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Prevalence and Factors Associated with Anastomotic Leakage Among
Patients Undergoing Bowel Resection and Anastomosis.



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Prevalence and Factors Associated with Anastomotic Leakage Among Patients Undergoing Bowel Resection and Anastomosis.

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Abstract.

Purpose: This study aimed at giving evidence on prevalence and factors associated with anastomotic leakage among patients undergoing bowel resection and anastomosis at Bugando Medical Centre (BMC) and Sekou Toure Regional Referral Hospital (SRRH).

Methodology: A descriptive cross-sectional analytical study was used involving patients undergoing bowel resection and anastomosis at Bugando Medical Centre and Sekotoure regional referral hospital over a four-month period from March 2017 to June 2017 inclusive.

Findings: Eight out of 144 patients (5.6%) developed anastomotic leakage. The common indication for surgery was sigmoid volvulus, the common performed anastomosis was ileo-ileo end to end, and double layer continuous anastomotic suture was the common method of anastomosis. Anemia (0.012), presence of premorbid illnesses ($p=0.003$), American association for anesthesia (ASA) greater than II ($p=0.001$), intraoperative contamination/sepsis ($p<0.001$), low ranked operator ($p=0.046$), prolonged duration of operation ($p=0.001$), and delayed passage of stool and flatus ($p=0.001$) were found to be variables associated with anastomotic leakage among study participants. Anastomotic leakage in our setting occurs in approximately 5.6% of patients operated. Several factors such as high American society for Anesthesiologist above III, premorbid condition such as uncontrolled Diabetes Mellitus, intraoperative contamination/sepsis, low ranked operator, prolonged duration of operation above 3 hours and prolonged ileus were among factors that the present study found to be associated with high risk of anastomotic leakage.

Unique Contribution to Theory, Policy and Practise: These factors therefore, should be carefully considered when planning for patients for surgical interventions, so as to reduce the potential subsequent anastomotic leakage.

Keywords: *Bowel Anastomosis, Gastrointestinal Tract Pathology, Anastomotic Leakage, Sigmoid Volvulus, Premorbid Illnesses.*

1 Introduction.

Bowel anastomosis is a surgical procedure to establish communication between two ends of resected bowel. This procedure restores bowel continuity after removal or bypass of a pathologic condition affecting the bowel. The art of bowel anastomosis dates back into the 19th century. Nicholas Senn's review (1844–1908, Chicago) performed in 1893 detected approximately 60 different techniques for intestinal suture, which he attributed to the ancient and modern methods, followed by an additional 33 recent methods of suturing bowel. Within the past 200 years, gastrointestinal anastomosis has been transformed from a life-threatening venture into a safe and routine. Later that century, Lembert countered this idea, instead advocating inverting sutures with serosal to serosal contact. Halsted noted that the submucosal layer was the strength-bearing layer in intestinal anastomoses. By the time that Treves published "A System of Surgery" in 1895 "Lembert Sutures" were recommended in intestinal anastomoses. The first acclaimed mechanical device to create a non-sutured anastomosis was Murphy's button introduced in 1892. It consisted of two mushroom shaped pieces, which were secured within bowel ends by purse string sutures. The pieces were then joined together. The bowel would heal as an inverted anastomosis. The excess inverted tissue would slough and the intact "button" would pass per rectum. Murphy's button gained considerable acceptance for several decades. Bowel anastomosis is one of the most commonly performed surgical procedures worldwide. Indications for bowel anastomosis can be broadly divided into two categories: restoration of bowel continuity after resection of diseased bowel and bypass of unresectable diseased bowel. However, bowel anastomosis is contraindicated in conditions where there is a high risk of anastomotic leak. In this case, a defunctioning stoma is recommended.

