BJS Open, 2025, zraf052
https://doi.org/10.1093/bjsopen/zraf052
Original Article

Organ/space surgical site infection and long-term outcomes of rectal cancer surgery: retrospective population-based cohort study

Carlota Matallana[1,2,3], Paula Manchon-Walsh[3,4], Eloy Espín[5], Marta Pascual[6], Sebastiano Biondo[7], Marta Jiménez-Toscano[6], Josep Maria Borràs[3,4], Josep M. Badia[8,9], Enric Limón[9,10,11], Luisa Aliste[3,4], Rebeca Font[3,4] and Miguel Pera[12,13,*]

[1]Department of Surgery, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain
[2]Department of Surgery, Hospital Universitari Parc Taulí, Sabadell, Spain
[3]Catalan Cancer Plan, Health Department, Duran i Reynals Hospital, Barcelona, Spain
[4]Biomedical Research Institute of Bellvitge (IDIBELL), University of Barcelona, Barcelona, Spain
[5]Colorectal Surgery Unit, Vall d'Hebrón University Hospital, Barcelona, Spain
[6]Department of Surgery, Hospital del Mar, Barcelona, Spain
[7]Department of Surgery, Hospital Universitari de Bellvitge, Barcelona, Spain
[8]Department of Surgery, Granollers General Hospital, School of Medicine, Universitat Internacional de Catalunya, Barcelona, Spain
[9]Health Department, VINCat Program, Surveillance of Healthcare Related Infections in Catalonia, Barcelona, Spain
[10]Department of Public Health, Mental Health and Mother–Infant Nursing, Faculty of Nursing, University of Barcelona, Barcelona, Spain
[11]Infectious Diseases Networking Biomedical Research Centre (CIBERINFEC), Carlos III Institute, Madrid, Spain
[12]Department of General and Digestive Surgery, Institute of Digestive and Metabolic Diseases (ICMDM), Hospital Clínic Barcelona, University of Barcelona, Barcelona, Spain
[13]Gastrointestinal and Pancreatic Oncology Group, August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain

*Correspondence to: Miguel Pera, Department of General and Digestive Surgery, Institute of Digestive and Metabolic Diseases (ICMDM), Hospital Clínic Barcelona, Villarroel 170, 08036 Barcelona, Spain (e-mail: pera@clinic.cat)

Abstract

Background: Anastomotic leak and subsequent organ/space surgical site infection (O/S-SSI) after colorectal cancer surgery are associated with poor short-term outcomes; however, the evidence regarding long-term outcomes is inconclusive. This population-based retrospective cohort study aimed to evaluate the association between O/S-SSI and both tumour recurrence and long-term survival after curative rectal cancer surgery.

Methods: Data was obtained for all adults who underwent curative oncological resection of the rectum in the periods 2011–2012 and 2015–2016 ($n = 2208$) in Spain. Multivariable analysis (Cox proportional hazards model) was used to evaluate the effects of clinical and pathological characteristics, as well as the occurrence of O/S-SSI, on recurrence and survival.

Results: In all, 2208 adults underwent curative rectal cancer resection, 1464 of whom were male (66.3%); the median patient age was 69.1 years. O/S-SSI occurred in 291 patients (13%). Independent predictors of recurrence included tumour stage III (hazard ratio (HR) 1.95, 95% confidence interval (c.i.) 1.06 to 3.58; $P = 0.032$), a positive resection margin (HR 4.03, 95% c.i. 2.58 to 6.29; $P < 0.001$), and poor quality mesorectal excision (HR 1.81, 95% c.i. 1.11 to 2.95; $P = 0.018$), but not O/S-SSI (HR 1.02, 95% c.i. 0.78 to 1.34; $P = 0.888$). However, O/S-SSI was independently associated with reduced overall survival at 1 year (HR 2.20, 95% c.i. 1.39 to 3.48; $P < 0.001$), 2 years (HR 1.75, 95% c.i. 1.25 to 2.43; $P < 0.001$), and 5 years (HR 1.33, 95% c.i. 1.05 to 1.68; $P = 0.017$).

Conclusion: In this study, O/S-SSI had a negative impact on the long-term survival of patients who underwent rectal cancer surgery, but was not associated with increased tumour recurrence.

Introduction

Colorectal cancer is the third most common malignancy worldwide and the fourth leading cause of cancer death in men and women, with 30–35% of all colorectal tumours arising in the rectum[1]. Although the introduction of total mesorectal excision and neoadjuvant chemoradiation has improved oncological outcomes, the 5-year risk of recurrence remains at approximately 20%, with tumour stage being the main prognostic factor[2,3]. Surgery-related factors, such as the quality of surgical resection[4] or postoperative complications[5], may also have an impact.

One of the most serious complications of colorectal cancer surgery is anastomotic leak (AL), which occurs in 3–21% of operations, depending on tumour location and the definition of the leak[1]. AL is associated with considerable morbidity and may reduce quality of life[6]. Several studies have shown that AL and subsequent organ/space surgical site infections (O/S-SSIs) are also associated with higher rates of local and systemic tumour recurrence and cancer-specific mortality[7–9]. A recent meta-analysis of 43 studies with 154 981 patients found that AL and postoperative O/S-SSI had a significant negative impact on

Received: January 18, 2025. Accepted: February 27, 2025

disease-free survival, local recurrence, and overall recurrence[10]. This association has also been reported after the resection of liver metastases and other gastrointestinal malignancies[11]. Moreover, the severity of postoperative infection is directly correlated with the risk of recurrence[12]. However, other studies have found no such associations[13,14]. Therefore, whether AL and O/S-SSI contribute to disease recurrence remains contentious and requires further investigation.

The aim of this population-based study was to evaluate the effect of O/S-SSI on the 5-year recurrence (locoregional, systemic, and overall) and survival of patients who had undergone curative rectal cancer surgery.

Methods

Study design, setting, and participants

This was a retrospective population-based cohort study including all patients who underwent curative rectal cancer surgery between 2011 and 2012 and between 2015 and 2016 in public hospitals in Catalonia, Spain (7.7 million inhabitants). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed[15].

Study outcomes, variables, and definitions

The primary outcomes of this study were cancer recurrence (locoregional and/or systemic) and overall survival (OS).

Locoregional recurrence was defined as cancer recurrence at the surgical site, and systemic recurrence was defined as the spread of cancer to organs outside the surgical field. These findings were confirmed histologically or via imaging. Recurrence was categorized as isolated locoregional recurrence (LR), locoregional recurrence with or without systemic recurrence (LR+/−SR), and systemic recurrence (SR). Global recurrence (GR) included all categories.

OS was defined as the time from surgery to death from any cause. Data were also collected for conditional survival (CS), defined in the present study as OS among patients who survived for at least 30 days, 90 days, 6 months, and 1 year after surgery.

The main exposure variable was the occurrence of O/S-SSI based on descriptions and diagnoses in discharge summaries and according to the Centres for Disease Control and Prevention National Healthcare Safety Network classifications of operative procedures[16]. On this basis, an O/S-SSI in rectal surgery is an infection occurring within 30 days of the surgical procedure and involving any part of the body deeper than the fascial/muscle layers that are opened or manipulated during surgery. In addition, at least one of the following associated conditions must also be met: purulent drainage from a drain placed into the organ/space; identification of an organism(s) from fluid or tissue in the organ/space by culture- or non-culture-based microbiological testing methods, performed for the purpose of clinical diagnosis or treatment; an abscess or other evidence of infection involving the organ/space, detected on gross anatomical or histopathological examination; or definitive or equivocal evidence of infection on imaging tests or histopathologic examination or definitive evidence on imaging tests.

