



Prehabilitation approaches for gastrointestinal cancer surgery: a narrative review

Sergii Girnyi^{1*}, Luigi Marano^{1,2*}, Jarosław Skokowski^{1,2}, Piotr MocarSKI¹, Witold KyCler³, Gaetano Gallo⁴, Agnieszka Dyzmann-Sroka⁵, Karolina Kazmierczak-Siedlecka⁶, Leszek Kalinowski^{6,7}, Tomasz Banasiewicz⁸, Karol Polom^{2,3}

¹Department of General Surgery and Surgical Oncology, "Saint Wojciech" Hospital, "Nicolaus Copernicus" Health Center, Gdansk, Poland

²Department of Medicine, Academy of Applied Medical and Social Sciences (AMiSNS), Elblag, Poland

³Department of Gastrointestinal Surgical Oncology, Greater Poland Cancer Centre, Poznan, Poland

⁴Department of Surgery, Sapienza University of Rome, Rome, Italy

⁵Cancer Registry, Greater Poland Cancer Centre, Poznan, Poland

⁶Department of Medical Laboratory Diagnostics — Fahrenheit Biobank BBMRI.pl, Medical University of Gdansk, Gdansk, Poland

⁷BioTechMed Centre/Department of Mechanics of Materials and Structures, Gdansk University of Technology, Gdansk, Poland

⁸Department of General, Endocrinological Surgery and Gastroenterological Oncology, Poznan University of Medical Sciences, Poznan, Poland

*These authors share first authorship.

ABSTRACT

Gastrointestinal (GI) cancer patients undergoing surgery are particularly vulnerable to malnutrition, which can significantly impact surgical outcomes. Prehabilitation interventions encompassing nutritional, physical, and psychosocial support have gained attention for their potential to mitigate these risks. However, the efficacy of multidisciplinary prehabilitation programs in this context remains underexplored. This narrative review synthesizes existing literature to evaluate the effectiveness of prehabilitation interventions in improving outcomes for GI cancer patients undergoing surgery. Drawing on a comprehensive analysis of available evidence, the review examines the integration of nutritional, physical, and psychosocial interventions and explores the implications for clinical practice and future research. The review highlights the importance of standardized protocols and interdisciplinary collaboration in optimizing prehabilitation programs for GI cancer patients. It identifies gaps in current research, particularly regarding the synergistic effects of integrating various intervention modalities and the role of innovative strategies such as immunonutrition. Moreover, the review underscores the need for larger studies to assess the effectiveness of multimodal prehabilitation approaches and establish standardized outcome measures.

In conclusion, despite advancements in understanding the importance of prehabilitation, significant gaps persist in the literature, warranting further research to refine prehabilitation protocols and improve perioperative outcomes for GI cancer patients. By addressing these research gaps and fostering interdisciplinary partnerships, future studies have the potential to enhance the effectiveness of prehabilitation interventions and optimize perioperative care in this population.

Key words: prehabilitation; gastrointestinal cancer; surgery; nutritional intervention; multimodal care; frailty

Rep Pract Oncol Radiother 2024;29(5):1-13

Address for correspondence: Karol Polom, Department of Gastrointestinal Surgical Oncology, Greater Poland Cancer Centre, Garbary 15, Poznan, Poland; e-mail: karol.polom@wco.pl

This article is available in open access under Creative Common Attribution-Non-Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) license, allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially

Introduction

Gastrointestinal (GI) cancers represent an increasing public health challenge, having substantial effects on morbidity and mortality rates. In 2022, the worldwide occurrence of GI cancers reached an estimated 4.8 million new cases [1]. This category encompasses cancers of the stomach, liver, esophagus, pancreas, and colorectum, collectively constituting over 26% of cancer incidence and contributing to 35.4% of cancer-related fatalities [2, 3]. Surgery entails purposeful and controlled tissue damage, initiating a cascade of physiological and metabolic changes leading to catabolism [4, 5]. In individuals with GI cancers, pre-existing comorbidities, including frailty and malnutrition [6, 7], combined with additional impairments from chemoradiotherapy before and/or after surgery, exacerbate the impact of the surgical stress response, further elevating the risk of postoperative complications [8, 9]. Although there have been advancements in clinical practice and technology, resulting in better post-operative outcomes over the years, surgical treatment for GI cancers continues to be linked with higher rates of post-operative morbidity and mortality. Up to 44% of patients undergoing major surgery experience postoperative complications, impacting mortality rates, hospitalization durations, and healthcare expenses [10]. Furthermore, their effect on patients' quality of life extends beyond the immediate post-surgical period, intensifying with complication severity and persisting for at least 12 months post-surgery [11]. Widely regarded as a formidable challenge in the surgical domain, complications pose significant hurdles for patients and the healthcare system, necessitating heightened attention and innovative solutions [12]. Additionally, even in the absence of postoperative complications, many patients experience a decline in physical function and a significant reduction in quality of life following major GI surgery [13].

The concept of prehabilitation, defined as tailored interventions aimed at enhancing the functional status of cancer patients prior to the initiation of treatment, has gained increasing recognition in recent years [14]. This concept encompasses activities from the time of cancer diagnosis until surgery or the initiation of cancer therapy, incorporating nutritional, psychological, and physical assess-

ments and interventions to mitigate the functional decline associated with treatment and its subsequent consequences [15]. The primary objective of prehabilitation programs is to integrate targeted interventions to enhance patients' health and functional capacity, improve their tolerance to prescribed cancer therapies and, ultimately, enhance clinical outcomes and quality of life [14, 16]. While acknowledging the potential optimization of effects through multicomponent interventions, prior research has often examined isolated components due to the evolving nature of the prehabilitation concept [14, 15]. These programs often integrate evidence-based practices and interventions to prevent or minimize surgery-related complications and promote safer surgical procedures [8]. Collaboration among highly specialized clinicians in a multidisciplinary approach allows for the development of tailored plans for each individual patient. Despite recommendations and an expanding evidence base, prehabilitation is not yet standard practice, lacking clinical guidelines for patients undergoing GI surgery [17]. Clinical prehabilitation services typically cover the entire spectrum of gastrointestinal cancer surgeries, including hepato-pancreato-biliary (HPB) surgery and oesophago-gastric (OG) surgery, despite their distinct subspecialties [18]. Notably, the existing evidence base for prehabilitation in this realm either encompasses a wide range of elective surgeries beyond upper GI surgery or focuses solely on specific subspecialties within upper GI surgery, thus constraining clinical implementation [19, 20]. Therefore, we analyzed current evidence to delineate prehabilitation programs designed for gastrointestinal cancers and their impact on pre- and post-surgery clinical outcomes. In doing so, our objective is to offer valuable insights to improve the preparation of patients diagnosed with GI cancer for surgery, thereby increasing their chances of survival and decreasing the morbidity.

Methods

Initially, all authors convened for a pre-planning meeting to delineate the scope of the review and assign specific sections of the article. Subsequently, each author independently conducted a thorough literature review using databases such as PubMed, ScienceDirect, and Google

Scholar. Key terms related to gastrointestinal surgery, rehab, prehab, prehabilitation, sarcopenia, oncology, nutrition, diet, quality of life, exercise, and cancer were utilized in various combinations to ensure comprehensive coverage. Additionally, terms related to ERAS surgery, ERAS outcomes, ERAS gastrointestinal surgery, ERAS implementation, and healthcare spending were searched on Google Scholar. Each author individually scrutinized English-language abstracts of search results spanning the past 15 years to determine their relevance for inclusion in their respective sections. Following this initial review, a second meeting was convened to discuss the outcomes of the literature search and finalize section allocations, outline, writing objectives, and timeline. During the review process, authors focused on identifying studies that established correlations between sarcopenia and outcomes, studies outlining ERAS guidelines as potential foundations for prehabilitation, and studies investigating multimodal prehabilitation programs in gastrointestinal malignancies. Articles presenting reproducible models and deemed applicable within the healthcare framework were included and analyzed. The individual sections were then submitted to the senior author, who amalgamated them into a manuscript form and edited them to ensure stylistic consistency and grammatical accuracy. A draft version of the manuscript was subsequently distributed to each author for independent and collective review during a final meeting prior to the final submission.

Prehabilitation programs

Establishing a causal relationship between prehabilitation and outcomes presents a significant challenge due to the absence of consensus regarding the components of an ideal program, resulting in notable heterogeneity among prehabilitation studies. The complexity and variability within oncology, especially among GI surgical patient populations, make it clear that a universally applicable prehabilitation program is impractical. Nevertheless, it is essential to evaluate the effects of selecting a unimodal versus multimodal prehabilitation program, as well as to explore the impacts of various exercise programs concerning frequency, intensity, type, duration, and timing²¹. This assessment is crucial for maximizing the potential

for a statistically and clinically significant positive impact on outcomes. While a unimodal program focuses solely on pre-operative exercise, a multimodal program integrates additional components, such as nutrition and physical therapy, to supervise and guide exercise progression, case management and/or social work to address social determinants and establish goals, and nurse involvement for periodic patient check-ins to ensure adherence to the program and manage any injuries sustained during prehabilitation. Although a multimodal program like this would address other critical factors influencing patient outcomes, its implementation would require more resources. Moreover, a pilot study conducted in colorectal cancer patients demonstrated that a multimodal prehabilitation program could enhance functional capacity and result in improvements in self-reported physical activity and health-related quality of life [22].

