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PERI-OPERATIVE OUTCOMES IN ELDERLY UNDERGOING MINIMALLY INVASIVE RIGHT HEMICOLECTOMY

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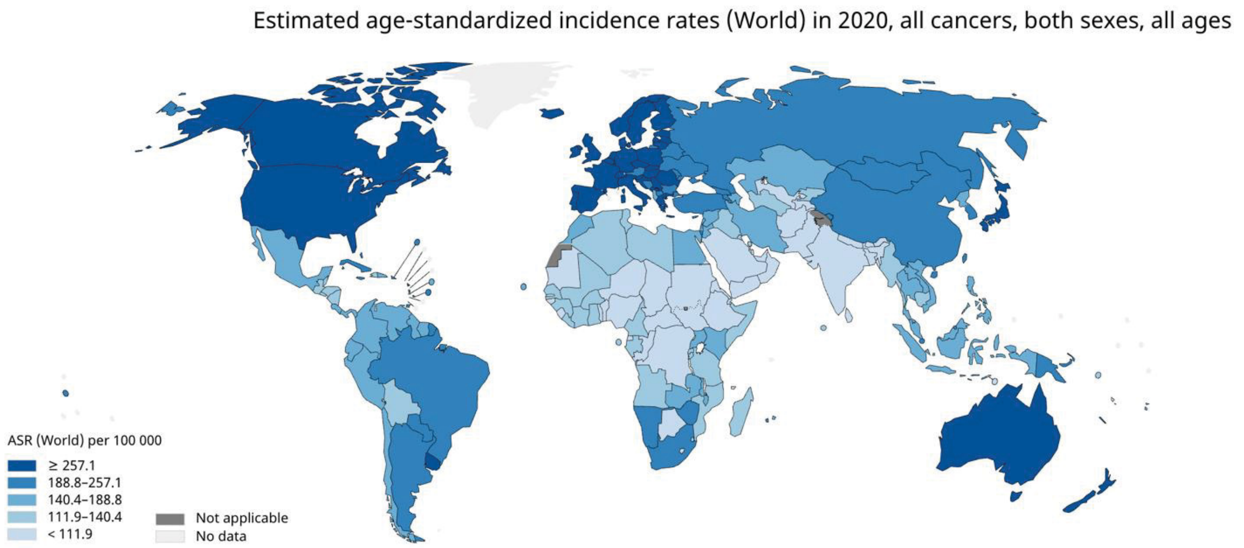
1. INTRODUCTION

1.a Epidemiology of colon cancer

Colorectal cancer (CRC) accounts for approximately 10% of all annually diagnosed cancers and cancer-related deaths worldwide. [1] It is the second most common cancer diagnosed in women and third most in men. [1-3]. With more than 600 000 deaths estimated each year, CRC is the fourth most common cancer-related cause of death globally.[2] In women, incidence and mortality are approximately 25% lower than in men. These rates also vary geographically, with the highest rates seen in the most developed countries (Figure 1). The growing incidence in some countries reflects a modification in lifestyle and its consequences related to 'Westernisation' such as obesity, physical inactivity, alcohol consumption, high red meat intake and cigarette smoking. [3, 4] Some data suggest a putative role in colon cancer carcinogenesis due to factors that cause imbalances in gut microbiota. [5, 6] As developing countries continue to advance, the incidence of colorectal cancer worldwide is predicted to increase to 2·5 million new cases in 2035. [2, 4] Stabilizing and decreasing trends tend to be seen in highly developed countries only. These have been primarily attributed to nationwide screening programs and increased uptake of colonoscopy in general, although lifestyle and dietary changes might also contribute. [6]

In Europe, the mortality rate is 15-20 per 100 000 in males and 9-14 per 100 000 in females and has decreased over time, particularly in females. The incidence in Italy in 2020 has been estimated to be around 45,000 new cases (24,000 in men and 21,000 in women) [7]. In affected European individuals, 5-year survival ranges from 28.5% to 57% in men and from 30.9% to 60% in women, with a pooled estimation in 23 countries of 46.8% in men and 48.4% in women.6 The risk of developing colon cancer depends on factors which can be classified into lifestyle or behavioural characteristics and genetically determined factors. Screening tests are modulated according to the individual probability of developing CRC. [6]



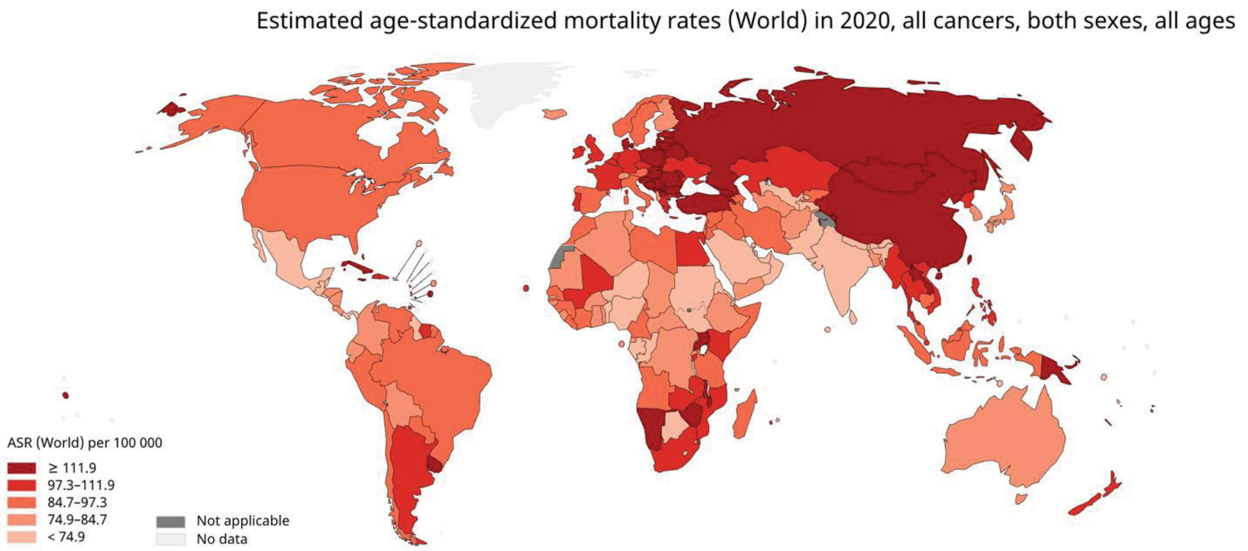
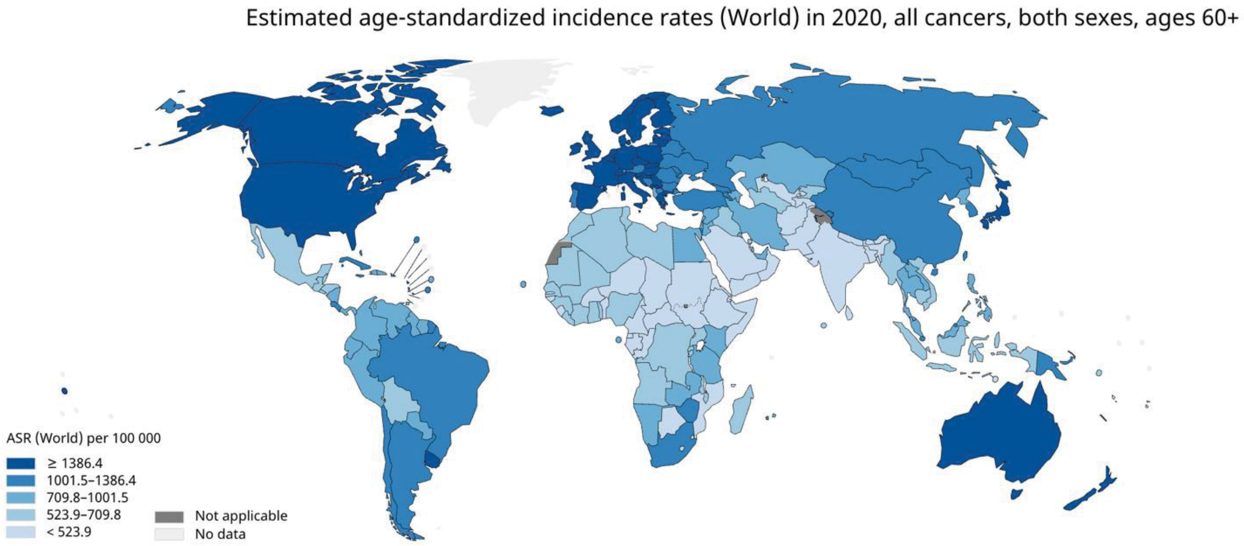


