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The Clavien-Dindo Classification a useful tool in measuring postoperative complications following colorectal cancer surgery at Colombo South Teaching Hospital

Degree Project in Medicine

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Abstract

Background: Colorectal cancer (CRC) is increasing in Sri Lanka. Surgery is the cornerstone of treatment for cure. Postoperative short-term complications are commonly measured by the Clavien-Dindo classification (CDC), which grades the severity of complications based on the level of treatment required. The CDC is not frequently used in Sri Lanka, although it is well-established globally. Moreover, to what extent age above 60 years affects the overall complication rate has not previously been studied in Sri Lanka. **Objectives:** The primary objective was to determine the types and Clavien-Dindo grade (≥II) of postoperative complications following CRC surgery at Colombo South Teaching Hospital (CSTH), Sri Lanka, and to evaluate the applicability of the CDC in the studied setting. The secondary objective was to investigate whether age above 60 years affects the complication rate.

Methods: This study was a retrospective medical record review and involved 88 patients who have undergone surgery from first of January 2017 to 29th of January 2020.

Results: One or more postoperative complications occurred in 45.5 % of the patients. The most common complications were postoperative anemia (22.7 %) and incisional surgical site infection (11.4%). Severe complications (\geq grade III) were observed in 5.7 % and no patient died. There was no statistically significant difference in rates of complications between patients <60 and \geq 60 years of age.

Conclusions: The CDC is a useful tool in measuring postoperative complications after CRC surgery at CSTH and can be used in other hospitals in Sri Lanka. More research is needed concerning at what age the postoperative risks increase. The number of severe complications seems to be low at CSTH. It would be advantageous to decrease the number of blood transfusions and reduce the antibiotic utilization.

Key words: colorectal cancer, postoperative complications, Clavien-Dindo, Sri Lanka

Abbreviations

- NCDs Non-communicable diseases
- WHO The World Health Organization
- SDGs Sustainable Developing Goals
- CCS Country Cooperation Strategy
- CRC Colorectal cancer
- FAP Familial adenomatous polyposis
- LOS Length of hospital stay
- CDC The Clavien-Dindo classification
- ICU Intensive care unit
- SSI Surgical site infection
- CSTH Colombo South Teaching Hospital
- BHT Bead hed ticket
- ERAS Enhanced Recovery After Surgery
- ASA American Society of Anesthesiologists
- SPSS Statistical Package for the Social Sciences
- ARDS Acute respiratory distress syndrome
- NIPPV Noninvasive Intermittent Positive Pressure Ventilation

Background

Short on history and development in Sri Lanka

The island nation Sri Lanka is located in the Indian Ocean and belongs to South-East Asia. The country has a population of 21.2 million. Sri Lanka has experienced major changes in the past century concerning politics, economic growth and health. The country was previously a British colony, but became independent in 1948. Later on, the country suffered from a civil conflict during three decades until 2009. The economy has grown a lot, especially after the end of the conflict. (1) The World Bank recently upgraded Sri Lanka from a lower middleincome country to an upper middle-income country. (2)

Healthcare in Sri Lanka and Non-communicable diseases

Great progresses have been achieved during the last 90 years regarding neonatal, child and maternal mortality rates, which are low compared to nearby countries. Also, longevity has increased and the life expectancy at birth was 74.9 years in 2015. These factors indicate a demographic transition. Sri Lanka has achieved impressive improvements in health and can serve as a role model for other countries in the region. Still, in order to catch up with more developed countries, remaining problems have to be addressed. One of the challenges is the ongoing epidemiological transition in the country. The disease burden is shifting from infectious diseases such as Malaria, Tuberculosis, Japanese encephalitis, infectious diarrhea and acute respiratory infections, to non-communicable diseases (NCDs). (1) NCDs are commonly long-lasting diseases and develop slowly. The mortality and morbidity of NCDs consists of four major groups; cardiovascular disease, cancers, diabetes and chronic respiratory diseases. (3) The World Health Organization (WHO) estimates that NCDs account for 83 % of total deaths in Sri Lanka. (4) Cancers, including colorectal cancer, are now the second most common cause of death. A decade ago, cancer was only at fourth place. (1)

WHO predicts that mortality and morbidity from NCDs will increase in the future in the South-East Asian Region, including Sri Lanka. (3) The increased disease burden from NCDs is partly due to higher life expectancy, which is an important risk factor for NCDs. Moreover, as many people start working in the service-sector instead of farming and move into cities, life-style is changing. This includes increase in unhealthy diet, stress and low physical activity, which are also risk factors for NCDs. (1) One of the targets of the 2030 Agenda for Sustainable Developing Goals (SDGs), is to address the NCDs (SDG target 3.4). The goal is to reduce premature mortality due to NCDs by one-third. Premature mortality is defined as death before the age of 70 years. Low-and middle-income countries, including Sri Lanka, stand for 85 % of the premature mortality from NCDs. (5) Sri Lanka has previously ratified the Agenda 2030. The Government and WHO have together developed strategies to achieve the SDGs, which are presented in the fourth Country Cooperation Strategy (CCS). The CCS also emphasizes the lack of information concerning healthcare parameters, such as mortality and morbidity on both local as well as national level. The deficient documentation and reporting of information results in difficulties to compile statistics and improve healthcare. Additionally, the CCS describes a need of more research studies in the country. (1)

Healthcare is free of charge for all citizens in Sri Lanka and there are many centers for both primary and specialized healthcare. However, accessibility of human resources for healthcare is still deficient in more rural areas. Moreover, although healthcare is intended to be free, out of pocket spending is increasing. Approximately 5 % of inpatient care and 55 % of outpatient care is provided by the private sector. (1)

