Commentary

Prehabilitation and Its Role in Geriatric Surgery

Alfred WC Kow, 1,2,3 MBBS, FRCSEd (Gen Surg), FAMS

Abstract

As the world's population ages rapidly, many elderly people are living to a much more advanced age than before. Consequently, medical conditions that require surgical interventions such as solid organ cancers are also getting more common. While young and fit patients may be able to withstand surgical stresses and recover rapidly after operation, older adults may find these challenging. Rehabilitation that is instituted in the postoperative period aims to help patients regain physical fitness and robustness to preoperative levels. However, recent studies have shown that prehabilitation may be more effective in bringing the fitness level of elderly patients to a higher level before they go for surgery. There are many controversies regarding the effectiveness of prehabilitation, the components of this intervention—be it mono- or multimodalities—and the duration of prehabilitation. This paper looks at the current evidence of this hot topic revolving geriatric surgery.

Ann Acad Med Singapore 2019;48:386–92 Key words: Frail, Nutritional Intervention, Preoperative exercise, Psychological support

Introduction

The population in Singapore is ageing rapidly. According to statistics, by 2030, 1 in 2 adults in Singapore will be >65 years old.¹ As the life expectancy of the population has improved significantly in the past few decades, a substantial portion of this rapidly ageing population will place a hefty burden on the resources of society, in particular, the healthcare system. Many elderly people are living longer and enjoying a good quality of life. This, however, means that medical conditions requiring surgical care will also rise in similar proportion. For example, more than half of patients with colorectal cancer in Singapore are >65 years old (50.3% are male and 55.5% are female). About 21.9% of male colorectal cancer patients in Singapore were >75 years old (between 2011 to 2015) and 31.6% of female colorectal cancer patients were >75 years old.² Many of these patients required surgery to treat colorectal cancers. Similar patterns were observed in the Western population as well. Cheema et al reported that elderly patients have increasingly frequent access to surgery due to the continuous growth in life expectancy—as an example, almost 40% of colorectal cancers are diagnosed after 75 years and most of them are operated.³

Undergoing surgery imposes a stressful challenge to the normal physiology of the body. Major surgery induces a high systemic inflammatory response associated with a marked increase in oxygen consumption in the immediate postoperative period.^{4,5} This is coupled with the need for anaesthesia to facilitate the surgery, risk of intraoperative blood loss and tissue injury as a result of the operation, and

¹Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, University Surgical Cluster, National University Hospital, Singapore ²Liver Transplantation, National University Centre for Organ Transplantation, National University Hospital, Singapore

³Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Address for Correspondence: A/Prof Alfred Kow Wei Chieh, Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, University Surgical Cluster, National University Hospital, 1E Kent Ridge Road, Level 8, NUHS Tower Block, Singapore 119228.

Email: alfred kow@nuhs.edu.sg

healing of the body that can only take place after the surgery is done. Such challenges may prove difficult to handle in elderly patients with poor cardiorespiratory reserve, leading to an inability to withstand this increased demand, resulting in morbidity and mortality.⁶

Paradigm Shift in Elderly Surgery Care

Strategies to minimise the effect of surgical stress response and metabolic deconditioning, and accelerate the return to baseline levels of functional capacity have focussed on the intra- and postoperative periods.⁷ Traditionally, rehabilitation has been the mainstay of efforts to improve recovery with the focus being placed on the postoperative period. However, physicians have realised that rehabilitation does not improve muscular and functional reserve at the time of major surgery. Poor preoperative physical performance has been shown to increase mortality and postoperative complications, and delay postoperative recovery.^{8–10} As shown in Figure 1, if no effort is made to try to improve the physical fitness of the patients, frail and elderly patients will usually have very little reserve to withstand surgical stress and may develop morbidity, even succumbing to mortality after surgery. Frail patients tend to lose their fitness at a much steeper rate compared to prefrail and fit patients.

Rehabilitation in the postoperative period is currently the main interventional strategy for returning patients to preoperative physical fitness. It is, however, important to recognise that frail patients have a much lower baseline of fitness and poorer reserves—they will take a much longer time to recover compared to fitter patients. The rate of loss of such fitness seems to be much faster in frail patients compared to other categories of elderly patients.

