





# Reactivation leakages following stoma reversal after rectal cancer surgery: an underestimated problem

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Presented at: NVVH Chirurgedagen (Surgical Days from the Dutch Society for Surgery), May 2023; CCA Conference, July 2023; Digestive Disease Days, September 2023.

## Introduction

To prevent anastomotic leakage (AL) and to reduce its clinical consequences, diverting stomas are often constructed during index rectal cancer surgery. While this approach decreases short-term incidence of symptomatic AL, a subclinical leak can still develop and might become symptomatic at a later stage<sup>1,2</sup>. In the case of primarily non-diverted symptomatic AL, secondary faecal diversion is the mainstay of treatment<sup>3</sup>. Several weeks or months after index surgery, the anastomosis is assessed using endoscopic and/or radiological examination. If healing is confirmed, the diverting stoma is usually closed. However, some patients might develop a symptomatic AL within weeks to even years thereafter, which is also referred to as reactivation leakage.

Reactivation leakage seems to occur in 2–16% of patients after stoma closure. It is characterized by dense fibrosis as a result of chronic inflammation, which impairs subsequent treatment and clinical outcomes<sup>2,4–6</sup>. As a national referral centre for pelvic sepsis, many patients with reactivation leakage were evaluated, often with long-standing complaints and several interventions preceding referral, and severely impaired quality of life. The current literature on this topic is scarce and does not adequately describe the management and relevant outcomes for these patients. The aim of this study was to determine the proportion of reactivation leakage within a cohort of patients with pelvic sepsis referred to a tertiary hospital, to describe the clinical presentation, salvage treatment and subsequent outcomes, and to compare this with a group of pelvic sepsis patients who never underwent stoma closure.

## Methods

From January 2010 until January 2020, all patients referred to the Amsterdam University Medical Centres (AUMC), location AMC, for treatment of acute or chronic pelvic sepsis after prior rectal cancer resection were prospectively registered. This database

has previously been described<sup>7</sup>. For the purpose of the present study, patients were stratified according to closure of a diverting stoma in the period between index surgery and referral with pelvic sepsis: patients were assigned to the group with reactivation leakage if they underwent stoma closure, and patients were assigned to the comparison group if the primary or secondary diverting stoma was still in situ at the time of referral. Patients who never received a diverting stoma or patients with a primary Hartmann's procedure as index surgery were excluded for this study. The study has been approved by the medical ethical committee of the AUMC—location AMC (reference number W21\_099 # 21.112).

For outcome parameters, definitions and statistical methods, see [Supplementary Methods](#).

## Results

In total, 120 patients were included in this study ([Fig. S1](#)). Baseline characteristics of the group with reactivation leak ( $n = 55$ ; 46%) and the comparison group ( $n = 65$ ; 54%) are displayed in [Table S1](#). The median time to develop symptoms related to a reactivation leak after stoma closure was 16 months (i.q.r. 4–43; [Table 1](#)). Reactivation leakages initially presented in most cases with pain in the back, leg or anus (27%), as low anterior resection syndrome (26%), or as a fistula (24%). Twenty-nine of 55 patients with a reactivation leak (53%) had no leak-related symptoms during index admission. Patients who were asymptomatic after the index surgery demonstrated a longer time after stoma reversal to develop symptoms related to the reactivation leak, compared to patients who became already symptomatic after index surgery; 29 months versus 10 months, respectively.

In the group with reactivation leak, the median time from index surgery to referral was 39 months (i.q.r. 18–92), which was significantly longer than 9 months (i.q.r. 3.5–18.5) in the comparison group ([Table S2](#)). All the details regarding treatment modalities and outcomes are also presented in [Table S2](#).

Received: October 04, 2023. Revised: October 31, 2023. Accepted: November 05, 2023

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Before referral, the mean number of major surgical re-interventions (0.84 versus 0.48,  $P=0.048$ ) was higher in the group of patients with reactivation leaks.

After referral to our tertiary centre, primary treatment of pelvic sepsis consisted of intersphincteric resection of the leaking anastomosis with end colostomy in 58% of patients with a reactivation leakage, while this was 29% in the comparison group (OR 3.37 (95% c.i. 1.58 to 7.19)).

Mean length of follow-up since index surgery was 92 months (s.d. 49), with a mean length of 118 months (s.d. 49) in the reactivation leakage group compared to 71 months (s.d. 39) in

the comparison group (Table 2). At the end of follow-up, a permanent stoma was more often present in the reactivation leakage group (71% versus 46%; OR 2.84 (95% c.i. 1.33 to 6.06)). Median time to healing of pelvic sepsis since index surgery was 55 months (i.q.r. 28–114) after reactivation leakage compared to 20 months (i.q.r. 12–47) in the comparison group. Overall rate of healed pelvic sepsis was similar (91% versus 89%; OR 1.21 (95% c.i. 0.36 to 4.05)).

## Discussion

Reactivation leakage was the cause of pelvic sepsis in almost half of the patients included in this study and treatment of reactivation leaks is leading to a permanent stoma in the majority of patients.

The high contribution of reactivation leakages in a cohort of pelvic sepsis patients can possibly be explained by two factors: a delayed diagnosis and delay of proper treatment of such leakages. Both factors contribute to more complex problems following AL with a risk of developing pelvic sepsis. The current study clarifies that it often takes a long time before it becomes apparent that the anastomosis was not definitively healed, with a median period of 16 months after stoma closure. It was shown that most reactivation leakages presented as pain in the back, leg or anus, as severe low anterior resection syndrome, or as a fistula. These symptoms should be recognized as warning signs during clinical follow-up after stoma reversal.

