

# Should we resect colorectal cancer in patients over the age of 85?

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October 20, 2020

## Abstract

**Rationale, aims and objective** The prevalence of colorectal cancer in the elderly is increasing with older patients undergoing surgery. The aim of the study was two-fold: to evaluate the post-operative outcomes for patients [?] 85 years old following colorectal cancer resection as well as evaluating the outcomes of laparoscopic resection of colorectal cancer in patients over 85. **Methods** The study was divided into two parts. For part one, patients were divided into two groups based on age: those age [?] 85 years old and those aged 75-84 years old. Short term surgical outcomes and clinicopathological features were compared using appropriate parametric and non-parametric testing. For part two, patient's over 85 years old were divided into two groups based upon operative technique: laparoscopic vs open colorectal resection. Short-term post-operative outcomes of each approach were assessed. **Results** The median length of stay (LOS) between patients over 85 and those aged 75-85 was eight days, with no statistically significant difference in LOS between the groups ( $p=0.29$ ). No significant difference was identified between the older and younger groups with regards to severity of complications ( $p=0.93$ ), ASA grading ( $p=0.43$ ) or 30-day mortality (2 vs 2%,  $p=0.96$ ). Patients over 85 who underwent laparoscopic colorectal resection were compared to those who underwent an open resection. The median length of stay between the group was similar (8 vs 9 days respectively) with no significant difference in length of stay ( $p=0.18$ ). There was no significant difference in 30-day mortality rates (0% vs 9%,  $p=0.063$ ) or severity of complication grades ( $p=0.46$ ) between the laparoscopic and open surgical groups. **Conclusion** No significant short term surgical differences were identified in patients [?] 85 years old when compared to those 75-85 years old. There is no difference in short term surgical outcomes between laparoscopic or open colorectal resections in patients over 85.

## Should we resect colorectal cancer in patients over the age of 85?

Colorectal surgery in the elderly

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The corresponding author has not received funding nor a research scholarship for this project.

This article is not based on any previous communication at a society or meeting

**Key Words:** Aged, Colorectal Neoplasms, General Surgery, Atrial Laparoscopy, Open Abdomen Techniques

## Introduction

The elderly population is increasing worldwide. In Australia, people over the age of 65 makes up 15% of the population while those aged over 85 make up 2.1% of the population<sup>1</sup>. Colorectal cancer is a leading cause of morbidity and mortality in the western world with incidence rates steadily increasing in the elderly.

Historically, there was an adopted view amongst clinicians that the peri-operative risks were too high for those at the extremes of age, with older patients being offered less aggressive and palliative oncological treatments<sup>2</sup>. However, evidence is starting to favour surgical intervention for colorectal cancer<sup>3</sup> in select patients at the extremes of age. Previous studies have investigated the outcomes of colorectal resection in different age ranges (over 75's, over 80's ect) and demonstrated favourable results, however there is a paucity of information on the role of colorectal cancer resection specifically in those over 85 (commonly referred to as "the oldest old")<sup>4</sup>.

The question of laparoscopic surgery vs open surgery in the elderly population has also been explored with several randomised control trials demonstrating favourable outcomes in 'elderly patients'<sup>5,6</sup>. Once again, many of these studies focus on patients in the 6<sup>th</sup> and 7<sup>th</sup> decade of life, with a scarcity of studies investigating laparoscopic outcomes in those over 85<sup>7,8</sup>.

In order to compare the short-term outcomes from surgery, post-operative complications must be assessed and compared. In previous studies, there has been a lack of consistency in grading complications. Terms such as 'mild', 'moderate' and 'severe' have been inconsistently used and compared, leading to bias. The Clavien-Dindo classification of post-operative complications has been shown to provide a reproducible and objective classification of post-surgical outcomes. The classification is based upon the severity and required treatment for each complication grade and is graded from grade I-V with Grade V being mortality, the gravest of complications. The classifications have been widely used to standardise outcomes in a variety of surgical subspecialties<sup>9-11</sup>.

The aim of this study is two-fold: to investigate the short-term outcomes of patients over the age of 85 undergoing colorectal cancer resection and the use of laparoscopic colorectal cancer resection in those over the age of 85.

## Methods

### *Study Design and Data Source*

A single institution, retrospective study of patients undergoing colorectal cancer surgery at The Prince Charles Hospital.

Patients were divided in two age groups in order to assess the short-term outcomes of patients over 85. The comparison group was chosen to be those between 75-84 years of age. The demographic features, comorbidities, surgical characteristics, short-term outcomes and complications were compared between the two groups.

