# Emergency Management of Patients with Colorectal Cancer

by
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## Abstract

Background: According to the literature, up to 30% patients with colorectal cancers (CRCs) present to the emergency department (ED) with surgical emergencies. The most common surgical presentations of these patients are: intestinal obstruction, perforation and bleeding. Palliative surgical interventions in these patients are believed to carry high risks of morbidity and mortality. Moreover, management options tend to be individualized in most cases, if not all.

Methodology: A systematic review of published literature was conducted. Articles meeting inclusion criteria were summarized. Quantitative data regarding study characteristics were analyzed and expressed as descriptive statistics. Primary outcomes of interest were post-operative complications, mortality and 5-year disease free status.

Results: 304 articles were collected from searching online data bases. Eight articles were found to match the research question and underwent a full text review. Five more articles were added from searching the grey literature. After final review, 11 articles were selected to be included in the systematic review.

Papers were assessed for methodological validity. 81.8% of studies used regression models in their analyses. Mean number of patients included in the papers was 3,567 (min= 145, max= 30,790). 50.2% of all patients were males. Most of the included studies reported mean age of more than 60 years. The mean follow-up period in days was 399.5. Analysis of different variables revealed that, CRC patients who received emergency surgery had more comorbidities (95% CI, OR=1.42 P=0.05), higher American Society of Anesthesiology classes (95% CI, OR=1.33 P=0.08), and more advanced disease (95% CI, OR=1.09 P=0.02) than CRC patients who receive surgical intervention on elective basis. Moreover, resection rate was higher in the elective group (95% CI, OR=0.5 P=0.04). In contrast, stoma creation rate was higher in the emergency group (95% CI, OR=5.08 P=0.003). Furthermore, emergency patients had higher rates of postoperative complications (95% CI, OR=4.6 P=0.007) and mortality (95% CI, OR=5.38 P=0.0001).

Conclusion: Patients requiring emergency surgery for CRC often have complex comorbidities and acute instability, and are at very high risk of postoperative complications. These findings highlight an important opportunity for the development of comprehensive systems of emergency surgical care, and, ultimately, improvement of patient outcomes.

## Preface

- Chapter one - Systematic review: The idea of this study was established by Dr Morad Hameed (MH) who is my thesis supervisor and myself as a first author (RM). Key word searches and study selection criteria were established by myself with the help of Mr Dean Guistini (DG), under supervision of Dr. Hameed. Searching the databases and obtaining initial titles and abstracts was performed by myself. The initial phase of selecting the title-relevant articles was performed by Dr. Hameed and myself. The second phase of full text review and further exclusion of articles was performed by myself. Data extraction, data and entry and data analysis was performed by myself. Writing the manuscript was done by myself with guidance from Dr. Hameed.

- Chapters two and three – Retrospective cohort study: was conducted under the supervision of the research group. Dr Hameed and myself were responsible of formulating the research objectives, the study design, and obtaining the ethical approval. I was responsible of the data collection (chart review), data analysis and writing the manuscript.

- Parts of this thesis were presented at the Trauma Association of Canada conference in Halifax in May 2016. Two abstracts were submitted to the 2016 Canadian Surgical Forum.

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## List of Abbreviations

**ACS:** American College of Surgeons
**AJCC**: American Joint Committee on Cancer
**ASA:** American Society of Anesthesiology
**CI:** Confidence Interval
**CRC:** Colorectal Cancer
**ED:** Emergency Department
**EGS:** Emergency General Surgery Services
**EL**: Elective
**EM**: Emergency
**EMBASE:** Excerpta Medica database
**ERAS**: Enhanced Recovery After Surgery
**GI:** Gastrointestinal
**GRADE:** Grading of Recommendations, Assessment, Development and Evaluations
**LOS:** Length of Stay
**MeSH:** Medical Subject Headings
**NEJM:** New England Journal of Medicine
**NSQIP:** National Surgical Quality Improvement Program
**OR:** Odds Ratio
**PCIS:** Patient Clinical Information System
**PMC:** PubMed Central
**PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta Analyses
**SSI**: Surgical Site Infection
**VCHRI:** Vancouver Coastal Health Research Institute
**VGH:** Vancouver General Hospital

## Acknowledgements

I sincerely thank my supervisor, Dr Morad Hameed for his continuous support and guidance throughout my project.

I express my sincere gratitude to Dr Garth Warnock for accepting to be my external examiner. It is an honor. Many thanks to Dr Richard Simons as well for being a member of my supervisory committee.

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My sincerely gratitude to my mentors Dr Abdullah Al-Harthy, Dr Hani Al Qadhi and Dr Zainab Al-Balushi for supporting me, not only in my training, but also most aspects of life.

## Dedication

To my father, who passed away when I was in my second year of medical school. You were, and continue to be, a source of continuous support and courage to move forward in my life. I will work hard to always make you prouder.

To my mother, who continues to be supporting and understanding, despite that she wanted me to join a specialty that is less demanding than general surgery.

To my sisters, my best friends. Yes, I have crazy loud sisters and I love them.

To my eldest nephews: Hamdan_I and Khalifa: you always remain a source of joy and happiness to me. To my youngest nephew Hamdan_II who was born while I'm away and I've never seen him yet: I can't tell how much I'm dying to meet you my sweetheart!

To My best friend and partner in crime: Najla: You've got such a beautiful heart. I wish you all the best in life.

To my dear friends and surgical family: we're all going to come back one day to build up our dear country Oman.

# Chapter 1

## A Systematic review of emergency versus elective surgical care of patients with colorectal cancer

## 1.1 Introduction

### 1.1.1 Background:

Cancer is the second most common cause of death worldwide, and the top most common cause of death in Canada (1). Patients diagnosed with malignancies are at risk of different emergency conditions during their life time. These complications are either related to their primary disease or secondary to treatment (2).

Potential emergency conditions in patients with GI malignancies can be life threatening. These cases are more likely to present to emergency general surgery services. It is estimated that up to 37% of the consultations of patients with GI malignancies presenting to the emergency department are related to acute surgical emergencies (3). Surgical complications in patients with colorectal cancer (CRC) are particularly common. Up to 30% of patients with CRC present to the emergency department with surgical emergencies (4). Among these, GI bleeding, perforation and intestinal obstruction are the most frequently encountered surgical emergencies in patients with CRC, with the later accounting for at least 20% of acute surgical admissions (5, 6). Emergency surgical interventions in these patients are believed to carry high risks of post-operative complications including: sepsis, venous thromboembolism, re-operation and also death. (2).

In general, management options in these situations tend to be individualized in most of cases, if not all (7). Given the acuteness of these conditions and the potential detrimental impact on patients' life, they are most commonly managed without any preceding multidisciplinary board discussions. In addition, the literature lacks the appropriate protocols and guidelines to follow in these situations.

### 1.1.2 Aim

We conducted a systematic review of emergency versus elective surgical management in patients with CRC. We aimed to study the characteristics and processes of care in patients with CRC managed on an emergency basis and to measure the association between emergency surgical care and outcome.

### 1.1.3 Objectives

**Primary:**

- To compare rates of post-operative mortality of patients with CRC in emergency and elective groups

- Secondary:

- To examine the different characteristics of patients with CRCs presenting to the emergency surgical services and compare them with elective cases (including: age, disease stage at presentation, and co-morbidities)

- To highlight the differences in processes of care between both groups

- To evaluate the differences in outcome (i.e. short term outcomes, adequacy of resection, disease-related survival, and disease recurrence) between emergency and elective cases

## 1.2 Methodology

### Research question with PICO framework:

Our research question was "what are the characteristics, processes of care and outcomes of patients with colorectal cancer who undergo surgical intervention on emergency or basis, and how do they differ in comparison to patients with CRC who are managed electively?" Understanding these differences will help in identifying potential areas for improvement in processes and eventually patient care. Moreover, we hope this work will serve as a gap analysis of the literature and as a basis for future research in this field of emergency general surgery.

P: Patients > 18 years diagnosed with CRC presenting with surgical complications
I: Operative management
C: Patients > 18 years diagnosed with CRC who are managed on elective basis
O: short term outcomes, completeness of resection, disease recurrence, and mortality.

### 1.2.1 Criteria for inclusion of studies in the review:

We included studies that were conducted on patients aged > 18 years with colorectal cancer presenting with surgical emergencies. Types of Studies to be reviewed included comparative studies between emergency and elective cases including observational, case-control, retrospective cohort and prospective cohort studies. We looked only at studies which evaluated surgical management as the type of intervention being performed. Outcomes of interest were: post-operative complications, recurrence of disease, disease related survival and mortality. Finally, we limited our search to published studies in English language.

### 1.2.2 Search Strategy/Description:

Available literature was searched through different databases including: Medline, EMBASE, PubMed and Cochrane Controlled Trials register. The search was performed

using both MeSH terms and key words including: colorectal cancer, emergency surgery, elective surgery, comparative study, complications and outcome. A detailed description of search strategy is attached to in Appendix 1.

Grey Literature:

PubMed Central (PMC) archives, Google Scholar, online journals, and bibliographies were searched and search study results were title screened. Four articles found to match the search question and were included for full article review.

304 studies were imported into Mendeley® software where duplicates were identified and removed. Remaining studies were then imported into an excel sheet. Studies were screened by title and abstract and studies that met the search question were identified and selected. Full text review of the selected was then performed.

Quality assessment:

Identified studies that met the publication criteria were grouped into one of the following categories: prospective cohort studies, retrospective cohort studies, cross sectional studies, observational studies, and textual/opinion papers. These studies were then assessed independently for methodological validity by two reviewers using the Newcastle-Ottawa Quality Assessment Scale (Appendix 2 and 3) and National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (Appendix 4), prior to inclusion in the review. The agreeability between the two reviewers was very good (kappa statistic= 84.6 %) Disagreements between the reviewers were resolved through discussion or assistance of a third reviewer.

### 1.2.3 Data Extraction:

The papers were grouped according to whether they are retrospective cohort studies, prospective cohort studies and cross sectional studies. A data extraction sheet was developed looking into the following information:

1- Title
2- Primary author
3- Year of publication
4- Research question
5- Study design
6- Use of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP)
7- Use of regression models
8- Number of patients
9- Outcomes measured
10- Main results
11- Interpretation of results

12-Length of follow up

The initial data sheet was tested by extracting data from a sample of articles and re-examined by two investigators. After co-approval of the data extraction form, we decided to use it for all of the papers included within the review. One reviewer (myself) performed data extraction.

### Data Synthesis:

Data entry and analysis were performed in Microsoft Excel 2016 and R© _version 0.98.1091. Forest graphs were created using Review Manager software version 5.3. Results were expressed in terms of descriptive statistics and appropriate representative charts.

## 1.3 Results

### Results of study selection process

A total of 304 articles were collected from searching through Medline, PubMed, EMBASE and Cochrane data bases. These articles were imported into Mendeley® reference manager software. 99 duplicate articles were detected by the software and were removed. Remaining studies were reviewed in three phases:

1- One reviewer (myself) screened the articles by titles.
2- Two reviewers (Dr Morad Hameed and myself) reviewed the articles by title and abstract.
3- Full text articles were finally reviewed by myself.

**Grey Literature:** Searching through PubMed Central (PMC) archives identified 612 articles that contained at least one of the key words mentioned above. Google Scholar, bibliographies and few online journals including: The New England Journal of Medicine (NEJM), the American Journal of Surgery, and Journal of the American College of Surgeons were searched as well and articles were title screened. Four more articles were found to match the search question and were included for full text review.

The following flow chart summarizes the steps performed in selecting the articles (Figure 1).

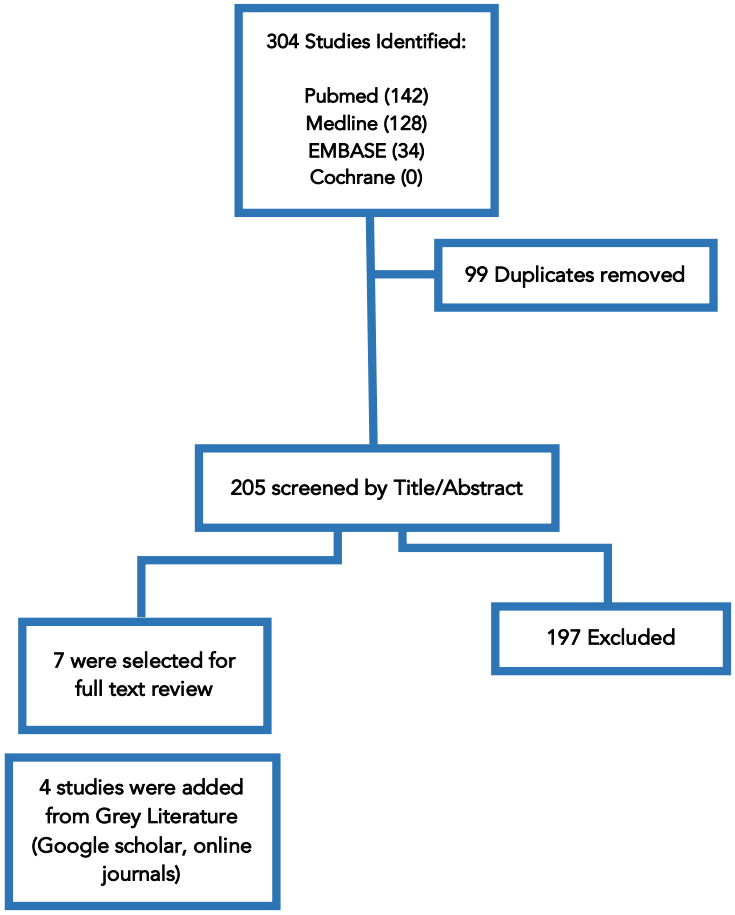



Figure 1: PRISMA flow diagram

## Characteristics of selected studies:

54.5% all of the included studies were retrospective cohort studies, with almost one third being prospective cohort studies. The following table (Table 1) illustrates the types of studies included in the final review.

Table 1: Types of studies included in the review

| Type of Study | Frequency |
|---|---|
| Prospective Cohort Studies | 4 |
| Retrospective Cohort Studies | 6 |
| Cross Sectional Studies | 1 |

Quality assessment of the included studies was carried out using the Newcastle – Ottawa Quality Assessment Scale for Cohort studies and the one used for cross-sectional studies (Tables 2 and 3), and National Institute of Health Quality Assessment

Tool for Observational Cohort and Cross-Sectional Studies (Table 4).