A disastrous complication of bowel anastomosis is anastomotic leak resulting in peritonitis or enterocutaneous fistula, which is associated with high morbidity, mortality and prolonged hospital stay. Anastomotic leakage rates vary from region to region, hospital to hospital, and from surgeon to surgeon. Globally, the prevalence of anastomotic leakage following bowel anastomosis has been reported to range from 1% to 30%. However, the prevalence of anastomotic leak varies widely because of the divergences in what constitute a leak. If a leak is defined on the basis of only those requiring surgery, the cited rate is 1.9% but may be as high as 15.9% for radiologically sought leaks.

The risk factors for anastomotic leakage may be multifactorial, including patient-specific factors, such as male gender, older age, poor nutritional status, leukocytosis, cardiovascular disease immunodeficiency states, high ASA status, smoking, alcohol renal condition like uremia, neonates. Technical factors, including local ischemia, anastomotic tension, extensive surgery following Tumor resection require creation of difunctional stoma to prevent Anastomotic leakage other factors are low anastomosis, poor blood supply emergency surgery, local sepsis presence of distal obstruction, steroid use, chemotherapy and radiation therapy. The rate of anastomotic leakage also varies depending on sites or location of the bowels anastomosed the presence of any of these risk factors calls into question the safety of the planned anastomosis. Despite the fact that anastomotic leakage is a major cause of postoperative mortality, morbidity and prolonged hospital stay following gastrointestinal

surgery in our setting, little work regarding this subject has been done in Tanzania and Bugando Medical Centre and SRRH in particular. Most of previous study have shown that anastomosis leakage has associate with high mortality, morbidity and prolonged hospital stay, If this is true, then This study aimed at establishing the prevalence of anastomotic leakage among patients undergoing bowel resection and anastomosis at Bugando Medical Centre and sekotoure regional referral hospital and to identify factors associated with its occurrence

2 Methods and Methodology.

A hospital based primary Data were collected at BMC and SSRH in the period of 3 months from March to June 2017, then a statistical test used to determine the prevalence and factors associated with of anastomotic leakage among patients undergoing bowel resection and anastomosis The study was conducted in the surgical wards of Bugando Medical Centre and SRRH. Bugando Medical Centre is one of the four largest tertiary care hospitals in the country and serves as a referral centre for tertiary specialist care for a catchment population of approximately 13 million people from neighboring regions. BMC has a total of 950 bed, of which 140 beds have been dedicated to general surgery services.

The study population included all patients undergoing bowel resection and anastomosis at Bugando Medical Centre Sekou- Toure Regional Referral hospital (both electively and emergency) during the period of study above 28days. The patient who die immediately after surgery (bowel resection and anastomosis), Patients with anastomosis protected by a proximal diverting stoma and Patients developing complications other than leakage like hemorrhage, stenosis and diverticular formation are excluded from the study

a. Sample Size Estimation.

The minimum sample size of this study was calculated using Yamane Taro (1973).

$$n = \frac{N}{(1+N(e)^2)}$$

Where;

n=sample size

N= population under study that is 243 patient who had bowel anastomosis at BMC for the past year 2006

e margin of error 0.05

$$n = 243$$

$$(1+243(0.05)^2)$$

$$N = 152$$

The minimum sample size was expected to be **152 patients**; but during the study period a total of 144 patients were enrolled. Convenience sampling of patients who meet the inclusion criteria was performed until the sample size was reached

Recruitment of patients to participate in the study was done in the surgical wards of Bugando Medical Centre and SRRH. Anastomotic leakage was diagnosed if there is one of the following criteria: 1) Presence of enterocutaneous fistula; 2) Anastomotic breakdown was identified by high index of suspicion of peritonitis that was confirmed by ultrasound or laparotomy 3) Clinical features of a leak confirmed by rectal examination, water-soluble contrast enema or

contrast computed tomography (CT) in cases of low anterior resection. A leak was considered major if there is peritonitis, with systemic features such as fever, tachycardia, confusion or signs of shock, or high output enterocutaneous fistula whereas a leak that lacks these features and does not warrant surgical intervention was considered minor.

b. Data Management.

i. Data collection.