Colorectal cancer

Globally, colorectal cancer (CRC) is the second most common cancer among women and the third most common cancer among men. Moreover, CRC has reached the fourth highest mortality rate of all types of cancer. The incidence of CRC is expected to increase in the future. More developed regions, such as Europe, Northern America, Japan, New Zeeland and Australia, stand for the majority of CRC cases. This is due to a higher socioeconomic level in those countries, leading to a larger population of elderly and higher presence of unhealthy diet, smoking, low physical activity and obesity, which are all risk factors for CRC. Both environment and genetics contribute to the development of CRC. Approximately 75 % of cases are sporadic and 25 % are genetically linked, including 5-10% caused by hereditary syndromes. Lynch syndrome and Familial Adenomatous Polyposis (FAP) are the most common hereditary syndromes, comprising specific DNA-mutations. Also, Inflammatory Bowel Disease is a risk factor for CRC due to chronic inflammation in the bowel. (6)

CRC is detected either by screening or by patients seeking healthcare for symptoms. CRC can give rise to a wide spread of symptoms, including bloody stools, altered bowel habits, weight loss, stomach pain, fatigue and symptoms of anemia. Screening for CRC is increasing worldwide and it makes it possible to detect the disease before it causes symptoms. The established method for screening is tracing occult blood in feces, and if blood is present followed by colonoscopy. Research of alternative screening methods, such as faecal testing for genetic markers is going on in several centers. Screening of CRC will probably affect incidence and mortality to a large extent the following 15 years. Colonoscopy is also golden standard for diagnosis. Biopsies of the cancer-suspected lesion are taken during the procedure, and histological patterns give the definitive diagnosis. Furthermore, colonoscopy offers the opportunity to perform polypectomi. Most of colorectal tumors evolve from benign polyps

and therefore, cancer is prevented by removing them. (6) The outcome of CRC depends on in what stage the disease is detected and treatment can be started. If confined to the bowel wall the outcome is favorable and most patients survive. However, once growing through the bowel and metastasize the chance of survival is limited. (7)

Surgery is the cornerstone of treatment for cure. Furthermore, surgery can be indicated as a part of the palliative care to treat symptoms like bleeding, obstruction and perforation in noncurable cases. (8) Obstructive ileus and perforation can also be indications for doing an acute operation in non-metastasized cancers. However, it is highly preferable to perform elective surgeries in order to avoid postoperative complications. Figure 1 demonstrates different types of colorectal resections, depending on the localization of the tumor. The resections are based on the anatomy of the blood vessels, in order to remove the lymph vessels and nodes together with the resected bowel segment. A crucial part is to ensure that the resection margins are free of cancer cells. (9) A potential perioperative adverse event is to injure other abdominal organs, such as the ureters, duodenum, pancreas and spleen. Additionally, in order to avoid anastomotic leakage, which is a very severe complication, the anastomosis has to be made tension-free and torsion-free. Lastly, the surgery can be performed as open or laparoscopic, both are considered equally safe. (6)

In more advanced stages of rectal cancer, neoadjuvant chemotherapy and radiation is beneficial. Also, adjuvant chemotherapy for colon cancer and adjuvant chemoradiotherapy for rectal cancer is sometimes used to minimize the risk of recurrence. For this reason, a multidisciplinary approach is important. (6)

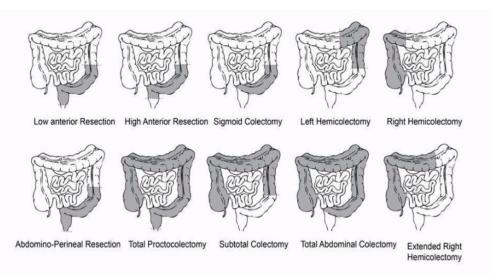


Figure 1: In colorectal cancer surgery, different types of surgical resections can be performed,(10)illustrated in this picture. The choice of resection type depends on where in the bowel the tumor islocalized.

Short-term outcome

Short-term outcome after surgery often includes postoperative complications and mortality. The timeframe of 30 days is generally considered to be the golden standard. However, it is not possible in many parts of the world since the patients are not followed up after discharge. Thus, the Lancet Commission on Global Surgery defines the timeframe as prior to discharge. (11)

A study of short-term outcome by Longo et al. (12) included 5.853 patients who had undergone resection due to colon cancer, obtained from the National Veterans Affairs Surgical Quality Improvement Program database. The results showed that 28 % of the patients suffered from one or more complications occurring within 30 days post surgery.

Length of hospital stay (LOS) is also commonly included in short-term outcome and used as an indicator of healthcare quality. Prolonged hospital stay is associated with multiple postoperative complications and worse patient recovery. (13) Furthermore, prolonged hospital stay significantly increases healthcare costs. (14) The Clavien-Dindo classification (CDC) is a widely used scoring system for postoperative complications. The system is clinically validated and offers the opportunity to rank the severity of all types of complications in an easy and objective way. Both medical and surgical complications are involved in the classification. Complications are classified as grade I-V, depending on the level of treatment required. For example, a complication is classified as grade I if pharmacological treatment is sufficient and as grade IV if intensive care unit (ICU) management is required. Definitions of all grades are shown in table 1. The CDC was presented for the first time in year 2004, in the article "*Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey*" by Dindo D, Demartines N and Clavien PA. (15) They defined complications as "any deviation from the normal postoperative course". Also, the authors published a list of clinical examples of how to grade different postoperative complications. Later on, Clavien PA et al. presented 11 cases of postoperative complications, which were considered especially difficult to rank. In the article "*The Clavien-Dindo Classification of Surgical Complications: Five-year experience*", they suggest adequate interpretations of the difficult cases. (16)

Medical complications observed after CRC surgery involves different types of infections, cardiovascular events, thromboembolism, neurological complications, urinary retention and renal failure. (8) (9)

