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A.K. Warps [a, b], R.A.E.M. Tollenaar [a, b], P.J. Tanis [c], J.W.T. Dekker [d, *], on behalf of the Dutch ColoRectal Audit

[a] Leiden University Medical Centre, Department of Surgery, Albinusdreef 2, 2333, ZA, Leiden, the Netherlands
[b] Dutch Institute for Clinical Auditing, Rijnsburgerweg 10, 2333, AA, Leiden, the Netherlands
[c] Amsterdam University Medical Centres, Department of Surgery, University of Amsterdam, Cancer Centre Amsterdam, 1117 Boelelaan, 1081, HV, Amsterdam, the Netherlands
[d] Reinier de Graaf Groep, Department of Surgery, Reinier de Graafweg 5, 2625, AD, Delft, the Netherlands

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ABSTRACT

Background: Complications after colorectal cancer surgery can worsen long-term survival. The aim of this nationwide study was to determine the impact of different types of complications on overall survival (OS) and conditional survival if still alive one year postoperatively (CS-1) after colorectal cancer surgery.
Materials and methods: All patients registered in the Dutch ColoRectal Audit after resection of primary colorectal cancer between 2011 and 2017 and with known survival status were included. Multivariable Cox regression models were used to assess the association of complications with OS and CS-1, thereby calculating the Hazard Ratio (HR) with 95% Confidence Interval.
Results: 43,908 colon and 16,955 rectal cancer patients were included. Median follow-up time was 66.1 and 66.5 months, respectively. Five-year OS after colon cancer resection was 73.2% without complications, and 65.4% with surgical, 52.9% with non-surgical and 51.8% with combined type of complications ($p < 0.001$). Corresponding 5-year OS for rectal cancer patients was 76.9%, 72.7%, 64.9%, and 63.2% ($p < 0.001$). In colon cancer, multivariable analyses revealed HR 1.198 (1.136–1.264) for surgical, HR 1.489 (1.423–1.558) for non-surgical and HR 1.590 (1.505–1.681) for combined type of complications. For rectal cancer, these HRs were 1.193 (1.097–1.2297), 1.456 (1.346–1.329), and 1.489 (1.357–1.633). Surgical complications were associated with worse CS-1 in rectal cancer (HR 1.140 (1.050–1.260), but not in colon cancer (HR 1.007 (0.943–1.075)).
Conclusion: Non-surgical complications have higher impact on survival than surgical complications. The impact of surgical complications on survival was still measurable after surviving the first year in rectal cancer but not in colon cancer patients.

1. Introduction

Colorectal cancer surgery is accompanied by a considerable complications rate (>40%) [1,2]. Studies found that postoperative complications might negatively impact overall survival (OS) and disease recurrence. However, the impact depends on the type of complications and differs for colon and rectal cancer patients [1–9]. For example, it was found that colon cancer patients who suffered from postoperative complications have a worse survival than rectal cancer patients and patients without complications [1]. Breugom et al. demonstrated that surgical complications, such as anastomotic leakage, excessive blood loss, and sepsis were associated with a decreased 1-year OS. Furthermore, anastomotic leakage, abscess, and delirium were associated with an impaired 5-year OS and conditional survival (CS) [2]. It has been suggested that surgical complications cause an inflammatory microenvironment that

* Corresponding author. Hospital: Reinier de Graaf Groep, Department of Surgery, Address: Reinier de Graafweg 5, 2625, AD, Delft, the Netherlands.
E-mail address: J.W.T.Dekker@rdgg.nl (J.W.T. Dekker).