## Table 2: Quality assessment using Newcastle – Ottawa scale cohort studies

| No. | Title | Selection | Comparability | Exposure/Outcome | Overall Score |
|---|---|---|---|---|---|
| 1 | An evaluation of treatment results of emergency versus elective surgery in colorectal cancer patients. Bayar et al, 2015. | *** | | ** | 5/9 |
| 2 | Clinico pathological analysis of colorectal cancer: a comparison between emergency and elective surgical cases. Ghazi et al, 2013. | *** | | *** | 6/9 |
| 3 | Comparison of Hospital Performance in Nonemergency Versus Emergency Colorectal Operations at 142 Hospitals. Ingraham et al, 2009. | *** | * | *** | 7/9 |
| 4 | Colorectal cancer treatment in octogenarians: elective or emergency surgery? Ming-gao et al, 2014. | *** | | ** | 5/9 |
| 5 | Elective and emergency abdominal surgery in patients 90 years of age or older. Racz et al, 2011. | *** | | ** | 5/9 |
| 6 | Emergency surgery for colorectal cancer does not result in nodal understaging compared with elective surgery. Patel et al, 2014. | *** | ** | *** | 8/9 |
| 7 | Outcome after emergency subtotal/total colectomy compared to elective resection in patients with left-sided colorectal carcinoma. Omejc et al, 1998. | *** | | ** | 5/9 |
| 8 | Short term outcome after emergency and elective surgery for colon cancer. Sjo et al, 2009. | *** | | ** | 5/9 |

| No. | Title | Selection | Comparability | Exposure/Outcome | Overall Score |
|---|---|---|---|---|---|
| 9 | A prospective study of outcomes of emergency and elective surgeries for complicated colonic cancer. | *** | ** | ** | 7/9 |
| 10 | Elective versus emergency surgery for patients with colorectal cancer. Anderson etal, 1992. | *** | | ** | 5/9 |

## Table 3: Quality assessment using Newcastle – Ottawa scale Cross Sectional studies

| No. | Tile | Selection | Comparability | Exposure/Outcome | Overall Score |
|---|---|---|---|---|---|
| 1 | Burden of Emergency and Non emergency Colorectal Cancer Surgeries in West Virginia and the USA | *** | * | *** | 7/9 |

## Table 4: National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

| Criterion | Bayar et al (2015) | Shah et al (2013) | Ghazi et al (2013) | Ingraham et al (2009) | Ming-gao et al(2014) | Racz et al(2011) | Patel et al(2014) | Omejc et al (1998) | Sjo OH et al (2009) | Biondo S et al (2005) | Anderson et al (1992) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Was the research question or objective in this paper clearly stated? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 2. Was the study population clearly specified and defined? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 3. Was the participation rate of eligible persons at least 50%? | NR | NR | NR | NR | NR | NR | Yes | NR | NR | NR | Yes |
| 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre specified and applied uniformly to all participants? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 5. Was a sample size justification, power description, or variance and effect estimates provided? | Yes | No | Yes | Yes | No | Yes | No | No | Yes | Yes | No |
| 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? | No | No | No | No | No | No | No | No | No | No | No |

| Criterion | Bayar et al (2015) | Shah et al (2013) | Ghazi et al (2013) | Ingraham et al (2009) | Ming-gao et al(2014) | Racz et al(2011) | Patel et al(2014) | Omejc et al (1998) | Sjo OH et al (2009) | Biondo S et al (2005) | Anderson et al (1992) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 10. Was the exposure(s) assessed more than once over time? | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 12. Were the outcome assessors blinded to the exposure status of participants? | NR | NR | Yes | NR | NR | NR | NR | NR | NR | NR | NR |
| 13. Was loss to follow-up after baseline 20% or less? | NA | NA | NA | NA | NA | NA | NR | NA | NR | NR | NR |
| 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s) | No | Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes |
| Overall rate | Good | Good | Good | Good | Fair | Good | Good | Fair | Good | Good | Good |

*NA: not applicable, NR: not reported

Table of summary of study characteristics is attached in appendix 4.

Nine out of 11 (81.8%) studies clearly mentioned the use of regression models in their analyses. Only 1 group used ACS NSQIP spell this out data set in their study. Mean number of patients included in the papers was 3,567 (with min= 145 and max= 30,790). 50.2% of all patients were males. Most of the included studies reported mean age of more than 60 years (Table 5). The mean follow-up period in days was 399.5.

Table 5: Summary of Patients' Age in all papers

| No | Author | Age (mean, median or %) | |
|---|---|---|---|
| | | Emergency | Elective |
| 1 | Bayar et al, 2015 | Mean 62 Y | Mean 62 Y |
| 2 | Ming-gao et al, 2014 | Median 83.5 Y | Median 84.7 Y |
| 3 | Patel et al, 2014 | 81.4% > 60 Y | 72.2% > 60 Y |
| 4 | Ghazi et al, 2013 | Total mean 69.2 Y | Total mean 69.2 Y |
| 5 | Shah et al, 2013 | 68.2% > 65 Y | 68% > 65 Y |
| 6 | Racz et al, 2011 | Median 91 Y | Median 91.5 Y |
| 7 | Ingraham et al, 2009 | Mean 64.1 Y | Mean 61.3 Y |
| 8 | Sjo OH et al, 2009 | Median 76 Y | Median 74 Y |
| 9 | Biondo S et al, 2005 | Mean 67.24 Y | Mean 67 Y |
| 10 | Omejc et al, 1998 | Mean 68.5 Y | Mean 62.1 Y |
| 11 | Anderson et al, 1992 | 55.3% > 65 Y | 55.3% > 65 Y |

## Comparing rates of co-morbidities in patients with CRC who undergo elective or emergency surgical management.

Six studies demonstrated the differences in rates of co-morbidities between emergency and elective groups. Patients had at least one co-morbidity pre operatively, mostly cardiovascular.

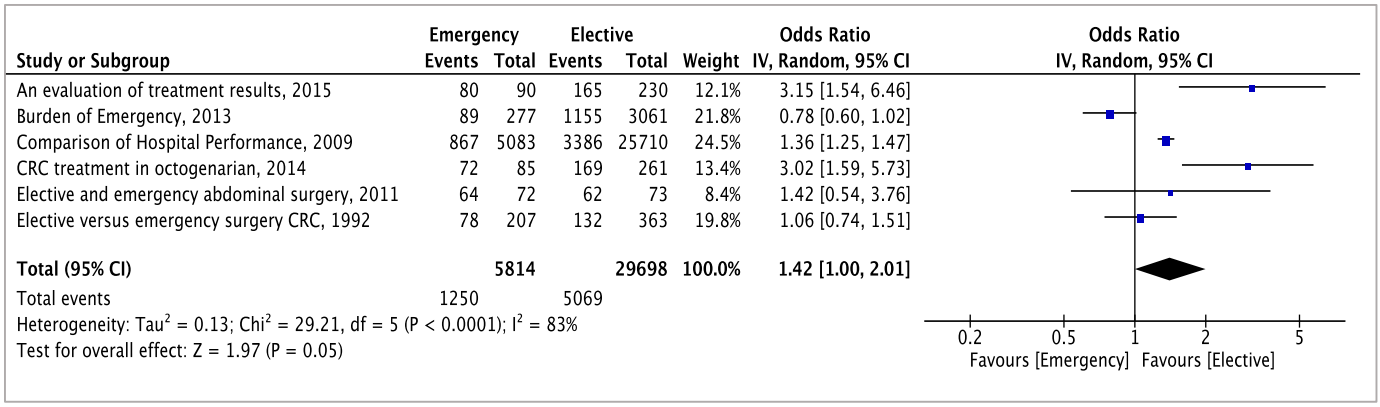
Most of studies reported at least one co-morbid condition in their study population. The most commonly reported co-morbidities were cardiovascular including hypertension and coronary artery disease. Type 2 diabetes was among the most commonly reported endocrinological co-morbidities. In general, rates of co-morbid conditions were higher in patients with CRC who received emergency surgical intervention as summarized in Table 6.

Table 6: Characteristics and main findings of studies reporting rates of co-morbidities in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Bayar et al, 2015 | Retro-spective cohort study | Adults with CRC | 320 | **Age**:<br>Mean EL: 62 Y<br>Mean EM: 62 Y<br>**Male:** 62.8% | Elective vs emergency surgery | 88.9% of EM group had comorbidities vs 71.7% of EL group (P-value <0.001) |
| 2 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**:<br>Median EL: 84.7 Y<br>Median EM: 83.5 Y<br>**Male:** 44.2% | Elective vs emergency surgery | 84.7% of EM group vs 64.8% of EL group had comorbidities. (OR: 3.02, 95% CI). |
| 3 | Shah et al, 2013 | Cross-sectional comparison of a national sample | Adults with CRC | 3,338 | **Age:**<br>EL: 68% > 65 Y<br>EM: 68.2% > 65 Y<br>**Male:** 48.5% | Elective vs emergency surgery | No significant difference in rate of comorbidities in both groups. (P-value 0.179) |
| 4 | Racz et al, 2011 | Retro-Spective cohort study | Adults with surgical conditions including CRC | 145 | **Age**:<br>Median EL: 91 Y<br>Median EM: 91 Y<br>**Male:** 36.6% | Elective vs emergency surgery | 84.9% of EL vs 88.9% of EM group. (No P-value). |
| 5 | Ingraham et al, 2009 | Retro-spective cohort study | Adults with CRC | 30,793 | **Age**:<br>Mean EL: 61.3 Y<br>Mean EM: 64.1 Y<br>**Male:** 47.8% | Elective vs emergency surgery | 24% of EL vs 48.2% of EM group. (P-value <0.0001). |
| 6 | Anderson et al, 1992 | Pro- spective study | Adults with CRC | 570 | **Age:**<br>EL: 55.3% > 65 Y<br>EM: 55.3% > 65 Y<br>**Male:** 50% | Elective vs emergency surgery | 36% of EL vs 38% of EM group. |

Figure 2 subjectively describes the differences in rates of patients' co-morbidities across these studies. There were fewer co-morbidities patients in the elective group (OR= 1.42, 95% CI, *P-value*= 0.05).

Figure 2: Forest graph of comorbidities in emergency and elective groups




## Comparing ASA classes in patients with CRC who undergo elective or emergency surgical management.

In most studies, ASA classes were grouped in 3 categories (ASA classes I-II, ASA class III and ASA class IV). Only 3 studies reported patients in ASA class V. In general, the reported difference in ASA classes were statistically significant. CRC patients who underwent emergency surgery had worse ASA classes in most of studies (Table 6).

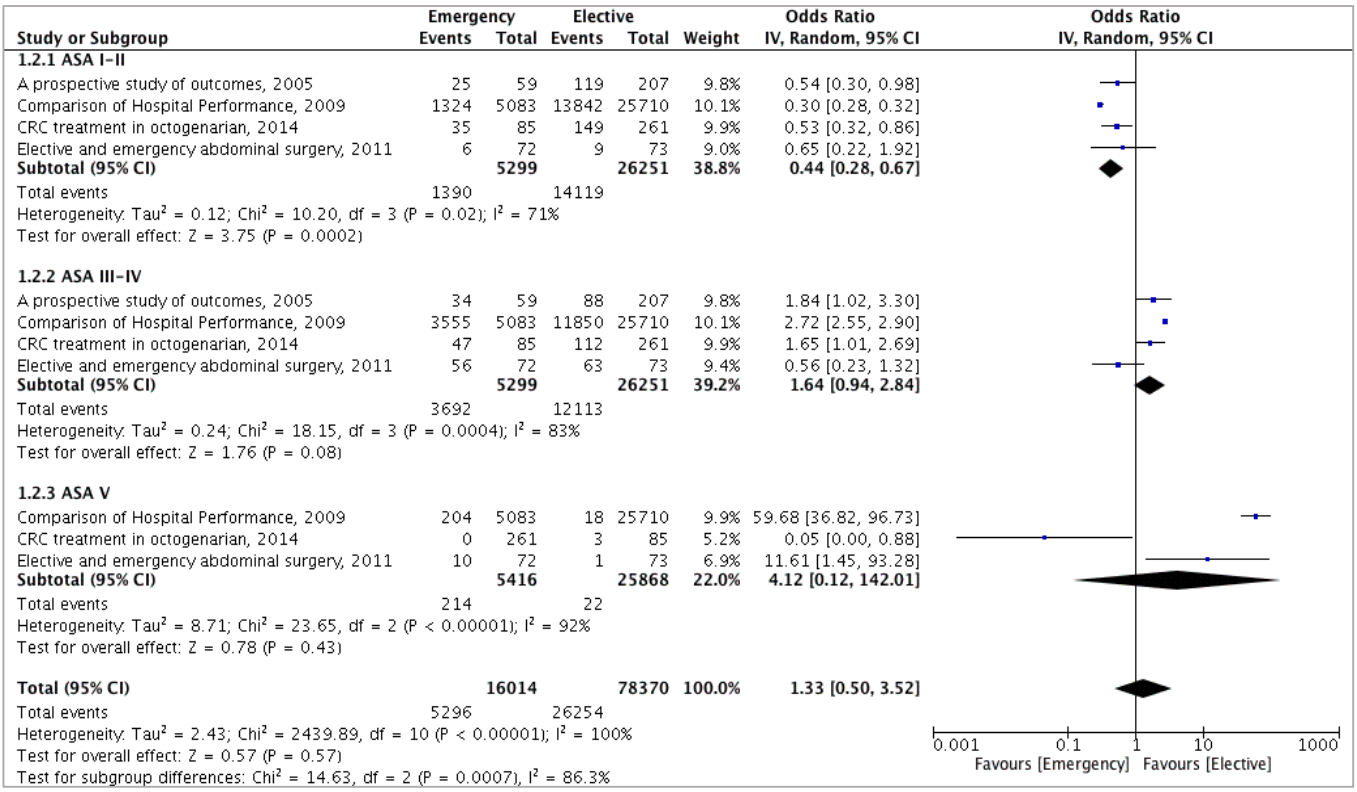
Table 7: Characteristics and main findings of studies reporting ASA classes in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**: Median EL: 84.7 Y Median EM: 83.5 Y **Male:** 44.2% | Elective vs emergency surgery | **ASA Classes I-II:** 41.2% of EM group vs 57.1% of EL group. **ASA Classes III-IV:** 55.3% in EM group vs 42.9 in EL group. (P-value <0.01) |
| 2 | Racz et al, 2011 | Retro-Spective cohort study | Adults with surgical conditions including CRC | 145 | **Age**: Median EL: 91 Y Median EM: 91 Y **Male:** 36.6% | Elective vs emergency surgery | **ASA classes I-II:** 12.3% in EL group vs 8.3% in EM group. **ASA classes III-IV:** 86.3% in EL |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | group vs 77.8% in EM group. |
| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
| 3 | Ingraham et al, 2009 | Retro-spective cohort study | Adults with CRC | 30,793 | **Age**:<br>Mean EL: 61.3 Y<br>Mean EM: 64.1 Y<br>**Male:** 47.8% | Elective vs emergency surgery | **ASA classes I-II:** 53.8% in EL group vs 4.3% in EM group. **ASA classes III-IV:** 46.1% in EL group vs 69.9% in EM group. (P-value <0.0001). |
| 4 | Biondo S et al, 2005 | Pro spective cohort study | Adults with CRC | 266 | **Age**:<br>Mean EL: 67 Y<br>Mean EM: 67.24 Y<br>**Male:** 63.2% | Elective vs emergency surgery | **ASA classes I-II:** 57.4% in EL group vs 42.3% in EM group. **ASA classes III-IV:** 42.6% in EL group vs 57.7% in EM group. (P-value 0.05). |

Odds ratios are in favour of the elective group as they have less severe ASA classes (OR= 1.33, 95% CI). A closer look at each subgroup of figure 3 highlights the differences in rates of patients in each subgroup.

