PRESIDENTIAL LECTURE

Prehabilitation in HBP surgery

Chol-Kyoon Cho, MD, PhD

Department of Surgery, Chonnam National University Medical School, Gwangju, Korea

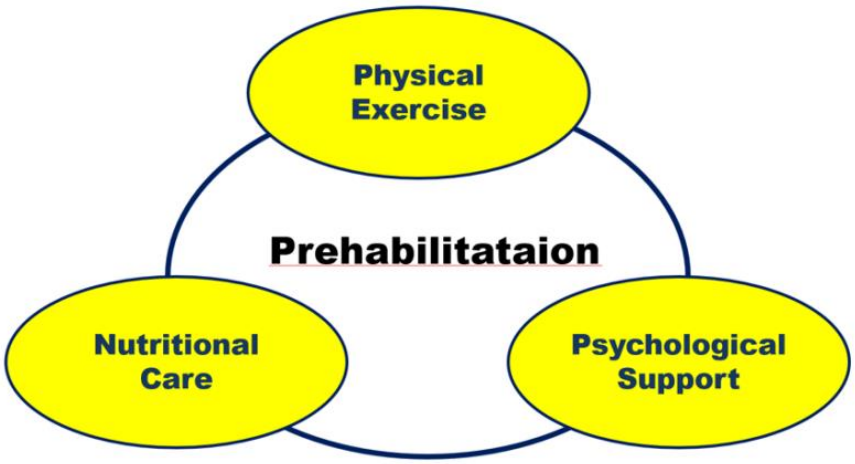
Lecture :

Introduction

Many patients with hepato-biliary-pancreatic (HBP) cancer are malnourished due to anorexia, malabsorption, cancer cachexia and metabolic derangement. In addition, data regarding to operation in the last decade have shown that surgical candidates are getting older in age. These weakened patients are often more susceptible to symptoms and have less ability to withstand both cancer and surgical insults. Previous interventions that aimed at improving recovery after major surgery have largely focused on the postoperative which is rehabilitation. However, investigations into modifiable risk factors have identified preoperative physical fitness, physical activity, and nutritional status as predictors of surgical complications and recovery. The preoperative period is an optimal time to invest in modifiable risk factors, such as exercise, diet, and psychological support.

Definition of prehabilitation

Prehabilitation is defined as the process of creating a buffer against the potentially deleterious effects of a significant stressor by enhancing an individual's functional and mental capacity . In a surgical setting, this includes preoperative physical, nutritional and mental conditioning to prevent an anticipated, surgery-related declines in function and well-being.1



This means that not only physical exercise, but also every modifiable risk factor such as nutrition, smoking cessation, and psychological support need to be targeted. A randomized controlled trial (RCT) in patients undergoing colorectal surgery reported poor surgical outcomes in the prehabilitation group and identified some predictive factors of poor outcomes and poor compliance, including high anxiety, psychological stress, and a catabolic state. This suggests that improving physical capacity only may not be sufficient and that prehabilitation should also include preoperative nutrition and anxiety treatments.2

Frailty and prehabilitation

Frailty is a state of extreme vulnerability to stressors, such as surgical insult and chemotherapy, leading to adverse health outcomes. It is a complex, multidimensional, and cyclical state of diminished physiological reserve that results in decreased resiliency and adaptive capacity, and increased susceptibility to stress.3 It is assessed with various methods. The Frailty Index was developed from the Canadian Health and Aging Study (CHAS) and is based on a cumulative deficit model. It includes 70 items, which range from vague to very specific signs, symptoms, diseases, and disabilities. 4 Velanovich et al proposed an 11–item modified Frailty Index (11–item mFI) which maps the 70 variables from the CHAS Frailty Index to 11 preexisting variables from the National Surgical Quality Improvement Program (NSQIP) data.5 More recently, Divino et al proposed the 5–item modified Frailty index (5–item mFI) and reported that the 5–item mFI and the 11–item mFI were equally effective predictors of mortality and postoperative complications.6 Using a single–item assessment tool is a quick and easy way to assess a patient's frailty, and the most commonly used single–item assessment tools are gait speed, a Timed Up–and–Go score, and a 6–minute walk test.7–9 Irrespective of the assessment tool used, a number of studies have indicated that frailty is associated with surgical outcomes and survival.5–13 Therefore, it is considered that frail patients may be possible candidates for prehabilitation.

