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Low Incidence of Anastomotic Insufficiency in Rectal Cancer Resections in Sri Lanka

Degree Project in Medicine

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Abstract

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Background: Colorectal cancer is increasing in Sri Lanka, along with an increasing life expectancy. One of the most severe complications of colorectal surgery is anastomotic insufficiency. It is most common following rectal resections.

Aim: To investigate the incidence and presentation of anastomotic insufficiency in rectal cancer resections and to look at different risk factors on the influence of this complication.

Method: A retrospective medical record review including 66 patients who have undergone rectal cancer resections at Colombo South Teaching Hospital, Sri Lanka, during the time period of 1st of January 2012 – 30th of October 2017.

Results: Of the 66 patients there were 37 women and 29 men and the mean age was 61 years. Three of the 66 patients suffered an anastomotic insufficiency. All three were male, two of them had received neoadjuvant chemotherapy. Adverse events occurred during surgery for two of them. The postoperative length of hospital stay was 5, 19 and 60 days respectively. All three patients were reoperated.

Conclusions: It was found that the patient group who undergo rectal cancer resections in Sri Lanka are younger compared to patients in other countries and the incidence of anastomotic insufficiency appears to be low. However, because of the small sample size and low incidence of anastomotic insufficiency, the results need to be verified in a more extensive study.

Key words: Rectal cancer, Anastomosis, Anastomotic leakage, Risk factors

Introduction

Sri Lanka, in South Asia, a rapidly developing country that has made great achievements in the health sector. The maternal mortality ratio and child mortality rate (under 5 years of age) continues to decline. In 2012 the life expectancy at birth was 75 years, an increase of 5 years during the period 2000-2012 (1). It is calculated that by 2026s almost 20 % of the population will be 60 years or older (2). New challenges occur with an ageing population. Noncommunicable diseases (NCDs), such as cardiovascular diseases, cancers, diabetes, and chronic respiratory diseases are increasing and account for almost 70 % of deaths in the country. NCDs are also the largest contributor to burden of disease, accounting for 85 % of disease adjusted life years (DALY) (2).

One of the most common malignancies is colorectal cancer. 2012 colorectal cancer was the third most common cancer worldwide comprising 9.7 % of all cancer cases diagnosed, just after lung cancer (13.0 %) and breast cancer (11.9 %). In Sri Lanka it accounts for 4.0 % of all cancers. (3) A study made in Sri Lanka investigated change in incidence of colorectal cancer between the periods 1992-1997 and 1996-2004. The result showed an increase from 1.9 per 100 000 to 3.2 per 100 000 in women and 4.9 in men: from these figures one can conclude that colorectal cancer in Sri Lanka is on the rise (4).

Colorectal cancer is the collective name for cancers located somewhere in the large intestine or rectum. The reason why it develops is not fully known, but risk factors are a diet rich in protein and fat, if combined with low fibre intake the risk is increased. Inflammatory bowel disease, radiation towards the pelvic area, colorectal polyps, previous colon cancer, family history of colorectal cancer and adenomatous polyps are other risk factors. The median age at diagnosis, in western societies, is 74 years and it is rare before the age of 40, making age the greatest risk factor (5).

The only way to obtain permanent cure is to surgically remove the tumour with radical surgery. A section of the intestine is excised along with supplying blood vessels and lymph nodes. The remaining ends are then sutured together as an anastomosis, making it possible for the content of the intestine to pass through. Anterior resection (AR) is the procedure where part of rectum, sigmoid colon and descending colon is removed. High AR involves the rectosigmoid junction, low AR involves lesions in mid to upper rectum and ultralow AR is for low rectal lesions. Hartmann's procedure is performed in cases where it is not advisable to make an anastomosis at the same time as the resection is done. Instead, after the lesion is resected, the proximal segment is exteriorised and a stoma is created and the distal segment is closed. This procedure can be reversed on a later occasion and an anastomosis can be created.

One of the most severe complications after colorectal surgery is anastomotic insufficiency (5), which can lead to leakage of gas, pus and faecal discharge. It is associated with prolonged hospital stay, high reoperation rate and high mortality, affecting both long term and short term survival (6). Anastomotic insufficiency is more common when the anastomosis involves rectum (7-12).