Figure 1 Data source: GLOBOCAN 2020 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization

Age is considered the major unchangeable risk factor for sporadic colon cancer: nearly 70% of patients are >65 years of age and this disease is rare before the age of 40 years, despite data from Western registries showing an increased incidence in the 40-44-year age group. [6] (Figure 2)

In contrast, a worrying rise in patients presenting with colorectal cancer younger than 50 years has been observed, especially rectal cancer and left-sided colon cancer. [6] Although genetic, lifestyle, obesity and environmental factors might have some association, the exact reasons for this increase are not completely understood. [6]



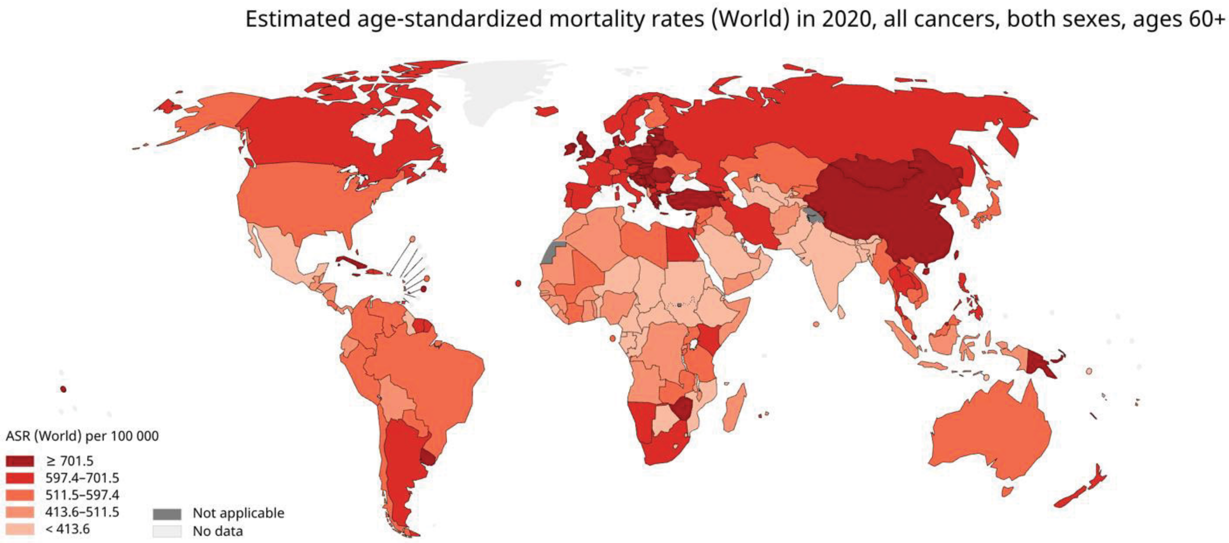


Figure 2 Data source: GLOBOCAN 2020 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization

1.b Epidemiology of ageing

The rising trend towards an ageing population ageing has been observed worldwide. This finding reflects the spread of better socio-economical conditions and a longer life expectancy.

According to the WHO estimates in 2019, the number of people aged 60 years and older was 1 billion. This number is expected to increase to 1.4 billion by 2030 and 2.1 billion by 2050. As a result, the elderly already constitute the majority of both colorectal cancer and surgical volume.

1.c Management of non-metastatic colon cancer

Surgery is the cornerstone of the management of CRC with curative intent treatment. Quality of colorectal cancer resection is crucial and can be assessed with objective parameters. [6]

Surgery for colon cancer has been optimized by the use of sharp dissection along the embryological planes within the mesofascial interface, according to the so called complete mesocolic excision principle. A still controversial topic is the extent of lymphadenectomy because no evidence shows the beneficial impact of extensive (D3) versus more limited (D2) dissection on oncological outcome and it might increase morbidity. [8]

The first laparoscopic colectomy was described by Jacobs in 1991 [9]. Laparoscopy has rapidly become the standard technique for colon cancer in many countries worldwide, with proven short-term benefits in randomized trials and population studies. Minimally invasive colorectal surgery has many advantages: small incisions, better aesthetic results, less postoperative pain, faster intestinal function recovery, shorter hospital stays, lower postoperative mortality and morbidity with similar oncological outcome compared to open surgery [10, 11]. However, laparoscopy has some intrinsic limitations such as two-dimensional (2D) visualization, reduced ergonomics in confined spaces, tremor effect and possible incoordination between the surgeon's eye and hand. [12, 13].