It therefore makes sense to try to improve the physical fitness of patients even before the surgery is done. By building up the fitness level of frail patients to a higher level, patients would be able to stock up on more reserves, moving themselves up to prefrail or even fit levels as shown in Figure 1. After surgery, even if their fitness

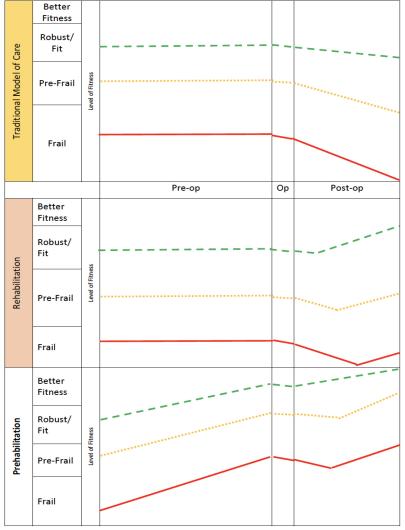


Fig. 1. Charts illustrating the potential differences in the pre- and postoperative fitness of patients who are subjected to traditional model of care, care with rehabilitation and the potential benefits of prehabilitation. Op: Operation

deteriorates, these patients will have sufficient reserves to withstand these losses before regaining them. Concurrently, the rate of fitness loss may be less steep if they are fitter before surgery. As such, the concept of prehabilitation has emerged and gained much popularity recently as the preoperative period is thought to be a more relevant period for increasing the physical condition with the intention of reducing postoperative morbidity of major surgery. While prehabilitation is fairly established in cardiovascular and thoracic surgery,^{12–14} the evidence of prehabilitation is less established in digestive surgery including oncology. In addition to frailty assessments in elderly patients needing abdominal surgery, the focus of prehabilitation also includes reserving muscle loss and improving nutritional status before surgery.

Definition of Prehabilitation

The process of enhancing an individual's functional capacity before scheduled surgery, aimed at improving the patient's tolerance to upcoming physiologic stress, has been termed as prehabilitation.¹¹

Prehabilitation has emerged as a concept that has shown to be helpful in cardiovascular surgery patients (i.e. cardiac prehabilitation), and its use has demonstrated improvement in cardiovascular status, respiratory recovery and improved postoperative outcomes.12-14 However, the body of evidence for prehabilitation in abdominal surgery is still controversial. From an encouraging angle, a systematic review demonstrated that prehabilitation in the form of preoperative exercises could improve postoperative morbidity and physical function.¹⁵ On the other hand, Carli et al reported worse outcomes in patients who complied with a more intense exercise programme before undergoing colorectal surgery.¹⁶ Lemanu et al¹⁷ questioned the benefit of prehabilitation as the studies reported on this topic were highly heterogeneous. The lack of standardised physical exercises was often quoted as the key concern. Other criticisms included the varying type of surgery and some studies did not include nutritional and psychological care.¹⁷

Prehabilitation and the Key Areas of Consideration

Prehabilitation should not be focussed on just preoperative exercise alone. Recently, a multidisciplinary preoperative programme aiming to improve physical condition, nutritional status and preoperative anxiety (the so-called "trimodal" approach) was proposed (Fig. 2). The trimodal programme has evolved to combine moderate physical activity with nutritional counselling and whey protein supplementation together with coping strategies to address mental health and improve programme compliance.¹⁸

The pioneer of the prehabilitation programme was piloted at Department of Surgery, Khoo Teck Puat Hospital (KTPH) in 2007. Tan et al¹⁹ from KTPH's Department of Surgery

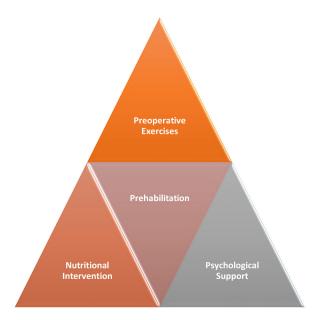


Fig. 2. Trimodal approach in prehabilitation uses preoperative exercise, nutritional intervention and psychological support.

first described the Geriatric Surgery Service (GSS) as specifically focussing on colorectal surgery patients. The programme involved complex and multifaceted care for elderly (>75 years old) surgical patients undergoing major colorectal resections at the hospital. Prior to GSS, the 30day mortality rate following major colorectal resection was nearly 10% and the major morbidity rate was about 30%. When GSS was started in 2007, it initially involved a surgeon and a nurse who anchored the service. This was subsequently expanded to include an anaesthetist, a geriatrician, cardiologist, physiotherapist, dietitian and medical social worker. Through a process of continuous improvement, the GSS team at KTPH revised and enhanced the workflow and care models for elderly surgical patients undergoing colorectal resections.¹⁹