Effect of prehabilitation

Prehabilitation is strongly endorsed in the ERAS® recommendation.14 However, the effect of prehabilitation in patients with HBP cancer is still unclear. In a randomized controlled study that analyzed the impact of prehabilitation on postoperative outcomes in patients undergoing pancreaticoduodenectomy (PD), prehabilitation did not reduce postoperative complications. However, delayed gastric emptying was reduced.15 Perlmutter et al also reported that prehabilitation did not affect hospital stay, complications, and 90–day readmission rates after PD.16 In another RCT, however, Barberan–Garcia et al reported that prehabilitation enhanced postoperative outcomes in high–risk candidates for elective major abdominal surgery.17 Katsourakis et al carried out a RCT which evaluated the impact of prehabilitation on quality of life (QoL) in patients who underwent pancreatic resection. They reported that exercise improved QoL after pancreatectomy.18 In a large–scale retrospective study, Yamaue et al reported that prehabilitation might reduce postoperative pulmonary complications and shorten postoperative hospital stay after PD.19 Fard–Aghaie et al demonstrated enhanced liver regeneration after ALPPS by means of physical prehabilitation in an animal experiment.20 Lin et al reported the feasibility of prehabilitataion in improving the Liver Frailty Index, functional capacity, and survival in liver transplantation candidates.21 Because of the heterogeneity of the studies, the results of meta–analyses are inconclusive.22–25 On the one hand, a meta–analysis by Dagorno et al, with regard to HBP surgery, reported that prehabilitation had no effect on length of stay (LOS) or the rate of postoperative complications.22 On the other hand, Lambert et al reported a shortened LOS associated with prehabilitation.24 Bundred et al reported improvement in LOS, DGE, muscle mass, and functioning following prehabilitation, but no effect on postoperative outcomes.23 Daniels et al reported decreased postoperative complications in multimodal prehabilitation, but not in "exercise only" prehabilitation. Despite the divergency of the above results, many studies have, nevertheless, demonstrated the possible benefits of prehabilitation suggesting that such a program may improve surgical outcomes, survival, and QoL.21, 27

How to do “prehabilitation”?

An international research consortium on prehabilitation created a “best practice” approach for multimodal prehabilitation for colorectal cancer surgery in 2016. This four-pillar program consists of high-intensity interval training on endurance and strength; nutritional support with protein and vitamin supplementation; mental support; and a smoking cessation program.28 This program has been adopted in many clinical studies, as well as in response to subsidiary requests for patients with diseases other than colorectal cancer. Hence prehabilitation should be multimodal, and physical exercise should be individualized according to the functional capacity of the patient.

Closing Remarks

Frailty is an important risk factor for patients with HBP cancer, and a frailty assessment should be considered in older patients before a planned surgery. The waiting period for surgery is an optimal time for physical and psychological conditioning to improve the functional capacity of patients. There are evidences that improvement in functional capacity may be related to improvement in surgical outcome and survival. The “marginal gain” obtained from prehabilitation may, therefore, induce a significant improvement in outcomes when aggregated with other strategies.