The robotic technique was developed through the evolution of conventional laparoscopy [12, 14]. The robotic technique for colorectal surgery was introduced in 2002 by Weber [14]. Robotic surgery provides several advantages such as three-dimensional (3D) high-definition vision, greater freedom and control on operating instruments, flexible wrists, and filtration of hand tremor to improve maneuverability and operative comfort [15].

1.d The use of minimally invasive techniques in elderly

With an increase in the elderly population, there will also be an increase in the number of elderly undergoing surgery for colon cancer. Elderly patients inherently have higher rates of frailty, and a higher associated risk of postoperative complications and healthcare utilization that drives higher costs [16-18]. Laparoscopic surgery for colorectal cancer in the elderly has been proven safe and feasible. However, the available literature on this topic is scarce and studies on current utilization, clinical, and financial advantages for colorectal cancer in the elderly are needed.

Keller et al in a recent national evaluation of the utilization, clinical, and financial outcomes for laparoscopic colorectal cancer surgery in the elderly, found that laparoscopy improved patient outcomes and costs, with lower index and readmission costs, shorter length of stay, and lower complication and readmission rates. [16]

Previous studies have supported the improvement in short-term outcomes that elderly colorectal cancer patients obtain with laparoscopy compared with the open approach, especially within an enhanced recovery protocol [18-22]. These benefits have been seen specifically in patients with pulmonary and cardiac comorbidities [23]. Previous studies have also revealed the advantages of laparoscopic surgery for faster recovery in the elderly, comorbid patients, with preservation of postoperative independence, a major consideration in this population

[24-27]. Recent published works have shown overall rates of minimally invasive surgery for curative rectal cancer between 50.1 and 55.3% and colon cancer between 44 and 52% in the USA [28-30], both with modest increases over time.

However, the rates increased slowly and have more recently declined, which has corresponded with a rise in open surgery, in other words, in the US, despite its proven advantages, the laparoscopic approach is used less than the open approach in the elderly.

There are several possible reasons for the disparity in use of laparoscopy for CRC in the elderly. The first is the influence of age itself; age has a major influence on the perception around different treatment modalities [31]. With limited literature regarding the impact, financial benefits, and advantages of laparoscopic surgery for colorectal cancer in the elderly population, there may be a reluctance to offer a laparoscopic approach to elderly patients [32].

Secondly, the lower use of laparoscopy as compared to open surgery in the adjusted cohorts is reported as a lack of education for surgeons and patients around the safety of laparoscopy in elderly patients. From the surgeon's standpoint, education is needed to dispel concerns of physiological and cardiorespiratory complications from surgical duration, positioning, and pneumoperitoneum to change the perception and increase application of laparoscopy [16, 21, 27].

A third reason is concerns around the perceived risks of laparoscopic colectomy in the elderly population in relation to age-associated increase in co-morbidities and significantly longer operative times, in addition to the unknown physiological effects that prolonged time under anaesthesia and CO_2 pneumoperitoneum have upon multiple co-morbid conditions in the elderly. [33]

In the literature, there are even fewer studies that evaluate the effects of robotic surgery in the elderly patient. Only one study compares robotic colorectal resection to laparoscopic colorectal resection surgery in elderly patients [13]. In this retrospective study, there are similar results between the two approaches in terms of operative and oncological outcomes, despite longer operative times for the robotic surgery [34]. Unlike previous studies, we considered surgeons with a proven record in both robotic and laparoscopic surgery.

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3. STUDY

3.a INTRODUCTION

The last few decades have witnessed an increasing incidence of colorectal cancer (CRC) worldwide, which has coincided with the general trend towards an ageing of population and longer life expectancy [1, 2].

The incidence of CRC in Italy in 2020 is estimated to be around 45,000 new cases (24,000 in men and 21,000 in women) [3]. Approximately 90% of new cases are diagnosed in patients older than 50 years, with 60% of whom are > 65 years old [4].

Surgical resection is the mainstay of the curative treatments for CRC. During the last 30 years, surgery for CRC has witnessed the introduction and development of new technologies and an increasing move towards minimally invasive techniques.

In the late 1990s to 2000s, laparoscopic surgery for CRC, and more recently robotic surgery, were widely adopted. Minimally invasive surgery has already been proven to be safe and feasible for CRC and has many advantages: small incisions, better aesthetic results, less postoperative pain, faster recovery of intestinal function, shorter hospital stays, lower postoperative mortality and morbidity, with similar oncological outcome compared to open surgery [8, 9].

Beyond these benefits, several studies demonstrate the advantages of minimally invasive colonic resections in improving short-term postoperative outcomes, such benefits are reported to be more advantageous to elderly patients than in younger patients [10-17].

However, although several studies revealed that the operative mortality in CRC surgery remains relatively low, the incidence of postoperative complications remains as high as 10–50% [18, 19].

In particular, elderly patients are expected to have more comorbidities, including cardiovascular disease, respiratory disease, and renal dysfunction, as compared to younger patients, and these could negatively affect the post-operative outcomes. Therefore, it is crucial to take into consideration the general condition of elderly patients on an individual basis to ensure the best choice of treatment strategy. Currently, because there are no detailed guidelines by age group, the treatment strategy for elderly patients with CRC depends on the policies of each institution and surgeon. When considering the clinical management of elderly patients, realising the impact of age and frailty on postoperative outcomes is important for guiding treatment decisions [20, 21, 22]. The aim of this study was to investigate the safety and feasibility of minimally invasive right hemicolectomy for elderly patients with colon cancer aged over 75 years by retrospectively comparing their operative outcomes with those of the non-elderly using a propensity score matching (PSM) model based on age and Charlson Comorbidity Index (CCI).

3.b MATERIALS AND METHODS

This is a multicenter retrospective study combining four prospectively maintained databases of consecutive patients undergoing elective right hemicolectomy between January 2013 and December 2020.

Patients undergoing right hemicolectomy in an emergent/urgent setting, for different indications other than malignant disease or with advanced metastatic disease were excluded. Resections were designated as emergent in patients who had been admitted with obstructed or perforated right colon cancer and were operated within 24 h of admission.

The primary endpoint of the study was to analyse the short-term postoperative results of minimally invasive right hemicolectomy in elderly patients. The incidence of major surgical complications, defined as Clavien-Dindo III-IV grade complications, represented the primary outcome. Secondary outcomes included risk factors for complications and prolonged operative time.

