

Predicting the Risk and Diminishing the Consequences of Anastomotic Leakage After Anterior Resection For Rectal Cancer

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rezime **INTRODUCTION:** Anastomotic leakage is one of the most serious early complications of any intestinal anastomosis. The morbidity and mortality are high and patients may be at increased risk of cancer recurrence. In colorectal surgery the risks are particularly high following low anterior resection. Factors which increase and decrease the risks are discussed. **METHODS:** A review of the main published risk factors for anastomotic leakage after anterior resection for rectal cancer together with the authors personal experience is reported. A review of a recent large randomized trial of a defunctioning stoma versus no stoma is outlined. **RESULTS:** The main factor influencing anastomotic leakage is the height of the anastomosis above the anal verge with the lower the anastomosis the higher the risk. All anastomoses within 7 cm of the anal verge are at increased risk which includes all patients who have had a total mesorectal excision. Neoadjuvant therapy (in particular long course radiotherapy or chemoradiotherapy) increases the risk. Male sex, older age, smoking, alcohol in excess, short course radiotherapy, obesity, general fitness, immunosuppression have been reported in some series as increasing the risk. A temporary diverting stoma decreases the consequences of leakage and reduces the need for emergency re-operation. Anastomotic leakage is associated with an increased postoperative death rate, reoperative rates, need for a permanent stoma and possibly an increase in local recurrence and decreased cancer specific and overall survival. **CONCLUSION:** Anastomotic leakage is a serious early complication following surgery for rectal cancer. The height of the anastomosis and neoadjuvant therapy are the main predictors of an increased risk. A diverting stoma diminishes the consequences of risk and reduces the need for emergency re-operation.

Key words: anastomotic leakage, early complication
rectal cancer

INTRODUCTION

Anastomotic leakage after anterior resection for rectal cancer is one of the most serious early complications¹ and continues to account for approximately 30% of postoperative deaths^{2,3}. The reported clinical leakage rate after anterior resection varies from 3% to 22%^{4,5,6}. There are a number of recognized risk factors that increase the risks of leakage and now an almost universal acceptance that a proximal defunctioning stoma reduces both the need for emergency re-operation and the consequences of leakage^{1,2,3}. The immediate adverse consequences of leakage include postoperative death from sepsis, the need for emergency re-intervention and a stoma in most cases, prolonged intensive care and overall hospital stay and a major impact on quality of life and recovery.

Furthermore, in the medium to long term, patients who have had surgery for cancer and develop anastomotic leakage may be unfit for post-operative adjuvant therapy with detrimental effects on disease survival. Additionally anastomotic leakage itself may be associated with an increase in local recurrence and a reduction in overall, and disease free, survival⁷. In the longer term, from a bowel functional point of view, a large proportion of patients are left with a permanent stoma and those in whom intestinal continuity is restored generally have poor neorectal function^{1,2,4}. Furthermore the increasing utilization of minimal access surgery has not had the hoped for reduction in leakage and it appears that the risks are the same, and may even be higher, compared with open surgery.

For these reasons predicting and diminishing the risks of leakage, together with early diagnosis and aggressive management of those who leak, continue to be an important topic in rectal cancer surgery. A recent large randomized clinical trial comparing patients with, and without, a proximal diverting stoma after surgery for rectal cancer has been very informative and illustrates some of the complex issues involved¹.

DEFINITION OF AN ANASTOMOTIC LEAK

One of the fundamental aspects accounting for much of the confusion surrounding the incidence and complications of anastomotic leakage revolves around the lack of a universally accepted definition of leakage. A recent proposed definition and grading of leakage is informative and helps to clarify some of the discrepancies suggesting that an "anastomotic leak should be defined as a defect of the intestinal wall (including suture lines and staples of neo-rectal reservoirs) leading to a communication between the intra and extraluminal compartments"⁸. The authors go on to suggest that leakage should be graded into Grade A in which the leak results in no change in the patients management, Grade B requiring intervention, such as radiological drainage and Grade C requiring a re-laparotomy or re-laparoscopy⁸. This definition, and grading system, would be useful if universally accepted and would allow comparison between series and an indication of the severity of the leak and intervention required.

