*Int Surg* 2014;**99:**112–119
DOI: 10.9738/INTSURG-D-13-00059

# Incidence and Mortality of Anastomotic Dehiscence Requiring Reoperation After Rectal Carcinoma Resection

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**Anastomotic dehiscence (AD) requiring reoperation is the most severe complication following anterior rectal resection. We performed a systematic review on studies that describe AD requiring reoperation and its subsequent mortality after anterior resection for rectal carcinoma. A systematic search was performed on published literature. Data on the definition and rate of AD, the number of ADs requiring reoperation, the mortality caused by AD, and the overall postoperative mortality were pooled and analyzed. A total of 39 studies with 24,232 patients were analyzed. The studies varied in incidence and definition of AD. Systematic review of the data showed that the overall rate of AD was 8.6%, and the rate of AD requiring reoperation was 5.4%. The postoperative mortality caused by AD was 0.4%, and the overall postoperative mortality was 1.3%. We found considerable risk and mortality for AD requiring reoperation, which largely contributed to the overall postoperative mortality.**

*Key words:* Anastomotic dehiscence – Anterior resection – Rectal carcinoma – Complication – Mortality – Treatment

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During the past several decades, total mesorectal excision has dramatically increased the proportion of sphincter-saving procedures applied in the treatment of rectal carcinoma. However, an increased risk of anastomotic dehiscence (AD) is associated with total mesorectal excision which potentially endangers the blood supply of the rectal stump. AD requiring reoperation, the most invasive type of intervention, should be considered as an important point in clinical research. These patients are exposed to the risks of a second anesthetic and operative intervention, and they are usually managed by Hartmann procedure with takedown of anastomosis and future operation to restore intestinal continuity. Several authors have also reported data showing impaired oncologic outcome for patients with AD who underwent reoperation.[1–3]

This study aims to perform a systematic review of studies that describe AD requiring reoperation and its subsequent mortality compared with the overall postoperative mortality after anterior resection for rectal carcinoma. Given the impact that total mesorectal excision and stapling devices have had on AD, only studies using these techniques after the year 2000 will be included in this review.

## Methods

### *Search strategy*

Relevant studies published between January 2000 and December 2012 were identified by searching the databases of Medline, Embase, and The Cochrane Library. The following search terms were used: ("rectum," "rectal," or "proctectomy") and ("dehiscence," "leak," "leakage," "failure," "integrity," "insufficiency," "breakdown," "defect," or "separation.") The electronic search was restricted to English-language publications and was carried out on December 5, 2012.

### *Inclusion and exclusion criteria*

During the first step of the literature search, titles and abstracts of all original papers were screened for potentially relevant references that focus on laparotomic or laparoscopic anterior resection for rectal carcinoma and provide data of dehiscence, including randomized, controlled, multicenter, single-center, prospective, and retrospective studies. During the second step of the literature search, full articles of the selected references were assessed to identify relevant articles. Important inclusion criteria in our analysis were the availability of an incidence rate and the subsequent management of AD. These parameters could be used to count the number of events of AD requiring reoperation in the included studies.

The studies that were excluded from analysis were those that underwent low anterior resections only, included abdominoperineal resections, considered preoperative chemoradiation therapy as the study object, or used surgical techniques such as robot-assisted surgery. To avoid counting the same patients more than once in our analysis, we also excluded studies with the same affiliation and duplicate timing of the patients' date.

### *Data extraction*

Data on the rate of AD and the number of AD patients requiring reoperation were extracted. If available, data on the mortality caused by AD and overall postoperative mortality were also extracted. To increase the sensitivity of the search strategy, reference lists of the retrieved literature were cross-searched manually for additional relevant publications. Two researchers (C.Z. and H.L.) independently performed the collection and comparison of data. Any discrepancies were resolved by discussion.

### *Statistical analysis*

We performed a systematic review on AD requiring reoperation, mortality caused by dehiscence, and overall postoperative mortality with a random effects model. The number was small in most studies, and the SD of the random effects was zero. Thus, the data over studies could be pooled. The overall percentages of the outcomes were the number of events over studies divided by the total number of patients over studies. PASW version 16.0 (SPSS Inc, Chicago, Illinois) was used for statistical analysis.

