

A comparison of extracorporeal side to side or end to side anastomosis following a laparoscopic right hemicolectomy for colon cancer

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Key words

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Introduction

Colorectal cancer is a significant global health concern, and within Australia, colorectal cancer was estimated to be the second leading cause of cancer-related death in 2020 after lung cancer.¹ The search for optimal surgical and oncological outcomes has resulted in the development of a variety of colorectal anastomosis techniques. Stapled anastomoses in colorectal surgery have been shown to significantly shorten operation duration and promote faster and better recovery with

Abstract

Background: This study aimed to investigate whether an extracorporeal side-to-side (SS) or end-to-side (ES) stapled anastomosis impacts short-term and long-term outcomes after an oncological laparoscopic right hemicolectomy.

Methods: A retrospective cohort study of prospectively collected data from two Victorian tertiary referral hospitals was performed. Patients who underwent oncological resection for colorectal cancer between February 2010 and September 2020 were selected from the colorectal neoplasia database. Patients were divided into two groups depending on the type of stapled anastomosis: Group 1 (functional end-to-end/side-to-side (SS)); and Group 2 (end-to-side (ES)). Primary outcomes were anastomotic leak, postoperative ileus, mortality and morbidity, length of stay post-surgery, readmission to hospital, and 30-day mortality.

Results: This large case series of 1040 patients (SS = 625, ES = 415) demonstrated that the type of stapling technique impacted operative duration and postoperative ileus rates. Patients in the SS group had a faster operation of 108 min rather than 130 min in the ES group ($p < 0.001$). The SS group were more likely to experience a post-operative ileus ($p < 0.001$) with no impact on length of stay (SS, 7 days versus ES, 7 days; $p = 0.14$). There were no differences between the two groups with respect to lymph node yield, lymph node ratio, anastomotic leaks, return to theatre, 30-day mortality and 5-year overall survival.

Discussion: The type of extracorporeal stapled anastomosis following an oncological laparoscopic right hemicolectomy has minimal impact on morbidity and survival outcomes; however, a side-to-side stapled anastomosis is more likely to be a faster operation with a higher postoperative ileus rate.

minimal impact on anastomotic leak rates.² Following a right hemicolectomy, constructing a stapled ileocolonic anastomosis can be performed using two configurations: a functional end-to-end anastomosis/side-to-side (SS) using a linear stapler; or an end-to-side anastomosis (ES) using a circular stapler, first described by Steichen in 1968.³ Which technique to use is often down to the individual choice of the surgeon based on their experience.⁴ SS has become a commonly preferred technique in recent times⁵ however, ES configuration has been shown to have a lower incidence of anastomotic leakage.⁶

Anastomotic failure is associated with several patient-, disease- and technique-specific factors. Gender, tumour location, body mass index (BMI) and anastomotic technique are some of the many published contributory factors for anastomotic leak.^{7,8} The clinical outcomes of an ES or SS anastomosis have only been investigated in two retrospective studies and one small randomized clinical trial.^{4,6,9} Accordingly, we aimed to determine whether the type of extracorporeal stapled anastomosis had any impact on surgical and oncological outcomes following a laparoscopic right hemicolectomy.

Methods

The Cabrini Monash University Colorectal Neoplasia database¹⁰ was investigated for patients who had undergone right hemicolectomy or extended right hemicolectomy surgical resection for colon cancer between January 2010 and September 2020 under the care of 11 colorectal surgeons at The Alfred and Cabrini hospitals in Melbourne, Australia. A retrospective analysis of prospectively collected data entered into this database was performed. Human Research Ethics Committee approval was obtained before the commencement of the study (CHREC #03-25-06-18).

Patients with a hand-sewn anastomosis were excluded from the study. Patients who underwent conversion from laparoscopic surgery were also excluded. The remaining patients were divided into two groups, Group 1 (functional end-to-end/side-to-side (SS)), and Group 2 (end-to-side (ES)). Data was extracted from the database for patient demographics, comorbidities, surgical and medical complications and hospital length of stay. Data pertaining to the operation acuity and duration of operation performed was also collected.