Nonetheless, it is of note that, in all the studies, patients were required to meet certain criteria for exercise participation at baseline. In a randomized controlled trial conducted by Moug et al., patients were excluded based on their mobility baseline, which hindered their ability to engage in a walking intervention, or if they already met the recommended government guidelines for weekly physical activity (assessed using the Scottish Physical Activity Screening Questionnaire) [23]. The pilot study by Alejo et al. recruited patients with an Eastern Cooperative Oncology Group performance status of less than 3 but excluded those who were transfusion-dependent or using psychoactive drugs [24]. Heldens A et al. defined exclusion criteria as having a medical condition that contradicted exercise or an inability to cooperate with the training and testing process²⁵. Another pilot study by Loughney et al. [26] enrolled patients with a World Health Organization performance status of less than 2 and excluded individuals with lower limb dysfunction preventing cardiopulmonary exercise testing (CPET) or bicycle exercise, or those who underwent non-standardized neoadjuvant chemoradiotherapy (NACRT) [26]. Singh et al. required participants to have the baseline ability to walk 400 meters unaided and to obtain medical clearance from their general practitioner [27]. Similarly, West et al. excluded patients who were unable to perform CPET or bicycle exercise at baseline [28].

Physical training plan

Patients with gastrointestinal cancers undergoing complex surgical procedures often encounter significant physical challenges [15]. Suboptimal physical fitness preoperatively increases the risk of postoperative complications [29]. Therefore, prehabilitation programs aim to optimize patients' physical and functional status through structured physical activity interventions, enhancing the prospects for improved recovery and treatment response. Recent research underscores the significant correlation between better preoperative cardiorespiratory exercise test values, such as peak VO_2 , and enhanced postoperative outcomes in cancer surgery patients. For instance, studies have examined VO_{2max} at anaerobic threshold (AT), revealing that lower values are associated with increased morbidity, mortality, and prolonged hospital stays [30, 31]. Dunne et al. [32], in one of the pioneering studies on the effectiveness of a prehabilitation program for liver resection, implemented a 4-week exercise regimen conducted three times weekly. This regimen included a warm-up, thirty minutes of aerobic cycle training alternating between moderate and vigorous intensity, and a cool down. By monitoring VO_{2max} at AT as the primary outcome measure, this exercise program resulted in a significant increase in VO_{2max} , thereby reducing the number of patients classified as high-risk before surgery [32]. Conversely, Wang et al. employed a 2–4-week program comprising deep breathing exercises four times daily, along with lower body strengthening exercises and thirty minutes of aerobic walking activity five times weekly [33]. Focused on assessing the effect on clinical outcomes, this study found a significantly lower incidence of post-operative complications and reduced hospital stays in the prehabilitation group. Oversight of the physical activity component within prehabilitation programs is typically provided by qualified professionals, such as physical therapists or specialized exercise physiologists. These professionals tailor optimal exercise regimens, often incorporating strategies like prescribed exercise diaries and participation in individual or group exercise sessions, including telehealth options [8]. Nonetheless, further investigation is necessary to determine the optimal type, intensity, and frequency of exercise interventions across different cancer types. In 2018, the American College of Sports Medicine

(ACSM) multidisciplinary roundtable developed exercise recommendations for cancer survivors based on randomized clinical trials, which could serve as a robust foundation for the exercise component of prehabilitation programs [34]. These evidence-based recommendations advocate for aerobic exercise at 60–80% of maximum heart rate for at least 90 minutes weekly, and resistance training at 60–80% of one-rep max intensity, performed at least twice weekly with varying repetitions, frequencies, durations, and lengths based on individual exercise goals and specific cancer populations.

In the perioperative setting, subjective clinician estimates using the American Society of Anesthesiologists (ASA)'s Physical Status Classification System or metabolic equivalent of tasks (METs) often serve as the basis for physical fitness assessment, determining fitness to proceed if the patient exceeds four METs without symptoms [35]. Nevertheless, significant discordance exists between clinician-assessed and patient-reported exercise capacity, limiting predictive accuracy [36]. This has led to calls for systematic and objective screening at the contemplation stage for surgery [37]. Screening procedures are essential but may face challenges due to resource limitations and may not always be necessary for all patients awaiting surgery. A tiered approach involving universal screening to identify individuals requiring comprehensive assessment is suggested [38]. Commencing screening close to diagnosis, using concise digital tools for scalability, is advisable. The screening instrument should possess adequate sensitivity to identify high-risk patients, enabling referral for specialized evaluation and personalized care direction. While there is controversy regarding the accuracy of self-reported screening tools, aggregate data from Patient Reported Outcome Measures (PROMs) have been integrated into routine healthcare practices and perioperative research for an extended period. In the United Kingdom, these data have been utilized to evaluate healthcare provider performance within the primary care Quality and Outcomes Framework (QOF) and in surgical populations through the Patient Reported Outcome Measures (PROMs) initiative [39, 40]. Objective physiological evaluation should complement self-reported screening rather than replace it. Individualized assessment necessitates a comprehensive scru-

tiny of physical fitness using validated clinical measurement techniques administered by registered healthcare professionals, ideally directed at patients surpassing prognostically significant screening thresholds. Cardiopulmonary exercise testing stands out as the established gold-standard for preoperative risk evaluation, offering a dynamic integrated appraisal of cardiopulmonary, neuromuscular, metabolic, and musculoskeletal systems [41]. Impaired CPET performance predicts immediate postoperative complications, enduring morbidity, and mortality risks, while also revealing undiagnosed pathologies and providing parameters guiding prehabilitation programs. Key focus areas include oxygen uptake at the anaerobic threshold and ventilatory capacity, which display the best predictive potential [42]. Alternatively, when the logistical demands or expenses of preoperative CPET hinder its implementation, results from alternative assessments, such as the six-minute walk test (6-MWT) and Incremental Shuttle Walk Test (ISWT), correlate with CPET-derived results and show associations with postoperative outcomes [42, 43]. Although natriuretic peptide, a biomarker of cardiac dysfunction, modestly correlates with CPET variables [36], its application in preoperative testing holds promise in predicting postoperative cardiac complications, especially for patients with concurrent cardiac comorbidities [44].

Future studies could investigate different GI cancer groups with differences in types, frequencies, durations, and intensities of exercise to evaluate their distinct effects on changes in VO_{2max} at AT, along with other functional outcome measures such as the 6-minute walk test, TUG test, handgrip strength, body composition changes, and various patient-reported outcome measures.

Nutritional intervention

Malnutrition represents a global health issue impacting individuals across all age groups, with particularly grave consequences among vulnerable demographics like GI cancer patients. They exhibit a range of comorbidities and medical profiles tailored to their specific surgical needs, presenting symptoms such as dyspepsia, altered bowel habits, and loss of appetite, all of which heighten the risk of malnutrition [45]. Moreover, surgical oncology patients commonly suffer from anemia, accompa-

nied by symptoms like appetite loss, weight loss, and cachexia [46]. Indeed, malnutrition within this cohort can precipitate severe and adverse outcomes, including sarcopenia and functional decline [47, 48]. Furthermore, malnutrition can compromise the immune system, rendering cancer patients more susceptible to infections and other negative events, while diminishing their capacity to withstand adverse events such as surgical stress. Consequently, this may result in prolonged hospitalization, heightened infection rates, and an elevated risk of disability, institutionalization, and mortality [49, 50]. Given the significant predisposition to malnutrition among GI surgical patients due to their underlying health conditions, proactive preoperative screening for nutritional status, followed by timely interventions, is essential to improve overall surgical outcomes [51].

Assessment and identification of malnutrition should adhere to established guidelines. The American Society for Parenteral and Enteral Nutrition (ASPEN), the European Society for Clinical Nutrition and Metabolism (ESPEN), and the Academy's Oncology Nutrition Evidence Analysis Library Work Group have endorsed definitions and features of malnutrition that encompass a range of parameters, rather than relying solely on traditional indicators like weight loss, low body mass index (BMI), or decreased serum protein levels (e.g., albumin) for identification [52, 53]. However, serum albumin level is considered an inadequate measure of nutritional status and should not be utilized in malnutrition assessments for this patient cohort, as it is more indicative of disease severity and inflammatory status [54].