## Results

### *Included studies*

We identified 807 studies, of which 41 were included. The most common reason for not meeting the inclusion criteria was that the study described the rate of AD without providing specific data on the intervention of AD. Two studies with the same affiliation and duplicate time of patients' date as two other studies were also excluded.[4,5] A total of 39 studies were included in our analysis.[6–44]

The included studies had a total population of 24,232 patients, with sample sizes ranging from 82 to 2729 patients. Four randomized, controlled trials were included, and the number of nonrandomized prospective and retrospective clinical trials was 12 and 23, respectively (Table 1).

*Definition of AD*

Among the 39 studies included, 31 (79.5%) provided a definition of AD, whereas 8 did not. Among the 31 studies that provided a definition of AD, 27 had a detailed description of AD, whereas 4 had a limited definition of AD. Based on the clinical symptoms of a patient, most definitions of AD consisted of a clinical suspicion that was subsequently confirmed by endoscopy, imaging using contrast agents, and during reoperation. Only one study[6] reported on ADs based on the standard definition proposed in 2010 by the International Study Group of Rectal Cancer.[45]

The reported symptoms comprised the signs of localized or generalized peritonitis (22 studies), fecal discharge from the wound and/or drain (23 studies), abscess (17 studies), rectovaginal fistulas (16 studies), pus discharge per rectum (11 studies), and fever and leukocytosis (5 studies). Active intervention was described in 2 studies to define a clinically relevant AD.[30,43] However, another study excluded perirectal abscess and rectovaginal fistula from AD based on the absence of a definite fecal discharge and the results of computed tomography alone.[36] Two other studies excluded pelvic abscess, which was not proven by imaging to show anastomotic insufficiency.[8,22]

*Incidence of AD*

We used the number of ADs as defined in the studies. A total of 2075 dehiscences were confirmed in 39 studies. The overall pooled rate of AD was 8.6%. A large variation in AD rates was observed. The highest and lowest reported AD rates were 20.6% and 1.2%, respectively (Fig. 1).

*Incidence of AD requiring reoperation*

According to the management of AD described in these 39 studies, we extracted the number of events of AD requiring reoperation. A total of 1309 patients were confirmed in this analysis, indicating that 63.1% (1309 of 2075) of ADs after resection for rectal carcinoma require reoperation. The overall incidence rate of AD requiring reoperation was 5.4%, with the highest being 12.0% and the lowest being 0% (Fig. 1). Twenty-three authors reported on the surgical procedure of reintervention for AD patients. In these studies, 536 ADs required reoperation, of which 480 (89.6%) needed diverting stoma construction (temporary or permanent).

*Definition of mortality*

For this analysis, we used the number of postoperative deaths as described in the studies. Of the 39 studies, 25 reported data on both mortality caused by AD and overall postoperative mortality.[6–30]

A total of 12 studies did not specify their definition of mortality. The definition of postoperative mortality in the remaining studies differed. Nine studies[7–15] reported postoperative mortality as all patients who died within 30 days after operation, regardless of the location (in-hospital or after discharge). One study[16] considered all in-hospital deaths as postoperative mortality rate, without specification of timing. Three studies[17–19] specified postoperative mortality as death occurring during the hospital stay or within 30 days of surgery.

*Mortality caused by AD and overall postoperative mortality*

The total number of patients who underwent anterior resection in the 25 studies was 14,159. Dehiscence occurred in 1194 patients, of whom 715 required reoperation. A total of 59 patients died as a direct consequence of AD. Thus, the pooled mortality rate in AD patients requiring reoperation reached as high as 8.3% (range, 0%–54.6%). The pooled mortality caused by AD in the patients of the 25 studies was 0.4% (range, 0%–1.8%), and the overall postoperative mortality rate after anterior resection was 1.3% (range, 0%–3.0%). Thus, almost one third of the overall postoperative mortality was caused by AD. This percentage ranged from 0% to 100% (Fig. 2).