Data was collected using a pre-tested coded questionnaire. Data administered in the questionnaire include; demographic characteristics (e.g. age, sex),

ii. Statistical data analysis.

Statistical data analysis was done using STATA version 12, with help of medical statistician. Categorical variables were summarized in form of proportions, frequent tables, bar and pie charts whereas the mean, median, mode, standard deviation and histograms was used to summarize continuous variables. Chi-square test was used to test for the significance of association between the predictor and outcome variables in the categorical variables. Rank sum test was used to compare the difference between median age of patients with and without anastomotic leak. Significance was defined as a p-value of less than 0.05

Predictor (independent) variables are Socio-demographic characteristics (e.g. age, sex, area of residence, education hospital at which attended, occupation, socio-economic status). Pre-operative information example duration of illness, ASA status, preoperative laboratory, investigation, and need for blood transfusion, type of surgery whether emergency or elective if diabetic RBG where be taken preoperatively. Intraoperative variables example Rank of the operator/surgeon (registrar, resident or specialist), Type of anastomosis (enteroenteric, enterocolic, colocolic, colorectal) Number of anastomosis done, Suture technique used (two layers continuous or interrupted suture, and Time of doing the anastomosis. Outcome (dependent) variables is anastomotic leakage associated morbidity

iii. Data quality control.

To ensure internal validity of the study the following precautions was taken into considerations: 1) The data collecting tool was being pre-tested. 2) Research assistants were oriented on how to administer the questionnaire and to collect data. 3) The principle investigator ensured completeness and consistency of data collected

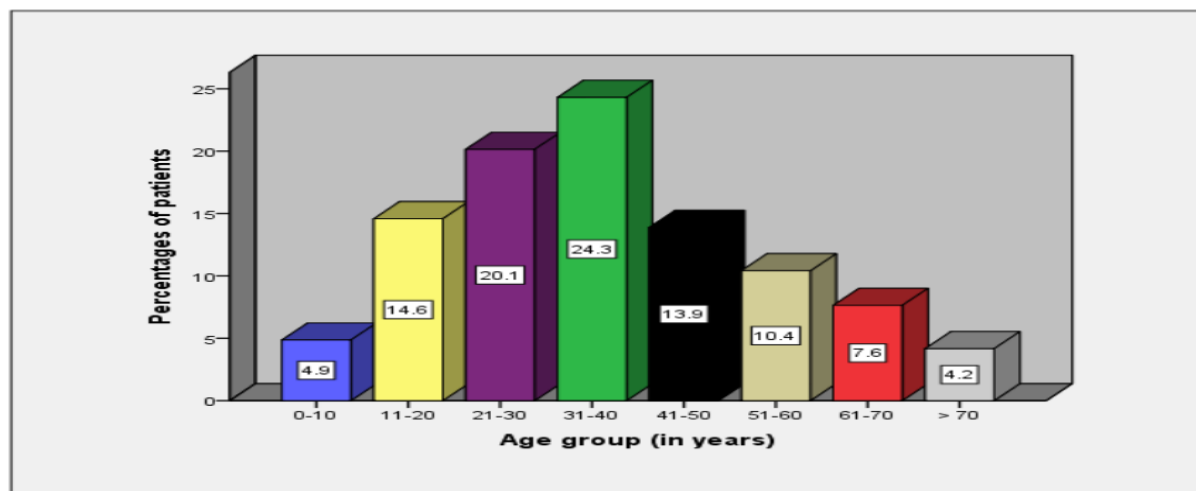
3 Results and Findings.

a. Patient's baseline characteristics

During the period of study, a total of 149 patients underwent bowel resection and primary anastomosis at BMC and SRRH. Five patients out of 149 were excluded from the study due failure to meet the inclusion criteria. The patient's ages ranged from 4 to 94 years with the, median age (IQR) of 34.59 (23-53.5) years. The modal age group was 31-40 years, accounting for 35 (24.3%) as shown in a Figure 1. Another social demographic result is shown in the Table 1 below.