INCIDENCE OF ANASTOMOTIC LEAKAGE

The reported incidence of anastomotic leakage after anterior resection for rectal cancer varies considerably between reported series^{4,5,61}. Whilst the rates reported vary between 3% and 22% for large series^{4,5,6}, these rates may partly represent case selection and both referral and treatment bias. It now seems that overall the rate is in the region of 10% after restorative resection for rectal cancer as reported in National Data base publications^{9,10} and from large rectal cancer randomised controlled trials such as the Dutch TME trial¹¹. In the Norwegian National registry report in 2005⁹ the leak rate was 11.6% (228/1958) and the odds ratio for leakage were increased by 1.6 for males, 2.2 for those who had preoperative radiotherapy and by 5.5 for those with an anastomosis below 3cm. A defunctioning stoma reduced the chances of leakage by 60%⁹. A recent publication from the Danish Colorectal Study Group¹⁰ reported a remarkably similar overall leak rate to the Norwegian Registry report with a leak rate of 11% in 1495 patients. The risks were higher in males, patients with tumours below 10cm, smokers and were also higher in proportion to the blood loss at surgery¹⁰. In the Dutch TME trial, where 1861 patient were randomised to preoperative radiotherapy and TME or TME surgery alone, the leak rate was 11% in patients who had pre-operative radiotherapy and TME compared with 12% in the TME alone group¹¹. Whilst this might suggest that pre-operative short course radiotherapy has no impact on the leak rate, unlike the well documented detrimental effect on perineal wound healing in those who had an abdominoperineal¹¹, it is salutary to note that the radiotherapy group had a higher defunctioning stoma rate thus negating a possible adverse effect of preoperative radiotherapy.

PROXIMAL DIVERTING STOMA AFTER ANTERIOR RESECTION

Proximal faecal diversion by a loop ileostomy or colostomy, whilst not abolishing the risk of leakage, undoubtedly mitigates the effects of leakage and markedly reduces

the serious consequences^{2,4,121}. Until recently this statement was not evidence based as there were only three small trials where patients had been randomised to a stoma or no stoma after an anterior resection for rectal cancer^{13,14,15} with conflicting result. However only 50¹³, 38¹⁴ and 36¹⁵ patients were randomized in these three studies with different terminology and definitions of leakage such that no firm conclusion could be drawn. These issues have recently been resolved by a very elegant study from Sweden entitled the RECTODES study¹. This study was conducted between 1999 and 2005 as a Swedish multicentre study in 21 hospitals. In total 234/ 821(28%) of patients who had a restorative resection were randomised. The main reason for exclusion was the fact that the surgeon considered that a stoma was needed due to a high risk of leakage or technical issues. Thus the 234 should theoretically be at a relatively low risk of leakage. There was strict definition of leakage including pelvic abscess, rectovaginal fistula and late leaks (often excluded in many reports on leakage). The results are illuminating. In total 10% of the 116 patients with a stoma had a leak, statistically less than the 28% of the 118 without a defunctioning stoma. At the end of the study, at a median (range) of 42(6-72) months, 13.8% of the patients randomised to have a defunctioning stoma still had a loop or an end colostomy compared with 16.9% of the group who had no stoma initially. The need for urgent reoperation of any type, at any hospital stay, was 10/116 (8.6%) in the stoma group compared with 30/118 (25%) in those without a stoma¹.

Of great interest was that only 60% of the anastomotic leaks were detected in hospital after surgery at a median (range) 8(3-18) days. The other 40% were diagnosed on re-admission at median day 24 (range 13 -172) following initial hospital discharge. Thus a defunctioning stoma significantly reduces the leak rate from 28% to 10% and significantly reduces the need for urgent re-operation from 24% to 8%¹. Furthermore a substantial proportion of the leaks are late and manifest after discharge from hospital following the initial surgery¹. Whilst these high leakage rates have been questioned, this undoubtedly results from the rigid definition and meticulous follow up and documentation and the authors are to be congratulated for their valuable addition to this complex area.

