni- and multi-modal approaches to prehabilitation, and determining both the independent and combined impact on physiological and psychological outcomes, are warranted.

Prehabilitation and behaviour change

Many existing pre-operative exercise studies involve supervised exercise sessions. Adherence to such interventions is often not reported; but where it is it tends to be good, with some studies reporting compliance of over 90% [35, 40]. However, it is acknowledged that if prehabilitation programmes are to be implemented in a sustainable way in current healthcare systems, community and home-based programmes are needed. A number of multi- and unimodal pre-operative interventions have included unsupervised, home-based elements, with mixed adherence rates [41]. These programmes often involve provision of written materials, CDs and follow-up telephone calls to encourage engagement; however, there is little evidence of the use of behaviour change theory to guide intervention components. Changing health behaviours is complex, and those designing future prehabilitation programmes can draw on a wealth of research from social, psychological and behavioural science that seeks to understand how best to support individual behaviour change. It is acknowledged that interventions that target specific mechanisms of action (often informed by behaviour change theory) are likely to be more effective [42]. Theoretically, informed approaches to behaviour change have proved promising in a rehabilitation context. For example, a systematic review and meta-analysis of physical activity and dietary interventions in cancer survivors, informed by social cognitive theory, concluded that they were effective in changing behaviour in the short and medium term [43]. Furthermore, we recommend that interventions follow a person-centred approach, that is to say they should be developed in collaboration with patients, understanding their needs and preferences and potential barriers to engagement. We encourage programme developers to consider this evidence when designing prehabilitation programmes. Key concepts are presented in the National Institute of Health Care Excellence guidelines for behaviour change [44], which provide a set of evidence-based generic principles for planning, delivering and evaluating behaviour change interventions.

Conclusions and future directions for research

Patients not only need to prepare physiologically for the demands of surgery but they also need to be mentally fit; it is increasingly acknowledged that prehabilitation should include psychological components [45]. Pre-operative anxiety, depression and low self-efficacy are consistently associated with worse physiological surgical outcomes and quality of life. However, there is currently insufficient evidence to be sure that pre-operative psychological interventions are of benefit, or which interventions are most effective. This probably reflects the considerable heterogeneity in the literature in terms of the characteristics of the patients who are included, the choice of intervention and the choice and timing of outcome measures. Furthermore, studies to date have not evaluated psychological morbidity at baseline, and thus null findings could relate to ceiling effects. It may be that a stratified approach is required, targeting patients with abnormal mood and low self-efficacy for prehabilitation. This would require routine psychological evaluation pre-operatively, which is not currently widespread practice. Additionally, in prehabilitation studies where multiple interventions are employed simultaneously, it is difficult to know which is the effective element of the package of care.

There is an urgent need for high-quality, contemporaneous prospective trials with baseline psychological evaluation, standardised interventions and agreement on the most appropriate psychological, quality of life and physiological outcomes measures. The Wessex fit for cancer surgery trial, codesigned with patients, is an example of a trial attempting to address some of these issues [46]. It is recruiting patients preparing for elective major intracavity cancer surgery into a 2–15 week fitness and/or psychological support programme in a factorial design. The trial will compare standard care with a supervised exercise intervention alone, a psychological intervention alone or a combined psychological and exercise intervention.

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Review Article

Pre-operative respiratory optimisation: an expert review

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Summary

Postoperative pulmonary complications are common and cause increased mortality and hospital stay. Smoking and respiratory diseases including asthma, chronic obstructive pulmonary disease and obstructive sleep apnoea are associated with developing postoperative pulmonary complications. Independent risk factors for such complications also include low pre-operative oxygen saturation, or a recent respiratory infection. Postponing surgery in patients who have respiratory infections or inadequately treated respiratory disease, until these can be fully treated, should, therefore, reduce postoperative pulmonary complications. There is evidence from several studies that pre-operative smoking cessation reduces such complications, with no agreed duration at which the benefits become significant; the longer the abstinence, the greater the benefit. Intensive smoking cessation programmes are more effective, and there are long-term benefits, as many patients become permanent non-smokers following their surgery. Supervised exercise programmes normally last 6–8 weeks, and although they reduce overall complications, the evidence of benefit for postoperative pulmonary complications is mixed. High-intensity interval training can improve fitness in just 2 weeks, and so may be more useful for surgical patients. Specific respiratory pre-operative interventions, such as deep breathing exercises and incentive spirometry, can help when used as components of a package of respiratory care. Pre-operative inspiratory muscle training programmes that involve inspiration against a predetermined respiratory load may also reduce some postoperative pulmonary complications. Pre-operative exercise programmes are recommended for patients having major surgery, or in those where pre-operative testing has shown low levels of cardiorespiratory fitness; interval training or respiratory interventions are more feasible as these reduce complications after a shorter pre-operative intervention.

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Introduction

'Postoperative pulmonary complication' is a widely used term encompassing almost any complication affecting the respiratory system in the postoperative period [1, 2]. Commonly included events are chest infections, including pneumonia; respiratory failure; acute respiratory distress syndrome; and surrogates for all of these such as a requirement for postoperative mechanical ventilation. The wide range of diagnoses and interventions included in the term has led to a recent multinational attempt to simplify and standardise its definition [3]. Postoperative pulmonary complications, however defined, are common, with the quoted incidence varying from 1% to 23%, depending on the definition used and population studied [2]. Overall, 2.8% of patients having non-cardiac, non-obstetric surgery develop a severe postoperative pulmonary complication [4]; these are known to be more common than cardiac complications and lead to increased hospital stay, cost and mortality.

This review focuses on interventions that may be undertaken in the pre-operative period to attempt to reduce a patient's chances of developing a postoperative pulmonary complication.

Optimising pre-existing respiratory disease: specific conditions

Many patients presenting for surgery already have respiratory disease, and a pre-operative history of smoking, asthma, chronic obstructive pulmonary disease or obstructive sleep apnoea have all been shown to be associated with developing a postoperative pulmonary complication. However, a large observational study of 5859 patients in Spain by Mazo et al. [5] did not find these labels to be predictive for developing a postoperative pulmonary complication; instead the study identified seven independent predictors, among which were low pre-operative oxygen saturation on air and a clinical history of a respiratory infection in the last month. This finding suggests it is not the respiratory diagnosis or smoking in themselves that lead to postoperative pulmonary complications, but their effects on the lungs at the time of surgery; that is, a patient with chronic obstructive pulmonary disease who is well, based on normal oxygen saturation and no recent infection, should have a similar risk to a patient without chronic obstructive pulmonary disease. Thus, it is important to identify patients whose respiratory system is not currently 'well' on these simple clinical grounds so they can be made better, thus reducing their risk, before surgery is undertaken.

Between 10 and 15% of the population of developed countries now have asthma; this is thus the most common respiratory comorbidity encountered by anaesthetists. Fortunately, the incidence of peri-operative bronchospasm in patients with asthma is reassuringly low at 1.7%, but patients who do develop bronchospasm are more likely to have had recent respiratory symptoms, clinical evidence of infection or medical interventions for their asthma in the pre-operative period [6]. Patients with symptomatic asthma should therefore, if time allows, have their treatment increased until symptom control is achieved before proceeding with surgery. Even for urgent or emergency surgery, more intensive treatment with bronchodilators and/or steroids may be possible within only a few hours. This is best achieved in collaboration with respiratory physicians.

For patients with chronic obstructive pulmonary disease, postponement of surgery after or during a recent exacerbation is advisable, although it has never been studied specifically; the study by Mazo et al. provides indirect evidence that this will reduce postoperative pulmonary complications. In patients with stable chronic obstructive pulmonary disease, treatment optimisation is also worth considering before elective surgery, but this is much less likely to be successful due to the long-term pathophysiological changes of the disease, such as remodelling of airways, chest hyperinflation reducing respiratory muscle efficiency and changes in respiratory muscle morphology [7]. None of these changes are easily reversible.

Patients with obstructive sleep apnoea are at higher risk of peri-operative complications including postoperative pulmonary complications [8]. Because obstructive sleep apnoea is often undiagnosed, most pre-assessment services now screen patients, most commonly using the STOP-BANG questionnaire [9]. The results are used either to further investigate patients with sleep studies and treat if required, or to alter the anaesthetic management of the patient by, for example, using fewer opioids as part of their pain management or by opting for enhanced postoperative monitoring. This screening is recommended by the Association of Anaesthetists for all obese patients undergoing surgery [9] and there is reasonable evidence that screening is worthwhile from studies of patients with obstructive sleep apnoea undergoing bariatric surgery. For example, treating patients with continuous positive airway pressure in the peri-operative period does not appear to reduce the incidence of complications [10], but reduces the requirement for admission to respiratory intensive care [11]. However, evidence for an outcome benefit of pre-operative continuous positive airway pressure in non-bariatric surgery is lacking, and details such as the minimum duration of continuous positive airway pressure required to reduce risks remain unknown. In practice, the urgency of many operations, and lack of compliance with continuous positive airway pressure treatment by patients, mean many will still undergo upon surgery with either undiagnosed or untreated obstructive sleep apnoea and so require more intensive monitoring.

Exercise testing

Many patients present for surgery with no history of respiratory disease, or may even deliberately play down their symptoms for fear that their proposed surgery may be postponed or declined. Patients' self-reported exercise tolerance is notoriously unreliable, and this has led to a variety of techniques for supervised assessment of functional capacity. Shuttle walk and 6-min walk tests are simple to perform but remain partly subjective, and so cardiopulmonary exercise testing has become the 'gold

standard' for pre-operative assessment of fitness [12]. Much of the research on cardiopulmonary exercise testing in the pre-operative period has focussed on using the measures obtained to assess patient risk, which then contributes to choosing the most appropriate surgical procedure and peri-operative management strategy, followed by shared decision-making with the patient. However, cardiopulmonary exercise testing will also identify patients who have undiagnosed or inadequately managed respiratory disease, allowing treatment to be initiated or increased before surgery as above. Recent work has suggested that a test-derived marker of respiratory inadequacy, the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}CO_2$), is a strong predictor of overall complications following oesophagectomy [13]. The measured and derived indices may also help identify which organ system is functionally limiting the patient and is hence prone to complications. For instance, reduced anaerobic threshold (AT) is associated with cardiac complications, whereas elevated $\dot{V}E/\dot{V}CO_2$ is associated specifically with postoperative pulmonary complications, in patients undergoing aortic aneurysm repair [14]. Finally, cardiopulmonary measurements may allow more intensive pre-operative interventions, as described below, to be targeted to individual patients [12].

Smoking cessation

In the developed world, the proportion of adults who smoke is slowly falling, being now around one-fifth. Despite this decrease, it is still the most prevalent modifiable risk factor for developing a postoperative pulmonary complication. Current smokers have a slightly increased 30-day mortality after surgery, and a substantially greater risk of a complication; this increase is directly related to the number of pack-years smoked [2]. Relative to lifetime non-smokers, ex-smokers also have an increased risk of developing postoperative pulmonary complications, this again being related to the total pack-years of smoking. It is worth noting that the study by Mazo et al. reported that independent predictors for postoperative pulmonary complications did not include smoking, again suggesting that a 'well' smoker may not be at increased risk. However, the greater the pack-years of smoking, the more likely the patient is to have an acute respiratory illness or significant lung disease at the time of surgery.

Many, although not all, studies suggest that the increased airway irritability associated with smoking causes a greater incidence of intra-operative cough, laryngospasm and breath-holding [15]. Desaturation in the recovery room is also more common in smokers and even in passive smokers, including children from homes where relatives smoke [16].

The required duration of smoking cessation to reverse these effects is unclear. The cardiovascular effects of carbon monoxide and nicotine will be reversed in a few hours, and airway sensitivity to inhaled ammonia reduces after 2–10 days [17]. Return to normal mucus secretion and clearance is likely to take many weeks, as this requires reversal of the hyperplasia of submucosal glands, a reduction in the number of goblet cells and reversal of the structural changes seen in the cilia of smokers.

Some older observational studies of patients undergoing cardiac surgery who smoked found more postoperative pulmonary complications in those who abstained for less than 8 weeks pre-operatively, compared with those who continued smoking until the day before surgery. These findings have been criticised due to the original studies having insufficient statistical power [15]. Several subsequent studies in a range of surgical specialities have failed to replicate these findings, and mostly conclude that smoking cessation is beneficial, and that the benefit increases with longer periods of pre-operative abstinence. Two systematic reviews with meta-analysis re-assessed these studies. The first included nine studies (two randomised) and, reassuringly, not only identified no detrimental effects of pre-operative abstinence but also found no significant reduction in pulmonary or overall complications with less than 8 weeks' cessation [18]. A second review included 21 studies (6 randomised and 15 observational) of pre-operative cessation and found a relative risk reduction (95%CI) of 41% (15–59%) in overall complications, with the magnitude of the effect increasing by 19% for each week of cessation, and becoming significantly larger with more than 4 weeks cessation [19]. The results were significant for both postoperative pulmonary complications and wound healing complications.

Current advice, supported by NICE [20], is therefore that smokers should always strive to stop smoking pre-operatively, and that the longer the period of cessation, the greater will be the benefit in terms of avoiding pulmonary complications. There is also evidence that undergoing major surgery motivates patients who smoke to stop permanently, and it is suggested that using the peri-operative period as a 'teachable moment' is the responsibility of all staff involved in a patient's care [21].

How best to support patients to help them stop smoking is unknown, but there is agreement that the more intensive the intervention, the more effective it will be [19]. Monitoring of the attempt to quit is important and is usually

done using hand-held expired carbon monoxide monitors. Counselling and behaviour therapy increase the likelihood of successful cessation, and may be delivered in person, by telephone or over the internet [22]. Nicotine replacement therapy should be considered in nicotine-dependent patients (normally evidenced by smoking within 30 min of waking in the morning). Many modes of nicotine replacement therapy are now available, but these should ideally be stopped 24 h before surgery, particularly for microvascular reconstructive procedures [20]. Finally, pharmacological support with varenicline or bupropion should be considered [22].

Exercise

Physical activity is associated with many long-term health outcomes, with widely accepted World Health Organization guidelines on the health benefits of regular exercise. Better physical fitness, as measured, for example, by cardiopulmonary exercise testing, is associated with improved peri-operative outcomes, including a reduction in postoperative pulmonary complications, in a variety of surgical specialities. But can we change respiratory outcomes by changing a patient's fitness before surgery? Exercise, fitness and sedentary behaviour in patients with cancer can affect outcomes such as disease progression and recurrence rates [12], but it is only recently that the possibility of changing fitness pre-operatively to improve outcomes has been considered.

Pulmonary rehabilitation is now an established component of the management of chronic obstructive pulmonary disease [23] and involves a programme of patient education, nutritional and psychological support, alongside a regular *supervised* exercise programme. Five sessions or more of 30 min of physical activity per week are required, with around half of these under the supervision of a healthcare worker, and continued for at least 6 weeks. For patients who complete the programme, these interventions increase exercise capacity and reduce dyspnoea symptoms [23]; in the treatment of chronic obstructive pulmonary disease the focus has now moved on to managing those more challenging patients who decline to join, or do not complete, a rehabilitation programme [24].