Other exposure variables included age, sex, American Society of Anesthesiologists (ASA) physical status classification, tumour variables, neoadjuvant therapy, surgical variables, and the grade of surgical complications according to the Clavien–Dindo classification.

Data sources and linkage of databases

Data were sourced from the periodic mandatory Catalan Cancer Plan (CCP) audits of rectal cancer[17,18], extracting detailed information on patient characteristics, preoperative diagnosis, surgical and adjuvant treatments, postoperative complications, oncological follow-up, and pathological examination of the excised specimen. These audits are conducted every 3–4 years, a time interval that is considered sufficient to detect potential changes in the quality of care provided to patients with rectal cancer. To validate the identification of O/S-SSI, CCP data were cross-checked against VINCat (The Infections Surveillance Programme VINCat from the Department of Health carries out standardized prospective surveillance of SSIs in colorectal surgery), a Catalan nosocomial infection surveillance program[19]. A detailed description of the linkage between the CCP and VINCat databases is provided elsewhere[20].

Inclusion and exclusion criteria

Eligible patients were those presenting with a tumour located no more than 13 cm from the anal verge (according to magnetic resonance imaging findings) who underwent oncological resection of the rectum for primary adenocarcinoma with curative intent in the periods 2011–2012 and 2015–2016. In the CCP, the most recent data are those corresponding to the 2015–2016 audit so that a follow-up of more than 5 years from the time of first surgery with curative intent is available.

Eligible surgical procedures included anterior rectal resection with total mesorectal excision (RAR), transanal total mesorectal excision (TaTME), abdominoperineal resection (APR), Hartmann procedure, total proctocolectomy, and pelvic exenteration.

The exclusion criteria were transanal local procedures, emergency surgery, stage IV tumours, non-resectable tumours, and palliative surgery.

Ethical considerations

Patient confidentiality and personal data protection were adhered to in accordance with European regulations by storing patient identifiers in a database that was independent of the clinical data used in the study and held by the CCP. The research ethics committee of the Bellvitge University Hospital approved this study (PR286/21). The study has been registered in ClinicalTrials.gov (NCT06382415).

Statistical analysis

Descriptive analysis used measures of central tendency and dispersion for continuous variables and absolute and relative frequencies for categorical variables. To measure the associations between baseline characteristics and the presence or absence of O/S-SSI, the χ^2 test was used for categorical variables and the non-parametric Mann–Whitney *U* test was used for continuous variables.

The Kaplan–Meier method was used to estimate the probability of OS and recurrence, and the log-rank test was used to evaluate the significance of differences between survival distributions.

To evaluate the effects of the exposure variables on recurrence and survival, multivariable analysis using the Cox proportional hazards model, adjusting for confounding factors was performed. The results are presented as hazard ratios (HRs) with 95% confidence intervals. All tests were considered statistically significant at $P \leq 0.050$. SPSS® (version 21.0; IBM Corp., Armonk, NY, USA) was used for all the analyses.

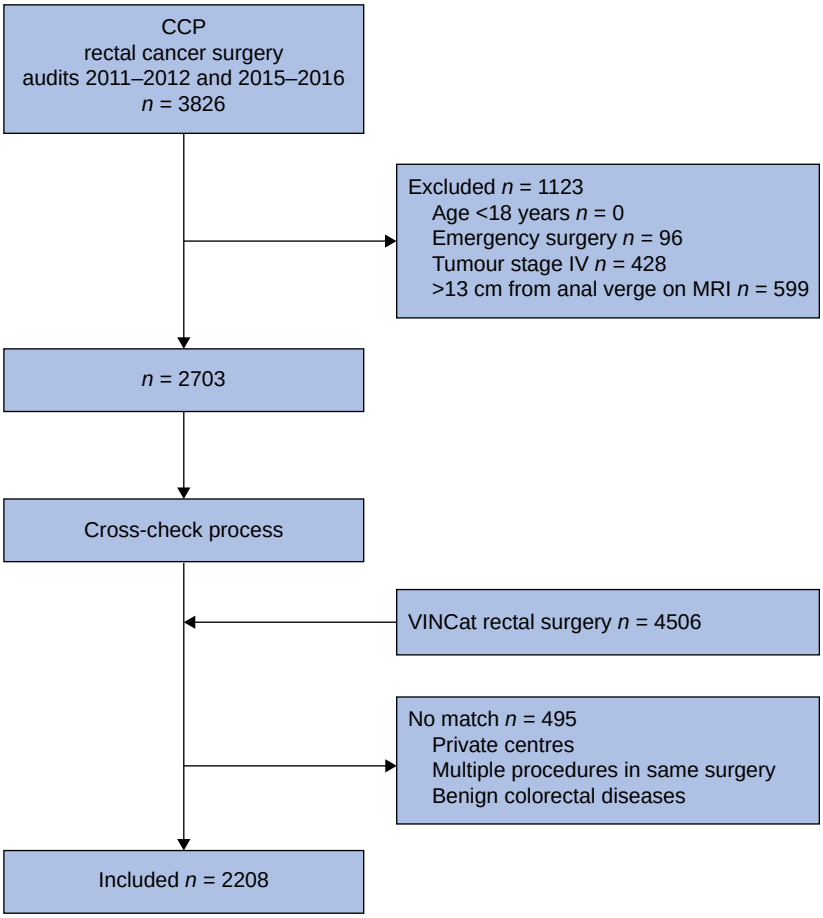

Fig. 1 Flow chart of participant inclusion in the study

CCP, Catalan Cancer Plan; MRI, magnetic resonance imaging; VINCat, Programme-Surveillance of Healthcare Related Infection in Catalonia.

Results

Data were retrieved for 3826 patients from the CCP audits (2011–2012 and 2015–2016), and for 4506 patients from the VINCat program for whom data were recorded during the same time periods. *Figure 1* illustrates the participant selection process. Of the patients included from the CCP audits, 1123 were excluded for various reasons. The remaining 2703 patients were cross-checked against the 4506 patients from the VINCat program; there was no match for 495 patients, who were excluded from the study. Ultimately, 2208 patients were included in this study. The characteristics of patients who were and were not in both databases are presented in *Table S1*.

Table 1 presents the characteristics of the sample. O/S-SSI occurred in 291 (13.2%) patients. O/S-SSI was more frequent in men than in women (14.9 *versus* 9.8%; $P = 0.001$), in patients with ASA grade III–IV than ASA grade I–II patients (15.8 *versus* 12%; $P = 0.016$), and in patients who underwent RAR/TaTME than in those who underwent PR/Hartmann procedures (14.3% *versus* 9.3%; $P = 0.001$). No association was found between neoadjuvant treatment and O/S-SSI ($P = 0.882$). In addition, there were no differences in the risk of O/S-SSI according to tumour location, tumour stage, or quality of surgery.

Assessing the Clavien–Dindo grade of surgical complications[21] in patients with O/S-SSI according to the type of surgical procedure, there were higher proportions of grade IIIB complications among those undergoing RAR and Hartmann procedures ($P = 0.039$), as shown in *Fig. S1*. RAR was the surgical procedure that led to the highest proportion of reinterventions under general anaesthesia (36.4%).

Recurrence

Cancer recurrence was diagnosed during follow-up in 486 patients (22.0%). There were no significant differences in the rate of global recurrence between patients with and without O/S-SSI (23.37 *versus* 21.81%; $P = 0.540$) or in the distribution of the type of recurrence between patients with and without O/S-SSI (*Fig. S2*).

Table S2 presents demographic, clinical, tumour-related, and surgical variables according to type of recurrence (LR, LR+/−SR, SR, and GR). Variables significantly associated with disease recurrence were the presence of stoma, pT classification, perineural invasion, and tumour stage.