RANDOMIZED CONTROLLED TRIAL OF ANAL STENT TO REDUCE LEAKAGE

We have looked at the possibility of a custom designed silicone anal stent to reduce the need for a defunctioning stoma and reported the outcome in 2003¹⁶. Of the 118 eligible patients only 76 (64%) were randomized as the other 42 were considered to require a stoma due to adverse features such as preoperative chemo radiotherapy or an air leak on intraoperative testing. The leak rate was similar in both groups, 2/35 (6%) in the stoma group compared with 3/41(7.5%) in the stent group. However all three in the stent group required emergency defunctioning whereas the 2 patients in the stoma group were treated non-operatively. The only significant difference was in the total hospital stay which was a median of 13 days in the stent

group compared with 27 days in the stoma group due to the added time required for reversal.

LEAKAGE AND CANCER RECURRENCE

It has been suggested that anastomotic leakage may predispose to both local and systemic recurrence, perhaps by the profound inflammatory reaction inducing abnormal local growth factors.

A recent meta-analysis of the published literature suggests an anastomotic leak increases the risk of local recurrence and impacts on survival, in addition to the increase in postoperative death rate⁷.

SUSPICION AND DIAGNOSIS OF A LEAK

Early detection and appropriate management of an anastomotic leak is crucial to diminish the serious consequences. Almost all problematic cases will not have a defunctioning stoma. A high index of suspicion is required and whilst the majority of leaks manifest in hospital, a substantial proportion may present much later and even several months after initial surgery¹. Data from a much quoted paper on leakage suggested that the mean time to detection was 10 with a range of 3-24 days⁴. However Mathieson et al¹ reported that in the 40% with late leaks the median time to detection was on day 24 (range 13 -172) following initial hospital discharge.

The usual presentation is unexplained pyrexia, often with tachycardia but some may present with symptoms and signs simulating a cardiorespiratory event¹⁷. Of 22 leaks over five years, 7 presented with peritonitis and the other 15 were misdiagnosed with 13/22 (58%) initially treated for cardiac complications¹⁷.

Abdominal signs are initially absent, particularly in an extra peritoneal anastomosis. It is likely that a number of patients have an anastomotic abscess which may rupture into the lumen and thus resolve or alternatively rupture outwards into initially a pelvic abscess or collection and subsequently into the peritoneal cavity with generalized peritonitis. When peritonitis occurs swift intervention is needed to reduce the profound sepsis which can rapidly occur and which is potentially lethal.

Prior to peritonitis, if a leak is suspected, either a water soluble contrast enema, carefully performed by an experienced radiologist, or alternatively a contrast enhanced CT scan can help to confirm or exclude a leak. There is ongoing debate as to the superiority of one test over the other, though undoubtedly CT can help to outline the degree of pelvic contamination and abnormal collections, though is less sensitive at detecting the actual anastomotic defect. Urgent discussion with a radio-logist is advised and optimal investigation agreed. Occasionally a combination of both imaging techniques is required.

Management of a confirmed leak involves immediate high dose intravenous antibiotics, and consideration for emergency surgical intervention. Whilst optimization of the general condition of the patient will help, few patients with faecal peritonitis will benefit from prolonged delays prior to emergency washout and defunctioning of the source. A personal approach is to perform a laparotomy with

the legs elevated in the modified Lloyd Davies position. Pelvic and peritoneal lavage is crucial and manual disruption of all loculations is required. The general tendency to take down the anastomosis and exteriorize the end in a Hartmans type procedure should be avoided, if feasible, as this may be associated with profuse bleeding, pelvic sepsis may continue and the patient may be left with a chronic perineal sinus and almost no hope of restoration of intestinal continuity. Large bore silicone drainage tubes should be placed in the pelvis to allow continuing drainage.