There are largely two main mechanisms for anastomotic insufficiency. Technical errors in constructing the anastomosis could lead to leakage, mainly occurring during one of the first days after surgery. The other chief factor behind insufficiency is necrosis of the anastomosis due to impaired blood supply and/or sepsis. This complication is more common in rectal surgery (11, 12) and often presents 5-7 days postoperative.

Anastomotic leakage is clinically found by fever, peritonitis or sepsis, even though the symptoms may be difficult to interpret. Raised CRP could verify the suspicion of anastomotic leakage (13, 14) and it is always advisable to perform a computer tomography (CT) to look for increased free air or concerning the rectum a gastrographine enema (15). Also, there

should be a high preparation to perform a relaparotomy/laparoscopy to confirm or exclude a leakage.

There are several risk factors causing necrosis of the anastomosis, both associated with patient factors and type of procedure (*Table 1*). However, there are conflicting views on the importance of life style related risk factors (16-18). Also, little is known about the influence on these risk factors in Sri Lankan colorectal cancer patients.

Table 1. Proposed Risk Factors, Predicting Anastomotic Leakage

Patient factors
Male gender (19)
Age (20)
Co-morbidity (such as diabetes, diverticulitis) (12, 21-25)
Obesity (26-28)
Smoking (29)
Drugs (30-35)
Preoperative radiation therapy (19, 36, 37)
Advanced tumor stage (6, 37)
Perioperative/technical factors
Low anterior resection (6, 19, 22, 23, 36-39)
Emergency Surgery (20, 25)
Prolonged operation time (22, 34)
“After-hour surgery” (26)
Adverse intraoperative events (for example malfunctioning devices, bleeding, injuries and contamination) (6, 34, 36, 37, 39, 40)

References are given in parentheses.

Aim

Aim of this study

To investigate the incidence and presentation of anastomotic insufficiency in rectal cancer resections and to look at different risk factors on the influence of this complication.

General objective

- To assess the incidence and presentation of anastomotic insufficiency in rectal cancer resections

Specific objectives

- To evaluate associated risk factors such as smoking, nutritional status, perioperative hypotension and blood loss, adverse events during surgery and neoadjuvant radio/chemo therapy
- To assess treatment modalities for anastomotic insufficiency