Table 1: Baseline social demographic features

Variable	No (%) or median (IQR)
Median age (IQR)Years	34.5(23-53.5) years
Sex	Male
	Female
Cigarette smoking and alcohol use status	Non
	Cigarette smoker
	Alcoholic users
	Both cigarette and alcohol users

**Figure 1: Distribution of patients according to age group (in years)**

b. Clinical characteristics among patient undergoing bowel resection and anastomosis at BMC and SRRH

Majority of patient presented with the history of abdominal pain, vomiting, constipation and other as it shown in the Table 2 below. Also, patient present with the history of pre-morbid medical illness. Duration of symptom ranged from 1-21 days with median of 6 days. Clinical characteristics like hemoglobin count, BMI, leucocyte count, erect X-rays are shown in the Table 3 below.

Table 2: Distribution of patients according to clinical presentation

Clinical presentation	Frequency(n); N=144	Percentage
Abdominal pain	138	95.8
Vomiting	120	83.3
Constipation	102	70.8
Abdominal distention	56	38.9
Diarrhea /constipation	34	23.6
Fever	26	18.1
Weight loss	24	16.7
Features of peritonism	68	47.2
Abdominal mass	20	13.9
Visible peristalsis	16	11.1
Succussion splash	13	9.0

Table 3: Clinical characteristics of patient associated with anastomotic leakage

Clinical characteristics	No (%)	
Co-morbid illness	Non	104(72.2%)
	Diabetes Mellitus	12(8.3%)
	Chronic Obstructive Pulmonary Disease	9(6.3%)
	Hypertension	8(5.3%)
	Others*	11(7.6%)
Duration of symptoms	Within 24hours	10(7%)
	24- 48hours	31(22%)
	48-72hours	21(14.7%)
	Above 72hours	82(57%)
Haemoglobin(g/dl)	Less than 6	10(7%)
	6 to 10	78(54.2%)
	More than 10	56(39%)
BMI (kg/m ²)	Less than 18	23(16%)
	18- 25	121(84%)
	Above25	0(0%)
Leucocyte count	Normal	81(56.25%)
	Leucocytosis	63(43.75%)
Erect x-ray findings	Up to 3 air fluid levels	23(15.97%)
	Multiple air fluid levels	121(84.03%)

All patients who were scheduled for operation (144) were assessed pre-operatively using the American Society of Anesthetists (ASA) pre-operative grading. The majority of patients, 132(92%) had ASA class I. The majority of patients, 120 (83.3%) were operated on emergency basis. Sigmoid volvulus was the most common indication for surgery accounting for 23.6% of cases, intraoperative majority of patient ended up with entero enteric anastomosis 93(64.6%), and intraoperative blood loss was less than 1litre in 119(82.6%) (See table 5)

Table 4: Preoperative and intraoperative factors of patients

Factor		Number (%)
ASA	ASA 1	132(92%)
	ASA II and III	9(6.3%)
	ASA IV and V	3(2.1%)
Nature of surgery	Emergency	120(83.3%)
	Elective	24(16.7%)
Indication for surgery	Sigmoid volvulus	34(23.6%)
	Inguinal hernias	32(22.2%)
	Aadhesions	28(19.4%)
	Intussusceptions	21(14.6%)
	Others*	29(20.1%)
Rank of surgeon	Resident or Registrar	99(68.8%)
	Specialist	45 (31.2%)
Technique suturing	Interrupted	8(6.6%)
Suture material used	Continuous suture	136(93.1%)
	Absorbable only	68(47.2%)
	Non-absorbable	24(16.8%)
Segment anastomosed	Both	52(36%)
	Enteroenteric	93(64.6%)
	Colocolic	36(25%)
	Enterogastric	14(9.7%)
Intraoperative contamination	Yes	8(6.9%)
	No	136(93.1%)
Intraoperative blood loss	Less than 1L	119(82.6%)
	More than 1L	23(17.4%)
Drain	Placed	78(54.2%)
	Not placed	66(45.8%)
Duration of surgery	Less than 3 hours	137(95.1%)
	More than 3 hours	7(4.9%)

c. Operative characteristics of study participant.

