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(RESEARCH ARTICLE)

Management of complicated colorectal cancer in Benghazi hospitals

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Abstract

Introduction: Colorectal cancer (CRC) is the third most frequent malignant disease in men and second most frequent in women. The treatment of emergency cases of CRC presented with complication is different than elective controlled cases.

Aim: of this study is to find the best way to treat a patient admitted as an emergency case of complicated colorectal cancer.

Methods: The medical data of 102 patients was retrospectively evaluated for those who were admitted as emergency cases with acute or subacute intestinal obstruction, perforation or bleeding colorectal cancer to Al-Jalla Hospital, Benghazi Libya. Three different emergency treatment methods were received as follow:

- Tumor resection,
- Damage control procedure with elective or semi elective resection, and
- No radical treatment.

Primary endpoints were 6 months mortality and morbidity. Secondary endpoints were length of hospital stay, number of lymph nodes, rate of radical R0 resections, and the number of patients who had received chemo-radiotherapy.

Results: 55 patients had immediate resection and colostomy. 33 patients were inoperable because the cancer was too advanced or they were too ill to tolerate an operation. 10 had damage control followed by elective resection. There was no statistically proven significant difference between immediate resections and 2-stage treatment. The patients who underwent staged treatment had a higher possibility of receiving a laparoscopic resection.

Conclusion: This study couldn't determine which treatment is better, even with using staging resection.

Keywords: Al-Jalla Hospital, BMC; Colorectal surgery; Obstructing colorectal cancer; Perforated colorectal cancer; Emergency surgery; Colorectal cancer

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1. Introduction

Colorectal cancer is the third most common cancer in men and the second most common cancer in women. In 2012, worldwide, there was estimated to have been 746 000 new cases in men (10.0% of all incident cancer cases in men) and 614 000 new cases in women (9.2% of all incident cancer cases in women). Almost 55% of these cases were in more developed regions. % In 2012) were found in less developed regions of the world, reflecting poor survival in these regions. Worldwide, mortality rates vary less than incidence rates, with mortality varying across regions by a factor of 6 in men and 4 in women. In both sexes, the highest estimated 2012 mortality rates (per 100 000 population) were in Central and Eastern Europe (20.3 deaths in men and 11.7 in women), and the lowest were in Western Africa (3.5 deaths in men and 3.0 in women). Colorectal cancer (CRC) is the third most frequent malignant disease in men and second most frequent in women. There are estimated to have been more than a million new cases per year worldwide.¹ more than 50% of these cases were found in developed countries. There is a considerable geographical variation in occurrence across the world, the highest estimated 2012 age-standardized incidence rates (per 100 000 population) were in Australia/New Zealand (44.8 and 32.2 cases in men and women, respectively), and the lowest were in Western Africa (4.5 and 3.8 cases in men and women, respectively). A significant proportion of these patients (14%-33%) were presented as emergency cases with bowel obstruction, perforation or bleeding.^{2,3} Even with the latest standardization applying for CRC, emergency cases still carry a bad prognostic outcome rather than elective cases.^{4,5} In BMC hospital all cases of CRC must be managed by surgeons who are particularly trained and experienced in colorectal surgery. The emergency cases must be managed by the on-call surgeon and the patient must be transferred to the relevant team/hospital as soon as possible. However, in Al-Jalla hospital, CRCs are usually managed by general surgeons, both as emergency or elective cases. The classic approach is done with a resection in emergency. The philosophy of "damage control," has recently emerged, in the UK, in this approach, the surgical complication can be treated in the emergency setting with minimal approach and procedures to control the acute condition (obstruction, perforation, or bleeding) until the patient becomes stable. Thereafter the definitive treatment of the CRC can be started under supervision of a specialized team.⁶ This retrospective study has been carried to provide further proof to confirm the choice of the best treatment for CRC, particularly immediate resection vs elective resection.