Patients were divided into three groups according to their age at the time of the operation: Group I (control group, < 60 years), Group II (>60-75), Group III (≧75). We decided to perform the comparative analysis censoring the data referring to the group of younger patients (Group I)

The patients were further divided according to the operative approach used: Laparoscopic (LrH) or Robotic (RrH) and Open resection (OrH).

Right hemicolectomy was defined as any resection extending from the cecum to, but without, the splenic flexure. Postoperative complications were classified as major surgical complications and major general complications, including infectious complications. Major surgical complications were defined as anastomotic leakage, or any complication required relaparotomy. Major general complications included cardiovascular complications (myocardial infarction, cardiac rhythm disturbances, heart failure, cerebral infarction, or pulmonary embolism), respiratory failure, or renal failure. Infectious complications included pneumonia and sepsis.

Post-operative complications were further grouped according to the Clavien Dindo classification [22]

Variables baseline demographic data (gender, Body Mass Index(BMI), American Society of Anaestesiologists (ASA) grade, Charlson Comorbidity Index (CCI), comorbidities, Previous abdominal surgery, CT location, size and stage of the tumour), intra-operative data (operative time, intra-operative complications, need and causes of conversion) and post-operative course (post-operative complications, time to flatus and length of stay) were investigated. Need for readmission and 90-days mortality were also included.

Similar datapoints were gleaned from patients undergoing open right hemicolectomy procedures in the same time period.

Statistical analysis

Data were processed using the MedCal statistical package (version 12.5). Qualitative variables were summarised by frequency and percentage, while non-normally distributed quantitative variables were described by the mean and standard deviation (SD). Student’s t-test and Fischer’s exact test were applied as appropriate. Statistical significance was determined ($P < 0.05$). Data were analysed on an intention to treat basis. Univariate and multivariate analyses were performed for the whole cohort to estimate the risk factors for prolonged operative time (> 180 minutes), general post-operative complications, and Clavien Dindo III complications. Gender, age, location of the tumour, BMI, intraoperative complications, tumor dimension and location and type of procedure were considered as independent factors for prolonged operative time.

Gender, age, location of the tumour, BMI, intraoperative complications, tumor dimension and location, conversion to open surgery and type of procedure were considered as independent factors for complications occurrence. Results were expressed as point and 95% confidence interval (95% CI) estimation of the odds ratios (OR).

3.c RESULTS

A total of 618 were included in the study. Of these, 267 (43.2%) were aged between 60 and 75 years, while 268 (43.4 %) were older than 75 years. The three groups statistically differed for the distribution of ASA group, Charlson score and comorbidities. The general characteristics are summarized in *Table 1*. According to the type of procedure, 337 (54.5) patients underwent LrH, 144 (23.3%) had a robotic procedure and in the remaining 137 (22.2%) an open approach was used.

These groups statistically differed for BMI (p=0.0079), location of the tumour at the pre-operative CT scan and size of the tumour (p=0.0140). (*Table 1)*

Analyzing the operative outcomes in patients aged > 60 years who had undergone a minimally invasive resection (LrH or RrH), there were no statistical differences for both operative time (p=0.148) and rate of intraoperative complications (p=0.938) between Group II and III. *(Table 2)*

An intracorporeal anastomosis was performed more frequently in the RrH group (p<0.0001).

Regarding the post-operative course, the age groups II and III did not differ for short term major surgical complications rate (p=0.392), nor for general major complications (13 Vs 8; p=0.380), no significative differences were noted in the incidence of Clavien Dindo III complications (8 vs 11; p=0.646). Class I and II complications according to Clavien-Dindo classification were higher in the age Group II. Length of hospital stay and readmission rate were comparable between the two groups (p=0.944 and p= 0.308 respectively). No mortality was observed. (*Table 3)*

None of the post-operative parameters analyzed differed when comparing LrH and RrH. (Table 3)

Mortality was not observed in the short term (within the first admission) nor in the long term (90 days after the operation). *(Table 3)*

When comparing patients aged > 60 who had undergone open or minimally invasive procedures (LrH/RrH) a statistically significant difference in intraoperative complications (6 vs 1; p=0.011) and estimated intra-operative blood loss (p=0.001) was observed. *(Table 4)*

The rate of post-operative complications was significantly higher in the OrH group (40 vs 82; p=0.22) considering both surgical and general complications (p= 0.039 and p<0.0001, respectively). Mortality at 90 days from the operation was observed in 5 patients (3.8%) in the OrH group. *(Table 4)*

Male gender and tumour location were identified as risk factors for prolonged operative time at univariate analysis but not in the multivariate analysis. Open procedures were associated with operative time >180 min in both univariate and multivariate analysis. *(Table 5)*

Conversion to open surgery resulted as a risk factor for complication occurrence *(Table 7)* and class III complications in both univariate and multivariate analyses *(Table 7),* while open procedure was a risk factor for Class III only at univariate analysis *(Table 7).*

3.d DISCUSSION

With the increasing trend towards an ageing population and prolonged life expectancy, the rate of CRC is expected to rise over the coming years. As a consequence, this will lead to a rise in the number of elderly patients needing surgical intervention for the management such neoplasia, with colorectal resection remaining the gold standard for treatment of non metastatic disease. In other words, the elderly constitute the vast majority of both colorectal cancer and surgical volume [21]

In recent years, thanks to improvement of anesthesiology and surgical technologies, indications for major surgery have also been extended to the elderly population [18]. However, it is generally expected for elderly people to have poorer post-operative outcomes compared to the younger population. Although elective surgery for colorectal cancer in the elderly generally has low perioperative mortality, the rates of postoperative complications are substantial, often exceeding 50%, and significantly higher than complication rates in non-elderly patients [18, 19, 21, 23, 24].

Older age is independently associated with having a complication [20, 25], and patients with preoperative frailty, functional impairment, and comorbidities have the highest risk of complications [25, 26]. Thus, there is a need to optimize outcomes for elderly colorectal cancer patients undergoing surgery.

Studies have shown that colorectal surgery in elderly patients is generally well tolerated although pre-morbid cardiopulmonary conditions do predispose to higher morbidity and mortality rates as compared to younger patients [26].