In the multivariable analysis, the independent predictors of LR+/−SR were stage III cancer (HR 1.95, 95% c.i. 1.06 to 3.58; $P = 0.032$), perineural invasion (HR 1.78, 95% c.i. 1.19 to 2.66; $P = 0.005$), positive resection margins (HR 4.03, 95% c.i. 2.58 to 6.29; $P < 0.001$), and poor-quality mesorectal excision (HR 1.81, 95% c.i. 1.11 to 2.95; $P = 0.018$). The independent predictors of GR were tumour stage II (HR 1.74, 95% c.i. 1.10 to 2.77; $P = 0.019$), tumour stage III (HR 2.81, 95% c.i. 1.81 to 4.37; $P < 0.001$), perineural invasion (HR 1.86, 95% c.i. 1.48 to 2.33; $P < 0.001$), lymph node involvement (HR 1.38, 95% c.i. 1.07 to 1.78;

Table 1 Baseline characteristics according to the presence or absence of O/S-SSI

	No O/S-SSI ($n = 1917$)	O/S-SSI ($n = 291$)	Total ($n = 2208$)	P*
Age (years)				0.348
<60	441 (23.0%)	78 (26.8%)	519 (23.5%)	
60–79	1165 (60.8%)	170 (58.4%)	1335 (60.5%)	
≥80	311 (16.2%)	43 (14.8%)	354 (16.0%)	
Sex				0.001
Male	1246 (65.0%)	218 (74.9%)	1464 (66.3%)	
Female	671 (35.0%)	73 (25.1%)	744 (33.7%)	
ASA grade				0.016
I–II	1184 (61.8%)	161 (55.3%)	1345 (60.9%)	
III–IV	655 (34.2%)	123 (42.3%)	778 (35.2%)	
Unknown	78 (4.1%)	7 (2.4%)	85 (3.8%)	
Surgical procedure				0.001
RAR/TaTME	1391 (72.6%)	232 (79.7%)	1623 (73.5%)	
APR/Hartmann	513 (26.8%)	53 (18.2%)	566 (25.6%)	
Others/TP/PE	13 (0.7%)	6 (2.1%)	19 (0.9%)	
Surgical approach				0.797
Laparotomy	474 (24.7%)	70 (24.1%)	544 (24.6%)	
Laparoscopy	1261 (65.8%)	188 (64.6%)	1449 (65.6%)	
Laparoscopy with conversion	158 (8.2%)	29 (10.0%)	187 (8.5%)	
Unknown	24 (1.3%)	4 (1.4%)	28 (1.3%)	
Neoadjuvant therapy				0.882
No	582 (30.4%)	89 (30.6%)	671 (30.4%)	
Yes, CTx and/or RTx	1324 (69.1%)	201 (69.1%)	1525 (69.1%)	
Unknown	11 (0.6%)	1 (0.3%)	12 (0.5%)	
Neoadjuvant CTx				0.832
No	709 (37.0%)	105 (36.1%)	814 (36.9%)	
Yes	1194 (62.3%)	183 (62.9%)	1377 (62.4%)	
Unknown	14 (0.7%)	3 (1.0%)	17 (0.8%)	
Stoma				0.001
No stoma	329 (17.2%)	40 (13.7%)	369 (16.7%)	
Defunctioning stoma	1066 (55.6%)	197 (67.7%)	1263 (57.2%)	
Definitive stoma	273 (14.2%)	33 (11.3%)	306 (13.9%)	
Unknown	249 (13.0%)	21 (7.2%)	270 (12.2%)	
pT groups				0.642
pT0–pT2	956 (49.9%)	141 (48.5%)	1097 (49.7%)	
pT3	841 (43.9%)	134 (46.0%)	975 (44.2%)	
pT4	100 (5.2%)	15 (5.2%)	115 (5.2%)	
Unknown	20 (1.0%)	1 (0.3%)	21 (1.0%)	
Tumour location				0.670
Distal rectum (<6 cm)	716 (37.4%)	101 (34.7%)	817 (37.0%)	
Middle rectum (6–10 cm)	953 (49.7%)	152 (52.2%)	1105 (50.0%)	
Higher rectum (11–13 cm)	248 (12.9%)	38 (13.1%)	286 (13.0%)	
Lymph nodes				0.148
<12	667 (34.8%)	85 (29.2%)	752 (34.1%)	
≥12	1205 (62.9%)	197 (67.7%)	1402 (63.5%)	
Unknown	45 (2.3%)	9 (3.1%)	54 (2.4%)	
Tumour stage				0.611
0/I	279 (14.6%)	40 (13.7%)	319 (14.4%)	
II	406 (21.2%)	69 (23.7%)	475 (21.5%)	
III	1232 (64.3%)	182 (62.5%)	1414 (64.0%)	
Positive resection margin				0.541
Radical surgery	1730 (90.2%)	257 (88.3%)	1987 (90.0%)	
Non-radical surgery	103 (5.4%)	20 (6.9%)	123 (5.6%)	
Unknown	84 (4.4%)	14 (4.8%)	98 (4.4%)	
Quality of ME				0.446
No ME registered	139 (7.3%)	19 (6.5%)	158 (7.2%)	
Complete ME	1396 (72.8%)	226 (77.7%)	1622 (73.5%)	
Nearly complete ME	162 (8.5%)	21 (7.2%)	183 (8.3%)	
Incomplete ME	172 (9.0%)	21 (7.2%)	193 (8.7%)	
Unknown	48 (2.5%)	4 (1.4%)	52 (2.4%)	

O/S-SSI, organ/space-surgical site infection; ASA, American Society of Anesthesiologists; RAR, rectal anterior resection with total mesorectal excision; TaTME, transanal total mesorectal excision; APR, abdominoperineal resection; TP, total proctocolectomy; PE, pelvic exenteration; CTx, chemotherapy; RTx, radiotherapy; ME, mesorectal excision. *χ^2 test.

$P = 0.014$), positive resection margins (HR 1.83, 95% c.i. 1.35 to 2.49; $P < 0.001$), and nearly complete mesorectal excision (HR 1.62, 95% c.i. 1.21 to 2.17; $P = 0.001$). However, there was no association between O/S-SSIs and any type of recurrence (*Table 2*).

There were no differences in the cumulative risk of cancer recurrence between patients with and without O/S-SSI at any time point after surgery (*Fig. 2*). *Fig. S3* shows the cumulative risk of different recurrence categories according to the occurrence of O/S-SSI.

Survival

In multivariable analysis (*Table 3*), O/S-SSI was independently associated with reduced OS at 1 year (HR 2.20, 95% c.i. 1.39 to 3.48; $P < 0.001$), 2 years (HR 1.75, 95% c.i. 1.25 to 2.43; $P < 0.001$),