2. Material and methods

The medical records of all consecutive patients with CRC admitted as emergency from May 2017 to August 2019 have been retrospectively analyzed under the care of the Colorectal Team of BMC Hospital and the General Surgery Team of Al-Jalla Hospital located in Benghazi, Libya. The Al-Jalla Hospital has 560 beds, whereas the BMC has 1200 beds, both serving the City of Benghazi with a population of approximately 850, 000.⁷ As they are also referral hospitals for most of the eastern half of Libya. Al-Jalla and BMC Hospitals are also affiliated to the University of Benghazi and the Libyan International Medical University (LIMU) located in Benghazi. Libya. The Colorectal Unit deals with about 60 new CRCs per year, both as elective and emergent cases. Emergency Surgery Department of Al-Jalla Hospital is one of the busiest emergency departments (EDs) in the Benghazi city. The patients' data regarding the treatment of their CRCs have been collected into an electronic database created with MS excel for windows 10, and the variables were checked for typos and missing Data. Variables with missing data >10% were rejected. Data was then analyzed using SPSS v 21. Continuous variables distribution was checked. The variables used in this study were gender, age, time between symptoms onset and admission, time between admission and first treatment, American Society of Anesthesiologists (ASA) score, type of Emergency presentation, and treatment for emergency cases such as ostomy, laparoscopic vs open approach, ultimately neoadjuvant or adjuvant chemotherapy. Frequencies are presented as number of cases and percentage. Values of p<0.05 had been considered significant. An initial evaluation was done to compare the data of the 2 contributing units and to check if there was any difference due to Hospital policies or attitude. Two groups had been compared: 1) patients who had emergency resection; and 2) patients treated with elective resection after initial stabilization and damage control procedures. The retrospective nature of this study made formal ethical approval unnecessary. However, the Ethical Committees of both the Al-Jalla Hospital and the BMC Hospital had been informed, whereas they both considered ethical approval and patient consent were not necessary on the following bases: 1) data were completely anonymized, 2) data were collected as part of normal treatment and subsequently analyzed within an audit aimed to improve the quality of care, 3) patients were treated according to national and international guidelines and 4) no experimental or new treatments/protocols are included in this study. All patients gave full informed consent to the treatment, either resection or non-operative management.

3. Results

98 medical records were reviewed, 44 from Al-Jalla Hospital and 54 from the BMC Hospital. Follow-up data and other clinical variables (I V fluids, blood transfusions and medicines) were not available because of local restrictions. Results

are summarized in Tables 1–6. The 2 initial groups were matched for age, gender, and type of case. Al-Jalla Hospital patients had a higher rate of metastatic cancers (45.5% vs 37.0%, p=0.059) (Table 1).

Table 1 patient's basic clinical data

	Total	Al-Jalla Hospital	BMC Hospital	P-value
Number of cases	98	44(44.9%)	54(55.1%)	
Gender				0.491
М	55(56.1%)	30(68.2%)	25(46.3%)	
F		14(32%)	29(53.7%)	
	43(43.9%)			
Age(years)	73.5	73.3	73.7	0.860
	74	73.5	74	
Presentation:				
Obstruction	88(89.8%)	40(91%)	48(90.6%)	
Perforation	6(6.1%)	2(4.5%)	4(7.4%)	
Bleeding	4(4.1%)	3(6.8%)	1(1.9%)	
Symptoms onset to admission (days)	19.3	19.9	18.7	0.004
	2	45	1	
Admission to 1 st treatment(days)	4.1	3	5.2	0.005
	0	0	1	
ASA				0.012
1	7(7.1%)	0	7(12.9%)	
2	43(43.9%)	20(45.5%)	23(42.6%)	
3	32(32.7%)	15(34.1%)	17(31.5%)	
4	15(15.3%)	8(18.2%)	7(12.9%)	
5	1(1%)	1(2.3%)	0	
Т				0.380
2	8(8.2%)	2(4.5%)	6(11.1%)	
3	48(49%)	30(68.2%)	18(33.3%)	
4	37(38%)	17(38.6%)	20(37%)	
missing	5	3	2	
N				0.340
0	35(36%)	19(43.2%)	16(29.6%)	
1	39(40%)	21(47.7%)	18(33.3%)	
2	20(20.4)	15	5(9.3%)	-
missing	4	1	3	-
М				0.059
0	45(46%)	19(43.2%)	26(48.1%)	1
1	40(41%)	20(45.5%)	20(37%)	

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Missing	3	2	1	
Location:				0.025
Right colon	42(43%)	20(45.5%)	22(40.7%)	
Left colon	40(41%)	17(38.6%)	23(42.6%)	
Rectum	7(7.1%)	4(9.1%)	3	
Emergency treatment:				0.000
Immediate resection	63(64.2%)	29(65.9%)	34(62.9%)	
DCS	15(15.3%)	8(18.2%)	7(12.9%)	
Palliative treatment	20(20.4%)	12(27.3%)	8(14.8%)	

Notes: National groups comparison (a mean ± standard deviation, median and range). Significant p-values are reported in bold.

