

Urgent Laparotomy in Patients with Metastatic Colorectal Cancer Presenting as an Acute Abdomen: A Retrospective Analysis

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ABSTRACT: **Background:** Unlike the elective treatment of metastatic colorectal cancer (MCRC), sufficient data and consensual guidelines on acute care are lacking.

Objectives: To analyze a cohort of MCRC patients who required urgent surgery due to acute abdomen and to identify risk factors contributing to the patient's perioperative mortality and morbidity.

Methods: A retrospective analysis was conducted of patients diagnosed with stage IV colorectal cancer who required urgent laparotomy at the Rabin Medical Center. Comparative analysis was performed using Pearson's chi-square and Student's *t*-test.

Results: Between 2010 and 2015, 113 patients underwent urgent laparotomy due to colorectal cancer complications, of which 62 patients were found to have a metastatic, stage IV, disease. Large bowel obstruction was the most common indication for urgent laparotomy. In-hospital mortality was 30% (n=19), and overall 30 day mortality was 43%. Fifteen patients (24%) required more than one surgery. The average length of hospital stay was 21 days. Age and lactate levels at presentation were the only prognostic factor found for mortality ($P < 0.05$).

Conclusions: MCRC laparotomy patients incur a significant burden of care and have a relatively high incidence of early mortality. Our data suggest high, verging on unacceptable, mortality and complication rates in this subgroup of patients. This finding is further accentuated in the subgroup of older patients presenting with lactatemia. These data should be considered by surgeons when discussing treatment options with patients and families.

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cause of cancer-related death [1]. Nearly 20% of patients with CRC present with metastasis at the time of diagnosis [2].

In recent years, median survival of metastatic colorectal patients (MCRC) has improved. Reported survival of these patients with contemporary treatment modalities (both surgical and medical) has risen to 30 months, compared with historical survival of 8 months without treatment [3].

There are few reports, however, on the management of MCRC patients presenting to the emergency department (ED) with an acute abdomen.

Emergency presentation of CRC is considered a marker of poor outcome and of advanced disease [4,5]. Emergency CRC surgery (regardless of stage) is associated with a high rate of complications and mortality [6].

However, practical implications of these observations revolve mostly around CRC screening improvement and early intervention to avoid emergency surgery for CRC complications. Sufficient data are lacking for aiding the clinician in deciding whether to operate on an already metastatic CRC patient who presents with an acute abdomen.

The aim of this study was to analyze a cohort of MCRC patients requiring urgent surgery and to identify risk factors contributing to a patient's perioperative mortality and morbidity.

PATIENTS AND METHODS

We performed a retrospective, descriptive analysis of patients diagnosed with stage IV CRC who required urgent laparotomy at the Rabin Medical Center, a tertiary care referral center in Israel.

Data were collected from the Rabin Medical Center's medical electronic registry. Patients with the diagnosis of CRC who underwent urgent laparotomy during their hospitalization were included in the cohort group if they had evidence of a known or newly diagnosed stage IV disease (using the TMN staging system) [7].

Data was imported into Microsoft Excel 2010® (Microsoft Corporation, USA) worksheets, and statistical analyses were

Colorectal cancer (CRC) is the third most common cancer diagnosed in both men and women in the United States, and when both genders are combined, it is the second leading

performed using Statistical Package for the Social Sciences software version 13 (SPSS Inc., Chicago, IL, USA). Quantitative variables were analyzed as mean ± standard deviation, and qualitative variables were described as frequency and percentage. A comparative analysis was performed using Pearson's chi-square test and Student's *t*-test. *P* < 0.05 was considered significant.

The Rabin Medical Center research ethics committee approved the study.

RESULTS

Between 2010 and 2015, 113 patients underwent urgent laparotomy due to colorectal cancer complications. Of these, 62 were found to have a metastatic, stage IV, disease (whether known or newly diagnosed) and were included in the cohort group.

Characteristics of the cohort group are presented in Table 1. Mean age was 70 years with a similar male to female distribution. Large bowel obstruction was the most common indication for urgent laparotomy among the metastatic colorectal cancer patients (53%), followed by small bowel obstruction (18%) and bowel perforation (14%).

Thirty-three patients (53%) presented to the ED with an already diagnosed metastatic disease. Eleven patients (18%) had already been diagnosed with CRC but were not known to have metastasis. Eighteen patients (29%) presented with a newly diagnosed stage IV malignant disease without previous history of malignant colorectal cancer.

Twenty-three patients of the known MCRC disease group (23/33, 69.6%) had received chemotherapy or radiotherapy prior to their acute presentation. From the previously diagnosed non-metastatic colorectal patients group, three patients (3/11, 27.2%) had received adjuvant chemotherapy.

