

# Review of Risk Factors Associated with the Anastomosis Leakage in Anterior Resection in Hospital Universiti Kebangsaan Malaysia

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## Summary

This is a retrospective study evaluating the risk factors for clinical anastomotic leakage after anterior resection in 64 patients with rectal cancer operated from November 2001 till August 2003. The percentage of anastomosis leakage was higher in those patients with diabetic, low albumin level, neoadjuvant radiotherapy, higher staging, and poorly differentiated tumour. However, these differences were statistically not significant. There was a significant difference ( $p=0.03$ ) of anastomosis leakage in those patients with very distal tumour of < 4cm from anal verge (42%), when compare to those patients with proximal tumor of > 15cm from anal verge (4.3%). The mortality associated with this complication was 30%. Hence, a surgeon may consider a covering stoma or be more vigilant in operating patients with multiple risk factors.

**Key Words:** Anastomosis leak, Risk factors, Anterior resection, Colorectal carcinoma, Malaysia

## Introduction

Colorectal cancer is the third commonest cause of death in Malaysia. National census has recorded the rectal cancer constitutes about 50% of overall colorectal death. Rectal cancer accounts for more than 150,000 death annually worldwide<sup>1</sup>. However, there are no local published data available for the incidence and risk factors related to the anastomotic leakage after anterior resection in Malaysian population.

There are significant morbidities associated with the anastomotic leak following the colorectal resection. This anastomotic leakage has a recorded mortality rate of 6 to 22%. The leak can be detected clinically that may present as peritoneal abscess, peritonitis, sepsis, fistulae or even as death.

Patients with anastomosis leak may be subjected to relaparotomy and will have a longer recovery period. Prolong stay in hospital not only increases the cost but also the mental and physical suffering of patient. Therefore, patients with low anterior resections will need temporary stomas in the form of colostomy or ileostomy. However, there are some groups of practicing colorectal surgeons who are against any form of protective stoma. This is because stoma itself has various form of complications<sup>2</sup>.

The aim of this review is to evaluate the various risk factors associated with the anastomotic leakage after anterior resection for rectal cancer. The factors reviewed were patient's age, gender, co-morbidity, neoadjuvant radiotherapy, Duke staging, histological type, tumor distance from anal verge, operative findings and mortality associated with anastomotic leakage.

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## Materials and Methods

A retrospective review of 64 patients with rectal carcinoma operated from November 2001 until August 2003 in Hospital Universiti Kebangsaan Malaysia. Ten patients who had demonstrated anastomotic leakage were further analyzed using Chi-square test for any statistical significant difference between the leakage group and the non-leakage group of patients in term of various risk factors.

All patients were operated by two colorectal surgeons. Some of the patients underwent either short course (1 week) or long course (6 weeks) of neoadjuvant radiotherapy. Oral Fleet or Fortran was used in bowel preparation. Prophylactic antibiotic used was third generation cephalosporin and metronidazole. The distance of rectal tumor from the anal verge was recorded from the colonoscopy or the examination during surgery. Those tumors with a distance of 8cm or less were considered for low anterior resection. Anastomotic technique used was either hand sewn or double stapling. Those patients with clinical evidence of peritonitis or pelvic collection in immediate post-operative period were taken as anastomotic leak. The statistical test used was Chi-square test and  $p < 0.05$  was taken as significant.

## Results

### *Demographic data as risk factors:*

The percentage difference of anastomosis leak among patients with age below 60 year-old was lower 13% (4/30) versus those above 60 year-old 18% (6/34), but was not significant ( $p=0.738$ ). The percentage difference of leak between male 16.7% (5/30) versus female 14%(5/34) was not significant ( $p=0.549$ ).

### *Co-morbidities and nutritional status as risk factors:*

There were no significant differences in percentage of leak when compare between the ASA (American Society of Anesthesiology) 1 patients 11% (3/27) versus ASA 2, 19% (6/32) ( $p=0.487$ ), and ASA 1, 11% (3/7) versus ASA 3, 20% (1/5) ( $p=0.512$ ). The percentage of leak with diabetic 25% (3/9) was higher than non-diabetic 13% (7/52), but it was not significant ( $p=0.321$ ). The higher percentage of leak found in patients with low pre-operative albumin level (less than 34g/dl) was 17% (6/35), versus those with normal albumin level 13.8% (4/29) was not significant ( $p=0.494$ ).