Primary outcomes for this study were anastomotic leak, postoperative ileus, mortality and morbidity, length of stay post-surgery, readmission to hospital, and 30-day mortality. Secondary outcomes were lymph node yield and 5-year overall survival. Patients with benign polyps that were too large or unsafe to remove endoscopically were also included in the analysis.

All patients underwent laparoscopic surgery and mobilization of the right colon was performed in a standard fashion (e.g., medial to lateral and lateral to medial) at the discretion of the operating surgeon. After dissection of the diseased colon, extracorporeal anastomosis was performed. Amongst the 11 colorectal surgeons, differences exist in anastomotic technique and construction. SS anastomoses were typically performed with a combination of DST SERIES™ GIA™ reloadable staplers and/or Proximate® Reloadable Linear Stapler/DST Series™ TA stapler. ES anastomoses were performed with an ECHELON CIRCULAR™ stapler/DST Series™ EEA™ Stapler and Proximate® Reloadable Linear Stapler/DST Series™ TA stapler. Stapler length was typically 8 cm for linear staplers and 29 mm diameter for circular staplers. The types of anastomoses used in this study are pictured in Figures 1 and 2.

Patients suspected of an anastomotic leak based on clinical findings (e.g., fever, tachycardia, peritonitis, abdominal pain, etc.) or biochemical markers (e.g., leukocytosis and elevated C Reactive Protein) were further investigated radiologically with a CT abdomen and pelvis and/or were taken to the operative theatre for exploration. Anastomotic leak was defined by anastomotic dehiscence confirmed by intraoperative findings (faeculent or purulent peritonitis) or extravasation of enteric contrast from the anastomotic site on radiographic imaging. Post-operative ileus (POI) was defined as an absence of bowel function (no bowel movement) for greater than 1 week.

To ensure that any difference in survival noted in this analysis was not confounded by differences in surgical resection, lymph node ratio (LNR) was used as a surrogate marker to indicate similarity in oncological clearance between the two groups. The LNR was defined as the number of positive lymph nodes divided by the total number of lymph nodes harvested. Patients were divided into three LNR groups based on our previous published study: LNR0 (< 0.05), LNR1 (0.05–0.20) and LNR2 (> 0.20).¹¹ At least 12 harvested lymph nodes were accepted as an adequate number, and tumour staging was performed according to the seventh edition of the AJCC TNM manual.¹²