The question then arises: could a similar programme offer high-risk patients improved peri-operative respiratory outcomes? Mainly because such studies are relatively easy to perform, most research in this area has looked at using pre-operative exercise programmes to improve measures of fitness, usually using the results of cardiopulmonary exercise testing. The assumption is then made that, due to the strong association between these measures and outcomes, the changes will be clinically beneficial. Peak $\dot{V}O_2$ and anaerobic threshold have both been shown to improve with exercise training in some patient groups [25–27], but the studies did not report $\dot{V}E/\dot{V}CO_2$, which may be more relevant to respiratory outcomes [14].

Pre-operative exercise was first shown to benefit patients in a randomised study of patients undergoing cardiac surgery, when a twice-weekly exercise programme for 8 weeks reduced length of hospital stay and improved postoperative quality of life [28]. A systematic review in 2011 considered 12 studies of pre-operative exercise therapy and found no benefit in patients undergoing joint replacement surgery, but a significant effect on postoperative pulmonary complications in abdominal and cardiac surgery [29]. A recent Cochrane review of patients undergoing lung cancer resection surgery found a substantial reduction in postoperative pulmonary complications in patients who followed a pre-operative exercise programme, but the number of patients and quality of evidence were low [30]. Conversely, a small randomised study of 124 patients undergoing abdominal aortic aneurysm repair found that a 6-week supervised exercise programme significantly reduced overall complications and hospital stay, but the difference was only significant for cardiac and renal complications, and not for postoperative pulmonary complications [27]. The evidence for pre-operative exercise reducing postoperative pulmonary complications is therefore currently of low quality and shows mixed results. However, along with small numbers of studies and participants, there are other explanations for this lack of evidence, in particular heterogeneity within pre-operative exercise programmes. There is no agreement on how many weeks of exercise should be undertaken, with most interventions lasting around 6 weeks; this cannot include many patients whose surgery is too urgent for the intervention to be completed, for example, patients undergoing cancer surgery. The intensity of exercise varies, and even the way this is determined, with some studies using pre-determined proportions of predicted maximum heart rate or oxygen uptake, and others using patient-perceived intensity [12]. Finally, the pattern of exercise used is important, with a recent move towards high-intensity interval training (HIIT) in which participants repeatedly exercise at a high intensity for a short period of time. In non-surgical patients this form of training improves fitness more quickly than moderate-intensity exercise programmes [31], and this may also apply pre-operatively. In patients waiting for liver surgery, 4 weeks of high-intensity training improved both peak $\dot{V}O_2$ and anaerobic threshold [32], whereas in patients waiting for lung cancer surgery just

eight high-intensity sessions in a 25-day period improved $\dot{V}O_2$ peak significantly [33]. Only one study has looked at clinical outcomes: 25 days of high intensity interval training in lung cancer patients again improved exercise capacity based on $\dot{V}O_2$ peak and 6-min walk distance, and although the overall complication rate was unchanged from the conventional treatment group, there was a significant decrease in postoperative pulmonary complications in the high-intensity training group [34]. More intense training for a shorter period of time may, therefore, eventually be shown to be the more appropriate approach in surgical patients.

Pre-operative respiratory training

The mixed evidence for the efficacy of pre-operative exercise for preventing postoperative pulmonary complications may reflect the lack of specific respiratory components of these programmes. Other research has focussed on two types of interventions specifically aimed at improving respiratory function: incentive spirometry, deep breathing exercises and physiotherapy; and inspiratory muscle training. The first group is frequently used in the postoperative period in patients who have undergone major surgery. Multiple interventions are normally used together as a care package, with the aim of increasing lung volume, decreasing the work of breathing and facilitating clearance of secretions. Despite their widespread use, there is little evidence that the individual respiratory interventions reduce postoperative pulmonary complications [35]. There has been some success in reducing complications if the deep breathing exercises and incentive spirometry are used as part of a comprehensive package also including patient education, oral hygiene, frequent mobilisation and head-of-bed elevation [36], a care programme known as iCOUGH. For this package to be beneficial, the interventions need to be initiated pre-operatively in order to teach patients the various respiratory manoeuvres before they have pain and respiratory muscle dysfunction from their operation.

Inspiratory muscle training, in contrast to general exercise programmes, aims to specifically increase both inspiratory muscle strength and endurance. Postoperative inspiratory muscle weakness will not only lead to reduced resting lung volume and hence airway and lung collapse but will also impair the patient's ability to re-expand the atelectasis that develops in most patients having general anaesthesia for major surgery [2]. A typical inspiratory muscle training programme involves five to seven supervised sessions per week, each lasting 15–30 min, for 2 weeks before surgery [37]. In the sessions, patients breathe in through an inspiratory threshold-loading device at a pre-defined percentage of their maximal inspiratory strength (Pi_{max}). The inspiratory muscle training sessions do not continue postoperatively when pain and other effects of surgery would make this challenging manoeuvre almost impossible. A Cochrane review of pre-operative inspiratory muscle training programmes in cardiac and major abdominal surgery found no improvement in Pi_{max} values for patients in the inspiratory muscle training group, but significant clinical benefits from the intervention were found [37]. In the 695 patients from 12 trials included, there was a shorter length of hospital stay (1.33 days) and a significant reduction in postoperative atelectasis and pneumonia, with a risk ratio (95%CI) of 0.53 (0.34–0.82). These results suggest that for preventing respiratory complications, a more targeted intervention such as inspiratory muscle training is required; thus the time required to improve outcomes can be reduced to around 2 weeks.

Clinical use of pre-operative exercise

The preceding sections suggest that although the evidence of benefit for pre-operative exercise preventing post-operative pulmonary complications is not yet conclusive, there are clear enough improvements for this to be regarded as standard care in some patient groups. None of the studies described thus far have reported anything other than a low risk of adverse events from pre-operative exercise training [12, 38]. Recent clinical recommendations suggest that all patients undergoing major or complex surgery should be offered pre-operative training, in particular those found to have low cardiorespiratory fitness, normally based on the results of cardiopulmonary exercise training [38]. The training should be tailored to the individual patient, part of a wider multi-modal prehabilitation programme, and closely supervised and monitored. Delivery of these laudable aims in the UK will be a significant challenge, but worth pursuing if we are to continue to improve patient outcomes.

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Review Article

Pre-operative optimisation of the surgical patient with diagnosed and undiagnosed diabetes: a practical review

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Summary

Peri-operative hyperglycaemia, whether the cause is known diabetes, undiagnosed diabetes or stress hyperglycaemia, is a risk factor for harm, increased length of stay and death. There is increasing evidence that peri-operative hyperglycaemia is a modifiable risk factor, and many of the interventions required to improve the outcome of surgery must be instituted before the actual surgical admission. These interventions depend on communication and collaboration within the multidisciplinary team along each stage of the patient journey to ensure that integration of care occurs across the whole of the patient-centred care pathway.

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Introduction

Diabetes mellitus is the most prevalent long-term metabolic condition. Diabetes mellitus is a multi-system disorder that is characterised by chronic hyperglycaemia. It can be classified into the following general categories [1]:

1. Type 1 diabetes mellitus. This is due to β-cell destruction and usually leads to absolute insulin deficiency;
2. Type 2 diabetes mellitus. This is due to a progressive insulin secretory defect coupled with insulin resistance;
3. Gestational diabetes mellitus. This is diabetes diagnosed during pregnancy that may or may not resolve after delivery;
4. Other. This covers all the conditions that may predispose to hyperglycaemia, for example, diseases of the pancreas, glucocorticoid use and monogenic disorders causing maturity onset diabetes of the young.

There are recent data to suggest that there are several different subclasses of diabetes [2]. However, there are currently not enough data on peri-operative diabetes care to understand the implications of these subtypes on the outcomes of surgery.

The prevalence of diabetes is increasing. The most recent estimates from the International Diabetes Federation suggest that the number of people worldwide who have diabetes mellitus is about 425 million, that is, 1 in 11 adults. This number is predicted to rise to almost 700 million by 2045 [3]. Over 90% of these people have type 2 diabetes mellitus. In the UK, it is estimated that there are 3.8 million people with diabetes (8.6% of the adult population), this includes an estimated 940,000 people who have undiagnosed diabetes [4]. Diabetes accounts for up to 10% of heathcare expenditure in developed nations, and these huge costs are related in part to the excess number of hospital admissions [5]. People with diabetes (both diagnosed and undiagnosed) have: a significantly longer hospital length of stay; more major complications; a higher requirement for postoperative critical care admission; a

higher requirement for postoperative ventilation; and higher mortality rates and episode costs compared with people without diabetes admitted for the same conditions [6, 7]. In surgical patients, the length of hospital stay is up to 45% higher than those without diabetes, with general surgical and orthopaedic patients often having the longest stays [5, 8]. In addition, a significant proportion of patients with diabetes mellitus are often inappropriately denied day case surgery and this may contribute to the increased length of stay [9]. The mortality of surgical patients with diabetes is twice that of those without [10]; some of the causes for this are shown in Table 1. There is now increasing evidence that diabetes is a modifiable risk factor and that the care of the surgical patient with diabetes and pre-diabetes can be optimised, with a subsequent decrease in complications and mortality. It is therefore imperative that a consultation request by primary care for a surgical opinion mentions diabetes in the referral letter; a recent study showed that the presence of diabetes was not included in over 22% of all referral letters for people with the condition [11].

Table 1 Possible causes of adverse outcomes for surgical patients with diabetes mellitus.

Patients with undiagnosed diabetes
Failure to recognise that the surgical patient has diabetes with resultant additional requirements
Lack of institutional guidelines for management of diabetes
Lack of knowledge of diabetes and its management on the part of medical and nursing staff
Hypoglycaemia and subsequent neuroglycopaenia
Multiple comorbidities including microvascular and macrovascular complications, for example, coronary heart disease; renovascular disease; cerebrovascular disease and peripheral vascular disease
Associated obesity in patients with type 2 diabetes
Complex polypharmacy for the treatment of the diabetes, including misuse of insulin
Complex polypharmacy for the treatment of the co-existing morbidity
Inappropriate use of intravenous insulin
Electrolyte and fluid disturbances associated with the use of intravenous insulin and the coupled fluids
Management errors when converting from usual medication to intravenous insulin and back to usual medication
Hyperglycaemia resulting in peri-operative infection (surgical site or systemic, for example, lower respiratory tract infection, urinary tract infection)
Hyperglycaemia resulting in systemic complications, for example, acute coronary syndromes; acute kidney injury and cerebrovascular events
Hospital-acquired diabetic ketoacidosis

Pre-diabetes and undiagnosed diabetes

Pre-diabetes is the disorder where there is hyperglycaemia without the accepted criteria for diabetes; it is seen as a precursor to diabetes. Pre-diabetes is diagnosed by one of: a marginally elevated glycated haemoglobin (HbA1c) concentration; an impaired fasting glucose; impaired glucose tolerance. These diagnostic criteria for pre-diabetes do not describe the same populations, but they do overlap [12]. Depending on the organisation, the definitions are different. Table 2 shows the two most widely used criteria – from WHO and American Diabetic Association (ADA) – for the diagnosis of diabetes and pre-diabetes.

It is worth explaining the significance of HbA1c. Glycated haemoglobin reflects the average plasma glucose levels that the haemoglobin molecule has been exposed to over the preceding 3 months. It is used to diagnose diabetes and pre-diabetes, and to measure response to treatment. In 2011, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units ($mmol.mol^{-1}$) became the universally accepted units; the Diabetes Control and Complications Trial (DCCT) unit (%) is still in use despite being outmoded.

Undiagnosed diabetes is the condition in which the patient has diabetes but is yet to be diagnosed. The International Diabetes Federation currently estimates that worldwide just over 210 million people have undiagnosed diabetes [3]. This represents half of all people with diabetes. In the UK, in 2014, Public Health England estimated that the prevalence (95%CI) of pre-diabetes in the general population was 10.7% (10.2–11.1%); the prevalence (95% CI) of undiagnosed diabetes was 2.3% (2.1–2.6%) and the prevalence (95%CI) of diagnosed diabetes was 5.2% (4.9–5.5%) [13]. Despite this, the National Institute for Health and Care Excellence (NICE) does not currently recommend screening for diabetes in the 'at risk' surgical population [14]. This is despite there being evidence to suggest that undiagnosed diabetes mellitus is a greater risk factor for harm than diagnosed diabetes mellitus in the surgical population [10, 15]. It has been argued that this is a missed opportunity to improve surgical outcomes [16].

In a recently published single-centre Australian prospective study of patients aged > 54 years undergoing inpatient surgery, it was demonstrated that of 7565 patients, 2047 (27%) patients had diabetes, as defined by HbA1c ≥ 48 $mmol.mol^{-1}$ (6.5%); 2825 (37%) had pre-diabetes, as defined by HbA1c of 39–47 $mmol.mol^{-1}$ (5.7–6.4%); and only 2457 (32%) patients were normoglycaemic. In addition, 2825 patients were diagnosed with pre-diabetes,

Table 2 The WHO and ADA diagnostic criteria for the different types of dysglycaemia [3].

		'Pre-diabetes'		
	Diabetes	**HbA1c-diagnosed pre-diabetes**	**Impaired fasting glucose**	**Impaired glucose tolerance**
HbA1c criteria. IFCC units (DCCT %)	≥ 48 mmol.mol^{-1} (≥ to 6.5%) or	≥ 43 to ≤ 47 mmol.mol^{-1} (6.0–6.4%)		
Random glucose	> 11.1 mmol.l^{-1} or			
Fasting plasma glucose	≥ 7.0 mmol.l^{-1} or		6.1–6.9 mmol.l^{-1}	< 7.0 mmol.l^{-1} and
Two-hour plasma glucose following a 75-g oral glucose load	≥ 11.1 mmol.l^{-1}			≥ 7.8 to < 11.1 mmol.l^{-1}

IFCC, International Federation of Clinical Chemistry; WHO, World Health Organization; ADA, American Diabetes Association; DCCT, Diabetes Control and Complications Trial.

and 236 patients (3% of the total study population) were found to have undiagnosed diabetes mellitus [7].

Table 3 shows a list of characteristics that should lead to a person to being screened for diabetes before referral for surgery. If any person is found to have undiagnosed diabetes mellitus, appropriate treatment should be commenced. It is recommended that people with type 2 diabetes mellitus have treatment commenced or increased if the HbA1c exceeds 58 mmol.mol^{-1} (7.5%), whether surgery is planned or not [17].

Diabetes and surgical outcome

There are data from several surgical specialities to show that poor pre-operative glycaemic control (defined as either elevated blood glucose or HbA1c concentrations) is associated with harm [7, 18–25]. However, increasingly data have suggested that it is those people with previously undiagnosed hyperglycaemia who have the worst outcomes [10, 15, 26]. It may well be that this is because a known diagnosis of diabetes will almost always mean that a healthcare professional will observe and monitor the patient more often, if only to have a bed-side capillary glucose measurement taken, and at such time, it may be noticed if the patient is becoming more unwell. This is described in a recent study that showed that the higher the pre-operative HbA1c, the more frequently capillary glucose concentrations were measured, and the more likely patients were to be started on an intravenous insulin infusion [27]. If an individual's glycaemic status is not known, they are likely to be observed less often.

