Title: Outcomes in Patients Undergoing Urgent Colorectal Surgery

Short Title: Urgent Colorectal Surgery

by

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ABSTRACT

Introduction: Urgent surgery for acute intestinal presentations is generally associated with worse outcomes than elective procedures. This study assessed the outcomes of patients undergoing urgent colorectal surgery.

Methods: Patients were identified from a prospective database. Surgery was classified as urgent when performed as soon as possible after resuscitation and usually within 24 hours. Outcome measures included 30-day mortality, return to theatre, anastomotic leak, and overall survival.

Results: 249 patients were included in the analysis. Median age was 65 years (IQR 48-74). The most common presentations were obstruction (52.2%) and perforation (23.6%). Cancer was the disease process responsible for presentation in 47.8% of patients. Thirty-day mortality was 6.8%. Age (OR 1.08 95%CI 1.02–1.15; p=0.01), ASA 4 (OR 7.14 95%CI 1.67–30.4; p=0.008), and cancer (OR 6.61 95%CI 1.53–28.45; p=0.011) were independent predictors of 30-day mortality. Re-laparotomy was required in 6 (2.4%) cases. A primary anastomosis was performed in 156 (62.6%) patients. Anastomotic leak occurred in 4 (2.5%) patients. In patients with cancer overall 5-year survival was 28% (95%CI 19-37), corresponding to 54% (95%CI 35-70) for Stages I and II, 50% (95%CI 24-71) for Stage III, and 6% (95%CI 1-17) for Stage IV disease. Urgent surgery was independently associated with worse overall survival (HR 2.65; 95%CI 1.76-3.99; p<0.001).

Conclusion: In patients undergoing an urgent resection within a colorectal unit, performing a primary anastomosis is feasible and safe in the majority, re-laparotomies are required in a minority, and urgent surgery is an important predictor of worse prognosis in those with colorectal cancer.

INTRODUCTION

It is widely accepted that patients who require urgent surgery for intestinal conditions tend to have worse outcomes when compared with those who undergo elective procedures (1–3). However, divergent results in regards to the 30-day mortality rates for these patients have been reported. Multiple factors are thought to influence the outcomes of patients undergoing urgent surgery. These relate to the condition requiring surgery, the treatment, or the patient's comorbidities (4,5). Also, specialty training in colorectal surgery has been shown to improve outcomes in the elective and acute settings (6–8). The literature is lacking current data on outcomes for patients undergoing urgent surgery for colorectal conditions in Australia.

The surgical management of acute intestinal conditions has changed significantly in the past 2 decades (9). Non-restorative resections with diversion used to be the norm, but accumulating evidence shows that primary resection and anastomosis, with or without a covering loop ileostomy is feasible and safe in many instances (10–15). The aim of this study was to characterise the postoperative 30-day mortality, return to theatre rate, anastomotic leak rate, and overall survival in patients undergoing urgent intestinal resections performed by a group of colorectal specialists.

METHODS

All patients undergoing urgent surgical resections were identified from a prospectively maintained database. The database includes all cases performed or directly supervised by 5 colorectal surgeons in 3 hospitals. One surgeon dataset ranges from 1996 to 2012 and the other 4 from 2006 to 2013. An independent nurse performed data entry, including information on patient demographics, pathology, operative details, and postoperative outcomes, including morbidity and mortality.

The current analysis is focused on patients who underwent urgent surgery as per the United Kingdom National Bowel Cancer Audit definition: i.e. "operation performed as soon as possible after resuscitation and usually within 24 hours". None of the patients in the database fitted the definition of emergency, which is an immediate and life-saving operation, simultaneous with resuscitation, usually within 2 hours.

Exclusion criteria included laparotomy without resection and patients who underwent only small bowel resection. Health status was assessed by American Society of Anesthesiologists (ASA) class, as assigned by a consultant anaesthetist. Outcomes measures included mortality within 30 days, return to theatre within 30 days, anastomotic leakage, and overall survival for patients with malignant disease. Information was also collected on the disease process, type of surgery, type of anastomosis, and the requirement for a defunctioning stoma or an end stoma.