Material and Method

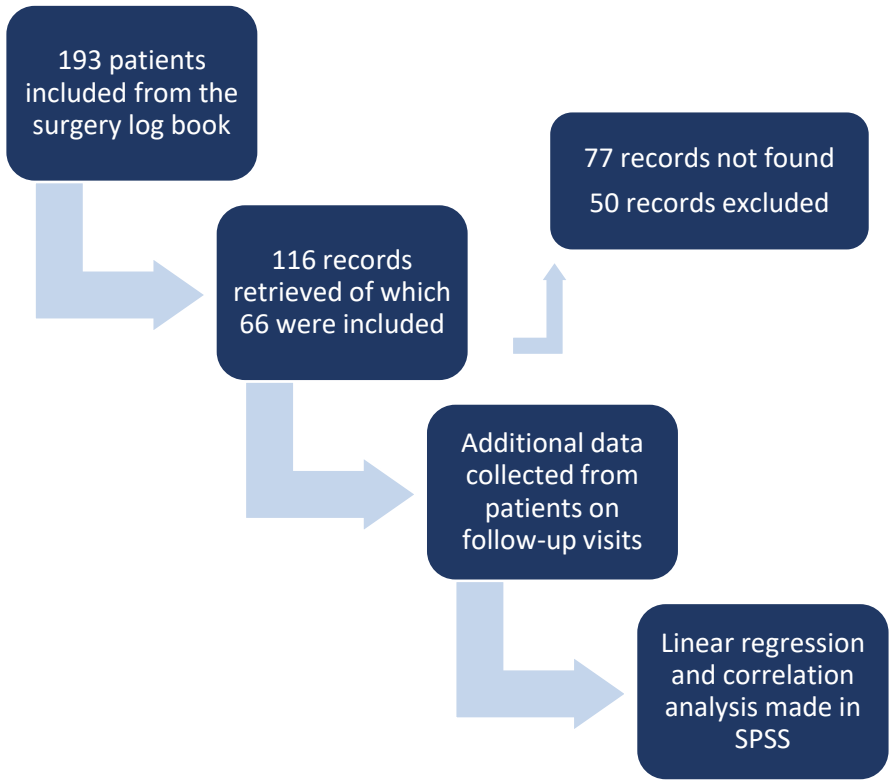

Figure 1. Patient selection flow chart.

Study design

This study is a retrospective medical record review. Data was collected from the medical records and registered in excel, using a separate document for coding the patients. The data was then exported to SPSS for statistical analyses. A few patients who came for follow-ups during the time the study was conducted were interviewed to get additional information.

Study population

Patients who had undergone rectal cancer resections with the construction of anastomosis at Colombo South Teaching Hospital (CSTH) in Colombo, Sri Lanka between the 1st of January 2012 and the 30th of October 2017 were included in the study.

Enrolling patients

At CSTH all patients who undergo surgery are registered in a log book in the operation theatre. In this book the bed head ticket (BHT), name of patient, type of surgery, date of surgery and ward is registered. By using the log book patients who had undergone colorectal surgery was found and a list of 193 patients was compiled. This list was then taken to the wards and using the BHT's and names, we could find admission date and contact information through the admission book.

After approval of the hospital director the list was given to the medical record room in order to obtain the medical records for those patients. Since they don't have computerized records in Sri Lanka the storage space limits the length of time they can keep the records available. Unfortunately there were no records from 2012 available and only 5 of the 22 from 2013 were found. Out of the 193 patients in the original list 77 were not found and another 50 were excluded. Patients were excluded if the surgical procedure did not involve an anastomosis or

the anastomosis did not involve the rectum or the reason for surgery was other than colorectal cancer. A total of 66 patients were included in the study.

Data about smoking were often missing. Only 11 of 66 records had a note about smoking and these were all men. Smoking in women is only at 0.1% in Sri Lanka (41) and therefor the women in the study were assumed to be non-smokers. Calls were made to the male patients in those cases there was a contact number available, for follow-up questions about smoking. Of the 10 patients where a contact number could be acquired, only 4 could be reached. Another 2 patients had died since discharge and a relative answered the follow-up questions in their place.

The population of Sri Lanka do not have identification numbers. Once they have been discharged from the hospital their medical records are archived and filed under their temporary BHT-number. For the follow-up visits patients bring their own notebook for the doctor to make notes and it is then kept in the patient's home between visits. Only for a few patients there is contact information available. Therefore there is no way to know what happens to the patients after discharge.

Statistical Methods

SPSS was used to make descriptive analyses of frequencies, correlation analyses and linear regression analyses.

Ethics

The study aligned to the principles of the Helsinki Declaration. The project was approved by the Ethics Review Committee, Faculty of Medical Sciences at University of Sri

Jajewardenepura, Sri Lanka. For the patients anonymity they were given a coded number and the coding key was kept in a separate document.

Results

66 patients were included in the study. The information in the medical records was often not complete, therefore data is missing for some variables.

Characteristics of the patients

Of the 66 patients included in the study 37 were women and 29 were men. The mean age was 61 years for both groups, with a span from 23 to 84 for men and 33 to 78 for women (*figure* 2). A majority (82 %) were in the ages 45-75 years old.

Data about smoking was accessible in 52 out of 66 patients (after assuming that all women were never smokers as described above). 67 % were never smokers, 6 were ex-smokers and 2 were current smokers.

Comorbidity was registered as the sum of diseases given under medical history. The occurring diseases and frequencies are listed in table 2. 38 % of the patients had no comorbidity, while 53 % had one or two comorbidities. 5 patients had three comorbidities and 1 had four (figure 3).

Physical status was classified according to the American Society of Anesthesiologists physical status classification system (ASA class) (table 3). ASA class was registered according to records if specified, if not it was assessed using the available information in the records. 28 patients were ASA 1, 37 were ASA 2 and one was ASA 3.

