

# Oncological outcome after incidental perforation in radical rectal cancer surgery

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## Abstract

**Purpose** Identification of risk factors of poor oncological outcome in rectal cancer surgery is of utmost importance. This study examines the impact of incidental perforation on the oncological outcome.

**Methods** Using the Swedish Rectal Cancer Registry, patients were selected who received major abdominal surgery for rectal cancer between 1995 and 1997 with registered incidental perforation. A control group was also selected for analysis of the oncological outcome after 5-year follow-up. Multivariate analysis was performed. Registry data were validated, and additional data were supplemented from medical records.

**Results** After validation and exclusion of non-radically operated patients, 118 patients with incidental perforation and 155 controls in TNM stages I–III were included in the analysis. The rate of local recurrence (LR) [20% (23/118) vs. 8% (12/155) ( $p=0.007$ )] was significantly higher among patients with perforation, whereas the rates of distant metastasis [27% (32/118) vs. 21% (33/155) ( $p=0.33$ )] and overall recurrence (OAR) [35% (41/118) vs. 25% (38/155)

( $p=0.087$ )] were not significantly different between the groups. Overall as well as cancer-specific 5-year survival rates were significantly reduced for the patients with perforation [44 vs. 64% ( $p=0.002$ ) and 66 vs. 80% ( $p=0.026$ ), respectively]. In the multivariate analysis, perforation was a significant risk factor of increased rates of LR and OAR as well as reduced 5-year overall and cancer-specific survival.

**Conclusions** Incidental perforation in rectal cancer surgery is an important risk factor of poor oncological outcome and should be considered in the discussion concerning postoperative adjuvant treatment as well as the follow-up regime.

**Keywords** Rectal neoplasms · Intestinal perforation · Neoplasm recurrence local · Neoplasm metastasis · Survival rate · Risk factors

## Introduction

Incidental perforation in rectal cancer surgery is considered to affect the oncological outcome adversely in terms of increased risk of tumour recurrence and reduced survival. However, only a few studies address the impact of incidental perforation on the oncological outcome, and the majority of these studies were performed before the introduction of modern treatment strategies for rectal cancer [1–5]. Since the 1990s, significant changes in rectal cancer management have taken place concerning preoperative assessment, use of pre- and postoperative radiotherapy (RT), chemotherapy and surgical technique. All these advancements have decreased the local recurrence (LR) rate and improved survival [6–8]. Further advancements demand identification of potential risk factors of poor oncological outcome.

This paper is not based on a previous communication to a society or meeting.

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In 1995, the Swedish Rectal Cancer Registry (SRCR) was launched to supervise and assure the quality of the management of rectal cancer [7]. SRCR has gathered a great deal of data, making it an excellent resource for studies that aim to identify potential risk factors of poor oncological outcome.

In a recently published study on unvalidated registry data from the SRCR, we found that incidental perforation of the rectum during rectal cancer surgery significantly increased the risk of LR [9]. The present study was performed primarily to explore this finding by analysing additional data from the medical records and further investigating the impact of incidental perforation on the rates of distant metastasis, overall recurrence (OAR), overall survival and cancer-specific survival specifically. In cases with incidental perforation, special considerations were taken concerning the potential impact of preoperative RT and rectal washout. In addition, validation of the data in the SRCR was achieved for the patients included in the study.

## Patients and methods

### Patients

Since 1995, data for all patients with newly diagnosed rectal cancer in Sweden are prospectively registered in the SRCR. A detailed description of the SRCR has been published previously [7]. SRCR includes over 97% of patients when the registry is linked to the Swedish Cancer Registry. In the SRCR, 5-year follow-up data have been reported for more than 98% of the patients.

Data on preoperative assessment, surgical treatment and early postoperative complications are registered on a primary registration form and reported to the SRCR 30 days after surgery or at diagnosis in cases with no surgical treatment. Late complications, tumour recurrence and death are annually registered on a follow-up registration form for 5 years. During the studied period, there was no standardised national follow-up strategy, but the patients were followed according to each hospital's routines.