Laparoscopic colorectal resection is rapidly becoming the gold standard of treatment for both malignant and benign colorectal lesions [2,3,18]. The benefits of laparoscopy have been attributed to less post-operative pain, better pulmonary function and reduced stress response [27]. These outcomes are particularly important in elderly patients who are at higher risk of post-operative morbidity and mortality. However, there are concerns regarding the safety of laparoscopic surgery in elderly patients, mainly related to supposedly longer operative time [26] as well as physiological stresses associated hypercapnia, reduced venous return and increased peak airway pressure and decreased pulmonary compliance may all potentially increase the risk of cardiorespiratory complications [27].

Given the proven benefits of minimally invasive surgery, in the form of laparoscopic colorectal resection and more recently robotic resection, it seems reasonable to postulate that elderly patients could benefit from the advantages linked to these approaches more so than younger patients.

Several studies have described laparoscopic colectomy as safe and feasible in the elderly population [10-17]
However, the literature analysing short term outcomes of minimally invasive surgery in elderly people is scarce and there are several limitations. [18].

The first limitation is due to the definition of elderly. Though chronological age of 60 has been used as a discriminant, the general condition of the so called elderly according to this definition vary enormously. However, it is expected that number of comorbities and the general dysfunction associated with aging may vary enormously. Our study reflected the expectation of an increase in both ASA score and Charlson comorbity index in the oldest patient group. (Andrea puoi aggiun)

The second bias in the current literature is that the studied series are often hybrid dealing with both rectal and colonic resection, therefore, there is controversy over outcomes in this group. Roscio et al. compared patients over 80 years with those between 60 and 69 years and reported that complication rate after laparoscopic surgery for CRC was not significantly different [28]. Conversely, Kang et al. reported that the postoperative complication rates were significantly higher, and hospital stay was significantly delayed in the patients aged over 80 years. Moreover, they reported that age emerged as the only significant risk factor associated with the development of postoperative complications [29]. Bare et al. found that there is an association between older age and higher rate of pneumonia, sepsis, cardiac dysfuction, and organ failure (heart, renal, or respiratory) [17].

As it is known that left colonic resection are burdened by higher post-operative morbidity, we chose to analyze the post-operative outcomes of minimally invasive right hemicolectomy, being technically easier.

In this regard, Utsumi et al. comparing patients aged > 80 years to younger patients undergoing laparoscopic right hemicolectomy. They demonstrated that, although the median length of postoperative hospital stay in elderly patients was significantly longer than that of the non-elderly, it was not associated with a statistically significant difference in post-operative complication rate [18]. Conversely, in the Quyn et al analysis, LrH was associated with a significantly longer operative time compared to OrH. In our study, LrH was not associated with reduced post-operative morbidity or significantly shorter length of hospital stay [26]. Given the heterogeneity of the results available in the literature and the lack of conclusive guidelines on the choice of approach, surgical management depends on the local institution policies and on the surgeons experience. A recent study in the US demonstrated an increasing rate of laparoscopic surgery for CRC in the elderly until 2013, followed by a decline associated with increasing rates of open surgery. [21]

Another consideration raised, is the introduction and increased application of robotic surgery in colonic resection. [30, 31] The rationale of the introduction of robotics was to overcome the drawbacks that are intrinsic to laparoscopic surgery with the goal being better post-operative outcomes. [31] The superiority of robotics as compared to laparoscopic surgery in colorectal resection is yet to be demonstrated and its safety in the elderly population is uncertain.

In this study, no significant differences in the rate of overall postoperative complications with Clavien–Dindo classification grade III were observed. Importantly, the univariate analysis revealed that gender, tumor location, operation time, and conversion to open surgery, but not the age, were the significant risk factors for grade III or higher overall postoperative complications.

Moreover, there were no statistical differences between LrH and RrH in terms of intra-operative outcomes or post-operative course.

Conversely, comparing the post-operative outcomes of OrH in the same age group, there was a statistical difference in post-operative complication rate, with open procedure being a risk factor for a poorer post-operative course with an associated longer hospital stay.

These results suggest that indication for laparoscopic surgery should not be abandoned for elderly patients solely based on older age. Meanwhile, older people tend to have a variety of underlying conditions and poorer general health than younger people. Therefore, elderly patients need thorough care and pre-operative planning, including rehabilitation and palliative care considerations. The decision of optimal surgical procedure should be taken based on the individual patient condition, life expectancy, and patient's wishes and not specifically based on patient age.

The major limitation of the present study is the selection bias of the surgical approach because of the retrospective nature of this study despite using a PSM model.

In conclusion, laparoscopic surgery is considered technically safe in patients with right colon cancer in people aged over 60 and 75 years. The older age is not a risk factor for postoperative complications after laparoscopic colorectal cancer surgery.

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4. APPENDIX A (Tables)

Table 1. General characteristics of the studies population before performing the propensity score matching