Important surgical postoperative complications in patients undergoing colorectal surgery are anastomotic leakage, intraabdominal abscess, bleeding, wound complications and bowel obstruction. (13, 17) Anastomotic leakage, which is considered to be the most severe complication, stands for one-third of deaths post colorectal surgery. Identified risk factors are male gender, previous abdominal surgery and tumors in the rectum. In addition to higher

overall morbidity and mortality, anastomotic leakage is associated with higher risk of cancer recurrence. Symptoms can be discharge of pus or feces from draining catheters, pelvic abscess and peritonitis. CT is often used to confirm the diagnosis. For pelvic abscesses, treatment is radiology-guided percutaneous drainage, given that the patient is hemodynamically stable. In free anastomotic leakage, reoperation is frequently required. (17) Wound complications, including incisional surgical site infection (SSI), bleeding and rupture, affect up to 13 % of patients post colorectal surgery and results in a significant number of reoperations. (13) In addition, incisional SSI increases the risk of wound rupture, which sometimes requires reoperation. Bowel obstruction is another potential surgical complication. However, the frequency is relatively low immediately post surgery. (9) Lastly, postoperative bleeding is uncommon in colorectal surgery. (17)

Colorectal cancer in Sri Lanka

The incidence of CRC in Asia is increasing. (18) Unfortunately, Sri Lanka lacks reliable statistics concerning CRC. The National Cancer Control Programme has established a cancer registry, but data is only collected and reported sporadically. Moreover, the information is obtained entirely from institutions. Thus, the data do not cover the total Sri Lankan population. (19) The cancer registry mainly presents data of cancer incidences. In the latest published report, from the year 2011, CRC was estimated to have the fourth highest incidence of all types of malignancies among men and the fifth highest incidence among women. No data concerning short-term outcome after surgery such as mortality, complications or LOS is presented in the registry. (20)

Colombo South Teaching Hospital

Colombo South Teaching Hospital (CSTH), is a public hospital located in Colombo District. It has a bed capacity of 1110 and covers a wide range of tertiary specialties. (21) The Department of Surgery consists of two different wards each admitting around 1000 patients per month with a wide variety of different surgical conditions, both acute and elective. Of these, gastrointestinal disorders make up a minor and CRC an even smaller proportion of these conditions. The CRC surgeries are performed both as open and laparoscopic procedures.

The surgical unit at CSTH follows the Enhanced Recovery After Surgery (ERAS) program in the perioperative care. ERAS is a concept for shortening recovery time after major surgery and preventing postoperative complications. The ERAS protocol for colorectal surgery includes guidelines for thrombosis prophylaxis, pain relief, mobilization, postoperative diet and other issues. The guidelines are evidence-based and used worldwide to improve recovery and decrease the number of complications after surgery. (22)

Hypothesis

The Clavien-Dindo classification (CDC) is not frequently used in measuring short-term postoperative outcome in Sri Lanka, although the system is well-established globally. (15) Moreover, age is a risk factor for postoperative complications, due to a higher presence of comorbidities. (17) Studies have shown younger age in Sri Lankan CRC patients, compared to western countries, with observed median ages of 60 (23) and 61 (24) years, respectively. For instance, in Sweden the mean age for colon cancer at presentation is 72 years and for rectal cancer 70 years. (25) To what extent age above 60 years affects the overall complication rate has not previously been studied in Sri Lanka.

Thus, the hypothesis with this study was that the degree of postoperative short-term complications at CSTH were possible to measure by the Clavien-Dindo classification (CDC) and that the rate of complications did not differ between patients <60 and \geq 60 years of age.

Aim

The aim of this study was to investigate short-term outcome after colorectal cancer surgery at Colombo South Teaching Hospital (CSTH).

Specific objectives

The primary objective was to determine the prevalence, types and Clavien-Dindo grade of postoperative complications occurring before discharge and to evaluate the applicability of the CDC in the studied setting. Additionally, determine length of hospital stay (LOS) for these patients. The secondary objective was to compare prevalence of overall complications and severe complications between patients <60 and \geq 60 years of age.

Material and methods

Study design

This thesis is a retrospective medical record review. Data was collected by the author in Colombo, Sri Lanka, during six weeks. The project involves patients who have undergone colorectal cancer resection at Colombo South Teaching Hospital (CSTH) from first of January 2017 to 29th of January 2020.

Enrolling patients and data collection

The hospitals in Sri Lanka provide every patient with a unique bed head ticket (BHT) number on each admission. All medical recording during the current hospitalization, such as daily notes, lab results and radiology reports, is marked with the BHT. This BHT-number serves as a temporary patient identification number during a current hospitalization, since national personal identity numbers are not used in the Sri Lankan medical record system. If the patient is readmitted at a later moment, he or she will receive a new BHT-number. These different BHT-numbers are only written down by the patient and if lost no medical records can be retrieved later on. At CSTH, all BHTs (medical records) are paper based and stored at the Medical Records Department for a few years. No digital storage exists.

All performed surgeries at CSTH are documented in a log book in the operation theatre. Date of surgery, name of the patient, type of procedure and the BHT-number are recorded. The BHT-numbers of all colorectal resections performed during the observed time period were collected from the log book. Included colorectal resections were right and left-sided hemicolectomy, transverse colectomy, extended right hemicolectomy, sigmoid colectomy, total colectomy, total proctocolectomy, anterior resection, abdominal perineal resection and Hartmann's procedure. The collected BHT-numbers were submitted to the staff at the Medical Records Department, who retrieved the medical records. The records were mostly handwritten. The following basic characteristics of patients and surgeries were obtained from the medical records and documented in Excel; age, gender, tumor localization (colon or rectum), physical status according to the American Society of Anesthesiologists (ASA) classification, date of surgery, type of surgery, if the procedure was performed open, laparoscopic or converted and if the surgery was acute or elective. If documentation of ASAclassification was missing, comorbidities were reviewed and the patient was graded according to the classification system, (26) demonstrated in table 2. Colorectal resections with indications other than cancer were excluded. Furthermore, length of hospital stay (LOS) was calculated. LOS was defined as the number of days from date of surgery to discharge. Thereafter, the entire medical record was reviewed, aiming to find postoperative complications and the treatment required. The severity of complications was graded by the

Clavien-Dindo classification (CDC). The assessment and grading of the postoperative

complications are described in more detail in a subsequent section.