A recent scoping review investigated prehabilitation interventions for cancer patients, encompassing all cancer types, with a specific emphasis on nutritional assessment and interventions, revealing a scarcity and inconsistency of evidence in this domain [55]. Patients diagnosed with GI cancer are typically advised to follow a balanced high-calorie, high-protein diet before undergoing surgery [52]. It is important to avoid unnecessary dietary restrictions, especially those that may lead to inadequate intake of energy, protein, fat, vitamins, or minerals. While there are no specific dietary patterns known to cure cancer or prevent its recurrence, the focus is on consuming palatable and well-tolerated foods to ensure sufficient oral intake, particular-

ly in individuals with malnutrition or at risk of it [52]. In cases where oral nutrition intake is deemed insufficient, oral nutrition supplements should be considered to enhance the overall adequacy of nutrient intake. To this address, several studies explored the impact of nutritional interventions on the nutritional status of patients undergoing GI surgery [56, 57]. Notably, no significant differences were observed in outcomes before or after surgery among patients undergoing esophageal surgery or liver transplant [35, 58]. However, both studies were categorized as having “some concerns” in their risk of bias assessment due to small participant numbers, which limited the power to detect changes in postoperative outcomes [8]. Conversely, recent studies have shown that a single consultation session with a dietician can enhance protein intake, underscoring the importance of personalized guidance regarding protein and energy intake [57]. Furthermore, Deftereos et al. [56] demonstrated the feasibility and advantages of implementing a personalized perioperative nutrition pathway across a GI service with patients undergoing three different types of upper GI surgery. Nonetheless, larger studies of this nature are warranted to facilitate better intervention development for patients with GI cancers. Within this framework, immunonutrition, which entails providing targeted nutrients to regulate immune responses, arises as a promising approach to alleviate the heightened inflammatory response observed in surgical patients [47, 59, 60]. Several prospective randomized trials have explored the effects of immunonutrition on outcomes post major surgeries, demonstrating reduced length of stay and a notable decrease in postoperative infectious complications [61–34]. Recent experimental investigations have provided further insights, suggesting that the efficacy of immunonutrients is enhanced when administered both pre- and post-surgery, surpassing the benefits observed with postoperative administration alone [65, 66]. Of particular interest is the finding that, regardless of patients’ initial nutritional status, immunonutrition’s benefits were evident even in well-nourished patients who typically experience a decline in host defense mechanisms following surgery [65]. In the same way, other studies explored the effects of short-term immunonutrition interventions on the surgical stress response in GI patients [67, 68]. Although there was a significant

serum response to immunonutrition interventions between baseline and surgery, the effects on postoperative complications were varied. While two studies reported significant improvement in infectious complications [68, 69] and one in systemic inflammatory response syndrome (SIRS) [69], three studies showed an improvement in the severity of complications [68, 70, 71]. Only one study reported a significant reduction in hospital length of stay [68]. Despite encouraging preliminary results, further research into immunonutrition in upper GI surgical populations is necessary to draw definitive conclusions regarding their inclusion in preoperative interventions. Although nutritional interventions are a fundamental aspect of cancer prehabilitation guidelines, there remains ample room for additional research in this area, particularly concerning multimodal interventions for patients undergoing upper GI surgery. A systematic review and meta-analysis investigating the effects of nutritional prehabilitation, with and without exercise, in patients undergoing colorectal surgery found a reduction in hospital admission length by two days [72]. Optimal nutrition and the prevention of weight loss are crucial for patients undergoing upper GI surgery, as they are linked to improved outcomes [73]. Therefore, they may play a central role in optimizing other aspects of the prehabilitation pathway, such as exercise.

Given the absence of standardized guidance, there is a need for the development and consensus of a core outcome set encompassing both short- and long-term outcomes to evaluate nutritional interventions and their impact on functional capacity across different types of upper GI surgery. This would enhance opportunities for evidence synthesis to inform the nutritional components of future multimodal prehabilitation interventions [8].

Psychosocial support

The significance of psychological support and behavior modification within prehabilitation, alongside exercise and nutrition, is underscored in medical literature [8]. Cancer diagnosis and subsequent surgery have profound psychological implications, with approximately half of patients experiencing clinically significant distress across various cancer types [74]. Elevated distress levels are linked to higher mortality rates and poorer postoperative outcomes, including pain, delayed

wound healing, and extended hospital stays [75]. Depression and anxiety at diagnosis predict lower quality of life and may impact treatment decisions for up to two years post-surgery [76]. Systematic reviews demonstrate a consistent association between psychological distress and adverse post-operative outcomes within the first 30 days [77]. Conversely, positive psychological traits, like self-efficacy and optimism, correlate with improved recovery, suggesting the potential for interventions to enhance patient well-being and compliance with treatment [41]. Biologically plausible mechanisms implicate psychological distress in cancer progression and wound healing through inflammatory responses, immunological dysregulation, and hormonal imbalance [78, 79]. Individuals with distress may also engage in risky behaviors, such as smoking and poor diet, further exacerbating health outcomes [80, 81]. Recognizing psychological distress as a vital sign, international guidelines emphasize its integration into cancer care alongside physiological measures [82]. Screening tools like the Distress Thermometer enable fast, scalable assessment, triggering referrals for comprehensive evaluation when distress levels exceed predefined thresholds [83]. Following screening, formal assessment by registered psychological professionals is recommended using validated tools like the Generalized Anxiety Disorder 7 (GAD-7) and Patient Health Questionnaire (PHQ-9) for anxiety and depression, respectively [84, 85]. While operational models for psycho-oncological assessment exist, further research is essential to refine their efficacy and applicability [86, 87]. From a clinical point of view, despite the paucity of evidence in surgical and cancer patient populations, preliminary findings suggest potential benefits on postoperative outcomes, immunologic function, and patient-reported quality of life [88, 89]. Notably, a study examining psychological intervention for pancreatic surgery patients revealed reduced preoperative emotional distress and postoperative emotional pain following a one-hour consultation session with a psychologist [90]. However, the study was considered to have a high risk of bias across various domains, and no significant effects on post-operative complications or hospital length of stay were observed. Furthermore, limitations in patient sample sizes may have prevented conclusive recommendations.

The “Surgery for Frails” innovative approach: objectives and decision-making

Recent research has unequivocally demonstrated that age alone does not predict complications following elective surgery in older patients; instead, cognitive or functional frailty emerges as the key risk factor [91]. However, frailty, characterized by physical and cognitive vulnerability and a reduced ability to withstand stressors, is often misunderstood, overlooked, or conflated with aging [92]. Consequently, older individuals, particularly among cancer patients, may be less likely to be referred for surgery despite evidence showing that post-operative recovery is not age-dependent. Referring physicians and evaluating surgeons should not base surgical decisions solely on chronological age; rather, decisions should be informed by a comprehensive geriatric assessment (CGA), considering cognitive, functional, nutritional, socioeconomic, and emotional factors [93]. Surgeons who have recognized the significance of comorbidities and physiological factors beyond age have consistently achieved positive outcomes. Early multidisciplinary management of older patients can profoundly impact outcomes, with surgical risk assessments extending beyond age. Despite compelling evidence in acute medical settings, the surgical community has been slow to adopt this collaborative care model for cancer patients. Notably, Harari and colleagues pioneered research on multidisciplinary geriatric involvement in elective surgery for older patients, demonstrating remarkable improvements in morbidity and mortality [94]. Orthopedic practices, in particular, have embraced multidisciplinary team (MDT) care and orthogeriatricians, offering strong evidence in support of this approach [6].

Establishing a standardized preoperative assessment is advisable to identify frailty-related factors and high-risk patients, involving them in decision-making [6, 7]. Interdisciplinary care protocols aim to address vulnerabilities, prevent complications, and enhance communication among healthcare providers, patients, and caregivers [93]. Discussions on treatment and healthcare objectives are crucial, focusing on patient priorities. Surgery discussions should consider postoperative function, living arrangements, and caregiver burden. Addressing code status, advanced

directives, and life-sustaining therapy is essential. Patients should review decision-making processes with surgical team members for confidence in their choices. A comprehensive care plan must address identified vulnerabilities, discussed in multidisciplinary meetings and shared with patients, families, and primary care physicians. Standardization of postoperative management is vital, especially for frail patients, to mitigate risks and ensure consistent treatment [95, 96]. Frailty tools have high sensitivity but low specificity, limiting clinical reliability [97]. Comprehensive geriatric assessment is recommended over “short” instruments; assessing various factors like functional disability, cognition, and nutritional status, along with Handgrip Strength measurement, should be mandatory pre-surgery tasks. Prior to scheduling surgery, surgeons with a geriatrician co-management must understand and provide the patient’s vulnerability-frailty status. While 90% of patients may undergo standard care, the remaining 10% identified as frail should undergo additional risk assessment, participate in shared decision-making informed by risk, engage in prehabilitation, or consider alternatives to major surgery if it’s not in their best interest. This approach could significantly reduce mortality rates over time and highlights the importance of establishing strong connections with patients’ support systems to facilitate transitional care, ensuring a smooth return home after rehabilitation. In some instances, restructuring palliative care integration preoperatively may offer patients a clearer understanding of their upcoming procedure, avoiding postoperative reactions in the ICU. These criteria serve as the cornerstone of the innovative “Surgery for Frails” model, guaranteeing thorough and enhanced patient care. Supporting this model is the study by Hall et al. [98] which assessed the impact of frailty screening on surgical outcomes. Frail patients underwent administrative review, with perioperative plans adjusted based on multidisciplinary input. Among 9,153 patients undergoing major, elective, noncardiac surgery, implementing frailty screening led to a significant reduction in 30-day mortality, from 1.6% to 0.7%. Mortality rates among frail patients notably decreased from 12.2% to 3.8%. Similar trends were observed at 180 and 365 days post-surgery. Multivariable analysis confirmed improved survival post-frailty score implementation, irrespective of

age, frailty, and predicted mortality. These findings underscore the potential benefits of preoperative frailty screening and system-level initiatives to enhance surgical outcomes, emphasizing the need for further research to establish causality definitively.