Details on the surgical procedures that had been performed are presented in Table 2. The most common procedure performed was stoma formation (colostomy or ileostomy) (42.7%), 8 out of 35 of these were combined with resection of the colon,

and 4 as a second surgery after anastomotic leaks. There were 13 right hemicolectomies (16%), of which 10 were with primary anastomosis. Two of these patients underwent a second surgery due to leakage. There were four cases of left colectomies with primary anastomosis, of which two required a second operation due to leakage. Another common procedure was a small bowel resection (16%).

Fifteen patients (24%) required more than one surgery (average of 1.4 procedures per patient). Eighteen patients (29%) required mechanical ventilation with an average of 8.2 ventilation days. Seven (11%) patients required admission to an intensive care unit (ICU) during part or all of their hospitalization.

Postoperative complications are listed in Table 3. Surgical site infection was the most common complication (29%). Other

Table 1. Cohort patient characteristics

Cohort group of 62 patients (emergency + metastatic disease)	
Age, years (range)	70 (35–94)
Gender (male/female)	29/33
Indication, n (%)	
Large bowel obstruction	33 (53)
Small bowel obstruction	11 (18)
Perforation of bowel	9 (14)
Sepsis	4 (6)
Gastrointestinal bleeding	2 (3)
Site of primary malignancy, n (%)	
Colon	50 (80)
Rectum	12 (20)
Metastatic extent, n (%)	
Liver: unilobar	20 (32)
Liver: bilobar	16 (26)
Carcinomatosis	48 (77)
Both (liver metastasis + carcinomatosis)	22 (35)

Table 2. Surgical procedure

Surgery	Number (%)
Colostomy/ileostomy	35 (42.7)
Subtotal + end ileostomy	3 (3.6)
Right colectomy	13 (16)
Primary anastomosis	10
With ileostomy	3
Left colectomy	4 (4.8)
Primary anastomosis	2
With end colostomy	2
Anterior resection	1 (1.2)
Sigmoidectomy	4 (4.8)
Primary anastomosis	2
With end colostomy	2
Small bowel resection	13 (16)
Peritoneal lavage	5 (6.1)
Lysis of adhesions	1 (1.2)
Drainage of abscess	2 (2.4)
Gastrostomy	1 (1.2)

Table 3. Morbidity and mortality

Morbidity	
Length of hospital stay, days	21
Number of surgeries (range)	1.4 (1–8)
Ventilator days	2.4 (40 max, 148 total)
Complications, n (%)	
Surgical site infection	18 (29)
Intra-abdominal collection	11 (18)
Pulmonary (non pulmonary emboli)	11 (18)
Wound dehiscence	7 (11)
Evisceration	5 (8)
Arrhythmia	5 (8)
Early anastomotic leak	4 (6)*
Early small bowel obstruction	3 (5)
Pulmonary emboli	2 (3)
Mortality	
In-hospital	19 (30)
30 day	8 (13)
Overall mortality	27 (43)

*Relative to the number of anastomosis made overall (15), the rate rises to 26%

complications included formation of intra-abdominal collections (18%), wound dehiscence (11%), and anastomotic leak (6% of patients, 26% of overall primary anastomosis).

Nineteen patients (30.6%) died during their hospitalization [Table 4]. By the end of 30 days, an additional eight patients died, raising the mortality rate to 43% (n=27). Within 90 days, four additional patients died, setting the overall 90 day mortality at 50% (n=31).

Albumin and lactate upon presentation were evaluated. The average albumin level was 3.17 g/dl and no statistically significant differences were found between patients who died during admission (in-hospital mortality) and those who survived. The cohort's average lactate level was 26.1 mg/dl with 37 mg/dl measured in the in-hospital mortality group vs. 18.3 mg/dl among those who survived their admission (P = 0.03).

Patient age was found to be statistically significant in predicting mortality [Table 4]. In our cohort, 28 patients (45%) were over the age of 75 years. In this age group, the 30 day mortality rate was 57%, and when combining a lactate level of ≥ 25, the 30 day mortality rose to 88%.

The indication for laparotomy, extent of metastatic disease, and patient co-morbidities were not found to be significant in predicting mortality.

DISCUSSION

There are no clear consensual guidelines for the surgical treatment of acutely presenting stage IV CRC patients. While it is well established that within this population emergency surgery cannot offer a cure, the benefits of a palliative surgical procedure remains controversial.

