



Managing elderly with colorectal cancer

Rhan Chaen Chong, Marc Weijie Ong, Kok Yang Tan

Department of General Surgery, Khoo Teck Puat Hospital, Singapore, Singapore

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Correspondence to: Rhan Chaen Chong, MBChB, MRCS. Department of General Surgery, Khoo Teck Puat Hospital, 90 Yishun Central, Singapore, Singapore. Email: lestercrc@gmail.com.

Abstract: The aging population is an increasing healthcare concern in developing countries. In Singapore, 25% of the local population are expected to be older than 65 years old by 2030. Colorectal cancer (CRC) is ranked third most diagnosed cancers worldwide with up to 1.8 million new cases diagnosed in 2018. 60% of newly diagnosed CRC are among patients who are 70 years or older and hence majority of these patients will invariably face challenges with frailty and multiple comorbidities that require appropriate assessment and stratification. The standard of care in patients with stage I or II CRC is surgery with curative intent. For patients with stage III CRC, upfront surgical resection of tumor along with adjuvant chemotherapy is the internationally recommended treatment approach. As for those patients with metastatic disease, they are usually managed within a multidisciplinary team and considered for surgical resection if deemed feasible. Elderly patients are mostly burdened with frailty, functional dependency and existing co-morbidities, all of which are predictors of early postoperative mortality and morbidity in patients with CRC. This article thus aims to review existing evidence to discuss the intricate decision-making process for the surgical management of elderly patient with CRC.

Keywords: Colorectal surgery; colorectal cancer in elderly (CRC in elderly); transdisciplinary care; frailty

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Introduction

The aging population is an increasing healthcare concern in developing countries. In Singapore, a quarter of its will be expected to be 65 years of age or older by 2030 (1).

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The International Society of Geriatric Oncology (SIOG) recommended patients who are going for colorectal resection at the age of 65 or above should have a comprehensive geriatric assessment (CGA) prior to surgery. The involvement of a geriatrician grants the opportunity to identify comorbidities for optimization as well as address psychological needs. This article thus aims to review existing evidence to discuss the intricate decision-making process for the surgical management of elderly patient with CRC.

Physiology of elderly and impact on colorectal surgery

One of the major challenges is the heterogeneity inherent with that of older patient population due to the myriad of medical illnesses, psychological and social care issues.

The perils of multiple comorbidities and limited functional reserve make operating on elderly patients a particular challenge (2). Hence, it is not unexpected that geriatric patients were found to have a higher incidence of perioperative complications, with pulmonary and cardiovascular complications increasing significantly with age.

The geriatric population generally have a higher blood pressure, stroke volumes and cardiac outputs when compared to younger counterparts (3). With labile blood pressure and also susceptibility to hypotension during anaesthesia, the impact on the sympathetic response to surgical stimuli and ultimately the depth and type of anaesthesia required can be profound.

The common changes in lung function in the elderly population are secondary to changes in compliance of the respiratory system resulting in efficiency in oxygenation and hence hampering response to hypoxia. These changes in lung mechanics also affect a geriatric patient's gas exchange and predispose to small airway collapse and atelectasis. Hence several studies have demonstrated that age alone can independently increase the risk of perioperative pulmonary complications (4).

Consequently, these changes in physiology and limited functional reserve in these patients make surgical management of these patients a complex undertaking (5). Aside from the medical comorbidities, psychosocial health components are crucial peri-operative considerations of a major surgery. All these psychological issues are likely to increase stress to the patient predisposing them to further risk of malnutrition during the post-operative period (6).

According to the World Health Organization (WHO), health is defined not purely as a lack of disease or ailment but rather a state of well-being that encompasses physical, mental and social welfare. It is pivotal to preserve patient's functional status and independence whilst at the same time minimizing morbidity and mortality risks that are exposed to. Hence a holistic approach in managing such patients is paramount in achieving good clinical outcome.

With the increasing emphasis on surgery in the geriatric population, clinicians that are managing this subset of patient need to be accustomed to age-related changes that occur in this fragile group so that we can improve clinical

outcomes by minimizing compromising insults the limited physiologic reserve of the elderly patient. There are various risk stratifying tools to aid surgeons in identifying elderly patients at risks of developing morbidity or mortality. This also facilitates pre and post-operative transdisciplinary interventions.