Figure 3: Forest graph of ASA classes in emergency and elective groups




## Comparing disease stages in patients with CRC who undergo elective or emergency surgical management.

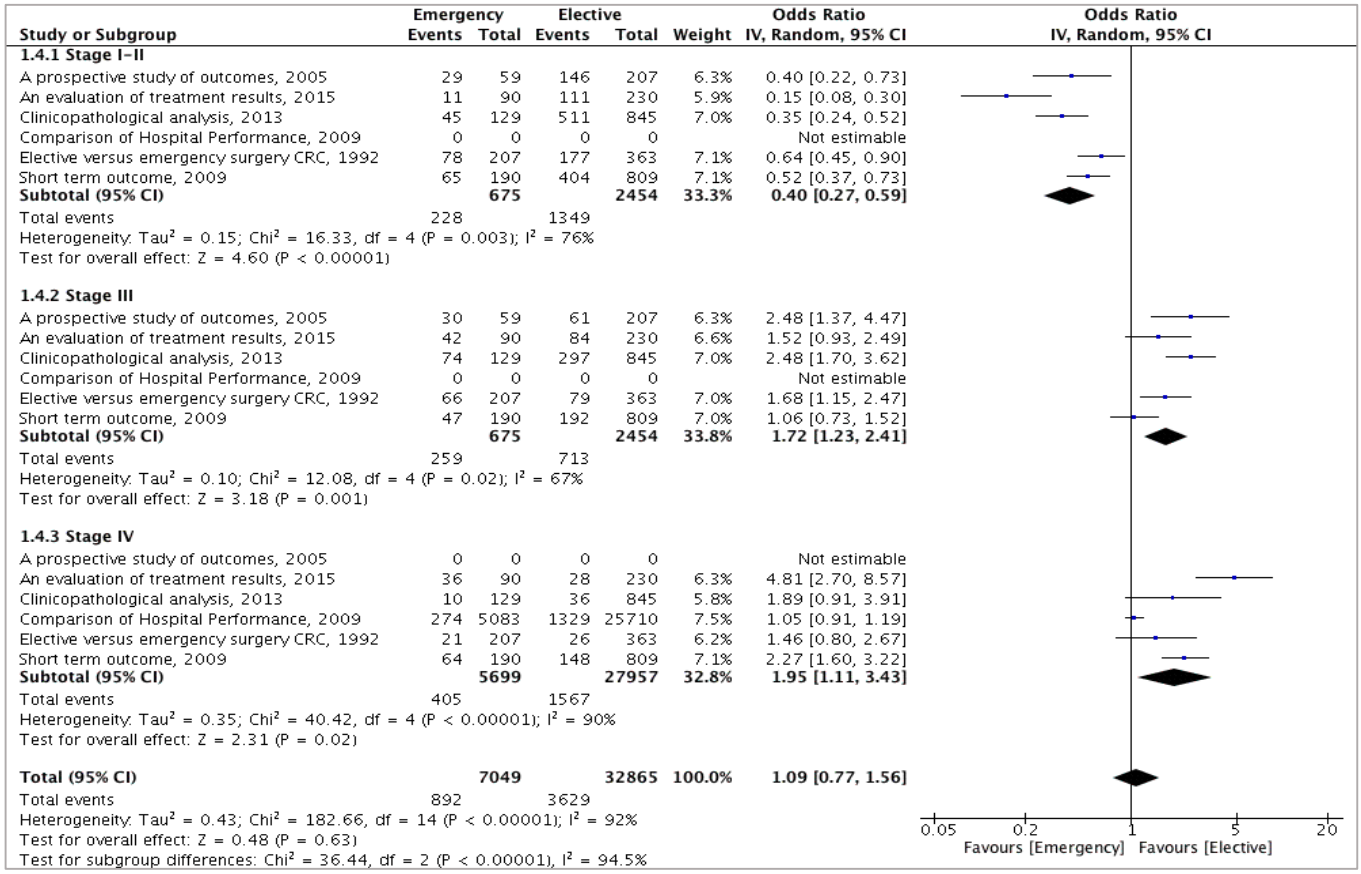
To measure CRC stages, most studies used the American Joint Committee on Cancer (AJCC) staging system. Only one study that reported disease stages using the Duke's classification system. 5 Studies showed higher rates of advanced stages of CRC in patients who underwent emergency surgery (Table 8). One study by Ingraham et al. showed no revealed no difference in disease stages in both groups.

Table 8: Characteristics and main findings of studies reporting disease stages in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Bayar et al, 2015 | Retro-spective cohort study | Adults with CRC | 320 | **Age**:<br>Mean EL: 62 Y<br>Mean EM: 62 Y<br>**Male:** 62.8% | Elective vs emergency surgery | Stage 1- 3 disease were more common in EL patients, while patients with more advanced stages constituted the EM group. (P-value <0.001) |
| 2 | Ghazi et al, 2013 | Retro-spective cohort study | Adults with CRC | 976 | **Age**: 69.2 Y (mean)<br>**Male:** 52.6% | Elective vs emergency surgery | **Stages 1 – 2:** 60.5% in EL group vs 35.1% in EM group. (P-value 0.002).<br>**Stages 3 – 4:** 39.4% in EL group vs 64.8% in EM group. (P-value <0.0001). |
| 3 | Ingraham et al, 2009 | Retro-spective cohort study | Adults with CRC | 30,793 | **Age**:<br>Mean EL: 61.3 Y<br>Mean EM: 64.1 Y<br>**Male:** 47.8% | Elective vs emergency surgery | Disseminated cancer was found in 5.2% of EL group and 5.4% of EM group. (P-value 0.52). |
| 4 | Biondo S et al, 2005 | Pro spective cohort study | Adults with CRC | 266 | **Age**:<br>Mean EL: 67 Y<br>Mean EM: 67.24 Y<br>**Male:** 63.2% | Elective vs emergency surgery | **Stage 1 - 2:** 49.2% in EM group vs 70.5% in EL group.<br>**Stage 3:** 50.8% in EM group vs 29.5% in EL group. |
| 6 | Anderson et al, 1992 | Pro- spective study | Adults with CRC | 570 | **Age:**<br>EL: 55.3% > 65 Y<br>EM: 55.3% > 65 Y<br>**Male:** 50% | Elective vs emergency surgery | **Stage 1 - 3:** 69.6% in EM group vs 70.5% in EL group.<br>**Stage 4:** 10% in EM group vs 7% in EL group. |

Analyzing pooled patients' data from these studies showed statistically significant differences between emergency and elective cases in stages III and IV is as illustrated in figure 4 (OR= 1.72, 95% CI, *p-value*= 0.001 and OR= 1.95, 95% CI, *p-value*= 0.02, respectively).

Figure 4: Forest graph of disease stages in emergency and elective groups




## Comparing resection rates, adequacy of surgical resection, stoma creation rates, level of surgical training of surgeons performing resections in patients with CRC who undergo elective or emergency surgical management.

In this section, we studied differences in processes of care in patients with CRC in both emergency and elective groups. These processes include: resection rate, adequacy of surgical resection in terms of resection margin and the number of harvested lymph nodes, rates of stoma creation, and differences in surgical training levels in surgeons who performed these surgeries. Table 9 showed the differences in resection rates in both groups. All studies included in this table concluded that, higher rated of surgical

resection are likely to be achieved in CRC patients undergoing elective surgery.

**Table 9: Characteristics and main findings of studies reporting resection rates in patients with CRC managed on elective or emergency basis**

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Bayar et al, 2015 | Retro-spective cohort study | Adults with CRC | 320 | **Age**:<br>Mean EL: 62 Y<br>Mean EM: 62 Y<br>**Male:** 62.8% | Elective vs emergency surgery | Resection rates 52.2% vs 79.6% in EM and EL groups respectively. (P-value < 0.001). |
| 2 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**:<br>Median EL: 84.7 Y<br>Median EM: 83.5 Y<br>**Male:** 44.2% | Elective vs emergency surgery | Curative resection was achieved in 89.7% of EL group compared to 71.8% in EM group. (P-value <0.01). |
| 3 | Sjo OH et al, 2009 | Pro-spective cohort study | Adults with CRC | 999 | **Age**:<br>Median EL: 74 Y<br>Median EM: 76 Y<br>**Male:** 45.8% | Elective vs emergency surgery | Resection was achieved in 94.3% of EL group compared to 84.7% in EM group. (P-value <0.01). |
| 4 | Anderson et al, 1992 | Pro- spective study | Adults with CRC | 570 | **Age:**<br>EL: 55.3% > 65 Y<br>EM: 55.3% > 65 Y<br>**Male:** 50% | Elective vs emergency surgery | Curative resection was achieved in 58% of EL group compared to 45% in EM group. |

Two studies reported the differences in adequacy of surgical resection as shown in Table 10. Petal et al. investigated the differences in number of harvested lymph nosed and found that there was no statistical significance in number of harvested nodes in both arms.

On the other hand, Ghazi and his group assessed the adequacy of surgical resection in regard to whether the resected margin was involved with malignancy or not. They concluded that, higher rates of negative surgical margin are likely to be achieved in

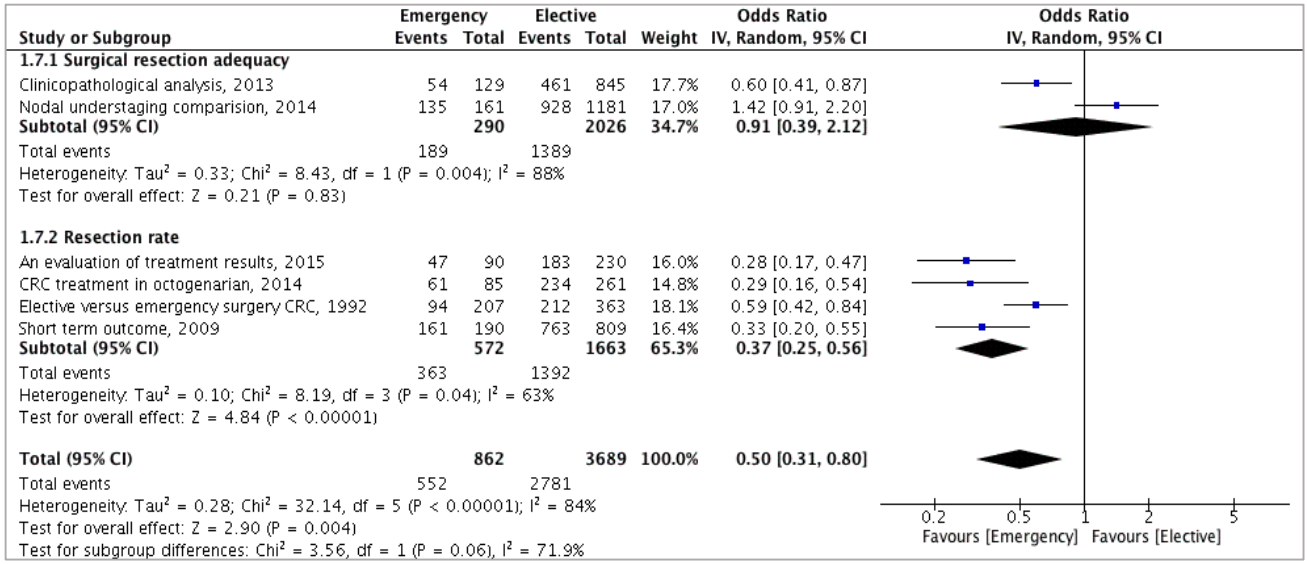
patients undergoing elective surgery.

Table 10: Characteristics and main findings of studies reporting adequacy of surgical resection in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Patel et al, 2014 | Pro- spective cohort study | Adults with CRC | 1,279 | **Age:** EL: 72.2% > 60 Y EM: 81.4% > 60 Y **Male**: not mentioned | Elective vs emergency surgery | Adequate (≥ 12 nodes) LN were harvested in 83.0% of EL cases and 83.9% of EM cases. (P-value 0.79). |
| 2 | Ghazi et al, 2013 | Retro- spective cohort study | Adults with CRC | 976 | **Age**: 69.2 Y (mean) **Male**: 52.6% | Elective vs emergency surgery | Infiltrative margin was setected in 45.5% of EL vs 58.1% of EM cases. (P-value 0.008). |

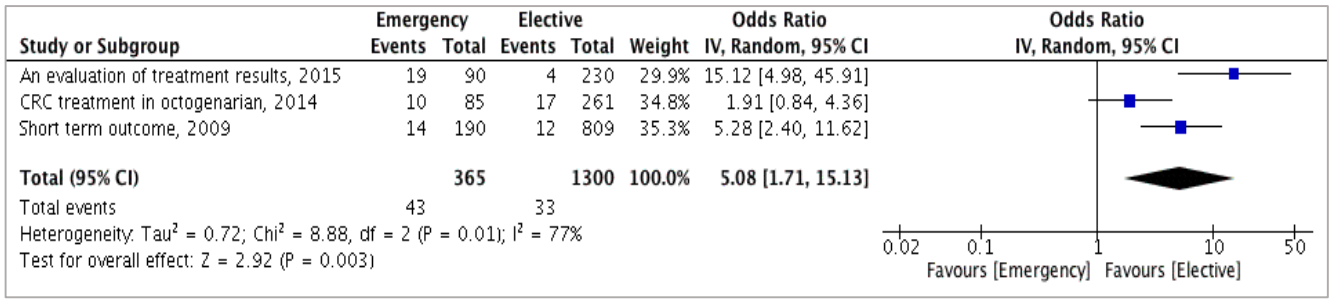
Figure 5 describes the differences in resection rates between emergency and elective groups. Resection intention is defined here as curative resection with or without stoma creation. Adequacy of surgical resection is defined as negative margin on the resected specimen and adequate number of lymph nodes. Analysis of pooled data in figure 5 failed to show any significant difference in adequacy of surgical resection between the emergency and the elective groups (OR= 0.91, 95% CI, *p-value*= 0.83). However, emergency patients had lesser resection rates compared to patients managed electively (OR= 0.5, 95% CI, *p-value*= 0.004).