The majority of operations were performed by junior doctors (registrar and residents). Enteroenteric anastomosis was the most common anastomotic segment performed in 56.3% of cases. Intraoperative blood transfusions were administered in 25 (17.4%) patients. In 78 (54.2%) patients, there was placement of drain in the vicinity of the anastomosis, while in the rest of 66(45.8%) patients; no drain was placed. The duration of operations was more than 3 hours in 7(4.9%) patient. Postoperatively, nasogastric decompression was done in 113(89%) patients, while in 14(11%) patients it was not done both absorbable suture and non-absorbable suture were used, and intraoperative diagnosis was similar to preoperative one in 92.3% (see table 4 above)

d. Prevalence and factors associated with anastomotic leakage.

Out of 144 patients who underwent bowel resection and primary anastomosis out of those 32(36.1%) were operated at SRRH and the rest 112(63.9%) were operated at BMC. The prevalence of anastomotic leakage was 5.6% (8/144) out of those with anastomotic leakage

7(87.5%) were from BMC and one (12.5%) was from SRRH. The mean postoperative period for the diagnosis of anastomotic leak was 3.63 ± 1.30 days (range 3 and 6 days). The diagnosis of leakage was made clinically by identifying enterocutaneous fistula in 6(75.0%) patients and in one (12.5%) patients it was made radiologically by contrast study. The diagnosis of anastomotic leakage in the remaining one (12.5%) patient was identified at laparotomy for peritonitis.

e. Preoperative, Intraoperative and Postoperative factors associated with anastomotic leakage.

High ASA class ($p=0.001$), intra operative contamination ($p < 0.001$), premorbid illness ($p=0.003$), low hemoglobin ($p= 0.012$), low ranked operator ($p= 0.046$), and), prolonged duration of surgery ($p= 0.001$) were found to be statistically significantly associated with anastomotic leakage (see table 5 and 6).

Table 5: Preoperative factors associated with anastomotic leakage

Predictive factor	Anastomotic leakage		p value
	Leakage (n, %)	No leakage (n, %)	
Median age	23.5(21-35)	35(23-59)	0.145
Sex	Male	6(75%)	0.365
	Female	2(25%)	
Facility at which attended	BMC	7(87.7%)	0.435
	SRRH	1(12.5%)	
ASA	ASA I	1(12.5%)	0.001
	ASA II and III	6(75%)	
	ASA IV and V	1(12.5%)	
		1(5.7%)	
Hemoglobin	Less than 6	2(25%)	0.012
	6 to 10	6(75%)	
	More than 10	0(0%)	
Social behavior	Non	2(25%)	0.229
	Smoking	2(25%)	
	Alcohol	3(37.5%)	
	Bboth	1(12.5%)	
	Non	5(62.5%)	
	DM	2(25%)	
Premorbid conditions	COPD	1(12.5%)	0.003
	Others	0(0%)	
		11(8.1%)	

Table 6: I intraoperative and postoperative factors associated with anastomotic leakage among study participants