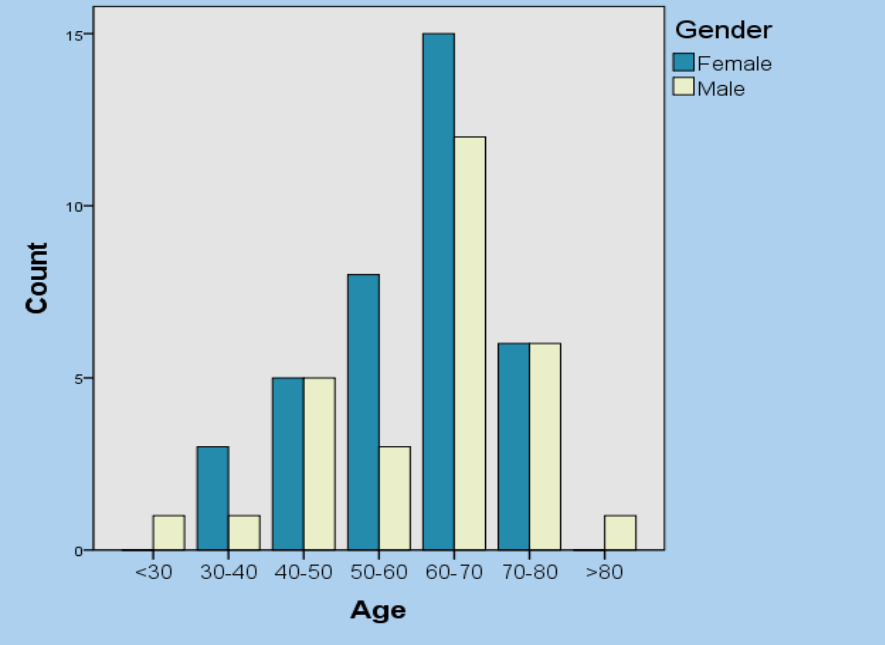

Figure 2. Age distribution separated into gender.

Table 2. The patient's comorbidities and how often they occur.

Comorbidity	Number (n=x)
Hypertension	22
Diabetes mellitus	19
Bronchial asthma	13
Dyslipidemia	7
Ischemic heart disease	3
Liver cirrosis	1
Hypothyroid	1
Chronic obstructive pulmonary disease	1
Fibrosing alveolitis	1
Reumatoid arthritis	1
Chronic kidney disease	1

Table 3. Classification of physical status according to the ASA classification*

ASA Physical Status Classification	
ASA 1	A normal healthy patient
ASA 2	A patient with mild systemic disease
ASA 3	A patient with severe systemic disease
ASA 4	A patient with severe systemic disease that is a constant threat to life
ASA 5	A moribund patinet who is not expected to survive without the operation
ASA 6	A declared brain-dead patient whose organs are being removed for donor purposes