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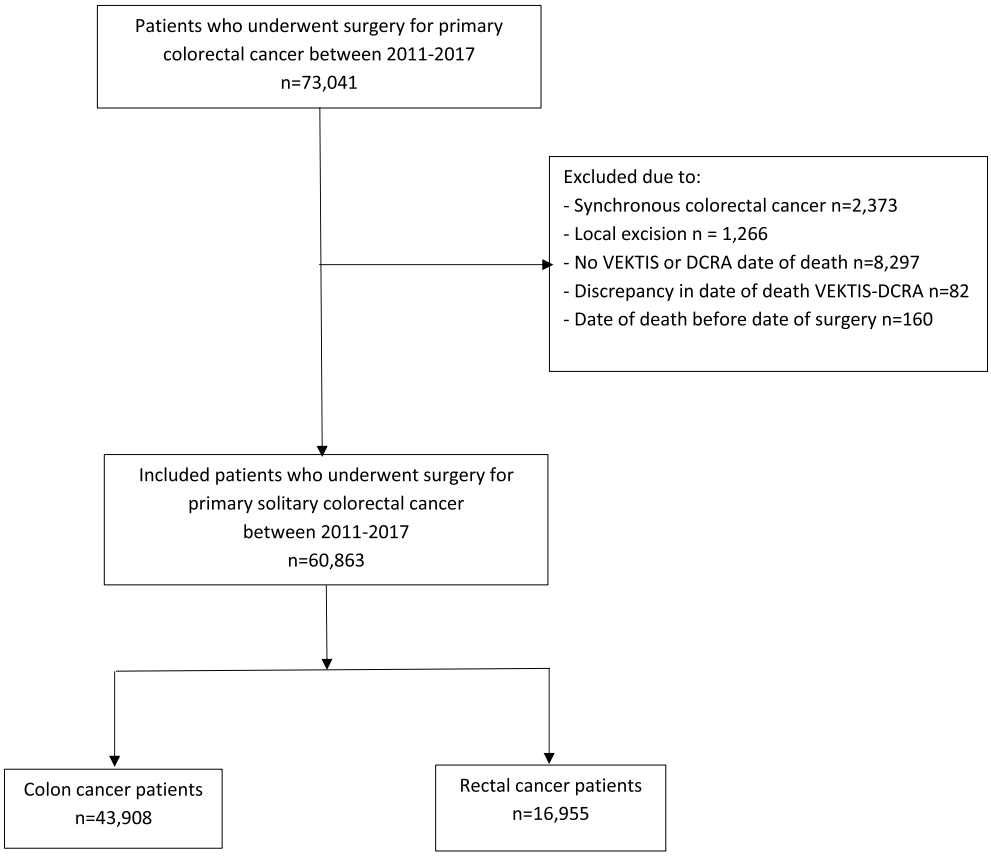


Fig. 1. Study flowchart
Fig. 1: flow chart of the present study.

contributes to local recurrence and metastases development, and might therefore have the biggest impact on survival [6,10–12]. Non-surgical complications, e.g., delirium or pneumonia, have been related to patients preoperative condition [2,13], which might lead to an impaired recovery process and reduced survival.

Most studies regarding colorectal cancer survival solely present OS [1,4–8], but OS can be influenced by postoperative mortality. The excess mortality during the first year is mainly caused by a prolonged surgical impact, especially when perioperative complications occurred [14,15]. The CS is used to show an excess mortality under the condition that a specific period is survived (e.g. postoperative period) [14,15]. The aim of the study was to assess the association between different types of complications after colon and rectal cancer surgery with OS and conditional survival if still alive after 1-year.

2. Materials and methods

This national observational cohort study linked data from the Dutch ColoRectal Audit (DCRA) with data from a national database based on insurance expense reports, Vektis [16]. This study required no informed consent or ethical approval by Dutch law and is reported according to the STROBE guidelines [17].

2.1. Combining the DCRA and VEKTIS-datasets

Since 2009, the DCRA registers patient, tumour, surgical and 30-day follow-up characteristics of all colorectal cancer patients who underwent surgery in the Netherlands (95% completeness) [18]. To provide survival information beyond 30-day follow-up, the DCRA was combined with the Vektis database that records information of medical expense reports of Dutch insurance companies [16]. Since health care insurance is obligatory in the Netherlands and ends when a patient dies, all Dutch deceased patients with date of death are recorded by Vektis [16,19,20].