Current gaps in the literature and future research

Despite advancements in understanding the importance of prehabilitation in improving outcomes for GI cancer patients undergoing surgery, there are still significant gaps in the current research. One key gap is the lack of clear guidelines specifically for prehabilitation programs for GI cancer surgeries [8]. This means that healthcare providers may not have consistent standards to follow when implementing prehabilitation, which could lead to variations in patient care and outcomes [99]. Additionally, most research focuses on individual aspects of prehabilitation, like exercise or nutrition, rather than looks at how different components work together [21, 72]. This limits our understanding of how comprehensive prehabilitation programs, including nutritional, physical, and psychosocial support, can impact patient outcomes. Larger studies are needed to fully assess the effectiveness of these multimodal prehabilitation approaches. Furthermore, the role of nutritional interventions, such as immunonutrition, in GI cancer prehabilitation is not well explored, and more research is needed to understand how these interventions work and how they can improve outcomes for patients [47, 70, 71, 100]. Establishing standardized outcome measures and guidelines is crucial to advance the field of prehabilitation and ensure that GI cancer patients receive the best possible care before surgery.

To further enhance prehabilitation programs, additional support service should be considered in gastrointestinal cancer patients’ protocols. The programs should also analyze drug interaction consultations, smoking and alcohol cessation programs, oncofertility consultations, and stoma information for colorectal patients.

Conclusions

In conclusion, this narrative review underscores the crucial role of comprehensive prehabilitation programs in enhancing the perioperative care of

GI cancer patients. Drawing upon insights from existing literature, it is evident that multidisciplinary preoperative interventions targeting nutritional, physical, and psychosocial domains hold a significant potential for optimizing surgical outcomes and improving patient well-being. Our analysis aligns with previous research, emphasizing the necessity of standardized protocols and interdisciplinary collaboration in preoperative care pathways. Future investigations should focus on elucidating the synergistic effects of integrating various intervention modalities and refining prehabilitation protocols to supply the unique needs of GI cancer patients. Furthermore, exploring novel strategies, such as immunonutrition as well as frailty, warrants attention for their potential to further enhance prehabilitation outcomes. By addressing these research gaps and fostering interdisciplinary partnerships, we can advance the field of prehabilitation and pave the way for improved perioperative care and outcomes in GI cancer surgery.

References

- Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024; 74(3): 229–263, doi: [10.3322/caac.21834](https://doi.org/10.3322/caac.21834), indexed in Pubmed: [38572751](https://pubmed.ncbi.nlm.nih.gov/38572751/).
- Arnold M, Abnet CC, Neale RE, et al. Global Burden of 5 Major Types of Gastrointestinal Cancer. *Gastroenterology.* 2020; 159(1): 335–349.e15, doi: [10.1053/j.gastro.2020.02.068](https://doi.org/10.1053/j.gastro.2020.02.068), indexed in Pubmed: [32247694](https://pubmed.ncbi.nlm.nih.gov/32247694/).
- Cavaliere D, Parini D, Marano L, et al. SICO (Italian Society of Surgical Oncology). Surgical management of oncologic patient during and after the COVID-19 outbreak: practical recommendations from the Italian society of Surgical Oncology. *Updates Surg.* 2021; 73(1): 321–329, doi: [10.1007/s13304-020-00921-4](https://doi.org/10.1007/s13304-020-00921-4), indexed in Pubmed: [33184782](https://pubmed.ncbi.nlm.nih.gov/33184782/).
- Dobson GP. Addressing the Global Burden of Trauma in Major Surgery. *Front Surg.* 2015; 2: 43, doi: [10.3389/fsurg.2015.00043](https://doi.org/10.3389/fsurg.2015.00043), indexed in Pubmed: [26389122](https://pubmed.ncbi.nlm.nih.gov/26389122/).
- Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth.* 1997; 78(5): 606–617, doi: [10.1093/bja/78.5.606](https://doi.org/10.1093/bja/78.5.606), indexed in Pubmed: [9175983](https://pubmed.ncbi.nlm.nih.gov/9175983/).
- Boccardi V, Marano L. The Geriatric Surgery: The Importance of Frailty Identification Beyond Chronological Age. *Geriatrics (Basel).* 2020; 5(1), doi: [10.3390/geriatrics5010012](https://doi.org/10.3390/geriatrics5010012), indexed in Pubmed: [32121144](https://pubmed.ncbi.nlm.nih.gov/32121144/).
- Marano L, Carbone L, Poto GE, et al. Handgrip strength predicts length of hospital stay in an abdominal surgical setting: the role of frailty beyond age. *Aging Clin Exp Res.* 2022; 34(4): 811–817, doi: [10.1007/s40520-022-02121-z](https://doi.org/10.1007/s40520-022-02121-z), indexed in Pubmed: [35389186](https://pubmed.ncbi.nlm.nih.gov/35389186/).
- Stiger RJ, Williams MA, Gustafson OD, et al. The effectiveness of prehabilitation interventions on biopsychosocial and service outcomes pre and post upper gastrointestinal surgery: a systematic review. *Disabil Rehabil.* 2024 [Epub ahead of print]: 1–24, doi: [10.1080/09638288.2024.2310765](https://doi.org/10.1080/09638288.2024.2310765), indexed in Pubmed: [38323587](https://pubmed.ncbi.nlm.nih.gov/38323587/).
- Erkul O, Cekic AB, Cansu A, et al. Effects of Sarcopenia on Postoperative Outcomes in Patients Who Underwent Gastrectomy for Gastric Cancer. *J Surg Res.* 2022; 274: 196–206, doi: [10.1016/j.jss.2021.12.051](https://doi.org/10.1016/j.jss.2021.12.051), indexed in Pubmed: [35183030](https://pubmed.ncbi.nlm.nih.gov/35183030/).
- Jakobson T, Karjagin J, Vipp L, et al. Postoperative complications and mortality after major gastrointestinal surgery. *Medicina (Kaunas).* 2014; 50(2): 111–117, doi: [10.1016/j.medici.2014.06.002](https://doi.org/10.1016/j.medici.2014.06.002), indexed in Pubmed: [25172605](https://pubmed.ncbi.nlm.nih.gov/25172605/).
- Downey CL, Bainbridge J, Jayne DG, et al. Impact of in-hospital postoperative complications on quality of life up to 12 months after major abdominal surgery. *Br J Surg.* 2023; 110(9): 1206–1212, doi: [10.1093/bjs/znad167](https://doi.org/10.1093/bjs/znad167), indexed in Pubmed: [37335925](https://pubmed.ncbi.nlm.nih.gov/37335925/).
- Gemici K, Okuş A, Yıldız M, et al. A surgeon's nightmare: Complications. *Ulus Cerrahi Derg.* 2015; 31(2): 90–91, doi: [10.5152/UCD.2015.2785](https://doi.org/10.5152/UCD.2015.2785), indexed in Pubmed: [26170757](https://pubmed.ncbi.nlm.nih.gov/26170757/).
- Zuckerman RB, Sheingold SH, Orav EJ, et al. Readmissions, Observation, and the Hospital Readmissions Reduction Program. *N Engl J Med.* 2016; 374(16): 1543–1551, doi: [10.1056/NEJMsa1513024](https://doi.org/10.1056/NEJMsa1513024), indexed in Pubmed: [26910198](https://pubmed.ncbi.nlm.nih.gov/26910198/).
- Crevenna R, Palma S, Licht T. Cancer prehabilitation — a short review. *Mag Eur Med Oncol.* 2021; 14(1): 39–43, doi: [10.1007/s12254-021-00686-5](https://doi.org/10.1007/s12254-021-00686-5).
- Yaceczko S, Baltz J. Evaluation of nutrition components within prehabilitation programs in gastrointestinal cancers: Is prehab worth the hype? *Nutr Clin Pract.* 2024; 39(1): 117–128, doi: [10.1002/ncp.11079](https://doi.org/10.1002/ncp.11079), indexed in Pubmed: [37772471](https://pubmed.ncbi.nlm.nih.gov/37772471/).
- Piotrowski T, Ryzkowski A, Kalendralis P, et al. Forecasting model for qualitative prediction of the results of patient-specific quality assurance based on planning and complexity metrics and their interrelations. Pilot study. *Rep Pract Oncol Radiother.* 2024; 29(3): 318–328, doi: [10.5603/rpor.101093](https://doi.org/10.5603/rpor.101093), indexed in Pubmed: [39144260](https://pubmed.ncbi.nlm.nih.gov/39144260/).
- Siriwardena AK. Centralisation of upper gastrointestinal cancer surgery. *Ann R Coll Surg Engl.* 2007; 89(4): 335–336, doi: [10.1308/003588407X183265](https://doi.org/10.1308/003588407X183265), indexed in Pubmed: [17535606](https://pubmed.ncbi.nlm.nih.gov/17535606/).
- Perry R, Herbert G, Atkinson C, et al. Pre-admission interventions (prehabilitation) to improve outcome after major elective surgery: a systematic review and meta-analysis. *BMJ Open.* 2021; 11(9): e050806, doi: [10.1136/bmjopen-2021-050806](https://doi.org/10.1136/bmjopen-2021-050806), indexed in Pubmed: [34593498](https://pubmed.ncbi.nlm.nih.gov/34593498/).
- Bausys A, Mazeikaite M, Bickaite K, et al. The Role of Prehabilitation in Modern Esophagogastric Cancer Surgery: A Comprehensive Review. *Cancers (Basel).* 2022; 14(9), doi: [10.3390/cancers14092096](https://doi.org/10.3390/cancers14092096), indexed in Pubmed: [35565226](https://pubmed.ncbi.nlm.nih.gov/35565226/).
- O'Callaghan N, Douglas P, Keaver L. The persistence of nutrition impact symptoms in cancer survivors' post-treatment. *Proc Nutr Soc.* 2022; 81(OCE4), doi: [10.1017/s0029665122001859](https://doi.org/10.1017/s0029665122001859).
- Kichena S, Kamani A, Fricke B. Potential of prehabilitation in hepatocellular carcinoma: a narrative review of available evidence. *Ann Palliat Med.* 2024; 13(1): 101–111, doi: [10.21037/apm-23-175](https://doi.org/10.21037/apm-23-175), indexed in Pubmed: [37993401](https://pubmed.ncbi.nlm.nih.gov/37993401/).