For the second aim of the study, patients over the age of 85 who underwent laparoscopic colorectal surgery were compared to those who underwent open surgery.

Patient charts were individually reviewed and data extracted by trained medical personnel. Data was obtained from previous admissions, current admissions as well as correspondence letters, follow up documentation and outpatient/readmission notes.

Inclusion criteria included those who underwent surgical resection of biopsy proven colorectal cancer at The Prince Charles Hospital between January 2010 and December 2018. Patients were excluded if they had endoscopic resection of the malignant lesion without surgical intervention.

### *Demographic and comorbidity characteristics*

Basic demographic data including age, gender, date of birth, height, weight, body mass index (BMI) and American Society of Anaesthesiologists (ASA) grade was documented. Specific pre-operative conditions were grouped into comorbid groups and documented for each patient: cardiovascular (ischemic heart disease, previous coronary artery bypass grafting, previous percutaneous coronary intervention, pacemaker insertion, defibrillator insertion, previous valve repair, heart failure, cardiomyopathy, hypertension, pulmonary hypertension and atrial fibrillation), respiratory (asthma, COPD, bronchiectasis, cystic fibrosis and obstructive sleep apnoea), metabolic (type I diabetes, type II diabetes and hyperlipidaemia), autoimmune (rheumatoid arthritis, psoriasis, polymyalgia rheumatica, and systemic lupus erythematosus) and renal disease.

### *Surgical and pathological features*

Surgical data included the operation performed, urgency of surgery, operative approach, and length of stay (LOS). Pathological data included tumour histopathology, histological grade and TNM stage of disease.

### *Short term post-operative outcomes*

Short term outcomes reviewed included complications, 30-day mortality and length of stay. Complications were Graded from I to V according to the Clavien-Dindo Classification of surgical complications (Appendix I).

Post-operative complications were defined as those that arose up to 14 days post-operatively.

### *Statistical analysis*

Differences in demographic features, comorbidities and surgical/pathological features between the two complication groups were assessed using t-tests, chi squared test and Fisher's exact tests as appropriate. Statistically significant results were defined as those with p value  $\leq 0.05$ . Data was analysed with Stata v14 software (StataCorp).

Ethics approval for this database was granted by the Prince Charles Hospital Human Research Ethics Committee (Reference: HREC/17/QPCH/295).

## **Results**

### *Patient demographics*

From January 2010 to December 2018, five hundred and thirty-three patients underwent colorectal cancer resection at our institution. No patients were excluded from the study. One hundred and thirty-six patients were aged between 75-85 years old at the time of surgery. Forty-eight patients were aged 85 or above at the time of surgery. These two groups were compared with the demographic features of each group outlined in Table 1.

The distribution of ASA grading was similar between the two groups, with no significant difference in distribution or prevalence. Hypertension was the most common cardiac comorbidity in both groups (75-85 age group, 63% vs 85+ age group, 71%,  $p=0.38$ ) with coronary artery bypass grafting being more prevalent within the 75-85 years old group (15% vs 11%,  $p=0.025$ ). There was also a significantly higher proportion of women in the over 85 group (69% vs 51%,  $p=0.043$ ). There was no significant difference between the two groups with regards to distribution of other cardiac comorbidities.

Asthma (15% vs 8 %,  $p=0.33$ ), COPD (16% vs 8%,  $p=0.23$ ) and obstructive sleep apnoea (7% vs 0%,  $p=0.066$ ) in both groups were not statistically different. There was no significant difference in metabolic or autoimmune comorbidities between the two groups. Those in the 85+ group had a higher incidence of renal disease (pre-operative eGFR less than 60) compared to those in the 75-85 year old group (25% vs 46%,  $p=0.007$ ).

### *Surgical and pathological characteristics*

The surgical and pathological characteristics of the cohort is outlined in Table 2. The majority of colorectal cancer resections in both age groups were urgent procedures that occurred within 30 days of diagnosis (75-85 age group, 74% vs 85+ age group, 79%,  $p=0.35$ ). Laparoscopic procedures were more common in both groups (67% vs 77%,  $p=0.50$ ) when compared to open procedures. Both age groups demonstrated a high number of right sided colon cancers (61% vs 73%,  $p=0.24$ ), with no significant difference in cancer locations between the two groups. In keeping with tumour location, the most common surgical procedure in both groups was a right hemicolectomy (59% vs 71%,  $p=0.49$ ).