Figure 5: Forest graph of resection adequacy and resection rates in emergency and elective groups




Three studies measured the differences in stoma creation rates in CRC patients in emergency and elective groups. Rates were higher in the emergency group, as shown in figure 6. The difference in stoma creation rates between the emergency and elective groups was statistically significant (OR= 5.08, 95% CI, *p-value*= 0.003).

Figure 6: Forest graph of stoma creation rates in emergency and elective groups




Only one study compared surgical performance in adequacy of nodal harvest among different surgical subspecialties. There was no significant difference in the numbers of lymph nodes harvested by surgeons from different subspecialties as described in table 11.

Table 11: adequacy of lymph node harvest in emergency and elective groups across different surgical specialties.

| Surgical specialty | Emergency (%) | Elective (%) | P value |
|---|---|---|---|
| Colorectal | 17.3 | 9.7 | 0.28 |
| Surgical Oncology | 18.4 | 6.3 | 0.23 |
| General Surgery | 16.5 | 19.5 | 0.44 |

*Emergency surgery for colorectal cancer does not result in nodal under-staging compared with elective surgery. Patel et al, 2014.

On the other hand, the differences in rates of elective and emergency surgeries performed by consultant and non-consultants was significant (Table 12). According to the study conducted by Anderson et al, elective CRC cases are more likely to be performed by consultants (*p-value*= 0.001).

Table 12: Levels of training in surgeons performing emergency and elective CRC surgeries.

| Training Level | Emergency (%) | Elective (%) | P value |
|---|---|---|---|
| Consultant | 49.3 | 63.1 | 0.001 |
| Non consultant | 39.6 | 24.2 | 0.0001 |

***** Elective versus emergency surgery for patients with colorectal cancer. Anderson et al, 1992.

## Comparing rates of post-operative complications and length of hospital stay in patients with CRC who undergo elective or emergency surgical management.

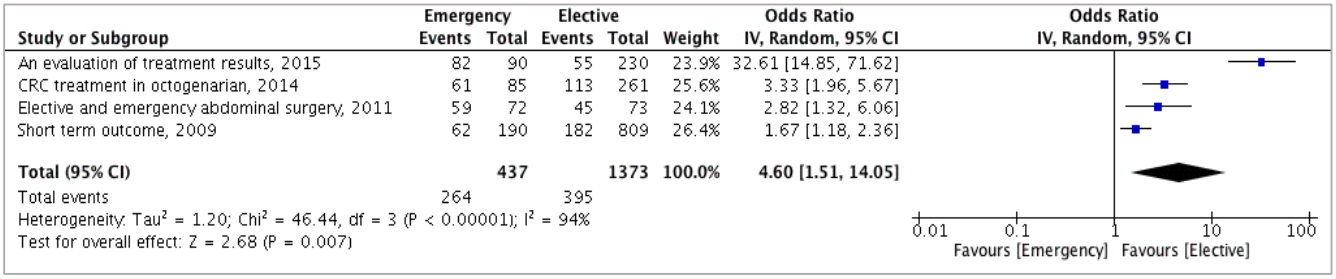
In the next two sections, we assessed the differences in post-operative short and long term outcomes in RC patients who undergo emergency or elective surgical intervention. Four studies reported the occurrence of at least 1 post-operative complication in their study groups (Table 13). All four studies reported higher rates of post-operative complications in the emergency group. Bayar et al. reported surgical site infections, evisceration and atelectasis are the most frequently encountered complications.

Table 13: Characteristics and main findings of studies reporting post-operative complications in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Bayar et al, 2015 | Retro-spective cohort study | Adults with CRC | 320 | **Age**:<br>Mean EL: 62 Y<br>Mean EM: 62 Y<br>**Male**: 62.8% | Elective vs emergency surgery | At least 1 post-operative complication occurred. 91.1% vs 23.9% in EM and EL groups respectively. (P-value <0.05). Most common reported complications: SSI, atelectasis and evisceration. |
| 2 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**:<br>Median EL: 84.7 Y<br>Median EM: 83.5 Y<br>**Male:** 44.2% | Elective vs emergency surgery | 76.6% of EM group had post-operative complications compared to 36.4% of EL group. (P-value < 0.02). |
| 3 | Racz et al, 2011 | Retro-Spective cohort study | Adults with surgical conditions including CRC | 145 | **Age**:<br>Median EL: 91 Y<br>Median EM: 91 Y<br>**Male:** 36.6% | Elective vs emergency surgery | Post-operative complications rate 61.6% in EL group and 81.9% in EM group. (P-value <0.007). |
| 4 | Sjo OH et al, 2009 | Pro-spective cohort study | Adults with CRC | 999 | **Age**:<br>Median EL: 74 Y<br>Median EM: 76 Y<br>**Male:** 45.8% | Elective vs emergency surgery | Post-operative complications rate 24% in EL group and 38% in EM group. (P-value <0.01). |

The analysis of pooled patients' data described in figure 7 shows that emergency CRC patients are more likely to experience post-operative adverse events compared to their elective counterparts (OR= 4.60, 95% CI, *p-value*= 0.007).

Figure 7: Forest graph of post-operative complications in emergency and elective groups




Differences in median hospital length of stay was demonstrated by two studies. Patients managed on emergency basis had significantly longer LOS than patients managed electively. Statistical significance of these differences is shown in table 14.

Table 14: Median Length of hospital stay in emergency and elective groups

| No | Study | Emergency | Elective | P value |
|---|---|---|---|---|
| 1 | Colorectal cancer treatment in octogenarians: elective or emergency surgery? Ming-gao et al, 2014. | 21 | 12 | <0.01 |
| 2 | Elective and emergency abdominal surgery in patients 90 years of age or older. Racz et al, 2011. | 12 | 8 | <0.001 |

## Comparing rates of post-operative mortality, recurrence rates and disease related survival in patients with CRC who undergo elective or emergency surgical management.

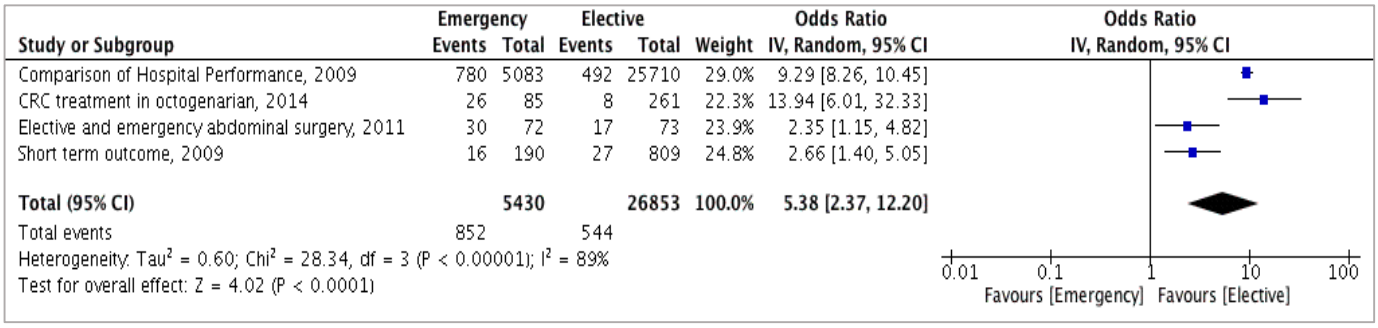
Here, we assessed differences in rates of post-operative mortality, disease recurrence and disease related survival in both groups. Four studies described at least 30-days post-operative mortality. While most of these studies showed higher mortality rates in emergency groups, Ming-gao and his colleagues showed no difference in mortality between both groups.

Table 15: Characteristics and main findings of studies reporting post-operative mortality in patients with CRC managed on elective or emergency basis

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**: Median EL: 84.7 Y Median EM: 83.5 Y **Male:** 44.2% | Elective vs emergency surgery | No significant difference in post-operative mortality. (P-value <0.25). |
| 2 | Racz et al, 2011 | Retro-Spective cohort study | Adults with surgical conditions including CRC | 145 | **Age**: Median EL: 91 Y Median EM: 91 Y **Male:** 36.6% | Elective vs emergency surgery | **In-hospital mortality:** 9.6% in EL group vs 20.8% in EM group. (P-value <0.06). |
| 3 | Ingraham et al, 2009 | Retro-spective cohort study | Adults with CRC | 30,793 | **Age**: Mean EL: 61.3 Y Mean EM: 64.1 Y **Male:** 47.8% | Elective vs emergency surgery | 1.9% in EL group vs 15.4% in EM group. (P-value <0.0001). |
| 4 | Sjo OH et al, 2009 | Pro-spective cohort study | Adults with CRC | 999 | **Age**: Median EL: 74 Y Median EM: 76 Y **Male:** 45.8% | Elective vs emergency surgery | 3.5% in EL group vs 10.4% in EM group. (P-value <0.01). |

Figure 8 shows analysis of pooled data in regard to post-operative mortality. Rates were higher in the emergency group as compared to their elective counterparts (OR= 5.38, 95% CI, *p-value*= 0.0001).

Figure 8: Forest graph of post-operative mortality in emergency and elective groups




Only one study reported disease recurrence rates in emergency and elective groups. Biondo and his group reported disease recurrence rates of 30.5% and 29% in emergency and elective groups, respectively (OR= 0.371, 95% CI, P= 0.006).

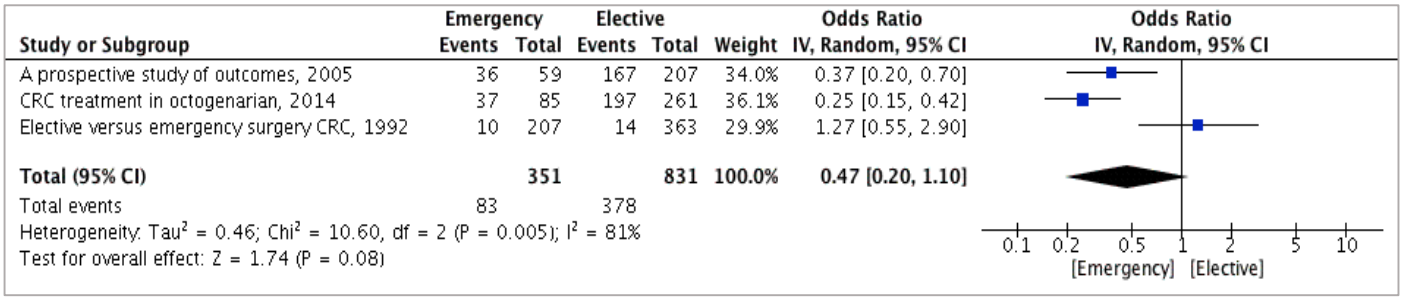
Three of the included studies measured rates of at least 1-year disease related survival in emergency and elective groups.

**Table 16: Characteristics and main findings of studies reporting disease related survival in patients with CRC managed on elective or emergency basis**

| No. | Author | Study design | Population | Number of patients | Characteristics | Intervention | Main results |
|---|---|---|---|---|---|---|---|
| 1 | Ming-gao et al, 2014 | Retro-spective cohort study | Adults with CRC | 346 | **Age**:<br>Median EL: 84.7 Y<br>Median EM: 83.5 Y<br>**Male:** 44.2% | Elective vs emergency surgery | **1-year survival:** 43.8% in EM group vs 60% in EL group. (P-value 1.00).<br>**3-year survival:** 10.9% in EM group vs 10.0% in EL group. (P-value 1.00). |
| 2 | Biondo S et al, 2005 | Pro spective cohort study | Adults with CRC | 266 | **Age**:<br>Mean EL: 67 Y<br>Mean EM: 67.24 Y<br>**Male:** 63.2% | Elective vs emergency surgery | **3-year survival after radical surgery:** 80.4% in EM group vs 94.5% in EL group. (P-value 0.3). |
| 3 | Anderson et al, 1992 | Pro- spective study | Adults with CRC | 570 | **Age:**<br>EL: 55.3% > 65 Y<br>EM: 55.3% > 65 Y<br>**Male:** 50% | Elective vs emergency surgery | **5-year survival:** 36% in EM group vs 64% in EL group. |

Figure 9 shows analysis of pooled patients' data. Disease related survival rates are lower in the emergency than in the elective group (OR= 0.47, 95% CI, *p-value*= 0.08).

**Figure 9: Forest graph of disease related survival in emergency and elective groups**



## 1.4 Discussion

Emergency general surgery services (EGS) encounter high volumes of patients presenting with emergency conditions including surgical complications related to colon cancer. These patients are generally sicker and more complex than their counterparts with CRC who present without complications. Unfortunately, little is known about processes of care for, or outcomes of these patients on organized emergency general surgery services. Patients presenting with complications of CRC may face issues of access to timely primary care, and they may have more comorbidities or other barriers to surgical intervention. They also may have suboptimal surgical or adjuvant therapy for their cancers, and they may face a higher rate of complications or long-term adverse outcomes.

We conducted this systematic review to analyze the different characteristics in patients with CRC who present for surgical management as emergency or elective basis. Basic demographic characteristics were quite comparable, including male to female ratio and median ages of included patients in both the emergency and elective groups. In general, most of the studies reported mean age of more than 60 years (Table 5).

Rates of co-morbidities were significantly different between patients with CRC who were managed on emergency basis compared to those managed electively. Patients managed on emergency basis were reported to have higher rates of co-morbidities as shown in figure 3. Most of the included studies reported at least one co-morbid condition in their patients. Among these, cardiovascular conditions were the most frequently reported co-morbidities in these studies.

Most studies used the ASA classification as an indication to pre-operative assessment of physical status. Analysis of ASA classification in patients managed on emergency basis showed that these patients are more likely to have worse pre-operative physical status compared to their elective counterparts (Figure 4). However, it failed to demonstrate statistical significance of the observed difference in ASA classification between the two groups as indicated by p-value of 0.57. In contrast, patients with CRC who were managed on elective basis were more likely to have better ASA classes (ASA classes I & II), than patients managed on emergency basis (OR= 0.44, 95% CI, *p-value*= 0.0002).

We also looked into the differences in CRC stage at presentation between patients managed on elective and emergency basis. Figure 5 demonstrated that patients in the elective group are more likely to have less advances disease (stages I and II). The statistical significance of this observation was indicated with a *p-value* of less than

0.00001. In general, patients with CRC who are managed on emergency basis have more advanced disease (stages III and IV) than their elective counterparts (*p-value*= 0.001 and 0.02 for stages III and IV respectively).