Statistics

The median and inter-quartile range (IQR) were used as descriptive statistics. Associations between categorical variables were tested using Chi-square tests. Logistic regression was used to model the effects of various independent covariates on 30-day mortality. Overall survival was determined using the Kaplan-Meier technique in patients presenting with colorectal cancer. Patients were followed up until date of death or study censor date (10 June 2013). Date of death was determined from linkage of patient identifiers to the state based death registry on a regular basis. Cox regression was used to model the effects of various independent covariates on overall survival using a larger cohort of patients that included those undergoing elective surgery. Likelihood ratio tests were used to include or exclude covariates from the adjusted model and to identify any potential plausible interaction terms at the 5% level. All analysis was performed using Stata 12.0 (Statacorp, USA).

RESULTS

Overall 249 patients were included in this analysis. Patient characteristics stratified by indication for surgery are summarised in Table I. The most common presentations were obstruction (52%), perforation (23%) and abscess (11%). Cancer was the disease process responsible for presentation in 119 (47.8%) patients, followed by inflammatory bowel disease 44 (17.6%), and diverticulitis 42 (16.8%).

Early Postoperative Outcomes

Postoperative outcomes stratified by surgical procedure are presented in Table II. Older age ($p=0.008$) and higher ASA score ($p=0.001$) were associated with a longer LOS on univariate analysis. On multivariate analysis only ASA score was significantly associated with longer LOS ($p<0.0001$). Return to theatre within 30 days was required in 6 cases (2.4%). Overall, the 30-day mortality was 6.8% (17 patients). Logistic regression analysis demonstrated that age (OR 1.06 95% CI 1.01 – 1.12; $p=0.009$), ASA 4 (OR 7.4 95% CI 1.8 – 30.9; $p=0.005$) and cancer (OR 6.1 95% CI 1.7 – 21.2; $p=0.004$) were independently associated with 30-day mortality.

Primary Anastomosis

A primary anastomosis was performed in 156 patients (62%). On multivariable analysis, patients with higher ASA scores were less likely to have a primary anastomosis fashioned ($p<0.001$; Table III), while age had no impact ($p=0.9$). On univariate analysis receiving an endstoma was

associated with longer length of stay (p=0.03; Table III) and higher mortality (p=0.02; Table III), but such associations disappeared once ASA was included in the multivariate models. Of the patients who received a primary anastomosis, 83 (53%) received a covering stoma. For the most part covering stomas were used in patients who were receiving a primary anastomosis to the rectum (Table IV).

Overall there were 6 (2.4%) cases of postoperative intra-abdominal septic complication (4 anastomotic leaks and 2 abscesses). Five cases occurred in patients who received a primary anastomosis (3.2%) and 1 case in a patient who received an end stoma (1.07%; p=0.3). Anastomotic leak occurred in 4 (2.5%) cases, 2 in patients with and 2 in patients without a covering stoma. The rate of leak stratified by type of anastomosis is presented in Table IV. Treatment for anastomotic leak was antibiotics in 1 case, percutaneous image-guided drainage in 1 case and re-operation in 1 case. One of the leaks was a radiological diagnosis without clinical implications. Abscesses developed in 2 patients, one was treated with antibiotics and one required a second laparotomy.

Patients with cancer

One hundred and thirty three patients had cancer as the cause for the acute presentation. Sixty-seven (55%) patients had Stage IV and 19 (16%) had Stage III disease. R0, R1 and R2 resections were achieved in 76 (69.4%), 5 (4.6%), 28 (25.9%) patients, respectively. The resection was considered curative in 52 (42%) patients. The median follow-up was 3.1 years (IQR 1.4-5.8) and the overall 5-year survival was 28% (95% CI 19-37). The overall 5-year survival stratified by stage was: Stage I and II 54% (95% CI 35-70), Stage III 50% (95% CI 24-71) and Stage IV 6% (95% CI 1-17). Median overall survival for patients with cancer was 1.9 years (IQR 0.52 – 9.8).

Median survival for Stage III disease was 5.4 years (IQR 3.6 – not reached) and for Stage IV disease 0.75 (IQR 0.16 – 1.6).

When elective procedures were included, another 1051 patients who underwent surgery for colorectal cancer were identified. A multivariable fractional polynomial model demonstrated that age doesn't exhibit a linear association with survival. Therefore a transformed age was included in the Cox regression model. After adjusting for age (transformed), ASA, Stage, extramural vascular invasion and adjuvant chemo-radiotherapy, urgent surgery remained an independent predictor of worse prognosis (HR 2.65; 95% CI 1.76-3.99; $p<0.001$; Table V). Even when only patients with Stage IV disease were considered, urgent surgery was still associated with worse prognosis (Figure 1).