For the majority of cases in both groups, histopathological analysis identified adenocarcinoma of no special type (86% vs 79%,  $p=0.46$ ) with a low histological grade of cancer (72% vs 72%,  $p=1.0$ ). There was no significant difference between groups with regards to stage of disease at time of surgery. In both groups, the most common stage of cancer progression at time of surgery was Stage IIa (29% vs 23%,  $p=0.57$ ).

### *Complications*

Patients within both groups experienced a variety of complications which are outlined in Table 4. The most common complication in both groups was a prolonged ileus (75-85 age group, 17% vs 85+ age group, 11%). There was a particularly high number of patients in the 75-85 years old group with cardiac arrhythmias (13% vs 5%) when compared to the older group. However, there was a higher percentage of abdominopelvic collections (2% vs 8%) and incidences of respiratory failure (3% vs 8%) in the over 85's group.

### *Short Term Outcomes*

The median length of stay in the 75-85 year age group and the 85+ year age group was the same at 8 days (Table 3). There was a non-statistically significant increase in the proportion of patients who stayed longer than 14 days in the 85+ year age (29% vs 38%,  $p=0.29$ ). However, the 30-day mortality was the same between both groups (2% vs 2%,  $p=0.96$ ). There was also a very similar distribution of post-operative complications between both groups. Thirty seven percent of patients in the 75-85 year old group had no complications which is similar to the thirty-five percent in the over 85's group.

There was a similar incidence of high-grade complications (Clavien-Dindo Grade >III) between the two groups (22% vs 16%) however this difference was not statistically significant ( $p=0.93$ ).

### *Open vs Laparoscopic surgery in the over 85 group*

Patients over the age of 85 were analysed as to which surgical approach was used (Table 5). Forty-eight patients over the age of 85 underwent surgical resection. Eleven patients had an open procedure (23%) while thirty-seven had a laparoscopic procedure (77%).

The median length of stay between the open and laparoscopic groups was similar at 9 and 8 days respectively. The percentage of patients whose stay was over 14 days was higher in the open technique group (open group, 55% vs laparoscopic group, 32%,  $p=0.18$ ). The 30-day mortality between the groups was also similar (9% vs 0%,  $p=0.063$ ). Open procedures were more likely to be emergency surgical procedures (6/11, 55% vs 3/37, 8%,  $p=0.002$ ).

There were no major differences in the distribution of the Clavien-Dindo grading or severity of complications between the two groups ( $p=0.46$ ). High-grade post-operative complications occurred in 9% of open procedures compared to the 6% of laparoscopic procedures.

## **Discussion**

The results of our study demonstrate that there is no significant difference between the short-term surgical outcomes between patients over 85 and those 75-85 years old who undergo colorectal cancer resection in terms of median length of stay, grading of complications and 30-day mortality. The results also indicate that the short-term outcomes from laparoscopic resection in those over 85 are similar to those of open surgery. This study is one of the first studies to utilise the Clavien-Dindo grading of complications for the assessment of short-term outcomes in this demographic.

Kunio et al.<sup>12</sup> examined a similar cohort of patients (75-85 year old's vs over 85 year old's) and compared the same three short-term outcomes following colorectal cancer surgery. The results stipulated that patients over 85 years old have a significantly higher mortality when compared to those in the 75-84 year old group (24% vs 9%,  $p=0.048$ ). However, there was no significant difference in length of stay or post-operative complications. The paper investigated the prevalence of specific complications (such as 'pulmonary complications' or 'anastomotic leak'). They demonstrated a higher incidence of pulmonary complications in the 85+ population but no other remarkable differences in complications. This study concluded that the mortality rate was higher for the 85+ population but interestingly our data demonstrates similar post-operative mortality rates between the groups.

The decision to perform a colorectal surgical resection in those over 85 is based on numerous factors including patient preference, disease stage, patient comorbid status and frailty. Although our patients over 85 have a similar comorbid burden to those aged 75-85, this may not reflect a patient's frailty which can play a large part in determining therapy for a patient. Certain surgical scales of frailty such as the Modified Frailty Index have been shown to predict mortality in general surgical procedures<sup>13,14</sup> for patients over 60. Unfortunately frailty scales are rarely utilised by colorectal surgical teams but can play a large role as a factor in determining whether to offer surgery.

From our research we can conclude that the short-term outcomes from surgery in the over 85 year old's group are comparable to those who are 75-85 year old. This should serve to support surgical intervention in appropriate patients over 85.