22. Li C, Carli F, Lee L, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg Endosc.* 2013; 27(4): 1072–1082, doi: [10.1007/s00464-012-2560-5](https://doi.org/10.1007/s00464-012-2560-5), indexed in Pubmed: [23052535](https://pubmed.ncbi.nlm.nih.gov/23052535/).
23. Moug SJ, Mutrie N, Barry SJE, et al. Prehabilitation is feasible in patients with rectal cancer undergoing neoadjuvant chemoradiotherapy and may minimize physical deterioration: results from the REX trial. *Colorectal Dis.* 2019; 21(5): 548–562, doi: [10.1111/codi.14560](https://doi.org/10.1111/codi.14560), indexed in Pubmed: [30657249](https://pubmed.ncbi.nlm.nih.gov/30657249/).
24. Alejo LB, Pagola-Aldazabal I, Fiuza-Luces C, et al. Exercise prehabilitation program for patients under neoadjuvant treatment for rectal cancer: A pilot study. *J Cancer Res Ther.* 2019; 15(1): 20–25, doi: [10.4103/jcrt.JCRT_30_17](https://doi.org/10.4103/jcrt.JCRT_30_17), indexed in Pubmed: [30880749](https://pubmed.ncbi.nlm.nih.gov/30880749/).
25. Heldens AF, Bongers BC, de Vos-Geelen J, et al. Feasibility and preliminary effectiveness of a physical exercise training program during neoadjuvant chemoradiotherapy in individual patients with rectal cancer prior to major elective surgery. *Eur J Surg Oncol.* 2016; 42(9): 1322–1330, doi: [10.1016/j.ejso.2016.03.021](https://doi.org/10.1016/j.ejso.2016.03.021), indexed in Pubmed: [27156145](https://pubmed.ncbi.nlm.nih.gov/27156145/).
26. Loughney L, West MA, Dimitrov BD, et al. Physical activity levels in locally advanced rectal cancer patients following neoadjuvant chemoradiotherapy and an exercise training programme before surgery: a pilot study. *Perioper Med (Lond).* 2017; 6: 3, doi: [10.1186/s13741-017-0058-3](https://doi.org/10.1186/s13741-017-0058-3), indexed in Pubmed: [28228938](https://pubmed.ncbi.nlm.nih.gov/28228938/).
27. Durrand J, Singh SJ, Danjoux G. Prehabilitation. *Clin Med (Lond).* 2019; 19(6): 458–464, doi: [10.7861/clinmed.2019-0257](https://doi.org/10.7861/clinmed.2019-0257), indexed in Pubmed: [31732585](https://pubmed.ncbi.nlm.nih.gov/31732585/).
28. West MA, Lythgoe D, Barben CP, et al. Cardiopulmonary exercise variables are associated with postoperative morbidity after major colonic surgery: a prospective blinded observational study. *Br J Anaesth.* 2014; 112(4): 665–671, doi: [10.1093/bja/aet408](https://doi.org/10.1093/bja/aet408), indexed in Pubmed: [24322573](https://pubmed.ncbi.nlm.nih.gov/24322573/).
29. Steffens D, Ismail H, Denehy L, et al. Preoperative Cardiopulmonary Exercise Test Associated with Postoperative Outcomes in Patients Undergoing Cancer Surgery: A Systematic Review and Meta-Analyses. *Ann Surg Oncol.* 2021; 28(12): 7120–7146, doi: [10.1245/s10434-021-10251-3](https://doi.org/10.1245/s10434-021-10251-3), indexed in Pubmed: [34101066](https://pubmed.ncbi.nlm.nih.gov/34101066/).
30. Kasisvisvanathan R, Abbassi-Ghadi N, McLeod ADM, et al. Cardiopulmonary exercise testing for predicting postoperative morbidity in patients undergoing hepatic resection surgery. *HPB (Oxford).* 2015; 17(7): 637–643, doi: [10.1111/hpb.12420](https://doi.org/10.1111/hpb.12420), indexed in Pubmed: [25994624](https://pubmed.ncbi.nlm.nih.gov/25994624/).
31. Stuart SR, Poço JG, Rodrigues MV, et al. Can we predict who will benefit from the deep inspiration breath hold (DIBH) technique for breast cancer irradiation? *Rep Pract Oncol Radiother.* 2023; 28(5): 582–591, doi: [10.5603/rpor.96867](https://doi.org/10.5603/rpor.96867), indexed in Pubmed: [38179291](https://pubmed.ncbi.nlm.nih.gov/38179291/).
32. Dunne DFJ, Jack S, Jones RP, et al. Randomized clinical trial of prehabilitation before planned liver resection. *Br J Surg.* 2016; 103(5): 504–512, doi: [10.1002/bjs.10096](https://doi.org/10.1002/bjs.10096), indexed in Pubmed: [26864728](https://pubmed.ncbi.nlm.nih.gov/26864728/).
33. Wang B, Shelat VG, Chow JJ, et al. Prehabilitation Program Improves Outcomes of Patients Undergoing Elective Liver Resection. *J Surg Res.* 2020; 251: 119–125, doi: [10.1016/j.jss.2020.01.009](https://doi.org/10.1016/j.jss.2020.01.009), indexed in Pubmed: [32135382](https://pubmed.ncbi.nlm.nih.gov/32135382/).
34. Patel AV, Friedenreich CM, Moore SC, et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med Sci Sports Exerc.* 2019; 51(11): 2391–2402, doi: [10.1249/MSS.0000000000002117](https://doi.org/10.1249/MSS.0000000000002117), indexed in Pubmed: [31626056](https://pubmed.ncbi.nlm.nih.gov/31626056/).
35. Fan ST, Lau WY, Wong KK, et al. Pre-operative parenteral nutrition in patients with oesophageal cancer: a prospective, randomised clinical trial. *Clin Nutr.* 1989; 8(1): 23–27, doi: [10.1016/0261-5614\(89\)90021-6](https://doi.org/10.1016/0261-5614(89)90021-6), indexed in Pubmed: [16837262](https://pubmed.ncbi.nlm.nih.gov/16837262/).
36. Wijesundera DN, Pearse RM, Shulman MA, et al. METS study investigators. Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet.* 2018; 391(10140): 2631–2640, doi: [10.1016/S0140-6736\(18\)31131-0](https://doi.org/10.1016/S0140-6736(18)31131-0), indexed in Pubmed: [30070222](https://pubmed.ncbi.nlm.nih.gov/30070222/).
37. van Kooten RT, Bahadoer RR, Peeters KC, et al. Preoperative risk factors for major postoperative complications after complex gastrointestinal cancer surgery: A systematic review. *Eur J Surg Oncol.* 2021; 47(12): 3049–3058, doi: [10.1016/j.ejso.2021.07.021](https://doi.org/10.1016/j.ejso.2021.07.021), indexed in Pubmed: [34340874](https://pubmed.ncbi.nlm.nih.gov/34340874/).
38. Bates A, West MA, Jack S, et al. Preparing for and Not Waiting for Surgery. *Curr Oncol.* 2024; 31(2): 629–648, doi: [10.3390/curren31020046](https://doi.org/10.3390/curren31020046), indexed in Pubmed: [38392040](https://pubmed.ncbi.nlm.nih.gov/38392040/).
39. Roland M, Guthrie B. Quality and Outcomes Framework: what have we learnt? *BMJ.* 2016; 354: i4060, doi: [10.1136/bmj.i4060](https://doi.org/10.1136/bmj.i4060), indexed in Pubmed: [27492602](https://pubmed.ncbi.nlm.nih.gov/27492602/).
40. Kyte D, Cockwell P, Lencioni M, et al. Reflections on the national patient-reported outcome measures (PROMs) programme: Where do we go from here? *J R Soc Med.* 2016; 109(12): 441–445, doi: [10.1177/0141076816677856](https://doi.org/10.1177/0141076816677856), indexed in Pubmed: [27923896](https://pubmed.ncbi.nlm.nih.gov/27923896/).
41. Levett DZH, Grimmett C. Psychological factors, prehabilitation and surgical outcomes: evidence and future directions. *Anaesthesia.* 2019; 74 Suppl 1: 36–42, doi: [10.1111/anae.14507](https://doi.org/10.1111/anae.14507), indexed in Pubmed: [30604423](https://pubmed.ncbi.nlm.nih.gov/30604423/).
42. Argillander TE, Heil TC, Melis RJF, et al. Preoperative physical performance as predictor of postoperative outcomes in patients aged 65 and older scheduled for major abdominal cancer surgery: A systematic review. *Eur J Surg Oncol.* 2022; 48(3): 570–581, doi: [10.1016/j.ejso.2021.09.019](https://doi.org/10.1016/j.ejso.2021.09.019), indexed in Pubmed: [34629224](https://pubmed.ncbi.nlm.nih.gov/34629224/).
43. Karlsson E, Egenvall M, Farahnak P, et al. Better preoperative physical performance reduces the odds of complication severity and discharge to care facility after abdominal cancer resection in people over the age of 70 - A prospective cohort study. *Eur J Surg Oncol.* 2018; 44(11): 1760–1767, doi: [10.1016/j.ejso.2018.08.011](https://doi.org/10.1016/j.ejso.2018.08.011), indexed in Pubmed: [30201418](https://pubmed.ncbi.nlm.nih.gov/30201418/).
44. Rodseth RN, Biccard BM, Le Manach Y, et al. The prognostic value of pre-operative and post-operative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. *J Am Coll Cardiol.* 2014; 63(2): 170–180, doi: [10.1016/j.jacc.2013.08.1630](https://doi.org/10.1016/j.jacc.2013.08.1630), indexed in Pubmed: [24076282](https://pubmed.ncbi.nlm.nih.gov/24076282/).
45. Williams DGA, Molinger J, Wischmeyer PE. The malnourished surgery patient: a silent epidemic in perioperative outcomes? *Curr Opin Anaesthesiol.* 2019; 32(3): 405–411, doi: [10.1097/ACO.0000000000000722](https://doi.org/10.1097/ACO.0000000000000722), indexed in Pubmed: [30893119](https://pubmed.ncbi.nlm.nih.gov/30893119/).
46. Peixoto da Silva S, Santos JMO, Costa E Silva MP, et al. Cancer cachexia and its pathophysiology: links with sar-