A defunctioning stoma is fashioned and the distal limb is irrigated to evacuate all faecal matter from the bowel downstream from the stoma. This is facilitated by peranal insertion of a proctoscope.

The anastomosis is inspected peranally and any defect is enlarged. With this strategy, in a series of 24 major leaks, 3/24 patients died from sepsis, 11/21 survivors had the stoma eventually closed and of these 9 had good function with 2 having poor rectal function⁴.

A recent novel approach to a leak has been the use of an "endosponge" placed peranally into the defect with the application of continuous suction with promising results in some cases^{18,19}. This method may provide more rapid resolution of local sepsis but will not address the problem of peritonitis in those with a major leak who require the above strategy combined with the addition of a peranal mini-vac procedure in selected cases

CONCLUSION

Anastomotic leakage continues to be a major risk in anterior resection for rectal cancer and is associated with major post-operative morbidity, a substantial risk of morbidity and almost always requires emergency re-operation. The use of a defunctioning stoma mitigates the consequences, as illustrated by a recent randomized trial, and should be considered for all patients undergoing low anterior resection and where omitted a high index of suspicion should be maintained in those without a stoma. Early detection and aggressive management is essential to prevent disastrous outcomes from those unfortunate to develop what is not an uncommon complication after surgery for rectal cancer.

SUMMARY

PREDVIDJANJE RIZIKA I SMANJENJE POSLEDICA DEHISCENCIJE ANASTOMOZE POSLE PREDNJE RESEKCIJE ZBOG KARCINOMA REKTUMA

Uvod: Dehiscencija anastomoze je jedna od najozbiljnijih komplikacija bilo koje intestinalne anastomoze. Morbiditet i mortalitet su visoki i pacijenti mogu imati visok rizik od recidiva karcinoma. U kolorektalnoj hirurgiji su rizici naročito visoki nakon prednje resekcije rektuma. Diskutovani su faktori koji utiču na povećanje i smanjenje rizika.

Metode: Prikazan je pregled najčešćih objavljenih faktora rizika za dehiscenciju anastomoze posle prednje resekcije rektuma sa ličnim iskustvima autora. Pregled skorije objavljenih velikih randomizovanih studija sa protektivnim stomama nasuprot nekeriranju stoma je izložen.

Rezultati: Glavni faktor koji utiče na dehiscenciju anastomoze je visina anastomoze iznad ano-kutane linije gde je povećan rizik sa nižom pozicijom anastomoze. Sve anastomoze u okviru 7 cm iznad ano-kutane linije imaju povećani rizik, u šta se ubrajaju svi pacijenti kod kojih je uradjena totalna mezorektalna ekscizija. Neoadjuvantna terapija (naročito dugotrajna radioterapija ili hemioterapija) povećavaju rizik. Muški pol, starije životno doba, pušenje, alkoholizam, kratkotrajna radioterapija, gojaznost, opšta kondicija, imunosupresija su raportirani u nekim serijama kao faktori rizika. Privremena protektivna stoma smanjuje posledice dehiscencije i smanjuje ratu potrebu urgentne reoperacije.

Dehiscencija anastomoze udružena je sa povećanom postoperativnom smrtnošću, brojem reoperacija, potrebom za trajnom stomom i mogućim povećanjem incidence lokalnog recidiva i smanjenim kancer specifičnim i ukupnim preživljavanjima.

Zaključak: Dehiscencija anastomoze je ozbiljna rana komplikacija nakon operacije karcinoma kolona. Visina anastomoze i neoadjuvantne terapije su glavni prediktori povećanog rizika. Protektivna stoma smanjuje posledice rizika i smanjuje potrebu za urgentnom reoperacijom.

Ključne reči: dehiscencija, anastomoza, rane komplikacije, karcinom, kolon

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