Risk stratification

Due to the diversity that exists within the elderly population, risk stratification and careful surgical preparation is crucial to ensure safe and appropriate surgical care is provided to these patients.

Risk stratification is performed by assessing pre-existing medical conditions as well as investigating biochemical and physiological health indicators. Several risks stratification tools already exist and they are used in conjunction to assess the overall risks of patients undergoing major surgery such as the American Society of Anaesthesiologists classification and the weighted Charlson comorbidity index.

The ASA scoring system determines risk based on a patient's preoperative medical issues and is simple to adopt. This tool does not predict post-operative morbidity or mortality. The Charlson comorbidity index was historically designed to assess long term mortality of the geriatric patients but it has been since modified for use in the surgery (7). Geriatric surgeons should consider using this index as part of their assessment of elderly surgical patients along with ASA score as a Charlson comorbidity index score >5 and ASA score >3 have been shown to be independent predictors of morbidity (8).

Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSUM) score is a surgical scoring system used to predict for both mortality and morbidity which comprised 12 preoperative and 6 intraoperative variables. The pitfall of this assessment tool is its tendency to overestimate mortality rates in low-risk patients, which consequently led to the development of the (Portsmouth) P-Possum score (9). When combining the 2-scoring system, they complement each other in predicting morbidity and mortality of patients undergoing surgical intervention and these scoring systems are validated for the use in general surgery. Last but not least, in the context of colorectal surgery, Cr-Possum, was derived from the core foundation of the POSSUM score and evidence suggest that it predict mortality in patients undergoing colorectal surgery better than both of the above (10).

All the above risk stratification tools assess patients

based on clinical parameters and also biochemical tests. Frailty, conversely has been studied and used extensively in medical models and there is consensus that the core features include impairment in a series of linked systems, leading to a reduction in an individual's ability to withstand stressors (11). The interesting concept about frailty is that it does not necessarily need to coexist in patients with a myriad of medical conditions. For instance, an elderly with minimal comorbidities may still show signs of frailty. As such, frailty has emerged as a useful tool to identify patients at risks of adverse surgical outcome that were not previously identified through conventional clinical and biochemical parameters.

Preliminary findings of a prospective study conducted in Japan and Singapore was able to demonstrate that patients who have frailty syndrome were found to have 4-fold increased risk of encountering major complications in patients undergoing CRC surgery (12). This phenomenon may be caused by an elderly patient's decreased resilience to surgical insult secondary to dampened physiological systems, inflammatory response and immunity in frail patients. With the existence of variety of tools that is available at our disposal, geriatric surgeons should be more well versed with some of the physiological scoring system as well as one that emphasizes on frailty. As such, it is crucial all surgeons and geriatricians looking after the elderly population are accustomed to using of these amalgamations of risk assessment tools so that a tailored surgical plan can be provided to each patient.

Therefore, a thorough geriatric assessment should be carried out for all patients undergoing major CRC surgery so that patients at risks of developing post-operative complications and functional decline can be identified early and further assessed if they will benefit from some form of prehabilitation program before embarking on major definitive surgery.

Frailty and geriatric assessment

CGA is a multi-faceted evaluation of general well-being of an elder based on combination of screening tools that assist in identifying a list of medical problems. CGA is different from traditional evaluation treatments as it involves a multidisciplinary approach and comprehensive diagnostic processes that encompasses patient's overall health. CGA is useful in identifying health issues that are overlooked in routine history and physical examination, allows for risk assessment, aid surgical planning and assist in targeted

pre-operative optimization and improved post-operative outcomes (13).

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) and the American Geriatrics Society (ASG) guidelines place great emphasis on accurate preoperative assessment of the geriatric surgical patients, including multiple facets of CGA which include domains such as functional status, cognition, psychosocial wellbeing and nutritional status.