## Discussion

AD is a predominant cause of morbidity and mortality after anterior resection. This effect is more obvious for ADs requiring reoperation, which commonly require additional operative interventions and a prolonged hospital stay.[41,46,47] Aside from its adverse effects on late functional results, AD also impairs the long-term prognosis of patients

*Table 1 Details of the included articles*

| Author | Year | Patients, No. | Study design | Author | Year | Patients, No. | Study design |
|---|---|---|---|---|---|---|---|
| Zhao *et al* | 2012 | 158 | Prospective single-center | Miyajima *et al* | 2009 | 995 | Retrospective multicenter |
| Yamamoto *et al* | 2012 | 111 | Prospective single-center | Eberl *et al* | 2008 | 472 | Retrospective single-center |
| Smith *et al* | 2012 | 1127 | Retrospective single-center | Jung *et al* | 2008 | 1391 | Retrospective single-center |
| Penninckx *et al* | 2012 | 1815 | Retrospective multicenter | Ito *et al* | 2008 | 180 | Retrospective single-center |
| Akagi *et al* | 2012 | 82 | Retrospective single-center | Matthiessen *et al* | 2007 | 234 | Randomized multicenter |
| Mroczkowski *et al* | 2011 | 356 | Retrospective single-center | Kruschewski *et al* | 2007 | 276 | Prospective single-center |
| Rutegård *et al* | 2011 | 2023 | Retrospective national study | Bianchi *et al* | 2007 | 104 | Prospective single-center |
| Lin *et al* | 2011 | 999 | Retrospective single-center | Brennan *et al* | 2007 | 100 | Retrospective single-center |
| Akiyoshi *et al* | 2011 | 363 | Retrospective single-center | Lee *et al* | 2006 | 499 | Retrospective single-center |
| Chen *et al* | 2011 | 750 | Retrospective single-center | Vlot *et al* | 2005 | 144 | Retrospective single-center |
| Warschkow *et al* | 2011 | 527 | Retrospective single-center | Gastinger *et al* | 2005 | 2729 | Prospective multicenter |
| Xiao *et al* | 2011 | 398 | Randomized controlled trial | Eriksen *et al* | 2005 | 1958 | Prospective single-center |
| Choi *et al* | 2010 | 178 | Prospective single-center | Peeters *et al* | 2005 | 924 | Retrospective single-center |
| Bretagnol *et al* | 2010 | 178 | Randomized multicenter | Kanellos *et al* | 2004 | 93 | Retrospective single-center |
| Shin *et al* | 2010 | 1838 | Retrospective single-center | Law *et al* | 2004 | 91 | Retrospective single-center |
| Maggiori *et al* | 2010 | 200 | Retrospective single-center | Matthiessen *et al* | 2004 | 432 | Retrospective multicenter |
| Huh | 2010 | 223 | Prospective single-center | Schmidt *et al* | 2003 | 788 | Prospective single-center |
| Kim *et al* | 2009 | 105 | Prospective single-center | Scheidbach *et al* | 2002 | 231 | Prospective multicenter |
| Cong *et al* | 2009 | 738 | Retrospective single-center | Tocchi *et al* | 2000 | 115 | Randomized controlled trial |
| Joh *et al* | 2009 | 307 | Prospective single-center | | | | |

with rectal carcinoma, particularly when reoperation is required.[1–3] The mechanisms of the negative prognostic effects of AD requiring reoperation include more pronounced immune system suppression caused by reoperation, more marked inflammation associated with AD requiring surgical revision, such as endotoxin that switches off apoptosis and thus leaves mitosis to shift the balance in favor of tumor growth, or transmission of viable exfoliated carcinoma cells during further surgery.[48,49]

The incidence of AD after anterior resection is an essential measure to determine the clinical value of different operative and perioperative interventions because of its effect on the postoperative course and long-term survival of a patient. Thus, the incidence of AD after anterior resection is often selected as a primary end point in clinical trials. However, the