There is work to show that poor surgical outcomes occur when the HbA1c concentration is raised, but still within the non-diabetic range; this association begins at 43 mmol.mol^{-1} (6.0%) [28, 29]. There are, however, currently no prospective studies examining surgical outcome after randomly allocating patients with poor glycaemic control to either no diabetes treatment or to diabetes treatment. In addition, this study may never occur as it may be deemed unethical to randomly allocate patients with diabetes to no treatment. Thus, although it may seem 'intuitive' to optimise pre-operative HbA1c concentrations, there are few data to support this [30]. The exceptions to this are cardiac and liver transplant surgery [31, 32]. There are also data to support improving glucose control to reduce surgical site infections [33].

Pre-operative glycaemic optimisation

Given that the epidemiological data suggest that 'good' pre-operative glycaemic control is associated with a lower risk of postoperative complications, it has been advocated that HbA1c concentrations should be optimised before an elective procedure, if it is safe to do so [34]. For some patients, the risk of iatrogenic hypoglycaemia outweighs the benefits of better glycaemic control, and pre-operative optimisation is not safely possible. For practical reasons,

Table 3 Proposal for who should be screened for diabetes before referral for surgery.

Age > 40 years old (> 30 years in people of South Asian origin)
Family history of diabetes
Personal history of gestational diabetes
Personal history of hypertension
Personal history of dyslipidaemia
Personal history of pre-diabetes
BMI > 25 kg.m^{-2} (23 kg.m^{-2} in those of South Asian origin)
Those on long-term glucocorticoid treatment

suggestions from the UK advocate postponement of elective surgery only if the HbA1c is ≥ 69 mmol.mol^{-1} (8.5%) [34]; whereas, the US Society for Ambulatory Anesthesia (SAMBA) suggests 53 mmol.mol^{-1} (7.0%) [35]. The National Institute for Health and Care Excellence now suggests that HbA1c is a vital test that should be offered to all patients with diabetes if it has not been performed in the 3 months before the anticipated date of surgery [14]. Data from the Peri-operative Quality Improvement Programme (PQIP) 2017–2018 annual report demonstrated that, despite a pre-operative HbA1c being recommended in all patients with known diabetes, only 69% of such patients in that study had the pre-operative HbA1c performed [36].

Review of glycaemic control, and any subsequent glycaemic optimisation, should commence at the time of the referral for a surgical consultation and should continue at all stages of the patient journey: primary care; surgical outpatients; pre-operative assessment clinic; hospital admission; theatres and recovery; postoperative ward; and discharge home [34]. At all of these stages, communication between the relevant staff and the patient is vital to help to ensure that optimal glycaemic control is achieved and maintained. Pre-operative glycaemic optimisation should be facilitated by either primary care or hospital specialists [34].

Pre-operative optimisation of comorbidity and drug therapy

Diabetes is a multi-system disease and is associated with several other comorbidities. These most frequently include cardiovascular disease, peripheral vascular disease, renal disease, hypertension and obesity; 90% of adults with type 2 diabetes aged 16–54 years are overweight or obese [37]. Many of these co-existing conditions are also associated with increased surgical complications, and there is substantial evidence that patients with less severe comorbidity have better outcomes than those with severe and uncontrolled comorbidity [38]. In addition, there is now emerging evidence that pre-operative optimisation of these associated conditions can lead to an improvements in outcomes; many are discussed in detail in other sections of this journal supplement. Furthermore, the peri-operative strategies that are used to manage the associated conditions are changing and are associated with less morbidity. For example, Douketis et al. demonstrated that peri-procedural interruption of warfarin, for atrial fibrillation, with no anticoagulant bridging was not inferior to low molecular heparin bridging for the prevention of arterial thrombo-embolism, but decreased the risk of peri-procedural major bleeding [39].

The National Institute for Health and Care Excellence has produced many clinical guidelines for the optimisation of diabetes and its associated conditions [14, 17, 40–44]. However, it is being increasingly realised that these guidelines often only consider the disease in isolation. This has the unintended consequence of potentially causing either drug–disease interactions or drug–drug interactions if medical practitioners apply the recommendations from the guidelines in isolation and do not consider the co-existing diseases and drugs. Pre-operative optimisation of the surgical patient with diabetes, therefore, demands careful scrutiny and optimisation/rationalisation of the existing medication to reduce the potential of peri-operative adverse drug events including: hypotension; bleeding; bradycardia; ventricular arrhythmias; altered plasma concentrations; and hypo/hyperkalaemia caused by drug–disease or drug–drug interactions [45].

Prevention of peri-operative dysglycaemia

It has been demonstrated that peri-operative hypoglycaemia and hyperglycaemia are both associated with harm and death. Hypoglycaemia is often defined as capillary blood glucose < 4.0 mmol.l^{-1} and severe hypoglycaemia is defined as capillary blood glucose < 3.0 mmol.l^{-1} [46]. There are now data to demonstrate that hospital length of stay and risk of death actually increase with capillary blood glucose ≤ 4.0 mmol.l^{-1} [47, 48]. In addition, studies in which tight glycaemic control (4.5–6.0 mmol.l^{-1}) using intensive insulin therapy has been compared with a liberal target of 8.0–10.0 mmol.l^{-1} have showed increased harm in the former group [49]. Therefore, the UK peri-operative guidelines now recommend that the lowest acceptable peri-operative capillary blood glucose in patients taking glucose lowering medication should be 6.0 mmol.l^{-1}, with the US guidelines suggesting reconsideration of treatment at 5.6 mmol.l^{-1} [5, 34, 50]. Due to data suggesting that the treatment for hyperglycaemia is associated with harm, many societies and guidelines suggest treating inpatient hyperglycaemia only once the capillary blood glucose is above 10.0 mmol.l^{-1} [5, 34, 50]. Thus, there is a universal consensus that the optimal peri-operative target zone is approximately 6.0–10.0 mmol.l^{-1} [5, 34, 50–52]. This target is almost identical to the range recommended by Alberti in 1979, who suggested 5.0–10.0 mmol.l^{-1} [53]. In addition, the UK guidance recognises the dangers of glucose-lowering medication and suggests that an upper limit of 12.0 mmol.l^{-1} may be acceptable [34].

As well as hyperglycaemia predisposing the patient to both infective and non-infective complications, the patient with type 1 diabetes mellitus is also prone to diabetic ketoacidosis. Hospital-acquired diabetic ketoacidosis is defined as a patient developing diabetic ketoacidosis once in hospital for another reason, makes up almost 8% of all cases of diabetic ketoacidosis, and is thus its third commonest cause [54]. At present the exact incidence of hospital-acquired diabetic ketoacidosis in the surgical population is unknown. It is anticipated that the current National Confidential Enquiry into Patient Outcome and Death will be able to provide more data. The UK guidelines suggest the continuation of basal insulin, albeit at a reduced dose, to prevent this highly undesirable complication [34, 50].

In addition to identifying patients with previously undiagnosed hyperglycaemia, there are several strategies to prevent peri-operative dysglycaemia. These are summarised in Table 4. Precise details on the exact implementation of these strategies are beyond the scope of this article but have been previously published [50].

The unifying aspect for the successful implementation of all of these strategies is meticulous pre-operative assessment by staff with expertise in the peri-operative management of diabetes. Effective communication with the patient and the ward staff on the chosen management plan is vital. The diabetes drugs must be safely prescribed, and to facilitate safe day-of-surgery admission, it is recommended that these drugs are prescribed in the pre-operative assessment clinic. In addition, treatment in the event of both hypoglycaemia and hyperglycaemia should be prescribed at the pre-operative assessment clinic, so that dysglycaemia can be managed if required from the moment of hospital admission.

Safe use of insulin

Insulin remains one of the most frequently misprescribed and misadministered drugs [55]. These medication errors include the wrong dose; administration at the wrong time; and inappropriate omission of a dose. It remains important to prescribe the correctly named insulin. Insulin should be prescribed by the complete brand name – including the strength and origin (e.g. human, animal or analogue). Importantly, the word 'unit' should be written out in full, never abbreviated as 'U' [56]. The mode of administration should also be included – pre-filled pen, needle and vial or cartridge. When in doubt, always ask for help from the diabetes team. Furthermore, when insulin is administered it should always be given using an insulin syringe – these allow for 1-unit increments to be given.

Unresolved issues

In this section, we will deal with the topic of stress hyperglycaemia before looking ahead to the future of peri-operative diabetic management.

The term stress hyperglycaemia describes transient elevations in blood glucose in patients without a history of diabetes that occur during acute illness or stress [57]. Several observational studies have reported higher morbidity and mortality in surgical patients with newly recognised hyperglycaemia when compared with those even with known diabetes [58, 59]. In general surgery, the development of peri-operative hyperglycaemia is associated with up to a fourfold increase in complications and twice the risk of death compared with patients maintaining normoglycaemia; this risk begins with a capillary blood glucose $\geq$ 7.8 mmol.l^{-1} [10]. In a recent US study, the incidence of stress hyperglycaemia was found to be 21%; there are currently no studies from the UK [60]. It is currently unknown whether it is patients with pre-diabetes who develop stress hyperglycaemia. If this was the case, it would further strengthen the argument for pre-operative screening using HbA1c for all patients having a major surgery. At present there are no pre-/peri-operative studies examining whether these patients can be identified or whether treatment can affect the outcome of stress hyperglycaemia. The work by Van den Berghe et al. in critically ill patients suggests that among other strategies insulin therapy may have a role, but more work is required [61, 62].

The future remains full of potential in the field of peri-operative glycaemic control. Data from the 2017–2018 PQIP showed that, among those participating hospitals, care of surgical patients with diabetes can be improved, and has been identified as the foremost national improvement opportunity for 2018–2019 [36]. These data show that diabetes is taking a more prominent position in peri-operative care than previously.

Although there are outcome studies currently going on in this area (e.g. the Optimising Cardiac Surgery ouTcomes in People with diabeteS (OCTOPus) trial – HTA project number 16/25/12 – Professor R. Holt, personal communication), there remain few data on the outcomes and effects of intervention on those not known to have diabetes. Given the rising prevalence of obesity this is an important 'missing link' in the field.

There also needs to be more research about the epidemiology of stress hyperglycaemia, and its optimal treatment. The optimal agents/strategies needed to prevent peri-operative dysglycaemia also remain to be determined. The ideal agents would not cause hypoglycaemia and would

Table 4 Summary of the strategies available for peri-operative glycaemic control.

Strategy	Pre-requisite	Advantages	Disadvantages
No changes	Diet-controlled T2DM with an HbA1c < 8.5%	Minimal risk of iatrogenic complications	Will not control additional stress hyperglycaemia
Modification of normal glucose lowering medication	• Adequately controlled DM with a pre-existing HbA1c < 8.5% • Short starvation period (< 1 missed meal) • Patient able to understand instructions on how to modify normal medicines	Simple, effective	• Not suitable for prolonged starvation • Some of the drugs are contraindicated in the peri-operative period
Initiation of basal insulin with correction dose insulin	• T2DM on oral hypoglycaemic agents T2DM on oral hypoglycaemic agents • Short starvation period (< 1 missed meal)	Overcomes the concern that the product data sheets of some oral hypoglycaemic agents suggest discontinuation in the peri-operative period	• Need to be seen by a diabetes specialist to facilitate safe transfer from oral hypoglycaemic agents • All the intrinsic risks of insulin prescription and administration
CSII	• Normally on CSII • Short starvation period (< 1 missed meal) • Patient able to understand instructions on how to modify CSII	Minimal disruption to normal diabetes management	• Lack of familiarity by staff • Pump manufacturers now suggesting avoidance of use in the presence of diathermy
VRIII	• Dedicated cannula • Ability for staff to safely establish the VRIII with associated fluid • Ability for staff to check CBG hourly • Ability for staff to establish and discontinue VRIII safely • Needs two pumps	Theoretically has the ability to achieve the best degree of glycaemic control	• Lack of hourly checking of CBG predisposes to hypoglycaemia/ hyperglycaemia. • Issues with initiation and discontinuation can predispose to DKA • Choice of substrate fluid may predispose to electrolyte imbalance. • Difficult to use in day surgery
GIK infusion Potassium (GIK) infusion		Simple and relatively safe Effective absorption as administered intravenously Only needs one pump	• Wasteful due to need to replace whole fluid bag if CBG falls out of target zone. • Will need additional fluids to prevent electrolyte imbalance
'Sliding scale' subcutaneous insulin boluses		Simple	• Does not prevent dysglycaemia • Discredited and not recommended

CBG, capillary blood glucose; DKA, diabetic ketoacidosis; DM, diabetes mellitus; CSII, continuous subcutaneous insulin infusion; T2DM, type 2 diabetes mellitus; VRIII, variable rate intravenous insulin infusion; GIK, glucose-insulin- potassium.

Figure 1 Comprehensive care pathway of the elective surgical patient with diabetes.

be safe to use at times of acute illness. The use of the sodium glucose cotransporter-2 inhibitors is associated with an increased risk of diabetic ketoacidosis and should be avoided during periods of acute illness, and there continue to be concerns about the use of metformin in renal impairment. The peri-operative use of drugs acting on the incretin pathway, the dipeptidyl peptidase-4 inhibitors and the glucagon-like peptides, have shown promise in preventing

peri-operative hyperglycaemia; however, their use may be limited by side-effects, including nausea and vomiting [63]. Finally, the increasing use of technology may help to reduce the risk of dysglycaemia associated with insulin use, as well as reducing the impact on staff time. The use of 'closed loop' glucose sensors and insulin delivery devices has shown promise in early trials in the inpatient population [64–66]. However, due to the difficulties of individualising the algorithms and how they change with the changing situation in the hospitalised patient, this technology remains some way from routine clinical use.

Implications for practice

It has become increasingly apparent from the success of enhanced recovery partnership programmes that better outcomes are achieved by having a patient pathway that commences at primary care referral. This pathway is summarised in Fig. 1. Management of the surgical patient with diabetes is no different. For the reasons stated, at the time of initial referral, diabetes and other comorbidities should have been optimised where it is safe to do so. The referral letter to the surgical team should detail all relevant pathology and medication as well as the current HbA1c. Currently, this is poorly done [11]. If diabetes is not optimally managed at the time of referral, advice from the diabetes team should be sought as soon as possible, to facilitate optimisation. Optimisation generally takes about 3 months. Identifying poorly controlled or undiagnosed diabetes at a pre-operative clinic just before elective surgery, especially if the referral was made several weeks or months previously, should no longer be acceptable.

Patients should be advised on how to manage their diabetes to facilitate day-of-surgery admission, and day surgery is recommended if the surgery is appropriate. Diabetes is no longer a contraindication to day surgery. Day surgery provides less time for iatrogenic complications and thus is an integral part of NHS England's 'Choosing Wisely' and 'Getting it Right First Time' initiatives [67, 68].

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Review Article

Peri-operative optimisation of elderly and frail patients: a narrative review

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Summary

With increasing life expectancy and technological advancement, provision of anaesthesia for elderly patients has become a significant part of the overall case-load. These patients are unique, not only because they are older with more propensity for comorbidity but a decline in physiological reserve and cognitive function invariably accompanies ageing; this can substantially impact peri-operative outcome and quality of recovery. Furthermore, it is not only morbidity and mortality that matters; quality of life is also especially relevant in this vulnerable population. Comprehensive geriatric assessment is a patient-centred and multidisciplinary approach to peri-operative care. The assessment of frailty has a central role in the pre-operative evaluation of the elderly. Other essential domains include optimisation of nutritional status, assessment of baseline cognitive function and proper approach to patient counselling and the decision-making process. Anaesthetists should be proactive in multidisciplinary care to achieve better outcomes; they are integral to the process.