### *Neoadjuvant radiotherapy as a risk factor:*

The percentage of leak was higher in those who had neoadjuvant therapy 22% (6/27) versus those without 11% (4/37), but the difference was not significant ( $p=0.18$ ).

### *Stage and histological type of tumor as risk factors:*

Patient with Duke A did not have any leak. The percentage of leak in Duke B 13% (5/38) versus Duke C, 21% (5/24) was not significant ( $p=0.646$ ). The percentage of leak in various type of tumor base on histology was shown in Table I.

### *Distance of tumor from anal verge as risk factor:*

There was significant difference ( $p=0.03$ ) of leak with those very distal tumor of less than 4 cm from anal verge 42% (3/7) when compare to those very proximal tumor of more than 15 cm from anal verge 4.3% (1/23). It was shown in Table II. Technically it was easier and able to achieve a more perfect anastomosis with lesser tension if anastomosis was performed very proximally, rather than performed it deep in the pelvis.

### *Type of surgery and Intra-operative finding as risk factors:*

The leak percentage was lower in anterior resection 10% (4/39) versus low anterior resection 24% (6/25), but it was not significant ( $p=0.260$ ). The hand-sewn group had a higher percentage of leak 33% (1/3) versus stapling 14.7% (9/61) but the difference was not significant ( $p=0.386$ ). The percentage of leak with stoma 23% (6/26) versus non-stoma 11% (4/38) was not significant ( $p=0.156$ ). Twenty-three patients had covering ileostomy and 3 had colostomy, but 6 patients still had leak form the ileostomy group. There was no significant difference in the leak group with blood loss of more than 1 Litre, 20% (3/15) versus less than 1 Litre, 14% (7/49) ( $p=0.616$ ). The duration of surgery did not appear to have any correlation with the anastomosis leakage as shown in Table III.

Ten patients or overall of 6.25% had anastomotic leak in this study. They had combination of complications like abscess, peritonitis, sepsis and fistulae. Four patients required relaparotomy while others were treated with conservative or radiological aspirate and drainage. The mortality of anastomotic leak was 30% (3/10).

**Table I: Histological type of tumour**

	Well differentiated adenocarcinoma	Moderately differentiated adenocarcinoma	Poorly differentiated adenocarcinoma	Mucinous type
No leak	33	13	6	2
Leak	4 (10.8%)	1 (7.1%)	3 (33%)	2 (50%)

**Table II: Distance of tumour from anal verge**

Distance from anal verge	<4cm	4-7.9cm	8-14.9cm	15-20cm
No leak	4	9	19	22
Leak	3 (42%)	4 (30.7%)	3 (15.7%)	1 (4.3%)

**Table III: Intra-operative duration of surgery**

Duration (hr)	2-4	4-5	5-6	6-7
Leak (n)	1	5	2	2

## Discussion

There is currently no universally accepted definition of anastomotic leak<sup>3</sup>. Its presentation can be at times remains in subclinical or overt with sign and symptoms such as intra-peritoneal abscess formation, fistulae or sepsis. In this hospital we did not routinely performed radiological contrast study to confirmed leak. This is to avoid contrast-related complications.

There have been studies designed to identify factors that contribute to the occurrence of rectal anastomotic leak<sup>4,5</sup>. By understanding these, surgeons may be able to reduce the rate of anastomosis leak. The complications of leak and sepsis may adversely affect on survival and contributes to increase in local recurrence of carcinoma<sup>6</sup>. The anastomotic leak rate in published literatures was reported ranging from 3% to 13%<sup>7-21</sup>. This corresponds well with our leak rate of 15.6%.

In the past, anastomotic leakage was believed related to a surgeon's skill<sup>22</sup>. However, even in a technically successful surgery of an experience surgeon did not reveal a consistent result. This study showed that surgical related factors such as stapling or hand sewn, stoma or non-stoma, intra-operative blood loss and duration of surgery, did not show any significant differences between the leak and non-leak group of patients.

Male patients had a higher rate of leak. This may be contributed to the narrow pelvis in males. Hence, technically it is more difficult to perform a deep-sited anastomosis in them<sup>23</sup>. Male patients in our study had a higher leak rate when compare to female, but the difference was small and statistically not significant.