Table 4. Statistical analysis: factors predicting mortality, multivariate analysis

		Overall 30 day mortality				P
		Survived		Died		
		n	%	n	%	
Age (average, years)		67		76		< 0.05
Diagnosis	New	10	28.6	8	30.8	0.9
	Known malignancy	6	17.1	4	15.4	
	Known metastatic disease	19	54.3	14	53.8	
Indication	Large bowel obstruction	22	61.1	14	53.8	0.242
	Perforation	5	13.9	4	15.4	
	Sepsis	0	0.0	1	3.8	
	Mesenteric ischemia	0	0.0	3	11.5	
	Small bowel obstruction	8	22.2	3	11.5	
	GI bleeding	1	2.8	1	3.8	
Liver	No metastasis	17	47.2	9	34.6	0.3
	Unilobar	12	33.3	8	30.7	
	Bilobar	7	19.4	9	34.6	
Carcinomatosis	None	7	19.4	7	26.9	0.49
	Present	29	80.6	19	73.1	
Diabetes	No	29	80.6	20	76.9	0.73
	Present	7	19.4	6	23.1	

Previous studies have shown that acutely presenting CRC patients have high rates of perioperative mortality and morbidity [8-10]. Rosen and colleagues [10], in an almost exclusively elective (non-emergency) setting, described 120 patients who initially presented with a stage IV disease and underwent laparotomy. Their findings showed that in patients older than 65 years of age, carcinomatosis and extensive liver involvement were associated with decreased survival and increased postoperative morbidity.

Biondo and co-authors [11] prospectively compared emergency laparotomy for complicated CRC patients (defined as non-MCRC patients arriving with obstruction/peritonitis) versus elective surgery and showed that there was a poor prognosis for acute presentation in stage IV. However, in stage II patients, and to some extent those at stage III, no statistical difference was found concerning survival [11].

To the best of our knowledge, our study population is among the largest reporting on patients with CRC who arrived at an acute state and underwent an emergency surgery. These patients were characterized by an early high mortality rate reaching 43% within 30 days and 50% within 90 days, as well as a high rate of complications, many requiring additional surgery.

Among possible prognostic factors, including co-morbidities, extent of metastatic disease, and initial indication for laparotomy, only age and lactate levels at presentation were found to be statistically significant in predicting mortality. The combination of these two factors (age > 75 years and a lactate level of ≥ 25) yielded in an 88% mortality rate.

Metastatic CRC patients who survived an emergency laparotomy had a long length of hospital stay, increased usage of operation theaters and ICU beds, and more days on the ventilator. These factors placed a heavy burden on both the patients as well as the medical institution.

In the elderly population, precise tools for assessing when to offer maximal treatment have long been lacking [12], and although there are few, if any, reports of this specific cohort of MCRC patients with an acute abdomen, the high mortality rate should not be surprising. Studies dealing equally ill elderly patients have reported similar mortality and complications rate [13].

While stenting may offer some palliation for selected patients arriving with large bowel obstruction, accumulating data suggests that the use of endoscopic colonic stenting by self-expanding metallic stents can provide only temporary palliation and may only serve as a bridge for surgery [14-16].

Although surgery remains the mainstay of treatment for CRC patients presenting with acute abdomen, the benefits of surgery in metastatic patients are not well described. Our data suggest that surgeons must consider the high mortality and complication rates in this subgroup of patients. This morbidity and mortality rate seems to be unrelated to the extent of the metastatic disease and is further accentuated in the subgroup of older patients presenting with lactatemia.

CONCLUSIONS

It is important to consider offering palliative end-of-life care as viable alternatives for the treatment of MCRC patients presenting with acute abdomen. In view of the high morbidity and mortality rate, it is important that our decision-making be informed, realistic, and shared and discussed openly with the patient and family. Laparotomy in patients with MCRC is an understudied field and further studies are needed to determine which subgroup of these patients might benefit from an urgent laparotomy, thus empowering the surgeon's decision-making process, minimizing unnecessary distress, and maximizing the use of the already limited resources most centers have.