Table 2 Multivariable Cox proportional hazards regression analysis of recurrence at the 5-year follow-up

	n	Locoregional recurrence		Locoregional with or without systemic recurrence		Systemic recurrence		Global recurrence	
		HR	*P*	HR	*P*	HR	*P*	HR	*P*
O/S-SSI									
No	1917	1 (Reference)	0.724	1 (Reference)	0.671	1 (Reference)	0.693	1 (Reference)	0.888
Yes	291	0.90 (0.51, 1.59)	0.724	0.90 (0.55, 1.47)	0.671	1.07 (0.77, 1.48)	0.693	1.02 (0.78, 1.34)	0.888
Age (years)									
<60	519	1 (Reference)	0.445	1 (Reference)	0.125	1 (Reference)	0.561	1 (Reference)	0.594
60–79	1335	0.79 (0.50, 1.23)	0.298	0.78 (0.52, 1.15)	0.207	1.16 (0.89, 1.51)	0.283	1.02 (0.82, 1.28)	0.828
≥80	354	1.02 (0.56, 1.85)	0.946	1.19 (0.72, 1.97)	0.498	1.13 (0.77, 1.65)	0.530	1.16 (0.86, 1.57)	0.338
Sex									
Female	744	1 (Reference)	0.300	1 (Reference)	0.085	1 (Reference)	0.392	1 (Reference)	0.120
Male	1464	1.25 (0.82, 1.89)	0.300	1.38 (0.96, 2.00)	0.085	1.11 (0.88, 1.40)	0.392	1.17 (0.96, 1.43)	0.120
ASA grade									
I–II	1345	1 (Reference)	0.420	1 (Reference)	0.739	1 (Reference)	0.710	1 (Reference)	0.943
III–IV	778	1.20 (0.80, 1.80)	0.384	1.12 (0.79, 1.60)	0.516	0.90 (0.71, 1.15)	0.414	0.97 (0.79, 1.18)	0.742
Unknown	85	1.64 (0.70, 3.84)	0.257	1.25 (0.54, 2.89)	0.598	0.93 (0.51, 1.71)	0.815	1.01 (0.62, 1.66)	0.960
Surgical procedure									
RAR/TaTME	1623	1 (Reference)	0.001	1 (Reference)	0.005	1 (Reference)	0.375	1 (Reference)	0.216
APR/Hartmann	566	1.18 (0.77, 1.80)	0.449	1.15 (0.80, 1.67)	0.448	1.16 (0.90, 1.48)	0.251	1.15 (0.94, 1.41)	0.184
Others/TP/PE	19	7.07 (2.47, 20.25)	<0.001	5.44 (1.93, 15.34)	0.001	0.46 (0.06, 3.32)	0.443	1.74 (0.71, 4.26)	0.225
Tumour stage									
0/I	319	1 (Reference)	0.034	1 (Reference)	<0.001	1 (Reference)	<0.001	1 (Reference)	<0.001
II	475	0.74 (0.34, 1.59)	0.437	0.79 (0.38, 1.67)	0.540	2.58 (1.42, 4.70)	0.002	1.74 (1.10, 2.77)	0.019
III	1414	1.49 (0.80, 2.78)	0.212	1.95 (1.06, 3.58)	0.032	3.58 (2.01, 6.39)	<0.001	2.81 (1.81, 4.37)	<0.001
Perineural invasion									
No	1706	1 (Reference)	0.128	1 (Reference)	0.006	1 (Reference)	<0.001	1 (Reference)	<0.001
Yes	356	1.53 (0.95, 2.47)	0.079	1.78 (1.19, 2.66)	0.005	1.89 (1.44, 2.48)	<0.001	1.86 (1.48, 2.33)	<0.001
Unknown	146	0.49 (0.09, 2.64)	0.405	0.35 (0.07, 1.83)	0.214	1.01 (0.52, 1.98)	0.973	0.87 (0.48, 1.58)	0.646
Lymph nodes									
No	1768	1 (Reference)	0.450	1 (Reference)	0.372	1 (Reference)	0.054	1 (Reference)	0.047
Yes	278	1.02 (0.61, 1.73)	0.931	1.20 (0.77, 1.85)	0.423	1.46 (1.07, 2.00)	0.016	1.38 (1.07, 1.78)	0.014
Unknown	162	0.34 (0.06, 1.83)	0.210	0.47 (0.12, 1.83)	0.278	1.21 (0.65, 2.24)	0.556	0.99 (0.57, 1.71)	0.960
Positive resection margin									
Radical surgery	1987	1 (Reference)	<0.001	1 (Reference)	<0.001	1 (Reference)	0.446	1 (Reference)	<0.001
Non-radical surgery	123	4.53 (2.73, 7.53)	<0.001	4.03 (2.58, 6.29)	<0.001	1.06 (0.68, 1.67)	0.789	1.83 (1.35, 2.49)	<0.001
Unknown	98	1.35 (0.53, 3.43)	0.526	1.32 (0.57, 3.07)	0.518	0.67 (0.35, 1.27)	0.219	0.84 (0.50, 1.40)	0.500
Quality of ME									
Complete ME	1622	1 (Reference)	0.038	1 (Reference)	0.033	1 (Reference)	0.174	1 (Reference)	0.013
No ME registered	158	2.04 (1.10, 3.81)	0.025	1.67 (0.93, 3.00)	0.089	1.01 (0.64, 1.58)	0.968	1.18 (0.83, 1.69)	0.359
Nearly complete ME	183	1.75 (0.96, 3.21)	0.069	1.82 (1.09, 3.05)	0.022	1.55 (1.09, 2.21)	0.015	1.62 (1.21, 2.17)	<0.001
Incomplete ME	193	1.88 (1.08, 3.30)	0.027	1.81 (1.11, 2.95)	0.018	1.14 (0.78, 1.66)	0.511	1.32 (0.98, 1.78)	0.069
Unknown	52	1.72 (0.61, 4.83)	0.303	1.54 (0.61, 3.86)	0.361	0.86 (0.40, 1.85)	0.708	1.03 (0.57, 1.85)	0.923
Neoadjuvant therapy									
No	671					1 (Reference)	0.030	1 (Reference)	0.169
Yes: CTx and/or RTx	1525					1.13 (0.83, 1.52)	0.434	1.10 (0.86, 1.41)	0.447
Unknown	12					4.83 (1.48, 15.79)	0.009	2.91 (0.91, 9.33)	0.073

Values in parentheses are 95% confidence intervals. HR, hazard ratio; OS-SSI, organ/space surgical site infection; ASA, American Society of Anesthesiologists; RAR, rectal anterior resection with total mesorectal excision; TaTME, transanal total mesorectal excision; APR, abdominoperineal resection; TP, total proctocolectomy; PE, pelvic exenteration; ME, mesorectal excision; CTx, chemotherapy; RTx, radiotherapy.

and 5 years (HR 1.33, 95% c.i. 1.05 to 1.68; $P = 0.017$). Other factors independently associated with reduced 5-year OS were age over 80 years (HR 3.70, 95% c.i. 2.76 to 4.97; $P < 0.001$), male sex (HR 1.21, 95% c.i. 1.00 to 1.45; $P = 0.047$), ASA grade III–IV (HR 1.93, 95% c.i. 1.62 to 2.31; $P < 0.001$), tumour stage III (HR 1.94, 95% c.i. 1.40 to 2.68; $P < 0.001$), APR/Hartmann procedures (HR 1.31, 95% c.i. 1.09 to 1.58; $P = 0.004$), perineural invasion (HR 1.57, 95% c.i. 1.27 to 1.94; $P < 0.001$), lymph node invasion (HR 1.58, 95% c.i. 1.25 to 2.00; $P < 0.001$), positive resection margins (HR 2.17, 95% c.i. 1.66 to 2.83; $P < 0.001$), and high-quality mesorectal excision (HR 1.38, 95% c.i. 1.01 to 1.87; $P = 0.043$). In contrast, neoadjuvant therapy was associated with increased OS (HR 0.78, 95% c.i. 0.63 to 0.96; $P = 0.019$).

In patients who lived beyond 30 and 90 days after surgery, 1-year and 2-year conditional survival was lower in those with than without O/S-SSI ($P < 0.050$). There was no association between O/S-SSI and CS in patients who lived beyond 6 months after surgery (*Table S3*).

As shown in *Fig. 3*, 5-year CS was reduced among patients with *versus* without postoperative O/S-SSI for those who lived for >30 days (76.3 *versus* 69.4%; $P = 0.013$, χ^2), as was 2-year CS for those with *versus* without postoperative O/S-SSI who lived beyond 30 days (91 *versus* 85.9%; $P = 0.013$, χ^2) and 90 days (91.4 *versus* 87.1% $P = 0.026$, χ^2).