Variables	Age groups (years) Before matching			*p*	Procedure group Before matching			*p*
	≤60 (n=83)	61-75 (n=267)	>75 (n=268)		LrH (n=337)	RrH (n=144)	OrH (n=137)	
Gender [m, n(%)]	50 (60.2)	152 (56.9)	124 (46.3)	0.0016	177 (52.5)	77 (53.5)	72 (52.5)	0.0079
BMI [mean, Kg/m²±SD]	25.6±4.5	26.05±4.3	25.47±4.2	0.168	26.4 ±4.44	24.9±3.51	25±4.63	0.0079
ASA group [n(%)]								
ASA I [n(%)]	29 (34.9)	54 (20.2)	44 (16.4)	0.001	60 (17.8)	45 (31.2)	22 (16)	0.145
ASA II [n(%)]	47 (56.6)	124 (46.4)	112 (41.8)	0.057	166 (49.2)	59 (40.9)	58 (42.3)	0.0765
ASA III [n(%)]	7 (8.4)	85 (31.8)	103 (38.4)	<0.001	105 (31.1)	39 (27.1)	51 (37.2)	0.0739
ASA IV [n(%)]	0	4 (1.5)	9 (3.3)	0.116	6 (1.8)	1 (0.7)	6 (4.4)	0.0896
CCI [mean ± SD]	3.2±1.57	4.2±1.75	5.2±2.23	0.085	4.6±2.07	4.9±1.89	4±2.23	0.2144
Cardiovascular disease [y, n(%)]	20 (24.1)	133 (49.8)	173 (64.5)	<0.001	167 (49.5)	69 (47.9)	90 (65.7)	0.138
Pulmonary disease [y, n(%)]	3 (1.12)	32 (12)	48 (17.9)	0.0025	49 (14.5)	13 (9)	21 (15.3)	0.0716
Neurocognitive disorder [y, n(%)]	2 (2.4)	11 (4.1)	33 (12.3)	0.0003	22 (6.5)	12 (8.3)	12 (8.7)	0.0385
Diabetes [y, n(%)]	5 (6)	49 (18.3)	46 (17.2)	0.0243	56 (16.6)	20 (13.9)	24 (17.5)	0.0356
Comorbidities >1 [y, n(%)]	22 (26.5)	117 (43.8)	162 (60.4)	<0.001	147 (43.6)	70 (48.8)	84 (61.3)	0.139
Albumin pre-op [g/dl, mean ± SD]	4.2 ±0.71	4.1±0.81	3.6±0.73	0.0656	4.1±0.74	4±0.83	3.4±0.76	0.0078
Tumour Location at CT scan [n(%)]								
Ascending colon [n(%)]	34 (40.9)	102 (38.2)	103 (38.4)	0.0187	137 (0.41)	52 (36.1)	49 (35.8)	0.0482
Cecum [n(%)]	37 (44.6)	108 (40.4)	106 (39.5)	0.0329	133 (39.5)	60 (41.7)	58 (42.3)	0.0260
Hepatic flexure [n(%)]	11 (13.2)	43 (16.1)	48 (17.9)	0.0412	53 (15.7)	28 (19.4)	21 (15.3)	0.0438
Transverse colon [n(%)]	1 (1.2)	14 (5.2)	11 (41)	0.0644	14 (4.1)	4 (2.8)	9 (6.5)	0.0634
Tumour size [cm, mean ± SD]	4.6±2.26	4.6±2.95	4.9±2.69	0.200	4.3±2.31	4.5±2.02	5.5±3.33	0.0140
Tumour p-stage [y, n(%)]								
pT 1/2 [y, n(%)]	54 (65.1)	151 (56.5)	131 (48.9)	0.110	171 (50.7)	92 (63.9)	74 (54)	0.0294
pT 3/4	29 (34.9)	116 (43.4)	137 (51.1)	0.110	166 (49.2)	52 (36.1)	63 (46)	0.0294
pN - [y, n(%)]	68 (81.9)	219 (82)	214 (79.8)	0.795	272 (35)	118 (81.9)	111 (81)	0.951
pN+ [y, n(%)]	15 (18)	48 (18)	54 (20.1)	0.795	65 (19.3)	26 (18)	26 (19)	0.951
Previous surgery [y, n(%)]	39 (47)	121 (45.3)	150 (56)	0.102	163 (48.4)	59 (41)	88 (64.2)	0.160

°ASA=American Society of Anesthesiologists; BMI= body mass index; SD=standard deviation; CCI= Charlson Comorbidity Index

Table 2. Operative outcomes for patients aged > 60 according to age group and type of procedure (RrH or LrH)

Variables	Age groups (years)		p	Procedure group		p
	61-75 (n=211)	>75 (n=193)		LrH (n=292)	RrH (n=112)	
Operative Time [min, mean ± SD]	127.7±38.04	122.5±33.75	0.1488	121.4±36.51	135.2±33.16	0.005
Inta-operative Complication [y, n(%)]	1 (0.47)	2 (1.03)	0.938	3 (1.03)	0	0.667
Type of intraoperative complications						
Bleeding [y, n(%)]	1 (0.47)	2 (1.03)	0.938	3 (1.03)	0	0.667
Estimated Blood loss [ml, median ± SD]	0 ± 87.73	0 ± 154.18	0.612	0 ± 150.61	0 ± 18.90	0.127
Type of anastomosis [y, n(%)]						
Intracorporeal [y, n(%)]	84 (39.8)	59 (30.56)	0.082	49 (16.78)	94 (83.92)	<0.0001
Extracorporeal [y, n(%)]	127 (60.19)	134 (69.43)	0.061	243 (83.21)	18 (16.07)	<0.0001
Hand sewn [y, n(%)]	70 (33.17)	81 (41.96)	0.097	145 (49.65)	5 (4.46)	<0.0001
Stapled [y, n(%)]	141 (66.82)	112 (58.03)	0.097	147 (50.34)	107 (95.53)	< 0.0001
Resection of adjacent organs [y, n(%)]	8 (3.79)	13 (6.73)	0.369	14 (4.79)	7 (6.25)	0.700
Conversion [y, n(%)]	14 (0.63)	21 (0.88)	0.157	28 (9.58)	7 (6.25)	0.329
Reasons for conversion [y, n(%)]						
Adhesions [y, n(%)]	11 (5.21)	17 (8.80)	0.173	23 (7.87)	6 (5.35)	0.518
Size of the lesion [y, n(%)]	2 (0.94)	0	0.499	1 (0.34)	1 (0.89)	0.478
Visceral fat [y, n(%)]	0	2 (1.03)	0.227	2 (0.68)	0	ns
Bleeding [y, n(%)]	1 (0.47)	2 (1.03)	0.608	3 (1.03)	0	0.563

Table 3. Post-operative outcomes for patients aged > 60 according to age and type of procedure (RrH or LrH)