Between 1 January 1995 and 31 December 1997, 4,153 patients were registered in the SRCR. These patients constitute the cohort of this study. Major abdominal surgery [anterior resection (AR), abdominoperineal resection (APR), or Hartmann's procedure (HA)] was performed in 3,196 patients, and out of these patients incidental rectal perforation was registered in 208 (7%). All patients with a registered perforation were subjected to further analysis. Controls were selected randomly among patients that had undergone major abdominal surgery without a registered perforation during the same period. The number of controls

was the same as the number of cases. In the end, this study comprised 416 patients.

Primary data and 5-year follow-up data from surgery in the SRCR database were validated. Medical records from hospital stays including the operation notes, pathology reports from the preoperative and the surgical specimens, and the outpatient visits were collected. Extracted additional data were information on preoperative RT (25 Gy/5 days or 50 Gy/25 days course), details of the surgical procedure (Total Mesorectal Excision (TME) and abdominal drainage), the perforation (location of the perforation, moment of perforation and peroperative faecal contamination), macroscopic type of the tumour (ulcerative/polypoid or annular), tumour position (anterior, posterior or lateral), tumour grade (well, moderate or poor differentiation), separate registration of the T stage, circumferential resection margin (CRM), and residual tumour status. In patients with perforation, the complete medical record was impossible to retrieve in four patients, and in five patients the requested information was incomplete. In controls, the corresponding figures were five and four patients. When requested data were not possible to retrieve, the data in the SRCR were used in the analyses.

### Definitions

*Rectal cancer* in the SRCR is by definition an adenocarcinoma that is completely or partly located within 15 cm from the anal verge as measured with a rigid sigmoidoscope during withdrawal.

*TME* is defined as a sharp dissection under direct vision in embryological avascular planes with removal of the rectum with the intact mesorectum down to the pelvic floor. For most of the tumours situated close to the very upper limit of the rectum, the rectum and the mesorectum were divided 5 cm below the tumour corresponding to what some authors call a partial mesorectal excision.

*Incidental perforation* is defined as an unintended perforation of the rectum during the course of surgical resection. In this study, perforations are further divided into perforations in the tumour or in another part of the rectum. Unsuccessful stapling with intraoperative leakage and transection of tumours are also included. Thus, the term incidental perforation here comprises any unintended situation with possible spread of tumour cells into the pelvic cavity during surgery. Preoperative perforations as well as perforations in other parts of the bowel were not registered in the SRCR during the studied period.

*Rectal washout* denotes peroperative irrigation of the rectum after cross-clamping below the tumour and before transection in order to eliminate exfoliated malignant cells.

A *locally radical procedure* (R0) is defined as no macroscopic tumour growth left after completed surgery

as judged by the surgeon and no microscopic tumour growth at the resected specimen margins as judged by the pathologist (CRM >1 mm). When there is disagreement, the resection is classified as an R1 procedure (also including the group of patients with CRM ≤1 mm). If both the surgeon and the pathologist agree that tumour growth is left behind, the resection is by definition an R2 procedure.

*LR* is defined as the presence of tumour growth at the anastomotic site, perirectally, in the lesser pelvis (including vagina, bladder and lateral pelvic lymph nodes), perineum, or at another site (in the rectal stump after HA, at the top of the stoma after APR or HA, which is synonymous with the proximal resection margin) as documented by clinical, radiological, or pathological examination or examination at surgery or autopsy.

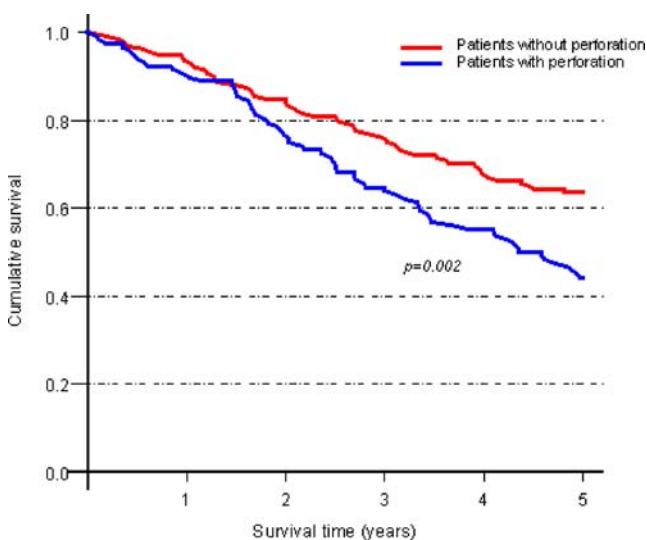
*Distant metastasis* is defined as the presence of tumour growth in any lymph node outside the pelvis, in the ovary, liver, lung, peritoneum, bone, brain or in any other organ as documented by clinical, radiological, or pathological examination or examination at surgery or autopsy.