DISCUSSION

The results of this study demonstrate that satisfactory outcomes are achievable in patients presenting with acute intestinal conditions requiring urgent surgical management. Our mortality rate of 6.8% is comparable to previous reports of mortality ranging from 5.7-15.3% (4,11,15). In our analysis age, the ASA score and cancer were the most important independent determinants of 30-day mortality. This study has also highlighted how colorectal cancer still results in a majority of the presentations in this class, and that a majority of these patients have Stage IV disease. This group of patients had the poorest outcomes.

The use of primary resection and anastomosis in surgical emergencies is still debated, particularly in the management of left-sided colonic pathology. In this analysis, performing a primary anastomosis in selected patients did not lead to worse outcomes in regards to mortality, hospital stay, intra-abdominal septic complications or re-operations. This is in accordance with previous studies of patients with any left-sided large bowel (11) or specifically acute diverticulitis (10,12,14). In our series more than 60% of patients received a primary anastomosis. Patients with lower ASA scores were more likely to have a primary anastomosis performed. Intra-abdominal septic complications (anastomotic leak and abscess formation) occurred in 3.2% of patients receiving a primary anastomosis, which is comparable to reported rates for elective surgery. Only 1 of the 4 patients with anastomotic leak required re-operation. Our usage of covering ileostomy (53%) was higher than that report by Zorcolo et al. (8.0%) (11). In their series of 176 patients with primary anastomosis 9 (5.1%) had anastomotic leak and all these patients required a second laparotomy. In regards to the location of the primary disease process, the use of primary resection was indeed higher in patients with right-sided conditions, but our

results suggest that primary resection and anastomosis is feasible and safe with good outcomes in selected patients.

The principle of a re-laparotomy and lavage in patients with peritonitis has been entrenched in surgical care, but has more recently been challenged. A randomised controlled trial of 232 patients suggested that even in those with severe secondary peritonitis, planned re-laparotomy does not improve outcomes and is associated with longer length of stay and greater resource utilization in comparison to on-demand surgery. In accordance, in this study only 2.4% of patients required a second laparotomy. Out of 59 patients with bowel perforation only 1 required a second operation. The fundamentals of managing intra-abdominal sepsis dictate control of the primary source, and if this can be achieved, then subsequent outcomes are improved.

A significant proportion of patients with colorectal cancer still present with obstruction or perforation (9). While contemporary Australian data are lacking, figures between 8-29% for obstruction and 3-8% for perforation are quoted for developed countries with screening programs (16). Historically, patients presenting as a surgical urgency were less likely to have their cancers resected than patients undergoing elective surgery (17). However, more recently it has been shown that resectability in the emergency and elective settings are similar (15). An R0 resection was achieved in all patients with Stage I-II, 95% of those with Stage III and 34% of those with Stage 4 disease. The long-term survival impact of surgery in the acute setting for colorectal malignancy is controversial. While some have described significantly worse long-term outcomes (18), other suggested that when a radical procedure is performed in the urgent setting, results are only slightly worse than stage-matched elective procedures (15,19). Two studies have suggested

that the worse prognosis of patients presenting acutely is due to higher peri-operative death rates (19,20). In our series, urgent surgery was an independent predictor of worse overall survival even after adjustment for age, ASA, stage, number of lymph nodes resected, number of involved lymph nodes, extramural vascular invasion, and adjuvant chemoradiation (Table V). Even when only patients with stage IV were considered, urgent surgery was independently associated with worse overall survival (Figure I).

Our study has several limitations. Firstly, it represents the results from consultants with specialty training in colorectal surgery, which has been shown to be associated with decreased morbidity and mortality in the acute setting (6). Secondly, we have limited data on intra-operative factors such as degree of contamination and severity of peritonitis. Specifically, in regards to patients with diverticulitis, the lack of data on Hinchey classification prevents more direct comparisons with previous studies. Similarly, the types of urgent presentations to a group of colorectal surgeons may not be representative of the overall burden of urgent surgery that may present to some Australian emergency departments.