*ASA = The American Society of Anesthesiologists

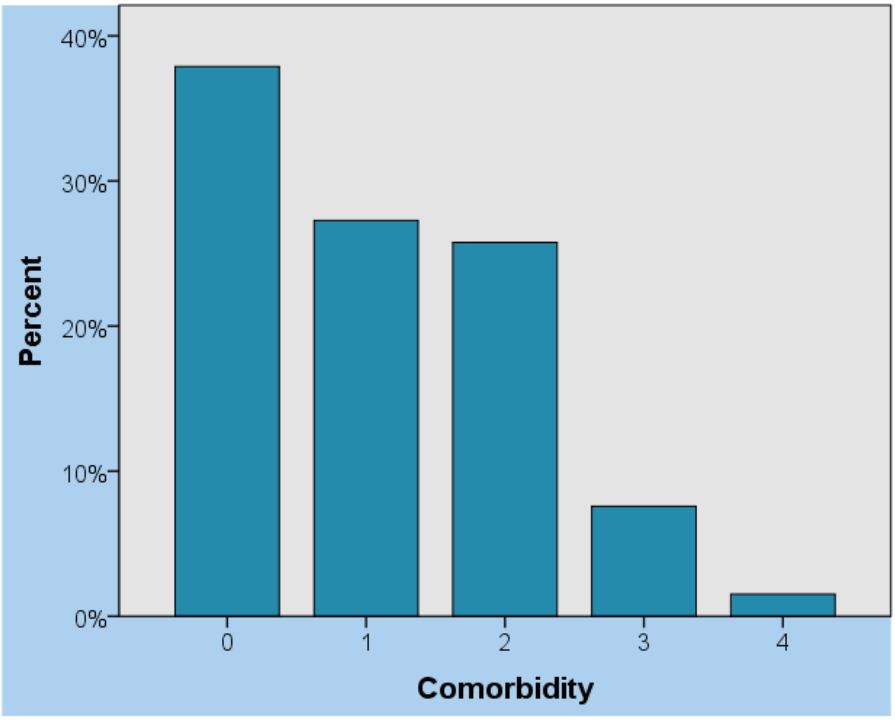

Figure 3. Proportion of patients by number of comorbidities.

Characteristics of surgery

This study includes eight different types of surgical procedures. High AR and Low AR was most common (42 % and 32 % respectively), followed by Reversal of Hartmann's procedure (8 %), Sigmoid Colectomy (8 %) and Ultra Low AR (6 %).

32 of the procedures were performed by laparoscopic technique, but had to be converted to open surgery in 5 cases and 34 were done by open surgery. The procedures were mainly performed by two different surgeons (47 % and 26 % respectively), 26 % were performed by others and data was missing for one patient. Defunctioning ileostomy (DI) was performed for 13 out of 65 patients and data was missing for one patient.

Adverse events were reported in 5 cases and included stapler malfunction, bleeding (n=2), purulent spilling and extensive adhesions. Three of those were initiated laparoscopically and were converted to open, the other two were performed as open surgery from the start.

Outcome

The incidence of AI was 4.5 % (3 out of 66 patients). Logistic regression analysis was attempted to estimate correlation between AI and different risk factors, but the sample size and low incidence of AI made the analysis unreliable. Instead the AI cases will be described as they were, see also table 4.

Table 4. Characteristics of the patients with anastomotic insufficiency.

	Case 1	Case 2	Case 3
Age	61	61	37
Gender	Male	Male	Male
Number of Comorbidities	1	2	0
Intraoperative blood loss (ml)	550	350	-
Serum albumin (g/l)	41	21	-
Neoadjuvant treatment	Chemo	None	Chemo
Procedure	Low AR**	High AR	Low AR
Defunctioning ileostomy	Yes	No	-
Adverse events	Yes	Yes	-
Diagnostic procedure for AI*	Endoscopy	Clinically	Radiology
Days after surgery	8	0	2
Length of hospital stay	19	5	60
Reoperation	Yes	Yes	Yes

**AI = Anastomotic insufficiency. ** AR= Anterior resection.*

All 3 AI patients were men, one of them was a never smoker, one ex-smoker since 25 years and for one data was missing. Adverse events occurred during surgery for two of the AI patients, data is missing for the third patient. The incidence of adverse events for patients without AI was 5 %.

Neoadjuvant treatment was registered in four categories: radiotherapy, chemotherapy, radiochemotherapy and no neoadjuvant treatment. Two of the AI patients had received chemotherapy and one patient had not received any neoadjuvant treatment.

Two of the AI patients had open surgery and one was converted from laparoscopic to open. One had High AR and two had Low AR.

Diagnostic procedure was radiology for one and endoscopy for one, data missing for one. Time from surgery until diagnosed insufficiency was 0, 2 and 8 days respectively. All three were reoperated.

Length of hospital stay (LoHS) was registered as days from surgery until discharge (figure 4). The mean LoHS was 7 days for the entire population, with a variation from 3 to 60 days. The majority (91 %) stayed at the hospital for 9 days or less. There was a big variation in LoHS for patients with AI: 5, 19 and 60 days.