In a meta-analysis by Xue *et al.*, CGA was found to accurately predict post-operative complications in gastrointestinal cancer patients and revealed that Charlson comorbidity index ≥ 3 , polypharmacy, and activities of daily living (ADL) dependency were all valid predictive factors (14). Emphasis should be paid to optimization of comorbidity, minimize polypharmacy and also improve functional status of patients going for surgery. A complete medication reconciliation should be performed by the pharmacist to discontinue or modify medications and dosage whenever indicated to reduce the detriments of polypharmacy and further optimize pre-operative status of these patients. Pre-operative CGA could be helpful to identify potential health problems, guide risk stratification, aid surgical planning and implement goal directed geriatric interventions, thus allowing clinicians the opportunity of improve preoperative status of elderly surgical patients and enhancing peri-operative care (15).

It is important to promote CGA as a standard preoperative assessment among geriatric surgical patients as a recent survey showed only slightly over 6% of surgeons adopt CGA as their standard practice and only a handful of these surgeons assess for frailty (16). An important reason may be due to some screening tools of CGA are too complex to adopt, and hence impractical to be implemented in a high-volume surgical service. Another reason is that geriatric management interventions have not been robustly studied in cancer populations and thus prompting the need for development of novel quick assessment tool that can aid in predicting postoperative complications in geriatric patients following cancer surgery. More high-quality evidence is required to assess predictive values of various components of CGA in predicting post-operative complications.

Start to finish care

The success of post-operative outcomes and patient recovery can be improved by optimizing risk factors preoperatively.

The term “prehabilitation” is defined as improvement in functional capacity of a patient in order to withstand surgical stressors that will be imposed on them (17). Improving physical function and nutritional status before surgery may further reduce the impact of sarcopenia and malnourishment on postoperative complications. The window of opportunity for prehabilitation in colorectal surgery albeit small, may reap great potential benefits especially in older patients.

Prehabilitation has been shown in a recent randomised trial to be a protective factor for postoperative complication in high risk patients undergoing elective abdominal surgery (18). The personalised prehabilitation program employed in the latter study led to a significant increase in physical activity score and aerobic capacity which translated to almost 50% less complication rate in the intervention group. Other studies have also shown clearly that prehabilitation has a positive benefit on morbidity however no proven benefit for length of stay (19).

This concept has also led to the development of multimodal care programs as a means to boost perioperative resilience, prevent decline postoperatively and ultimately have beneficial effects on postoperative outcome. A recent systematic review by Souwer *et al.* included both prehabilitation and rehabilitation into their multidisciplinary program for elderly patients undergoing colorectal surgery but did not demonstrate a clear effect on perioperative complications and mortality after implementation (20). Additionally, Bruns *et al.* (21) acknowledges in his systematic review that prehabilitation has a positive effect on overall fitness of older patients undergoing colorectal surgery; but evidence on reduction of complications or length of stay is lacking. Nevertheless, a study conducted by Chia and colleagues, demonstrated that a multimodal programme led to a reduction in the length of hospital stay of approximately 3 days after multimodal prehabilitation (22).

The challenges surrounding prehabilitation include the heterogeneity which exists in terms of duration of intervention and the modalities of exercise training. Integrating prehabilitation into overall care of older patients requires a tailor-made approach to obtain compliance as well. This also applies to multimodal programs, which include psychological as well as nutritional assessment in conjunction with physical training.

For patients undergoing elective colorectal resection and (neo)adjuvant chemotherapy and/or radiotherapy, prehabilitation might prove to be cost-effective in all patients. Cost-effectiveness should be expected, and

therefore evaluated, in terms of fewer postoperative complications, fewer reoperations, a shorter length of stay, fewer readmissions, shorter rehabilitation periods, and earlier resumption of work.

Enhanced recovery in elderly

Enhanced recovery after surgery (ERAS) protocols have been well established resting on the concepts on a multidisciplinary, multimodal approach to resolving issues that might delay postoperative recovery. The elements of care are implemented by various professionals including nurses, dieticians, physiotherapists alongside physicians and surgeons. A successful implantation of ERAS guidelines and protocols amongst 30 colorectal units in Netherlands have shown to decrease mean length of hospital stay from 9–10 days to 6 days (23). Another study revealed that compliance rates above 70% with the ERAS protocols led to significant drop in mortality rates after adjusting for variables including sex, age, American Society of Anesthesiologists scores and surgical procedures performed (24).

