Review Article (Current Strategies in Colon Cancer Management)

Minimally invasive surgery in the geriatric patient with colon cancer

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Abstract: As the global population ages, the number of geriatric patients requiring surgery for colon cancer would inevitably increase. Radical oncological surgery in the elderly colorectal cancer patient has been recognized to be associated with a higher rate of postoperative complications and mortality compared to the young. While less aggressive management options may be reasonable in patients with limited life expectancy and significant comorbidities, many elderly patients have preserved function despite their chronological age. The advances in minimally invasive surgery (MIS) now provide a feasible means of achieving safe oncological treatment for these geriatric patients. This review focuses on the evidence behind MIS in the geriatric patient with colon cancer.

Keywords: Laparoscopy (LAP); colorectal; elderly; geriatric

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Introduction

The World Health Organization (WHO) reported an increase in global average life expectancy from 66.5 to 72.0 years between 2000 and 2016, and data from the Global Health Observatory (GHO) has estimated that the global population aged 60 years could expect to live another 20.5 years on average in 2016 (1). Coupled with the fact that the incidence of colon cancer rises with age, the number of geriatric patients requiring surgery for colon cancer is expected to increase. A review of the Nationwide Inpatient Sample from 2001 to 2010 already reported that 63.8% of colorectal cancer operations in the United States were being performed on patients 65 years and older (2). While uncommon, there have also been reports of patients in the extreme age groups—octogenarians, nonagenarians and centenarians—undergoing surgery (3-6).

While the WHO classifies a 65-year-old to be of geriatric age, the definition of an elderly patient tends to vary between surgical publications, posing a challenge to inter-study comparisons and the pooling of data for statistical analysis (7). In addition, most studies on geriatric patients with colon cancer only take into account the chronological age of patients. While convenient for data collection and statistical interpretation, this tends to oversimplify the impact of age as a demographic factor. In reality, the perioperative outcomes of these patients correlate better with their functional, biological or physiological age. Acknowledging these limitations in the current literature, we review the evidence behind minimally invasive surgery (MIS) in the geriatric patient from two perspectives: MIS versus open surgery (OS) in the geriatric patient, and the outcomes of MIS in the geriatric patient versus the young.

MIS versus OS in the geriatric patient

The incorporation of MIS into cancer treatment for a

geriatric patient differs conceptually from adopting a minimally aggressive approach in the management of such a patient. The latter represents due consideration given to the life expectancy and comorbidities in a patient of advanced age, balanced against the potential merits of oncological treatment. For example, the risks involved in subjecting an elderly patient to radical resection after the complete endoscopic removal of a malignant polyp may justify the omission of surgery.

The role of MIS techniques, such as conventional laparoscopy (LAP) and robot-assisted LAP, is to reduce the amount of surgical trauma and the degree of physiological disruption to patients. There have been numerous publications detailing the short-term benefits of MIS when applied to a general population (8,9). These advantages in postoperative recovery are perhaps more compelling in the geriatric patient with limited reserves compared to a younger counterpart. However, in the context of colon cancer surgery, these should be achieved without compromising on the radicality of the oncological treatment. The COST Study Group Trial reported in 2004 that perioperative recovery was significantly (P<0.001) superior in the LAP group in terms of briefer use of parenteral narcotics and a shorter hospital stay compared to the OS group (9). While the duration of surgery was significantly longer in the LAP group (150 *vs.* 95 min, P<0.001), the rate and severity of complications in both groups were similar. The extent of resection was also comparable, with no difference in the number of lymph nodes harvested. After a median follow-up of 7 years, there were no significant differences between the two treatment groups in time to recurrence, 5-year disease-free survival and overall survival (10). Although the results were not stratified by age, a median patient age of 70 years in the LAP group would suggest that the majority of patients were geriatric. However, as the COST study was devised mainly to prove the safety or noninferiority of LAP compared to OS, patients with "severe medical illnesses" were excluded from the study. And with 86% of patients in the LAP group categorized as ASA 2, these patients were probably relatively healthy despite their age.