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References

1. American-Cancer-Society. Key statistics for colorectal cancer: how common is colorectal cancer? [Available from: <https://www.cancer.org/cancer/colon-rectal-cancer/about/key-statistics.html>]. [Accessed October 2016].
2. Steinberg SM, Barkin JS, Kaplan RS, Stablein DM. Prognostic indicators of colon tumors. The Gastrointestinal Tumor Study Group experience. *Cancer* 1986; 57 (9): 1866-70.
3. Kopetz S, Chang GJ, Overman MJ, et al. Improved survival in metastatic colorectal cancer is associated with adoption of hepatic resection and improved chemotherapy. *J Clin Oncol* 2009; 27 (22): 3677-83.
4. Brown SC, Abraham JS, Walsh S, Sykes PA. Risk factors and operative mortality in surgery for colorectal cancer. *Ann R Coll Surg Engl* 1991; 73 (5): 269-72.
5. Amri R, Bordeianou LG, Sylla P, Berger DL. Colon cancer surgery following emergency presentation: effects on admission and stage-adjusted outcomes. *Am J Surg* 2015; 209 (2): 246-53.
6. Askari A, Malietzis G, Nachiappan S, et al. Defining characteristics of patients with colorectal cancer requiring emergency surgery. *Int J Colorectal Dis* 2015; 30 (10): 1329-36.
7. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, eds. *AJCC cancer staging manual* (7th ed). New York, NY: Springer; 2010.
8. Chen HS, Sheen-Chen SM. Obstruction and perforation in colorectal adenocarcinoma: an analysis of prognosis and current trends. *Surgery* 2000; 127 (4): 370-6.
9. Peloquin AB. Factors influencing survival with complete obstruction and free perforation of colorectal cancers. *Dis Colon Rectum* 1975; 18 (1): 11-21.
10. Rosen SA, Buell JF, Yoshida A, et al. Initial presentation with stage IV colorectal cancer: how aggressive should we be? *Arch Surg*. 2000 135 (5): 530-4; discussion 534-5.
11. Biondo S, Martí-Ragué J, Kreisler E, et al. A prospective study of outcomes of emergency and elective surgeries for complicated colonic cancer. *Am J Surg* 2005; 189 (4): 377-83.
12. Friedmann R, Shapiro D. The oldest old in internal medicine wards: can prognostic predictors be used for making clinical decisions? *IMAJ* 2010; 12 (1): 42-4.
13. Anwar MA, D'Souza F, Coulter R, Memon B, Khan IM, Memon MA. Outcome of acutely perforated colorectal cancers: experience of a single district general hospital. *Surg Oncol* 2006; 15 (2): 91-6.
14. Sebastian S, Johnston S, Geoghegan T, Torreggiani W, Buckley M. Pooled analysis of the efficacy and safety of self-expanding metal stenting in malignant colorectal obstruction. *Am J Gastroenterol* 2004; 99 (10): 2051-7.
15. Horesh N, Dux JY, Nadler M, et al. Stenting in malignant colonic obstruction--is it a real therapeutic option? *Int J Colorectal Dis* 2016; 31 (1): 131-5.
16. Gibor U, Perry Z, Tirosh D, et al. Comparison of the long-term oncological outcomes of stent as a bridge to surgery and surgery alone in malignant colonic obstruction. *IMAJ* 2017; 19 (12): 736-40.

Capsule**Type 2 poliovirus detection after global withdrawal of trivalent oral vaccine**

Mass campaigns with oral poliovirus vaccine (OPV) have brought the world close to the eradication of wild poliovirus. However, to complete eradication, OPV must itself be withdrawn to prevent outbreaks of vaccine-derived poliovirus (VDPV). Synchronized global withdrawal of OPV began with serotype 2 OPV (OPV2) in April 2016, which presented the first test of the feasibility of eradicating all polioviruses. **Blake** et al. analyzed global surveillance data on the detection of serotype 2 Sabin vaccine (Sabin-2) poliovirus and serotype 2 vaccine-derived poliovirus (VDPV2, defined as vaccine strains that are at least 0.6% divergent from Sabin-2 poliovirus in the viral protein 1 genomic region) in stool samples from 495,035 children with acute flaccid paralysis in 118 countries and in 8528 sewage samples from four countries at high risk for transmission. The samples were collected from 1 January 2013 until 11 July 2018. The prevalence of Sabin-2 poliovirus

in stool samples declined from 3.9% at the time of OPV2 withdrawal to 0.2% at 2 months after withdrawal, and the detection rate in sewage samples declined from 71.0% to 13.0% during the same period. However, 12 months after OPV2 withdrawal, Sabin-2 poliovirus continued to be detected in stool samples (< 0.1%) and sewage samples (8.0%; 95% confidence interval 5.0–13.0) because of the use of OPV2 in response to VDPV2 outbreaks. Nine outbreaks were reported after OPV2 withdrawal and were associated with low coverage of routine immunization (odds ratio 1.64 per 10% absolute decrease) and low levels of population immunity (odds ratio 2.60 per 10% absolute decrease) within affected countries. In a perspective, **Pallansch** calls for ending the use of OPV altogether.

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Eitan Israeli

“We’ve all got both light and dark inside us. What matters is the part we choose to act on. That’s who we really are”

J.K. Rowling, (born 1965), author, best known for writing the *Harry Potter* fantasy series