It may be argued that the elderly need strategies such as ERAS to optimize speed of recovery and to avoid postoperative complications and their sequelae. A systematic review conducted by Bagnall has demonstrated shorter hospital stay along with fewer complications in elderly patients managed within an ERAS programme than with conventional care (25). It also showed that ERAS programmes employed amongst elderly patients was safe with similar mortality rates and no observed difference in rate of postoperative pulmonary complications compared to younger counterparts. Furthermore, in the LAFA trial, the combination of laparoscopic colectomy and perioperative ERAS management has been proposed as the achieving optimal outcomes for patients undergoing colectomy for colon cancer (26).

Reduced overall compliance with ERAS protocols remains a key predictor of delayed discharge, morbidity and readmission with pooled compliance being 69%, 72% and 53% with pre, peri and post-operative ERAS protocol adherence in one study (27). ERAS protocol deviation is most critical in the post-operative stage as it is likely to represent either the development of complications or, if these have been excluded, impaired functional recovery. It is observed that the higher compliance rate to ERAS protocols yielded greater reduction in mean hospital length stay as compared to those with lower compliance rates

(4.6 vs. 8 days) (28). Similarly, Nygren and colleagues (29) highlighted the importance of being compliant to ERAS protocol as it demonstrated a reduction of postoperative complications by 27%.

Despite the advantages associated with ERAS protocol, pick up rate in some institutions across the globe remain low possibly due to organizational and cultural barriers. Kehlet *et al.* has postulated that some reasons include scepticism about their reproducibility outside clinical trials, time-limitation issues, challenges in setting up multidisciplinary teams due to lack of domain experts and in achieving the logistical requirements, reimbursement problems and liability issues as result of shorter hospitalization (30). As such, a highly-committed multi-disciplinary team with the appropriate skills-set is required to maximize patient adherence and compliance to these protocols so that desired outcome of the care pathway can be achieved.

Notwithstanding, ERAS remains a feasible program and obtains better outcomes compared to the traditional way of care after colorectal surgery and should be implemented without reservations in elderly patients. In order to achieve a high compliance rate within this age group, major efforts will be required focusing on patient education and social factors. Goals and benefits expected in this population would be the same as found in other age groups.

Surgical considerations

Surgical intervention in patients with advanced CRC is limited. According to guidelines from the National Comprehensive Cancer Network, patients with stage 4 CRC should only undergo surgery if they develop tumor related complications or have potentially resectable metastases.

Approximately 30% of patients with CRC develop a colorectal liver metastasis (CRLM) within 15 years of diagnosis of the primary tumour. Without treatment, less than 20% of the patients are alive 3 years, and survival beyond 5 years is the exception. Patients who have CRLM are divided into three groups: non-resectable metastases, clearly resectable metastases, and advanced metastases of borderline resectability. Unfortunately, less than 20% of patients with CRLM are considered eligible for resection, while rest have unresectable CRLM at presentation (31). A systematic review and meta-analysis of 142 have shown 5-year survival rates ranging from 16–71%, for patients with CRC after surgical resection of liver metastases (32). Adam and colleagues evaluated the outcome of liver

surgery for CRLM in patients over 70 years old in a large international multicentre cohort and concluded that elderly patients were less likely to undergo major hepatic resection and receive adjuvant or palliative chemotherapy (33). They also observed that the elderly surgical patients have a higher 60 days post-operative morbidity and mortality when compared to their younger counterparts. However, the long-term survival rate at 3 years was similar between the elderly (60.2%) and older (57.1%) cohort.

CRC patients presenting as an emergency often necessitates prompt treatment with significantly more of the elderly patients present in such a manner. Patients generally fair worse when they are operated as an emergency case as compared to those who undergo elective surgery as a result of a higher perioperative mortality rate related to the more advanced tumour stage and poor physical status of patients in an emergency presentation. Clinicians frequently have to decide whether major surgery is justified in elderly patients with a limited life expectancy. A systematic review of 34,194 patients in 2,000 of the management of CRC in elderly patients found a more advanced disease stage at presentation, increased emergency presentation rates, increased frequency of postoperative morbidity and mortality with progressive age, also suggesting that age alone is a pivotal driver in decision for surgery in elderly patients (34).