The MRC CLASICC was another trial that supported the oncological safety of LAP, although the study design included both colonic and rectal tumors, with only 52% of the study population involving the former. The results were, similarly, not stratified by patient age, with the mean age in the LAP colorectal group being reported as 69±11 years (11).

Interestingly, a multivariate analysis of data from the COLOR trial showed significantly worse disease-free survival and overall survival in older patients. Further analyses indicated that the worse outcomes were not due to a higher incidence of recurrence. The median age of patients in the LAP group was reported as 71 (range, 54–84) years, but the study was not designed to examine the impact of patient age and the authors merely attributed the differences to that expected of a general population (12).

These earlier studies were initiated in the 1990s, when the aim was to generate evidence to support the use of MIS for colectomies in the general population. More recent studies have compared the outcomes of MIS versus OS specifically in the elderly, possibly addressing concerns of how the longer operating time and physiological demands of sustained pneumoperitoneum and steep positioning potentially affect this group of patients. One such study published in 2013 retrospectively analyzed 434 patients who underwent elective resection for colon cancer between 2000 and 2009 (13). The authors reported lesser intraoperative blood loss (100 *vs.* 120 mL, P<0.0001), lower cardiac complication rate (3.70 *vs.* 11.5%, P=0.003), lower mortality rate (0.5% *vs.* 4.0%, P=0.043), and a shorter hospital stay in the LAP group (5 *vs.* 7 days, P<0.0001). This was despite a longer operating time (150 *vs.* 115 min, P<0.0001). The overall 5-year survival rates were similar between LAP and OS. Although the two groups of patients did not differ in terms of age, gender, comorbidities, ASA, or stage of disease, there could inevitably be an element of selection bias as the choice of LAP or OS was left to the discretion of the surgeon. Potential confounders such as the specific type of comorbidities, performance status and BMI of the patients, previous abdominal surgeries, and tumor size were not reported. Consequently, the benefits of LAP in this study likely reflect the superior outcomes from a preferentially-selected group of patients who were more suited to undergo MIS. In an attempt to minimize the effect of these confounders, a meta-analysis of 66,592 patients was performed by Antoniou *et al.* (14). The authors reported that the clinical outcomes remained in favour of LAP even after sensitivity analyses. Another systematic review of elective LAP versus OS in colorectal patients older than 85 years showed no significant difference in morbidity or mortality, although the pooled data analysis demonstrated reduced morbidity in the LAP group (P=0.032) (15). Out of the six retrospective studies included in that review, only two reported on 'time to oral diet'—both showed significantly shorter times to oral diet in the LAP group.

Pooled data of all six studies showed an overall average hospital stay of 13.1 and 18.9 days in the LAP and OS groups, respectively (P<0.0001).

Other publications comparing LAP and OS in the elderly have also either shown equipoise or benefits of the former in terms of lesser blood loss, reduced complications, faster recovery, and shorter lengths of hospital stay (16). In particular, Law *et al*. showed a significant reduction in cardiopulmonary morbidity (7.7% *vs*. 22.4%, P=0.033) in the LAP group (17). In their series of 535 patients who had been randomly assigned to LAP or OS, Frasson *et al*. showed that LAP was associated with reduced morbidity (20.2 *vs*. 37.5%, P=0.01) and a shorter length of hospital stay (9.5 *vs*. 13 days, P=0.001) when compared to OS in patients aged 70 years or older (18). Interestingly, it was only within the OS group that a higher morbidity rate and longer length of hospital stay was reported in the elderly. The LAP group reported similar outcomes regardless of age. The authors attributed this finding to the lower rate of pneumonia and cardiopulmonary complications, and a quicker recovery of self-care ability associated with LAP. In one of the most recent publications comparing OS and LAP in the elderly colorectal patient, Keller *et al*. performed an adjusted analysis of the United States Premier Inpatient Database, controlling for all differences in the patient and hospital characteristics across OS and LAP in patients aged 65 years and older undergoing elective colorectal resections between 2010 and 2015 (19). The authors reported significantly lower complication and readmission rates, lengths of stay, and total inpatient costs in the LAP group.

In summary, notwithstanding the limitations of registry data and retrospective analyses, it would seem that the literature lends support to the adoption of MIS in the geriatric patient with colon cancer.