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Introduction

Global life expectancy has been increasing over the last few decades. In the UK for example, the proportion of population aged 65 or above is expected to increase from 16.9% to 24.7% between 2006 and 2046 [1], and provision of healthcare is one of the biggest concerns with this change. In the past, major surgery was seldom performed on patients older than 80 years. With advancements in surgical techniques and peri-operative care, surgery may be a viable treatment even at very advanced age [2]. Although chronological age itself predicts surgical outcome poorly, age-related decline in physiological reserve and functional capacity are inevitable, and affect all organ systems. When people live longer, more comorbidities appear; this will result in higher rates of peri-operative morbidity and mortality. This is already imposing a significant burden on healthcare systems, by increasing both the utilisation of intensive care facilities and length of hospital stay [3, 4]. Therefore, it is imperative to deliver both high-quality and efficient peri-operative care for elderly patients.

The 'elderly' represent a unique group of patients, with many challenges for the peri-operative care team. In this article, we review the following aspects of anaesthesia in the elderly: (1) the role of comprehensive geriatric assessment and innovative models of care; (2) the implications of frailty and its assessment; (3) the assessment and optimisation of nutritional status; (4) the assessment of neurocognitive dysfunction; and (5) patient counselling and approach to decision-making.

Comprehensive geriatric assessment and innovative models of care

Comprehensive geriatric assessment is an established method for evaluating and optimising physical, psychological, functional and social issues in elderly patients to improve long-term outcomes [5]. It involves a multidomain assessment, which necessitates collaboration from multidisciplinary teams in planning and implementing investigations and treatment, as well as arranging discharge and follow-up plans. Table 1 lists the main components of comprehensive geriatric assessment. This requires collaboration between all those involved in the peri-operative pathway, including anaesthetists, surgeons, geriatricians, nurses, therapists and dieticians [6]. Systematic review has confirmed its role in enhancing postoperative outcomes in elderly patients undergoing elective surgery [5].

Various care models have evolved, but none have proven to be superior to others because the setup, as well as the efficacy, is influenced by local resources, population distribution, the specific facilities of certain centres and available expertise [7]. We will describe some examples of well-known models.

Table 1 Components of comprehensive geriatric assessment.

Domain	Items to be assessed
Medical	Comorbid condition and diseases severity
	Medication review
	Nutritional status
Mental health	Cognition
	Mood, anxiety and fears
	Decision-making capacity
	Risk factors for postoperative delirium
Functional capacity	Activities of daily living
	Gait and balance
	Activity/exercise status
	Use of visual, hearing, mobility aids, dentures
Social circumstances	Informal support from family or friends
	Social network such as visitors or daytime activities
	Eligibility for receiving care resources
Environment	Home comfort, facilities and safety
	Transport facilities
	Accessibility to local resources
Risk score	Pathology-specific, for example, Nottingham Hip Fracture Score
	Frailty scores

Some services can be described as geriatrician-led. Here, pre-operative comprehensive geriatric assessment is provided by a consultant geriatrician-led multidisciplinary team, who liaises with the surgical teams about peri-operative medical care, focusing on functional optimisation and discharge planning for both emergency and elective patients. Examples of this model include the Pro-active care of Older People undergoing Surgery service at Guy's and St Thomas' NHS Foundation Trust [8] and the Systematic Care Older Patients undergoing Elective Surgery at Nottingham University Hospitals NHS Trust [9].

Other services are led by anaesthetists. In this model, patients are triaged based on predicted peri-operative risk of mortality. Those at higher risk will attend an anaesthetist-led clinic, where the anaesthetist will stratify the risk in detail by assessing patients' functional reserve, either by clinical assessment, or with objective physiological tests such as cardiopulmonary exercise testing. They will then discuss with the patients and their families about risks and benefits of surgery based on the assessment result. The clinic is supported by different streams of healthcare professionals providing expert advice and support. An example of this model is the Torbay Pre-operative Preparation Clinic, South Devon Healthcare NHS Foundation Trust [10].

Other models of care include peri-operative optimisation of senior health developed at Duke University School of Medicine [11], and the Michigan Surgical Home and Optimisation Program developed at the University of Michigan [12].

Frailty and its peri-operative implications

Traditional surgical risk assessment tools are typically organ specific. A classic example is the Goldman Cardiac Risk Index, which was published in 1977 [13]. Subsequently, various risk tools have been developed for predicting adverse outcomes in different organ systems such as pulmonary [14], renal [15] and neurological [16].

There is a growing interest in integrating concepts drawn from gerontology to peri-operative care of the elderly. Specifically, frailty has been used to provide additional prognostic insight for elderly patients not captured by organ-based risk scoring systems. 'Frailty' is defined as a state of high propensity for adverse health outcomes, including disability, dependency, falls, need for long-term care and mortality [17]. It is an age-related, progressive decline in multiple physiological reserves that results in diminished resilience, loss of adaptive capacity, and increased vulnerability to stressors [18]. Therefore, it is not surprising that frailty has been associated with adverse

postoperative outcomes, including postoperative medical complications, prolonged hospitalisation, institutionalisation, readmission and short- and long-term mortality [17, 19–21].

The prevalence of frailty is greater among women and increases with age. It is seen in 40% of patients aged 80 years or older (vs. 10% for those aged between 65 and 75) [22]. It is vital to assess frailty to predict the risk of adverse postoperative outcomes. Notably, the American College of Surgeons National Surgical Quality Improvement Program/American Geriatrics Society (ACS NSQIP/AGS) 2012 *Guidelines for the optimal pre-operative assessment of the geriatric surgical patient* outlined frailty assessment as a critical component in the pre-operative setting [23]. Moreover, the AGS and the National Institute on Aging published a major consensus statement in 2015 on '*Frailty for specialists*', which highlighted the importance of incorporating frailty assessment into the pre-operative journey [18].

Despite these guidelines and consensus, there is no single generally accepted definition of frailty. The two most commonly studied frailty assessment tools are the 'phenotypic' model and the 'deficit accumulating' model.

In 2001, Fried et al. first developed and operationalised a standardised phenotype of frailty, using data from over 5300 men and women over age 65 in the Cardiovascular Heart Study [17]. They proposed that frailty is a distinct clinical syndrome driven by the ageing process (including mitochondrial dysfunction, cellular senescence etc.), which contributes, along with comorbid diseases, to a pernicious cycle of frailty associated with sarcopenia and declining energetics and reserve. This phenotypic model encompasses decreased strength, decreased walking speed, low physical activity, self-reported exhaustion and unintentional weight loss (Table 2). It is a powerful prognostic tool for falls, incident disability, worsening mobility, hospitalisations and death. However, it does not account for changes in cognition or mood. Although this frailty evaluation is recognised by the ACS/AGS guidelines, subsequent authors have called for future work focused on the development of scales specific to the surgical population [18].

Table 2 Frailty phenotype [17].

Characteristic of frailty	Measurement
Weakness	Grip strength: lowest 20% (by sex, body mass index)
Slowness	Time taken to walk 15 feet: slowest 20% (by sex, height)
Low level of physical activity	kcal.week^{-1}: lowest 20% Men: < 383 kcal.week^{-1} Women: < 270 kcal.week^{-1}
Exhaustion, poor endurance	'Exhaustion' (self-report)
Weight loss	Unintentional weight loss > 10 lb in prior year

'Positive' for frailty phenotype: ≥ 3 criteria present. Pre-frail: 1 or 2 criteria present. Robust: no criteria present.

Another method to evaluate frailty utilises the deficit accumulation model, which is also known as the Rockwood Frailty Index. It was developed from the Canadian Study of Health and Aging by incorporating a predefined set of 70 clinical deficits in the domains of comorbidities, mood disorders, cognition, functional status and nutrition, with the likelihood of being frail increasing with the accumulation of more deficits [20, 24]. The frailty index is expressed numerically by dividing the number of deficits found by the number of potential deficits. This approach states that frailty is the result of an age-associated accumulation of health deficits and the more deficits an individual has, the greater their risk for an adverse outcome. It is a continuous variable and can stratify those with moderate to severe frailty more precisely than the categorical phenotypic model [25]. It has been applied to various elderly populations being exposed to stresses, and has been shown to be strongly predictive of mortality and other adverse outcomes.

Both the phenotypic model and the deficit accumulating model have invited criticism because their performance is time consuming and labour intensive when included in routine pre-operative assessment. Particularly, the Fried frailty criteria require the use of special equipment such as a dynamometer and the measurement of gait speed, whereas the original Rockwood Frailty Index requires assessment of 70 potential clinical deficits. Both models have been modified and studied in surgical populations. For instance, Huded et al. utilised modified Fried frailty assessment to predict the risk of institutionalised discharge in patients undergoing transcatheter aortic valve implantation [26]. Robinson et al. revealed six strong predictors for both 6-month mortality and post-discharge institutionalisation in patients undergoing major general, thoracic, vascular and urologic surgery [27]. Further work by the same group has demonstrated the ability of frailty scoring to forecast adverse outcomes in patients after elective colorectal and cardiac operations [28, 29]. Farhat et al. measured 11 deficits, which are collected as part of the ACS NSQIP, out of the 70 deficits in the initial Rockwood study, to create the modified frailty index. They demonstrated its high predictive value for both postoperative 30-day mortality and postoperative infection in over 35,000 patients undergoing general surgery [30].

The same index was applied to over 230,000 patients undergoing orthopaedic, vascular and general surgery, and was found to be predictive of postoperative complications and 30-day re-admissions [31].

The Clinical Frailty Scale was developed to enable frailty measurement in the outpatient setting [32]. It is a semi-quantitative tool that stratifies the elderly according to their relative degree of vulnerability using simple clinical descriptors [20]. It provides a global score ranging from 1 (robust health) to 9 (terminally ill). It is an attractive tool as it is simple and can be completed by any trained staff.

The Edmonton Frail Scale (EFS) [33] is a 17-point scale validated for use by non-geriatricians that can be completed within 5 min. The scale incorporates 10 domains, including medication use, cognitive impairment, balance and mobility. The 'get-up-and-go' test of the EFS has been shown to predict morbidity and mortality across surgical specialties [34]. Although the test is not applicable in emergency operations, it is valuable in the anaesthetic assessment clinic.

Undoubtedly, frailty is associated with adverse surgical outcomes [26, 35–37] but the recognition of frailty is only useful if it can modify peri-operative care and improve outcomes. At the anaesthetic clinic, we can discuss anticipated outcomes with patients and their families based on the magnitude of the frailty score and co-existing morbidities. This can enable them to have an insight into what could happen, and helps plan the subsequent care and location of subsequent care on discharge from hospital. In terms of surgical planning, for the frailest patients, we can advise surgeons to adopt the least invasive approach, or even consider a staged or 'damage control' approach, so as to minimise the stress induced by major surgery. In all circumstances, anaesthetists play an important role in initiating an appropriate level of monitoring, choosing and titrating anaesthetics meticulously intra-operatively [38], as well as maintaining normothermia, which can help to minimise complications for the most vulnerable.

Unfortunately, there is still a lack of evidence that frailty can be attenuated or reversed once it is established, although supervised exercise training programmes before surgery may improve mobility and functional ability in selected cases. Other adjuvant interventions include nutritional screening, red cell mass optimisation [39] and correction of sarcopenia (discussed later in this article). Further large-scale, multi-centre studies are required to determine what peri-operative programme will be most useful in minimising the deleterious impact of frailty on peri-operative outcomes.

Assessment and optimisation of nutritional status

Malnutrition is a strong independent predictor of higher peri-operative mortality, morbidities, length of hospital stay and re-admission rates. It thus increases the burden on healthcare systems [40–43]. The American Society for Enhanced Recovery and Peri-operative Quality Initiative (ASER/POQI) summarised the current challenges of peri-operative nutrition screening and therapy [40]. Two out of three patients undergoing gastrointestinal surgery are malnourished, which renders them three times more likely to suffer from complications and five times more likely to die. However, only around one-fifth of hospitals have a formal nutrition screening programme, and only one out of five patients receives nutritional support. The majority of surgeons believe peri-operative nutritional optimisation will reduce complication rates. It has also been shown that for every one unit of currency spent on nutrition therapy in hospitalised patients, 52 units will be saved in hospital costs. The group has also highlighted the urgent need to improve peri-operative nutrition assessment and interventions.

The European Society for Clinical Nutrition and Metabolism 2017 guidelines emphasised the importance of nutritional screening and interventions in enhanced recovery pathways [44]. They defined malnutrition as a body mass index (BMI) less than 18.5 $kg.m^{-2}$. Also, patients who sustained weight loss of more than 10% (or 5% within 3 months), in addition to low BMI or low fat-free mass index also fulfilled the diagnostic criteria of malnutrition. For older patients, a higher cut-off for BMI is preferred because research indicates that the risk for all-cause mortality increases starting at a BMI of 24 $kg.m^{-2}$ for the aged population, and doubles when BMI is < 22 $kg.m^{-2}$ for men and < 20 $kg.m^{-2}$ for women [45].

The ASER/POQI developed and proposed a peri-operative nutrition screening algorithm based on patient's BMI (cut-off at 18.5, or 20 if age > 65 years), recent weight loss more than 10% in 6 months, reported recent decreased oral intake and pre-operative hypoalbuminaemia (cut-off at 3 $g.dl^{-1}$) [43]. Checking serum albumin levels is inexpensive and routinely available, and represents a strong predictor of surgical risk and mortality. Its use as an indicator of malnutrition has been criticised because it is neither specific nor sensitive [46]. However, until a better marker is available, albumin level is still recommended as a component of the peri-operative nutrition screen.

Patients at high risk of malnutrition should be referred to a dietician for a comprehensive nutritional assessment [43, 44, 47]. Nutritional therapy is indicated in patients with, or at risk of, malnutrition. It should also be initiated if the

patient will not be able to have adequate oral intake for more than 5 days peri-operatively [43]. In principle, oral nutritional supplements should be considered before tube feeding, unless contraindicated. If oral and enteral routes are impossible, intolerable or inadequate (< 50% recommended protein/caloric requirement achieved), then parenteral nutrition is recommended. Oral nutritional supplementation, particularly with high protein content, can reduce the risk of developing pressure ulcers in the elderly. Achieving a goal of overall protein intake > 1.2 $g.kg^{-1}.day^{-1}$ is more important than achieving a total calorie intake.

Unnecessary prolonged pre-operative fasting should be avoided. In patients with minimal risk of aspiration, unrestricted access to solids and clear fluids should be allowed up to 6 h and 2 h, respectively, before anaesthesia. A pre-operative drink containing at least 45 g of carbohydrate is recommended in patients undergoing major surgery, except for patients with insulin-dependent diabetes [48]. Carbohydrate loading carries an additional benefit of reducing peri-operative discomfort and anxiety. Postoperatively, a high-protein diet should be commenced as tolerated, except in patients with significant bowel pathology. Traditional 'clear liquid' and 'full liquid' diets should not be routinely used.

Immunonutrition has been proposed as a risk reduction strategy in surgical patients [43, 48]. Particularly, arginine, omega-3 fatty acid and antioxidants are included in various nutritional formulae. Arginine is rapidly depleted after surgical stress, and it is important for the activation of T lymphocytes, promotion of T-helper cells and phagocytosis [49]. It is also a precursor of nitric oxide and proline, which are both important for anastomotic and wound healing. Nitric oxide promotes vasodilation and tissue oxygenation, whereas proline contributes to collagen deposition during healing. Omega-3 fatty acids play a wide range of anti-inflammatory roles and can reduce oxidative injury. Pre-operative immunonutrition should be considered for patients undergoing elective major abdominal surgery [43].