Abbreviations: ASA, American Society of Anesthesiologists; DCS, damage control surgery.

Twenty patients (20.4%) did not have a radical treatment. eight out of 33 patients were managed only with medical palliative treatment, whereas 25 underwent an invasive procedure. However, 7 patients had laparotomy exploration with no active procedure. Fifteen patients (45.5% of the non-resectable Patients) had diversion procedures (Table 2). Most cases (66.3%) had the first treatment within 24 hours from admission. This rate was higher in the Al-Jalla Hospital group (79.5% vs 55.6%, p=0.001). The majority of cases had done open surgery. Most of the cases in BMC had laparoscopic procedure for treatment. (42%) of patients had a stoma as 1st option (Table 2).

Table 2 Comparison of emergency treatment in Al-Jalla hospital vs BMC

	Total	Al-Jalla Hospital	BMC Hospital
Total	98	44(44.9%)	54 (55.1%)
Radical resection	65	30(46.2%) (68.2% within group)	35 (53.8%) (64.8% within group)
Immediate resection:	55	29 (52.7%)	26 (47.3%)
Right colectomy	17 (30.9%)	5 (17.2%)	12 (46.2%)
Extended right	4 (7.8%)	3 (10.3%)	1 (3.8%)
colectomy	10 (18.2%)	7 (24.1%)	3 (11.5%)
Left colectomy	1 (1.8%)	0	1 (3.8%)
Extended left colectomy	7 (12.7%)	5 (17.2%)	2 (7.7%)
Hartmann's	2 (3.6%)	0	2 (7.7%)
Sigmoid colectomy	1 (1.8%)	1 (3.4%)	0
Anterior resection	3 (5.5%)	2 (6.9%)	1 (3.8%)
Subtotal colectomy	10(18.2%)	9 (31%)	1 (3.8%)
Total colectomy			
Damage control	10	7 (70%)	3(30%)
Loop colostomy	8 (80%)	6 (85.7%)	3 (100%)
Stent	2 (20%)	2 (28.6%)	0
Palliative treatment:	33	11 (24.2%)	22(75.8%)
Terminal colostomy	1 (3%)	1 (9.1%)	0
Loop colostomy	7 (21.2%)	2 (18.2%)	5 (22.7%)
Terminal ileostomy	3 (9.1%)	3 (27.3%)	0
Loop ileostomy	6 (18.2%)	4 (36.4%)	2(9.1%)
Ileotransverse bypass	3 (9.1%)	0	3 (13.6%)
Diagnostic laparoscopy	2 (6.1%)	0	2 (9.1%)

Exploratory laparotomy	3 (9.1%)	1 (9.1%)	2 (9.1%)
Stent	0	0	0
Medical treatment	8 (24.2%)	1 (9.1%)	7(31.8%)
Colostomy	22 (22.4%)	10 (22.7%)	12 (22.2%)
Ileostomy	20 (20.4%)	12 (27.3%)	8 (14.8%)
No stoma	56 (57.1%)	22 (50%)	34 (62.9%)
Laparotomy	68 (69.4%)	35 (79.5%)	33 (61.1%)
Laparoscopy	18 (18.4%)	3 (6.8%)	15 (27.8%)
Conversion lap-open	2 (2%)	2 (4.5%)	0
No operation	10 (10.2%)	4 (9.1%)	6(11.1%)
Emergency surgery 24h	65 (66.3%)	35 (79.5%)	30 (55.6%)
Delayed surgery 🛛 24 h	22 (22.4%)	8 (18.1%)	14 (25.9%)
Medical treatment	11(11.2%)	1 (2.3%)	10 (18.5%)

Notes: a total number of ostomies, including protective stomas and palliative stomas. P-values of the comparison between the two series (Al-Jalla vs BMC) are reported in bold.

