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EDITORIAL

Prehabilitation

The next challenge for anaesthesia teams

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Death within 30 days of surgery is the third most common cause of death (approximately 1 in 13 deaths).[1] Globally, this represents a significant public health challenge and is argued to be a hidden pandemic.[2] The magnitude of this pandemic is further highlighted in a study that interrogated the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database and reported that 19% of patients had not returned home within 30 days of surgery.[3] Postoperative complications were key drivers for these unfavourable outcomes.

A two-fold to three-fold increase in surgical services will be required to meet the increased burden of degenerative disease, cardiovascular disease and cancer that accompanies the ageing global population, through increasing life expectancy. Ageing is also accompanied by an increased burden of comorbid disease, polypharmacy, sedentary lifestyle and frailty. By extrapolating the impact of the ageing population, we should expect a greater than 10% increase in the incidence of postoperative morbidity annually, with increased healthcare expenditure. This is underpinned by the fact that the population segment older than 80 years is expected to increase by 351% by 2050. The predicted morbidity of those greater than 80 years old (compared with <65 years old) increases by 27.5% after major surgery.[4]

It is essential that peri-operative pathways are re-engineered to promote early referral of patients to perioperative medicine specialists, including anaesthesiologists, to ensure sufficient time to optimise physiological and psychological resilience (prehabilitation programme) to withstand the pending stressor of major surgery. The pre-operative period should address maladaptive behaviours (smoking, alcohol abuse, sedentary lifestyle) and optimise comorbid disease (malnutrition, anaemia, diabetes, pulmonary and cardiac disease), preferably without delaying surgery.[5,6] Such re-engineering is essential, especially in high-risk patients, to enable individualised risk assessment to guide the decision to proceed to surgery or not, replacing the post hoc evaluation of fitness for surgery after the patient has been informed that an operation is needed. This shared decision-making process will support patient-centred choice in high-risk patients, in whom the risks and benefits of surgery are often difficult to evaluate.[7]

Prehabilitation is the process of enhancing physiological, nutritional and psychological resilience to increase patients' functional capacity in advance of a known physiologically stressful event, for example, surgery or cancer therapy.[8] Prehabilitation aims to empower patients, reduce the risk of postoperative morbidity, improve the rate of postoperative recovery, and ultimately, through sustained behavioural change and improved management of comorbidities, to improve long-term health outcomes.

Deconditioning, predominantly through sedentary lifestyle and frailty, is a modifiable risk factor. Other modifiable pre-operative risk factors include poor respiratory muscle strength, poor nutritional status, smoking, iron deficiency anaemia, excess alcohol consumption, anxiety, depression and poor self-efficacy.[9] The prevalence of modifiable risk factors in surgical patients is unknown, but we estimate that approximately one-third of surgical patients are affected. Timely identification and referral of these patients to prehabilitation services will require close liaison with primary care clinicians, allied health professionals, surgeons and nursing and administrative staff.

There is evidence that surgeons are supportive of prehabilitation. A survey of colorectal surgeons and anaesthesiologists revealed that surgeons in particular

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would consider postponing surgery for prehabilitation to reduce the incidence of postoperative complications, increase the likelihood of achieving postoperative adjuvant therapy and improve long-term survival for their patients.[10] Similarly, feedback from prehabilitation services and limited international trials to date suggest that patients are enthusiastic about participation in prehabilitation programmes,[9,11] especially when their risk stratification data is shared with them pre-operatively.[12] Importantly, patients should be involved in the design of prehabilitation programmes to include information technology solutions, telemedicine and community programmes. For example, a recent survey reported patients' preference for supervised, group exercise interventions.[11] To this end, the UK Royal College of Anaesthetists in collaboration with Cancer MacMillan (UK) published a document outlining the principles and guidance for prehabilitation for people with cancer.[9]

In addition to individualised prehabilitation programmes, patients and their relatives find significant benefit in attending supportive pre-operative educational interventions. Such interventions empower the patient and support behavioural change in the 'teachable moment' before surgery when a patient may be particularly responsive to health advice. Preoperative educational interventions also address pain management and the principles of enhanced recovery after surgery (ERAS), emphasising the importance of early DREAMing (drinking, eating and mobilisation) postoperatively to ensure patients understand how to engage with care delivery after surgery for best outcomes.

Several studies have demonstrated that cardiopulmonary exercise testing has good discriminative ability to identify deconditioned patients,[13] and that such deconditioning is associated with increased risk of postoperative complications in high-risk[14] and intermediate-risk[15] surgical cohorts. In a systematic review and meta-analysis, we reported that deconditioned patients (anaerobic threshold $<11\ ml\ kg^{-1}\ min^{-1}$) undergoing major colorectal surgery were three to five times more likely to suffer postoperative complications.[16] Adding insult to injury, patients with postoperative complications are less likely to achieve postoperative adjuvant chemotherapy,[17] and have reduced long-term survival.[18]

Meaningful changes in postoperative functional exercise capacity can be achieved with prehabilitation programmes.[19,20] Studies to date report that supervised in-hospital high-intensity exercise programmes can improve functional capacity [peak maximal oxygen consumption (VO_2) and anaerobic threshold] by 2 to $3\ ml\ kg^{-1}\ min^{-1}$ within a period of 2 to 3 weeks.[20] Such interventions have been shown to be safe and feasible, with good patient adherence (more than 90%) and consequent improvements in patients' quality of life.[21]