Despite the above-mentioned benefits of peri-operative nutritional interventions, there are many uncertainties which make its routine implementation difficult [48]. For instance, postoperative ileus and the potential benefits of early feeding are still poorly understood, and are controversial. Surgeons typically wait until the bowel function returns, or until it is clear that there are no immediate postoperative complications. Placement of enteral feeding tubes is not always easy, and sometimes even requires radiological confirmation. Moreover, it is difficult to ensure that elderly patients will take adequate supplementation, even with the assistance of a dietitian [47]. Therefore, it is essential to provide pre-operative education to patients and their families to improve compliance. Frequent and repeated assessment of nutritional status should be conducted for patients during their hospital stay [44].

The European Working Group on Sarcopenia in Older People (EWGSOP) defines sarcopenia as a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death [50]. Sarcopenia is common in the elderly and can worsen personal health and produce a burden for the healthcare system. Buettner et al. recommended including sarcopenia in identifying frail patients at greatest risk for one-year mortality after gastrointestinal cancer surgery [48]. Although there is no standardised approach to diagnosing sarcopenia, the EWGSOP has proposed a screening algorithm for patients aged 65 years and above [50]. The diagnosis of sarcopenia is based on low muscle mass, together with either low muscle strength or poor physical performance. Physical performance is assessed by gait speed, with a cut-off of 0.8 $m.s^{-1}$; the lower the speed, the poorer the physical function. Muscle strength is assessed by grip strength, with cut-offs of < 30 kg for men and < 20 kg for women. Muscle mass is assessed by dual-energy X-ray absorptiometry, with cut-offs established using an appendicular skeletal mass index. The use of CT or MRI scanning for body composition measurement is advocated, especially for patients with cancer, because these imaging modalities are part of the workup in disease staging.

Nutrition and exercise are synergistic for the growth and maintenance of muscle. Elderly people are less able to utilise amino acids for protein synthesis at muscle level, due to anabolic resistance to a physiological dose of amino acids. Protein and leucine metabolites are key dietary components that contribute to muscle accretion and synthesis [51]. The combination of resistance training and an intake of high amounts of protein favours muscle mass deposition, and will improve strength and physical function. Optimisation of both diet and physical activity may help patients improve their tolerance to oncological treatment and health-related quality of life [52].

Postoperative cognitive disorders

Postoperative cognitive disorders are a spectrum of diseases ranging from immediate postoperative delirium to postoperative cognitive dysfunction. In a small group of unfortunate patients, the impairment can be long term and

permanent, which will substantially affect their quality of life. These disorders are commonly encountered in elderly surgical patients and will be elaborated in detail.

Delirium is an acute and fluctuating alteration of mental state of reduced awareness and disturbance of attention [53]. The diagnosis of delirium is challenging because symptoms wax and wane during the course of a day, and it is confounded by baseline cognitive impairment. Postoperative delirium, although transient, is not benign. Patients suffering from delirium often have a subsequent diagnosis of mild cognitive impairment or even dementia. It is also associated with prolonged hospitalisation, institutionalisation and higher long-term mortality [54]. The incidence of postoperative delirium varies in different groups. For example, it is reported as 4.0–53.3% in patients with hip fracture and 3.6–28.3% in all elective patients [55]. Common screening tools include the Confusion Assessment Method (CAM), Delirium Symptom Interview (DSI), and Nursing Delirium Screening Scale (NuDESC).

Pre-operative risk factors for postoperative delirium in the elderly include: frailty; pre-existing cognitive impairment; comorbidities (e.g. history of stroke, Parkinson's disease, depression, anxiety disorders and diabetes); malnutrition; prolonged fasting and dehydration; hypo- or hypernatraemia; use of anticholinergic drugs; alcoholism; and sensory impairment [56]. Peri-operative factors that increase the risk include: emergency surgery; duration and site of surgery (abdominal and cardiothoracic); greater intra-operative bleeding and transfusion requirement; hypothermia; urinary catheterisation; postoperative complications; and acute pain.

The European Society of Anaesthesiology recommends the implementation of fast-track surgery to prevent postoperative delirium in high-risk patients [53]. Routine premedication with benzodiazepines should be avoided. Depth of anaesthesia monitoring is advocated to avoid excessive depth and good pain control is important, including the use of a continuous intra-operative analgesic regimen such as remifentanil. The group also suggested implementing non-pharmacological measures to reduce postoperative delirium such as: cognitive orientation (clock, communication etc.); sensory enhancement with visual/hearing aids; noise reduction and good sleep hygiene; avoidance of unnecessary in-dwelling catheters; medication review; early mobilisation; and good nutrition. Medical evaluation is important to identify and manage triggering factors for postoperative delirium such as sepsis, dehydration, electrolyte imbalance, substance withdrawal, etc. [57]. Pharmacological treatments should be reserved for severe cases who could potentially cause harm to themselves or others. In such cases, drugs of choice include low-dose haloperidol or low-dose atypical neuroleptics. Total intravenous anaesthesia with propofol is associated with a lower rate of postoperative delirium than sevoflurane anaesthesia in elderly patients [58].

Unlike delirium, postoperative cognitive dysfunction does not have a uniform definition but, clinically, it can be defined as impairment of cognitive function, including memory, concentration, executive function and speed of mental processing [59–61]. In addition to mortality [62], postoperative cognitive dysfunction is associated with an increased risk of inability to work and social dependency, which imposes a huge burden on individuals and society [63]. According to a landmark study, the International Study on Postoperative Cognitive Dysfunction, postoperative cognitive dysfunction was present in 25.8% of elderly patients aged 60 years or above one week after major non-cardiac surgery, and in 9.9% of elderly patients 3 months after surgery. This compares with 3.4% and 2.8% in the respective control groups of similar patients who had not undergone surgery [64]. After cardiac surgery, rates of postoperative cognitive dysfunction lie between 43% and 81% at 1 week and between 6% and 39% at 3 months postoperatively. It can manifest days or weeks after surgery, and resolves more rapidly in younger populations [62]. However, it is difficult to reach the diagnosis, as different studies have adopted different time frames postoperatively for diagnosing the condition. Also, a baseline assessment of cognitive function before surgery is required for subsequent comparison. There is also a lack of consensus regarding which diagnostic tools should be used; formal psychometric testing is complicated and is impractical in the routine clinical setting.

Risk factors for postoperative cognitive dysfunction include: advanced age; lower educational level; history of stroke without residual impairment; pre-existing cognitive impairment; and depression. Peri-operative triggering factors include: long duration of surgery; type of surgery (cardiac, orthopaedic and vascular); postoperative delirium; respiratory complications; and infections [59, 60, 62, 64]. In cardiac surgery, the use of cardiopulmonary bypass has been implicated as a precipitating factor. However, no concrete evidence is available to support a direct causative relationship between anaesthesia, major surgery and postoperative cognitive dysfunction [65, 66]. Paradoxically, commonly encountered intra-operative events such as hypotension or hypoxia are not associated with the development of postoperative cognitive dysfunction [64].

To date there are no widely accepted management guidelines for postoperative cognitive dysfunction [53, 57,

67]. The adage 'prevention is better than cure' is apposite to this clinical condition and it is, therefore, important to identify high-risk patients and initiate appropriate preventive measures. The Association of Anaesthetists is currently preparing a guideline statement on the peri-operative care of people with cognitive impairment [68]. Pre-operatively, any pre-existing cognitive impairment or dementia should be documented. For high-risk cases, thorough discussion with, and counselling of, patients and families of the possibilities of cognitive change is highly recommended [59, 69]. Benzodiazepines must be avoided if possible. Minimally invasive surgery should be adopted, where appropriate, as it will decrease the extent of the inflammatory response.

There is growing evidence that processed electroencephalogram monitoring during anaesthesia reduces the incidence of postoperative cognitive dysfunction and delirium [70–72]. In a large randomised study, BIS™-guided anaesthesia, with a target of 40–60, was associated with a significant reduction from 14.7% to 10.2% in postoperative cognitive dysfunction at 3 months postoperatively [73]. The use of anaesthetics for non-anaesthetic purposes, for example, treating hypertension by increasing the dose of anaesthetic, is irrational and should be avoided. The use of near-infrared spectroscopy in cardiac surgery to avoid cerebral desaturation might be useful. There is no consistent evidence that any single anaesthetic agent or technique reduces the risk of postoperative cognitive dysfunction. In particular, there is no strong evidence that a propofol intravenous anaesthetic technique offers any advantages, although it may reduce delirium [58, 74]. Although it might be expected that regional anaesthesia would confer cognitive protection, once again evidence is lacking. Prolonged hospital stay, sleep deprivation and postoperative pain may all contribute to postoperative cognitive dysfunction. Minimising length of hospital stay by implementing fast-track surgery, optimising postoperative pain control (in particular avoiding opioids [75]), and improving sleep hygiene might decrease early postoperative cognitive dysfunction. All relevant staff should receive training in the evaluation and management of pain in patients with cognitive impairment [68].

Pre-operative counselling and shared decision-making

In a recent study, almost half of the patients over the age of 60 years wished to make decisions regarding medical care near the end of life. However, 70% of these patients lacked decision-making capacity [76]. It is important to have advance directives so that these individuals can receive care according to their wishes. Few patients undergoing high-risk surgical procedures have advance directives in place, and surgeons do not routinely discuss these issues pre-operatively [77, 78]. The best practices guideline 2016 from the ACS and the AGS on optimal peri-operative management of elderly patients provides several recommendations about patient counselling [79]. Pre-operatively, the healthcare team should explore and discuss with patients their personal values and treatment preferences, including specific outcomes that may be important to them, such as functional decline, loss of independence and the subsequent care burden. The team should ensure patients have an advance directive and a designated healthcare proxy; this information should be clearly documented in the patient's medical record. Whenever possible, early postoperative palliative care consultation should be considered in patients with a poor prognosis, especially those not expected to survive more than 6 months postoperatively. A structured approach to managing patients with existing advance directives should be in place.

Risk tools, such as the ASA physical status [80], Nottingham Hip Fracture Score [81] and mortality risk calculator [82], are useful in guiding decision-making. However, they are derived from heterogeneous observational data, which often require individualised adjustment. Furthermore, there may be a disparity between what doctors and patients view as 'risk' or 'acceptable risk'. Therefore, the manner and circumstances in which risk is conveyed are important [6, 83]. High-risk surgery should not be performed without a pre-operative commitment to appropriate postoperative care. If a patient is critically ill, the degree and appropriateness of intervention should be made in conjunction with senior surgeons, anaesthetists, intensivists, geriatricians and, most importantly, patients and their families.

In conclusion, as the world population ages, the demand for surgical care for elderly patients is increasing. These patients present unique challenges and need a tailored peri-operative care pathway. Anaesthetists should be proactive in both assessing and optimising medical conditions and the nutritional status of elderly patients pre-operatively. We should also explore social issues, and actively involve patients and their families in major decision-making. Peri-operative management should be multidisciplinary and patients' personal values and their quality of life should be the centre of any important clinical decision process.

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Review Article

Peri-operative care pathways: re-engineering care to achieve the 'triple aim'

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Summary

Elective surgical pathways offer a particular opportunity to plan radical change in the way care is delivered, based on patient need rather than provider convenience. Peri-operative pathway redesign enables improved patient experience of care (including quality and satisfaction), population/public health, and healthcare value (outcome per unit of currency). Among physicians with the skills to work within peri-operative medicine, anaesthetists are well positioned to lead the re-engineering of such pathways. Re-engineered pre-operative pathways open up opportunities for intervention before surgery including shared decision-making, comorbidity management and collaborative behavioural change. Individualised, risk-adapted, intra-operative interventions will drive more reliable and consistent care. Risk-adapted postoperative care, particularly around transitions of care, has a significant role in improving value through peri-operative medicine. Improved integration with primary care providers offers the potential for minimising errors around transitions of care before and after surgery, as well as maximising opportunities for population health interventions, including lifestyle modification (e.g. activity/exercise, smoking and/or alcohol cessation), pain management and sleep medicine. Systematic data collection focused on quality improvement is essential to drive continuous clinical improvement and will be enabled by technological development in predictive analytics, systems modelling and artificial intelligence.

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Introduction

The practice of peri-operative medicine is defined as the integrated, multidisciplinary medical care of patients from the moment of contemplation of surgery until full recovery [1, 2]. This simple definition has important and revolutionary implications for the care of patients for whom surgery may offer a treatment option. It also has profound implications for the future of anaesthesia as a medical specialty.

Peri-operative medicine is a new and rapidly evolving clinical science that addresses the needs of a growing patient population with increasingly complex medical needs. Peri-operative medicine offers the opportunity to go beyond the traditional anaesthetic and surgical focus on the care of a single patient in the immediate peri-operative period and to contribute as well to improving public/population health on a wider scale, thereby improving the

value proposition of anaesthesia as a specialty. Such an approach is perfectly aligned with the US Institute for Healthcare Improvement's widely supported 'triple aim' of improving patients' experience of care (including quality and satisfaction); improving population/public health; and reducing the per capita costs of healthcare [3, 4]. This 'triple aim' framework has now been explicitly integrated into the UK NHS Five Year Forward View [5]. Population health initiatives have typically focused on preventing, or slowing the progression of, chronic conditions. Less attention has been directed towards episodic peri-operative care, although in some systems such care accounts for over half of hospital costs [6]. Furthermore, elective peri-operative care takes place in a setting with substantial opportunities to rationalise and redesign pathways of care for patient benefit.

Delivering care based on the risk of adverse outcome for patients, a so-called risk-adapted approach, is essential to enhance healthcare value in the face of rising demand and inevitable resource constraints. Although such an approach may seem self-evident, many aspects of care have traditionally been organised around specialties or procedures, rather than around patient need. The growing prevalence of comorbid conditions [6], and harmful lifestyle characteristics (e.g. inactivity) coupled with an understanding that some surgery may be unnecessary or even harmful [7] are driving a re-appraisal of peri-operative processes. Approaches such as business process re-engineering are being applied with the aim of achieving fundamental systems redesign based on a comprehensive re-evaluation of process aims [8].

Patients who are candidates for surgery are often not ready for surgery. The implications of clusters of behavioural factors (activity/exercise, nutrition, consumption of social drugs) [9] and long-term conditions (comorbidity/multimorbidity) [10] are not well understood. The degree to which modification of such factors will affect outcome is also unclear. The incremental value of allocating resources to modify such risks adds a further layer of complexity. Costs are typically concentrated in a small proportion of care episodes with a high level of complexity [11]. Significant opportunity for value enhancement therefore lies within the understanding of these most complex episodes of care for the sickest patients. Finally, managing care around specialist 'silos' based on provider convenience is increasingly recognised as resulting in inefficient and ineffective care instead of serving patients' best interests.

The aims of this article are: to review the background and context of the current focus on innovation in peri-operative pathways; to summarise opportunities to improve peri-operative care through pathway re-engineering; and to highlight opportunities for further innovation to maximise value. To achieve these aims the manuscript is divided into two sections. The first section focuses on the contextual and conceptual issues underlying the evolution of peri-operative care and explores how peri-operative medicine meets the challenge of the 'triple aim': improved population health, healthcare and value. The second section focuses on specific opportunities to improve care and value through pathway modification in the pre-operative, intra-operative and postoperative phases.