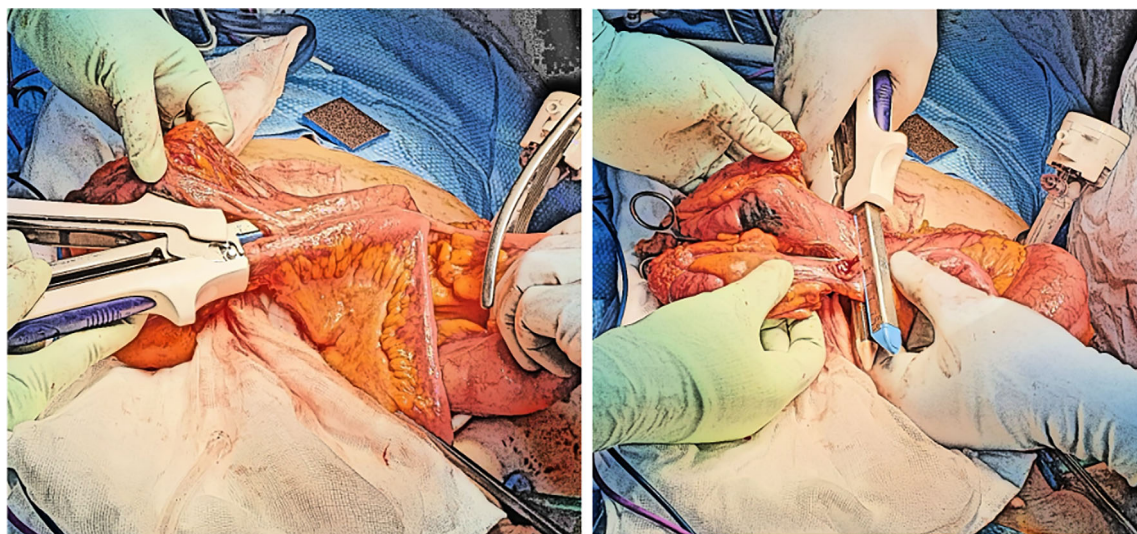


Fig. 1. Creation of the functional end-to-end stapled anastomosis. Surgical photos of a functional end-to-end/side-to-side (SS) anastomosis.

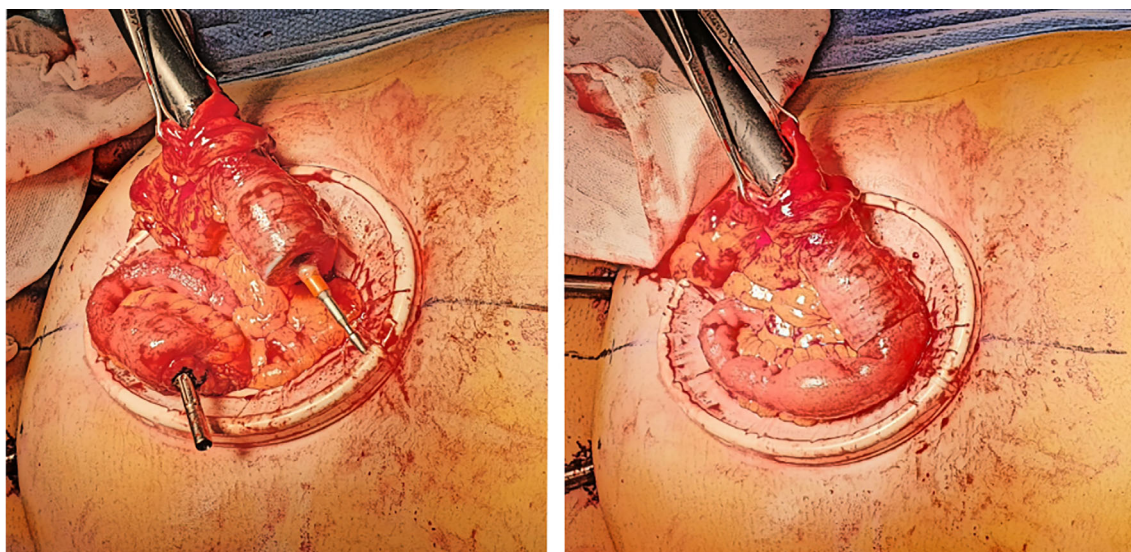


Fig. 2. Creation of the end-to-side stapled anastomosis. Surgical photos of an end-to-side (ES) anastomosis.

Pathological examination of lymph nodes in resected specimens relied on manual dissection by the pathologists.

All patients had cancer follow-up compliant with national guidelines.¹³ This included serial assessments of carcinoembryonic antigen (CEA), radiological examinations (CT of the chest, abdomen and pelvis) and colonoscopic visualization of the remaining bowel at timely intervals. In data analyses, follow-up was defined as the time from the date of primary surgery to a patient event, such as disease recurrence or death. Follow-up information was derived from the colorectal neoplasia database, and where necessary, additional data from patient hospital records were sourced.

Statistical analysis

Descriptive statistics are presented by frequencies and percentages. Categorical data were compared using chi-square (Fisher's) statistics, and continuous data were assessed by students' *t*-tests or non-parametric tests for median comparisons. Univariate and multivariate linear and logistic regression models were applied for examining the relationships between anastomosis technique and complications (surgical and medical), 30-day and inpatient mortality. Overall survival rates were assessed using survival analysis (Kaplan–Meier curve and log rank test). All analyses were carried out via GraphPad Prism (GraphPad Software, San Diego, USA), SPSS 26,¹⁴ and R 3.6.3.¹⁵ Significance was set as a *p*-value <0.05.