Another interesting finding was that half of these leakages were initially asymptomatic at index admission and only became evident after the stoma had been reversed. This demonstrates that occult leakages do matter and are of clinical significance, because a certain proportion will develop into chronic pelvic sepsis if left untreated. Furthermore, this finding illustrates the difficulty of evaluating the anastomosis and labelling it as intact during stoma closure, or to judge whether it is safe to close the stoma if there is still a small residual sinus present. Unfortunately, it was not possible to retrieve information about findings during assessment of the anastomotic integrity and subsequent decision making at the referring centres.

Most reactivation leakages occurred after having a primary stoma following index surgery and a diverting stoma hampers

**Table 1 Description of reactivation leaks in pelvic sepsis patients in a tertiary hospital**

	Proportion, frequency (n = 55)
Primary deviating stoma	49 (89.1)
Secondary deviating stoma	6 (10.9)
Time to symptoms after stoma closure in months, (median, i.q.r.)	15.9 (4.0–42.9) Min: 0, Max: 132.6
<b>Presentation of reactivation leak (initial symptoms)*</b>	
Back, leg or anal pain	15 (27.3)
Abdominal pain	5 (9.1)
Bowel obstruction	5 (9.1)
Rectal blood loss	7 (12.7)
Fistula originating from the anastomosis	13 (23.6)
LARS	14 (25.5)
Anaemia	2 (3.6)
Presacral abscess	9 (16.4)
Abscess leg or gluteal region	7 (12.7)
Fever	6 (10.9)
Purulent anal discharge	3 (5.5)
Sacral osteomyelitis	3 (5.5)
<b>Initially asymptomatic (during index admission)</b>	29 (52.7)
Time to symptoms after stoma closure in months, (median, i.q.r.)	29.2 (7.5–47.6) Min: 0, Max: 90.7
<b>Initially symptomatic (during index admission)</b>	26 (47.3)
Time to symptoms after stoma closure in months, (median, i.q.r.)	10.1 (1.9–23.3) Min: 0, Max: 132.6

Values are n (%) unless otherwise stated. \*Multiple symptoms possible per patient. LARS, low anterior resection syndrome.

**Table 2 End of follow-up reactivation leaks versus leaks with primary or secondary diverting stoma**

	Reactivation leak (n = 55)	Primary or secondary stoma until referral (n = 65)	Odds ratio (95% c.i.) or P†,‡,§
Follow-up time after index surgery referral centre (months), mean (s.d.)	117.7 (48.5)	71.1 (39.3)	<0.001
Follow-up time after surgery tertiary centre (months), mean (s.d.)	57.6 (33.7)	49.0 (29.8)	0.172
<b>Stoma present</b>	42 (76.4)	37 (56.9)	2.44 (1.11,5.41)
Permanent stoma	39 (70.9)	30 (46.2)	2.84 (1.33,6.06)
<b>Anastomosis present</b>	16 (29.1)	35 (53.8)	0.35 (0.16,0.75)
Functional anastomosis	13 (23.6)	28 (43.1)	0.41 (0.19,0.90)
Rectal stump present	2 (3.6)	5 (7.7)	0.45 (0.08,2.43)
Rectal extirpation	37 (67.3)	25 (38.5)	3.29 (1.55,7.00)
Healed pelvic sepsis	50 (90.9)	58 (89.2)	1.21 (0.36,4.05)
Time to healing since index surgery (months), median (i.q.r.)	55 (28–114)	18 (12–47)	<0.001§
Time to healing since surgery tertiary hospital (days), median (i.q.r.)	12 (7–110)	49 (12–246)	0.059§
Alive at end of follow-up	43 (78.2)	53 (81.5)	0.81 (0.33,1.99)

Values are n (%) unless otherwise indicated. †P after Mann–Whitney U-test (due to no normal distribution for all numerical variables in this table). ‡Odds ratio with 95% c.i. after Chi-square test for all categorical variables. §P after log rank test comparing Kaplan–Meier survival curves for variables with censored data.

early start of leakage treatment if there is no postoperative protocol for active diagnosis of occult leaks using C-reactive protein (CRP) and CRP-guided CT imaging with rectal contrast<sup>8</sup>. Relevant to this issue, it has been suggested that early and active treatment of AL with endoscopic vacuum therapy and transanal defect closure can significantly reduce chronic AL rates, especially when started within 2 weeks from index surgery<sup>9</sup>. This strategy could possibly reduce reactivation leakages too, as they most likely originate from a very small remaining defect after secondary healing. The interrupted mucosal barrier at the level of the anastomosis is the point where an anastomotic fistula and abscess will form, as a result of faecal passage with elevated intraluminal pressure following stoma closure. Eventually, permanent stoma rates might be reduced if proactive leakage management with surgical anastomotic reconstruction is able to reduce the incidence of reactivation leakages.

## Funding

No funding has been received by any author in relation to this article.

## Disclosure

The authors declare no conflict of interest.

## Supplementary material

[Supplementary material](#) is available at *BJS Open* online.

## Data availability

The data, analytic methods, and study materials that support the findings of this study are available from the corresponding author, upon reasonable request. This is not publicly available due to privacy or ethical restrictions.

## Author contributions

Kiedo Wienholts (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing—original draft, Writing—review & editing), Sarah Sharabiany (Data curation, Supervision, Writing—review & editing), Johannes De Wilt (Investigation, Supervision, Writing—review & editing), Roel Hompes (Investigation, Methodology,

Supervision, Writing—review & editing) and Pieter Tanis (Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing—original draft, Writing—review & editing)

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