Innovation, value and peri-operative care

The practice of anaesthesia and the pathway to surgery

Traditionally, the role of anaesthetists has been defined by the operating theatre, typically in the context of an in-patient episode. Patient assessment before surgery was considered important, but for in-patients (historically the vast majority of patients), routinely took place on the night before surgery. In the late 1980s and early 1990s, the move towards day-case or ambulatory surgery changed this framework. Pre-assessment clinics developed rapidly and patients were evaluated at a time separated from their in-patient episode. This trend was reinforced by the emphasis on day-of-surgery admission within Enhanced Recovery programmes and is now almost universal for most major operations. The benefit has been a substantial reduction in the in-patient bed utilisation associated with major surgery, alongside an increase in resources directed towards pre-operative assessment on an outpatient basis. However, for most patients travelling this 'journey', pre-assessment takes place a short time before surgery. A checklist approach effectively documents patient characteristics, and risk may be evaluated, but little can be achieved in the limited remaining time. The opportunity to intervene to improve health, either through optimising inter-current chronic illnesses (comorbidities) or through encouraging patients towards more healthy behaviours, has been lost. Critically, shared decision-making around choice of surgical and other treatments is much more challenging when the patient has been offered a surgical management plan several weeks previously. The opportunity to contribute to the care planning process and improve patient outcomes has been diminished, if not lost. Starting such conversations at a late stage in the process will also impoverish the patient experience: patients rightly expect that the teams offering options for the treatment of their underlying condition should act in a co-ordinated fashion as an integrated whole.

Value and peri-operative medicine pathways

The Harvard economist Michael Porter has written persuasively on the challenges of measuring and improving value, defined as outcome per unit currency, within healthcare [12]. Better value may be achieved through improving efficiency of particular processes with respect to cost (achieving more for the same or less) or through reducing demand for inefficient or ineffective processes. Peri-operative pathway modification may contribute to improving value in a variety of ways [8]. Streamlining pre-operative assessment through reducing the burden on low-risk patients may improve the efficiency of this process and free resources for higher risk patients. Collaborative (shared) decision-making [7] may result in patients at the highest risk of complications and prolonged length of stay choosing not to undertake surgery in circumstances when harm may outweigh benefit. Early intervention to manage comorbidities and initiate 'prehabilitation' may improve both short-term peri-operative outcome and long-term patient health [9]. The consequences of such interventions are not only better outcomes for the individual patient but also more efficient resource use for the healthcare system through economical delivery of effective interventions and avoidance of ineffective high-cost interventions. The resources so freed are then available to support better patient care and further public/population health initiatives.

Population/public health and peri-operative care

The closely intertwined concepts 'public health' and 'population health' encompass the notion of considering health at the level of the group, community or population level rather than at an individual level. Although nuances of definition may be important for those directly involved in these fields, in general the terms may be used interchangeably, with clinicians tending to refer to 'population health', and government and provider agencies tending to talk about 'public health'. The simple formulation that '*population health includes health outcomes, patterns of health determinants, and policies and interventions that link these two*' [13], whereas '*public health refers to the organised efforts of society to promote and protect people's health and wellbeing, and to prevent ill-health*' [14] may be useful.

Within this framework, the combination of progressive improvements in longevity, coupled with the increasing prevalence of multimorbidity with age [15], has resulted in a growing number of surgical procedures taking place in elderly patients with co-existing medical conditions [6]. Patients are living longer in chronic ill health; the requirement for surgery is both a consequence of that, and also made more complex by it. From a public/population health perspective, this group of patients offers extraordinary opportunities to intervene before the predictable 'injury' of surgery [6, 16–19]. Although this injury is viewed as necessary to improve the quality and/or quantity of life through treating the surgical problem, it may also bring unintended harm. Prehabilitation to improve patients' physical and psychological resilience to surgical injury focuses on improving physical activity/exercise, nutrition and psychological resilience, alongside behavioural change initiatives to minimise harmful social consumption of tobacco and alcohol [9]. Comorbidity management seeks to optimise management of long-term conditions such as anaemia and diabetes before surgery [9]. Both approaches offer the potential to improve short-term peri-operative outcomes and longer term postoperative health outcomes, given the well-recognised relationship between short-term harm and long-term mortality. Moreover, prehabilitation offers the possibility of long-term behavioural change, catalysed during the 'teachable moment' before surgery, with consequent improvements in individual and population level health outcomes. Shared (collaborative) decision making provides a mechanism to improve the patient experience and to better match clinical need with likely benefit [7]. Although some models of healthcare payment may work against such an integrated approach (e.g. fee-for-service), alternative mechanisms such as bundled payments or capitation may serve as a positive incentive.

Risk and surgery

Risk is the product of likelihood and consequence for an adverse event. The likelihood of any given peri-operative event is governed by two categories of risk determinant: patient characteristics and healthcare characteristics (including the types and magnitude of surgery and other elements of peri-operative care). Both of these categories of risk determinant may be lessened through changes to the peri-operative pathway.

Patient risk factors may be divided into those that are fixed and those that can be modified in the time available before surgery (Fig. 1). Some contributory risk factors, such as chronological age, sex, and genetic constitution, cannot be modified before surgery under any circumstances. Others may be partially modifiable; for instance, some aspects of chronic illness may in part be fixed (e.g. emphysema, myocardial injury) but in part modifiable (e.g. reversible airways disease, anaemia). Risks linked to patient lifestyle and behaviour may be substantially modifiable: activity/exercise, tobacco and alcohol consumption, diet

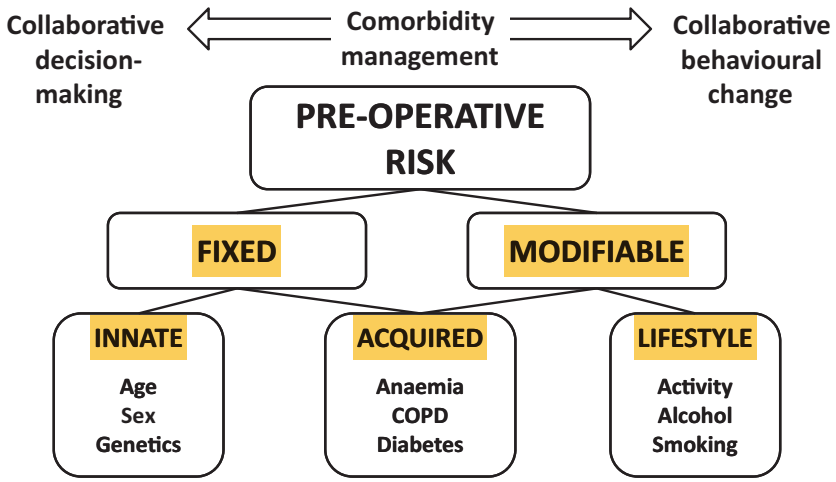

Figure 1 Fixed and modifiable patient risk factors.

and psychological wellbeing are all amenable to substantial change. Although the achievement of such a change may be challenging, the peri-operative period arguably offers unique opportunities ('teachable moments') to improve patient health and system value. From this framework, three categories of opportunity to improve pre-operative care present themselves: (1) shared (collaborative) decision-making; (2) comorbidity management; and (3) collaborative behavioural change. Fixed patient risk factors may shape the process of shared decision-making but are of less relevance to endeavours to manage comorbidities or patient behaviours. Modifiable comorbidities may be amenable to improved care through clinical input from peri-operative care teams or through specialist referrals. Modifiable behaviours are candidates for collaborative behavioural change interventions in patients who consent to such approaches. Each of these categories of peri-operative care modification will be considered in more detail below, and in other articles within this special issue of *Anaesthesia*.

Peri-operative care pathways

Adopting a patient perspective, the peri-operative care pathway should encompass five basic elements, the first of which leads inevitably to the remaining four. First, the patient should be at the centre of their own care, and their wishes, opinions and expectations should be central to the care process. Second, decision-making around surgery should result in their best interests being served. Third, they will be adequately prepared for surgery. Fourth, care during the peri-operative episode will be safe and effective. And finally, they will experience a full and timely recovery.

These patient expectations map onto different categories of clinical care. Decision-making about what care patients would like to receive is best served by formulating a pre-operative plan through a shared (collaborative) approach early in the peri-operative pathway [7]. Adequate preparation for surgery is addressed through efficient and effective comorbidity management and collaborative behavioural change (prehabilitation) [9]. To be effective, each of these three interventions must be commenced as early as possible after surgery is contemplated [8]. This requirement is the overriding justification for re-engineering the peri-operative pathway, so that patient evaluation can proceed in parallel with pathology evaluation [8]. In order to achieve this goal, early risk 'triage' to identify patients who will benefit from each of these three processes should occur as soon as possible after the initial contemplation of surgery, and the peri-operative physician (typically an anaesthetist) and patient should meet soon thereafter. Figures 2 and 3 illustrate the differences between a traditional pre-operative pathway and one set up to achieve the aims described above [8]. Safe, effective peri-operative care and a full and timely recovery are best achieved through individualised intra-operative and postoperative care plans based on a standardised 'menu' of options (see below). Individualisation of the intra-operative and postoperative care plans should be based on a careful evaluation of pre-operative risk factors and any changes that occur during the pre-operative journey.

Pre-operative care

Shared decision-making offers the potential for avoiding 'wrong-patient surgery', at the same time serving patients' best interests, reducing healthcare costs and improving the

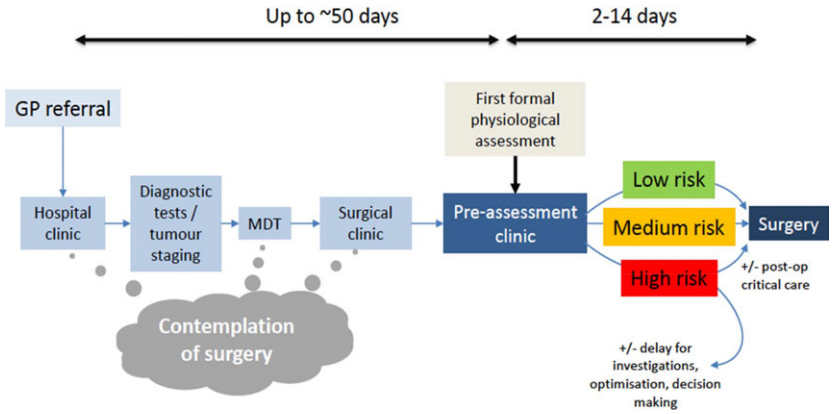

Figure 2 Traditional pre-operative pathway. MDT, multidisciplinary team.

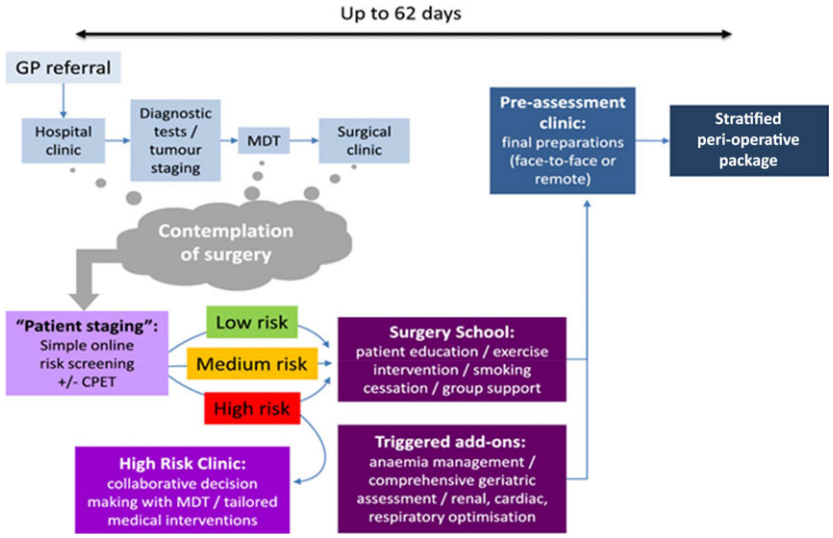

Figure 3 Proposed 're-engineered' pre-operative pathway.

patient and physician experience. Shared decision-making is covered in detail elsewhere in this journal Supplement [20]. An important implication of shared decision-making is that those patients most likely to choose not to have surgery are, in general, those patients who are at highest risk of adverse outcomes following surgery. Such patients are those in whom the harms of operative intervention do, or at least may, outweigh any potential benefits of surgery, and therefore they quite rationally make alternative healthcare choices (e.g. less aggressive surgery, alternative medical treatments including chemotherapy and palliative care). Importantly, patients at high risk of adverse outcomes contribute disproportionately to healthcare costs. Complications following surgery cost, on average, two or three times more than straightforward care [21] and those patients at the highest risk cost the most. The notion that a small number of patients contribute disproportionately to total cost is well recognised, both at an individual patient level (patient level cost attribution) and at a population level [11]. It is important to note that shared decision-making does not force patients to make decisions. Although some patients may choose, within a shared decision-making context, to accept advice from their doctor in a more paternalistic mode, others will seek to make their own independent decisions based on information provided by physicians. Many others lie on a spectrum between these two positions.

Co-existing disease is a powerful influence on risk in people undergoing major surgery, and the effective management of comorbidities is an important means of mitigating this risk. A variety of models of dedicated pre-operative clinics have emerged in recent years but a

number of themes are becoming clear. Such clinics are typically addressing common problems (e.g. anaemia, diabetes) and are based on an algorithmic approach supported by the contribution of specialists. These clinics may be face-to-face, or more commonly, 'virtual' clinics, with a face-to-face specialist clinic available for more complex cases. Pre-operative anaemia clinics are probably the most widespread at present and a number of reports from early adopters have appeared [22]. For pre-operative anaemia clinics, the savings achieved through reduced peri-operative blood transfusion readily supports the business case for establishing such a clinic; this may be more difficult for other diseases for which less evidence is available. Comorbid disease management before surgery may relate to patients with long-established diagnoses, in which case a conversation with, or even referral to, the long-term care specialist physician will be appropriate. Alternatively, new diagnoses may emerge during pre-operative preparations that are initially managed within the dedicated peri-operative clinic. For some patients, encounters with peri-operative physicians before surgery may constitute their first substantive health evaluation for many years. Established peri-operative clinics include: anaemia, diabetes, heart failure, cardiac ischaemia, cardiac devices (pacemakers, implantable cardiac devices), chronic obstructive airways disease, sleep/obstructive sleep apnoea and pain. Pre-operative pain clinics have become increasingly important with the emergence of the 'opioid epidemic', particularly in the US [23]. Peri-operative management of opioid dependence, whether from prescription, 'bystander' (consumption of someone else's prescription) or illicit drug use, is rapidly becoming more sophisticated with the extensive experience being accumulated in the US. Pathway re-engineering enables the effective delivery of such clinics by providing the necessary time for evaluation and intervention before surgery.