The transdisciplinary process was also described by Tan et al²⁰ in 2009. The transdisciplinary model of care aimed to address the pitfalls that were identified through a flattening of the hierarchy, heightened communication, increase in patient-centricity and role enhancements of the members of the team. Patients and their families also became an integral part of the team. This was a result of the realisation that patient and family buy-in was crucial to the whole process.²⁰ The transinstitutional "Start-to-Finish" programme was started in 2012 and it was propagated to all subspecialties in the Department of General Surgery using similar processes. The study found functional recovery to be >83% at 6 weeks after major surgery and >90% after 90 months.²¹ Throughout this whole process, major complication rates were reduced from 30.8% to 5.3%. Mortality rate was reduced from 9.6% to 1.7%. Functional recovery was now 98% for frail elderly patients, and the mean length of stay had been reduced from 11.0 days to 8.4 days. This was achieved despite having an increased number of frail patients who were operated on.¹⁹

Preoperative Exercises and Physiotherapy

The initial recommendation by Carli et al¹¹ was for a concentrated 3-month progressive exercise prehabilitation programme. This consisted of aerobic training at 45–65% of maximal heart rate reserve (%HRR), along with periodic high-intensity interval training (*90% HRR)4 times per week at 30-50 minutes per session, that was recommended for improving cardiovascular functioning. A strength training programme of about 10 different exercises focussed on large, multijointed muscle groups should also be implemented twice per week at a mean training intensity of 80% of 1-repetition maximum. Finally, a minimum of 140 g (*560 kcal) of carbohydrate (CHO) should be taken 3 hours before training to increase liver and muscle glycogen stores and a minimum of about 200 kcal of mixed protein-CHO should be ingested within 30 min following training to enhance muscle hypertrophy.¹⁰ This regimen seemed too complicated and difficult to follow.

In recent times, the 6-minute Walking Test (6MWT) has been the mainstay of evaluation of preoperative fitness and also the baseline to regaining strength after surgery. Gillis et al¹⁸ conducted a randomised controlled trial (RCT) comparing prehabilitation and rehabilitation in colorectal surgery. The primary outcome was functional walking capacity as measured by the 6MWT 8 weeks after surgery. The 6MWT—which has been validated in the colorectal surgical population-evaluates the ability of an individual to maintain a moderate level of physical endurance.²² Moderate to strong correlations have been found between the 6MWT and maximum oxygen consumption values obtained with other methods of exercise testing.²³ The 6MWT was created to test exercise tolerance but is now used clinically and in research to test functional exercise capacity, defined as "the ability to undertake physically demanding activities of daily living."24 Participants were instructed to walk back and forth along a 15-metre stretch of hallway for 6 minutes at a pace that would have tired them by the end of the walk. The total distance covered in 6 minutes was recorded in metres. Participants were allowed to rest, although any time spent resting was accounted for in the total distance covered within the 6 minutes.

Nutritional Intervention

Nutrition plays a pivotal role in the recovery of surgical patients, particularly in the elderly. Elderly patients may have poorer nutritional status because of underlying medical conditions (e.g. malignancy). This poses a significant challenge in the healing process after surgery. Nutritional prehabilitation is increasingly becoming an essential component of many surgical programmes worldwide. In a systematic review and meta-analysis on the effects of nutritional prehabilitation (with and without exercise) by Gillis et al, they have found that nutritional prehabilitation alone or combined with an exercise programme significantly decreased the length of stay by 2 days in patients undergoing colorectal surgery.25 They have suggested that multimodal prehabilitation with nutrition does add unique value to an enhanced recovery programme by contributing additional, complementary and functional benefits to colorectal surgical patients. Adherence to the intervention programme is key to a successful outcome for these patients. It was shown that adherence to nutrition-only interventions was consistently higher in patients (compared to multimodal interventions) as it allows patients to participate in the programme earlier and fully. However, 4 weeks after surgery, the nutritiononly interventions did not further enhance functional recovery, whereas the multimodal interventions significantly improved return to presurgical functional capacity.