MIS in the geriatric patient versus the young

There have been studies—again mainly retrospective reviews—that report no significant difference in postoperative morbidities and length of hospital stay between the elderly and the young after MIS colorectal surgery (20-24). Not surprisingly, patient demographics related to their difference in age, such as ASA and the number of medical comorbidities, tend to be statistically different. However, these retrospective analyses are inevitably subjected to the confounding of selection bias. None of the studies reported the number of geriatric patients who were managed non-surgically. Even if all consecutive patients undergoing surgery were studied, it would be logical to assume that the elderly patients with poor performance status and limited life expectancy would have been excluded from radical oncological surgery in the first place.

Most other reports tend to concur that MIS colorectal surgery in the elderly patient is still associated with greater risk than in younger patients. This is in part attributed to the fact that there tends to be preponderance of emergency surgeries and more advance disease in the elderly. Also, apart from the higher prevalence of comorbidities in the elderly, advanced age itself has also been shown to be an independent risk factor for morbidity and mortality (2,25). Kunitake *et al*. reported that the readmission rates in patients 80 years or older were nearly twice that of patients younger than 65 years (3). A systematic review of risk factors for 30-day readmission after colorectal surgery also identified older age as a consistent and significant predictor of readmission (26). The length of hospital stay, disposition to a short-term facility, and cost also steadily increased as patients aged (2).

Multivariate analysis of data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) showed an increased morbidity of 33% in the elderly, compared with 26% of the nonelderly (27). The same study also reported that the 30-day mortality rate was double for patients aged above 70 years, with an odds ratio (OR) of 4.3 (95% CI: 3.3–5.5) in patients more than 85 years old. Indeed, the impact of age on mortality might be even greater if the analysis was extended beyond the 30-day period, although this was not possible given the limitations of the ACS-NSQIP data set. In another review of 1,043,108 patients from the Nationwide Inpatient Sample from 2001 through 2010, Jafari *et al*. reported a significantly higher risk-adjusted in-hospital mortality in patients with advancing age: 65 to 69 years (OR 1.32; 95% CI: 1.18–1.49), 70 to 74 years (OR 2.02; 95% CI: 1.82–2.24), 75 to 79 years (OR 2.51; 95% CI: 2.28–2.76), 80 to 84 years (OR 3.15; 95% CI: 2.86–3.46), and 85 years and older (OR 4.72; 95% CI: 4.30–5.18) (2). A similar trend was noted in terms of morbidity, with almost all postoperative complications in the elderly being significantly higher.

In order for MIS to be safely incorporated into the treatment of the geriatric colon cancer patient, it is paramount to recognize the difference in outcomes between patients of different "ages"—specifically, their functional age. The knowledge of this distinction is important for preoperative counselling, perioperative optimization

and monitoring, and prognostication. Weerink *et al*. showed a reduction in overall survival from 66 months in octogenarian patients without complications to 13 months in those with postoperative complications (28). While elderly patients who survive the first year after surgery have a prognosis comparable to younger ones, older patients and sepsis are associated with higher 1-year overall, cancer-specific, and cardiovascular-specific mortality, highlighting the importance of formal geriatric assessment, multidisciplinary care, and cardiovascular optimization for older patients (29). With the substantial heterogeneity in the functional and physiological reserves of the elderly, tolerance to surgical stress can vary greatly among individuals of the same chronological age. Given the rising popularity of enhanced recovery after surgery (ERAS) protocols and prehabilitation pathways, future research should focus on multidimensional geriatric assessment tools to better identify the geriatric patient who would benefit from perioperative optimization. The other group that is frequently under-represented in trials are the geriatric patients with less-than-ideal cardiopulmonary function despite the best efforts at optimization. Their comorbidities place them at a high risk for surgery, but the alternative of withholding potentially curative treatment would subject them unnecessarily to the complications of cancer, including a premature demise. Acknowledging the benefits of MIS over OS, combined with the advancements in perioperative care, it is perhaps time to explore the feasibility and safety of MIS in this group of geriatric colon cancer patients.

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Footnote

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