	Immediate resection	Damage control	Palliative treatment	P-value
Total	50 (51%)	11 (11.2%)	37(37.8%)	
Gender				0.031
М	20 (40%)	10 (20%)	20 (40%)	
F	30 (62.5%)	1 (2%)	17 (35.4%)	
ASA				0.057
1	1 (12.5%)	2 (25.0%)	5 (62.5%)	
2	13 (46.4%)	5 (17.9%)	10 (35.7%)	
3	26 (57.8%)	4 (8.9%)	15 (33.3%)	
4	10 (62.5%)	0	6 (37.5%)	
5	0	0	1 (100%)	
Presentation				0.043
Obstruction	40 (50.6%)	9 (11.4%)	30 (37.9%)	
Perforation	8 (80%)	0	2 (20%)	
Bleeding	2 (22.2%)	2 (22.2%)	5 (55.6%)	
Location				0.000
Proximal colon	20 (50%)	0	20 (50%)	
Distal colon	27 (72.9%)	3 (8.1%)	7 (18.9%)	
Rectum	3 (14.3%)	8 (38.1%)	10 (47.6%)	

Note: Significant *p*-values are reported in bold.

Patients with a high ASA score along with female gender were more likely to receive an emergency resection. Obviously, cases with perforated cancers were resected in an emergency procedure, even if the patient was in a poor general condition. The majority of patients with left colon cancers underwent resection on emergency, while about one-third of

patients with rectal cancers had a 2-step procedure. Obviously, the high number of cases with right colon or rectal cancer did not receive radical treatment (Table 3).

The vast majority of patients received neoadjuvant chemo-radiotherapy or palliative chemotherapy. Young patients were more likely to receive chemo- or chemoradiotherapy. Neoadjuvant chemoradiotherapy was given only in rectal cancer patients, whereas adjuvant chemotherapy was more frequent in left colon cancers, and palliative chemotherapy in right colon cancers. The patients who had staged treatment were more likely to receive chemo- and/or radiotherapy (Tables 4 and 5).

	Neoadjuvant radio chemotherapy	Adjuvant chemotherapy	Palliative chemotherapy	No radiotherapy or chemotherapy	P-value
Total	6 (6.1%)	28 (28.6%)	12 (12.2%)	52 (53%)	
Al-Jalla	1 (2.3%)	18 (40.9%)	3 (6.8%)	22 (50%)	0.038
ВМС	5 (9.3%)	10 (18.5%)	9 (16.7%)	30 (55.6%)	
<70 y	5 (14.3%)	14 (40%)	6 (17.1%)	10 (28.6%)	0.004
>70 y	1 (1.6%)	14 (22.2%)	6 (9.5%)	42 (66.7%)	
ASA 1	1 (12.5%)	2 (25.0%)	1 (12.5%)	4 (50%)	0.317
ASA2	3 (10.3%)	7 (14.1%)	7 (14.1%)	12 (41.4%)	
ASA3	2 (4.4%)	14 (31.1%)	3 (6.7%)	25 (55.6%)	
ASA4	0	5 (31.3%)	1 (6.3%)	10 (62.5%)	
ASA5	0	0	0	1 (100%)	
proximal colon	0	10 (25%)	8 (20%)	22(55%)	0.000
distal colon	0	15 (42.9%)	2 (5.7%)	18 (51.4%)	
Rectum	6 (26.1%)	3 (13%)	2 (8.7%)	12 (52.2%)	
Immed. Resection	0	25 (38.5%)	0	40 (61.5%)	
DCS+ resection	5(50%)	3 (30%)	0	2 (20%)	0.004
Palliative treat.	1 (4.3%)	0	12 (52.2%)	10 (43.5%)	
Laparotomy	3 (3.3%)	26 (28.9%)	12 (13.3%)	49 (54.4%)	
Laparoscopy	3 (37.5%)	2(25%)	0	3 (37.5%)	

Table 4 Chemotherapy/radiotherapy

Note: Significant p-values are reported in bold

Table 5	Elective surgica	l procedures af	ter damage control
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	Total	Al-Jalla Hospital	ВМС
Hartmann	2 (20%)	2 (28.6%)	0
Left colectomy	2 (20%)	1 (14.3%)	1 (33.3%)
Abdomino-perineal Resection	1 (10%)	1 (14.3%)	1 (33.3%)
Anterior resection	2 (20%)	1 (14.3%)	1 (33.3%)
Exenteration	1 (10%)	0	0
l otal proctocolectomy	1 (10%)	1 (14.3%)	0
Extended right Colectomy	1 (9.1%)	1 (14.3%)	0
Colostomy	3 (30%)	2 (28.6%)	1 (33.3%)

lleostomy	3(30%)	4 (57.1)	1 (33.3%)
Colostomy	1 (10%)	0	1 (33.3%)
No stoma	3 (30%)	1 (14.3%)	0
Laparotomy	7 (70%)	4 (57.1%)	3(100%)
Laparoscopy	3 (30%)	3 (42.9%)	0
			<i>p</i> =0.058