Table 1: This table shows the Clavien-Dindo classification (CDC). It grades the severity of short-term postoperative complications depending on the treatment required. The severity is graded from I to V. Also, grade III and IV includes the subcategories a and b. (15)

The Clavien-D	pindo Classification
Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention.
Grade IIIa	Intervention not under general anesthesia.
Grade IIIb	Intervention under general anesthesia.
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management.
Grade IVa	Single organ dysfunction (including dialysis).
Grade IVb	Multiorgan dysfunction.
Grade V	Death of a patient.
*Brain hemorrh ischemic attacks	age, ischemic stroke, subarrachnoidal bleeding, but excluding transient s.

CNS= central nervous system; IC=intermediate care; ICU=intensive care unit

Table 2: The ASA Physical Status Classification System. The classification is used as an instrument to evaluate the fitness of a patient and the perioperative risks, based on the comorbidities. (26)

ASA PS Classification	Definition
ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes

ASA= American Society of Anesthesiologists. PS= Physical Status.

Study population

Initially, 130 BHTs were collected from the surgical log book at the operation theatre. Out of them, 100 medical records were reviewed at the Medical Records Department. As a consequence of the Corona pandemic, the author was compelled to leave Sri Lanka earlier than planned. Therefore, the remaining medical records were not possible to review due to lack of time. 12 medical records were excluded. The reason was that the indication for colorectal resection was other than cancer or that the type of surgery showed out not to be a colorectal resection. Hence, 88 patients were finally included in the study.

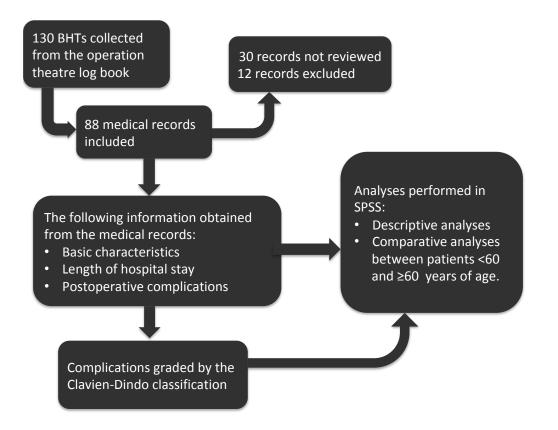


Figure 2: Flow chart of the method of the study, including patient enrollment, data collection and analyses. All steps were performed by the author. BHT is the identification number of a patient during a specific hospitalization and the corresponding medical record is marked with that number. The Clavien-Dindo classification is demonstrated in table 1.

BHT=Bed head ticket. SPSS=Statistical Package for the Social Sciences.

Assessment of postoperative complications

An excel-template from the website AssesSurgery(27) was used to code the postoperative complications. The columns listed in table 3 were copied from the template and pasted into the previous Excel-worksheet with the basic characteristics.

Only complications of grade II or higher were included in this study. The documentation of grade I complications in medical records was considered too unreliable, with risk of description bias. Previous studies (28, 29) have also excluded grade I complications and the Swedish Colorectal Cancer Registry limits the recording to grade II-V complications. (30)

Time from surgery till discharge was used as a timeframe for postoperative complications, as defined by Lancet Commission on Global Surgery. (11) The reason for not choosing 30 days post surgery as a timeframe was the lack of follow-ups. Also, the BHT-system makes it impossible to detect if a patient is readmitted, as explained above.

Urological complications that result in catheter at discharge do not have an obvious classification. Hence, such complications were classified as grade II, similarly as in the Swedish Colorectal Cancer Registry. (30) Moreover, although incisional surgical site infections (SSI) are commonly classified as grade I, as demonstrated in table 1, such infections were classified as grade II if systemic antibiotics were given, since pharmacological treatment belongs to grade II.

Table 3: Postoperative complications were obtained from the medical records and documented in Excel. The documentation of complications comprises these factors, obtained from an Excel-template published at the website Asses Surgery (27). "Grade" refers to Clavien-Dindo grade, demonstrated in table 1. "Description" includes how the complication was treated.

Complication yes/no	Type of complication A	Description of complication A	Grade of complication A	Type of complication B \rightarrow C, D, E,	Grade of Highest complication	Total number of complications

Statistical methods

The data was transferred from Excel to Statistical Package for the Social Sciences (SPSS) version 26. Firstly, descriptive analyses of frequencies were performed. Secondly, to test differences in rate of overall complications and severe complications between patient <60 and \geq 60 years of age, the Chi-squared test and Fisher's exact test were performed. P<0.05 was considered statistically significant.

Ethical considerations

The study aligns to the principles of the Helsinki Declaration. Ethical approval was received from the Ethics Review Committee of the Colombo South Teaching Hospital (Appendix A). Patients were given new identification numbers and thereby impossible to identify. Anonymity of patients was preserved during the collection of data.

Results

Characteristics of patients

53.4 % (n=47) of the patients were males and 46.6 % (n=41) were females. Mean age for males was 61.1 years and 60.4 for females. The age span was 23 to 92 years. The majority of patients (64 %) were 50-69 years old. A more detailed description of the age distribution is illustrated in figure 3. 40.9 % (n=36) of the patients were classified as ASA I, 54.5 % (n=48) as ASA II and 4.5 % (n=4) as ASA III. (Figure 4)

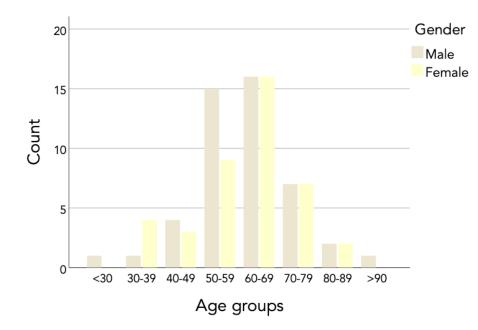


Figure 3: This graph shows the study population divided into different age groups. The age groups are also separated into gender.

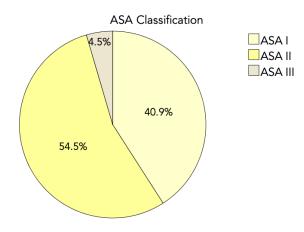


Figure 4: This figure shows how the patient physical status is distributed among the study population, according to the ASA-classification. The ASA-classification is explained and demonstrated in table 2. ASA= American Society of Anesthesiologists.