Despite the increasing use of laparoscopic surgery for colorectal cancer resections, there is a paucity of information on its use in patients at the extremes of age. As demonstrated in Table 5, there were no significant differences in the length of stay, 30-day mortality or grading of complications between open and laparoscopic procedures in those aged over 85.

There was a significantly higher proportion of open procedures for emergency operations (55% vs 8%,  $p=0.002$ ). This is understandable as the open approach affords ease of access, manoeuvrability and manipulation of distended or friable bowel in the setting of a bowel obstruction or perforation. Decisions on surgical approach are based upon multiple factors including urgency, anatomical considerations, surgeon expertise and personal preference. In general, there is a higher proportion of laparoscopic procedures performed on those aged over 85 at our institution.

These results demonstrate that there is no difference in short term outcomes between a laparoscopic or open approach in those over 85. This conclusion is supported by research from Francesc et al.<sup>15</sup> who demonstrated that laparoscopic approaches in those over 85 are not associated with an increase in morbidity or length of stay.

It should be noted that patients who underwent surgery in this study and those included within this cohort are those that were deemed appropriate candidates for surgery. There may have been patients who were too comorbid or frail for surgery who did not proceed with a surgical resection.

Colorectal cancer resection should be offered to appropriate patients, regardless of age. The short-term outcomes of those over 85 years old are not different to those aged 75-85 and demonstrate that age alone should not be a determining factor.

Our research also shows that laparoscopic resection of colorectal cancer has equitable short term post-operative outcomes to open resections.

## References

1. Australian Bureau of Statistics. *Australian Historical Population Statistics*. Canberra: ACT; 2016.
2. Hardiman KM, Cone M, Sheppard BC, Herzig DO. Disparities in the treatment of colon cancer in octogenarians. *Am J Surg*.2009;197(5):624-628.

3. Nakamura T, Sato T, Miura H, et al. Feasibility and outcomes of surgical therapy in very elderly patients with colorectal cancer. *Surg Laparosc Endosc Percutan Tech.* 2014;24(1):85-88.
4. Crews DE, Zavotka S. Aging, disability, and frailty: implications for universal design. *J Physiol Anthropol.* 2006;25(1):113-118.
5. Guillou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet.* 2005;365(9472):1718-1726.
6. Veldkamp R, Kuhry E, Hop WC, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol.* 2005;6(7):477-484.
7. Fugang W, Zhaopeng Y, Meng Z, Maomin S. Long-term outcomes of laparoscopy vs. open surgery for colorectal cancer in elderly patients: A meta-analysis. *Mol Clin Oncol.* 2017;7(5):771-776.
8. Shigeta K, Baba H, Yamafuji K, et al. Effects of laparoscopic surgery on the patterns of death in elderly colorectal cancer patients: competing risk analysis compared with open surgery. *Surg Today.* 2016;46(4):422-429.
9. Garcia-Garcia ML, Martin-Lorenzo JG, Liron-Ruiz R, Torralba-Martinez JA, Garcia-Lopez JA, Aguayo-Albasini JL. Perioperative complications following bariatric surgery according to the clavien-dindo classification. Score validation, literature review and results in a single-centre series. *Surg Obes Relat Dis.* 2017;13(9):1555-1561.
10. Téoule P, Bartel F, Birgin E, Rückert F, Wilhelm TJ. The Clavien-Dindo Classification in Pancreatic Surgery: A Clinical and Economic Validation. *J Invest Surg.* 2019;32(4):314-320.
11. Kishida N, Hibi T, Itano O, et al. Validation of Hepatectomy for Elderly Patients with Hepatocellular Carcinoma. *Ann Surg Oncol.* 2015;22(9):3094-3101.
12. Ng O, Watts E, Bull CA, Morris R, Acheson A, Banerjee A. Colorectal cancer outcomes in patients aged over 85 years. *Ann R Coll Surg Engl.* 2016;98(3):216-221.
13. Farhat JS, Velanovich V, Falvo AJ, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg.* 2012;72(6):1526-1530.
14. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. *J Surg Res.* 2013;183(1):104-110.
15. Vallribera Valls F, Landi F, Espín Basany E, et al. Laparoscopy-assisted versus open colectomy for treatment of colon cancer in the elderly: morbidity and mortality outcomes in 545 patients. *Surg Endosc.* 2014;28(12):3373-3378.

## Acknowledgments:

Nil

## Conflicts of Interest :

None of the authors of this publication have any conflicts of interest to declare.

## Figures:

Nil

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