The optimum management of patients with CRC is complete resection (22, 30) However, due to the acuteness of presentation of patients with complicated CRC, this aim might not be possible to be achieved in certain proportion of cases. Adequate surgical resection is defined here as achieving negative resection margins and 12 or more lymph nodes harvested (23, 24). Literature suggests a strong association between extensive lymph node harvest and better survival in patients with colon cancer (25).

It was interesting to see that our analysis of differences in adequacy of resection between the emergency and elective groups was not significant statistically (OR= 0.91, 95% CI, *p-value*= 0.83). However, the difference in resection rates between the two group was significant, suggesting that resection intention is more likely to be achieved in patients with CRC who are managed on elective basis (OR= 0.37, 95% CI, *p-value*= 0.00001).

On the other hand, stoma creation rates were likely to be higher in patients with CRC undergoing emergency surgical management (OR= 5.08, 95% CI, *p-value*= 0.003). Several factors can affect the decision whether to perform resection with or without stoma creation. Some of these factors are: patient's hemodynamic status, ASA classification, age, perioperative findings and tumor location (26).

Lots of emphasis is put on the importance of operating on CRC during the day time in presence of experienced surgeons and anesthetists (27). However, this might not apply to all cases, especially in emergency situations. Table 11 demonstrates the adequacy of lymph node harvest in CRC patients managed on emergency and elective basis by surgeons from three different subspecialties including: colorectal, surgical oncology and general surgery. This study showed no significant difference in the number of nodes harvested across these subspecialties in both groups. However, analysis demonstrated in table 12 suggests that elective CRC cases are more likely to be operated on by consultants compared to their emergency counterparts (*p-value*= 0.001).

One of the important short-term outcomes measured in patients with CRC who undergo surgical management are post-operative complications (Figure 8). There are significantly higher rates of post-operative complications in patients undergoing emergency surgical management of CRC (OR= 4.60, 95% CI, *p-value*= 0.007). Surgical site infection (SSI) and sepsis were the two most commonly reported post-operative adverse events (28, 29).

It is, hence, reasonable to predict that patients with CRC who undergo emergency surgery are likely to have longer hospital LOS due to the reasons suggested above. Table 14 compares median of hospital LOS in days between emergency and elective groups. There is a statistically significant higher median of LOS in patients in the emergency group (*p=value*= 0.01 and 0.001).

Despite efforts to perform curative resection, CRC is reported to recur in almost half of the patients (30). Several factors contribute to CRC recurrence after curative resection, most importantly: emergency surgery. Other factors include: anastomotic leakages, postoperative bacterial infections, and blood transfusions. However, the exact mechanism is still unknown (31). The study by Biondo et al showed significant difference in recurrence rates between emergency and elective groups (OR= 0.47, 95% CI, *p-value*= 0.006).

Survival after potentially curative resection of CRC remains poor. Literature reports a 5-year survival rate of almost 50% in these patients. Several factors are suggested to contribute to the poor post-operative survival in patients with CRC, including: grade, disease stage, resection margin and the presence of genetic mutation (32). Survival is decreased further in patients with CRC undergoing emergency surgery (33). Our analysis revealed that, there is a difference in disease related survival rates between emergency and elective groups as demonstrated in Figure 10. However, this difference was not statistically significant (OR= 0.47, 95% CI, *p-value*= 0.08).

## 1.5 Conclusion

Surgical complications in patients with CRC are not uncommon. Their physiology is quite challenged preoperatively as demonstrated by having more severe ASA classes pre operatively. Patients who present to EGS with surgical complications related to CRC carry higher risks of postoperative adverse outcomes compared to elective CRC patients. These complications include: surgical site infections and sepsis. Furthermore, they are likely to have higher rates of post-operative mortality and lower rates of disease related survival compared to their elective counterparts.

These facts must be kept in mind when managing patients with CRC who present with surgical complications. Moreover, emphasis should be put on the importance of directing more attention toward emergency CRC patients in terms of better preoperative optimization and resuscitation, in order to improve their outcomes.

Strengths and limitations:

One of the important strength points in the included studies is good number of patients, with a mean of 3,567 patients. Another point is the use of regression models in their analyses as this helps in controlling certain factors when comparting characteristics and outcomes between the two groups. Furthermore, most of the included studies looked into multiple characteristics and outcomes in comparing patients with CRC who undergo emergency and elective surgical management.

However, one of the main limitations in this review is the number of included studies. We hope that we might be able to update this review in future to include more studies and to include unpublished literature. Another point is the type of included studies, as most of these are retrospective studies. None of the included studies measured the correlation between time from ED to the operation room (OR) and outcomes in CRC patients receiving emergency surgery. We hope we will be able to include this correlation in future updates, as feasible. Furthermore, we would like to evaluate the relationship between use of neo-adjuvant and adjuvant chemo-radiotherapy and disease related survival in both arms.

Chapters 2

# Emergency and non-emergency surgery for colorectal cancer at a Canadian teaching hospital

## 2.1 Introduction

### 2.1.1 Background

The Vancouver General Hospital (VGH) has one of the busiest emergency general surgery services in the country, and cares for a high volume of patients presenting with emergency conditions related to colon cancer, including bowel obstruction, bowel perforation, and lower gastrointestinal bleeding. These patients are generally sicker and more complex than their elective counterparts who present without complications. Little is known about processes of care for, or outcomes of these patients on organized EGS services. Literature suggests that, patients presenting with complications of CRC may face issues of access to timely primary care, and they may have more comorbidities or other barriers to surgical intervention. They also may have suboptimal surgical or adjuvant therapy for their cancers, and they may face a higher rate of complications or long-term adverse outcomes.

***This study seeks to describe the population of CRC patients who present with emergency surgical complications, in terms of their risks for surgical emergencies and their short and long-term outcomes.*** Advances in our understanding of this population may suggest opportunities to address vulnerabilities and improve treatment.

### 2.1.2 Aim

To compare patient factors, and outcomes in the care of colon cancer patients presenting for non-emergency versus emergency surgical interventions using NSQIP data.

### 2.1.3 Objectives

Primary:

- To compare 30-days mortality rates between CRC patients requiring emergency or non-emergency surgeries

Secondary:

- To compare the differences in characteristics in both groups including: age, co-morbid conditions and ASA classes
- To compare their disease stages at presentation
- To measure the differences in rates of post-operative short-term outcomes including: SSI, pneumonia and DVT.

## 2.2 Methodology

**Study Design:** Retrospective Cohort Study

**Site:** Vancouver General Hospital (VGH)

**Time:** Records of patients diagnosed with CRC and admitted to VGH for surgeries during the period from January 2010 to December 2015.

**Study Population: (inclusion and exclusion criteria)**
Patients aged more than 18 years who were diagnosed with colorectal cancer and presented for surgical intervention on a non-emergency or emergency basis.

**Ethical approval** for both phases describes in chapters 2 and 3 was obtained from UBC Clinical Research Ethics Board. Operational approval was obtained from Surgery department at VGH.

**Data Collection and analysis**
In this phase of the study, we analyzed data collected for the National Surgical Quality Improvement Program. NSQIP collects data on sampled surgical patients. This analysis provides a broad overview of demographic, co-morbidity and short-outcome differences between non-emergency and emergency CRC patients.

We looked into the following variables:

- Age
- ASA classification
- Comorbidities
- Stage at presentation
- Length of stay
- Post-operative complications
- 30-day post-operative mortality

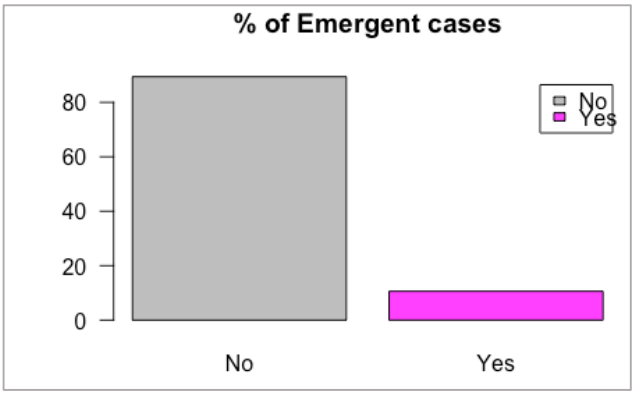
Data entry and analysis were performed in Microsoft Excel 2016 and R© _version 0.98.1091. Main characteristics analyses of the study population were highlighted using descriptive statistics. Comparisons were carried out using regression models.

**Data sets and sources**
**National Surgical Quality Improvement Program (NSQIP):** almost 100% of the non-emergency CRC cases and a sample of the emergency cases are captured by NSQIP. This data set helped us identify basic patient information; for e.g. demographics, date of admission.

## 2.3 Results

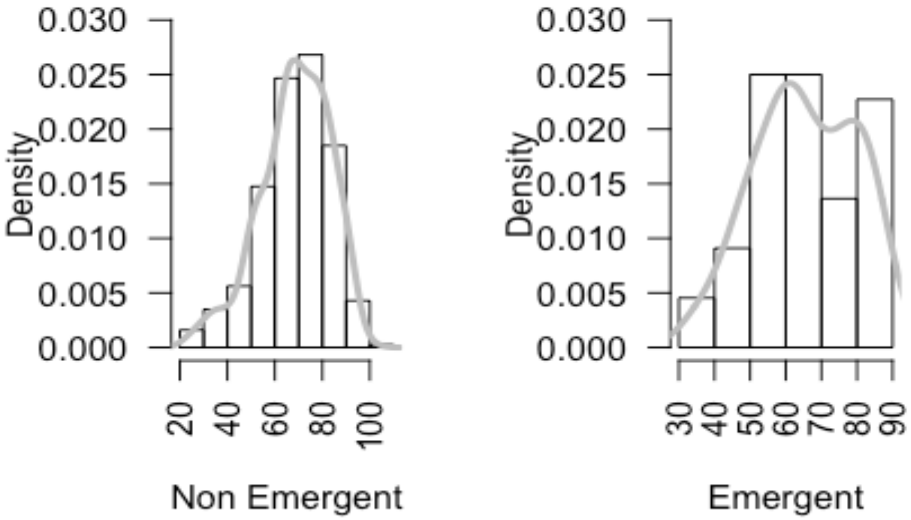
A total of 416 patients with CRC diagnosed within a year of presentation, were included in the NSQIP dataset during the period from 2010 to 2015. All of them underwent surgical intervention either on an emergency or non-emergency basis. Almost 11% of them were managed on emergency basis as shown in figure 10.

Figure 10: percentages of emergency and non-emergency cases in NSQIP dataset from 2010 to 2015.




The means of ages at time of surgery in the emergency and non-emergency groups were 65.4 and 68.4 years, respectively. The difference between the two mean was not statistically significant (95% CI, *p-value*= 0.09). Figure 11 demonstrates the distribution of age at time of surgery in both groups.

Figure 11: distribution of age at time of surgery in both groups



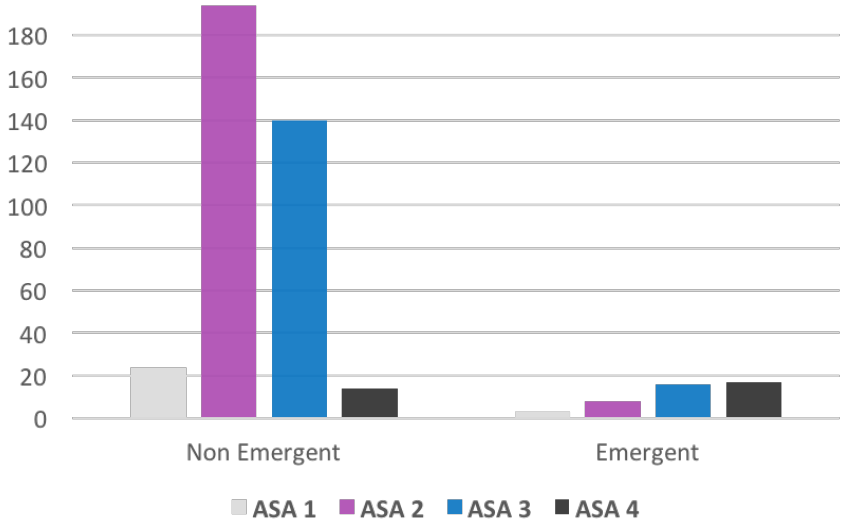
Both groups were evaluated in regard to rates of pre-operative co-morbid conditions. Around 50% of patients with CRC who underwent non-emergency surgery had at least one pre-operative co-morbidity, compared to 93% of patients in the emergency group (Table 17). This difference in rates of pre-operative co-morbidities was statistically significant at 95% CI (*p-value*= 0.000001).

Table 17: Pre-Operative risk factors in emergency and non-emergency groups

| Co-morbidities | Emergency Case | |
|---|---|---|
| | No | Yes |
| 0 | 171 | 3 |
| 1 | 150 | 12 |
| 2 | 43 | 11 |
| 3 | 8 | 10 |
| 4 | 0 | 5 |
| 5 | 0 | 2 |
| 6 | 0 | 1 |

Moreover, there was a significant difference in the ASA classification between patients managed on emergency basis compared to their non-emergency counterparts. At least 75% of those in the emergency group had ASA classes 3 and 4 compared to 41% of patients in the non-emergency group (95% CI, *p-value*= 0.00002). Figure 12 shows the distribution of patients across ASA classes in each group.

Figure 12: Distribution of patients across ASA classes in emergency and non-emergency groups.



NSQIP data also looks into the presence of disseminated disease at the time of surgery in CRC patients (Table 18). Analysis showed a significant difference in the rates of disseminated disease between those managed with emergency versus non-emergency surgery (13.6% versus 5.6% respectively, 95% CI, *p-value*= 0.04).

Table 18: Presence of disseminated disease at the time of surgery

| | Emergency | Non-Emergency | Marginal Row Totals |
|---|---|---|---|
| Disseminated Disease | 6 | 21 | 27 |
| No Disseminated Disease | 38 | 351 | 389 |
| Marginal Column Totals | 44 | 372 | 416 (Grand Total) |

When comparing the duration of surgery in patient with CRC who underwent emergency and non-emergency management, there was no significant difference in the two arms. The mean duration of surgery in minutes in the emergency group was 164 minutes, compared to 171 minutes in the non-emergency group (95% CI, *p-value*= 0.2).