Variables	Age groups (years)		*p*	Procedure group		*p*
	61-75 (n=211)	**>75 (n=193)**		**LrH (n=292)**	**RrH (n=112)**	
PC° [y, n(%)]	40 (18.9)	42 (21.8)	0.901	58 (19.9)	24 (21.4)	0.782
>1 PC° [y, n(%)]	5 (2.4)	7 (3.6)	0.562	8 (2.7)	4 (3.6)	0.744
Major surgical complications [y, n(%)]	13 (6.2)	8 (4.1)	0.380	37 (12.7)	20 (17.8)	0.201
Leak [y, n(%)]	7 (3.3)	3 (1.5)	0.344	8 (2.7)	2 (1.8)	0.729
Abscess [y, n(%)]	4 (1.9)	1 (0.5)	0.375	4 (1.4)	1 (0.9)	ns
Bleeding [y, n(%)]	2 (9.5)	4 (2)	0.427	3 (1)	3 (2.7)	0.376
Major general complications y, n(%)]	24 (11.4)	33 (17.1)	0.115	45 (15.4)	14 (12.5)	0.530
Wound infection [y, n(%)]	1 (0.5)	3 (1.5)	0.347	3 (1)	1 (0.9)	ns
Pneumonia [y, n(%)]	2 (0.9)	1 (0.5)	ns	2 (0.7)	1 (0.9)	ns
Intrabdominal fluid collection [y, n(%)]	1 (0.5)	0	ns	1 (0.3)	0	ns
Cardiovascular complications [y, n(%)]	1 (0.5)	3 (1.5)	0.352	3 (1)	1 (0.9)	ns
Anaemia [y, n(%)]	19 ()	15 ()	0.585	24 ()	10 ()	0.770
Urologic complications [y, n(%)]	0	5 (2.6)	0.024	4 (1.4)	1 (0.9)	ns
Temperature >38° [y, n(%)]	2 (0.9)	2 (1)	ns	4 (1.4)	0	0.579
Other [y, n(%)]	0	4 (2.1)	0.051	4 (1.4)	0	0.579
Clavien-Dindo I [y, n(%)]	14 (5.2)	0	0.0001	7 (2.4)	7 (6.2)	0.070
Clavien-Dindo II [y, n(%)]	39 (1.5)	0	<0.0001	18 (1.6)	21 (1.9)	0.0002
Clavien-Dindo III [y, n(%)]	8 (3.1)	11 (4.1)	0.646	15 (5.1)	4 (3.6)	0.608
Clavien-Dindo IV [y, n(%)]	0	1 (0.5)	0.477	1 (0.3)	0	ns
Reoperation [y, n(%)]	10 (4.7)	7 (3.6)	0.630	14 (47.9)	3 (2.7)	0.290
Blood transfusion [y, n(%)]	29 (13.7)	27 (14)	ns	38 (13)	18 (16.1)	0.424
Time to flatus [days, mean±SD]	2.6±1.23	2.7±1.34	0.440	2.7±1.29	2.5±1.25	0.103
Time to regular diet [days, mean±SD]	4.2±1.44	4.2±1.79	0.386	4.2±1.70	4.2±1.40	0.973
Length of hospital stay [days, mean±SD]	7.9±12.12	8±4.42	0.944	8.3±10.8	7.3±2.8	0.340
Readmission [y, n(%)]	6 (2.8)	10 (5.2)	0.308	14 (4.8)	2 (1.8)	0.253

°PC= post-operative complications; SD= standard deviation; y= yes

Table 4. Operative outcomes in open procedures (OrH) compared to minimally invasive approaches (LrH/ReH) according for patients aged > 60 years

Variables	Age groups (years)		*p*	Procedure group		*p*
	61-75 (n=267)	**>75 (n=268)**		**OrH (n=131)**	**LrH/RrH (n=404)**	
Operative Time [min, mean ± SD]	129.2±38.73	122.2±37.8	0.0364	127.3±44.92	125.2±36.11	0.590
Intra-operative complications [y, n(%)]	5 (1.9)	2 (0.7)	0.285	6 (4.6)	1 (2.5)	0.011
Type of intraoperative complications						
Bleeding [y, n(%)]	4 (1.5)	2 (0.7)	0.450	5 (3.8)	1 (2.5)	0.002
Duodenal injury	1 (0.4)	0	0.499	1 (0.8)	0	0.221
Estimated Blood loss [ml, median ± SD]	22.4±115.9	48.4±210.8	0.133	79.1±253.3	19.5±125.8	0.001
Type of anastomosis [y, n(%)]						
Hand sewn [y, n(%)]	97 (36.3)	115 (42.9)	0.092	62 (47.3)	150 ()	0.012
Stapled [y, n(%)]	168 (62.9)	149 (55.6)	0.107	64 (48.8)	254 (52.8)	0.0002
No anastomosis [y, n(%)]	2 (0.8)	3 (1.1)	ns	5 (3.8)	0	0.0008
Resection of adjacent organs [y, n(%)]	17 (6.4)	18 (6.7)	ns	14 (10.7)	21 (5.2)	0.067

Table 5. Post-operative outcomes in open procedures compared to minimally invasive approaches (LrH/ReH) according for patients aged > 60 years

Variables	Age groups (years)		p	Procedure group		p
	61-75 (n=267)	>75 (n=268)		OrH (n=131)	LrH/RrH (n=404)	
PC° [y, n(%)]	54 (20.2)	68 (25.4)	0.180	40 (30.5)	82 (20.3)	0.022
>1 PC° [y, n(%)]	7 (2.6)	14 (5.2)	0.180	9 (6.9)	12 (2.9)	0.066
Major surgical complications [y, n(%)]	15 (5.6)	20 (7.5)	0.484	14 (10.7)	21 (5.2)	0.039
Leak [y, n(%)]	9 (3.4)	10 (3.7)	0.819	9 (6.9)	10 (2.5)	0.050
Abscess [y, n(%)]	5 (1.9)	1 (0.4)	0.215	1 (1.7)	5 (1.2)	ns
Bleeding [y, n(%)]	1 (0.4)	9 (3.3)	0.0105	4 (3)	6 (1.5)	0.533
Major general complications [y, n(%)]	57 (21.3)	63 (23.5)	0.604	60 (45.8)	59 (14.6)	<0.0001
Wound complications [y, n(%)]	3 (1.1)	6 (2.2)	0.337	5 (3.8)	4 (0.9)	0.050
Anaemia [y, n(%)]	36 (13.5)	31 (11.6)	0.516	33 (25.2)	34 (8.4)	<0.0001
Pneumonia [y, n(%)]	2 (0.7)	1 (0.4)	0.623	0	3 (7.4)	0.576
Pulmonary embolism [y, n(%)]	0	1 (0.4)	ns	1 (0.8)	0	0.244
Pulmonary failure [y, n(%)]	0	1 (0.4)	ns	1 (0.8)	0	0.244
Dyspnoea [y, n(%)]	1 (0.4)	1 (0.4)	ns	2 (1.5)	0	0.059
Intrabdominal fluid collection [y, n(%)]	1 (0.4)	0	ns	0	1 (0.2)	ns
Cardiologic complications [y, n(%)]	4 (1.5)	4 (1.5)	ns	4 (3)	4 (0.9)	0.105
Urologic complications [y, n(%)]	0	6 (2.2)	0.03	1 (0.8)	5 (1.2)	ns
Renal failure [y, n(%)]	1 (0.4)	0	ns	1 (0.8)	0	ns
Temperature >38° [y, n(%)]	4 (1.5)	2 (0.7)	0.450	2 (1.5)	4 (0.9)	0.638
Bowel obstruction [y, n(%)]	2 (0.7)	2* (0.7)	ns	4* (3)	0	0.003
Other [y, n(%)]	2 (0.7)	8 (3)	0.106	6 (4.6)	4 (0.9)	0.016
Clavien-Dindo I [y, n(%)]	19 (7.1)	0	<0.001	5 (3.8)	14 (3.5)	0.790
Clavien-Dindo II [y, n(%)]	50 (1.9)	0	<0.001	11 (8.3)	39 (9.6)	0.732
Clavien-Dindo III [y, n(%)]	18 (6.7)	23 (8.5)	0.516	22 (1.7)	19 (4.7)	<0.0001
Clavien-Dindo IV [y, n(%)]	0	1 (0.4)	ns	0	1 (0.2)	ns
Reoperation [y, n(%)]	14 (5.2)	20 (7.5)	0.375	18 (13.7)	16 (3.9)	0.0002
Blood transfusion [y, n(%)]	39 (14.6)	50 (18.6)	0.245	31 (23.7)	56 (13.8)	0.013
Time to flatus [days, mean±SD]	2.7±1.2	2.8±1.4	0.301	3.2±1.5	2.6±1.3	0.0003
Time to regular diet [days, mean±SD]	4±1.4	4±1.8	0.178	4.8±1.7	4.2±1.6	0.001
Length of hospital stay [days, mean±SD]	6±12.5	7±7.8	0.420	8±12.9	7±9.3	<0.0001
Readmission [y, n(%)]	11 (4.1)	18 (6.7)	0.251	13.3 (9.9)	8 (4)	0.013
90-days mortality	2 (0.7)	3 (1.1)	ns	5 (3.8)	0	0.0008