Characteristics of surgery

Table 4 summarizes characteristics of the surgeries. One can see that the majority of tumors were localized to the rectum and laparoscopic surgery was more common than open surgery. Only one surgery was performed acute, due to severe bowel obstruction. The remaining 87 surgeries were elective. The frequencies of different types of surgeries performed are shown in figure 5. The vast majority was anterior resections. Transverse resection, total colectomy, total proctocolectomy and Hartmann's procedure were done only once. There were mainly two different senior surgeons who performed these operations. A minor part, approximately 18 %, was performed by other surgeons. For one patient, liver resection of a metastasis was performed together with the colorectal resection. Another patient underwent total hysterectomy and bilateral salpingo-oophorectomy immediately after the colorectal resection, due to postmenopausal bleeding. Additionally, for one patient distal pancreatectomy was performed simultaneously because of a cystadenoma in the tail of pancreas.

Table 4: Characteristics of the surgeries performed in this study, including localization of the tumor, choice of open, laparoscopic or converted procedure and if the surgery was performed acute or elective.

Tumor localization	Colon Rectum	Number 33 55	% 37.5 62.5
Procedure	Open	33	37.5
	Laparoscopic	49	55.7
	Converted	6	6.8
Planning	Acute	1	1.1
	Elective	87	98.9

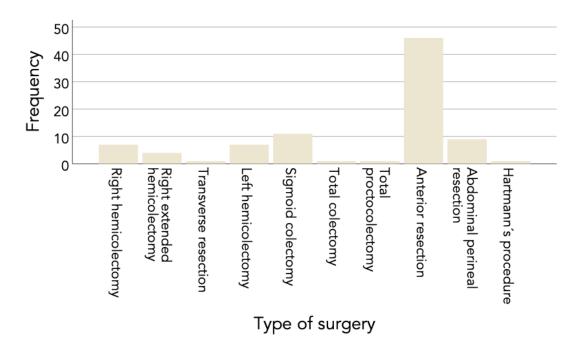


Figure 5: The different types of surgical resections performed are shown on the x-axis. The y-axis shows how many times the specific type of resection was performed in this study. Most of these resections are illustrated in figure 1.

Outcome

Altogether, one or more postoperative complications (\geq grade II) occurred in 45.5 % (n=40) of the patients. However, the number of complications was 51, since a patient could have more than one complication. The different complications were allocated as

grade II n = 46, grade III n = 3, grade IV n = 2 and grade V n = 0. A complete list of the specific types of complications is presented in table 5, together with the given treatment, Clavien-Dindo grade and number of cases. Since no patient developed grade IIIa or IVb complications, the grades are presented in the contracted forms, as grade III and IV. The most common complication, affecting 22.7% (n=20) of the patients, was postoperative anemia treated with blood transfusion. It was noticed during the data collection that most of these patients were anemic preoperatively, although the anemia became more severe after surgery. The second most common complication was incisional surgical site infection (SSI) (11.4%, n=10), treated with antibiotics and sometimes also removal of clips at bedside. In four patients, some kind of urinary tract injury, accidental or inevitable due to tumor overgrowth, was documented in the operation note and they required prolonged use of catheter. Four patients developed hypertension postoperatively, requiring antihypertensive medication. Three patients developed grade III complications; one case of wound rupture, another case of mechanical obstruction at stoma site and the third case was anastomotic insufficiency. The most severe complications occurred in two patients who developed respiratory dysfunction requiring ICU-management, and thus classified as grade IV. The first patient suffered from Acute Respiratory Distress Syndrome (ARDS) and was treated with Noninvasive Intermittent Positive Pressure Ventilation (NIPPV) and high amounts of oxygen. The second patient developed anastomotic insufficiency. In contrast to the other patient with anastomotic insufficiency, this patient required both reoperation (two times) and mechanical ventilation at ICU for eight days. There was no event of death among the patients.

Table 5: List of all postoperative complications (\geq grade II) observed in this study population, together with the corresponding Clavien-Dindo grade, the given treatment, number of cases and affected proportion of the total study population. Notice that one patient can have several complications documented in this table, not only the highest grade of complication.

Clavien-Dindo grade	Type of complication	Treatment	Number	%
Grade II			46 (total)	52.3
	Urinary tract injury	Catheter at discharge	4	4.5
	Urinary retention	α_1 –receptor antagonist	1	1.1
	Confusion	Antipsychotic medication	1	1.1
	Incisional SSI	Antibiotics	10	11.4
	Hypertension	Antihypertensive medication	4	4.5
	Hypotension	Noradrenaline infusion	1	1.1
	Atrial fibrillation	Antiarrhythmic medication	1	1.1
	NSTEMI	Routine medication	1	1.1
	Infection of unknown source	Antibiotics	1	1.1
	ACLF	Various medicines*	1	1.1
	Anemia	Blood transfusion	20	22.7
	Gastritis	Omeprazole	1	1.1
Grade III			3 (total)	3.4
	Wound rupture	Resuturing in G.A	1	1.1
	Anastomotic insufficiency 1	Reoperation in G.A	1	1.1
	Obstruction at stoma site	Reoperation in G.A	1	1.1
Grade IV			2 (total)	2.3
	ARDS	NIPPV at ICU	1	1.1
	Anastomotic insufficiency 2	Invasive ventilation at ICU	1	1.1
Grade V			0	

* Lactulose, Vitamin K, Tranexamic acid, antibiotic prophylaxis and plasma products. SSI= Surgical site infection, NSTEMI= Non ST elevation myocardial infarction, ACLF=Acute-on-chronic liver failure, ARDS= Acute respiratory distress syndrome, G.A= General anesthesia, NIPPV= Noninvasive positive pressure ventilation, ICU= Intensive care unit.

