Suitability of Enhanced Recovery after Surgery (ERAS) Protocols for Elderly Colorectal Cancer Patients

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ABSTRACT

Objective: Enhanced recovery after surgery (ERAS) provides a multimodal approach to postsurgical recovery, seeking to reduce a patient's stress response and promoting recovery. This study aimed to determine the suitability of ERAS protocols for elderly patients above 75 years of age.

Methods: This is a retrospective analysis of all patients who had undergone major colorectal resections under ERAS protocols in Khoo Teck Puat Hospital, Singapore and Faculty of Medicine Siriraj Hospital, Thailand between 2013 and 2014. Data collected included patient characteristics and outcomes, including length of hospitalization, and time to first flatus and mobilization.

Results: Of the 196 patients studied, 38 were above 75 years of age. Elderly patients were more likely to have more comorbidities, a higher ASA score and a higher POSSUM predicted mortality. They also had an increased risk of developing Clavien 2 complications (OR 2.41, 95% CI 1.10-5.29). Compared to their younger counterparts, elderly patients did not have a delay in first flatus or mobilization. However, they tended to stay longer (7.89 vs. 5.16 days, $p<0.001$). On multivariate analysis, ASA score of 3 and above was an independent risk factor for a length of stay over 1 week while age was not.

Conclusion: This study has shown that elderly patients achieve comparable functional recovery under an enhanced recovery approach. Enhanced recovery after surgery can be adopted regardless of a patient's age.

Keywords: Enhanced recovery; colorectal resections; elderly (Siriraj Med J 2020; 72: 18-23)

INTRODUCTION

Enhanced recovery after surgery (ERAS) had its roots from the 1990s in the early work of Henrik Kehlet[1], who proposed a multimodal approach to postsurgical recovery that could reduce both postoperative complications and duration of recovery. Enhanced recovery or 'fast-track' surgery challenges the conventional approach to postoperative care, and seeks to reduce the patient's stress response to surgery and promote recovery. Its key elements include preoperative counseling, avoidance of bowel preparation and premedication, reduction in preoperative fasting, maintenance of intraoperative normothermia, laparoscopic access where possible, avoidance of opioid analgesics, nasogastric and intra-abdominal drains, early removal of urinary catheters and early mobilization and feeding. At the beginning, these measures challenged what was then conventional wisdom and were met with resistance, but numerous publications

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over the years have validated its efficacy. A meta-analysis of six randomized controlled trials with 452 patients by *Varadhan et al*[2] in 2010 showed a reduction in hospital stay by 2.55 days (95% CI 1.85-3.24) and a reduction of complications with a relative risk of 0.53 (95% CI 0.44-0.64). While enhanced recovery was initially developed for colorectal surgery, it has now been evaluated or adopted in a number of other surgeries, including radical cystectomy, hepatobiliary and pancreatic surgery, total knee replacement and cardiovascular surgery.[3-7]

The management of an elderly patient undergoing surgery is an evolving challenge. In 2010, 524 million people were above the age of 65 years - 8 percent of the world's population. This number is expected to increase to 1.5 billion people, or 16 percent of the world's population by 2050.[8] A natural consequence of the demographic change has seen more major surgery being performed for elderly patients.[9,10] Surgery for the elderly is fraught with complexities as elderly patients have a higher incidence of co-morbidities, reduced functional reserves and are more likely to be frail. *Duron et al*[11] studied 3322 patients undergoing major digestive surgery in a multicenter prospective study and found that age above 65 years was shown to be an independent risk factor for mortality with an odds ratio of 2.21 (95% CI 1.36-3.59). Surgery in an elderly patient calls for a holistic approach with measures taken to address their increased postoperative risks.

This study aims to evaluate the comparative benefit of enhanced recovery after surgery (ERAS) protocols between elderly and young patients undergoing elective major colorectal resections in an Asian setting.

MATERIALS AND METHODS

All patients who had undergone elective major colorectal resections under ERAS protocols in the Khoo Teck Puat Hospital, Singapore and the Faculty of Medicine Siriraj Hospital, Thailand between January 2013 and December 2014 were reviewed. The elements of ERAS that were adopted in their care are detailed in Table 1. Data from our prospectively collected computer database was extracted and further clinical information was extracted from a review of the clinical notes. Individual comorbidities were recorded and quantified using the American Society of Anesthesiologist (ASA) system. Preoperative surgical risk was quantified with the Colorectal Physiological and Operative Severity for the enUmeration of Mortality and Morbidity (CR-POSSUM)[12] score. Body mass index (BMI), stage of malignant disease, site of surgery relative to the peritoneal reflection and surgical approach (open vs. laparoscopic) were noted.