There are suggestions that dietary intake of protein stimulates the transport of amino acids into muscle even at rest.²⁶ But this effect is less efficient without a utilisation process such as exercise. It is generally accepted that exercise provides the main anabolic stimulus and nutrition potentiates the muscle protein response.²⁷ Upon the trigger of resistance exercise, muscle protein synthesis and muscle protein breakdown are simultaneously stimulated.²⁸ Net protein balance (protein synthesis minus breakdown) in the muscle remains negative until exogenous amino acids are administered.²⁹ Amino acids stimulate not only the synthesis of structural proteins, such as myofibrillar proteins, but also the synthesis of mitochondrial proteins required for aerobic metabolism and maintenance of functional exercise capacity.³⁰

Nutrition and exercise are symbiotic in the prehabilitation interventions. The nutritional component of prehabilitation complements the exercise regimen, but it also stands alone to promote optimal patient outcomes. In this respect, sufficient protein intake is crucial in the pre- and postoperative period, not only to counter the catabolic effects of surgical stress but to also enhance the tissue healing process after surgery.³¹ It is known that most older adults do not meet the minimal dietary protein requirements established for healthy individuals. The major effect of surgery and critical illness to induce protein catabolism also needs to be understood and emphasised. Provisions of protein-independent of whether energy or total calorie requirements are met-can maintain lean muscle mass and reduce the risk of subsequent frailty in the elderly.^{32,33} The Quebec Longitudinal Study on Nutrition as a Determinant of Successful Aging³⁴ estimated that half of the cohort comprising 1793 community-dwelling older adults consumed <1 g protein/kg/day. This contrasts against optimal dietary protein requirements where at least 1.2-1.6 g/kg/day should be consumed to keep elderly patients in good health.35 A recent RCT of patients with abdominal and gastrointestinal cancer without clinical signs of malnutrition, under enhanced recovery after surgery (ERAS) care, also found that 14 days of supplementation with high-protein oral nutritional supplement before surgery resulted in fewer serious postoperative complications.³⁶ Finally, a recent trial conducted in colorectal surgery patients within an enhanced recovery pathway demonstrated that patients receiving high protein oral nutrition supplements postoperatively (consumption of >60% of protein needs over first 3 postoperative days) were associated with a 4.4-day reduction in length of stay (P < 0.001).³⁷ While some study populations may not be directly related to the geriatric population, the positive findings that are diseasespecific, such as those in some of the cancer groups, can be considered relevant to the elderly population based on good practice.

Provision of adequate total protein intake should be considered in nutritional prehabilitation and rehabilitation interventions. The key is to have allied health professionals work together in tailoring a programme that is acceptable for patients. While the evidence on this topic remains scarce, more studies in the future would help to strengthen the understanding in this area.

Management of Preoperative Anxiety and Psychological Support

Preparing for surgery can be very daunting for many patients, particularly so in the elderly patients. It is therefore essential to provide psychosocial support to these patients in the perioperative period, preferably starting in the preoperative phase. Many prehabilitation programmes have included healthcare personnel, such as a nurse clinician or psychologist, to help support the elderly surgical patients emotionally and psychologically. Indeed, it has been shown that a 60-min visit with a trained psychologist with certain home therapies, such as relaxation with breathing exercises, could help reduce the anxiety levels of patients.¹⁸

Emotional and psychological support—one of the key pillars in the trimodal approach in prehabilitation—should help in motivating patients to adhere to nutritional and exercise therapy. Some studies have shown that anxiety and depression often affect postoperative outcomes leading to longer hospitalisation, higher chances of infection and poorer recovery of patients.³⁸⁻⁴⁰

Duration of Prehabilitation

Prehabilitation confers many potential benefits on elderly patients. The most strategic approach to prehabilitation features an optimum duration and to achieve this, one must consider the effectiveness of the intervention, compliance and disease conditions of patients needing surgery. A prehabilitation programme of between 2 and 4 weeks seems to be ineffective⁴¹ whereas a regimen exceeding 3 months is associated with very poor compliance.¹⁰ If allowed by the underlying disease, a period ranging from 6–8 weeks seems to be a good compromise between feasibility and effectiveness. However, standardisation of each of the 3 modalities of prehabilitation is still lacking.

Challenges in Prehabilitation

Compliance to the preoperative exercise regimen is often challenging for elderly patients. Understandably, there will be a reduction in benefit if the regimen is not maintained with poorer postoperative outcomes. Attending preoperative exercise sessions at the hospitals are often challenging as elderly patients frequently need caregivers to take time off to bring them to such sessions. In Singapore, many caregivers rely on domestic helpers to play this role. As a result, elderly patients often decline such intervention, opting to stay home until surgery. Those who are more motivated are often the fitter and more robust patients.

Efforts to harness the ability of technology to monitor and track the performance of preoperative exercises are taking place rapidly. Wearable devices and telemonitoring using mobile devices are increasingly used to reduce face-to-face meets, and yet maintain compliance to such exercises. It is hoped that more meaningful solutions could be found for this area.