This study has been reported in line with STROCSS criteria.¹⁶ The research registry unique identifying number for this study is #7248 (www.researchregistry.com).

Results

A total of 1040 patients met the inclusion criteria and were included in the study. There were 914 patients with a right hemicolectomy procedure and 126 patients with an extended right hemicolectomy.

SS anastomosis was the most commonly performed anastomosis in 625 patients (60.1%). Elective surgery was performed in 943 (90.7%) patients. The follow-up median time was 2.17 years (range 0.01–8.58 years).

Patient and operative characteristics are shown in Table 1. There were no significant differences between the ES and the SS groups in terms of age, sex, lymph node yield or lymph node ratio. A median of 18 lymph nodes were harvested in each group. There were also no differences in the proportions of patients with different comorbidities or receiving antiplatelet treatments. A greater proportion of patients, 53.7%, in the ES group were American Society of Anesthesiologists (ASA) classification 3 and 4 compared with 42.3% in the SS group ($p < 0.001$). There were more patients with emergency or urgent surgery and Stage III and IV disease that received a functional end-to-end anastomosis (SS; Table 1). Patients in the ES group were more likely to be obese (BMI > 30) (26.1% versus 18% in the SS group). A significantly shorter median operating time was observed in the SS group than in the ES group (SS group Median 108.3 range 49–608 versus ES group 130.0 (76–421); $p < 0.0001$) (Fig. 3).

The incidence of postoperative ileus was the only postoperative complication that was significantly different ($p < 0.001$), with 42 instances in the SS group and 10 instances in the ES group (Table 2); however, this did not affect the overall length of stay between the two stapled groups which was 7 days. When right hemicolectomy and extended right hemicolectomy were examined separately, postoperative ileus was significantly lower in the ES group compared with the SS group (chi squared test, $p = 0.0193$) in patients undergoing right hemicolectomies but there was no difference between ES and SS groups in the extended right hemicolectomy patients (Fisher's Exact test, $p = 0.185$). The overall incidence of anastomotic leakage in this cohort was 1.5%. Anastomotic leakage occurred in seven and nine patients in the SS and ES groups, respectively. There were no differences in return to theatre, readmission within 30 days,

Table 1 Patient and operative characteristics

Factor	Stapled functional end-to-end (SS; <i>N</i> = 625)	Stapled end-to-side (ES; <i>N</i> = 415)	Total (<i>N</i> = 1040)	<i>p</i> -value
Patients (<i>n</i> = 1040)				
Sex				0.68
Male	257 (41.1%)	176 (42.4%)	433 (41.6%)	
Female	368 (58.9%)	239 (57.6%)	607 (58.4%)	
Age, mean (S.D.)	74 (11)	73 (12)	74 (12)	0.34
ASA score				< 0.001
1	111 (17.8%)	34 (8.2%)	145 (14%)	
2	249 (39.9%)	158 (38.1%)	407 (39.2%)	
3	218 (34.9%)	211 (50.8%)	429 (41.3%)	
4	46 (7.4%)	12 (2.9%)	58 (5.6%)	
BMI, mean (S.D.)	26.2 (5.2)	27.0 (5.2)	26.5 (5.2)	0.02
BMI >30	107 (18%)	104 (26.1%)	211 (21.3%)	< 0.001
Diabetes	97 (15.5%)	63 (15.2%)	160 (15.4%)	0.90
IHD	159 (25.4%)	122 (29.5%)	281 (27%)	0.15
Respiratory disease	92 (14.7%)	64 (15.5%)	156 (15%)	0.74
Antiplatelet agent	208 (33.3%)	153 (37%)	361 (34.7%)	0.22
Operative urgency				< 0.001
Emergency	24 (3.8%)	7 (1.7%)	31 (3%)	
Urgent	61 (9.8%)	5 (1.2%)	66 (6.3%)	
Elective	540 (86.4%)	403 (97.1%)	943 (90.7%)	
Overall AJCC stage				0.04
0	88 (14.1%)	46 (11.1%)	134 (12.9%)	
I	129 (20.7%)	104 (25.1%)	233 (22.4%)	
II	188 (30.1%)	142 (34.3%)	330 (31.8%)	
III	147 (23.6%)	92 (22.2%)	239 (23%)	
IV	72 (11.5%)	30 (7.2%)	102 (9.8%)	
Procedure type				<0.001
Right hemicolectomy	530 (84.8%)	384 (92.5%)	914 (87.9%)	
Extended right hemicolectomy	95 (15.2%)	31 (7.5%)	126 (12.1%)	
Duration of operation	108.3	130	118.7	<0.00
Median (IQR)	(51.2)	(41.3)	(46.7)	1
Lymph node yield	18 (9)	18 (8)	18 (9)	0.08
Median (IQR)				0.09
Lymph node ratio				
<0.05	445 (71.9%)	323 (78%)	768 (74.3%)	
0.05–0.20	104 (16.8%)	55 (13.3%)	159 (15.4%)	
>0.20	70 (11.3%)	36 (8.7%)	106 (10.3%)	