Likewise, the statistical difference in rates of post-operative SSI, pneumonia and DVT between the two groups was not significant at 95% CI (*p-values*= 0.9, 0.7 and 0.4 respectively). Moreover, stepwise regression analysis failed to identify any association between different variables (as shown in Table 19) and SSI. However, regression analysis showed that ASA class and the presence of disseminated disease are significant predictors of post-operative pneumonia (OR= 2.7 and 4.2, *p-value*= 0.001 and 0.03 respectively) (Tables 20).

Table 19: Stepwise regression analysis for the outcome SSI

| Variable | Average | Coefficient | StdErr | *P-value* | OR |
|---|---|---|---|---|---|
| Age | 68.127 | - 0.0190 | 0.0113 | 0.0929 | 0.9812 |
| Gender | 0.546 | 0.2357 | 0.3169 | 0.4569 | 1.2658 |
| Disseminated Dis. | 0.064 | - 0.0572 | 0.6120 | 0.9256 | 0.9444 |
| Emergent | 0.105 | - 0.1772 | 0.5402 | 0.7429 | 0.8376 |
| Co-morbidities | 0.882 | - 0.1351 | 0.1695 | 0.4253 | 0.8736 |
| ASA class | 2.4628 | 0.3672 | 0.2510 | 0.1435 | 1.4436 |
| Duration of surgery | 170.122 | 0.0027 | 0.0019 | 0.1419 | 1.0027 |

Overall Model Fit: Chi Square= 7.2497, DF= 7, *p-value*= 0.4034

Table 20: Stepwise regression analysis for the outcome Post-operative pneumonia

| Variable | *Coefficients* | *Std Error* | *t Stat* | *P-value* | OR |
|---|---|---|---|---|---|
| Intercept | -0.08 | 0.04 | -1.88 | 0.05 | |
| Disseminated Dis. | 0.10 | 0.05 | 2.21 | 0.03 | **4.18** |
| ASA class | 0.05 | 0.02 | 3.24 | 0.0013 | **2.696** |

Overall Model Fit: Chi Square= 28.8085, DF=2, *p-value*= 0.00007.

For both groups, patients with disseminated disease were 4.6 times more likely to return to the OR than those who did not have disseminated disease (*p-value*= 0.000008). Likewise, patients with worse ASA class were 3 times more likely to undergo a second operation (*p-value*= 0.0004) (Table 21).

Table 21: Stepwise regression analysis for the outcome Return to OR

| Variable | *Coefficients* | *Standard Error* | *t Stat* | *P-value* | OR |
|---|---|---|---|---|---|
| intercept | -0.09 | 0.04 | -2.27 | 0.024 | |
| Disseminated Dis | 0.21 | 0.05 | 4.51 | 0.000008 | **4.56** |
| ASA class | 0.06 | 0.02 | 3.56 | 0.0004 | **3.03** |

Overall Model Fit: Chi Square= 32.8753, DF=2, *p-value*= 0.00001

The mean hospital LOS in patients who underwent emergency surgery was 9 days, compared to 11 days in patients underwent non-emergency surgery. However, analysis failed to show a statistical significance of the difference in LOS between the two groups (95% CI, *p-value*=0.1). Figure 13 shows a boxplot of hospital LOS of patients in each group. Note the presence of an outlier in the non-emergency group, which might have affected the analysis. However, there was a significant correlation between duration of surgery and hospital LOS in the emergency group, as shown in figure 14 (*p-value* = 0.007).

Figure 13: Boxplot of hospital LOS of patients in emergency and non-emergency groups

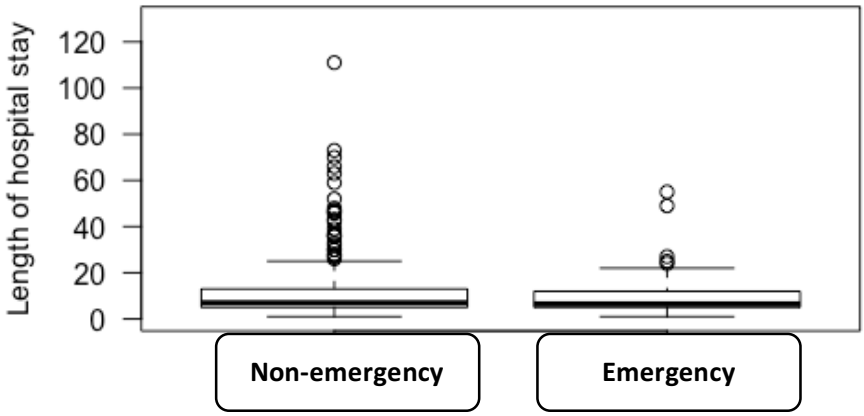
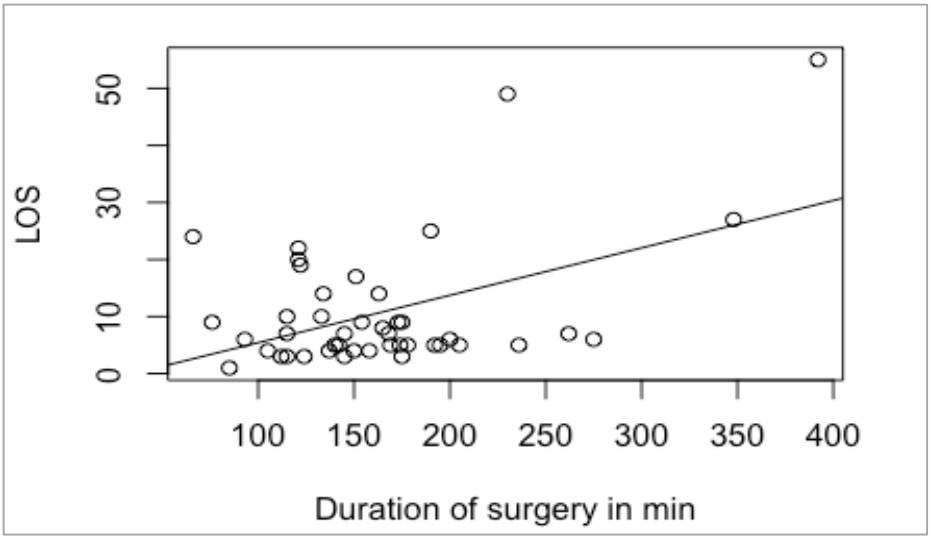



Figure 14: Correlation between duration of surgery and LOS in the emergency group




Emergency cases were more likely to have prolonged LOS as shown in table 22 (OR= 3.1, *p-value*= 0.00006). Likewise, those with prolonged surgery were likely to have prolonged LOS compared to those who did not.

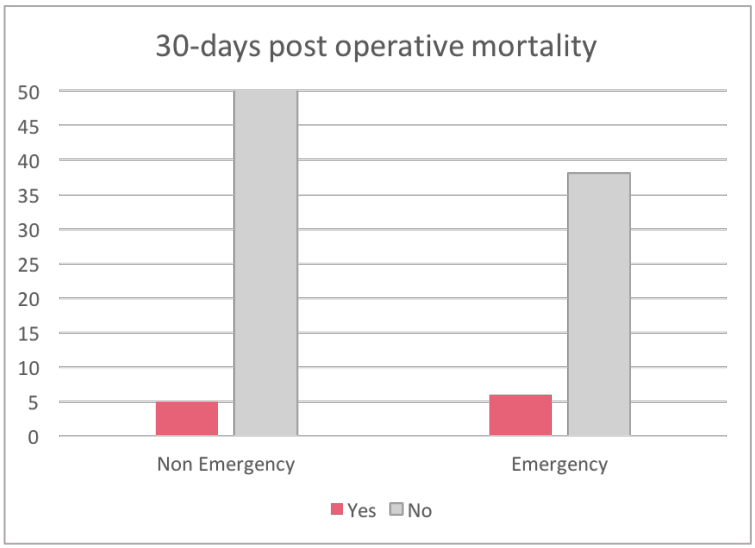
Table 22: Stepwise regression analysis for the outcome LOS

| Variable | Coefficients | Standard Error | t Stat | P-value | OR |
|---|---|---|---|---|---|
| Intercept | -0.01 | 0.26 | -0.04 | 0.97 | |
| Emergent | 1.34 | 0.33 | 4.05 | 0.00006 | 3.08 |
| Duration of surgery | 0.003 | 0.001 | 2.11 | 0.035 | 1.01 |

Overall Model Fit: Chi Square= 94.6679, DF=2, *p-value*= 0.00001

We also looked into the rates of 30-days mortality in both groups (Figure 15). Mortality within 30-days post operatively was higher in patients managed with emergency surgery as compared to their non-emergency counterparts (13.6% and 1.3% respectively, *p-value*= 0.000002).

Figure 15: 30-days post-operative mortality in emergency and non-emergency groups




Moreover, stepwise regression analysis revealed that there is a significant association between ASA class and post-operative 30-days mortality as shown in table 23 (OR= 3.2, *p-value*= 0.002). Likewise, emergency surgery was identified as an important predictor of mortality in this model (OR= 4.05, *p-value*= 0.0002). Although the significance is statistically weak, patients who had disseminated disease were 4 times more likely to have higher rates of 30-days Post-operative mortality (*p-value*=0.07).

Table 23: Stepwise regression analysis for the outcome 30-days Post-operative mortality

| Variable | *Coefficients* | *Standard Error* | *t Stat* | *P-value* | OR |
|---|---|---|---|---|---|
| Intercept | -0.07 | 0.03 | -2.61 | 0.009 | |
| Emergent | 0.095 | 0.025 | 3.725 | 0.0002 | **4.05** |
| Disseminated Dis | 0.056 | 0.031 | 1.796 | 0.073 | **3.76** |
| ASA class | 0.03 | 0.01 | 3.08 | 0.002 | **3.18** |

Overall Model Fit: Chi Square= 30.3867, DF= 3, *p-value*= 0.0001

## 2.4 Discussion

NSQIP data captures only a sample of CRC patients presenting to EGS in a cycle of 8 days. On the other hand, it captures almost 100% of patients managed on non-emergency basis. In our sample, CRC patients who underwent emergency surgery represented around 11% of the study population, as shown in figure 11.

The mean ages of patients in both groups were quite comparable (*p-value*= 0.09). Literature suggests that, advanced age is one of the significant risk factors for diagnosis of CRC, and the majority of patients are diagnosed at age of 65 years and older. Furthermore, the peak incidence of CRC increases in people 85 years and older (34). Marusch F et al suggested that, rates of emergency presentation, inoperability and peri-operative mortality were high in older patients with colorectal cancer (35). On the other hand, several recent studies showed that, age alone is not a predictor of outcome in these patients (36).

However, it was quite interesting to encounter cases with CRC presenting at ages younger than 30 years (Minimum age in emergency and non-emergency groups were 23 and 34 years, respectively).

Although there was no significant difference between means of ages at time of surgery in the two groups, it is worth noting that the distribution of ages in the emergency group showed two peaks at 50 to 70 years and at 80 to 90 years. On the other hand, the peak of the distribution of ages in the non-emergency group peaked around 60 to 80 years (Figure 12).

Analysis of pre-operative co-morbid conditions in patients underwent emergent and non-emergency surgery showed significant difference in rates of comorbidities between the two groups (95% CI, *p-value*= 0.000001). Almost half of patients with CRC who underwent non-emergency surgery had at least one pre-operative co-morbidity, compared to 93% of patients in the emergency group (Table 8). Studies demonstrated that, patients with CRC who present with surgical complications may also present with other emergencies including: metabolic, cardiovascular, infectious, and respiratory conditions. All these factors put them at significantly higher risks of post-operative morbidity and mortality (37).

Moreover, the difference in the ASA classification between patients managed on emergency basis compared to their non-emergency counterparts was significant at 95%CI. At least ¾ of those managed on emergency basis had ASA classes 3 or higher compared to only 41% of patients in the non-emergency group (*p-value*= 0.00002).

Based on this fact, emphasis should be put on the importance of pre-operative optimization and preparedness in CRC patients who undergo emergency surgery in order to minimize the risk of post-operative morbidity and mortality.

Table 9 shows the rates of disseminated disease in both groups. The difference in rates between emergency and non-emergency groups was quite significant. This observation suggests that, patients with CRC who present to EGS with surgical complications are more likely to have disseminated disease at time of surgery, compared to patients managed on non-emergency basis (*p-value*= 0.04).

In our study, there was no significant difference in the duration of surgery in patient with CRC who underwent emergency and non-emergency management. The means of the duration of surgery in minutes were 164 and 171 in the emergency and non-emergency groups, respectively (95% CI, *p-value*= 0.2). All cases included in this dataset were operated upon by general surgery attending staffs. Hence, there was no role for correlating the level of surgical training with the duration of surgeries.

Regarding post-operative complications, the statistical difference in rates of post-operative SSI, pneumonia and DVT between the two groups was not significant at 95% CI. However, stepwise regression analysis showed ASA class and disseminated disease as important predictors for post-operative pneumonia as shown in table 11 (OR= 2.7, *p-value*= 0.01). These three complications are among the most frequently encountered short term post-operative complications in CRC surgery in general (28, 29).

Using stepwise regression analysis, we were able to identify significant relations between the presence of disseminated disease and likelihood of return to the OR (OR= 4.6, *p-value*= 0.006). Furthermore, patients with worse ASA class were 3 times more likely to undergo a second operation (*p-value*= 0.003) as shown in Table 12.

In general, analysis did not show any statistical significance of the difference in LOS between the two groups (95% CI, *p-value*=0.1). The means of hospital LOS were 9 and 11 days in patients who underwent emergency and non-emergency surgery, respectively. The presence of an outlier in the non-emergency group might have affected the results, though. Furthermore, a significant proportion of the non-emergency cases were not included in the Enhanced Recovery After Surgery (ERAS) protocol, which might have influenced the results further. However, the correlation between duration of surgery and hospital LOS in the emergency group was statistically significant, as shown in figure 15 (*p-value* = 0.007) and Table 13 (OR= 3.1, *p-value*= 0.013). Furthermore, those with worse ASA classes and prolonged surgery were likely to have prolonged LOS as shown by stepwise regression analysis. Holloway et al

emphasized the burden created on health care systems by the increased LOS in CRC patients, as LOS after surgery is considered a major determinant of resource utilization (38).

Mortality within 30-days post operatively was higher in patients managed on emergency basis as compared to their non-emergency counterparts (*p-value*= 0.000002). Furthermore, we were able to identify emergency surgery, ASA class and disseminated disease as important predictors of 30-days post-operative mortality. In general, literature reports 30-days post mortality rate of 5% after CRC surgery (39). Rates are believed to increase further after emergency CRC surgery, as suggested by Park et al (33).