Anecdotally, it is observed that nutritional intervention has received much higher rate of compliance. It may be cultural, but elderly patients and caregivers are generally very interested to know what to eat and how much to eat to prepare for an upcoming surgery. The coordinated care provided, with lots of emotional and psychosocial support that comes together with it, is very much welcomed by patients and caregivers.

If possible, prehabilitation should also be incorporated into the ERAS protocol as the key components of ERAS are essential for rapid recovery of patients after surgery. More importantly, it must be emphasised that prehabilitation does not replace the need of good surgery. If there is poor surgical technique and the elderly patients suffer significant morbidity from it, all the good work from prehabilitation to building up reserves may be negated by it.

One of the main issues that is holding back widespread adoption of a standardised protocol for prehabilitation in geriatric surgery is inconsistent data from different surgeries in the literature. However, many studies are currently being conducted and we should see more evidence in the near future.

Conclusion

Prehabilitation represents a big paradigm shift in elderly surgical care. The current proposed multimodal intervention is shown to be the most effective method so far. More could be done to understand this better. We can add more quality to the longevity of elderly surgical patients in the future.

REFERENCES

- Ministry of Health, Singapore. Committee on Ageing Issues: Report on the Ageing Population. Available at: https://www.moh.gov.sg/docs/ librariesprovider5/resources-statistics/reports/committee-on-ageingissues-report-on-ageing-population.pdf. Accessed on 1 October 2019.
- National Registry of Diseases Office, Singapore. Singapore Cancer Registry Annual Registry Report 2015. Available at: https://www.nrdo. gov.sg/docs/librariesprovider3/Publications-Cancer/cancer-registryannual-report-2015_web.pdf?sfvrsn=10. Accessed on 1 October 2019.
- Cheema FN, Abraham NS, Berger DH, Albo D, Taffet GE, Naik AD. Novel approaches to perioperative assessment and intervention may improve long-term outcomes after colorectal cancer resection in older adults. Ann Surg 2011;253:867–74.
- Shoemaker WC, Appel PL, Kram HB. Role of oxygen debt in the development of organ failure sepsis, and death in high-risk surgical patients. Chest 1992;102:208–15.
- Older P, Smith R. Experience with the preoperative invasive measurement of haemodynamic, respiratory and renal function in 100 elderly patients scheduled for major abdominal surgery. Anaesth Intensive Care 1988;16:389–95.
- Boyd O, Grounds RM, Bennett ED. A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. JAMA 1993;270:2699–707.
- Carli F, Ferreira V. Prehabilitation: a new area of integration between geriatricians, anesthesiologists, and exercise therapists. Aging Clin Exp Res 2018;30:241–4.
- Wilson RJ, Davies S, Yates D, Redman J, Stone M. Impaired functional capacity is associated with all-cause mortality after major elective intraabdominal surgery. Br J Anaesth 2010;105:297–303.
- Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg 2013;206:544–50.
- Lawrence VA, Hazuda HP, Cornell JE, Pederson T, Bradshaw PT, Mulrow CD, et al. Functional independence after major abdominal surgery in the elderly. J Am Coll Surg 2004;199:762–72.
- Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. Curr Opin Clin Nutr Metab Care 2005;8:23–32.
- Asoh T, Tsuji H. Preoperative physical training for cardiac patients requiring non-cardiac surgery. Jpn J Surg 1981;11:251–5.
- Valkenet K, van de Port IG, Dronkers JJ, de Vries WR, Lindeman E, Backx FJ. The effects of preoperative exercise therapy on postoperative outcome: a systematic review. Clin Rehabil 2011;25:99–111.
- van Adrichem EJ, Meulenbroek RL, Plukker JT, Groen H, van Weert E. Comparison of two preoperative inspiratory muscle training programs to prevent pulmonary complications in patients undergoing esophagectomy: a randomized controlled pilot study. Ann Surg Oncol 2014;21:2353–60.

