

Colorectal cancer surgery in the very elderly patient: A systematic review of laparoscopic versus open colorectal resection.

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Keywords: “Laparoscopic colorectal surgery”, “Elderly”, “Colorectal cancer”, “Systematic Review”

Abstract

Introduction: Colorectal cancer is the second most common cause of death from neoplastic disease in men and third in women of all ages. Globally, life expectancy is increasing and consequently, an increasing number of operations are being performed on more elderly patients with the trend set to continue.

Elderly patients are more likely to have cardiovascular and pulmonary co-morbidities that are associated with increased peri-operative risk. They further tend to present with more locally-advanced disease, more likely to obstruct or have disseminated disease.

The aim of this study was to demonstrate the feasibility of laparoscopic colorectal resection in the very elderly patients, and the benefits over open surgery for colorectal cancer.

Methods: A systematic literature search was performed on Medline, Pubmed, Embase and Google Scholar. All comparative studies evaluating patients undergoing laparoscopic versus open surgery for colorectal cancer in the patients population over 85 were included.

The primary outcomes were 30-day mortality and 30-day overall morbidity. Secondary outcomes were: operating time, time to oral diet, number of retrieved lymph nodes, blood loss and 5-year survival.

Results: The search provided 1507 citations. 69 articles were retrieved for full text analysis and only 6 retrospective studies met the inclusion criteria. Overall mortality for elective laparoscopic resection was 2.92% and morbidity 23%. No single study showed a significant difference between laparoscopic and open surgery for morbidity or mortality but pooled data analysis demonstrated reduced morbidity in the laparoscopic group ($P=0.032$). Patients undergoing laparoscopic surgery are more likely to have a shorter hospital stay and a shorter time to oral diet.

Conclusion: Elective laparoscopic resection for colorectal cancer in the over 85 age group is feasible and safe and offers similar advantages over open surgery to those demonstrated in patients of younger ages.

Introduction:

Colorectal cancer is the second most common cause of death from neoplastic disease in men and third in women of all ages¹⁻³ with a peak incidence between the 7th and 8th decades⁴. Globally, life expectancy has increased and consequently an increasing number of operations are being performed on more elderly patients with the trend set to continue.

Elderly patients are more likely to have cardiovascular and pulmonary co-morbidities that are associated with increased peri-operative risk.⁵⁻⁸ In addition, elderly patients have been shown to present with more locally-advanced disease, more likely to obstruct or have disseminated disease at time of presentation.⁹⁻¹⁰ Age is an independent risk factor for both morbidity and mortality when adjusted for other co-morbidities.¹¹

Colorectal surgery has an increased risk of morbidity and mortality in the elderly population, with a direct correlation between risk and age, with the risk increasing according to the age, i.e. the oldest being further at risk¹². The benefits of laparoscopic colorectal resections over open surgery have been clearly demonstrated¹⁴⁻¹⁶ but in the elderly population the haemodynamic changes secondary to an increased intra-abdominal pressure caused by the pneumoperitoneum can be associated with post-operative complications¹³.

The aim of this study is to demonstrate the feasibility of laparoscopic colorectal resection in the very elderly patients, and the benefits over open surgery for colorectal cancer.

Methods:

Data sources and search strategy

After the development of a review protocol in compliance with the PRISMA guidelines for reporting systematic reviews¹⁷, two authors independently performed a comprehensive literature search of Medline, Pubmed, Embase and Google Scholar with no language, publication date or publication status restrictions.

An extensive search was conducted using the search terms in combination: “elective”, “colorectal cancer”, “laparoscopic surgery” and “elderly”. The last search was run on September 30th, 2015.

The reference list of the retrieved articles was searched to identify additional eligible studies.

Eligibility criteria and study selection

Inclusion criteria were as follows: (1) comparative studies evaluating patients undergoing laparoscopic versus open surgery for colorectal cancer in patient population over 85; (2) intention-to-treat analysis for the laparoscopic group (all procedures started laparoscopically were included in the laparoscopic group, even if converted); (3) complete follow-up data and losses clearly reported.

Studies including only hand-assisted, robotic and single incision laparoscopic surgery (SILS) patients were excluded. Indexed abstract of posters and podium presentations at international meetings were not included. Reviews were only checked to find further relevant studies, and when the same author and institution published the same case series in different articles, only the most recent paper was evaluated.

Two reviewers independently assessed the reports for eligibility at title and abstract level. In case of discrepancies, a third author was consulted and agreement was reached by consensus.

Data extraction, methodological quality appraisal and risk of bias assessment

Two authors independently retrieved the data from each included study filling an electronic database. For studies that reported insufficient data, the authors were contacted for further information, if no response was obtained after two reminders the study was excluded from the review.