*OAR* comprises either isolated LR or isolated distant metastasis or both.

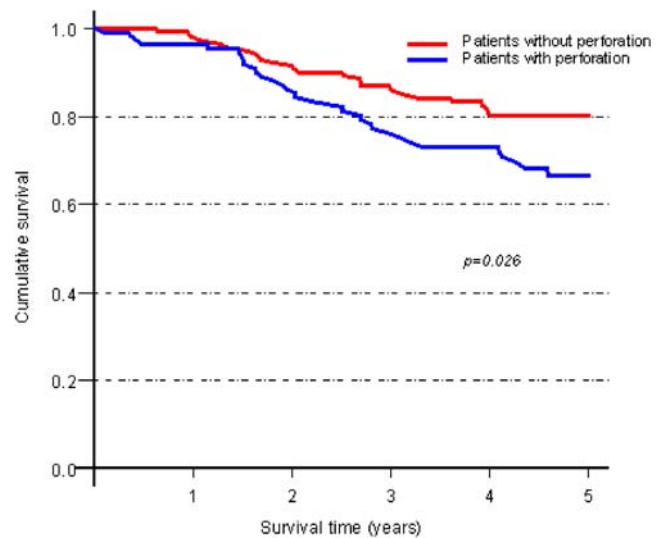
*Postoperative mortality* is defined as deaths within 30 days of surgery both in hospital and after discharge.

## Statistics

Data were analysed with the use of SPSS® version 15.0.0 for Windows® (SPSS, Chicago, Illinois, USA) statistical software. Figures were made in S-PLUS® version 6.0.2 for Windows® (Insightful Corporation, Seattle, Washington, USA). The Kaplan–Meier method was used in SPSS to calculate coordinates, and these were then used in S-PLUS to make the survival curves in Figs. 1 and 2. Cox regression



**Fig. 1** The 5-year overall survival rate of patients with and without perforation



**Fig. 2** The 5-year cancer-specific survival rate of patients with and without perforation

was used in Tables 4 and 5, and *p* values in results were calculated using the *t* test and  $\chi^2$  test.

## Ethics

All six Regional ethical review boards approved the study.

## Results

Validation of the SRCR yielded incorrect registration in 26 (13%) patients with perforation and in 17 (8%) controls. The reasons for exclusion are shown in Table 1. The following patients were withdrawn from further analysis: patients with tumours in TNM stage IV [30 (14%) patients with perforation, 20 (10%) controls]; patients where the TNM stage was unknown (two controls); and patients where local radicality was not achieved or it was uncertain [R1 resection: 13 patients (6%) with perforation, five (2%) controls; R2 resection: 20 (10%) patients with perforation, nine (4%) controls; uncertain local radicality: one patient with perforation]. Thus, 273 patients, 118 with perforation and 155 controls, were finally included in the calculations concerning the oncological outcome.

Table 2 shows the baseline characteristics of patients operated with locally radical surgery for tumours in TNM stages I–III as well as characteristics of the tumours and the treatment. Significant difference in tumour height with more low tumours among the patients with perforation was found ( $p < 0.001$ ). In addition, the type of surgery—there were more APRs among the patients with perforation—was significantly different ( $p < 0.001$ ). Also, preoperative faecal contamina-

**Table 1** Patients excluded after validation of perforations in SRCR 1995–1997 ( $n=43$ )

Group	Reasons for exclusion	No. of patients
Patients with perforation	No primary rectal cancer	
	High grade dysplasia	1
	Histopathology not adenocarcinoma	1
	Surgery for locally recurrent rectal carcinoma	3
	Preoperative perforation	9
	Perforation of small-bowel	1
	False registration of perforation	11
Controls	No primary rectal cancer	
	High grade dysplasia	3
	Sigmoid carcinoma registered as rectal carcinoma	3
	Perforation not registered	11

tion was significantly more common in the perforation group ( $p<0.001$ ). No other significant differences were found among studied parameters.