Abbreviations: ASA, American Society of Anaesthesiologists; BMI, body mass index; IHD, ischaemic heart disease; IQR = interquartile ranges.

or 30-day mortality when the type of stapled anastomosis was compared (Table 2).

The univariate and multivariate analyses of the associations between anastomosis technique and medical characteristics are in Tables 3 and 4, respectively. In both analyses, the type of anastomosis was only associated with the operative duration ($p < 0.001$) and had no impact on anastomotic leak rates. All other outcomes were not significantly different. There were also comparable lymph node ratios between the two groups.

Overall survival stratified by anastomotic technique demonstrated no 5-year survival differences between them (log rank test, $p = 0.16$; Fig. 4).

Discussion

Stapled anastomoses are now widely performed in gastrointestinal surgery as they are safe and improve recovery outcomes.² There are many published studies comparing different anastomotic techniques in colorectal surgery; however, the results are conflicting, and it is difficult to draw conclusions due to heterogeneous data which focus

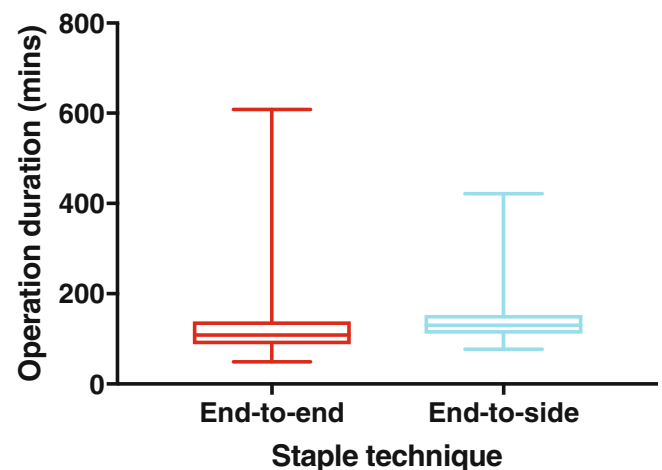


Fig. 3. Operation duration by stapled techniques. End-to-end (SS) patients; Median, 108.3; range, 49–608 min, $n = 487$ (Mean \pm SEM 119.8 \pm 2.3). End-to-side (ES) patients; Median, 130.0; range, 76–421 min, $n = 333$ (Mean \pm SEM 137.8 \pm 2.3). Unpaired 2-tailed t -test $p < 0.0001$.