Note: Significant *p*-values are reported in bold

Fifty patients had an immediate resection, whereas 11 had damage control and subsequent elective resection. No immediate resection was performed by laparoscopy. All patients with staged treatment were operated-on by subspecialist colorectal surgeons. (Table 6)

Table 6 Multivariate analysis on resected patients (89 cases)

Dependent variable	Independent prognostic factors	Correlation coefficient	P-value
Mortality			0.000
	ASA	0.152	
	Dukes	-0.112	
Morbidity			0.000
	ASA	0.165	
	Dukes	-0.132	
	Laparoscopic resection	-0.267	
LOS			0.000
	Admission to treatment	0.985	
	Onset to admission	0.062	
Ostomy	Distal cancer	0.447	0.000
Chemoradiotherapy	Age> 70	-0.301	0.004
LN analyzed			0.000
	ASA	-4.945	
	Distal cancer	-3.152	
LN adequate clearance			0.000
	ASA	-0.182	
	Dukes	0.131	
R+			0.000
	Laparoscopic resection	-0.225	
	Onset to admission	0.001	

Abbreviations: ASA, American Society of Anesthesiologists; LN, lymph nodes; LOS, length of stay.

4. Discussion

The treatment of emergency cases of CRC presented with obstruction, perforation, or significant bleeding – has yet to be standardized. Even the national guidelines and local protocols have widely followed for elective cases of CRC.⁸

However, it is not totally clear if the admitted patients should be treated by the emergency team or just stabilized with a damage control procedure and later transferred to the colorectal department for further evaluation and treatment. Obviously, there are cases that should undergo a resection procedure, but often the elective surgeries can be done at a later time to minimize the emergency complication.⁹ In obstructing CRC, damage-control surgery (DCS) is usually done to resolve bowel obstruction with a diversion procedure for instant an ileostomy or colostomy. CRC patients with bleeding can be treated at the emergency department with blood transfusions and resuscitation techniques. Up to 20% of patients who have acute obstruction due to CRC die within 1 month of the operation.¹⁰ Patients usually managed in emergency by no specialist general surgeons.¹¹ No palliative procedure can be done for most of the patients presented with advanced cancer. Ileostomy and colostomy procedures have no effect in the outcome of advanced cancer. A colostomy procedure can guarantee a good diversion with fewer side effects than an ileostomy procedure. Selfexpandable stents was one of the options for patients with acutely obstructing CRC.^{12,13} however in this study we didn't used colonic stenting, so this factor has not been analyzed. In patients with an operable disease, immediate or delayed resection can be done. ACPGBI 2007 guidelines.¹⁴ suggest immediate resection and anastomosis for obstructing CRC. based on the old studies.¹⁵ The recently published ACPGBI 2017 guidelines are less specific and suggest optimization of the patient in a high-dependency unit before considering emergency surgery or stenting.¹⁶ On the contrary, NCCN 2016 guidelines.^{17,18} consider both emergency resections and elective resections following ileostomy or colostomy as viable options. There is good evidence declaring that a series strategy of CRC management is carrying lower mortality and morbidity rates.¹⁹ A new study from Sweden revealed that a 2-stage treatment is associated with lower morbidity and safer nodal clearance compared to immediate resection.²⁰ On the other hand, a recent study from Korea recommended that every patient with obstruction due to CRC must have an emergency Subtotal Colectomy, because staged operations are associated with higher mortality and morbidity and longer hospital stay in comparison to immediate resections.²¹ Perforated CRC, almost always requires an emergency resection, regardless that these cancers are advanced in nature and carry a poor prognosis.^{22,23} An extensive operation on these patients is associated with higher morbidity and mortality rates.²⁴ therefore it is better to choose a conservative approach. In this study, all the cases of perforation underwent immediate resection. This study was planned to try to obtain some further physical evidence that could potentially be useful in the decision-making process. It is almost impossible to estimate the real incidence of complicated CRC in Libya on the basis of only the series from Benghazi, due to local factors. In our opinion, this may reflect the particular UK guidelines on the treatment of bowel cancer.²⁵ that suggest those cases with CRC should just be stabilized in the emergency department and then transferred to a specialized colorectal surgeon as soon as possible. If the patient is admitted during the weekend, they should stay until Sunday morning to be seen by the colorectal surgeon. These differences can also conduct why in Libyan hospitals the vast majority of patients underwent resection within 24 hours from admission, whereas in the UK, less than half had an emergency resection. The delay of emergency treatment may lead to an increase in hospital stay which might increase morbidity, thus suggesting that the decision-making process should be made as soon as possible. The higher incidence of advanced cancer may explain why only palliative treatment was used on more patients in Libva, compared to those in the UK.