Among the patients with perforation who received preoperative RT, 62/65 (95%) were given a short-term 25 Gy/5 days course and the rest were given a prolonged 50 Gy/25 days course. All 85 controls who received preoperative RT were given a short-term course. Preoperative chemotherapy was given to one patient with perforation and one control. Postoperative RT was given to five patients with perforation and one control. Postoperative chemotherapy was given to ten (9%) patients with perforation and 17 (12%) controls ( $p=0.70$ ).

#### Tumour recurrence

Within 5 years of primary surgery, 35/273 (13%) patients developed LR. Significantly more LR were registered among patients with perforation than among controls, 23 (20%) vs. 12 (8%) ( $p=0.007$ ).

Metachronous distant metastasis was diagnosed in 65/273 (24%) patients, but there was no significant difference between groups with 32 (27%) among the patients with perforation and 33 (21%) among the controls ( $p=0.33$ ). Together, this gives an OAR rate of 79/273 (29%) in the study. OAR tended to be more common among patients with perforation than controls, 41 (35%) vs. 38 (25%), but the difference was not significant ( $p=0.087$ ). Among patients with perforation and LR, isolated LR was detected in 11/23 (48%) patients, and in 12/23 (52%) patients LR were combined with distant metastasis. The corresponding figures for the 12 controls with LR were six (50%) isolated LR and six (50%) LR combined with distant metastasis ( $p=1.00$ ). Table 3 gives the time to LR, distant metastasis and OAR from primary surgery.

#### Survival

The overall postoperative mortality was six (2%) patients: two patients with perforation and four controls. The 5-year overall survival rate for patients with perforation was 44% and for controls 64% ( $p=0.002$ ) (Fig. 1). The 5-year cancer-specific survival rate was 66% for patients with perforation and 80% for controls ( $p=0.026$ ) (Fig. 2). Deaths within 30 days of surgery have been excluded in Figs. 1 and 2.

#### Perforations

Among patients with perforation, 46 (39%) perforations occurred in the tumour, 58 (49%) in another part of the rectum, 3 (3%) had a combination, and for 11 (9%) patients the medical record did not reveal where in the rectum the perforation had occurred. LR developed in 13 (28%) patients with perforation in the tumour, 8 (14%) in another part of the rectum, in none of the patients with a combination, and in two (18%) patients where the exact site was unknown ( $p=0.11$ ). Distant metastasis was diagnosed in 13 (28%) patients with perforation in the tumour, in 17 (29%) in another part of the rectum, in none of the patients with a combination, and in two (18%) patients where the site was unknown ( $p=1.00$ ). OAR occurred in 18 (39%) patients with perforation in the tumour, 20 (34%) in another part of the rectum, in none of the patients with a combination, and in 3 (27%) patients where the site was unknown ( $p=0.78$ ). The relation of the site of perforation and type of surgery is outlined in Table 4. Among patients with APR and perforation, 24 (32%) occurred during the abdominal phase of the surgical procedure, 43 (57%) during the perineal phase, and for 8 (11%) patients it was not stated in the medical record when the perforation occurred.

**Table 2** Baseline characteristics of the patients (with locally radical surgery for tumours in TNM stages I–III) of the tumours and of the treatment