The quality of the included studies was evaluated by the Newcastle-Ottawa Scale (NOS)¹⁸: on a scale of 9, a greater score was considered to be an indicator of better quality.

Outcome analysis:

The primary outcomes were 30-day mortality and 30-day overall morbidity. Secondary outcomes were: operating time, time to oral diet, number of retrieved lymph nodes, blood loss and 5-year survival.

Odds ratio (OR) and 95% confidence intervals (95% CI) were used as summary measures for dichotomous outcomes while Weighted Mean Difference (WMD) and 95% CI were used for continuous outcomes.

Statistical analysis was performed using STATA 12 statistical software (STATA Corp, College Station, Texas, USA).

Results:

Study selection:

The search of Medline, Pubmed, Embase and the Google Scholar provided 1507 citations, after exclusion of 1438 not relevant articles at title and abstract level, 69 full text articles were assessed for eligibility; 6 studies met the inclusions criteria. A flowchart is shown in Figure 1. No unpublished relevant studies were found.

All the included studies were retrospective. 5 were single centre studies,^{4,19-22} one was multicenter¹¹, 3 compared laparoscopic to open resection in the over 85 age group,^{19,20,22} 2 studies compared all colorectal resections between over and under 85 age groups.^{4,11} One study compared laparoscopic to open resections against multiple age groups²¹. The variables are displayed in *Table 1*.

Laparoscopic versus open:

Patient demographics:

3 studies reported no differences in the ASA grade between the two groups, while the fourth study did not report ASA grade, however no differences were demonstrated in comorbidities such as heart failure and diabetes ($P = 0.672$). In three studies, the open and laparoscopic groups were comparable for tumour stage while one study reported a significant difference, with less stage II and stage III patients in the laparoscopic group ($P = 0.009$). Two studies reported that the dimensions of the tumour were significantly larger in the open groups, ($P = 0.02$ and $P = 0.0371$).

Primary outcomes:

None of the studies demonstrated a significant difference in 30 day morbidity between the open and laparoscopic group. However, pooled data analysis demonstrated a significant

benefit for laparoscopic surgery (31/135 for the laparoscopic group, versus 54/157 for the open group, $P = 0.032$)

No difference was demonstrated in mortality. This was confirmed also at pooled data analysis (4/137 for the laparoscopic groups, 7/169 for the open groups, $p = 0.568$). The study results are shown in *Table 2* with pooled data and analysis displayed in *Table 3*.

Length of Hospital stay, Time to oral diet and postoperative analgesia:

All 4 studies¹⁹⁻²² reported length of hospital stay, two found no difference between the groups, the other two found significantly shorter hospital stay in the laparoscopic group ($P < 0.001$, $P = 0.0001$)^{20,22}. The mean length of stay varied between 10-20.2 days for laparoscopic and 15.4-21.7 for open. Pooled data showed an overall average stay of 13.1 and 18.9 days in the laparoscopic and open group respectively ($P < 0.0001$).

Two studies reported a significantly shorter time to oral diet in patients undergoing laparoscopic surgery, (means of 3.4 versus 4.2 days $P = 0.03$ and 2.7 versus 7.7 days, $P < 0.0001$)^{19,20}, while only one study assessed the use of postoperative analgesia showing a significantly reduced demand in the laparoscopic group ($P = 0.01$)¹⁹

Operating time and blood loss:

Of the three studies that measured length of operation all three found that laparoscopic surgery had statistically significantly longer operative times ($P < 0.01$, $P = 0.014$, $P = 0.0017$).^{19,20,22}

Intraoperative blood loss was less in the laparoscopic group in two studies, ($P < 0.001$, $P < 0.0001$)^{20,22}, while the third study demonstrated no differences.

Number of retrieved lymph nodes and 5 year survival:

Lymph node dissection was measured in three of the studies with varying results. One study found that significantly fewer lymph nodes were retrieved in the laparoscopic group, (means

of 11.4 versus 18.2, $P = 0.0181$),²² the other two studies found significantly more nodes were retrieved, ($P < 0.01, P = 0.032$).^{19,20}

Two studies reported 5 years survival demonstrating no difference in the two study populations.

Morbidity and Mortality in the over 85 patient population:

Two studies precisely compared morbidity and mortality for laparoscopic colorectal cancer resection in patients under the age of 85, and patients over the age of 85.^{11,21}

Pooled data analysis showed that the overall complication rate for all patients under 85 years old was 31.2% (142/455) and for the over 85 was 35.6% (32/90), ($P = 0.419$). Mortality in the under 85 age group was 4.2% (19/455) and 8.9% (8/90), ($P = 0.0597$) in the over 85.