However, it may also be due to the different approach toward advanced and metastatic disease, where UK guidelines suggest only palliative treatment, taking in consideration chemotherapy if indicated, while Libyan surgeons prefer to take a more aggressive approach. In this study, the choice of treatment was based according to the location of the tumor; staged treatment is the best option in distal cancers. It is well known that right colon cancers are frequently presented at a late stage in comparison to left colon cancers, which may explain why palliative treatment was more frequent in right colon cancers. It appears that an aggressive approach will give a long-term survival rate. In fact, younger patients (<65 years old) were often offered chemo-radiotherapy and had better nodal clearance. Mortality and morbidity higher in elderly patients and in those with multiple comorbidities, thus these patients should be treated carefully. While comparing the 2 methods of treatment there was no significant difference, but patients whom had immediate resection had higher mortality rates with worse nodal clearance and a lower rate of negative margins in regards to the patients who had delayed resections.²⁶ Unfortunately, like the previously published articles on this topic, our study lacks a longterm follow-up which could help establish the best treatment option, considering good nodal clearance and R0 resection as reliable factors, that affect the survival rate. In fact, while there is good evidence demonstrating that emergency cases are associated with poor survival rate.²⁷ other authors noted that worse survival in an emergency may not be due to the operation itself, but to some other clinical factors, like the higher stage at presentation.¹⁵ Patients with 2-stage treatment usually will have a stoma. In this study, the diversion of an ileostomy or colostomy is almost always the chosen procedure. The use of stents could reduce the option of the temporary stoma.⁵ However, multivariate analysis showed that stoma is independently associated with the distal location of cancer.

Staged treatment had a higher chance of getting resection by a laparoscopic mini-invasive approach, and chemoradiotherapy. Moreover, they were also being operated on by MIS subspecialized colorectal surgeons. As we know, the laparoscopic resections are associated with lower mortality and morbidity rates, shorter hospital stays, better nodal clearance, and a higher rate of R0 resection. Laparoscopic emergency resections are still performed in spite of the progress of laparoscopic colorectal surgery in elective cases.¹⁹ A laparoscopic approach in an emergency colorectal surgery is more difficult and can be associated with worse results; for that reason most of the surgeons are not enthusiastic perform it.²⁸ In these systematic reviews show that laparoscopic bowel resection in an emergency is possible and does not increase the mortality and morbidity rates.^{28,29} Long operative time is the only remaining issue, regardless in our point of view, it is not difficult, considering the use of mini-invasive surgery in cancer patients. This retrospective design has limitations. However, the total number of patients selected is significant and allows us to have satisfying conclusions.

Abbreviations

- CRCs: Colorectal cancer
- BMC: Benghazi Medical Centre.
- LIMU: Libyan International Medical University.
- ED: emergency department
- SPSS: Statistical Package for the Social Sciences
- ASA: American Society of Anaesthesiologists
- ACPGBI: Association of Coloproctology of Great Britain and Ireland.
- NCCN: The National Comprehensive Cancer Network.
- MIS: minimally invasive surgery
- DCS: damage control surgery.
- LN: Lymph nodes
- LOS: Length of stay

5. Conclusion

This study did not establish a clear advantage of staged elective treatment over immediate surgical resection, or vice versa, in case of resectable emergency CRCs, therefore both methods can be considered effective. However, 2-stage treatment is associated with lower mortality rates than in emergency resectable tumors. In summary, we recommend staged treatment as a viable option until new researches, and possibly proper randomized trials, show new proof.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

The study was approved by the Institutional Ethics Committee.

Statement of informed consent

All data collected from patients records.

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