		Patients with perforation (n=118)	Controls (n=155)	p value
Age (years) at primary surgery		73(45–90)*	71(39–87)*	0.10
Sex	M	69(59)	93(60)	0.90
	F	49(41)	62(40)	
Tumour height (cm)	Low: 0–5	57(48)	35(23)	<0.001
	Medium: 6–10	42(36)	65(42)	
	High: 11–15	18(15)	53(34)	
	Unknown	1(1)	2(1)	
Macroscopic type of tumour	Ulcerative/polypoid	31(26)	39(25)	0.90
	Annular	84(71)	114(74)	
	Unknown	3(3)	2(1)	
Tumour position <sup>a</sup>	Ant	35(42)	25(22)	0.20
	Post	17(20)	28(25)	
	Lat	10(12)	20(17)	
	Ant/lat	5(6)	8(7)	
	Post/lat	10(12)	10(9)	
	Ant/lat/post	1(1)	1(1)	
	Unknown	6(7)	22(19)	
Preoperative radiotherapy	No	53(45)	70(45)	1.00
	Yes	65(55)	85(55)	
Surgery	AR	32(27)	115(74)	<0.001
	APR	75(64)	32(21)	
	HA	11(9)	8(5)	
TME	No	17(14)	24(16)	1.00
	Yes	91(77)	129(83)	
	Unknown	10(9)	2(1)	
Peroperative faecal contamination	No	89(75)	152(98)	<0.001
	Yes	21(18)	2(1)	
	Unknown	8(7)	1(1)	
Rectal washout <sup>b</sup>	No	16(37)	29(24)	0.13
	Yes	27(63)	94(76)	
Abdominal drainage	No	37(31)	45(29)	0.67
	Yes	75(64)	106(68)	
	Unknown	6(5)	4(3)	
Anastomotic leakage <sup>c</sup>	No	25(78)	97(84)	0.57
	Yes	7(22)	18(16)	
Tumour grade	Well	6(5)	9(6)	0.79
	Moderate	90(76)	115(74)	
	Poor	19(16)	30(19)	
	Unknown	3(3)	1(1)	
TNM stage	I	24(20)	39(25)	0.65
	II	48(41)	59(38)	
	III	46(39)	57(37)	
T stage	1	4(3)	9(6)	0.018
	2	30(25)	44(28)	
	3	70(59)	96(62)	
	4	9(8)	1(1)	
	Unknown	5(4)	5(3)	
Median distal resection margin (mm) <sup>b</sup>		33(2–110)*	28(5–90)*	0.22

Values in parenthesis are percentage unless \* where it is range. *Ant* anterior, *Post* posterior, *Lat* lateral, *AR* anterior resection, *APR* abdominoperineal resection, *HA* Hartmann's procedure, *AL* anastomotic leakage

<sup>a</sup> For ulcerative/polypoid tumours

<sup>b</sup> For AR and HA

<sup>c</sup> After AR

**Table 3** Time to diagnosis of local recurrence, distant metastasis or overall recurrence from primary surgery after locally radical surgery for rectal cancer in TNM stages I–III

	Local recurrence				Distant metastasis				Overall recurrence <sup>a</sup>			
	Patients with perforation (n=23)	%	Controls (n=12)	%	Patients with perforation (n=32)	%	Controls (n=33)	%	Patients with perforation (n=41)	%	Controls (n=38)	%
1st year	8	35	4	33	6	19	7	21	11	27	10	26
2nd year	5	57	5	75	11	53	13	61	11	54	13	61
3rd year	6	83	2	92	9	81	5	76	12	83	7	79
4th year	0	83	1	100	2	88	1	79	1	85	2	84
5th year	4	100	0	100	4	100	7	100	6	100	6	100

% cumulative percentage.

<sup>a</sup> For overall recurrence the time is calculated to the first occurring recurrence, either local recurrence or distant metastasis

### Univariate and multivariate analyses of potential risk factors of tumour recurrence and survival

Univariate analysis of potential risk factors (age, gender, tumour height, preoperative RT, surgical procedure, TME, peroperative faecal contamination, rectal washout, tumour grade, TNM stage and T stage) of LR, distant metastasis, OAR and, reduced 5-year overall or 5-year cancer-specific survival was performed (data not shown). Multivariate analysis was performed of the potential risk factors with a *p* value  $\leq 0.10$  in the univariate analysis (Tables 5 and 6).

## Discussion

We have found that incidental perforation is an independent risk factor of LR, OAR and reduced 5-year overall as well as 5-year cancer-specific survival. However, we could not see any significant impact on the distant metastasis rate. This is in line with previous findings [1–5]. As Eriksen et al. stressed [5], the majority of the earlier studies are retrospective single-centre series with collection of data over a long period [1, 2, 4], a study design that reflects varieties in preoperative assessment, use of pre- or postoperative RT and chemotherapy as well as surgical

techniques. The prospectively assembled data in the German study [3] comes from a large registry from one institution, and the Norwegian study is based on the Norwegian Rectal Cancer Registry (NRCR) [5]. We present data for all patients with registered incidental perforation during a 3-year period and a randomly selected control group from the population-based SRCR. Presented data are prospectively registered, and the patients are followed for 5 years after primary surgery. In turn the SRCR data are validated and additional data are retrieved. Our study also reflects modern rectal cancer management with a high rate of patients treated with preoperative RT and TME since the studied period is after the implementation of these modalities in Sweden.