Table 2 Analysis of surgical complications

Factor	Stapled functional end-to-end (SS; <i>N</i> = 625)	Stapled end-to-side (ES; <i>N</i> = 415)	Total (<i>N</i> = 1040)	<i>p</i> -value
Anastomotic leak	7 (1.1%)	9 (2.2%)	16 (1.5%)	0.18
Prolonged ileus	42 (6.7%)	10 (2.4%)	52 (5%)	<0.001
LoS, median (IQR)	7 (6)	7 (4)	7 (5)	0.14
Returned to theatre	25 (4%)	20 (4.8%)	45 (4.3%)	0.52
Readmitted 30 days	26 (4.2%)	28 (6.8%)	54 (5.2%)	0.10
30-day mortality	5 (0.8%)	2 (0.5%)	7 (0.7%)	0.71*

Abbreviations: IQR, interquartile ranges; LoS, length of stay.

*Fisher's exact test.

on either inflammatory bowel disease (IBD)¹⁷ or include left-sided colorectal tumours¹⁸ or include patients with a hand-sewn anastomosis.^{6,19} The strengths of this study include being the largest single cohort, examining two extracorporeal stapling techniques and only focusing on right-sided colonic cancers, thereby excluding hand-sewn anastomosis or IBD patients.

Overall, the results show that both SS and ES anastomoses are comparable stapling techniques following a right hemicolectomy. The operative time was shorter in the SS group than in the ES group, which contrasts with a previous retrospective study that showed a shorter operative time in the ES group.²⁰ One explanation for the longer operative time could be that there were more obese patients (BMI > 30) in the ES cohort. The association of obesity with longer operative time is well-established.²¹ A recent randomized clinical trial in South Korea also found operative time was longer (160 min versus 150 min, *p* = 0.018) with ES patients compared with SS patients, however, their 130 patients had a mean BMI of 24.⁴ Five-year and overall survival for these groups were not impacted by the choice of anastomotic technique. Any impact of completeness of surgical resection was controlled for through comparison of LNY and LNR, which have been shown to impact disease-free and overall survival rate. Another finding is that there was no difference between the groups with respect to LNY which translated into comparable LNR and 5-year overall survival rates. It has been shown that both LNY and LNR impact on disease-free and overall survival rates.²²

Postoperative ileus (POI) following colorectal resections has an incidence of up to 10.2%.²³ Technical factors examining POI have usually compared stapled, and hand-sewn anastomosis in ileostomy closures and have shown a trend favouring stapled closures,

demonstrating lower POI rate and shorter operative time.²⁴ In this study, we identified that the overall POI rate was 5%, with patients in the SS group more likely to experience a POI. POI is usually associated with a higher prevalence of anastomotic leak and an increased inflammatory response; however, it is uncertain which of POI or anastomotic leak is the initiating event.²⁵ POI was also more common in patients undergoing SS in a previous study (13% versus 2.3%) however, the difference was not significant.²⁰ In contrast, a randomized controlled trial of 130 right hemicolectomy patients found no difference in POI when ES and SS groups were compared.⁴

Postoperative ileus is a common clinical condition following abdominal surgery causing increased length of hospital stay and patient morbidity.²⁶ POI is a complex process caused by neural mechanisms, intestinal inflammation and the use of anaesthetic drugs such as opioids during surgery.²⁶ Experiments in mice have also demonstrated slowed electrical waves and contractions of gut muscles after surgery.²⁷ Clinically, POI can be reduced with the use of laparoscopic surgery, opioid-reduced analgesia, continuous epidural local anaesthetic analgesia, and fluid management.²⁸ Peristalsis is governed by the synchronous movements of the longitudinal and circular muscles within the gut wall so arranged that both muscle layers contract and relax at the same time producing movement progressing down the colon.²⁹ It has been postulated that because of this arrangement of muscles, the circular ileal end of the ES anastomosis might cause less damage resulting in quicker recovery of gut function.²⁰ The ES method may also have other potential benefits despite it being considered technically more difficult⁹ it may sustain higher internal pressures than the SS technique³⁰; its point of attachment is more anatomical and is similar to

Table 3 Univariable analysis of the associations between anastomosis technique and medical characteristics (*n* = 1040). Anastomosis technique: End to end (SS) versus end to side (ES)