Obstruction is a common complication in patients with advanced CRC. As surgery could be a huge undertaking in elderly patients given their higher postoperative risk, several studies have sought to evaluate non-operative approach. Self-expanding metal stents (SEMS) have emerged as a bridge to avoid emergency surgery, relieve acute symptoms and to potentially avoid having a stoma creation. Stenting for malignant colorectal obstruction in older patients was shown to be technically feasible with success rates comparative to a younger population according to several retrospective studies (35,36). A large multicentre randomised trial conducted by Arezzo seems to suggest similar complication rates and oncologic outcomes when comparing colonic stenting with emergency surgery, albeit a significantly lower stoma rates in the stenting group (37).

The relationship between age and prognosis is complex and may potentially be confounded by differences in presenting symptoms, location of tumour, pre-existing medical conditions and the type of treatment received. Age-specific trends in studies have proven that elderly patients are indeed a heterogeneous group. It was noted that with advancing age, an increasing proportion of patients

underwent emergency surgery and correspondingly saw a diminishing proportion of them undergoing surgery that was curative (34). Hence an amplified need to screen for CRC and its risk factors among elderly patients are required to minimize late presentation and possibly circumvent emergency surgical intervention in this group of patients.

Moving forward: transdisciplinary care and restoration of functional outcome post-surgery

The provision of surgical care has become increasingly intricate in recent years. This is the result of developments in surgical options available to patients and thus there is a call for healthcare providers to explore their areas of expertise to greater depths whilst contributing to sub-specialisation care.

This results in a growing reliance on other subspecialists with other domain expertise in the care of patients. Consequently, fragmentation of care arises as from a mounting discrepancy between comprehensive care that every patient deserves and the ability of single healthcare provider to deliver this level of care. As such it is important for us to adopt a transdisciplinary model of care when providing surgical care to the elderly population. Transdisciplinary care aims to leverage on the success of multidisciplinary care and integrates knowledge of the different team members to facilitate the process of evaluating and treating a patient thereby circumventing fragmentation of care and duplication of services provided by different individuals.

One of the core features in the transdisciplinary model of care is to ensure early goal setting that is identifiable to the team. These goals should be individualized to a single patient and team members may deliberate the validity of these goals at initial assessment. Once common goal is set, the same individuals should follow through prehabilitation if required, see patient through surgery, are present for rehabilitation and solve problems with the patient as they arise. Through this transdisciplinary approach, Chia *et al.* were able to achieve a shorter hospital stay and full functional recovery in elderly frail patients who underwent colorectal surgery (22). It has also been demonstrated that transdisciplinary care is able to achieve good medium-term functional outcomes after major colorectal surgery (2).

The importance of return to functional baseline in elderly surgical patient cannot be stressed as independence post-surgery is an imperative consideration. Any deficit in return to their premorbid physical function after surgery

may affect their will to survive adversely even though benefits of surgical intervention have been achieved. Hence the facets of functional recovery plays as significant a role as solely focusing on improving morbidity and mortality.

As the landscape of geriatric surgery continue to shift, compelled by an aging population, transdisciplinary care should be considered as a new model of care in order for us to provide optimal, comprehensive healthcare for patients with a myriad of complex needs and simultaneously transforming our healthcare model into a cohesive one. It is vital to take postoperative quality of life and functional recovery into consideration when planning for an operative for an elderly patient so that the necessary interventions can be put in place prior to operation to ensure a respectable functional outcome.

Conclusions

The management of elderly patients with CRC can be a complex process, however outcomes for selected patients can still be excellent. There are specific strategies one can adopt to improve the care received in this vulnerable group. This can be achieved by surgeons not operating in isolation but by adopting a transdisciplinary model of care and through use of CGA tools to help to improve selection of candidates for intervention whilst prudently excluding high risk individuals.

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Footnote

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