As in our study, previous studies that have addressed the impact of incidental perforation on the LR rate have reported an increased risk [1–5]. We have only found one study that could not detect any difference in the LR rate between patients with and without perforation [10]. The analysis on the oncological outcome in this study was based on 15 patients with tumour perforation making the conclusions dubious. Patients with a contained preoperative pelvic and an incidental perforation were not analysed separately, and all patients with perforation were routinely referred for postoperative RT and chemotherapy. That the five largest series of patients [1–5] in addition to our study have found a negative impact on the LR rate makes this evidence solid even if it is based on subgroup analysis. However, the difference in our study is less pronounced than in other studies reporting an increased LR rate. In an earlier survey of the SRCR [9], we found a significantly increased LR risk after perforation only in non-irradiated patients when comparing the LR risk in irradiated and non-irradiated patients.

In this study, more than 50% of the patients were treated with preoperative RT. Although many patients were treated with RT in the study by Porter et al. [4], most of those patients were treated postoperatively and with suboptimal

**Table 4** The relation between site of perforation and type of surgery

Site of perforation	Type of surgery		
	AR (n=32)	APR (n=75)	HA (n=11)
Tumour	15 (47)	26 (35)	5 (46)
Another part of rectum	13 (41)	43 (57)	2 (18)
Combination	1 (3)	0	2 (18)
Unknown	3 (9)	6 (8)	2 (18)

Values in parentheses are percentage. AR anterior resection, APR abdominoperineal resection, HA Hartmann's procedure

**Table 5** Multivariate analysis of the impact of perforation on tumour recurrence after locally radical surgery for rectal cancer in TNM stages I–III

	No. of patients (events/total)	Univariate analysis			Multivariate analysis <sup>a</sup>		
		RR	CI 95%	<i>p</i> value	RR	CI 95%	<i>p</i> value
LR	35/267	2.53	1.24–5.15	0.010	2.52	1.12–5.69	0.026
DM	65/267	1.47	0.89–2.44	0.010	1.56	0.93–2.59	0.091
OAR	79/267	1.53	0.97–2.42	0.066	1.85	1.09–3.14	0.022

LR local recurrence, DM distant metastasis, OAR overall recurrence

<sup>a</sup> Adjusted for age, gender, tumour height, preoperative RT, surgical procedure, TME, peroperative faecal contamination, rectal washout, tumour grade, TNM stage and T stage. Deaths within 30 days of surgery have been excluded in the analysis

doses. In the study from Norway [5], the rate of RT was low and patients receiving pre- or postoperative RT were excluded from the analysis on LR and survival rate. In the other studies mentioned above, postoperative RT or chemotherapy was not used [1–3].

The importance of the use of rectal washout and its impact on the LR rate remain unclear and under debate [11]. No other study concerning incidental perforation has reported the use of rectal washout during AR and HA. The majority of patients in our study had rectal washout and omission was a significant risk factor in the multivariate analysis (data not shown).

The postulated mechanism of the development of LR after incidental perforation is that the bowel lumen contains viable cancer cells that are exfoliated and implanted in the pelvic cavity during the leakage of luminal contents from the perforation [12–14]. Anastomotic leakage (AL) has by the same implantation mechanism also been suggested as a potential risk factor of poor oncological outcome, a finding that we could not confirm in a recent paper [15]. The theory is that the systemic inflammatory response, enhanced by the AL, affects the immunity and facilitates implantation of cancer cells, increasing the LR risk [16, 17]. We hypothesise that the time for the occurrence of the leakage of luminal contents and the number of viable, intraluminal cancer cells at this time are more crucial. At the time of the perforation, the number of viable, intraluminal cancer cells might be high, resulting in a higher risk of implantation than after an AL. Leakage of luminal contents into the pelvic cavity after AL usually occurs several days after

surgery with probably a lower number of viable, intraluminal cancer cells and thereby a lower risk of LR. In our opinion, data in this study and our earlier study of the impact of AL [15] support this hypothesis. Preoperative RT in contrast to postoperative RT as well as rectal washout (if performed before the occurrence of the perforation), might to some extent eliminate or reduce the number of viable, intraluminal cancer cells capable of implantation and thereby diminishing the risk of LR. Our data does not prove this, but the data does indicate that this could partly explain the lower LR rate in our study compared to previous studies.