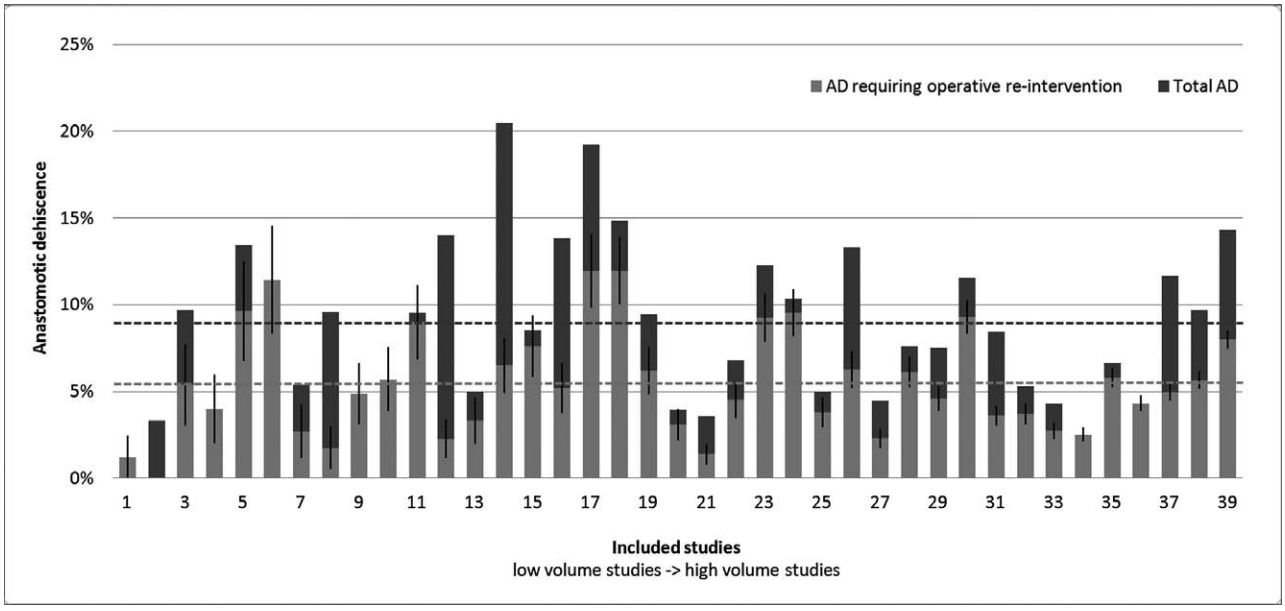


**Fig. 1** Rates of AD and AD requiring reoperation over the studies.

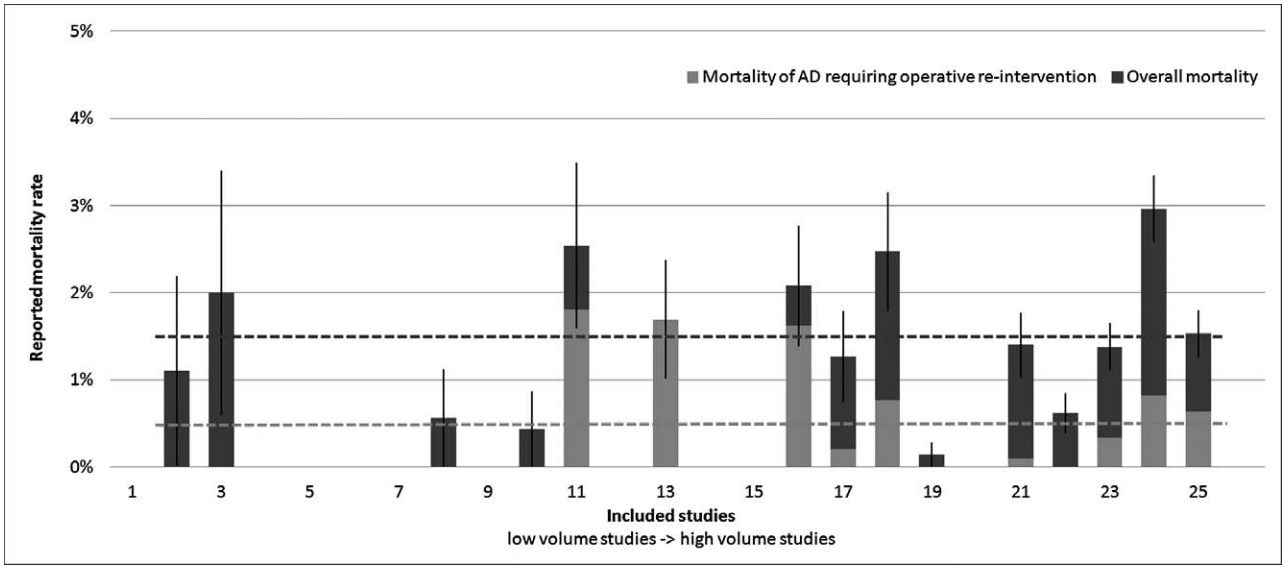


**Fig. 2** Mortality rate caused by AD requiring reoperation and overall postoperative mortality over the studies.

results of different studies varied, largely because of the lack of objectives and easily applicable definitions of AD, making comparisons complicated. Therefore, clear conclusions on the type of operative and perioperative management preferred in daily practice were hindered. In this analysis, we found that the definitions of AD and postoperative mortality varied over studies. Definitions were mainly based on clinical symptoms, and several authors disagreed about whether pelvic abscess or rectovaginal fistulas should be considered as AD.[8,22,36] To standardize reporting of clinical studies, the International Study Group of Rectal Cancer proposed a generally acceptable definition in 2010,[45] which can be adopted by clinicians for their studies and help the readers in comparing results of different reports. However, in this analysis, we found that only one author reported on ADs based on the standard definition.