Stepien et al⁴, compared a group of 94 patients over the age of 85, (mean = 88.9), with a random selection of 91 patients between the ages of 45-75, (mean = 56.4). They found that the older group presented with significantly more comorbidities ($P < 0.01$) and had a higher rate of emergency presentation (63%-34.1%) However this was for all surgical treatments and not specifically colorectal cancer. The study also showed a significant increase in rates of mortality in the older group ($P < 0.05$), but only for emergency admissions and not elective resection. Rates of overall complications for both emergency and elective admissions were found to be significantly different between the two groups, ($P < 0.01$). The study was unable to demonstrate any difference in length of hospital stay between the groups with a mean stay of 10.7 days in the older group versus 9.4 days in the control, ($P > 0.05$).

Jafadi et al¹¹, demonstrated a higher rate of co-morbidity in the over 85 age group using the "Elixhauser-Van Walraven co-morbidity score"²³, with the over 85 group demonstrating a mean score of 9 (SD 3). The study also showed that the over 85 group had a higher rate of emergency admission at 50.4% as compared to the other age groups. (45-64 = 29%, 65-69 = 29.6%, 70-74 = 31%, 75-79 = 34%, 80-84 = 39%.)

Similarly, this study found a significant increase in mortality rates ($P < 0.01$) when compared to the control group of 45-64 years old. The study then calculated the risk-adjusted in-hospital mortality with an odds ratio of 4.7 and confidence intervals (CI) 4.30-5.18.

Interestingly, the authors also found that over the 10 year observation period the overall rates

of mortality fell by an average of 6.6% per year with the over 85 age group having the highest rate of decreasing mortality at 9.1%.

The study also demonstrated a significant difference in mortality between the over 85 and the control age groups, ($P < 0.01$), and the risk-adjusted morbidity was calculated with the odds ratio of 1.96 (CI 1.89-2.03). Specific complications were also assessed and no difference in anastomotic leak, intra-abdominal abscess, intestinal fistula and ileus were demonstrated. However, other complications such as: acute renal failure, cardiac complications, respiratory failure, urinary tract infection and pneumonia were more commonly present in the over 85 group ($P < 0.01$). Finally the study acknowledges that the over 85 age group had the longest mean length of hospital stay at 12 days versus the control group at 9 days ($P < 0.05$).

Discussion:

The results of this study demonstrate that laparoscopic surgery is feasible and a safe alternative to open surgery in the very elderly. There were no reported differences in clinical outcomes between the two approaches. However there are no prospective randomised studies that have reported on this topic to date. Although there is limited information available regarding the most elderly groups of cancer resection, a trend towards reduced length of hospital stay, shorter time to oral diet and reduced 30-day morbidity has been demonstrated in our study. These preliminary data need to be confirmed in larger trials. On the basis of the results of our study it is possible to conclude that laparoscopic surgery for colorectal cancer is a safe option in the very elderly population aged over 85. This reflects current data of laparoscopic versus open surgery across all age groups even in high risk patients.²⁴

No significant difference in mortality has been demonstrated in laparoscopic versus open surgery in this patient population. Age in itself is an independent risk factor for mortality, however our study demonstrates a significant decrease in mortality over the past decade¹¹, which obviously reflects overall improvements and advances in healthcare, as well as more experience in the multidisciplinary management of an increasing aging population.²⁵ Our study has some limitations. The included studies have collected data over an extensive period of time that spans the introduction of laparoscopic colorectal resections. Moreover a tendency towards including more selected cases in the laparoscopic group was noted with that the larger tumours more likely to be resected via open surgery. However, as surgical experience

and confidence grows more difficult resections will be attempted laparoscopically³⁰. These operative outcomes will also improve with regards to length of operation and rate of conversion³¹.

As for the feasibility of surgery on the very old there is compelling evidence that we have yet to find an upper limit of age where elective resection becomes a non-viable option. Although age has been demonstrated as an independent risk factor for mortality separate from co-morbidity, this is across both elective and emergency admissions for open and laparoscopic surgery and is found to be 8%.¹¹ Not only is this set to improve based on the current trends but with regards to the laparoscopic studies examined the rates of mortality ranged from only 0-6.7%. It is important to have a robust pre-operative assessment to ensure that patient risk stratification can be accurately detailed and the risks of surgery discussed. Appropriate patient selection is even more important in achieving favourable clinical outcomes for this unique sub-group and involves a multidisciplinary approach between surgeons, anaesthetists and nursing colleagues. Pre-operative investigations and peri-operative planning with the use of high dependency and intensive care facilities is key to success.

Conclusion:

Elective laparoscopic resection for colorectal cancer in the over 85 age group is feasible and safe and offers similar advantages over open surgery to those demonstrated in patients of younger ages. This study demonstrates that advanced age must not be considered a contraindication to the laparoscopic approach.

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