- copenia, anorexia and asthenia. *J Cachexia Sarcopenia Muscle*. 2020; 11(3): 619–635, doi: [10.1002/jcsm.12528](https://doi.org/10.1002/jcsm.12528), indexed in Pubmed: [32142217](https://pubmed.ncbi.nlm.nih.gov/32142217/).
47. Boccardi V, Marano L. Improving geriatric outcomes through nutritional and immunonutritional strategies: Focus on surgical setting by a comprehensive evidence review. *Ageing Res Rev*. 2024; 96: 102272, doi: [10.1016/j.arr.2024.102272](https://doi.org/10.1016/j.arr.2024.102272), indexed in Pubmed: [38492809](https://pubmed.ncbi.nlm.nih.gov/38492809/).
 48. Norman K, Haß U, Pirlich M. Malnutrition in Older Adults-Recent Advances and Remaining Challenges. *Nutrients*. 2021; 13(8), doi: [10.3390/nu13082764](https://doi.org/10.3390/nu13082764), indexed in Pubmed: [34444924](https://pubmed.ncbi.nlm.nih.gov/34444924/).
 49. Jain R, Dotan E. Nutrition and Aging: a Practicing Oncologist's Perspective. *Curr Oncol Rep*. 2017; 19(11): 71, doi: [10.1007/s11912-017-0630-5](https://doi.org/10.1007/s11912-017-0630-5), indexed in Pubmed: [28884400](https://pubmed.ncbi.nlm.nih.gov/28884400/).
 50. Figura N, Marano L, Moretti E, et al. Helicobacter pylori infection and gastric carcinoma: Not all the strains and patients are alike. *World J Gastrointest Oncol*. 2016; 8(1): 40–54, doi: [10.4251/wjgo.v8.i1.40](https://doi.org/10.4251/wjgo.v8.i1.40), indexed in Pubmed: [26798436](https://pubmed.ncbi.nlm.nih.gov/26798436/).
 51. Marano L, Marmorino F, Desideri I, et al. NutriOnc Research Group. Clinical nutrition in surgical oncology: Young AIOM-AIRO-SICO multidisciplinary national survey on behalf of NutriOnc research group. *Front Nutr*. 2023; 10: 1045022, doi: [10.3389/fnut.2023.1045022](https://doi.org/10.3389/fnut.2023.1045022), indexed in Pubmed: [37125048](https://pubmed.ncbi.nlm.nih.gov/37125048/).
 52. Muscaritoli M, Arends J, Bachmann P, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017; 36(1): 11–48, doi: [10.1016/j.clnu.2016.07.015](https://doi.org/10.1016/j.clnu.2016.07.015), indexed in Pubmed: [27637832](https://pubmed.ncbi.nlm.nih.gov/27637832/).
 53. Thompson KL, Elliott L, Fuchs-Tarlovsky V, et al. Oncology Evidence-Based Nutrition Practice Guideline for Adults. *J Acad Nutr Diet*. 2017; 117(2): 297–310.e47, doi: [10.1016/j.jand.2016.05.010](https://doi.org/10.1016/j.jand.2016.05.010), indexed in Pubmed: [27436529](https://pubmed.ncbi.nlm.nih.gov/27436529/).
 54. Evans DC, Corkins MR, Malone A, et al. ASPEN Malnutrition Committee. The Use of Visceral Proteins as Nutrition Markers: An ASPEN Position Paper. *Nutr Clin Pract*. 2021; 36(1): 22–28, doi: [10.1002/ncp.10588](https://doi.org/10.1002/ncp.10588), indexed in Pubmed: [33125793](https://pubmed.ncbi.nlm.nih.gov/33125793/).
 55. Gillis C, Davies SJ, Carli F, et al. Current Landscape of Nutrition Within Prehabilitation Oncology Research: A Scoping Review. *Front Nutr*. 2021; 8: 644723, doi: [10.3389/fnut.2021.644723](https://doi.org/10.3389/fnut.2021.644723), indexed in Pubmed: [33898499](https://pubmed.ncbi.nlm.nih.gov/33898499/).
 56. Deftereos I, Hitch D, Butzkueven S, et al. Implementation of a standardised perioperative nutrition care pathway in upper gastrointestinal cancer surgery: A multisite pilot study. *J Hum Nutr Diet*. 2023; 36(2): 479–492, doi: [10.1111/jhn.13018](https://doi.org/10.1111/jhn.13018), indexed in Pubmed: [35441757](https://pubmed.ncbi.nlm.nih.gov/35441757/).
 57. Kasvis P, Viganò A, Bui T, et al. Impact of Dietary Counseling on Health-Related Quality of Life in Patients with Cancer Awaiting Hepato-Pancreato-Biliary Surgery. *Nutr Cancer*. 2023; 75(4): 1151–1164, doi: [10.1080/01635581.2023.2178961](https://doi.org/10.1080/01635581.2023.2178961), indexed in Pubmed: [36867443](https://pubmed.ncbi.nlm.nih.gov/36867443/).
 58. Le Cornu KA, McKiernan FJ, Kapadia SA, et al. A prospective randomized study of preoperative nutritional supplementation in patients awaiting elective orthotopic liver transplantation. *Transplantation*. 2000; 69(7): 1364–1369, doi: [10.1097/00007890-200004150-00026](https://doi.org/10.1097/00007890-200004150-00026), indexed in Pubmed: [10798755](https://pubmed.ncbi.nlm.nih.gov/10798755/).
 59. De Felice F, Cattaneo CG, Poto GE, et al. Mapping the landscape of immunonutrition and cancer research: a comprehensive bibliometric analysis on behalf of NutriOnc Research Group. *Int J Surg*. 2024; 110(1): 395–405, doi: [10.1097/JS9.0000000000000783](https://doi.org/10.1097/JS9.0000000000000783), indexed in Pubmed: [37737933](https://pubmed.ncbi.nlm.nih.gov/37737933/).
 60. Marano L, Porfida R, Pezzella M, et al. Clinical and immunological impact of early postoperative enteral immunonutrition after total gastrectomy in gastric cancer patients: a prospective randomized study. *Ann Surg Oncol*. 2013; 20(12): 3912–3918, doi: [10.1245/s10434-013-3088-1](https://doi.org/10.1245/s10434-013-3088-1), indexed in Pubmed: [23838912](https://pubmed.ncbi.nlm.nih.gov/23838912/).
 61. Braga M, Gianotti L, Vignali A, et al. Artificial nutrition after major abdominal surgery: impact of route of administration and composition of the diet. *Crit Care Med*. 1998; 26(1): 24–30, doi: [10.1097/00003246-199801000-00012](https://doi.org/10.1097/00003246-199801000-00012), indexed in Pubmed: [9428539](https://pubmed.ncbi.nlm.nih.gov/9428539/).
 62. Heslin MJ, Latkany L, Leung D, et al. A prospective, randomized trial of early enteral feeding after resection of upper gastrointestinal malignancy. *Ann Surg*. 1997; 226(4): 567–77; discussion 577, doi: [10.1097/0000658-199710000-00016](https://doi.org/10.1097/0000658-199710000-00016), indexed in Pubmed: [9351723](https://pubmed.ncbi.nlm.nih.gov/9351723/).
 63. Senkal M, Zumtobel V, Bauer KH, et al. Outcome and cost-effectiveness of perioperative enteral immunonutrition in patients undergoing elective upper gastrointestinal tract surgery: a prospective randomized study. *Arch Surg*. 1999; 134(12): 1309–1316, doi: [10.1001/archsurg.134.12.1309](https://doi.org/10.1001/archsurg.134.12.1309), indexed in Pubmed: [10593328](https://pubmed.ncbi.nlm.nih.gov/10593328/).
 64. Senkal M, Mumme A, Eickhoff U, et al. Early postoperative enteral immunonutrition: clinical outcome and cost-comparison analysis in surgical patients. *Crit Care Med*. 1997; 25(9): 1489–1496, doi: [10.1097/00003246-199709000-00015](https://doi.org/10.1097/00003246-199709000-00015), indexed in Pubmed: [9295822](https://pubmed.ncbi.nlm.nih.gov/9295822/).
 65. Braga M, Gianotti L, Radaelli G, et al. Perioperative immunonutrition in patients undergoing cancer surgery: results of a randomized double-blind phase 3 trial. *Arch Surg*. 1999; 134(4): 428–433, doi: [10.1001/archsurg.134.4.428](https://doi.org/10.1001/archsurg.134.4.428), indexed in Pubmed: [10199318](https://pubmed.ncbi.nlm.nih.gov/10199318/).
 66. Gennari R, Alexander JW. Arginine, glutamine, and dehydroepiandrosterone reverse the immunosuppressive effect of prednisone during gut-derived sepsis. *Crit Care Med*. 1997; 25(7): 1207–1214, doi: [10.1097/00003246-199707000-00024](https://doi.org/10.1097/00003246-199707000-00024), indexed in Pubmed: [9233749](https://pubmed.ncbi.nlm.nih.gov/9233749/).
 67. Ashida R, Okamura Y, Wakabayashi-Nakao K, et al. The Impact of Preoperative Enteral Nutrition Enriched with Eicosapentaenoic Acid on Postoperative Hypercytokinemia after Pancreatoduodenectomy: The Results of a Double-Blinded Randomized Controlled Trial. *Dig Surg*. 2019; 36(4): 348–356, doi: [10.1159/000490110](https://doi.org/10.1159/000490110), indexed in Pubmed: [29886499](https://pubmed.ncbi.nlm.nih.gov/29886499/).
 68. Uno H, Furukawa K, Suzuki D, et al. Immunonutrition suppresses acute inflammatory responses through modulation of resolvin E1 in patients undergoing major hepatobiliary resection. *Surgery*. 2016; 160(1): 228–236, doi: [10.1016/j.surg.2016.01.019](https://doi.org/10.1016/j.surg.2016.01.019), indexed in Pubmed: [26965712](https://pubmed.ncbi.nlm.nih.gov/26965712/).
 69. Okamoto Y, Okano K, Izuishi K, et al. Attenuation of the systemic inflammatory response and infectious complications after gastrectomy with preoperative oral arginine and omega-3 fatty acids supplemented immunonutrition. *World J Surg*. 2009; 33(9): 1815–1821, doi: [10.1007/s00268-009-0140-1](https://doi.org/10.1007/s00268-009-0140-1), indexed in Pubmed: [19629583](https://pubmed.ncbi.nlm.nih.gov/19629583/).
 70. Aida T, Furukawa K, Suzuki D, et al. Preoperative immunonutrition decreases postoperative complications by modulating prostaglandin E2 production and T-cell differentiation in patients undergoing pancreatodu-