*1 mechanical obstruction requiring intervention

Table 6. Factors associated with the risk of prolonged operative time (> 180 minutes)

	Univariate analysis			Multivariate analysis		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Gender [Male vs Female]	2.591	1.309-5.128	0.006	1.064	0.602-1.491	0.805
BMI				1.141	0.685-1.900	0.611
BMI ≤25 kg/m²	1.077	0.532-2.179	0.836			
BMI 25-30 kg/m²	1.004	0.493-2.044	0.990			
BMI 30-35 kg/m²	1.086	0.403-2.925	0.869			
BMI 35-40 kg/m²	/	/	0.296			
Age (years)				1.178	0.717-1.935	0.517
≤60 vs >75	0.731	0.257-2.081	0.557			
61-75 vs >75	1.466	0.752-2.858	0.260			
61-75 vs ≤60	1.122	0.461- 2.733	0.798			
Size of the tumour [>5 cm vs <=5 cm]	0.735	0.280-1.927	0.531			
Tumour location				0.607	0.359-1.028	0.063
Cecum [yes vs no]	1.699	1.157-2.496	0.006			
Ascending colon [yes vs no]	0.542	0.362-0.811	0.003			
Hepatic flexure [yes vs no]						
Transverse colon [yes vs no]	1.160	0.517-2.603	0.718			
IC° [yes vs no]	4.236	0.798-22.475	0.089	0.278	0.103-0.750	0.011
Type of procedure				0.331	0.187-0.587	0.0002
OrH vs LrH/RrH	0.402	0.253- 0.639	0.0001			
RrH vs LrH	1.164	0.509-2.659	0.718			

° IC=Intra-operative complications;

Table 7. Factors associated with the risk of general post-operative complications

	Univariate analysis			Multivariate analysis		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Gender [Male vs Female]	1.195	0.816-1.751	0.359	1.397	0.878- 2.224	0.157
BMI kg/m²				0.775	0.484-1.240	0.288
BMI ≤25 [yes vs no]	1.158	0.764-1.755	0.488			
BMI 25-30 [yes vs no]	0.991	0.648-1.514	0.967			
BMI 30-35 [yes vs no]	0.785	0.428- 1.441	0.435			
BMI 35-40 [yes vs no]	0.709	0.153- 3.287	0.660			
Age (years)				0.172	0.019- 1.520	0.113
≤60 [yes vs no]	0.746	0.412-1.353	0.335			
61-75 [yes vs no]	0.720	0.437-1.099	0.128			
>75 [yes vs no]	1.149	0.609-2.166	0.667			
Tumour location						
Cecum [yes vs no]	0.596	0.114-3.101	0.538			
Ascending colon [yes vs no]	2.169	0480-9.792	0.314			
Hepatic flexure [yes vs no]	0.811	0.096-6.819	0.847			
Transverse colon [yes vs no]	/	/	0.994			
Operative time (min)						
60-120 [yes vs no]	1.013	0.998-1.029	0.086			
>180 [yes vs no]	1.253	0.250-6.282	0.7783			
Conversion to open [yes vs no]	5.378	0.953-30.353	0.0567	6.509	1.050-40-351	0.044
Type of procedure				1.645	0.967- 2.798	0.066
OrH vs LrH/RrH [yes vs no]	1.650	1.041-2.613	0.032			
LrH vs RrH [yes vs no]	0.953	0.552-1.643	0.863			

Table 8. Factors associated with the risk of Clavien-Dindo III post-operative complications

	Univariate analysis			Multivariate analysis		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Gender [Male vs Female]	1.691	0874-3.271	0.118	1.717	0.877-3.362	0.114
BMI kg/m²				0.673	0.243-1.869	0.448
BMI ≤25 [yes vs no]	0.752	0.349-1.621	0.468			
BMI 25-30 [yes vs no]	0.587	0.259-1.328	0.200			
BMI 30-35 [yes vs no]	2.100	0.886-4.974	0091			
BMI 35-40 [yes vs no]	3.759	0.759-18.613	0.104			
Age (years)				1.247	0.472-3.292	0.655
≤60 [yes vs no]						
>61-75 [yes vs no]	0.770	0.405-1.462	0.424			
>75 [yes vs no]	1.29	0.683-2.466	0.427			
Tumour location				0.700	0.186-2.631	0.598
Cecum [yes vs no]	1.472	0.777-2.788	0.234			
Ascending colon [yes vs no]	1.032	0.537-1.984	0.922			
Hepatic flexure [yes vs no]	0.505	0.175-1.455	0.206			
Transverse colon [yes vs no]	0.486	0.064-3.690	0.485			
Operative time (min)				1.159	0.315-4.269	0.823
60-120 [yes vs no]	0.708	0.356-1.409	0.325			
>180 [yes vs no]	1.644	0.602-4.488	0.331			
Conversion to open [yes vs no]	1.470	0.415-5.206	0.550	1.383	0.381-5.017	0.621
Type of procedure				4.115	2.144-7.898	<0.0001
OrH vs LrH/RrH [yes vs no]	4.089	2.135-7.831	<0.0001			
LrH vs RrH [yes vs no]	1.462	0.474-4.504	0.508			

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