References

1. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. Curr Opin Clin Nutr Metab Care. 2005;8(1):23–32. doi: 10.1097/00075197-200501000-00005. PubMed PMID: 15585997.
2. Le Roy B, Selvy M, Slim K. The concept of prehabilitation: What the surgeon needs to know? J Visc Surg. 2016;153(2):109–12. Epub 20160203. doi: 10.1016/j.jviscsurg.2016.01.001. PubMed PMID: 26851994.
3. Ethun CG, Bilen MA, Jani AB, Maithel SK, Ogan K, Master VA. Frailty and cancer: Implications for oncology surgery, medical oncology, and radiation oncology. CA Cancer J Clin. 2017;67(5):362–77. Epub 20170721. doi: 10.3322/caac.21406. PubMed PMID: 28731537.
4. Rockwood K. A global clinical measure of fitness and frailty in elderly people. Canadian Medical Association Journal. 2005;173(5):489–95. doi: 10.1503/cmaj.050051.
5. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. Journal of Surgical Research. 2013;183(1):104–10. doi: 10.1016/j.jss.2013.01.021.
6. Subramaniam S, Aalberg JJ, Soriano RP, Divino CM. New 5-Factor Modified Frailty Index Using American College of Surgeons NSQIP Data. Journal of the American College of Surgeons. 2018;226(2):173–81.e8. doi: 10.1016/j.jamcollsurg.2017.11.005.
7. Afilalo J, Eisenberg MJ, Morin J-F, Bergman H, Monette J, Noiseux N, et al. Gait Speed as an Incremental Predictor of Mortality and Major Morbidity in Elderly Patients Undergoing Cardiac Surgery. Journal of the American College of Cardiology. 2010;56(20):1668–76. doi: 10.1016/j.jacc.2010.06.039.
8. Huisman MG, Van Leeuwen BL, Ugolini G, Montroni I, Spiliotis J, Stabilini C, et al. "Timed Up & Go": A Screening Tool for Predicting 30-Day Morbidity in Onco-Geriatric Surgical Patients? A Multicenter Cohort Study. PLoS ONE. 2014;9(1):e0086863. doi: 10.1371/journal.pone.0086863.

9. Hayashi K, Yokoyama Y, Nakajima H, Nagino M, Inoue T, Nagaya M, et al. Preoperative 6-minute walk distance accurately predicts postoperative complications after operations for hepato-pancreato-biliary cancer. Surgery. 2017;161(2):525-32. doi: 10.1016/j.surg.2016.08.002.
10. Paiella S, De Pastena M, Esposito A, Secchettin E, Casetti L, Malleo G, et al. Modified Frailty Index to Assess Risk in Elderly Patients Undergoing Distal Pancreatectomy: A Retrospective Single-Center Study. World Journal of Surgery. 2022. doi: 10.1007/s00268-021-06436-2.
11. Konstantinidis IT, Lewis A, Lee B, Warner SG, Woo Y, Singh G, et al. Minimally invasive distal pancreatectomy: greatest benefit for the frail. Surgical endoscopy. 2017;31(12):5234-40. doi: 10.1007/s00464-017-5593-y.
12. Mima K, Hayashi H, Nakagawa S, Matsumoto T, Kinoshita S, Matsumura K, et al. Frailty is associated with poor prognosis after resection for pancreatic cancer. International Journal of Clinical Oncology. 2021;26(10):1938-46. doi: 10.1007/s10147-021-01983-z.
13. Chen C-H, Ho C, Huang Y-Z, Hung T-T. Hand-grip strength is a simple and effective outcome predictor in esophageal cancer following esophagectomy with reconstruction: a prospective study. Journal of Cardiothoracic Surgery. 2011;6(1):98. doi: 10.1186/1749-8090-6-98.
14. Melloul E, Lassen K, Roulin D, Grass F, Perinel J, Adham M, et al. Guidelines for Perioperative Care for Pancreatoduodenectomy: Enhanced Recovery After Surgery (ERAS) Recommendations 2019. World J Surg. 2020;44(7):2056-84. doi: 10.1007/s00268-020-05462-w. PubMed PMID: 32161987.
15. Ausania F, Senra P, Melendez R, Caballeiro R, Ouvina R, Casal-Nunez E. Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva. 2019;111(8):603-8. doi: 10.17235/reed.2019.6182/2019. PubMed PMID: 31232076.
16. Perlmutter BC, Ali J, Cengiz TB, Said SA-D, Tang A, Augustin T, et al. Correlation between physical status measures and frailty score in patients undergoing pancreatic resection. Surgery. 2021. doi: 10.1016/j.surg.2021.10.030.
17. Barberan-Garcia A, Ubre M, Roca J, Lacy AM, Burgos F, Risco R, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Ann Surg. 2018;267(1):50-6. doi: 10.1097/SLA.0000000000002293. PubMed PMID: 28489682.
18. Katsourakis A, Vrabas I, Papanikolaou V, Apostolidis S, Chatzis I, Noussios G. The Role of Exercise in the Quality of Life in Patients After Pancreatectomy: A Prospective Randomized Controlled Trial. Journal of Clinical Medicine Research. 2019;11(1):65-71. doi: 10.14740/jocmr3675.
19. Kitahata Y, Hirono S, Kawai M, Okada K-I, Miyazawa M, Shimizu A, et al. Intensive perioperative rehabilitation improves surgical outcomes after pancreaticoduodenectomy. Langenbeck's Archives of Surgery. 2018;403(6):711-8. doi: 10.1007/s00423-018-1710-1.
20. Fard-Aghaie MH, Budai A, Daradics N, Horvath G, Oldhafer KJ, Szijarto A, et al. The effects of physical prehabilitation: Improved liver regeneration and mitochondrial function after ALPPS operation in a rodent model. J Hepatobiliary Pancreat Sci. 2021;28(8):692-702. Epub 20210404. doi: 10.1002/jhbp.945. PubMed PMID: 33742528.
21. Lin FP, Visina JM, Bloomer PM, Dunn MA, Josbeno DA, Zhang X, et al. Prehabilitation-Driven Changes in Frailty Metrics Predict Mortality in Patients With Advanced Liver Disease. The American journal of gastroenterology. 2021;116(10):2105-17. doi: 10.14309/ajg.0000000000001376. PubMed PMID: 34313620.