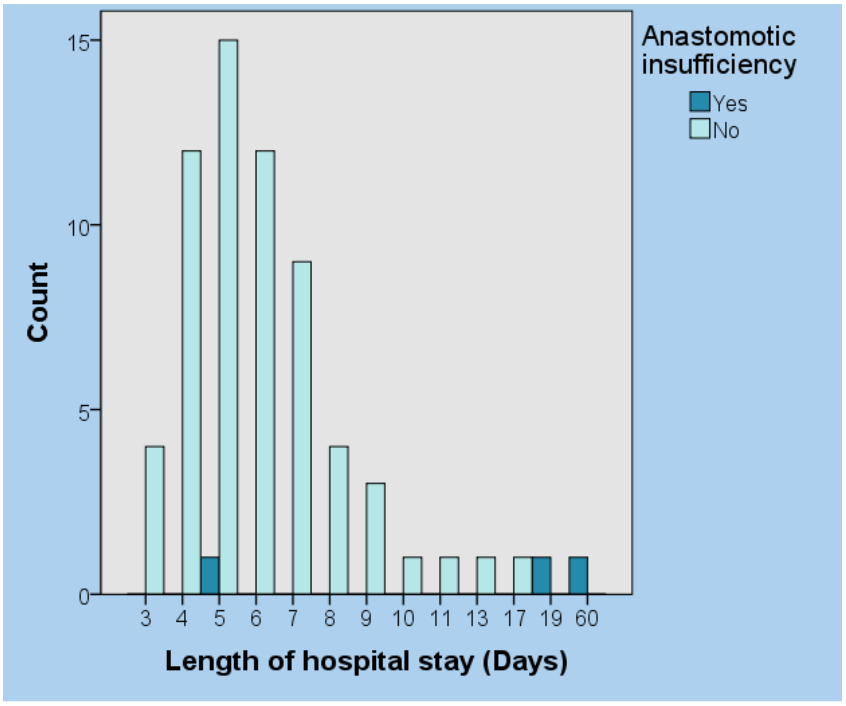

Figure 4. Postoperative length of hospital stay for patients with or without anastomotic insufficiency.

A test for correlation between LoHS and different risk factors was made and showed significant correlation between LoHS and AI ($c=0.64$ and $p<0.001$) as well as LoHS and Neoadjuvant treatment ($c=0.38$ and $p=0.002$). It also showed a not significant correlation with albumin, gender and open/laparoscopic surgery. Because AI seem to have a high impact on LoHS, the correlation test was repeated without the patients with AI. The result showed a significant correlation between LoHS and albumin ($c= -0.42$ and $p=0.005$), perioperative

systolic hypotension (c=340 and p=0.013) and open/laparoscopic surgery (c=0.28 and p=0.024). No correlation with gender was found.

Case report 1

A 61 year old man with hypertension who had received neoadjuvant chemotherapy. He underwent a Low AR which was converted from laparoscopic to open surgery. A defunctioning ileostomy was done. Adverse event during surgery was extensive adhesions and this was the reason the surgery was converted. On day 2 the patient presented with fever and pain. On day 3 a surgical site infection (SSI) was diagnosed and additional antibiotics was given. On day 7 he was diagnosed with wound sepsis and a wound washing was done.

On day 8 a sigmoidoscopy was performed and an unhealthy anastomotic site was found. There was also bleeding in the anastomotic site and a blood clot was lodged in the rectal part of the anastomosis. As a consequence of the findings an emergency laparotomy was executed, revealing an arterial bleeding in the sacrum and anastomotic breakdown with faecal contamination of pelvis. The artery was ligated and a washout of the pelvic cavity was performed. Wound debriment was done and a drain was put in. After surgery the patient was clinically improving and the wound looked better. On day 14 discharge continued from the wound, which was then kept open after removal of two sutures. On day 16 the rest of the sutures were removed, the wound cared for and culture and sensitivity testing done. After these steps the patient again improved clinically and could be discharged on day 19 with a healthy looking wound and a functioning ileostomy.