In conclusion, mortality rates of urgent intestinal are still higher than for elective procedures. Nonetheless, in patients presenting with urgent intestinal pathology, primary resection and anastomosis in possible in a majority with relatively low rates for septic complications. Re-operations, even in the presence of perforation, were noted to be uncommon. Finally, in patients with colorectal cancer, urgent surgical resection was an independent predictor for a worse overall survival.

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Table I. Patient characteristics by presentation

	Overall N=249	**Obstruction N=130**	**Perforation N=59**	**Abscess N=28**	**Failed Medical N=14**	**Other N=18**
Male:Female	113:136	58:72	29:30	13:15	6:8	7:11
Age (median; IQR)	65 (48-74)	68 (54-76)	65 (50-74)	48(27-65)	39(25-45)	68(45-74)
ASA						
I	12 (4.8%)	8 (6.1%)	1 (1.6%)	2 (7.1%)	0	1 (5.5%)
II	94 (37.7%)	53 (40.7%)	18 (30.5%)	15 (53.5%)	6 (42.8%)	2 (11.0%)
III	111 (44.5%)	54 (41.5%)	30 (50.8%)	10 (35.7%)	6 (42.8%)	12 (66.6%)
IV	32 (12.8%)	15 (11.5%)	10 (16.9%)	1 (3.5%)	2 (14.2%)	5 (27.7%)

IQR = interquartile range

Table II. Complications stratified by surgical procedure

	Hartmann's N=35	Anterior Resection N=63	Colectomy N=86	Subtotal N=40	Other N=25	Overall N=249
30-day mortality	4 (11.4%)	1 (1.6%)	7 (8.1%)	2 (5.0%)	3 (12.0%)	17 (6.8%)
Median LOS (days)	15 (10-21)	10 (9-13)	10 (8-13.5)	14 (10-16.5)	8 (7-14)	11 (8-14)
Primary anastomosis	0	63 (100%)	78 (90.7%)	12 (30.0%)	0	156 (62.6%)
Covering stoma	-	54 (85.7%)	19 (24.3%)	10 (83.3)	-	83 (53.2%)
Leak	-	1 (1.6%)	2 (2.5%)	1 (8.3%)	-	4 (2.5%)
Abscess	0	1 (1.6%)	0	0	1 (4.0%)	2 (0.7%)
Return to OT	0	1 (1.6%)	3 (3.5%)	1 (2.5%)	1 (4.0%)	6 (2.4%)

OT = operating theatre; LOS = length of stay

Table III. Comparison between patients with end-stoma and primary anastomosis

	End stoma N=93	**Primary anastomosis N= 156**	**P value**
Age	68 (50-76)	64 (46-73)	0.09
ASA			
I-II	26 (26.2%)	80 (51.2%)	Ref.
III	51 (51.5%)	60 (38.4%)	0.003 vs ASA I-II
IV	22 (22.2%)	10 (6.4%)	<0.001 vs ASA I-II
LOS	12 (8-18)	10 (8-13)	0.03
Leak or Abscess	1 (1.0%)	5 (3.2%)	0.24
Return to OT	2 (1.8%)	4 (2.7%)	0.74
30-day mortality	11 (11.4%)	6 (3.9%)	0.02

OT = operating theatre; LOS = length of stay;

Table IV. Complications stratified by type of anastomosis

	SB to Colon n=76	SB to rectum n=12	Colon to Colon n=5	Colon to rectum n=63	Total n=156
Covering stoma	18 (23.6%)	10 (83.3%)	1 (20%)	55 (87.3%)	83 (53.2%)
Leak	2 (2.7%)	1 (8.3%)	0	1 (1.6%)	4 (2.5%)
Return to OT	3 (3.9%)	0	0	1 (1.6%)	5(2.5%)
Abscess	0	0	0	1 (1.6%)	1 (0.6%)
Death	5 (6.5%)	0	1 (20.0%)	1 (1.6%)	7 (4.5%)