22. Dagorno C, Sommacale D, Laurent A, Attias A, Mongardon N, Levesque E, et al. Prehabilitation in hepato-pancreato-biliary surgery: A systematic review and meta-analysis. A necessary step forward evidence-based sample size calculation for future trials. J Visc Surg. 2021. Epub 20210903. doi: 10.1016/j.jviscsurg.2021.07.003. PubMed PMID: 34489200.
23. Bundred JR, Kamarajah SK, Hammond JS, Wilson CH, Prentis J, Pandanaboyana S. Prehabilitation prior to surgery for pancreatic cancer: A systematic review. Pancreatology. 2020;20(6):1243-50. Epub 20200803. doi: 10.1016/j.pan.2020.07.411. PubMed PMID: 32826168.
24. Lambert JE, Hayes LD, Keegan TJ, Subar DA, Gaffney CJ. The Impact of Prehabilitation on Patient Outcomes in Hepatobiliary, Colorectal, and Upper Gastrointestinal Cancer Surgery: A PRISMA-Accordant Meta-analysis. Ann Surg. 2021;274(1):70-7. doi: 10.1097/SLA.0000000000004527. PubMed PMID: 33201129.
25. Pouwels S, Stokmans RA, Willigendael EM, Nienhuijs SW, Rosman C, van Ramshorst B, et al. Preoperative exercise therapy for elective major abdominal surgery: a systematic review. Int J Surg. 2014;12(2):134-40. Epub 20131208. doi: 10.1016/j.ijsu.2013.11.018. PubMed PMID: 24325942.
26. Daniels SL, Lee MJ, George J, Kerr K, Moug S, Wilson TR, et al. Prehabilitation in elective abdominal cancer surgery in older patients: systematic review and meta-analysis. BJS Open. 2020;4(6):1022-41. doi: 10.1002/bjs5.50347.
27. Ngo-Huang A, Parker NH, Bruera E, Lee RE, Simpson R, O'Connor DP, et al. Home-Based Exercise Prehabilitation During Preoperative Treatment for Pancreatic Cancer Is Associated With Improvement in Physical Function and Quality of Life. Integr Cancer Ther. 2019;18:1534735419894061. doi: 10.1177/1534735419894061. PubMed PMID: 31858837; PubMed Central PMCID: PMCPMC7050956.
28. Molenaar CJL, Papen-Botterhuis NE, Herrle F, Slooter GD. Prehabilitation, making patients fit for surgery – a new frontier in perioperative care. Innovative Surgical Sciences. 2019;4(4):132-8. doi: 10.1515/iss-2019-0017.