Case report 2

A 61 year old man, sober alcoholic since 8 months. Stopped smoking 25 years ago. Had diabetes and liver cirrhosis, with a very low albumin level of 21 g/l (reference value 36-45 g/l). No neoadjuvant treatment was given. The surgery performed was an open High AR with

no defunctioning ileostomy. During surgery an adverse event occurred, malfunction of the stapler.

5 hours after surgery stool was coming out of the abdominal drain. Vitals were normal and no other complaints were reported. An exploratory laparotomy was performed where anastomotic dehiscence and faecal contamination of the pelvis was found. The pelvis was thoroughly washed and a Hartmann's procedure performed which means that the anastomosis is removed, the distal stump is closed and the proximal segment is exteriorised. A drain was inserted into the pelvis. Human albumin was given.

No further complications occurred and the patient was discharged on day 5.

Case report 3

This patient was enrolled at a follow-up, but his medical record was not found, therefor all data is information coming directly from the patient and a lot of data is missing.

A 37 year old man with no comorbidity who has never been a smoker. Had received neoadjuvant chemotherapy prior to surgery. Open Low AR was performed with no information about defunctioning ileostomy. No data about adverse events. AI was diagnosed 2 days after surgery using CT. The clinical presentation was fever. The AI was treated with reoperation and Hartmann's procedure was performed. The patient was kept in the intensive care unit for 14 days and after that another 45 days was spent at the ward. The patient was finally discharged 60 days after surgery. 2.5 years after surgery the patient still had a colostomy.

Discussion

Key findings

The study included 66 patients who had rectal surgery at Colombo South Teaching Hospital between the 1st of January 2013 and the 30th of October 2017. Three of these patients were diagnosed with anastomotic insufficiency after surgery. No mortalities occurred during the hospital stay, but since there is no registration of what happens after discharge nothing can be said about the long term survival rate. Data about smoking was scarce, even after contacting patients it only covered 55 % of the men. What we found was that 12.5 % of the men were current smokers, compared to 27.5 % in the population in general (41). The mean age of the patients in the study was 61 years (95 % CI: 57.8-63.9) giving a significantly younger population than presented in previous studies which show a mean age of 65-71 years (6, 9, 10, 14, 42).

The incidence of anastomotic insufficiency in this study was 4.5 %. Other studies have shown an incidence of 4.8-13 % for rectal resections (7-10). This might indicate that the incidence of AI in Sri Lanka is not higher than in western societies, on the contrary it might even be lower than in other countries. The sample size was too small to make further statistical analysis and no definitive conclusions can be drawn from it, but it gives cause for further investigation including more hospitals in the area, to confirm or deny these results. It is also interesting to see the combination of low AI incidence and a young population. It raises the question if there is a connection between these factors and it would be interesting to include them in future studies.

The patients with AI were diagnosed 0, 2 and 8 days after surgery. The two early diagnosis are consistent with leak due to problems in constructing the anastomosis. The later one suggests a leak due to necrosis, because of the late diagnosis, but as the patient presented with

symptoms on day two and was diagnosed with SSI on day three, it is likely that the AI was present already at this time. This indicates that all of the AIs were caused by construction problems and no one by necrosis. One explanation to the lack of necrosis caused AIs might lie in length of hospital stay (LoHS). As mentioned earlier the LoHS varied between 3 and 60 days. 31 of the patients were discharged after three to five days. As the necrosis usually presents after 5-7 days, it is possible that some patients were discharged before displaying symptoms. If the patient seek care at another hospital, this information would not be in the medical records.

Radiology was only used for diagnostics in one of the cases. All three AI patients were men which indicates that this might be an important risk factor, as in previous studies (43). No connection between smoking and AI could be identified. One of the objectives for this study was to assess treatment modalities. Though it's a small material to make an assessment, we can point out that all three patients were reoperated, compared to 35-50 % in other studies (9, 12). From this study there is no way to determine why we get this result, but it would be of interest to study what the indications for surgery are. If all the reoperations are justified it would imply that the AIs are more severe, even if they occur less often.