## 2.5 Conclusion

In this phase of our study, we demonstrated a comparison in basic characteristics and short-term outcomes between CRC patients who received surgical management on emergency and non-emergency basis. In general, patients with CRC who were managed on emergency basis had higher rates of pre-operative co-morbid condition and worse ASA classes compared to the non-emergency group. They are more likely to have advanced disease at time of surgery. Moreover, 30-days mortality were significantly higher in patients managed on emergency basis. Emergency surgery, ASA classes and disseminated disease were important predictors of 30-days post-operative mortality in our study. Most of these findings are keeping with observations reported in previous studies (37).

CRC patients presenting to EGS represent a challenge to the health care system on many dimensions. Understanding their unique characteristics and requirements helps in improving processes of care for these patients. Hence, improving their rates of morbidity and mortality after CRC surgery.

### Strength and limitations of the study

One of the main strengths of this study is its source of data. NSQIP dataset represents a high quality data source in the setting of emergency general surgery services. Utilizing this dataset can drive improvement in the quality of care provided by EGS services.

However, main limitations of the study are the small number of patients in the emergency group and the nature of the study which subjects it to risk of selection bias.

We hope to build on this study in future to include a bigger number of patients in order to obtain better statistical analyses. Moreover, we would like to assess the role of laparoscopy in emergency CRC surgery in this population.

# Chapter 3

# Emergency surgery for colorectal cancer: Patient and system characteristics

## 3.1 Introduction

This chapter is the second phase of the study described in chapter 2. In this phase of the study we seek to describe the population of CRC patients who present with emergency complications, in terms of processes of care and short-term outcomes. Advances in our understanding of these processes may suggest opportunities to improve patients' care.

### Objectives

Primary:

- To measure the relation between time to the operation room and 30-days post-operative mortality

Secondary:

- To measure the impact of time to OR on patient's length of stay.
- To measure resection rates and stoma creation rates in these patients
- To evaluate surgery adequacy in terms of resection margin and nodes harvested, and compare them to international standards

## 3.2 Methodology

This study was carried out after we obtained approval from UBC ethics board and Vancouver Coastal Health Research Institute (VCHRI) operational approval.

In this phase of the study we used the Vancouver General Hospital (VGH) Patient Clinical Information System (PCIS) data set to focus more specifically on CRC patients presenting with emergency surgical conditions. This dataset provides information on the processes of care and the nature of surgical intervention. After we combined data from NSQIP and the patients' electronic records, the resulting dataset provided better characterization of patient's clinical and oncologic presentations and the corresponding surgical care.

Processes of care and short term outcomes of the CRC cases presenting to EGS were analyzed in this phase of the study. Using both NSQIP and PCIS data, we were able to obtain more information and variables regarding date and time to OR and pathological characteristics of the resected specimens.

In this phase, we looked into the following variables:

- Time to OR
- Resection rate
- Stoma creation rate
- Pathological stage: resection margin and lymph nodes harvested

### Data sets and sources

**National Surgical Quality Improvement Program (NSQIP):** described in chapter 2.
**PCIS:** was accessed to obtain other missing information.

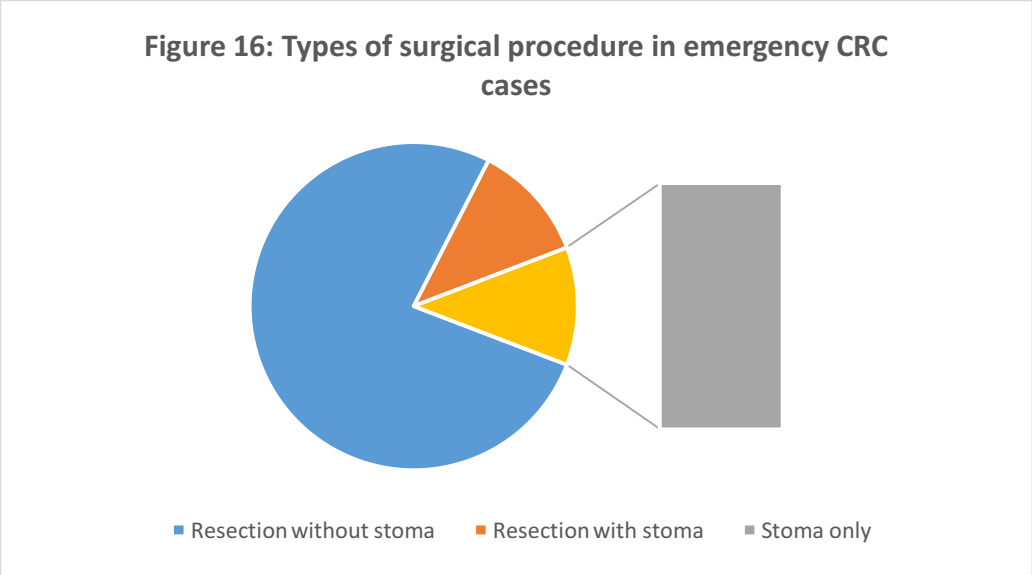
### Data security and Statement of Risks

Electronic medical records from VGH were queried to identify relevant patient records. Patients' demographic information and characteristics were obtained from these records. Each of the patient files was assigned a unique and anonymous study number, for the duration of the study, containing no additional identifiable information. The study data was maintained on the computer at the VGH Trauma Services office. The data will be kept for a period of 2 years following the completion of the study. At this point, all hard copies of data will be physically destroyed and electronic files will be erased.

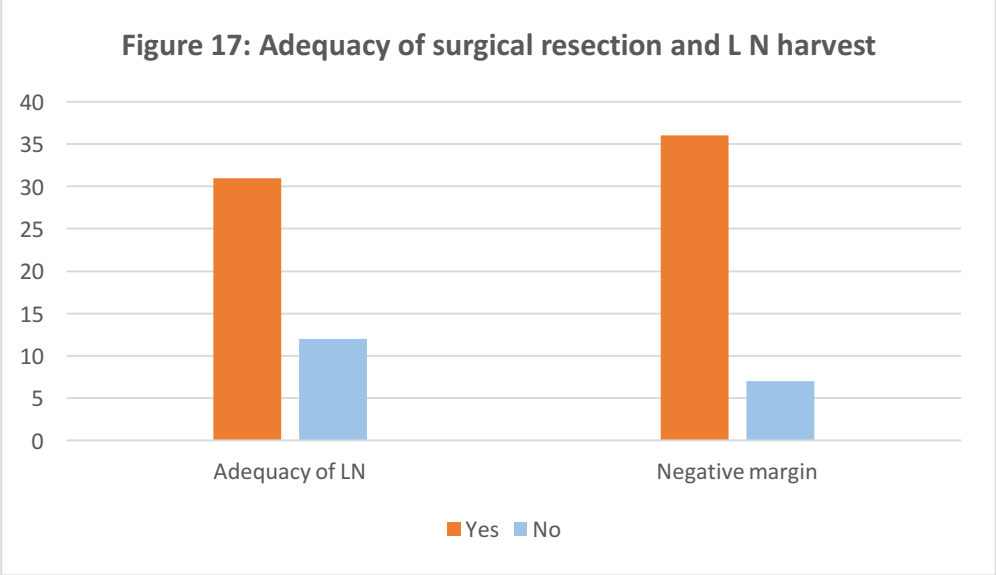
Risks associated with this observational study are negligible, as there is no study. Privacy and confidentiality issues are carefully addressed by using encrypted software, de-identified data and data analysis in secure settings.

## 3.3 Results

In this chapter, we looked primarily into resection rates, stoma creation rates and adequacy of surgical resection as indicated by the objectives earlier. We found that, 88.4% of CRC patients who underwent emergency surgery had their tumors resected. 13.2% of those who underwent resection had stoma (Figure 16).




Furthermore, 83.4% of resected specimens showed negative resection margin. Adequate lymph node harvest was achieved in 72.1% of cases (Figure 17). Adequacy of lymph node harvest was defined as more than or equal to 12 nodes. The mean number of harvested lymph nodes was 14 nodes (minimum 0 and maximum 34).




Analysis using stepwise regression model failed to show any significant association between time to OR and post-operative complications as shown in Table 24.

Table 24: Stepwise regression model of time to OR and post-operative complications.

| | *Coefficients* | *Standard Error* | *t Stat* | *P-value* |
|---|---|---|---|---|
| Intercept | -0.390878058 | 0.474325201 | -0.824 | 0.415 |
| Age | 0.00271373 | 0.006515566 | 0.416 | 0.680 |
| Co-morbidities | 0.180315344 | 0.168264221 | 1.071 | 0.291 |
| ASA class | 0.080364001 | 0.141240605 | 0.568 | 0.573 |
| Disseminated Dis. | 0.26957427 | 0.206871873 | 1.303 | 0.201 |
| Time to OR | -0.027203551 | 0.039080653 | -0.696 | 0.491 |
| Duration of surgery | 0.001848747 | 0.001454653 | 1.270 | 0.212 |

Likewise, it failed to predict probability of post-operative mortality using time to OR as an independent variable Table 25.

Table 25: Stepwise regression model of time to OR and mortality.

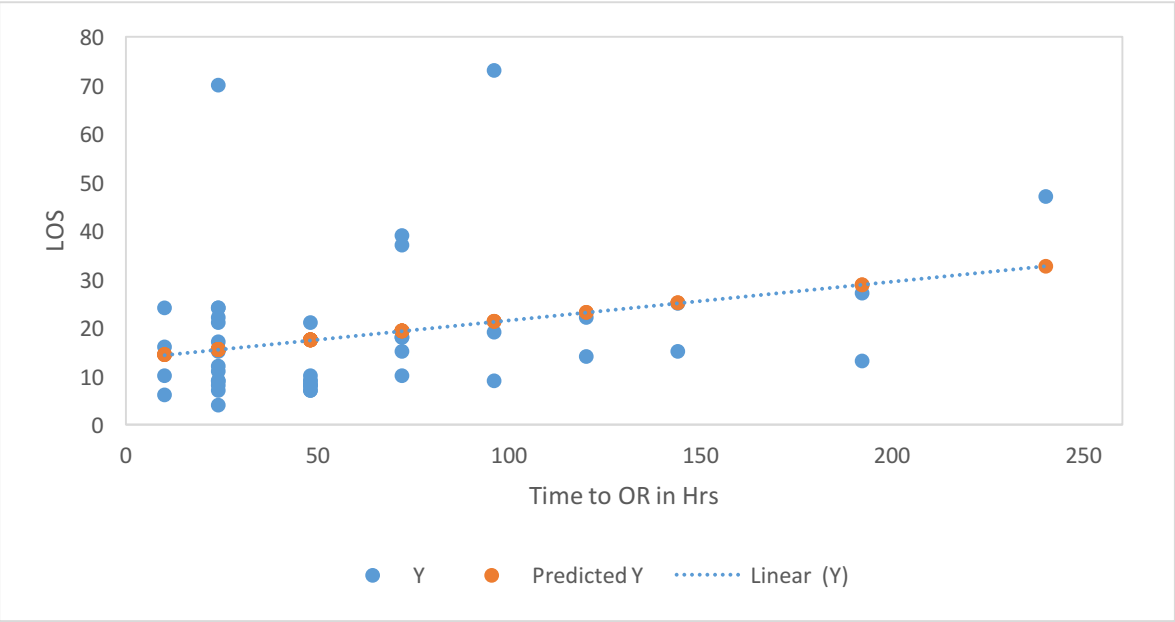
| | *Coefficients* | *Standard Error* | *t Stat* | *P-value* |
|---|---|---|---|---|
| Intercept | 0.197070452 | 0.268607045 | 0.733 | 0.467 |
| Age | 0.003079256 | 0.00365755 | 0.841 | 0.405 |
| Co-morbidities | 0.193560543 | 0.095294699 | 2.031 | 0.049 |
| ASA class | -0.053176563 | 0.079658104 | -0.667 | 0.508 |
| Disseminated Dis | 0.197118987 | 0.117131654 | 1.682 | 0.101 |
| Time to OR | 0.009606758 | 0.022133704 | 0.434 | 0.666 |
| Duration of surgery | -0.002292621 | 0.000788884 | -2.906 | 0.006 |

However, time to OR predicted LOS in linear regression model as shown in Table 26 and Figure 18.

Table 26: Linear regression model of time to OR and LOS.

| | *Coefficients* | *Standard Error* | *t Stat* | *P-value* |
|---|---|---|---|---|
| Intercept | 13.74383302 | 3.357357585 | 4.093 | 0.0002 |
| Time to OR | 1.872865275 | 0.98260726 | 1.906 | 0.063 |

Figure 18: Linear regression model of time to OR and LOS.




## 3.4 Discussion

This chapter assesses mainly processes of care for patients with CRC who underwent emergency surgical intervention. We examined the rate of resection, stoma creation rate and completeness of surgical resection. Majority of patients had resection with primary anastomosis. Only 11.6% of patients had diversion stoma without resection.

Likewise, most of cases had adequate lymph nodes harvest, with 12 or more lymph nodes. A minimum of 12 nodes has been recommended as a consensus standard for hospital-based performance for colon cancer surgery (41). However, Sandra and colleagues suggested that using the mere use of number of lymph nodes examined does not necessarily influence staging, use of adjuvant chemotherapy, or patient survival (42).

Regression models failed to predict the likelihood of post-operative complications or mortality. However, there was a significant association between the presence of co-morbid conditions and mortality in this group. Likewise, duration of surgery was identified as an important predictor of post-operative mortality. Moreover, linear regression analysis significantly predicts prolonged LOS in those who had long waiting time before OR (*p-value*= 0.06). Almost no studies performed in patients with CRC had ever discussed the relation between time to OR and outcome, which makes our finding in this study quite interesting.

## 3.5 Conclusion

In this phase of the study, we illustrated a significant relationship between time to OR and length of stay. Although emphasis should be put on the importance of preventing delays in surgical management of patients with CRC who present with acute surgical complications, one should also keep in mind the crucial role that pre-operative resuscitation plays in improving patient's outcomes.

### Importance of The Study

The Vancouver General Hospital has one of the busiest emergency general surgery services in the country, and cares for a high volume of patients presenting with emergency conditions related to colon cancer, including bowel obstruction, bowel perforation, and lower gastrointestinal bleeding. These patients are sicker and more complex than their counterparts with CRC who present without complications, and who are managed on non-emergency basis. Unfortunately, little is known about processes of care for, or outcomes of these patients on organized emergency general surgery services. Patients presenting with complications of CRC may face issues of access to timely primary care, and they may have more comorbidities or other barriers to surgical intervention. They also may have suboptimal surgical or adjuvant therapy for their cancers, and they may face a higher rate of complications or long-term adverse outcomes.

Ball. et al e suggested that EGS represents a dedicated system of services that provides quality care to patients with surgical emergencies in the best way to improve their outcomes. However, he also stated that it lacks the evidence-based improvements in outcomes (40). We believe that understanding the differences in characteristics of patients with CRC who present for surgical intervention is vital, as it's one of the important initial steps on the ladder to improving patients' outcomes.