	Coefficient	95% CI	<i>p</i> -value
LoS	−0.74	−1.66, 0.18	0.12
Operation duration	18.04	11.34, 24.75	<0.001
Lymph nodes harvested	−0.55	−1.56, 0.45	0.28
Positive nodes	−0.17	−0.52, 0.18	0.35
Lymph node ratio	−0.02	−0.03, 0.00	0.09
Odds ratio			
Return to theatre	1.20	0.66, 2.22	0.52
Inpatient death	0.60	0.09, 2.81	0.55
30-day mortality	0.60	0.09, 2.80	0.54
Readmitted within 30 days	1.26	0.78, 2.03	0.35
Anastomotic leak	1.96	0.72, 5.52	0.19

Table 4 Multivariate analysis of impact for anastomosis technique on medical characteristics (*n* = 1040)

	Estimate	95% CI	<i>p</i> -value
LoS	−0.72	−1.64, 0.21	0.13
Operation duration	18.01	11.30, 24.71	<0.001
Lymph node harvested	−0.50	−1.51, 0.50	0.33
Positive lymph nodes	−0.18	−0.53, 0.17	0.32
Odds ratio			
Return to theatre	1.22	0.67, 2.23	0.56
Readmitted 30 days	1.16	0.71, 1.89	0.58
30-day mortality	0.60	0.12, 3.12	0.43
Anastomotic leak	1.96	0.73, 5.31	0.33

Abbreviations: LoS, length of stay.

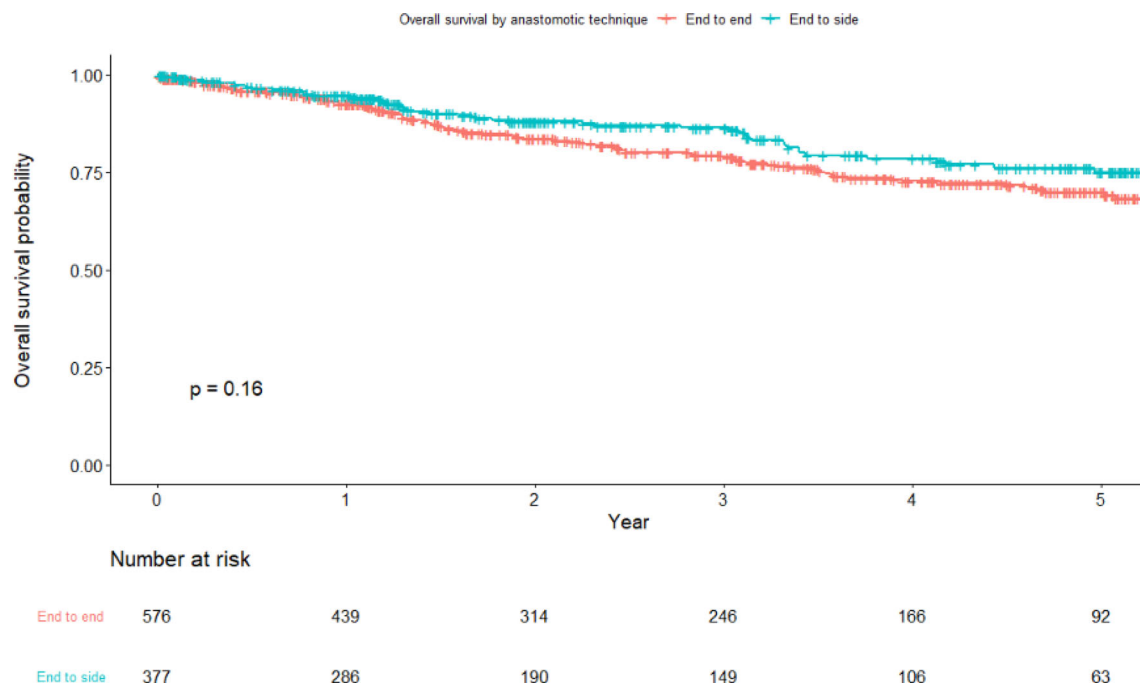


Fig. 4. Kaplan–Meier survival overall curves stratified by anastomotic technique.