Discussion

This population-based study showed an association between O/S-SSI and reduced long-term OS in patients who underwent curative rectal cancer surgery; however, there was no association with an increased risk of local or systemic recurrence during the 5-year follow-up period.

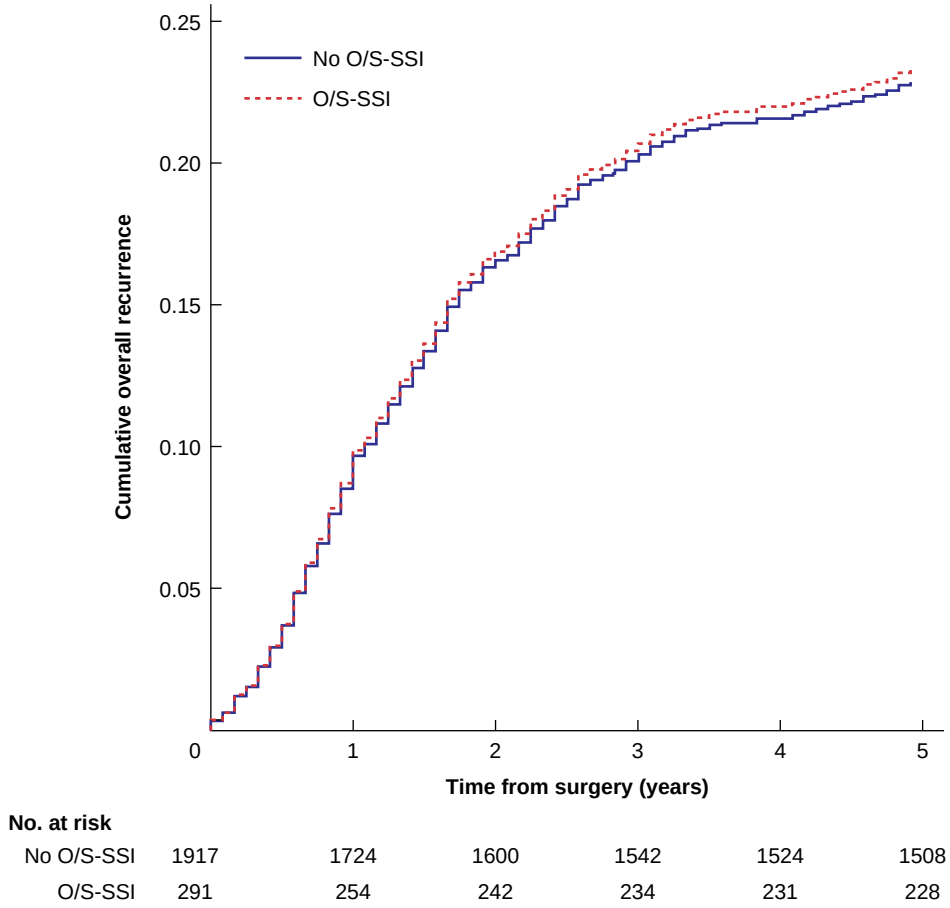

Fig. 2 Cumulative recurrence in patients with and without O/S-SSI

OS-SSI, organ/space surgical site infection. $P = 0.890$.

Although several studies have reported associations between O/S-SSI and poor short-term outcomes, evidence regarding long-term oncological outcomes remains inconclusive[22,23]. Some studies have reported an association between AL and O/S-SSI with tumour recurrence[24], whereas other studies have reported no such association[25,26]. The long-term follow-up of two multicentre randomized controlled trials comparing laparoscopic and open surgery for rectal cancer (CAO/ARO/AIO-94[27] and COLOR II[28]) showed that AL was an independent risk factor for local recurrence and decreased disease-free survival. Several recent meta-analyses have supported this association. Lawler *et al.* included 43 studies (154 981 patients) on colorectal cancer surgery and found that AL and postoperative O/S-SSI had a significant negative impact on disease-free survival, local recurrence, and overall recurrence[10]. In another meta-analysis of 18 cohort studies (34 487 patients), Ma *et al.* specifically investigated the effects of AL after anterior resection for rectal cancer[29]. In that analysis, AL was found to be associated with increased local recurrence and decreased disease-free survival, cancer-specific survival, and OS[29]. However, these results should be interpreted with caution because the main aim of the studies was not to assess outcomes after AL[27,28], or the findings were obtained from observational studies with a significant level of heterogeneity[10,24,29].

Population-based studies based on data from oncological registries that evaluate postoperative complications may be especially useful for understanding the relationship between O/S-SSI and oncological outcomes. These registries provide high-quality data for all treated patients, with standard definitions of events, standard methods for magnetic resonance imaging and pathological diagnosis, and uniform surgical techniques. Another retrospective population-based study including 22 855 rectal cancer patients recently evaluated long-term oncological outcomes after colorectal AL using data from the Netherlands Cancer Registry[30]. In that study, there were no differences in 4-year disease-free survival between patients with and without AL (81.4 *versus* 80.2%, respectively), and multivariable Cox proportional hazard regression revealed no association between AL and disease recurrence[30].

The variable quality of published studies, ranging from single-centre retrospective studies to population-based or propensity-matched cohort studies, may help explain their contradictory conclusions. Other explanations include differences in the definition of AL and the severity of O/S-SSI. Several studies have found negative effects on oncological outcomes in patients with the most severe complications requiring reintervention. In one observational study from the Colon/Rectum Carcinoma Group (University of Magdeburg, Germany), Ptok *et al.* investigated the influence of AL on oncological outcomes in 1741 patients undergoing curative resection of rectal cancer[8]. In that study, patients with AL who needed surgical treatment *versus* those without AL had a higher 5-year local recurrence rate (17.5 *versus* 10.1%; $P = 0.006$) and a lower 5-year disease-free survival rate (70.9 *versus* 75.4%; $P =$

Table 3 Cox proportional hazards regression analysis of independent factors influencing overall survival at 1, 2, and 5 years