Collaborative behavioural change becomes possible during the pre-operative period, as patients may be more susceptible to behaviour change interventions than during their 'normal' lives. Such interventions also offer a psychological boost at a time when patients may feel very limited control of their immediate destiny. Smoking cessation [24], alcohol cessation [25], nutritional optimisation [26] and physical activity and exercise [27] are covered in detail elsewhere in this supplement [28–31]. In each case, despite the current very limited evidence base, there are data available to point to the likelihood of significant clinical benefit in terms of improvements in short-term clinical outcomes. The notion that such changes in behaviour around the time of surgery may be long-lasting is intriguing and contributes to the paradigm that the practice of peri-operative medicine may provide population health benefits.

Intra-operative care

Developments in individualised, risk-adapted, intra-operative interventions should lead to more reliable, consistent care. Increasingly persuasive data suggest that many aspects of intra-operative care received by patients do not appear to represent either the best available evidence or a sound physiological basis: the factors that we might expect to drive delivered care are not necessarily those that do in 'real life' practice. An excellent example is that of fluid therapy, where recent studies in the US have demonstrated very substantial between-patient variations in volumes of fluid administered during major surgery [32]. Although we might expect such variation to be based on patient (e.g. age, risk) or surgical (e.g. duration, blood loss) characteristics, in fact the biggest determinants were the identity of the anaesthesia and surgical providers [32]. In other words, the clinicians' personal behaviours were more important that the patients' clinical situation. Furthermore, this variability is linked to clinical outcomes [33]. Similar patterns of variation in care pertain in peri-operative blood transfusion [34], oxygen therapy [35] and peri-operative ventilation [36]. These observations support the notion that intra-operative care should be both standardised and individualised; standardised to drive consistent patterns of care between different patients, and individualised to ensure that such care is based on individual patients' clinical risk. The adoption of a standardised risk-adapted approach to peri-operative fluid therapy [37] is an example of such an approach: standardised in that all patients are treated using the same risk-adapted framework, and individualised in that the precise management approach is based on the characteristics of the individual patient and their surgery [37]. An additional advantage of such a consistent approach to intra-operative patient management, and indeed to care in general, is that the evaluation of new interventions becomes easier due to an improvement in the relationship between 'signal' and 'noise'. Consistent routine care improves the likelihood that any signal of benefit (or harm) will be detected during formal evaluation such as quality improvement initiative or randomised controlled trial.

Postoperative care

Risk-adapted postoperative management, particularly around individualised care and transitions of care, has a significant role in improving value through peri-operative

medicine. In the short term, effective pre-operative risk characterisation and responsive postoperative care provision should ensure effective allocation of postoperative resources to those in need of them. Low-risk patients experiencing an uncomplicated recovery should be encouraged to return to normal function and discharged home as quickly as possible. Patients at higher risk of adverse outcome and/or who develop postoperative complications should be provided with the appropriate level of care in a timely manner, and on a preventative basis where possible. Effective management of the transitions from theatre to postoperative care, between postoperative care environments and from hospital to the community should maximise the benefit of previous interventions (surgery, behavioural change, comorbidity management) and minimise the risk of errors (e.g. failure to restart important long-term medications after surgery). Furthermore, linkage between primary and community care offers further opportunities to contribute to public health benefit by ensuring continuity of pre-operative behavioural change and comorbidity management interventions.

A number of principles can be seen to underpin effective postoperative care. First, the targeting of the limited available resources based on effectiveness of use, not traditional care silos: risk-adapted postoperative management. Second, achieving a balance between enhanced recovery principles and augmented care after surgery. Third, redefining postoperative care environments to meet the needs of patients that fall outside the current classification of levels of care (see next section). Fourth, the flexible use of physical medical and nursing/allied health professional resources to maximise effectiveness. Fifth, minimising risks inherent in transitions of care through more effective communication and implementation of systems (e.g. checklists) based on knowledge of human factors (see section below).

The individualised allocation of postoperative resources implies a move beyond current practice. Typically, a hospital offering major (in-patient) surgery will be able to offer some or all of the following range of postoperative care environments: Intensive Care (Level 3); Surgical High Dependency Care (Level 2); Postoperative Care Unit/Overnight Intensive Care (short stay unit that offers some level-3 facilities); augmented ward care; a postoperative outreach team and a peri-operative medicine team. Although the 'typical' postoperative journey involves the patients spending a few hours in recovery before returning to a surgical specialty ward, the variety of alternatives to this is increasing and the basis on which patients are triaged to different postoperative environments is changing.

Long-standing definitions of critical care (Levels 1/2/3) [38] are evolving as the spectrum of facilities becomes increasingly diverse. Although some hospitals offer augmented care within environments defined by these traditional criteria and staffed by intensivists or anaesthetists, other hospitals offer augmented care (monitored beds, cardiovascular support) in a ward-based environment with medical input from the surgical team. Furthermore, the criteria governing which patients are offered such care are changing. The notion that patients undergoing particular procedures are automatically cared for in intensive care or high dependency after surgery, although others are not, is evolving towards a framework of risk-adapted care defined by an individual patient's risk of postoperative harm in general, and specific risks in particular (e.g. airway problems following maxillofacial surgery). Although more 'high-risk' patients are being triaged to augmented care environments, low-risk patients undergoing higher risk procedures are often being 'fast-tracked' to the ward. A corollary of this approach is that it may make more sense to group patients in wards by risk and level of care, rather than by surgical specialty, in the immediate postoperative phase. An important consideration in this regard is that the advantages of a closely monitored, well-staffed environment aimed at avoiding 'failure to rescue' [39] need to be balanced against the more effective delivery of enhanced recovery goals that are typically achieved more effectively on general surgical wards. Consistent with the notion of 'critical care without walls', the characteristics of the care delivered are more important than its location. The level of staffing and monitoring, and the consequent capacity to safely execute complex postoperative interventions (e.g. vasopressors, non-invasive ventilation) is more important than the name over the ward door. Layered over the location of the patient is the availability of appropriately trained specialist postoperative care providers in a prompt and reliable manner. Peri-operative physician and critical care outreach teams may provide regular planned reviews of postoperative recovery as well as a rapid-response function to minimise the risk of failure to rescue. Finally, the concept of DrEaMing (Drinking Eating and Mobilising) [40] is increasingly being seen as important, both as marker of recovery that has utility in managing postoperative care (patients that achieve DrEaMing rarely develop subsequent complications) and as a benchmarking measure of the effectiveness of peri-operative care (see below) [40].

Transitions of postoperative care will still be necessary and effective communication is fundamental to safely managing these. Early transitions between recovery and ward or augmented care environment are best accompanied by direct verbal handover between medical staff to accompany ongoing clinical documentation. Checklist-type approaches are valuable to minimise the risk of human error in this context. Similarly, the lack of integration between secondary and primary care, coupled with the persistent use of out-dated technology (e.g. traditional mail, fax) contribute to patient dissatisfaction around the transition of care from home-to-hospital and hospital-to-home (community). Interventions targeted at improving transitions of care have, in general, been shown to improve clinical outcomes and patient satisfaction [41, 42], but the research literature in the peri-operative setting is very limited. Effective discharge planning commences at the moment that admission is contemplated. Length of hospital stay and requirements for postoperative care and services are largely predictable based on the patient's pre-operative circumstances and the nature of the intervention. Nevertheless, linkage with primary care is often poor, made worse through the limited use of effective electronic communication. The attention now typically given to in-hospital transitions of care should also be applied to transitions between primary and secondary care and within the broader community care network, including social services. Of note, the move within England towards integrated care organisations (e.g. Accountable Care Organisations, ACOs) may facilitate such a collaboration. Continuation of interventions (e.g. exercise rehabilitation) from before surgery, into recovery, and after discharge has the potential to maximise the public health benefits of peri-operative medicine. Effective integration between secondary care peri-operative medicine teams and primary care services can consolidate pre-operative behavioural changes and continue comorbidity management to match the evolving needs of patients following surgery. Two particular examples that merit attention across transitions of care are effective management of polypharmacy, and consistent attention to opioid minimisation/avoidance. Fundamental to the effective delivery of these aspirations will be the development of efficient and effective lines of communication with primary care and community providers. Linking effectively with general practice as well as community health and social care services will increase the likelihood of seamless delivery of care that functions in the patient's best interests.

Continuous improvement?

Pathway redesign, as with all changes to clinical care, brings with it the possibility of harm as well as benefit. Implementation of change within healthcare is notoriously slow and incomplete. Systematic data collection on processes and outcomes of care should be considered essential for quality care provision. Only through recording, and analysing the reliability of, delivery of processes can we evaluate whether we are actually providing the care we assume we are. Only through the systematic comparison of process reliability and risk-adjusted outcomes with benchmarking against peer institutions can we be confident that our care is the best it can be. Increasingly, such data management will be augmented by more advanced methods of analysis, presentation and modelling, including the use of predictive analytics, topological data analysis, systems modelling and artificial intelligence.

The professions of anaesthesia

In much of the developed world, anaesthetic care is provided by physicians. In low- and middle-income countries, non-physician providers often provide anaesthesia due to the limited availability of physicians. In the US, there is a long-standing mix of physician and non-physician (Certified Registered Nurse Anesthetists) providers; Certified Registered Nurse Anaesthetists can practice independently in more than half of US states. Technical solutions to the delivery of anaesthesia, including automated intelligent care delivery systems, robotic procedures and predictive analytics, will inevitably change the roles of anaesthesia providers of all types over time. Relying on the practice of anaesthesia delivery within the operating theatre/room to sustain the medical specialty of anaesthesia is likely to result in role displacement and loss of added value in the future. To paraphrase a quote about evolution that is often misattributed to Charles Darwin: *'It is not the most intellectual or the strongest that survives, but rather those that are best able to adapt or adjust to the changing environment in which they find themselves'* [43]. Failure to anticipate and adapt to the changing nature of anaesthetic service provision and technology, and the impact this will have on anaesthesia as a medical profession, risks professional decline and fall. In contrast, anticipation of this future, with a holistic focus on the broader spectrum of medical needs of patients contemplating and undergoing surgery, will ensure the vitality of anaesthesia as a medical specialty. The current time offers a particular opportunity for physician anaesthetists to align their interests with those of

their patients and embrace the future of peri-operative medicine.

Conclusion

Peri-operative medicine provides an opportunity to meet the challenge set down by the Institute for Healthcare Improvement's 'triple aim' of improving patient experience and population health while reducing costs. Anaesthetists are well positioned to lead the re-engineering of pre-operative care pathways needed to achieve this goal through shared decision-making, comorbidity management and collaborative behavioural change. Standardised, individualised (risk-adapted) intra-operative care leading to risk-adapted postoperative care, particularly around transitions of care, offers a further opportunity to improve value while contributing to improving patient and population health. Effective operationalisation of these ideas will be enabled by systematic data collection focused on quality improvement and supported by technological development in data analysis and presentation. For the medical specialty of anaesthesia, peri-operative medicine offers the opportunity to achieve a step-change in patient experience and contribute to improving public/population health and value while meeting the challenges associated with technological and workforce changes, that may otherwise result in role displacement and professional decline.

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Review Article

Pre-optimisation of patients undergoing emergency laparotomy: a review of best practice

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Summary

Although the concept of pre-operative optimisation is traditionally applied to elective surgery, there is ample opportunity to apply similar principles to patients undergoing emergency laparotomy. The key challenge is achieving meaningful improvements in a patient's condition without introducing delays to time-sensitive surgery, which may be required in a matter of hours. Optimisation can be considered in two parts: that of the patient's condition; and that of the care pathway. Optimising the patient's condition is less about improving long-term pathology, and more about correcting physiological derangement, such as electrolyte and fluid balance, blood loss, prompt treatment of sepsis, and ensuring appropriate continuation of medication in the peri-operative period. Optimising the care pathway involves ensuring that the system is designed to deliver reliably the appropriate interventions, such as prompt antibiotics, and access to computed tomography scanning and the operating theatre with minimal delay.

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Introduction

Approximately 30,000 emergency laparotomies are performed annually in England and Wales [1, 2]. Emergency laparotomy encompasses a wide range of procedures performed for a variety of surgical pathologies (Table 1). The presentation may be acute or subacute, and around 6% arise as complications of elective surgery. Almost half of patients are aged > 70 years, and 55% of patients have ASA physical status grade ≥ 3 [3].

The majority of patients undergoing emergency laparotomy have potentially life-threatening conditions that require prompt intervention (Table 2). The small proportion of patients who require an emergency laparotomy following elective surgery may have had the benefit of pre-optimisation for their elective procedure. However, for most, there is often limited time to carry out investigations and instigate treatment to optimise comorbidities. The time required to optimise a patient needs to be balanced against the risk of delay for time-sensitive pathologies. Data from the National Emergency Laparotomy Audit (NELA) shows that around 50% of patients have a surgical urgency < 6 h, 33% 6–18 h and 17% > 18 h [3]. As such, pre-optimisation for emergency surgery needs to be viewed in a different light to elective surgery. There is still significant opportunity to improve a patient's condition before emergency laparotomy, but this needs to be balanced against the surgical urgency.

Table 1 Primary surgical procedure performed during an emergency laparotomy (data from the 2018 National Emergency Laparotomy Audit). Values are proportion.

Primary surgical procedure	
Colonic resection	36%
Adhesiolysis	17%
Small bowel resection	16%
Drainage/washout of abscess/collection	5%
Peptic ulcer – suture repair of perforation	5%
Other	22%

Table 2 Main indications for an emergency laparotomy (data from the 2018 National Emergency Laparotomy Audit – N.B. more than one option may apply). Values are proportion.

Indication for surgery	
Small bowel obstruction	37%
Perforation	25%
Peritonitis	21%
Large bowel obstruction	14%
Sepsis	8%
Ischaemia	7%
Abdominal abscess	7%
Incarcerated hernia	5%
Colitis	4%
Volvulus	3%
Haemorrhage	3%

The approach to pre-optimisation can be considered in two parts: optimising the patient's condition; and optimising the care pathway to reduce delays.

Optimising the patient's condition

Timely antibiotics

Current recommendations advise that antibiotic prophylaxis for abdominal surgery is given on induction of anaesthesia or ≤ 60 min before the start of surgery [4, 5]. However, more than one-third of patients have signs of sepsis present on admission or at the time that the decision for surgery was made [3]. Patients with signs and symptoms consistent with sepsis should receive antibiotics as a matter of urgency after the diagnosis is suspected, irrespective of the timing of surgery. This may well mean that antibiotics are administered in the emergency department. The literature on sepsis describes a 'golden hour' for early administration of antibiotics, with observable increases in mortality for every hour of delay in delivering the first dose [6, 7].

Since the presentations and indications for emergency laparotomy are multiple, and antimicrobial stewardship is an important consideration, the urgent administration of broad-spectrum antibiotics will not apply to all patients. Hospitals should ensure they have their own systems in place to identify patients with sepsis and be able to manage them appropriately.

Rational approach to fluid resuscitation and electrolyte balance

Patients presenting with intra-abdominal pathology may be hypovolaemic, either due to fluid losses from the gastrointestinal tract through diarrhoea or vomiting, sequestration of fluid within the bowel lumen, intra-abdominal haemorrhage or a relative hypovolaemia due to distributive shock in the presence of sepsis or severe inflammation. In some cases, fluid resuscitation will need to continue before, during and after surgery. When presented with a hypovolaemic patient, the approach to fluid resuscitation should be consistent with the underlying cause.