- Santa Mina D, Clarke H, Ritvo P, Leung YW, Matthew AG, Katz J, et al. Effect of total-body prehabilitation on postoperative outcomes: a systematic review and meta-analysis. Physiotherapy 2014;100:196–207.
- Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. Br J Surg 2010;97:1187–97.
- Lemanu DP, Singh PP, MacCormick AD, Arroll B, Hill AG. Effect of preoperative exercise on cardiorespiratory function and recovery after surgery: a systematic review. World J Surg 2013;37:711–20.
- Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus rehabilitation. A randomized control trial in patients undergoing colorectal resection for cancer. Anaesthesiology 2014;121:937–47.
- Tan KY. Geriatric Surgery Service Our journey piloting in colorectal surgery and future challenges. Ann Acad Med Sing 2017;46:317–20.
- Tan KY, Konishi F, Tan L, Chin WK, Ong HY, Tan P. Optimizing the management of elderly colorectal surgery patients. Surg Today 2010;40:999–1010.
- Wang Z, Tan KY, Tan P. Functional outcomes in elderly adults who have undergone major colorectal surgery. J Am Geriatr Soc 2013;61:2249–50.
- Moriello C, Mayo NE, Feldman L, Carli F. Validating the six-minute walk test as a measure of recovery after elective colon resection surgery. Arch Phys Med Rehabil 2008;89:1083–9.
- Sinclair RC, Batterham AM, Davies S, Cawthorn L, Danjoux GR. Validity of the 6 min walk test in prediction of the anaerobic threshold before major non-cardiac surgery. Br J Anaesth 2012;108:30–5.
- Finch E, Brooks D, Stratford PW, Mayo NE. Physical Rehabilitation Outcome Measures. A Guide to Enhanced Clinical Decision Making. 2nd edition. Toronto: Canadian Physiotherapy Association; 2002. pp. 248–53.
- 25. Gillis C, Buhler K, Bresee L, Carli F, Gramlich L, Culos-Reed N, et al. Effects of nutritional prehabilitation, with or without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. Gastroenterology 2018;155:391–410.
- Wolfe RR. Protein supplements and exercise. Am J Clin Nutr 2000;72:551s-7s.
- Glover EI, Oates BR, Tang JE, Moore DR, Tarnopolsky MA, Phillips SM. Resistance exercise decreases eIF2B epsilon phosphorylation and potentiates the feeding-induced stimulation of p70S6K1 and rpS6 in young men. Am J Physiol Regul Integr Comp Physiol 2008;295:R604–10.
- Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. Am J Physiol Endocrinol Metab 1997;273:E99–107.
- Phillips SM. Protein requirements and supplementation in strength sports. Nutrition 2004;20:689–95.
- Wolfe RR. The underappreciated role of muscle in health and disease. Am J Clin Nutr 2006;84:475–82.
- Gillis C, Carli F. Promoting perioperative metabolic and nutritional care. Anesthesiology 2015;123:1455–72.
- Ferrando AA, Paddon-Jones D, Hays NP, Kortebein P, Ronsen O, Williams RH, et al. EAA supplementation to increase nitrogen intake improves muscle function during bed rest in the elderly. Clin Nutr 2010;29:18–23.
- Beasley JM, LaCroix AZ, Neuhouser ML, Huang Y, Tinker L, Woods N, et al. Protein intake and incident frailty in the Women's Health Initiative observational study. J Am Geriatr Soc 2010;58:1063–71.
- 34. Gaudreau P, Morais JA, Shatenstein B, Gray-Donald K, Khalil A, Dionne I, et al. Nutrition as a determinant of successful aging: description of the Quebec longitudinal study Nuage and results from cross sectional pilot studies. Rejuvenation Res 2007;10:377–86.
- Cawood AL, Elia M, Stratton RJ. Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. Ageing Res Rev 2012;11:278–96.

- 36. Kabata P, Jastrzebski T, Kakol M, Król K, Bobowicz M, Kosowska A, et al. Preoperative nutritional support in cancer patients with no clinical signs of malnutrition – prospective randomized controlled trial. Support Care Cancer 2015;23:365–70.
- 37. Yeung SE, Hilkewich L, Gillis C, Heine JA, Fenton TR. Protein intakes are associated with reduced length of stay: a comparison between enhanced recovery after surgery (ERAS) and conventional care after elective colorectal surgery. Am J Clin Nutr 2017;106:44–51.
- Munafo MR, Stevenson J. Anxiety and surgical recovery. Reinterpreting the literature. J Psychosom Res 2001;51:589–96.
- Gouin JP, Kiecolt-Glaser JK. The impact of psychological stress on wound healing; methods and mechanisms. Immunol Allergy Clin North Am 2011;31:81–93.
- Walburn J, Vedhara K, Hankins M, Rixon L, Weinman J. Psychological stress and wound healing in humans: a systematic review and metaanalysis. J Psychosom Res 2009;67:253–71.
- Dronkers JJ, Lamberts H, Reutelingsperger IM, Naber RH, Dronkers-Landman CM, Veldman A, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. Clin Rehabil 2010;24:614–22.