We saw that, a quite significant proportion of CRC patients presenting with surgical emergencies have more advanced or disseminated disease. This highlights the need to revise the available CRC screening protocols in order to detect cases at earlier stages, as feasible. Moreover, keeping in mind the extend of physiological challenge these patients go through when they present with complications, casts light on the importance of implementing strict pre-operative resuscitation and optimization protocols.

Understanding the differences in processes of care between patients with CRC who are managed on emergency or non-emergency basis also help in targeting areas of potential improvements in order to improve patients' outcomes. These processes

include: ED to OR time, duration of surgery and adequacy of surgical resection as compared to international standards.

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# Appendix 1:

## Detailed search strategies

MEDLINE was searched using OvidSP interface on the 6th of March 2016:

| | Searches | Results |
|---|---|---|
| 1 | Colorectal Neoplasms/ | 63963 |
| 2 | Emergencies/ | 36354 |
| 3 | Emergency Treatment/ | 9134 |
| 4 | ((emergency adj5 surg*) or emergen*).mp. | 337080 |
| 5 | 2 or 3 or 4 | 337080 |
| 6 | Comparative Study/ | 1728692 |
| 7 | 1 and 5 | 794 |
| 8 | 6 and 7 | 128 |

EMBASE was searched using OvidSP interface on the 19th of March 2016 for the period from 1974 to 2016 March 6th:

| | Searches | Results |
|---|---|---|
| 1 | colorectal tumor/ | 18329 |
| 2 | emergency/ | 44423 |
| 3 | emergency treatment/ | 14998 |
| 4 | ((emergency adj5 surg*) or emergen*).mp. | 481608 |
| 5 | 2 or 3 or 4 | 481608 |
| 6 | 1 and 5 | 278 |
| 7 | comparative study/ | 702602 |
| 8 | 6 and 7 | 34 |

Pubmed was searched using OvidSP interface on the 19th of March 2016 for the period from 1946 to 2016 March 19th:

(((((((colorectal OR colon OR rectum OR colonic OR rectal)) AND (neoplasm OR neoplasia OR neoplastic OR neoplasms OR neoplasias)) AND (cancer OR cancers)) AND (Malignancies OR malignancy OR malignant)) AND (emergency OR emergencies)) AND comparative study) AND (outcome OR outcomes) (142)

## Appendix 2:

### Newcastle - Ottawa Quality Assessment Scale Cohort Studies

| |
|---|
| Selection<br><br>(1) Representativeness of the exposed cohort<br>a) truly representative of the average _____ in the community<br>b) somewhat representative of the average _____ in the community<br>c) no description of the derivation of the cohort<br><br>2) Selection of the non exposed cohort<br>a) drawn from the same community as the exposed cohort<br>b) drawn from a different source<br>c) no description of the derivation of the non exposed cohort<br><br>3) Ascertainment of exposure<br>a) secure record (e.g. surgical records)<br>b) structured interview<br>c) written self report<br>d) no description<br><br>4) Demonstration that outcome of interest was not present at start of study<br>a) yes<br>b) no |
| Comparability<br><br>1) Comparability of cohorts on the basis of the design or analysis<br>a) study controls for _____ (select the most important factor)<br>b) study controls for any additional factor. (This criteria could be modified to indicate specific control for a second important factor.) |
| Outcome<br><br>1) Assessment of outcome<br>a) independent blind assessment<br>b) record linkage<br>c) self report<br>d) no description<br><br>2) Was follow-up long enough for outcomes to occur<br>a) yes (select an adequate follow-up period for outcome of interest)<br>b) no<br><br>3) Adequacy of follow-up of cohorts<br>a) complete follow-up – all subjects accounted for |

b) subjects lost to follow-up unlikely to introduce bias – small number lost -> ____ %(select an adequate %) follow-up, or description provided of those lost)
c) follow-up rate < ____ % (select an adequate %) and no description of those lost
d) no statement

## Appendix 3:

Newcastle - Ottawa Quality Assessment Scale Cross-sectional Studies

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| Selection: (Maximum 5 stars)<br><br>1) Representativeness of the sample:<br>a) Truly representative of the average in the target population. (all subjects or random sampling)<br>b) Somewhat representative of the average in the target population. (non-random sampling)<br>c) Selected group of users.<br>d) No description of the sampling strategy.<br><br>2) Sample size:<br>a) Justified and satisfactory.<br>b) Not justified.<br><br>3) Non-respondents:<br>a) Comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory.<br>b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.<br>c) No description of the response rate or the characteristics of the responders and the non-responders.<br><br>4) Ascertainment of the exposure (risk factor):<br>a) Validated measurement tool.<br>b) Non-validated measurement tool, but the tool is available or described.<br>c) No description of the measurement tool. |
| Comparability: (Maximum 2 stars)<br><br>1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.<br>a) The study controls for the most important factor (select one).<br>b) The study control for any additional factor. |
| Outcome: (Maximum 3 stars)<br><br>1) Assessment of the outcome:<br>a) Independent blind assessment.<br>b) Record linkage.<br>c) Self report.<br>d) No description.<br><br>2) Statistical test:<br>a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value).<br>b) The statistical test is not appropriate, not described or incomplete. |

## Appendix 4:

National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

| Criterion | No | Yes |
|---|---|---|
| 1. Was the research question or objective in this paper clearly stated? | | |
| 2. Was the study population clearly specified and defined? | | |
| 3. Was the participation rate of eligible persons at least 50%? | | |
| 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre specified and applied uniformly to all participants? | | |
| 5. Was a sample size justification, power description, or variance and effect estimates provided? | | |
| 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? | | |
| 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? | | |
| 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? | | |
| 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | | |
| 10. Was the exposure(s) assessed more than once over time? | | |
| 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | | |
| 12. Were the outcome assessors blinded to the exposure status of participants? | | |
| 13. Was loss to follow-up after baseline 20% or less? | | |
| 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s) | | |
| Overall rate | | |

# Appendix: 5

Characteristics and main findings of studies on elective versus emergency management of patients with CRC

| No. | Title | Primary author | Year of publication | Research question | Study design | Number of patients | Type of statistical analysis | Outcomes measured | Main results | Interpretation of results | Length of follow up |
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| 1 | An evaluation of treatment results of emergency versus elective surgery in colorectal cancer patients. | Bayar et al | 2015 | Determine factors associated with early diagnosis and survival in CRC patients by comparing demographics, surgical procedures, length of hospital stay, and postoperative treatment results among elective and emergent cases. | Retro-spective cohort study | 320 | Regression Models | - Post operative complications<br>- Hospital length of stay<br>- Post operative mortality | Statistically significant ($p<0.05$) difference in post-operative length of hospital stay, presence of co-morbid diseases, pathological stage, and postoperative complications. | Length of hospital stay, advanced stage on admission, complications were higher in patients in the emergency surgery group. | Not mentioned |
| 2 | Colorectal cancer treatment in octogenarians: elective or emergency surgery? | Ming-gao et al | 2014 | Assess characteristics of octo-genarian patients with CRC and compare specific outcomes due to different types of surgical procedures used. | Retro-spective cohort study | 346 | At least uni-variate analysis | - Anasto-mosis and stoma rates<br>- Post operative complications<br>- Hospital length of stay<br>- ICU admission<br>- Mortality | Emergent group had a more advanced Dukes' stage, higher ASA classes, lower anastomosis rate (40.2 vs 80.1%), higher stoma rate (30.6 vs 9.6%), more complications (71.8 vs 43.3%), longer length of hospital stay and higher (82.4% vs 36.4%) ICU admission rate. Higher mortality rate in the emergent group (30.6%) than the elective group (3.1%). | Octogenarians who undergo elective CRC surgery have better results than those requiring emergent surgery. | 36 months |

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| 3 | Emergency surgery for colorectal cancer does not result in nodal understaging compared with elective surgery | Patel et al | 2014 | To compare the adequacy of nodal staging in patients undergoing emergency surgery versus elective surgery for CRC. | Pro-spective cohort study | 1,279 | Logistic regression analysis | Number of nodes harvested during surgery | Mean number of nodes removed was higher in the emergency surgery group (mean difference +2.8, 95% confidence interval [CI] 0.6–5.1, p = 0.012). The proportion of patients with inadequate nodal staging did not differ between groups (emergent 16%, elective 17%, p = 0.79). The odds of adequate nodal staging, adjusting for site, type of resection, training and stage was no different between groups (OR 0.80, 95% CI 0.47–1.35, p = 0.41). | Emergency CRC cases are not understaged in terms of resection adequacy. | Not mentioned |
| 4 | Clinico pathological analysis of colorectal cancer: a comparison between emergency and elective surgical cases | Ghazi et al | 2013 | Compare the clinical and pathologic profiles of emergency and elective CRC cases. The main outcome measure was the difference in morphology between elective and emergency surgical cases. | Retro-spective cohort study | 976 | Univariate and multivariate analysis<br><br>Regression models | Difference in tumor morphology between elective and emergency surgical cases. | Emergency cases had more multiple tumors, higher AJCC tumor and node stage, peri-tumor lymphocytic reaction, high number of tumor-infiltrating lymphocytes, signet-ring cell mucinous carcinoma, desmoplastic stromal reaction, vascular and perineural invasion, and infiltrative tumor margin. | Emergency cases show a more aggressive histopathologic profile and a more advanced stage than do elective cases. | Not mentioned |

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| 5 | Burden of Emergency and Non emergency Colorectal Cancer Surgeries in West Virginia and the USA | Shah et al | 2013 | Determine the association between presenting with emergency condition and consequent outcomes of CRC surgery | Cross-sectional comparison of a national sample | 3,338 | - Descrip-tive analyses using chi-square statistic<br>- Multivariate regressions | - Length of stay (LOS)<br><br>- Total hospital charges<br><br>- Inpatient death | Emergency cases spent 51.9 % more days in the hospital than those who did not.<br>Hospital charges for those that underwent emergency resection were 68.3 % higher than those who did not.<br>Those underwent emergency surgery four times (OR 3.88; 95 % CI03.74–4.03) greater chance of in-hospital death. | Emergency cases are at higher risk of adverse outcomes than elective cases.<br>Hospital charges are likely to be higher in cases managed emergently. | Not mentioned |
| 6 | Elective and emergency abdominal surgery in patients 90 years of age or older | Racz et al | 2011 | Determine the outcomes of abdominal surgery in nonagenarians and to assess the performance of Physiologic and Operative Severity Score for enUmeration of Mortality and morbidity (POSSUM) as predictors of mortality. | Retro-Spective cohort study | 145 | Regression models | - In hospital mortality<br><br>- ICU admission<br><br>- Post operative complications<br><br>- 1-year mortality | 1-year mortality (49.1% v. 27.8%; p = 0.016), complication (81.9% v. 61.6%; p = 0.007) and intensive care unit admission rates (44.4% v. 11.0%; p < 0.001) were significantly higher among emergent than elective surgical patients.<br>POSSUM systems significantly over predicted mortality, particularly in higher risk groups. | Nonagenarians undergoing abdominal surgery have substantial operative morbidity and mortality, particularly in emergent surgical cases. | 1 year at least |
| 7 | Comparison of Hospital Performance in Nonemergency Versus | Ingraham et al | 2009 | To assess whether hospitals have comparable outcomes for | Retro-spective cohort study | 30,793 | Logistic regression models | 30-day morbidity and mortality | In non emergency CRC surgeries 23.9% patients | Hospitals with favorable outcomes after nonemergency colorectal | 30 days post operatively |

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| | Emergency Colorectal Operations at 142 Hospitals | | | emergency and nonemergency operations for patients with CRC. | | | | | experienced at least 1 complication 1.9% died. In emergency cases 48% experienced at least 1 complication, and 15.3% died. | resections do not necessarily have similar outcomes for emergency operations. | |
| 8 | Short term outcome after emergency and elective surgery for colon cancer. | Sjo OH et al | 2009 | To evaluate post-operative mortality and complications | Pro-spective cohort study | 999 | Regression models | - Post operative mortality<br><br>- Post operative complications | The mortality rate was 3.5% after elective and 10% after emergency operation with resection (P < 0.01), and the complication rate was 24% and 38% (P < 0.01), respectively | Emergency operation for colon cancer was associated with high rates of complications and mortality, indicating that immediate surgery should be avoided if possible. | 9 |
| 9 | A prospective study of outcomes of emergency and elective surgeries for complicated colonic cancer. | Biondo S et al | 2005 | To analyze the efficacy of curative emergency surgery in terms of tumor recurrence and cancer related survival compared with elective colonic surgery. | Pro spective cohort study | 266 | Regression models | - Post operative mortality<br><br>- Disease free survival | Postoperative mortality was higher in emergency group (P=.0004). Differences were observed for the overall survival in stage III tumors (P=.0007), and for the probability of being free from recurrence (P=.0011) and cancer-related survival (P=.0029) in stage II cancers. | Curative surgeries for complicated CRC are acceptable in emergency conditions. Cancer-related survival and recurrence in patients undergoing emergency surgery may approach that of elective surgery if surgical treatment with radical oncologic criteria is performed. | 10 |
| 10 | Outcome after emergency subtotal/total colectomy compared to elective resection in patients with left-sided colorectal carcinoma | Omejc et al | 1998 | To compare Long term survival of patients underwent CRC surgeries as elective and emergency bases | Retro-spective cohot study | 213 | At least uni variate analysis | - Mortality<br><br>- 5-year survival | Patients presented with intestinal obstruction were older than electively treated patients (68.5 versus 62.1 years), postoperative mortality was higher (13.8% | Post operative mortality was higher in emergent cases. 5-year survival for R0 resection was comparative in elective and emergency cases. | Not clear |

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| | | | | | | | | | versus 7.8%). 5-year survival rate of patients treated by R0 emergency subtotal/total colectomy was comparable to electively R0 resected patients (69% versus 61%). | | |
| 11 | Elective versus emergency surgery for patients with colorectal cancer. | Anderson et al | 1992 | To compare specific outcomes between CRC patients undergoing elective or emergency surgeries | Pro-spective study | 570 | Regression models | - Tumor resection rate<br><br>- Post operative mortality<br><br>- 5-year disease related survival | Elective group has higher proportion of resected tumors (77 versus 64 per cent, P less than 0.001), the operative mortality rate lower (9 versus 19 per cent, P less than 0.001) and the 5-year disease-related survival rate higher (37 versus 19 per cent, P less than 0.001). | Electively managed CRC patients had higher tumor resection rate, more favorable post operative outcomes and higher 5-year disease related survival. | At least 5 years |