54.5 % (n=48) of the patients had no postoperative complication (\geq grade II), 35.2 % (n=31) had one, 8.0 % (n=7) had two and only 2.3 % (n=2) developed three complications. (Figure 6) The calculation of highest degree of complication showed that 39.8 % (n=35) developed a grade II complication, 3.4 % (n=3) a grade III complication

and 2.3 % (n=2) grade IV as the most severe complication. (Figure 7) When defining Clavien-Dindo grade III or higher as a severe complication, the rate of severe complications becomes 5.7 %.

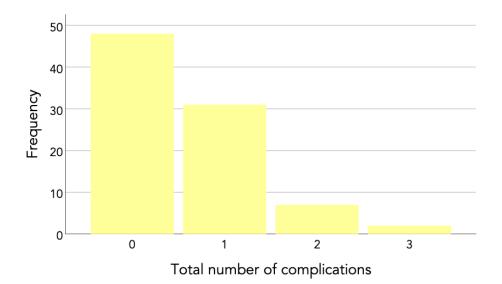


Figure 6: The number of patients who suffered from none, one, two or three postoperative complications (\geq grade II).

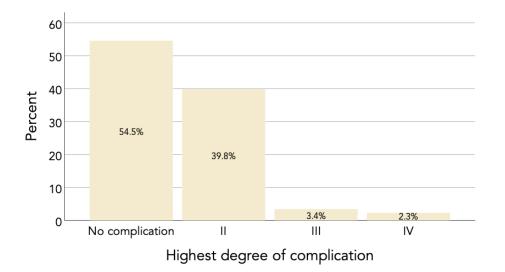


Figure 7: The x-axis shows the highest Clavien-Dindo grade of complication that a patient is suffering from. The y-axis shows how large proportion of the study population that belongs to respective scenario.

Median length of hospital stay (LOS) was 6 days. 85 % of the patients had a LOS of 4-8 days. The observed minimum LOS was 4 days and maximum 106 days. The latter can be considered as an outlier, as seen in figure 8. The patient suffered from anastomotic

insufficiency and was reoperated two times and intubated at the ICU with respiratory ventilation for eight days.

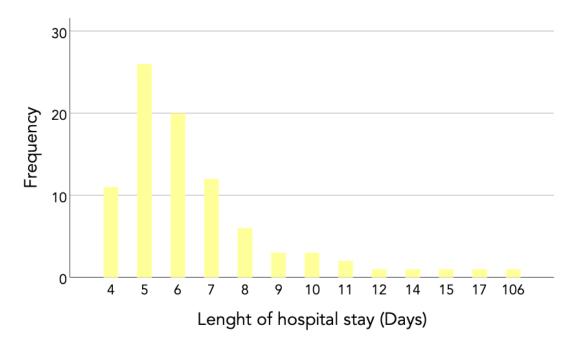


Figure 8: This graph demonstrates how many days patients stay at the hospital, measured from day of surgery to discharge.

Comparative analyses

The difference in overall complication rate (\geq grade II) between patients <60 and \geq 60 years of

age was not statistically significant. The subsequent analysis of difference in prevalence of

severe complications (≥grade III) showed no statistical significance either. (Table 6)

Table 6: Comparative analyses of overall complication rate (\geq grade II) and rate of severe complication (\geq grade III) between patients <60 and \geq 60 years of age.

Comparison	Age (Years)	Number of patients (%)	Р
One or more complications	<60 (n=37) ≥ 60 (n=51)	16 (43.2) 24 (47.1)	0.89*
Severe complication (≥ grade III)	<60 (n=37) ≥ 60 (n=51)	3 (8.1) 2 (3.9)	0.646**

*Chi-squared test, **Fisher's exact test

Discussion

The present study observed 45.5 % in overall prevalence of postoperative complications $(CDC \ge \text{grade II})$ before discharge in patients undergoing colorectal cancer (CRC) surgery at Colombo South Teaching Hospital (CSTH). For most patients with one or more complications, the highest degree of complication was Clavien-Dindo grade II. Out of these, the vast majority was postoperative anemia treated with blood transfusion. The second most common complication was incisional surgical site infection (SSI). A few patients (n=5) developed more severe complications, such as two cases of anastomotic insufficiency. Analyses did not show any difference in prevalence and severity of complications between patients <60 and \ge 60 years of age.

A study by Nakanishi et al. (31) investigated the influence of sarcopenia on complications after CRC surgery. The study have several similarities with ours by being retrospective, using time before discharge as a timeframe, publishing prevalence of Clavien-Dindo grade II or higher and having the same inclusion criteria for the total study population. The prevalence of one or more complications (≥grade II) was 33 % for the total study population (not only patients with sarcopenia). A possible explanation for the slightly higher prevalence (45.5 %) in our study could be that we classified all negative events as complications, even if not obviously caused by the surgery, as recommended by Clavien et al. (16). Postoperative anemia and hypertension are potentially examples of that scenario. Another explanation could certainly be a better perioperative healthcare in that study setting, especially since it was conducted in the developed country of Japan.

Regarding severe complications, comprising Clavien-Dindo ≥grade III, Nakanishi et al. reported 10 % in prevalence. (31) Another study observed a corresponding prevalence of 9 % after elective colorectal surgery. (32) These numbers are higher in comparison to the figures in this present study (5.7 %), which is a promising finding for CSTH. Another positive finding is that no patient died in our study, compared to a postoperative mortality of 2.2-8.5 % (23, 33, 34) in the previous research. However, the timeframe for observation was longer (30 days) than in our study, probably resulting in a higher detection rate of deaths. Also, the small patient sample and considerable large proportion of elective surgeries in the present study may affect mortality rate. Still, one can speculate whether CSTH's practice of the Enhanced Recovery After Surgery (ERAS) program contribute to the low number of severe complications and deaths. For instance, no thromboembolic event was observed, perhaps thanks to a strict usage of compression stockings, mobilization and guidelines for anticoagulation.