- denectomy. *Surgery*. 2014; 155(1): 124–133, doi: [10.1016/j.surg.2013.05.040](https://doi.org/10.1016/j.surg.2013.05.040), indexed in Pubmed: [24589090](https://pubmed.ncbi.nlm.nih.gov/24589090/).
71. Russell K, Zhang HG, Gillanders LK, et al. Preoperative immunonutrition in patients undergoing liver resection: A prospective randomized trial. *World J Hepatol*. 2019; 11(3): 305–317, doi: [10.4254/wjh.v11.i3.305](https://doi.org/10.4254/wjh.v11.i3.305), indexed in Pubmed: [30967908](https://pubmed.ncbi.nlm.nih.gov/30967908/).
 72. Gillis C, Buhler K, Bresee L, et al. Effects of Nutritional Prehabilitation, With and Without Exercise, on Outcomes of Patients Who Undergo Colorectal Surgery: A Systematic Review and Meta-analysis. *Gastroenterology*. 2018; 155(2): 391–410.e4, doi: [10.1053/j.gastro.2018.05.012](https://doi.org/10.1053/j.gastro.2018.05.012), indexed in Pubmed: [29750973](https://pubmed.ncbi.nlm.nih.gov/29750973/).
 73. Kenny E, Samavat H, Touger-Decker R, et al. Adverse perioperative outcomes among patients undergoing gastrointestinal cancer surgery: Quantifying attributable risk from malnutrition. *JPEN J Parenter Enteral Nutr*. 2022; 46(3): 517–525, doi: [10.1002/jpen.2200](https://doi.org/10.1002/jpen.2200), indexed in Pubmed: [34057749](https://pubmed.ncbi.nlm.nih.gov/34057749/).
 74. Mehnert A, Hartung TJ, Friedrich M, et al. Death-Related Anxiety in Patients With Advanced Cancer: Validation of the German Version of the Death and Dying Distress Scale. *J Pain Symptom Manage*. 2016; 52(4): 582–587, doi: [10.1016/j.jpainsymman.2016.07.002](https://doi.org/10.1016/j.jpainsymman.2016.07.002), indexed in Pubmed: [27521283](https://pubmed.ncbi.nlm.nih.gov/27521283/).
 75. Roche KN, Cooper D, Armstrong TS, et al. The link between psychological distress and survival in solid tumor patients: A systematic review. *Cancer Med*. 2023; 12(3): 3343–3364, doi: [10.1002/cam4.5200](https://doi.org/10.1002/cam4.5200), indexed in Pubmed: [36602400](https://pubmed.ncbi.nlm.nih.gov/36602400/).
 76. Foster C, Haviland J, Winter J, et al. Members of the Study Advisory Committee. Pre-Surgery Depression and Confidence to Manage Problems Predict Recovery Trajectories of Health and Wellbeing in the First Two Years following Colorectal Cancer: Results from the CREW Cohort Study. *PLoS One*. 2016; 11(5): e0155434, doi: [10.1371/journal.pone.0155434](https://doi.org/10.1371/journal.pone.0155434), indexed in Pubmed: [27171174](https://pubmed.ncbi.nlm.nih.gov/27171174/).
 77. Rosenberger PH, Jokl P, Ickovics J. Psychosocial factors and surgical outcomes: an evidence-based literature review. *J Am Acad Orthop Surg*. 2006; 14(7): 397–405, doi: [10.5435/00124635-200607000-00002](https://doi.org/10.5435/00124635-200607000-00002), indexed in Pubmed: [16822887](https://pubmed.ncbi.nlm.nih.gov/16822887/).
 78. Kiecolt-Glaser JK, Robles TF, Heffner KL, et al. Psycho-oncology and cancer: psychoneuroimmunology and cancer. *Ann Oncol*. 2002; 13 Suppl 4: 165–169, doi: [10.1093/annonc/mdf655](https://doi.org/10.1093/annonc/mdf655), indexed in Pubmed: [12401684](https://pubmed.ncbi.nlm.nih.gov/12401684/).
 79. Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003; 54(3): 269–282, doi: [10.1016/s0006-3223\(03\)00566-3](https://doi.org/10.1016/s0006-3223(03)00566-3), indexed in Pubmed: [12893103](https://pubmed.ncbi.nlm.nih.gov/12893103/).
 80. Grant BF, Hasin DS, Chou SP, et al. Nicotine dependence and psychiatric disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *Arch Gen Psychiatry*. 2004; 61(11): 1107–1115, doi: [10.1001/archpsyc.61.11.1107](https://doi.org/10.1001/archpsyc.61.11.1107), indexed in Pubmed: [15520358](https://pubmed.ncbi.nlm.nih.gov/15520358/).
 81. Burrows T, Kay-Lambkin F, Pursey K, et al. Food addiction and associations with mental health symptoms: a systematic review with meta-analysis. *J Hum Nutr Diet*. 2018; 31(4): 544–572, doi: [10.1111/jhn.12532](https://doi.org/10.1111/jhn.12532), indexed in Pubmed: [29368800](https://pubmed.ncbi.nlm.nih.gov/29368800/).
 82. Bultz BD, Carlson LE. Emotional distress: the sixth vital sign—future directions in cancer care. *Psychooncology*. 2006; 15(2): 93–95, doi: [10.1002/pon.1022](https://doi.org/10.1002/pon.1022), indexed in Pubmed: [16444764](https://pubmed.ncbi.nlm.nih.gov/16444764/).
 83. Cordova MJ, Riba MB, Spiegel D. Post-traumatic stress disorder and cancer. *Lancet Psychiatry*. 2017; 4(4): 330–338, doi: [10.1016/S2215-0366\(17\)30014-7](https://doi.org/10.1016/S2215-0366(17)30014-7), indexed in Pubmed: [28109647](https://pubmed.ncbi.nlm.nih.gov/28109647/).
 84. Spitzer RL, Kroenke K, Williams JBW, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006; 166(10): 1092–1097, doi: [10.1001/archinte.166.10.1092](https://doi.org/10.1001/archinte.166.10.1092), indexed in Pubmed: [16717171](https://pubmed.ncbi.nlm.nih.gov/16717171/).
 85. Kroenke K, Spitzer R. The PHQ-9: A New Depression Diagnostic and Severity Measure. *Psych Ann*. 2002; 32(9): 509–515, doi: [10.3928/0048-5713-20020901-06](https://doi.org/10.3928/0048-5713-20020901-06).
 86. Butow P, Price MA, Shaw JM, et al. Clinical pathway for the screening, assessment and management of anxiety and depression in adult cancer patients: Australian guidelines. *Psychooncology*. 2015; 24(9): 987–1001, doi: [10.1002/pon.3920](https://doi.org/10.1002/pon.3920), indexed in Pubmed: [26268799](https://pubmed.ncbi.nlm.nih.gov/26268799/).
 87. Hutchison SD, Steginga SK, Dunn J. The tiered model of psychosocial intervention in cancer: a community based approach. *Psychooncology*. 2006; 15(6): 541–546, doi: [10.1002/pon.973](https://doi.org/10.1002/pon.973), indexed in Pubmed: [16331595](https://pubmed.ncbi.nlm.nih.gov/16331595/).
 88. Mavros MN, Athanasiou S, Gkegkes ID, et al. Do psychological variables affect early surgical recovery? *PLoS One*. 2011; 6(5): e20306, doi: [10.1371/journal.pone.0020306](https://doi.org/10.1371/journal.pone.0020306), indexed in Pubmed: [21633506](https://pubmed.ncbi.nlm.nih.gov/21633506/).
 89. Tsimopoulou I, Pasquali S, Howard R, et al. Psychological Prehabilitation Before Cancer Surgery: A Systematic Review. *Ann Surg Oncol*. 2015; 22(13): 4117–4123, doi: [10.1245/s10434-015-4550-z](https://doi.org/10.1245/s10434-015-4550-z), indexed in Pubmed: [25869228](https://pubmed.ncbi.nlm.nih.gov/25869228/).
 90. Marinelli V, Danzi OP, Mazzi MA, et al. PREPARE: PreOperative Anxiety REduction. One-Year Feasibility RCT on a Brief Psychological Intervention for Pancreatic Cancer Patients Prior to Major Surgery. *Front Psychol*. 2020; 11: 362, doi: [10.3389/fpsyg.2020.00362](https://doi.org/10.3389/fpsyg.2020.00362), indexed in Pubmed: [32194490](https://pubmed.ncbi.nlm.nih.gov/32194490/).
 91. Han B, Li Q, Chen Xi. Effects of the frailty phenotype on post-operative complications in older surgical patients: a systematic review and meta-analysis. *BMC Geriatr*. 2019; 19(1): 141, doi: [10.1186/s12877-019-1153-8](https://doi.org/10.1186/s12877-019-1153-8), indexed in Pubmed: [31126245](https://pubmed.ncbi.nlm.nih.gov/31126245/).
 92. Fried LP, Tangen CM, Walston J, et al. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001; 56(3): M146–M156, doi: [10.1093/gerona/56.3.m146](https://doi.org/10.1093/gerona/56.3.m146), indexed in Pubmed: [11253156](https://pubmed.ncbi.nlm.nih.gov/11253156/).
 93. Ellis G, Gardner M, Tsiachristas A, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev*. 2017; 9(9): CD006211, doi: [10.1002/14651858.cd006211.pub3](https://doi.org/10.1002/14651858.cd006211.pub3), indexed in Pubmed: [28898390](https://pubmed.ncbi.nlm.nih.gov/28898390/).
 94. Harari D, Hopper A, Dhese J, et al. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. *Age Ageing*. 2007; 36(2): 190–196, doi: [10.1093/ageing/af1163](https://doi.org/10.1093/ageing/af1163), indexed in Pubmed: [17259638](https://pubmed.ncbi.nlm.nih.gov/17259638/).
 95. By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;