The mean LoHS was 7 days (95% CI: 5.26-8.80). This is significantly lower than in some other studies which have shown a mean of 11.6 and 12 days (8, 10). The reason for this difference we can only speculate about. Motivating factors could be the younger population, giving less comorbidities and better nutritional status. It would be of interest to further investigate this subject. A study with this focus could also include a wider range of procedures, not limiting it to only rectal resections and maybe even other causes like diverticulitis.

Study Limitations

The system for medical records keeping create a problem for this type of study as the records can only be kept for a period of time. The fact that the investigated type of surgery is only performed in a limited amount each year in combination with the low incidence of AI gives a problem of collecting enough data to make reliable statistical analyses. Another problem is that all the requested data is not registered in the records. Contact information is only available for a small part of the patients and it is difficult to get in touch with them after discharge. As the hospital don't hold records for the patients after they are discharged it is difficult to collect data about long term survival rate and complications occurring later.

The study included 37 women and 29 men (56 % women and 44 % men). This is in conflict with the expected distribution according to the study performed by Perera et al. which shows a higher incidence for men than for women. The expected distribution would be about 40 % women and 60 % men. This raises the question if the investigated population is representative for the intended group.

Conclusion

We found that the patient group who underwent rectal cancer resections at Colombo South Teaching Hospital in Sri Lanka were younger compared to patients in other countries and the incidence of AI appears to be low. The patients spent a shorter time at the hospital after surgery.

The results from this study are not conclusive and further investigation is needed to confirm or deny the results.

Further research

The fact that the majority of the AI patients experienced adverse events during surgery awakens new questions as to why this is, if there is a lower incidence of AI caused by necrosis and why this is. Other results that would be of interest to investigate further is the young patient group and the high reoperation rate.

Populärvetenskaplig sammanfattning:

Låg förekomst av läckage efter ändtarmscanceroperation på Sri Lanka

Tjocktarms- och ändtarmscancer är en av de vanligaste cancerformerna i världen. Orsaken till varför den utvecklas är fortfarande oklart, men ålder är den största riskfaktorn. Sri Lanka är ett land med en snabbt växande ekonomi och med en befolkning som blir allt äldre har man sett en ökning i antalet fall av tjocktarms- och ändtarmscancer.

För att bota denna cancerform krävs kirurgi som tar bort tumören i sin helhet. Kirurgin kan kombineras med annan typ av behandling, som strålning och cellgifter. Vid operation tas det segment av tarmen som är drabbat bort och, om möjligt, sys ändarna ihop med varandra och man kan få en fungerande tarm igen. Sammanfogningen av tarmändarna kallas anastomos.

En av de farligaste komplikationerna efter denna typ av kirurgi är att det blir ett läckage i anastomosen. Det kan då läcka ut avföring eller gaser i bukhålan och orsaka infektioner. I värsta fall kan det leda till att patienten avlider. Läckage är vanligare när man opererar ändtarmen.

Syftet med denna studie var att undersöka hur vanligt det är med läckage efter ändtarmsoperation på Sri Lanka och om man kan se samband mellan olika riskfaktorer som ålder, kön, rökning m.m. Studien omfattade 66 patienter som opererats för ändtarmscancer mellan 1 januari 2012 och 30 oktober 2017 på ett sjukhus i södra Colombo.

Det man fann var att tre patienter drabbats av läckage (4,5 %), vilket är en lägre andel än vad man sett i studier i andra länder där andelen legat på 4,8 - 13 %. Man såg även att medelåldern på de som opererades var lägre, vilket skulle kunna vara kopplat till att färre drabbas av läckage.

Alla drabbade var män, vilket talar för att manligt kön är en riskfaktor. Man kunde även se att tekniskt fel inträffade under totalt fem operationer varav två av dessa patienter senare fick läckage och man kan därför tänka sig att detta är ytterligare en riskfaktor. Vad gäller övriga faktorer som undersöktes kunde inga samband ses. Detta kan dels bero på att vissa uppgifter saknades i journalerna och därför inte kunde analyseras, dels kan det bero på att studien är så pass liten att svagare samband inte syns.

Eftersom det är en liten studie är resultaten inte helt tillförlitliga och större studier krävs för att kunna dra några definitiva slutsatser.

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