Rates of blood transfusions post colorectal resections vary a lot depending on surgeon and hospital. (35) Still, the goal should always be to minimize blood transfusions in this situation, as it is associated with adverse outcomes. More specific, research has shown an increased risk of SSI, pneumonia, thromboembolic events, prolonged hospital stay, cancer recurrence and overall mortality, when adding more blood transfusions. (36-38) The observed blood transfusion rate in the present study was 22.7 %. Thus, there is reason to make an effort to decrease the blood transfusions. It is recommended to achieve this by detecting and treating preoperative anemia with intravenous iron, several weeks before surgery. (39) Otherwise, there is a high risk that a preexisting anemia becomes aggravated by such a major surgery. As noticed during the data collection, most of the transfused patients were anemic already before surgery.

We presented 11.4 % in prevalence of incisional SSI. This is in line with other retrospective studies, which have found rates of 3.3-11.7% in colorectal surgery. (40, 41) The recommended treatment for incisional SSI is removal of sutures, without systemic antibiotics, in first hand. (42) Therefore, it is noteworthy that all SSI were treated with antibiotics. Especially in the light of the growing problem with antibiotic resistance. Moreover, if antibiotics not had been used for these SSI, the total number of grade II complications would have decreased considerably.

Regarding previous research on the Sri Lankan population, only a few minor clinical studies on CRC has been published. Out of them, a prospective study by Chandrasinghe et al. (24) in Gampaha District, involves the highest number of patients. The study analyzed 679 patients with CRC diagnosis at Colombo North Teaching Hospital from year 1997 to 2014. The results pointed out that both colon and rectal cancer increased during the observed time period. Also, in comparison with western countries, the patients in this cohort were younger and the cancer stage at diagnosis was more advanced. Over 25 % of the CRC patients were under the age of 50 years at presentation and the mean age was 58 years, which is low compared to other populations. This is in line with the observed mean age in the present study (males=61.1 years, females=60.4 years). As mentioned above in Background-Hypothesis, in a western country like Sweden the mean age for colon cancer is 72 years and for rectal cancer 70 years. (25) Furthermore, Chandrasinghe et al. emphasizes the deficiency of data concerning CRC in Sri Lanka. (24) A study by Perera et al., (23) also conducted in the Gampaha District, investigated mortality post CRC surgery as one of the objectives. They presented a 30-day mortality of 5 %, caused by myocardial infarction, anastomotic leakage and bronchopneumonia. The study involved 220 patients. Again, the shorter timeframe for

observation in our study may contribute to the lower mortality rate. None of the studies analyzed complications in general and did not use the Clavien-Dindo classification (CDC).

Focusing on length of hospital stay (LOS), Roulin et al. (43) investigated costeffectiveness of ERAS in colorectal surgery in Switzerland. LOS was compared between two groups, one treated according to the ERAS program and one receiving traditional care. The median LOS was 7 days for the ERAS group and 10 days for the other group. We observed a median LOS of 6 days, indicating that the ERAS protocol is functioning well at CSTH. In future research, it would be interesting to study rates of readmission post colorectal surgery at CSTH, to confirm that short LOS do not result in more readmissions.

There was no statistically significant difference in the rate and severity of complications between patients <60 years and ≥60 years of age. The reason for choosing 60 years as a cut-off was the previously observed significantly young age in CRC patients in the Sri Lankan population. (23, 24) The relatively high life expectancy (74.9 years) in Sri Lanka (1) suggests that the population is fit for surgery also in higher ages. On the other hand, the growing disease burden from non-communicable diseases (NCDs) (1) results in additional comorbidities among the patients, which can increase the postoperative risks even in younger ages. A study by Aquina et al., conducted in the USA, showed that complications after colon cancer surgery increased in patients of age 65-74 years and ≥75 years compared with patients <65 years of age. (44) Another study, by Chandrasinghe et al., (45) investigated short-term outcome following CRC surgery in different age groups in the Sri Lankan population. They observed a higher 30-day mortality in patients >70 years compared with patients <60 years and <50 years. Furthermore, the rate of three

types of complications were compared between patients >70 and <70 years, and also between patients >70 and <50 years. Cardiac complications were more common in the elderly in both analyses, but not infections or anastomotic complications. Together with the results from our study, one can speculate that the threshold for an increased postoperative risk is higher than 60 years in the Sri Lankan population, possibly around the age of 70 years.

During short visits at the surgical ward, as well as from the medical records, it was noted that many patients seemed to be underweight. A possible objective in future research could be to determine if underweight results in more postoperative complications in the Sri Lankan population. Another idea for further studies could be to survey differences in short-term outcome depending on the level of income, since low income is common among patients in public hospitals.

Strengths and weaknesses

This study has several limitations. Firstly, the retrospective review of physical medical records results in missing data. Nurses or doctors may not document every detail concerning the postoperative course of events and treatment. Furthermore, since the records are handwritten, it can be difficult to read. Additionally, interpretation of daily notes, compared with direct communication to the medical staff and seeing the patients with your own eyes, increases the risk of misunderstanding. Nevertheless, the data collection and grading were yet feasible and these problems exist more or less everywhere around the world during retrospective medical record reviewing. Moreover, the retrospective design makes it possible to include a larger number of patients, with respect to the short time of a student thesis. Secondly, lack of follow up and the medical

record system makes it impossible to detect complications occurring after discharge. For this reason, we were not able to use the golden standard timeframe (30 days). Thirdly, the small patient sample is a weakness. It makes it difficult to perform comparative analyses and draw conclusions. Considering our comparison of two age groups, if there actually is a difference, the likelihood is high that we failed to show it due to a small patient sample. A strength with this study is that one person performed all the data collection and grading. For this reason, all patients were interpreted and evaluated in the same way. Another strength is the usage of a well-established and clinically validated grading system for complications, which increases the reliability of the study. Furthermore, comparisons with other studies are facilitated by the worldwide usage of the Clavien-Dindo classification (CDC).