Previous studies showed that rectal carcinoma patients prefer to be involved in the decision-making process and to be informed on the risks of different treatment options.[50] Despite the vast body of evidence on the potential risk factors, AD remains difficult to predict in an individual patient. Because the selection process of high-risk patients remains imperfect, we emphasize that each patient should be counseled preoperatively on the risk of AD, the consequences including mortality, and the possibility of reoperation. Thus, clinicians need reliable and accurate information on the rates of AD requiring reoperation and the associated mortality after resection for rectal carcinoma.

Patients of AD who require reoperation are often quite ill. Most often, these patients have purulent/fecal drain contents in their drains and exhibit markedly increased infection parameters (leukocytosis, C-reactive protein). They usually have abdominal pain and fever, and subsequently develop signs of peritonitis (tenderness to palpation, abdominal wall rigidity, tachycardia, etc). If operative reintervention with control of the septic source is delayed or not performed, the clinical condition of these patients will deteriorate and ultimately result in sepsis with clinical signs of hypothermia, leukopenia, and organ failure. Imaging studies, such as computed tomography with transrectal instillation of contrast, reveal considerable leakage at the anastomotic site, with fluid collection in the pelvis.

In this thorough overview of studies describing AD requiring reoperation and subsequent mortality following resection of rectal carcinoma, we found that patients have a considerable pooled rate of 5.4% for AD requiring reoperation, which indicates that 63.1% of AD patients need reoperation. Moreover, 89.6% of patients with AD requiring reoperation need temporary or permanent diverting stoma construction. We also found that AD considerably contributed to mortality after rectal carcinoma surgery, accounting for almost one third of all postoperative mortality. AD is still the most frequent cause of death after anterior resection in this analysis, with a pooled postoperative mortality rate

of 8.3% in patients with AD requiring reoperation. This finding is supported by and comparable with the results of a nationwide population-based study in Sweden exclusively assessing patients who died following anterior resection of the rectum.[51] The study describes 140 of 6833 patients who died following rectal excision with anastomosis during the initial hospital stay or within 30 days, of whom 42% (59 patients) had AD as a cause of mortality, a result highly similar to our findings.

Although accurate prediction of risk is impossible, certain factors are known to influence AD rates. The clinical AD rate slightly increased after introduction of the total mesorectal excision technique.[52] Based on the cause analysis of AD after anterior resection for rectal carcinoma, numerous parameters, such as distance of the anastomosis from the anal verge, tension of the anastomosis, bacterial contamination, anastomotic blood flow, surgical techniques, and defunctioning stoma, were reported to be responsible for the adverse effects on anastomotic healing.[20–24,34–37] Early urgent therapeutic intervention is required to avoid the life-threatening consequences of clinical AD. For severe dehiscence without septic complications, a loop ileostomy or colostomy is necessary to prevent fecal contamination, especially for patients without defunctioning stoma in the initial operation. When a broad anastomotic insufficiency is accompanied by sepsis or peritonitis, a revision of the anastomosis is necessary. Only an aggressive surgical treatment can save the life of a patient under these circumstances. Hartmann operation is referred to as the "gold standard" technique when sepsis is present.[18,42,53]

The limitation of this article is that the publications were all sourced from English-language papers, and non–English-language papers were excluded in the analysis. A formal meta-analysis will provide more powerful evidence. The methodology used in the present study was not as powerful as a meta-analysis. However, our systematic review provides the summarized data on the AD rate and on mortality directly from the original publications.

Thus, the present study can be used for counseling patients preoperatively. With a considerable risk of reoperation and postoperative mortality, AD remains the most serious complication following anterior resection of the rectum for rectal carcinoma. Frequent feedback of these outcomes can support clinicians when informing patients about the risks of different treatment options and can facilitate the decision-making process.

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