- 71(7): 2052–2081, doi: [10.1111/jgs.18372](https://doi.org/10.1111/jgs.18372), indexed in Pubmed: [37139824](https://pubmed.ncbi.nlm.nih.gov/37139824/).
96. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg.* 2017; 152(3): 292–298, doi: [10.1001/jamasurg.2016.4952](https://doi.org/10.1001/jamasurg.2016.4952), indexed in Pubmed: [28097305](https://pubmed.ncbi.nlm.nih.gov/28097305/).
97. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age Ageing.* 2015; 44(1): 148–152, doi: [10.1093/ageing/afu157](https://doi.org/10.1093/ageing/afu157), indexed in Pubmed: [25355618](https://pubmed.ncbi.nlm.nih.gov/25355618/).
98. Hall DE, Arya S, Schmid KK, et al. Development and Initial Validation of the Risk Analysis Index for Measuring Frailty in Surgical Populations. *JAMA Surg.* 2017; 152(2): 175–182, doi: [10.1001/jamasurg.2016.4202](https://doi.org/10.1001/jamasurg.2016.4202), indexed in Pubmed: [27893030](https://pubmed.ncbi.nlm.nih.gov/27893030/).
99. Lee K, Zhou J, Norris MK, et al. Prehabilitative Exercise for the Enhancement of Physical, Psychosocial, and Biological Outcomes Among Patients Diagnosed with Cancer. *Curr Oncol Rep.* 2020; 22(7): 71, doi: [10.1007/s11912-020-00932-9](https://doi.org/10.1007/s11912-020-00932-9), indexed in Pubmed: [32537699](https://pubmed.ncbi.nlm.nih.gov/32537699/).
100. Shen J, Dai S, Li Z, et al. Effect of Enteral Immunonutrition in Patients Undergoing Surgery for Gastrointestinal Cancer: An Updated Systematic Review and Meta-Analysis. *Front Nutr.* 2022; 9: 941975, doi: [10.3389/fnut.2022.941975](https://doi.org/10.3389/fnut.2022.941975), indexed in Pubmed: [35845793](https://pubmed.ncbi.nlm.nih.gov/35845793/).