Perforation had no impact on the distant metastasis rate in our analysis. We have not been able to find any other publication separately reporting the impact on the distant metastasis rate after incidental perforation. The unaffected distant metastasis rate probably reflects the different origins of LR and distant metastasis. LR might occur as a consequence of local implantation of exfoliated cells in the immediate perioperative period as described above, whereas distant metastasis depends on the circulation of tumour cells in the lymph- or blood system [12–14, 18].

Significant impact on the OAR rate was also found in the multivariate analysis probably due to the impact of incidental perforation on the LR rate. This has been reported by Ranberger et al. [1], but they did not present data on LR and distant metastasis rate separately, thereby making it difficult to conclude if their findings were only reflecting the high reported LR rate or were due to an impact of the distant metastasis rate.

**Table 6** Multivariate analysis of the impact of perforation on 5-year overall and 5-year cancer-specific survival after locally radical surgery for rectal cancer in TNM stages I–III

	Univariate analysis			Multivariate analysis <sup>a</sup>		
	RR	CI 95%	<i>p</i> value	RR	CI 95%	<i>p</i> value
Overall survival	1.74	1.21–2.49	0.002	1.69	1.09–2.63	0.020
Cancer-specific survival	1.77	1.06–2.95	0.028	2.07	1.18–3.64	0.011

<sup>a</sup> Adjusted for age, gender, tumour height, preoperative RT, surgical procedure, TME, peroperative faecal contamination, rectal washout, tumour grade, TNM stage and T stage. Deaths within 30 days of surgery have been excluded in the analysis

We could not detect any difference in the time from primary surgery to occurrence of LR, distant metastasis or OAR among patients with and without perforation. Porter et al. [4] found the same result when addressing the time from primary surgery to LR.

Only the small study by Kagda et al. [10] has reported an equal 5-year overall survival rate in the patients with and without perforation. In line with our data, all other studies have reported a reduced 5-year overall survival rate of patients with incidental perforation [1–5]. The overall survival rates in our study, the German study [3], and in the Norwegian study [5] are markedly higher than in the other studies. Certainly, this reflects the importance of the refined TME and modern management of rectal cancer, although patients treated with preoperative RT were not included in the analysis of the oncological outcome in the studies from Germany and Norway, and the surgical technique was not stated in the German paper.

To our knowledge, we are the first to report on the impact of perforation on the 5-year cancer-specific survival rate. In our study, perforation significantly reduced the 5-year cancer-specific survival rate, a finding that probably reflects the high mortality among the patients developing LR.

In the study by Slanetz [2], a more marked impact on the LR rate and overall survival was seen when perforation occurred in the tumour rather than in the bowel, remote from the tumour. It was not specified whether remote from the tumour denoted in the rectum or if the perforation could be more proximal to the tumour in the colon. Zirngibl et al. [3] only included patients where perforation had occurred in the tumour in their analysis. We included perforations in the tumour as well as perforations in other parts of the rectum, and we saw a tendency for a higher LR rate among patients with perforation in the tumour. However, the difference was not statistically significant. This may be due to a rather small number of LR. We did not find any impact on the rates of OAR and distant metastasis irrespective of where in the rectum the perforation occurred. To answer the question of the importance of where in the bowel the perforation occurs, a greater number of patients need to be studied. Unfortunately, until 2007 it was not registered in the SRCR where in the bowel the perforation occurred. Our data come from the scrutiny of the medical records of the patients in our study. However, since 2007, when the SCRC was revised, the site of the perforation is registered.

Porter et al. [4] raised the question that incidental perforation might be a marker of an inferior operation, specifically in reference to closer lateral margins leading to increased LR risk. We have thoroughly reviewed the pathology report for all analysed patients ensuring a CRM >1 mm, and thus eliminating this confounder.