	n	1-year mortality		2- year mortality		5-year mortality	
		HR	P	HR	P	HR	P
O/S-SSI							
No	1917	1 (Reference)		1 (Reference)		1 (Reference)	
Yes	291	2.20 (1.39, 3.48)	<0.001	1.75 (1.25, 2.43)	<0.001	1.33 (1.05, 1.68)	0.017
Age (years)							
<60	519	1 (Reference)	<0.001	1 (Reference)	<0.001	1 (Reference)	<0.001
60–79	1335	2.29 (1.12, 4.67)	0.023	1.72 (1.13, 2.60)	0.011	1.74 (1.34, 2.26)	<0.001
≥ 80	354	4.69 (2.21, 9.98)	<0.001	3.36 (2.14, 5.29)	<0.001	3.70 (2.76, 4.97)	<0.001
Sex							
Female	744	1 (Reference)		1 (Reference)		1 (Reference)	
Male	1464	1.22 (0.79, 1.89)	0.371	1.19 (0.89, 1.59)	0.243	1.21 (1.00, 1.45)	0.047
ASA grade							
I–II	1345	1 (Reference)	0.001	1 (Reference)	<0.001	1 (Reference)	<0.001
III–IV	778	2.22 (1.46, 3.37)	<0.001	2.20 (1.66, 2.92)	<0.001	1.93 (1.62, 2.31)	<0.001
Unknown	85	1.69 (0.59, 4.82)	0.330	2.54 (1.40, 4.62)	0.002	1.62 (1.05, 2.52)	0.031
Surgical procedure							
RAR/TaTME	1623	1 (Reference)	0.093	1 (Reference)	0.043	1 (Reference)	0.004
APR/Hartmann	566	1.29 (0.84, 1.97)	0.245	1.22 (0.91, 1.63)	0.180	1.31 (1.09, 1.58)	0.004
Other/TP/PE	19	3.27 (1.00, 10.74)	0.050	2.83 (1.14, 7.04)	0.025	2.07 (0.97, 4.43)	0.059
Tumour stage							
0/I	319	1 (Reference)	0.524	1 (Reference)	0.001	1 (Reference)	<0.001
II	475	1.08 (0.54, 2.15)	0.837	1.34 (0.79, 2.27)	0.273	1.25 (0.89, 1.75)	0.198
III	1414	1.37 (0.71, 2.67)	0.348	2.20 (1.34, 3.62)	0.002	1.94 (1.40, 2.68)	<0.001
Neoadjuvant therapy							
No	671	1 (Reference)	0.101	1 (Reference)	0.006	1 (Reference)	0.662
Yes	1525	0.63 (0.40, 0.99)	0.045	0.60 (0.44, 0.82)	0.001	0.78 (0.63, 0.96)	0.019
Unknown	12	1.94 (0.26, 14.66)	0.520	1.01 (0.14, 7.40)	0.991	0.82 (0.20, 3.32)	0.776
Perineural invasion							
No	1706	1 (Reference)	0.117	1 (Reference)	<0.001	1 (Reference)	<0.001
Yes	356	1.64 (1.03, 2.64)	0.039	1.76 (1.29, 2.41)	<0.001	1.57 (1.27, 1.94)	<0.001
Unknown	146	1.13 (0.33, 3.86)	0.845	0.57 (0.24, 1.35)	0.201	0.64 (0.34, 1.20)	0.163
Lymph node invasion							
No	1768	1 (Reference)	0.015	1 (Reference)	0.004	1 (Reference)	<0.001
Yes	278	2.07 (1.26, 3.39)	0.036	1.73 (1.22, 2.44)	0.002	1.58 (1.25, 2.00)	<0.001
Unknown	162	1.09 (0.35, 3.36)	0.883	1.80 (0.93, 3.49)	0.080	1.03 (0.60, 1.78)	0.911
Positive resection margin							
Radical surgery	1987	1 (Reference)	0.106	1 (Reference)	0.003	1 (Reference)	<0.001
No radical surgery	123	1.84 (1.04, 3.26)	0.036	1.96 (1.33, 2.87)	<0.001	2.17 (1.66, 2.83)	<0.001
Unknown	98	1.24 (0.49, 3.15)	0.654	1.16 (0.61, 2.19)	0.651	0.99 (0.63, 1.56)	0.961
Quality of ME							
Complete ME	1622	1 (Reference)	0.471	1 (Reference)	0.032	1 (Reference)	0.049
No ME registered	158	1.35 (0.69, 2.65)	0.385	1.29 (0.80, 2.07)	0.290	1.38 (1.01, 1.87)	0.043
Nearly Complete ME	183	1.70 (0.93, 3.11)	0.087	1.67 (1.11, 2.51)	0.015	1.38 (1.05, 1.83)	0.023
Incomplete ME	193	1.15 (0.61, 2.19)	0.661	1.12 (0.72, 1.74)	0.609	1.09 (0.82, 1.45)	0.550
Unknown	52	1.48 (0.45, 4.86)	0.514	2.17 (1.11, 4.21)	0.023	1.46 (0.86, 2.47)	0.159

Values in parentheses are 95% confidence intervals. HR, hazard ratio; OS-SSI, organ/space surgical site infection; ASA, American Society of Anesthesiologists; RAR, rectal anterior resection with total mesorectal excision; TaTME, transanal total mesorectal excision; APR, abdominoperineal resection; TP, total proctocolectomy; PE, pelvic exenteration; ME, mesorectal excision; CTx, chemotherapy; RTx, radiotherapy.

0.020); however, there was no association between AL not requiring surgical intervention and worse oncological outcomes[8]. Takahashi *et al.* evaluated the long-term outcomes of 615 patients who underwent curative resection of colorectal cancer without postoperative complications *versus* 44 similar patients who experienced AL[31] (grade A in 7 patients, grade B in 21 patients, and grade C in 16 patients, according to criteria proposed by the International Study Group of Rectal Cancer[32]). Patients with grades A and B AL received conservative treatment, whereas those with grade C AL received surgical treatment. The grade C group had significantly worse recurrence-free survival and cancer-specific survival[31]. This is particularly relevant because one proposed mechanism for the negative effect of AL is a surgery-induced inflammatory response that leads to the release of soluble factors capable of stimulating viable residual tumour cells as well as dormant micrometastases[33,34].

Although there was no association between O/S-SSI and an increased risk of local or systemic recurrence in the present study, the association with reduced 1-year, 2-year, and 5-year survival is highly relevant. When the analysis included only patients who lived beyond 30 and 90 days after surgery, the 1-year and 2-year survival rates were still lower in patients with than without O/S-SSI. Interestingly, previous studies have also demonstrated reduced long-term OS in patients with AL and O/S-SSI, without an increase in cancer recurrence. For example, Odermatt *et al.* investigated the impact of major complications (Clavien–Dindo IIIb–IVb) in 844 colorectal cancer resections[35]. After excluding postoperative or in-hospital deaths, 39 major complications (5%) remained in the analysis. After a median follow-up of 5.7 years, the estimated crude 5-year OS probability was 78% in the group without major complications and 65% in the group with major complications[35]. Furthermore, major complications were a significant negative predictor for OS (HR 2.42, 95% c.i. 1.41 to 4.14), but not for time to recurrence (HR 1.29, 95% c.i. 0.56 to 2.99)[35]. Arnarson *et al.* analyzed the effect of postoperative complications following radical resection