TABLE 1. Enhanced Recovery after Surgery (ERAS) Protocol.

Variable	Age
Preoperative	Patient education and counselling
	Anaesthesia assessment
	Low residue diet until day before surgery, clear fluids until 2 hours before surgery
	Fluids for carbohydrate loading
	Avoidance of bowel preparation (except for low rectal lesion)
Intraoperative	Epidural analgesia for open surgery (upper midline)
	Mechanical venous thromboemolism and antibiotic prophylaxis
	Zero-balance fluid management
	Bilateral TAP block for laparoscopic/subumbilical incisions +/- PCA
	Removal of NG tube before extubation
Postoperative	Allow free fluids at the earliest opportunity
	Give fluids at 1 ml/kg/hr - Prompt cessation of IV fluids
	Discontinue PCA by POD2, Epidural/TAP cathethers by POD3
	Oral analgesia prescribed - Paracetamol +/- NSAIDS
	Sit out of bed and ambulation by physiotherapist from POD1
	Remove urinary cathether if there are no specific requirements

Outcome measures of morbidity were quantified with the Clavien scoring system.[13] Other outcome measures included the length of stay, day of first flatus or mobilization, the need for re-operations and postoperative mortality. Analysis for factors correlating to the development of postoperative complications and mortality were performed using factors that were identified to be useful predictors by previous studies. The outcomes of patients with age over 75 years were compared with those with a younger age.

Bivariate analysis was performed using Chi-square test in Statistical Package for the Social Sciences for Windows (SPSS Inc, Chicago, USA), version 20.0 on a personal computer. Results were expressed as odds ratios with 95% confidence intervals. Stepwise logistic regression analysis was used in multivariate analysis to identify parameters that independently had affected outcomes.

Institutional review board statement: The study was approved by the institutional review board [DSRB Reference Number: 2017/00130 and SIRB Number: Si 482/2560].

RESULTS

Among the 196 patients who underwent colorectal resections, 38 were above the age of 75 years. The demographic and characteristics of the patients who were operated under ERAS protocols are shown in Table 2. Elderly patients above 75 years of age were more likely to have two or more co-morbidities, with 44.7% of elderly patients having an ASA score of 3 and above compared to 17.7% ($p<0.001$) for younger patients. Elderly patients also had a higher mean CR-POSSUM predicted mortality of 5.86% compared to 1.79% ($p<0.001$) for younger patients. There was no significant difference in gender, BMI, stage of disease and site of surgery.

Bivariate analysis showed that elderly patients had increased risk of postoperative morbidity. The odds ratio for developing Clavien 2 complications and above was 2.41 (95% CI 1.10 – 5.29) for elderly patients (Table 3). However, age was not shown to be an independent risk factor for developing Clavien 2 complications and above on multivariate analysis (Table 4). Instead, having two or more co-morbidities and BMI above 25 were found to be independent risk factors. The elderly were not shown to

TABLE 2. Patient Demographics and Operation Characteristics.

Variable	Age		*P*-value
	Above 75	Below 75	
Male gender	39.5% (15/38)	55.5% (88/158)	0.072
2 or more co-morbidities	**63.2% (24/38)**	**28.5% (45/158)**	**<0.001**
ASA 3 and above	**44.7% (17/38)**	**17.7% (28/158)**	**<0.001**
Mean POSSUM predicted Mortality (SD)	**5.86% (4.43)**	**1.79% (1.52)**	**<0.001**
BMI > 25	21.1% (8/38)	32.3% (51/158)	0.176
Stage 3 disease and above	36.8% (14/38)	47.5% (75/158)	0.238
Below peritoneal reflection	39.5% (15/38)	50.9% (79/158)	0.244
Laparoscopic	**18.4% (7/38)**	**36.1% (57/158)**	**0.037**

TABLE 3. Patient outcomes on bivariate analysis (Odds Ratio).

Variable	Age		Odds Ratio	*P*-value
	Above 75	Below 75	(95% CI)	
Reoperation	2.6% (1/38)	1.9% (3/158)	1.40 (0.14 - 13.81)	0.774
Clavien ≥2 complications	**34.2% (13/38)**	**17.7% (28/158)**	**2.41 (1.10 - 5.29)**	**0.025**
Clavien ≥3 complications	5.3% (2/38)	3.8% (6/158)	1.41 (0.94 - 1.10)	0.682
Hospitalization death	2.6% (1/38)	0.6% (1/158)	4.24 (0.26 - 69.42)	0.271

TABLE 4. Multivariate analysis correlating to Clavien 2 or more complications and length of stay ≥1 week.