Factor	Anastomotic leakage		P value	
	Leakage	No leakage		
Anastomosed segment	Enteroenteric	7(87.5%)	86(63.2%)	0.550
	Colocolic	1(12.5%)	35(25.7%)	
	Enterogastric	0(0%)	49(36%)	
Intraoperative contamination/ sepsis	Yes	3(37.5%)	127(93.4%)	<0.001
	No	5(62.5%)	9(6.6%)	
Nature of operation	Emergency	6(75%)	114(83.8%)	0.397
	Election	2(25%)	22(16.2%)	
Rank of surgeon	Resident and registrars	8(100%)	91(66.9%)	0.046
	specialist	0(0%)	45(33.1%)	
Suture material	Absorbable only	5(62.5%)	63(46.4%)	0.550
	Non-absorbable	0(0%)	24(17.6%)	
	Both	3(37.5%)	49(36%)	
Technique of anastomosis	interrupted	0(0%)	10(7.3%)	0.554
	continuous	8(100%)	126(92.7%)	
No of layers	single	2(25%)	16(11.8%)	0.271
	double	6(75%)	120(88.2%)	
Drain	yes	5(62.5%)	73(53.7%)	0.456
	no	3(37.5%)	63(46.3%)	
Duration of surgery	Less than 1 hour	0(0%)	20(14.7%)	0.001
	2 to 3 hour	2(25%)	115(84.6%)	
	More than 3 hours	6(75%)	1(0.7%)	
Resume of bowel sound	24 to 48	0(0%)	126(92.7%)	0.001
	48 to 72	0(0%)	10(7.3%)	
	More than 72	100(100%)	0(0%)	
oral sips initiation	Less than 72 hours	4(50%)	136(100%)	0.001
	More than 72 hours	4(50%)	0(0%)	
Complain postoperative	Abdominal pain	0(0%)	136(100%)	0.001
	Abdominal distension	2(25%)	0(0%)	
	Fecal discharge	6(75%)	0(0%)	
Post-operative NGT	Placed	2(25%)	53(39%)	0.349
	Not placed	6(75%)	83(61%)	

f. Management of anastomotic leakage.

Out of the 8 patients who developed anastomotic leakage, 5 (62.5%) were managed operatively and the remaining 3(37.5%) patients had conservative management. Of the patients who were managed operatively, 3(60.0%) had diverting ileostomy after another exploratory laparotomy and washout of peritoneal cavity and repair of the leak, and 2 (40.0%) patients had exploratory laparotomy and management of the leak by re-anastomosis.

4 Discussion.

Anastomotic leakage following bowel resection and primary anastomosis is a major clinical problem and it is associated with increased morbidity and mortality worldwide. In this study, the prevalence of anastomotic leakage was 5.6%, a figure which is higher than 2.7% reported in other studies the prevalence of intraperitoneal anastomotic leak varies in the literature between 0.5% and 30%, but is generally between 2% and 5%. Differences in exposure to several risk factors for anastomotic leakage may be responsible for this regional variation. Anastomotic leakage typically occurs between the 3rd

and the 6th post-operative days [19]. In the present study, the mean postoperative period for the diagnosis of anastomotic leak was 3.6 days which is within the range reported in literature.

In the present study, male gender was not consistently being identified as a risk factor for anastomotic leak. The gender risk has been related predominantly to low rectal procedures and the male's narrow pelvis which makes dissection technically more difficult and more prone to complications. However, this observation does not explain the higher rate of anastomotic leak seen in colonic and small bowel surgery. It has also been postulated that hormonal differences in men influence intestinal microcirculation and may contribute to higher risk of anastomotic leakage in this group. This study showed no clinical anastomotic leaks in the group of patients undergoing rectal procedures. However, the overall number of rectal procedures in the present study was low. As such, specific analysis of pelvic procedures as a risk factor for anastomotic leakage could not be undertaken, the only explanation in this study was predominance of male patient in this study

Some studies have demonstrated that increasing age or age >60 is associated with an increased risk of anastomotic leakage. In our study it shows insignificance difference between increase in age and increase in risk of anastomotic leakage. Smoking, alcohol use or both has been shown to be a risk factor for anastomotic leak in multiple studies on various types of GI anastomoses especially low colonic anastomosis. This study, there were no difference in developing anastomotic leakage between smokers and non-smokers

Although there is conflicting evidence for an increased risk of anastomotic leakage in patients with Co-morbid illness, two studies have suggested an increased anastomotic leakage rate in ileo-colic anastomoses or low anterior resection, whereas another paper has demonstrated no change in anastomotic leakage rate but higher mortality and increased length of stay in those who do sustain a leak. Our study has demonstrated that Co-morbid condition, like Diabetes mellitus, COPD, HIV, PVD and chronic liver disease are associated with higher risk of anastomotic leakage following bowel resection and primary anastomosis.