Diabetic patients and higher ASA classified patients had a higher leak rate<sup>24</sup>. This may be due to poorer tissue perfusion and increase infection risk at the anastomotic site in diabetic or cardiac failure, poorly controlled hypertension or renal impaired patients. The leak rate in our study was higher in diabetic and higher ASA patients. However, it was not statistically significant.

Poor nutritional status of patient can contribute to poor anastomotic site healing<sup>24</sup>. We looked into the pre-operative albumin level. A higher leak rate was noted among patient with lower albumin level of less than 34g/dl. However, this finding was not statistically significant.

Bowel preparation was used in all our patients but we did not have any comparative controlled group to conclude if it has any prophylactic role. However, some surgeons believe bowel preparation has no role in anastomosis leak and do not bowel prepared their patients before operation<sup>24</sup>. Prophylactic antibiotic was routinely given in all our patients. Previous study indicated that single prophylactic antibiotic is sufficient<sup>25</sup>.

Patients who received either a short or long course of neoadjuvant radiotherapy may have more tissue fibrosis and less tissue perfusion or vascularity at the pelvic region as compared to those without neoadjuvant radiotherapy. The leak rate was higher in those who underwent neoadjuvant radiotherapy, but the difference was statistically not significant.

There are no published papers assessing Duke's staging or tumour type as risk factors for anastomotic leak. Patient with Duke C or those poorly differentiated type of tumours would have tumour infiltrated to surrounding structures. Usually this can make the anastomotic reconstruction become technically more difficult to perform. However, our study did not show any significant differences between different Duke staging and tumour types.

The distance of tumour from the anal verge has been assumed as the most important factor in determining leak and decision for protective stoma<sup>26</sup>. Finish study showed all the anastomotic leaks, developed in those who had anastomosis less than 7cm from anal verge<sup>27</sup>. Rullier reported almost 33% of cases that leaked, had tumor distance from anal verge of 4cm or lower<sup>23</sup>. Our study also supported such findings.

Completeness of resected proximal and distal bowel rings (Doughnuts) after double stapling is not a sufficiently reliable indicator of an intact anastomosis<sup>24</sup>. All cases in our study had complete doughnuts, but anastomotic leak still did occur. However, incomplete doughnut reflects the difficulty in creating anastomosis and which can be used as additional factor when predicting the fate of anastomosis<sup>24</sup>.

Manually constructed (hand sewn) technique anastomosis is equally safe as stapled one in colorectal surgery<sup>27</sup>. However, in low anastomosis, the use of double stapling technique makes reconstruction of anastomosis easier and perhaps safer. In our study the stapler anastomosis had lower leak rate when compare with hand sewn, but the difference was statistically not significant.

Intra-operative blood loss may induce immunosuppression and predisposes patients to various infections<sup>28,29</sup>. In our study, there was higher anastomotic leak rate in those who had blood loss of more than 1000ml, when compare to those with blood loss of less than 1000ml. However, the difference was not statistically significant. Moreover, it is difficult to associate a single variable as a causative factor.

Longer duration of surgery may associate with increasing bacterial exposure and issue trauma, which results in increasing surgical site infection. Nevertheless, our study and other studies did not show any correlation of this factor with the anastomotic leak.

This anastomotic leakage has a recorded mortality rate of 6 to 22%, which usually occurred within a month after surgery<sup>24</sup>. However, this figure is much lower than our mortality rate. This is because the period that we had taken into consideration for mortality varies. In many cases of post-operative deaths with anastomotic leak, it is difficult to make certain the death is directly related to the leak. This is because others factors could still have contributed to the mortality.

The use of protective stoma in colorectal anastomosis does not decrease the leak rate, but it has been shown to reduce relaparotomy and post-operative death if leak does occur<sup>30,32</sup>. In our study the higher leak rate was from the stoma group. This can be explained by selection bias of the surgeons. The majorities of patients with covering stoma had multiple risk factors, such as construction of a very low anastomosis, difficult intra-operatively dissection where tumour had infiltrated to the bladder and pelvic structures, or fecal contamination occurred after iatrogenic bowel perforation.

In conclusion this study shows that anastomotic leak is associated with high mortality. The distance of tumor from the anal verge is a significant risk factor. The other risk factors did not found to be significant in this study, may be due to a small sample size. A surgeon may consider a covering stoma or be more vigilant in operating patients with multiple risk factors. Further understanding of factors contributing to anastomosis leak, not only can prevent both physical and psychological morbidities of patients, but also reducing cost of prolonged hospital treatment.

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