As in our study, a higher perforation rate for APRs than other resections has been reported in several papers [3, 5, 19, 20]. In the Norwegian study, the perforation rate was high for HA, but the authors claimed that this might be the case because HA was chosen as a result of a perforation or other complications that may influence the perforation rate. In some cases, this might also be true for the choice of performing an APR due to an intraoperative adverse event. Perforation is also reported to be more common during the perineal phase of the APR [4]. The higher perforation rate in our study for APRs than ARs might to some extent be explained by a suboptimal surgical technique when performing an APR. During the studied period, the conventional technique for APR was dominating in Sweden. In the abdominal phase of the APR the mesorectum was followed down to the pelvic floor and dissected of the upper parts of the levator muscles. The perineal part was then performed with the patient in the supine position and the anal canal and lower parts of the levator muscles excised, often resulting in a waist of the specimen. At the waist, the outer border of the specimen is thin as it consists of the outer muscle layer of the rectal tube. In turn this outer border constitutes the CRM. As the specimen here is thinner than in other parts and also due to the limited visualisation during this part of the operation the risk of perforation is high. Another consequence of the waist is a high risk of CRM involvement with a subsequent negative impact on the oncological outcome [19–22]. To overcome these problems, APR by an extended posterior approach was introduced in Sweden [21]. With this technique the abdominal part of the procedure is terminated at the upper borders of the levator muscles. The patient is then turned to the prone jack-knife position, and the dissection is continued from below until the insertions of the levator muscles on the pelvic side walls. This ensures proper visualisation for the surgeon and results in a cylindrical, thicker specimen as the levator muscle is attached to the specimen. Thereby the risks of perforation and CRM involvement are decreased. Lower perforation rates and improved oncological outcome have been reported after APR by an extended posterior approach, although the follow-up is short [21, 22]. Increased morbidity has not been observed with this technique [21, 22].

That incidental perforation reflects the inexperience of the surgeon, and thereby probability of an inferior operation resulting in a poor oncological outcome has been debated [5, 23]. From our data, it is not possible to draw conclusions concerning the impact of the experience of the surgeon. During the studied period, significant structural changes had taken place in Sweden with concentration of the management of rectal cancer to colorectal units. By these changes the rectal cancer surgery was performed in fewer hospitals and by fewer surgeons. That an inexperienced



surgeon alone managed rectal cancer was not likely during the studied period.

Limitations of the present study, as well as the earlier studies, are the relative rarity of perforation and tumour recurrence, conditions that make the analysed subgroups rather small. Another drawback of our study could be the choice of not matching the controls when selecting the control group. Tumour height, surgical procedure and peroperative faecal contamination were significantly different between patients with perforation and controls. Due to the rarity of peroperative faecal contamination, conclusions of this finding cannot be drawn. That low tumour and consequently APRs were more common among patients with perforations were not a surprising finding since low tumour is a reported risk factor of incidental perforation [5, 19, 20]. Since the controls were selected randomly among patients without a registered incidental perforation, we expected the ratios of the tumour height and the surgical procedure to be nearly the same as the reported ratios in the SRCR, which they were [7]. However, we used multivariate methods with adjustment for tumour height, surgical procedure and peroperative faecal contamination, as well as several other covariates in the analysis, which was the reason for not matching the controls. To our knowledge, multivariate methods have been applied only in two earlier studies [4, 5]. The number of selected controls could also be a matter for discussion, but since retrieval and extraction of data from medical records are complex and time consuming, we chose a number where the work and the possibility of obtaining the medical records without missing too much data was reasonable.

The validation excluded 10% of the patients due to incorrect registration. More patients with perforation than controls were excluded and this was to a great extent due to registration of preoperative perforations in the registry. This probably is explained by the fact that the studied cohort was assembled during the first years of the SRCR when the registration routines had not been settled. However, since the revision of the SRCR, preoperative perforations are registered separately. As in our two earlier works [9, 15], the assembly of medical records for the validation and addition of data proved the good order in the Swedish medical record system.

Less impact of incidental perforation on the oncological outcome was seen in our study than in previous studies, a finding that we believe is the result of the frequent use of preoperative RT, rectal washout and an improved surgical technique. Still incidental perforation significantly adversely affected the LR and the OAR rates as well as the overall and the cancer-specific 5-year survival rates. Therefore, great effort and attention must be taken to avoid this peroperative complication. Our data indicate that patients with incidental perforation should be considered for

postoperative RT, if not given preoperatively, and chemotherapy as well as extended follow-up.

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