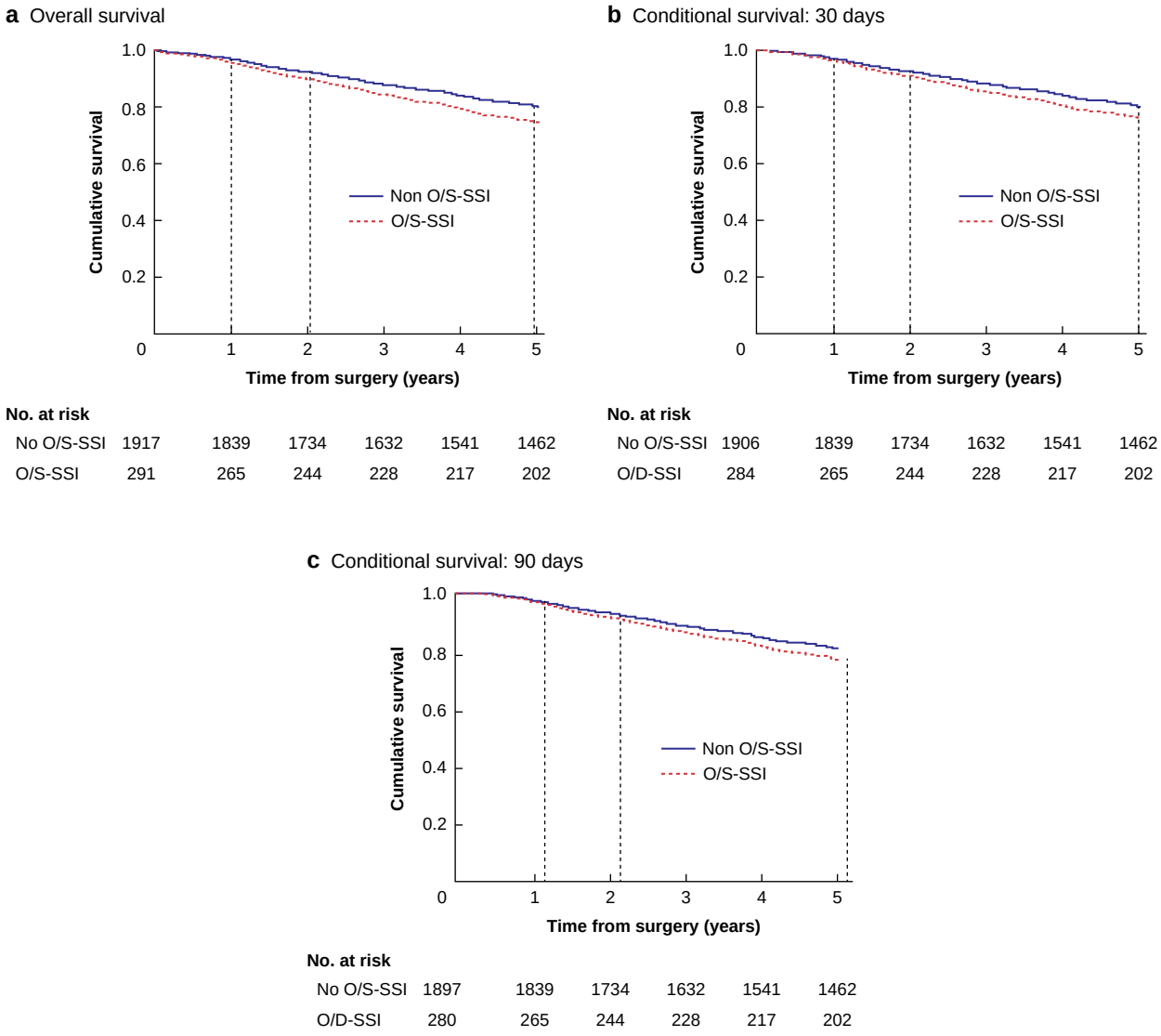

Fig. 3 Cumulative overall and conditional survival in patients with and without O/S-SSI

a Cumulative survival. Log rank $P < 0.001$, $P < 0.001$, and $P = 0.017$ at 1, 2 and 5 years, respectively. **b** Conditional survival: 30 days. Log rank $P = 0.020$, $P = 0.012$, and $P = 0.068$ at 1, 2 and 5 years, respectively. **c** Conditional survival: 90 days. Log rank $P = 0.047$, $P = 0.025$, and $P = 0.108$ at 1, 2 and 5 years, respectively. OS-SSI, organ/space surgical site infection.

for colorectal cancer on long-term outcomes using prospectively registered data from the Swedish Colorectal Cancer Registry[36]. In that study, the cohort of 6779 patients was divided into three subgroups: patients who developed severe postoperative complications (AL, reintervention, and septicaemia), patients who developed non-severe complications, and patients without any complications (controls). The 5-year overall OS rates were 60.3%, 64.2%, and 72.8% in the severe, non-severe, and control groups, respectively ($P < 0.010$)[36]. The recurrence rate was similar among the three groups. More recently, in a single-centre 10-year retrospective cohort study of colon cancer patients undergoing planned R0 colonic resection with primary anastomosis[37], patients with AL (57 of 686; 8.3%) had higher postoperative morbidity and mortality and lower long-term OS. However, AL did not affect local or distant recurrence[37].

It is unclear why AL is associated with reduced long-term OS but not with increased tumour recurrence. Possible explanations include unresolved inflammation that can lead to frailty and decompensation of co-morbidities[35,37]. Many of these patients with AL present chronic pelvic sepsis requiring frequent hospital readmissions and additional complications leading to a general deterioration. Long-term stoma-related complications may be another contributing factor. In this sense, long-term survival in patients who experience severe postoperative complications is directly related to a hospital's ability to implement surgical quality improvement initiatives focused on intermediate-term and long-term care, as well as perioperative care. For example, to manage the long-term sequelae of hospitalization for sepsis, the care model should include timely source control, post-discharge rehabilitation, screening for new chronic medical conditions, adequate medication reconciliation, and the assurance of adequate support systems. Patients treated at hospitals with poor failure-to-rescue performance had not only higher perioperative mortality rates but also worse long-term survival[38,39].

The present study has two main limitations. First, the retrospective data analysis does not allow the determination of causal associations. Second, cases of rectal cancer treated in

private hospitals (approximately 10% of all surgical cases) were not included because the CCP audit only covers public hospitals. The strengths of this study include its population-based design and the combination of clinical data from two different sources, specifically two robust registry systems that collect information on the occurrence of O/S-SSI. Both registries have a wide population coverage and a long trajectory in clinical monitoring[19,40]. The level of concordance in the detection of O/S-SSI between the two databases was satisfactory ($k = 0.69$, 95% c.i. 0.65 to 0.73)[20], validating their robustness. Furthermore, the O/S-SSI rate of 13% in the present study is consistent with the results of systematic reviews and data reported by the national colorectal cancer registries in Denmark, Norway and Spain[13,14,41]. The 5-year global recurrence rate of 22% is in line with recent data showing an improvement in oncological outcomes after rectal cancer treatment over the past decade. A recent nationwide Danish cohort study, including 34 166 patients with colorectal cancer found that the risk of recurrence decreased in patients with stage I–III disease from 2004 to 2019. Recurrence rates for rectal cancer specifically decreased from 29.4% in the period 2004–2008 to 24.9% in the period 2009–2013 and to 18.3% in the period 2014–2019[2]. Therefore, the consistency of these results reflects the quality and external validity of the analysed data.

Funding

This research was funded by the Departament de Recerca i Universitats de la Generalitat de Catalunya i l'AGAUR" (Grant number 2021 SGR 00808). The authors thank CERCA Programme/Generalitat de Catalunya for institutional support.

Acknowledgements

The authors thank Julia Turner for editorial support.

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

Data supporting this study are not publicly available due to privacy and confidentiality restrictions and ethical reasons.