SB = small bowel; OT = operating theatre

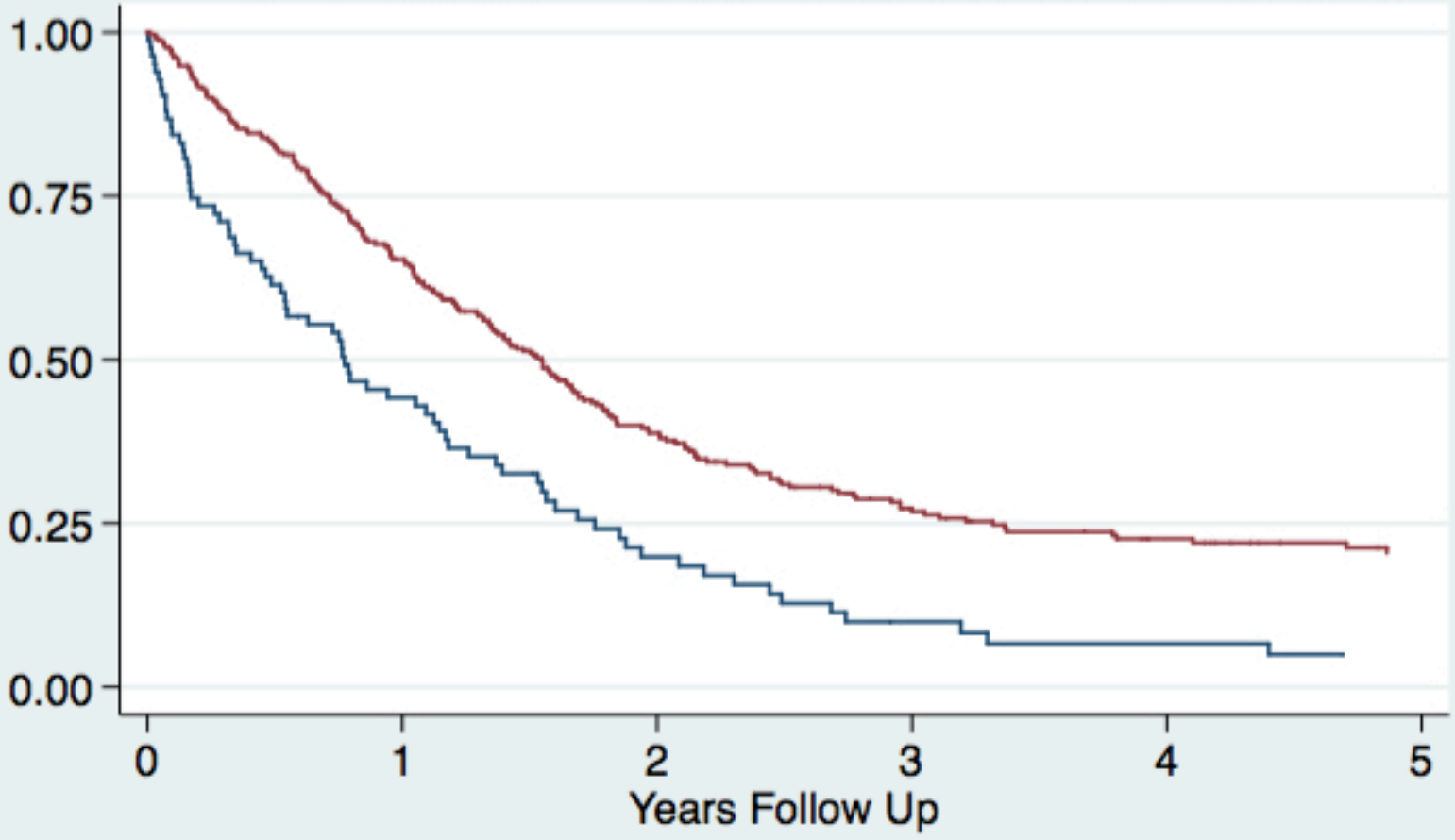
Table V. Cox regression of overall survival of patients with colorectal cancer

	Hazard ratio	95% CI	P value
Age (transformed)	2.15	1.2-3.85	0.010
ASA			
I-II	(ref)		
III	2.37	1.75-3.21	<0.001
IV	3.69	2.04-6.69	<0.001
Stage			
I-II	Ref.		
III	2.36	1.49-3.74	<0.001
IV	9.42	6.50-13.65	<0.001
EMV	1.67	1.23-2.25	0.001
Chemoradiation	0.40	0.27-0.60	<0.001
Urgent surgery	2.65	1.76-3.99	<0.001

EMV = extramural vascular invasion

Figure I. Effect of urgency on survival of patients with Stage IV cancer

Overal Survival for Stage IV Colorectal Cancer by Urgency.



Number at risk						
Timing = urgent	83	35	14	6	4	2
Timing = elective	312	192	99	55	37	26

Timing = urgent Timing = elective