Conclusions and implications

The present study shows that the Clavien-Dindo classification (CDC) is a useful tool in measuring short-term complications following colorectal cancer surgery at Colombo South Teaching Hospital (CSTH). The system is even possible to use retrospectively, based on sufficient information in the medical records. This finding suggests that the system also can be used in other hospitals in the country. Since the CDC is used world wide in research, it would be beneficial to make it more established in Sri Lanka, in order to become on a par with more developed countries. Furthermore, quality reporting systems following colorectal surgery will hopefully be started in the future in the country. Therefore, the usability of the CDC is an important knowledge. Moreover, the results showed no increased risk of complications in patients ≥ 60 years of age. There is a need for more research considering at what age the postoperative risk increases, in order to prevent complications in these patients even more effectively and be able to evaluate the benefits of surgery relative to

the risks. Additionally, the present study indicates a quite large number of overall complications, to a large extent consisting of incisional SSI and postoperative anemia treated with blood transfusion. The number of severe complications seems to be low and there was no number of deaths in this study population. However, further research including a larger patient group, is needed to draw any conclusions. In order to improve the outcomes for this patient group, the hospital should work towards a decrease in the number of blood transfusions. For the healthcare as a whole, it would be favorable to reduce the antibiotic utilization, in view of the growing antibiotic resistance. Also, improvements of the medical record system would increase the opportunities to perform research in the country.

Populärvetenskaplig sammanfattning

Att mäta komplikationer efter operation av tjock-och ändtarmscancer på ett Sri Lankesiskt sjukhus

Tjock-och ändtarmscancer ökar på Sri Lanka i takt med att befolkningen blir äldre och ohälsosamma levnadsvanor ökar, vilka båda är riskfaktorer för sjukdomen. Kirurgi utgör grundstenen för botande behandling. Det är en stor operation, som innebär risker för komplikationer. Allvarlighetsgraden av komplikationer som inträffar kort tid (maximalt 30 dagar) efter kirurgi graderas vanligtvis utefter den s.k. Clavien-Dindo klassifikationen. Det är en femgradig skala (I-V), där graden bestäms av vilken behandling som krävs. Till exempel grad II om läkemedel är tillräckligt som behandling och grad IV om intensivvård behövs. Trots att Clavien-Dindo klassifikationen är väletablerad globalt, används den sällan på Sri Lanka. Vidare, ålder är en riskfaktor för komplikationer och tidigare studier har observerat påfallande låg ålder hos patienter med tjock-och ändtarmscancer i den Sri Lankesiska befolkningen. Det har inte tidigare studerats huruvida ålder över 60 år ökar risken för komplikationer.

Syftet med studien var att undersöka komplikationer hos patienter som genomgått operation för tjock-och ändtarmscancer på *Colombo South Teaching Hospital* och i förlängningen ifall Clavien-Dindo klassifikationen var ett passande verktyg för sådan studie. Syftet var också att undersöka huruvida patienter över 60 år löpte större risk att drabbas av komplikation jämfört med patienter under 60 år. Informationen hämtades från handskrivna journaler tillhörande 88 patienter som opererats under de senaste tre åren.

Resultaten visade att förekomsten av komplikationer överlag var relativt hög i jämförelse med internationella siffror. Majoriteten bestod av läkemedelsbehandlade tillstånd, motsvarande grad II, och utav dem framför allt sårinfektioner och blodbrist som behandlades med

blodtransfusion. Förekomsten av allvarliga komplikationer, motsvarande grad III eller högre, visade sig däremot vara förhållandevis låg. Tre av dessa patienter behövde opereras igen och två utvecklade så pass allvarliga tillstånd att intensivvård krävdes. Ingen patient dog innan utskrivning. Ingen skillnad kunde påvisas gällande mängden komplikationer hos patienter som var under respektive över 60 år gamla.

Sammanfattningsvis var Clavien-Dindo klassifikationen ett användbart verktyg för att mäta komplikationer efter operation av tjock-och ändtarmscancer på *Colombo South Teaching Hospital.* Detta motiverar att systemet med fördel även skulle kunna användas på andra sjukhus i Sri Lanka. Resultaten antyder att risken för komplikationer inte ökar när man fyllt 60 år, utan först vid en högre, ännu okänd, ålder. Det krävs fler och större studier för att ta reda på vid vilken ålder som operationen blir extra riskfylld. Studien tyder på en låg förekomst av allvarliga komplikationer och död kort tid efter operation, vilket är lovande för sjukhuset. Utifrån ett nationellt perspektiv, är denna studie ett exempel på att systemet med handskrivna journaler är problematiskt när man ska bedriva forskning. Det vore således gynnsamt att förbättra systemet för att lättare kunna föra statistik och utföra nya studier.

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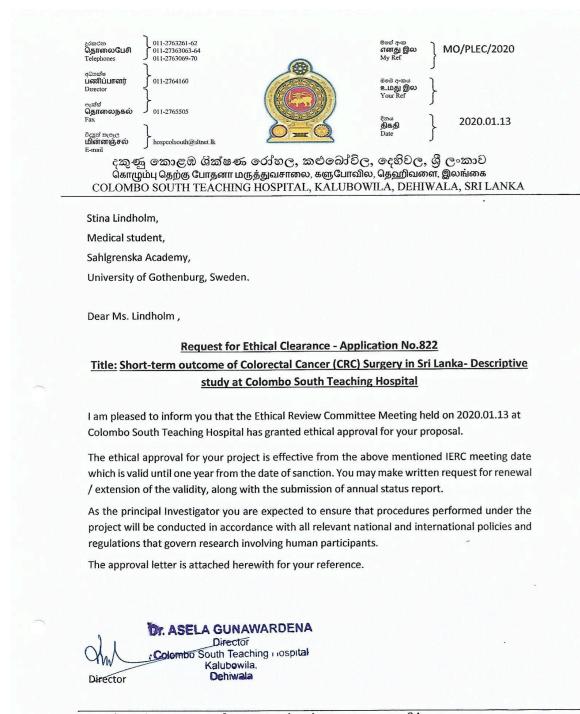
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Appendices

Appendix A: Ethical Approval



காஜீஜை கோல் கோல் குகை மனப்பாங்குடனான பராமரிப்பு DEDICATION TO CARE