In addition to unimodal prehabilitation with exercise, trials have evaluated the efficacy of multimodal programmes where aerobic exercise and strength training are combined with nutritional optimisation and psychological support (motivational interviewing, counselling and anxiety reduction) and smoking and alcohol cessation interventions (Table 1).[19,20,22–36]

A number of single-centre trials of such interventions have reported up to 50% reduction in postoperative complications, reduced readmission rates[37] and sustained behavioural change 3 months postoperatively.[30,38] Recent systematic syntheses of multimodal prehabilitation trials report reduced length of hospital admission, accelerated postoperative recovery and improved disease-free survival in colorectal cancer patients undergoing prehabilitation.[39,40] Other prehabilitation interventions reduce postoperative pulmonary complications. In a recent Cochrane

Table 1 Randomised, controlled trials with proposed and successfully tested, unimodal or multimodal treatments during prehabilitation (listed chronologically)

Reference	Year	Number of modalities	Number of patients[a]	Physical exercise training	Nutritional support	Psychological support
Kim *et al.*[22]	2009	Unimodal	14/7	Yes	–	–
Carli *et al.*[23]	2010	Unimodal	58/54/0	Yes	–	–
Dronkers *et al.*[24]	2010	Unimodal	22/20	Yes	–	–
Kaibori *et al.*[25]	2013	Bimodal	25/26/0	Yes	Yes	–
Li *et al.*[26]	2013	Trimodal	42/45	Yes	Yes	Yes
Banerjee[27]	2013	Unimodal	N/A (total 30)	Yes	–	–
Gillis *et al.*[19]	2014	Trimodal	38/39	Yes	Yes	Yes
Jensen *et al.*[28]	2015	Unimodal	50/57	Yes	–	–
West *et al.*[20]	2015	Unimodal	22/17	Yes	–	–
Dunne *et al.*[29]	2016	Unimodal	20/18	Yes	–	–
Barberan-Garcia *et al.*[30]	2018	Trimodal	73/71	Yes	Yes	Yes
Bousquet-Dion *et al.*[31]	2018	Trimodal	41/39	Yes	Yes	Yes
Marchand *et al.*[32]	2019	Unimodal	20/20	Yes	–	–
Bhatia *et al.*[33]	2019	Unimodal	74/77	Yes	–	–
Ausania *et al.*[34]	2019	Bimodal	18/22	Yes	Yes	–
Liu *et al.*[35]	2019	Trimodal	37/36	Yes	Yes	Yes
Minnella *et al.*[36]	2019	Trimodal	35/35	Yes	Yes	Yes

[a] Intervention 1/intervention 2/no intervention.

Table 2 Specific prehabilitation diagnostic and treatment options

Multidisciplinary team	Specific diagnostic and treatment options				
Exercise physiologist/ physiotherapist	Cardiopulmonary exercise testing	Pulmonary function testing	Frailty score	Structured responsive exercise programme	Inspiratory muscle training
Dietitian	Malnutrition screening score	Dietitian review	Albumin surveillance	Daily nutritional plan	Protein supplement, for example, postexercise
Psychologist	Hospital anxiety and depression scale (HADS)	Coping strategies to reduce anxiety	Relaxation/breathing exercises (imagery/ visualisation)	Motivational techniques/ coaching	Recording for home-exercise
Nursing team	Educational interventions	Smoking and alcohol cessation programmes	Bundled care with re-orientation, oral hygiene, head of bed elevation in patients at increased risk of pulmonary complications	Enhanced recovery after surgery programmes	
Medical team	Medical optimisation of diabetes heart failure COPD anaemia pain treatment	Enhanced recovery after surgery programmes	Audit Quality improvement initiatives		

COPD, chronic obstructive pulmonary disease.

review, inspiratory muscle training reduced postoperative pulmonary complications by up to 50% in single-centre studies.[41] Likewise preoperative physiotherapy reduced postoperative pneumonia and 1-year mortality after elective abdominal surgery.[42] Although these small single-centre trials[30,38,42] may overestimate treatment effects, these findings warrant urgent exploration in large multicentre trials, some of which are under way.[43]

Prehabilitation is currently delivered heterogeneously across centres (Table 2), and while personalised care tailored to the individual patient is essential, future studies should identify the most effective elements and explore interactions between elements, for example, the permissive effect of adequate nutrition on exercise training. Studies must include sufficient high-risk patients (avoiding healthy patient selection bias and recruitment of those patients who are willing to exercise), report the type, intensity and responsiveness of exercise interventions, the detail of psychological or behavioural change interventions and patient adherence.[44]

Putative mechanisms attributed to the effectiveness of prehabilitation include the pleiotropic effects of exercise, which, through numerous physiological systems, may impact on surgical outcome. Exercise stimulates bone marrow-derived cells, improving vascular function and wound healing.[45] An episode of maximal exercise mobilised progenitor populations into the peripheral circulation in some patients, and this was associated with fewer postoperative complications. Exercise also generates erythropoietin, increasing red cell count and stimulates natural killer cell production, which may modulate the tumour defence response.[46] Recent evidence suggests that preoperative exercise may down-stage tumour grade.[47] This may be driven by antioxidant and anti-inflammatory pathways that are affected by exercise.

Prehabilitation may engender resilience that better prepares patients for surgery. Although there is a consistent short-term and medium-term improvement in clinical outcomes in prehabilitation as an intervention, we should recognise the limitations of small single-centre studies and the potential for recruitment bias, and further research is needed. The pre-operative period is a window of opportunity, a teachable moment when patients faced with a potentially life-threatening event may be persuaded to address maladaptive lifestyle behaviours with the aim of improving the postoperative outcome.

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