the way to ileum joins the caecum,⁴ and it produces a smaller blind pouch than the SS technique.²⁰

Despite the significant difference in POI rate in this study, no difference in anastomotic leak rates was observed between the two anastomotic techniques on univariate or multivariate analysis. Furthermore, the leak rate of 1.6% in this study was also low compared to the literature, which reported leak rates reported in up to 3–19% of patients.^{31,32} The 2015 European Society of Coloproctology Collaborating Group (ESCCG) performed a multicentre study to determine the relationship between stapling technique and anastomotic failure for right-sided colonic resections but also failed to identify any difference in anastomotic leak rates according to the type of stapling device used to close the apical aspect.⁷ The ESCCG identified, however that general surgeons had higher leak rates in comparison to colorectal surgeons. The lower leak rate in this study may be attributed to the fact that all resections included in both private and public settings were performed or supervised by a specialist colorectal surgeon. Although no general surgeons contribute patients to our database, there were no differences between the 11 colorectal surgeons at both hospitals for leak rates. Furthermore, there was no difference in leak rates for patients operated on within either a public or private setting.

In the public setting, the performance of colorectal surgery is usually by senior general surgical trainees and/or a colorectal fellow in an appropriately supervised environment. A recent meta-analysis of 19 non-randomized studies including 14 344 resections did not show a difference in leak rates (3.2% versus 2.5%, OR 0.77, $p = 0.08$) or cancer-specific survival (HR 0.76, $p = 0.13$) between expert and expert-supervised trainees.³³

The effect of retrospective analysis of patients is minimized in this study as the data was extracted from a prospectively maintained database.¹⁰ Procedural variables that exist when constructing an

anastomosis were not analysed for example, which part of the anastomosis was oversewn and the timing of firing the stapler (immediately or waiting before cutting to let potential oedema resolve). The presence of any postoperative oedema was also not recorded. Some of these anastomotic procedural factors are a protective factor against leaks.³⁴ It is also worth noting that even though a standard linear staple anastomotic technique is used in this study (8 cm linear stapler), the size and shape of the side-to-side or functional end-to-end anastomosis can be varied. The final luminal diameter of a linear anastomosis depends on intraoperative factors like the number of firings and surgeon preference for neo caecum size and is therefore variable between patients and surgeons. Equally, the standard luminal diameter for a circular anastomosis would be determined by the circular staple size (29 mm in this study). The currently available range of circular staplers in everyday use by Australian surgeons varies between 20 and 33 mm. Another important limitation is that relevant post-operative data was not collected in the database (e.g., time to passing flatus). Despite these limitations, this is the largest cohort study investigating the impact of extracorporeal anastomotic configuration on patient outcomes following a laparoscopic right hemicolectomy.

In conclusion, a side-to-side stapled anastomosis is more likely to be a shorter operation with a higher postoperative ileus rate. Overall, however, the type of extracorporeal stapled anastomosis following a laparoscopic right hemicolectomy is comparable for morbidity, mortality and survival outcomes.

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Author contributions

Ali Riaz Baqar: Conceptualization; formal analysis; methodology; writing – original draft; writing – review and editing. **Simon Wilkins:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; writing – original draft; writing – review and editing. **Wei Chun Wang:** Conceptualization; formal analysis; investigation; methodology; writing – original draft; writing – review and editing. **Karen Oliva:** Conceptualization; data curation; formal analysis; investigation; methodology; writing – original draft; writing – review and editing. **Suelyn Centauri:** Conceptualization; formal analysis; investigation; methodology; project administration; writing – original draft; writing – review and editing. **Raymond Yap:** Conceptualization; formal analysis; investigation; methodology; writing – original draft; writing – review and editing. **Paul McMurrick:** Conceptualization; funding acquisition; investigation; methodology; project administration; resources; supervision; writing – original draft; writing – review and editing.

Conflict of interest

None declared. Let's Beat Bowel Cancer was not involved in the conduct of this study nor the writing of this manuscript.

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