Factor	Clavien ≥2 Complications OR (95% CI, *P*-value)	Length of stay ≥1 week OR (95% CI, *P*-value)
Age >75	1.46 (0.59 – 3.63, 0.414)	1.22 (0.45 – 3.33, 0.701)
Male gender	1.02 (0.49 – 2.16, 0.950)	1.00 (0.44 – 2.27, 0.992)
2 or more co-morbidities	**2.61 (1.13 – 6.00, 0.024)**	**2.06 (0.82 – 5.18, 0.127)**
ASA 3 and above	1.66 (0.69 – 3.97, 0.256)	2.58 (1.02 – 6.54, 0.460)
BMI >25	**2.62 (1.05 – 6.52, 0.038)**	**2.50 (0.91 – 6.89, 0.076)**
Stage 3 disease and above	0.85 (0.40 – 1.81, 0.670)	1.45 (0.64 – 3.31, 0.373)
Below peritoneal reflection	0.82 (0.37 – 5.89, 0.577)	0.83 (0.36 – 1.89, 0.652)
Laparoscopic	1.29 (0.58 – 2.87, 0.529)	0.98 (0.40 – 2.42, 0.964)

be at significant risk for developing more major (Clavien 3 and above) complications. There was no statistically significant difference in the rate of reoperations or in-hospital death.

Elderly patients were found to have an increased length of stay at an average of 7.89 days compared to 5.16 days ($p<0.001$) in younger patients (Table 5), but demonstrated good functional recovery, with no significant difference in the day of first flatus or first mobilization. Once again, age was not shown to be an independent risk factor for a length of stay beyond one week on multivariate analysis (Table 4). An ASA score of 3 and above was shown to be an independent risk factor for increased length of stay.

TABLE 5. Patient outcomes (comparison of means).

Variable	Age		
	Above 75	**Below 75**	***P*-value**
Length of stay (SD)	**7.89 days (6.24)**	**5.16 days (3.42)**	**<0.001**
Day of first flatus (SD)	1.97 days (1.30)	1.88 days (1.22)	0.638
Day of first mobilization (SD)	1.50 days (0.95)	1.32 days (0.72)	0.052

DISCUSSION

This review of two cohort of patients from Singapore and Thailand showed that elderly patients 75 years of age and above undergoing major colorectal resections under ERAS guidelines were more likely to develop Clavien 2 and above complications and to have an increased length of stay. Although elderly patients experienced more complication and longer hospital stay, they could achieve comparable functional recovery as of a younger age group within an ERAS protocol. Interestingly, old age was not shown to be an independent risk factor for either outcome on multivariate analysis. In fact, two or more co-morbidities and BMI above 25 were found to be independent risk factors for major postoperative complication, and ASA score of 3 and above was an independent risk factor for increased length of stay.

While age above 75 years was associated with the development of Clavien 2 and above complications, it was not found to lead to more major complications (Clavien 3 and above) requiring admission to an intensive care unit or further procedural or surgical re-interventions. Elderly patients were also not found to have a significant difference in mortality rates. This suggests that enhanced recovery interventions can be safely applied to elderly patients. Several previous studies have shown that ERAS reduced complications and duration of hospitalization when applied to the elderly, and there was no significant difference in outcomes between the elderly and the young.[14-16] While the present findings are comparable to those in the literature, it may be subject to Type 2 sampling error given the sample size and the low probabilities of major adverse events, with only one patient in each cohort (age above or below 75 years) suffering from in-hospital death.

Another consideration for an increased length of stay in elderly patients was the reduced use of a laparoscopic approach, which reduces postoperative pain, improves functional recovery and shortens hospital stay.[17-18] In the present study, elderly patients were more likely to be selected for open surgery partly due to relative contraindications to a laparoscopic approach relating to their co-morbidities.

Despite an increased length of stay, there was no significant difference in the functional recovery of an elderly patient under an enhanced recovery program. They had similar average day of first flatus and first mobilization as their younger cohort. This suggests that the elderly derive a comparable benefit from enhanced recovery measures. Furthermore, what differentiate elderly patients from their younger counterparts is their own expectations when they agree to undergo surgery. Long-term survival is often not as important as a return to pre-morbid function and the retention of functional independence.[19] The application of ERAS protocols to reduce functional impairment after surgery could have an even greater significance in the elderly population.

CONCLUSION

Compared to a younger patient, an elderly patient may develop increased complications or require a longer duration of hospitalization if they have increased co-morbidities or a higher ASA score. Nevertheless, this study has shown that elderly patients achieve comparable functional recovery under an enhanced recovery approach. Enhanced recovery after surgery should be adopted regardless of a patient's age.

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