Patients with acute haemorrhage may require blood products as opposed to large quantities of clear fluids. Although the evidence suggests that a restrictive approach to the management of upper gastrointestinal bleeding is preferable [8, 9], shocked patients or those with evidence of continuing significant bleeding should be managed with early, balanced transfusion. Hospitals should therefore ensure they have the capacity to supply packed red blood cells (O negative or cross-matched) and other blood products rapidly in the event of major haemorrhage. Applying evidence from the trauma literature, access to thromboelastography may also help to rationalise the use of specific blood products. In the event of major haemorrhage, tranexamic acid should be considered as part of resuscitation, along with the avoidance of hypothermia, acidosis and coagulopathy. In any patient with continuing bleeding, the priority should be urgent haemostasis, either through surgery, endoscopic intervention or interventional radiology [10].

Patients presenting for emergency surgery due to cancer causing bowel obstruction may also be anaemic. Treatment with intravenous (i.v.) iron before elective surgery is becoming an established part of pre-operative optimisation that reduces allogenic transfusion requirements. However, its role within the emergency situation is unclear [11, 12]. Guidelines suggest that in the absence of evidence of iron deficiency, the routine use of iron supplementation is not recommended during critical illness [13]. For planned surgery, the target pre-operative haemoglobin concentration is ≥ 130 $g.l^{-1}$, however, a

range of 70–90 $g.l^{-1}$ is generally acceptable for critically ill patients, unless modified due to specific comorbidities or acute illness [13, 14].

Patients with significant gastrointestinal tract fluid loss may be both fluid volume and electrolyte depleted. There remains significant debate over the best (or least bad) fluid to use in this situation. In critically ill patients, a balanced crystalloid solution would appear preferable to saline, in order to avoid a high sodium and chloride load [15]. Hydroxyethyl starch solutions have been widely withdrawn from routine use; however, this remains the subject of review [16, 17]. Although hydroxyethyl starch solutions do remain available for the initial management of hypovolaemia secondary to acute haemorrhage, they should not be used in sepsis or other critical illness, and UK guidelines continue to recommend against their use for fluid resuscitation [17, 18]. Other colloids, such as gelatins and albumin, remain available, but any additional benefit over crystalloids remains unproven [19]. Patients with subacute presentation, such as acute-on-chronic bowel obstruction, may have suffered several weeks of worsening fluid losses resulting in chronic fluid and electrolyte imbalance. Restoration of intracellular cations is unlikely to be accomplished by peripheral administration of i.v. fluids alone. Central venous cannulation may be required in order to administer concentrated potassium or other electrolyte infusions. However, the time required to restore electrolyte concentrations to normal levels, when the maximum infusion rate for K+ is 10 $mmol.h^{-1}$, needs to be balanced against surgical urgency.

In the patient with relative hypovolaemia secondary to vasodilation, fluid resuscitation may only be transiently effective. Excessive administration of fluid may cause an increase in extravascular lung water (compromising oxygenation or ventilation) or worsen tissue oedema (affecting healing of wounds and surgical anastomoses, and compromising organ perfusion). These patients are likely to require the use of vasopressors or inotropes in addition to i.v. fluid; however, the end-points to aim for are not clear. There is research in progress to ascertain whether the intra-operative use of goal directed fluid therapy benefits patients undergoing emergency laparotomy [20].

In general, patients undergoing emergency laparotomy require meticulous monitoring of fluid input and output, including from urinary catheters, stomas, drains, nasogastric tubes and other gastrointestinal losses. Clinicians should bear in mind that in patients with obstruction or ileus, the bowel lumen may contain a significant volume of unmeasured fluid. Intravenous fluid for maintenance and i.v. fluid for resuscitation should be viewed separately, with resuscitation fluid given as titrated boluses. Intravenous fluid resuscitation should be de-escalated as early as possible, and high continuing fluid input should be prompt review by a senior clinician [18].

Omitting/optimising medications

The approach to adjusting or omitting medications should be individualised for the patient, considering their past medical history and the clinical situation.

Acute kidney injury is not uncommon in patients requiring emergency laparotomy due to fluid and electrolyte imbalance, coupled with an elderly patient population. Nephrotoxic medications should be reviewed and omitted where possible, especially in the shocked patient. NHS England introduced an acute kidney injury alert system in 2014 to standardise the identification and treatment of acute kidney injury [21]. It is likely that such patients will have been 'flagged' by a hospital's pathology results system, and it is important that this information is recorded and acted upon. Renal function and blood pressure should be considered before giving any antihypertensive drugs, especially ACE-inhibitors or angiotensin receptor blockers [22]. Administration of β-blockers to patients who are already on therapy should be reviewed on a case by case basis, since there is evidence to support continuing their existing use peri-operatively [23]. The same also applies to patients who are already prescribed statins.

Where the absorption of medication via the enteral route is not possible due to the surgical pathology, consideration should be given to finding alternatives for certain essential medications (anti-epileptics, treatment for Parkinson's disease, immunosuppression for transplant patients, etc). These patients should be discussed with the relevant speciality and the pharmacist to try to identify alternative options in the peri-operative period.

Medications with a narrow therapeutic window should be monitored due to the effect that acute illness or drug interactions may have on metabolism and clearance.

Anticoagulants and antiplatelet medications should not be discontinued without first establishing why they were originally prescribed. Patients taking antiplatelet medications following recent endovascular stenting should be discussed with the relevant speciality. In many instances, it may be necessary to stop or reverse anticoagulation, but the indication for the anticoagulant will determine what additional action is required [24, 25]. For instance, patients with a mechanical aortic value will require bridging therapy with low molecular weight or unfractionated heparin, as will patients with a recent venous thromboembolism. Patients

with a recent venous thromboembolism in whom full anticoagulation is contraindicated may benefit from insertion of a temporary inferior vena cava filter [26]. Again, the specific circumstances of the patient should be considered.

This list is by no means exhaustive, and early discussion with a pharmacist and the relevant medical specialties is advised for other medications.

Nutrition

Adequate nutrition is vital for recovery from major surgery and it is recommended that nutritional status be formally assessed both pre- and postoperatively [27]. Where time allows, the nutritional status of patients should be optimised pre-operatively in discussion with a dietician.

Peri-operative nutritional therapy is indicated in patients with malnutrition or those at risk, such as patients not anticipated to be able to eat for > 5 days peri-operatively, or those not expected to be able to maintain > 50% of their recommended intake for > 7 days [27]. Although the enteral route is preferred, numerous indications for emergency laparotomy are contraindications to enteral feeding. In these instances, parental feeding is an alternative. It is common to site a multilumen central venous catheter during surgery, and reserve one lumen for parenteral feeds only.

Even if oral diet or feeding via the enteral route is possible, if energy and nutritional requirements cannot be met (e.g. an intake < 50% of calorific requirement) for 7 days, supplementation with parenteral nutrition is recommended. Where it is indicated, parenteral nutrition should be administered as soon as possible [27].

Glycaemic control

Periods of fasting, either before surgery or because enteral nutrition is not tolerated, coupled with the stress response associated with acute illness, are likely to affect the glycaemic control of diabetic patients.

Due to the unpredictable nature of the timing, duration and recovery from emergency surgery, most patients with diabetes who require emergency laparotomy should be managed with i.v. insulin and glucose, either in the form of a variable rate i.v. insulin infusion or a glucose-potassium-insulin infusion, depending on the specific hospital guideline [28, 29]. Patients usually treated with an insulin pump should be managed according to the local policy.

Once an i.v. insulin infusion is established, most regular oral antidiabetic medications should be stopped until the patient is eating and drinking normally, with the exception of GLP-1 analogues, which may be continued [28, 29]. Although there are no formal UK guidelines at the time of writing, SGLT-2 inhibitors should be stopped 2–3 days before surgery due to the risk of euglycaemic ketoacidosis. If this is not possible, blood ketones should be monitored in addition to blood glucose [30–32]. If the patient usually takes a long-acting subcutaneous insulin, this may be continued at 80% of the normal dose together with i.v. insulin, as this may help to stabilise glycaemic control and facilitate return to the patient's normal regimen [28, 29].

Any patient undergoing urgent surgery who is receiving insulin will require regular monitoring of blood glucose and continuous supply of substrate. Aiming for tight glycaemic control is not recommended, but instead the target blood glucose level in the pre-operative or anaesthetised patient should be 6–10 mmol.l^{-1}, accepting values of ≤ 12 mmol.l^{-1} in patients where control is more difficult [28, 29].

Patients with diabetes should be managed in an environment where the staff are familiar with their care. Early involvement of the hospital's diabetes team should be considered.

Pre-operative chest physiotherapy

Postoperative pulmonary complications are common after major abdominal surgery. Some small studies have demonstrated that pre-operative prophylactic physiotherapy can reduce the incidence of such complications [33, 34]. These studies do not account for the specific challenges relating to emergency surgical patients, and were not powered to examine outcomes such as mortality or length of stay. As such, there are no formal recommendations for prophylactic physiotherapy, but this could be a useful area for further study.

Damage control surgery

Although typically associated with trauma patients, some of the elements of damage control surgery are equally applicable to unstable general surgical patients with significant peritoneal contamination or major intra-abdominal haemorrhage. Here the focus is on short-term physiological correction rather than definitive surgery [35]. There are four phases to the process of damage control surgery, as outlined in Table 3. Phases 0 to 3 could be viewed as an extended period of optimisation before the final definitive procedure in phase 4.

Clearly not every emergency laparotomy requires this approach, but the principles should be considered when dealing with patients with significant physiological disturbance or haemodynamic compromise.

Table 3 Phases of damage control surgery.

Phase	Location	Aims	Priority
0	Pre-operative (e.g. Emergency Department, ward)	Resuscitation Prompt access to an operating theatre Avoidance of hypothermia	Physiological optimisation
I	Operating theatre	Damage control laparotomy Control of bleeding Washout of contamination	
II	Critical Care Unit	Further resuscitation Physiological/organ support	
III	Operating theatre	Restoration of bowel continuity, ± closure of abdomen	Definitive procedure

Optimising the care pathway

Reducing delays

Since one of the challenges of emergency surgery is the limited time for pre-operative investigations and optimisation of the patient, it is vital that the care pathway runs as smoothly as possible to avoid unnecessary delays. Delay to emergency surgery has been associated with lower rates of survival [36]. Hospitals should investigate the performance of their own internal systems to ensure that: patients requiring an emergency laparotomy are promptly identified and referred to senior decision makers; any pre-operative investigations can be requested and the results reviewed in a timely manner; and there is sufficient capacity to allow access to an operating theatre in a timeframe appropriate to the clinical urgency.

Hospital systems are complex, and a patient requiring emergency laparotomy will require input from numerous professionals from multiple departments. There is not, therefore, a single right way to structure this pathway, but different solutions will work best according to a hospital's own specific infrastructure and resources. Clinicians should endeavour to optimise this pathway through regular data collection and quality improvement methodology.

Timeliness of access to and reporting of radiology and CT investigations

Interventional radiology plays an important part in the treatment of certain surgical pathologies and may avoid the need for emergency laparotomy. It is the treatment of choice for some types of abdominal bleeding and drainage of abdominal collections. The lack of universal availability of interventional radiology may be overcome through network arrangements with neighbouring hospitals, such that there is a defined pathway to refer patients who would benefit from Interventional radiology and potentially avoid an emergency laparotomy.

It is recognised that for some patients the decision to perform emergency laparotomy can be taken based on clinical findings alone, and that not all patients require an abdominal computed tomography (CT) pre-operatively. However, the majority of patients who go on to have an emergency laparotomy will have had a CT scan performed before surgery [3]. In such a case, it is important that patients have timely access to diagnostic radiology services, and that these images can be reported by a suitably experienced radiologist so that the results aid surgical decision-making without adding delay.

Such targets for access and reporting of CT scans exist for patients admitted following major trauma (CT access available < 15 min and reported by a consultant radiologist < 60 min of the scan) [37], so it is not unreasonable that similar results could be achieved before an emergency laparotomy. Agreements with the radiology department that ensure appropriate scans are performed and reported urgently would assist surgical planning by identifying the likely extent of pathology, and hopefully reduce the number of non-therapeutic (open-and-close) laparotomies in the event of advanced or untreatable disease.

Standardisation/surgical pathways

National audit data have shown that there are considerable variations in the standards of care that patients undergoing emergency laparotomy receive, both between hospitals and within hospitals [3].

Intra-hospital variation can be reduced through standardisation of processes and modification of systems, such that barriers to providing appropriate care are reduced and inappropriate deviation from good care is made more difficult.

This is not to underestimate the importance of the role that clinicians play in ensuring that management is individualised to the specific patient. Good care pathways should overcome access barriers and serve as prompts to clinicians, so that important evidence-based interventions and national recommendations are at least considered, even if they are not applicable in every case.

Optimising the care of the patient

Recognising high risk (or assuming high risk until proven otherwise)

A strong message from the National Emergency Laparotomy Audit has been that appreciation of risk is associated with improved standards of care for high-risk patients. Pre-operative assessment and documentation of risk has been encouraged, initially using the P-POSSUM model and more recently the NELA risk prediction model, which was developed from the population of patients undergoing emergency laparotomy in England and Wales.

Applying population-level data to an individual patient for risk prediction is difficult and should only assist, not replace, clinical judgement. With an overall 30-day mortality rate of 9.5%, emergency laparotomy is high-risk surgery [3]. It is, therefore, reasonable to treat all patients undergoing emergency laparotomy as high risk unless both clinical judgement and risk prediction scores suggest otherwise.

Consultant-led care – right intervention, right time, right place, right people

Considering the high-risk nature of the surgery, it is important to have consultant-led care throughout the process. This applies not only to the technical aspects associated with performing or overseeing the operation but also the decision to operate, or indeed not to operate.

Early consultant input from surgical and anaesthetic specialities, plus critical care and elderly medicine where appropriate, should aim to ensure that the right operation is carried out, at the right time, performed by the right people, with the right facilities available.

Informed consent, shared decision-making and information to family

All patients with capacity should provide fully informed consent before any surgical intervention [38]. The time pressure that comes with the emergency nature of the surgery, coupled with the baseline characteristics of the population undergoing emergency laparotomy, can make this particularly challenging. The process of shared decision-making is another area where the non-technical expertise of consultants is of vital importance.

Although national data provide high-quality information on postoperative mortality and survival, at present the data relating to quality of life and other patient-reported outcomes are very limited. These quality of life factors may be more important to patients and their families than traditional mortality outcomes. Work is underway to assess the feasibility of collecting quality of life outcomes after emergency laparotomy [39]. However, until data on quality of life are available, consultants overseeing the care of these patients must draw on their experience to ensure that they have considered all options, both invasive and more conservative, and are able to reach a shared decision with the patient who is consistent with their wishes and expectations in terms of quality and quantity of life.

Conclusion

Pre-optimisation of patients undergoing emergency laparotomy needs to be viewed in a different light to elective surgery. The reduced time-frames available due to surgical urgency mean that prompt and senior decision-making is required to minimise delays. The time taken to correct any abnormalities needs to be balanced against the need for prompt surgery, particularly in time-sensitive situations involving sepsis or hypovolaemia. Corrective action and surgery may need to occur simultaneously. Although patients might require active treatment to correct abnormalities, it is equally important to ensure that normal medications are continued where appropriate, and omitted where they may be harmful. The reduced timeframe available for pre-optimisation also means that there needs to be robust systems in place to ensure care is provided promptly and consistently, with minimal delays.

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