References

1. Feeney G, Sehgal R, Sheehan M, Hogan A, Regan M, Joyce M *et al.* Neoadjuvant radiotherapy for rectal cancer management. *World J Gastroenterol* 2019;**25**:4850–4869
2. Nors J, Iversen LH, Erichsen R, Gotschalck KA, Andersen CL. Incidence of recurrence and time to recurrence in stage I to III colorectal cancer: a nationwide Danish cohort study. *JAMA Oncol* 2024;**10**:54–62
3. Leonard D, Penninckx F, Laenen A, Kartheuser A. Quantitative contribution of prognosticators to oncologic outcome after rectal cancer resection. *Dis Colon Rectum* 2015;**58**:566–574
4. Agger EA, Jörgren FH, Lydrup MLA, Buchwald PL. Risk of local recurrence of rectal cancer and circumferential resection margin: population-based cohort study. *Br J Surg* 2020;**107**:580–585
5. Oh CK, Huh JW, Lee YJ, Choi MS, Pyo DH, Lee SC *et al.* Long-term oncologic outcome of postoperative complications after colorectal cancer surgery. *Ann Coloproctol* 2020;**36**:273–280
6. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. *Br J Surg* 2015;**102**:462–479
7. Sánchez-Velázquez P, Pera M, Jiménez-Toscano M, Mayol X, Rogés X, Lorente L *et al.* Postoperative intra-abdominal infection is an independent prognostic factor of disease-free survival and disease-specific survival in patients with stage II colon cancer. *Clin Transl Oncol* 2018;**20**:1321–1328
8. Ptok H, Marusch F, Meyer F, Schubert D, Gastinger I, Lippert H. Impact of anastomotic leakage on oncological outcome after rectal cancer resection. *Br J Surg* 2007;**94**:1548–1554
9. Akabane S, Egi H, Takakura Y, Sada H, Kochi M, Taguchi K *et al.* The prognostic value of organ/space surgical site infection in stage I colorectal cancer recurrence. *Int J Colorectal Dis* 2020;**35**:1689–1694
10. Lawler J, Choynowski M, Bailey K, Bucholc M, Johnston A, Sugrue M. Meta-analysis of the impact of postoperative infective complications on oncological outcomes in colorectal cancer surgery. *BJS Open* 2020;**4**:737–747
11. Markar S, Gronnier C, Duhamel A, Mabrut JY, Bail JP, Carrere N *et al.* The impact of severe anastomotic leak on long-term survival and cancer recurrence after surgical resection for esophageal malignancy. *Ann Surg* 2015;**262**:972–980
12. Artinyan A, Orcutt ST, Anaya DA, Richardson P, Chen GJ, Berger DH. Infectious postoperative complications decrease long-term survival in patients undergoing curative surgery for colorectal cancer: a study of 12,075 patients. *Ann Surg* 2015;**261**:497–505
13. Espín E, Ciga MA, Pera M, Ortiz H, Lujan J, Fraccalvieri D *et al.* Oncological outcome following anastomotic leak in rectal surgery. *Br J Surg* 2015;**102**:416–422
14. Bertelsen CA, Andreasen AH, Jørgensen T, Harling H. Anastomotic leakage after curative anterior resection for rectal cancer: short and long-term outcome. *Colorectal Disease* 2010;**12**:76–81
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;**335**:806–808
16. National Healthcare Safety Network. *Surgical Site Infection Event (SSI)*. 2022 December. https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (accessed January 2025)
17. Manchon-Walsh P, Borras JM, Espinas JA, Aliste L. Variability in the quality of rectal cancer care in public hospitals in Catalonia (Spain): clinical audit as a basis for action. *Eur J Surg Oncol* 2011;**37**:325–333
18. Manchon-Walsh P, Aliste L, Espinàs JA, Prades J, Guarga A, Balart J *et al.* Improving survival and local control in rectal cancer in Catalonia (Spain) in the context of centralisation: a full cycle audit assessment. *Eur J Surg Oncol* 2016;**42**:1873–1880
19. Arroyo-Garcia N, Badia JM, Vázquez A, Pera M, Parés D, Limón E *et al.* An interventional nationwide surveillance program lowers postoperative infection rates in elective colorectal surgery. A cohort study (2008–2019). *Int J Surg* 2022;**102**:106611
20. Matallana C, Pera M, Espin-Basany E, Biondo S, Badia JM, Limon E *et al.* Quality check: concordance between two monitoring systems for postoperative organ/space-surgical site infections in rectal cancer surgery. Linkage of data from the Catalan

Cancer Plan and the VINCat infection surveillance programme. *World J Surg Oncol* 2024;**22**:1–8
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;**240**:205–213
22. Boström P, Haapamäki MM, Rutegård J, Matthiessen P, Rutegård M. Population-based cohort study of the impact on postoperative mortality of anastomotic leakage after anterior resection for rectal cancer. *BJS Open* 2019;**3**:106–111
23. Weber MC, Berlet M, Stoess C, Reischl S, Wilhelm D, Friess H *et al.* A nationwide population-based study on the clinical and economic burden of anastomotic leakage in colorectal surgery. *Langenbecks Arch Surg* 2023;**408**:1–11
24. Mirnezami A, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* 2011;**253**: 890–899
25. Crippa J, Duchalais E, Machairas N, Merchea A, Kelley SR, Larson DW. Long-term oncological outcomes following anastomotic leak in rectal cancer surgery. *Dis Colon Rectum* 2020;**63**:769–777
26. Jang JH, Kim HC, Huh JW, Park YA, Cho YB, Yun SH *et al.* Anastomotic leak does not impact oncologic outcomes after preoperative chemoradiotherapy and resection for rectal cancer. *Ann Surg* 2019;**269**:678–685
27. Sprenger T, Beißbarth T, Sauer R, Tschmelitsch J, Fietkau R, Liersch T *et al.* Long-term prognostic impact of surgical complications in the German Rectal Cancer Trial CAO/ARO/ AIO-94. *Br J Surg* 2018;**105**:1510–1518
28. Koedam TWA, Bootsma BT, Deijen CL, Van De Brug T, Kazemier G, Cuesta MA *et al.* Oncological outcomes after anastomotic leakage after surgery for colon or rectal cancer: increased risk of local recurrence. *Ann Surg* 2022;**275**:E420–E427
29. Ma L, Pang X, Ji G, Sun H, Fan Q, Ma C. The impact of anastomotic leakage on oncology after curative anterior resection for rectal cancer. *Medicine (Baltimore)* 2020;**99**:e22139
30. Arron MNN, Greijdanus NG, Bastiaans S, Vissers PAJ, Verhoeven RHA, ten Broek RPG *et al.* Long-term oncological outcomes after colorectal anastomotic leakage a retrospective Dutch population-based study. *Ann Surg* 2022;**276**:882–889
31. Takahashi H, Haraguchi N, Nishimura J, Hata T, Yamamoto H, Matsuda C *et al.* The severity of anastomotic leakage may negatively impact the long-term prognosis of colorectal cancer. *Anticancer Res* 2018;**38**:533–539
32. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A *et al.* Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery* 2010;**147**:339–351
33. Salvans S, Mayol X, Alonso S, Messeguer R, Pascual M, Mojal S *et al.* Postoperative peritoneal infection enhances migration and invasion capacities of tumour cells in vitro: an insight into the association between anastomotic leak and recurrence after surgery for colorectal cancer. *Ann Surg* 2014; **260**:939–944
34. Alonso S, Pascual M, Salvans S, Mayol X, Mojal S, Gil MJ *et al.* Postoperative intra-abdominal infection and colorectal cancer recurrence: a prospective matched cohort study of inflammatory and angiogenic responses as mechanisms involved in this association. *Eur J Surg Oncol* 2015;**41**:208–214
35. Odermatt M, Miskovic D, Flashman K, Khan J, Senapati A, O'Leary D *et al.* Major postoperative complications following elective resection for colorectal cancer decrease long-term survival but not the time to recurrence. *Colorectal Dis* 2015;**17**: 141–149
36. Arnarson Ö, Butt-Tuna S, Syk I. Postoperative complications following colonic resection for cancer are associated with impaired long-term survival. *Colorectal Dis* 2019;**21**:805–815
37. Brito da Silva F, Lopes P, Cavadas D, Pereira Gonçalves B, Bernardo M, Abecasis N *et al.* The impact of anastomotic leakage after curative colon cancer resection on long-term survival: a retrospective cohort study. *Cir Esp (Engl Ed)* 2023; **102**:3–10
38. Portuondo JI, Farjah F, Massarweh NN. Association between hospital perioperative quality and long-term survival after noncardiac surgery. *JAMA Surg* 2022;**157**:258–268
39. Pera M. Anastomotic leak in colorectal cancer surgery: short term outcomes have long term consequences. *Cir Esp (Engl Ed)* 2024;**102**:185–187
40. Gudiol F, Limón E, Fondevilla E, Argimon JM, Almirante B, Pujol M. The development and successful implementation of the VINCat program. *Enferm Infecc Microbiol Clin* 2012;**30**:3–6
41. Eriksen MT, Wibe A, Norstein J, Haffner J, Wiig JN. Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. *Colorectal Dis* 2005;**7**:51–57