Majority of operations were performed by junior doctors who may have little experiences in performing bowel anastomosis, our study demonstrated association between the rank of the surgeon and anastomotic leakage rates. This observation is at variant with other studies that reported an association between surgeon's rank and the risk of anastomotic leakage. This finding reflects differences in experiences in performing bowel anastomosis. The present study demonstrated association between single-layer versus double-layer and the risk of anastomotic leakage. Invariably, most authors have concluded that single-layer anastomoses are faster and easier to construct and associated with low rates of anastomotic leakage. In our study single layer interrupted anastomosis was seen as a safe option to those patients who are at high risk of anastomotic leakage than compared to double layer continuous which has high tendency of disruption.

Present study which showed a strong association between intraoperative septic conditions and anastomotic leak. The use of defunctioning loop ileostomy in all patients undergoing bowel surgery in intraoperative septic conditions is beneficial and safe and has resulted in no anastomotic leak rate and considerable low morbidity as it was seen in our study. So according to our study, we strongly recommend defunctioning loop ileostomy as a routine procedure in patients undergoing bowel surgery in septic conditions.

Anaemia has been long associated with increased anastomotic leak rates. In addition, blood transfusion in the perioperative period has a very high association with anastomotic leak. In our study, anaemia with haemoglobin less than 6, intraoperative high blood loss was associated with an increased

anastomotic leak rate. However, intraoperative blood transfusion of more than 2 packed red blood cells was associated with increased risk of anastomotic leak.

In this study, postoperative NGT placement did not influence the risk of anastomotic leakage. Similar observations were also reported by other authors [16]. In the present study, delayed passage of flatus following bowel resection and primary anastomosis was not found to be an independent factor associated with anastomotic leakage. This calls for surgeons to have a high index of suspicion to diagnose an anastomotic leak early as most of patients with anastomotic leakage presents with prolonged ileus, increased postoperative abdominal pain, fever, tachycardia and leucocytosis. In our series, approximately two third of patients with anastomotic leakage were managed surgically with defunctioning stoma and re-anastomosis this was in keeping with other studies that recommend same method of management though with advent in technology stenting and percutaneous drainage of accumulation at the anastomotic site are other option.

5 Conclusions and Recommendations.

a. Conclusions.

Anastomotic leakage in Mwanza city occurred in approximately 5.6% of patients undergoing surgical interventions at BMC and SRRH. High ASA, intraoperative contamination/sepsis, anemia, low rank of the operator, prolonged duration of surgery and prolonged ileus were factors found to be associated with high rates of anastomotic leakage. Pre-morbid condition such as uncontrolled Diabetes Mellitus, intraoperative contamination/sepsis, low ranked operator, prolonged duration of operation above 3 hours and prolonged ileus were among factors that the present study found to be associated with high risk of anastomotic leakage Majority of patient with anastomotic leakage were managed by ileostomy, re anastomosis or colostomy

b. Recommendations.

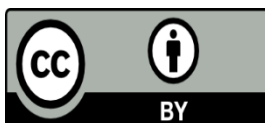
High index of suspicion is required for early diagnosis of anastomotic leakage before it manifest. Understanding of risk factors for anastomotic leakage and proper decision making is important on when to do or not do the anastomosis to avoid potential subsequent leakage. Further studies are recommended to elucidate more on anastomotic leakage basing on long term prospective studies.

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