The DCRA and Vektis datasets were combined in September 2020 (date of last follow-up: September 25, 2020), by a third trusted party, Medical Research Data Management (NEN 7510:2011 and ISO 27001:2013 certified) [21], to guarantee patients' privacy.

2.2. Patient population

All patients who underwent colorectal cancer resection between January 1, 2011, and December 31, 2017, were potentially eligible (N = 73,041) (Fig. 1). Patients with multiple colorectal carcinomas (N = 2,3737) or who underwent local excision (N = 1266) were excluded. The time between primary surgery and death or last follow-up was calculated. Patients were excluded if the date of death was missing in both databases (N = 8297), if there was a discrepancy in date of death between the databases (N = 82) or if the date of death was before the registered date of surgery (N = 160), resulting in the inclusion of 60,836 patients. Patients who underwent an abdominoperineal excision, a total mesorectal excision, a partial mesorectal excision, or a low anterior resection for a tumour located ≤10 cm from the anal verge were assigned to the rectal cancer population.

2.3. Primary outcomes and definitions

Primary outcomes of the study were 5-year OS and 5-year

Table 1
Baseline characteristics of the total colon and rectal cancer study population.

		Colon cancer (n = 43,908)		Rectal cancer (n = 16,955)	
		n	%	n	%
Preoperative characteristics					
Age (years)	<60	6270	14.3	3692	21.8
	60-70	13,359	30.4	5853	34.6
	70-80	15,348	35.0	5294	31.3
	≥80	8899	20.3	2100	12.4
Sex	Male	23,188	52.8	10,737	63.3
	Female	20,715	47.2	6214	36.6
	Missing	5	0.0	4	0.0
BMI (kg/m^2)	<18.5	2382	5.4	686	4.0
	18.5–25.0	16,736	38.1	6601	38.9
	25.0–30.0	16,782	38.2	6863	40.5
	≥30.0	7940	18.1	2794	16.5
	Missing	68	0.2	11	0.1
ASA score	I-II	32,383	73.8	13,948	82.3
	III+	11,464	26.1	2997	17.7
	Missing	61	0.1	10	0.1
CCI	0-2	38,454	87.6	15,383	90.7
	>2	5454	12.4	1572	9.3
Tumour characteristics					
Tumour-related complications*	No	27,275	62.1	13,192	77.8
	Yes	16,463	37.5	3691	21.8
	Missing	170	0.4	72	0.4
cT stage	cT1-2	4702	10.7	4664	27.5
	cT3	7135	16.2	9820	57.9
	cT4	1671	3.8	1622	9.6
	cTx	30,400	69.2	849	5.0
cN stage	cN0	11,662	26.6	6983	41.2
	cN1-2	5368	12.2	9065	53.5
	cNx	26,878	61.2	907	5.3
Preoperative therapy					
Neoadjuvant radiotherapy	No	–	–	5383	31.7
	SCRT	–	–	5525	32.6
	CRT	–	–	5633	33.2
	Other RTx scheme	-	–	408	2.4
	Missing	-	-	6	0.0
Neoadjuvant chemotherapy	No	42,212	96.1	–	–
	Yes	885	2.0	-	–
	Missing	811	1.8	-	-
Surgical characteristics					
Hospital type	Secondary	40,364	91.9	14,723	86.8
	Tertiary	3544	8.1	2232	13.2
Urgency	Elective	37,096	84.5	16,726	98.6
	Emergency	6780	15.4	219	1.3
	Missing	32	0.1	10	0.1
Approach	Open	15,422	35.1	4515	26.6
	Laparoscopic	28,310	64.5	12,345	72.8
	Missing	176	0.4	95	0.6
Multivisceral resection	No	39,572	90.1	15,634	92.2
	Yes	4173	9.5	1226	7.2
	Missing	163	0.4	95	0.6
Additional resection for metastasis	No	42,240	96.2	16,435	96.9
	Yes	1589	3.6	482	2.8
	Missing	79	0.2	38	0.2
Postoperative Tumour Stage					
(y)pTNM stage*	Stage I	9482	21.6	6447	38.0
	Stage II	15,277	34.8	4109	24.2
	Stage III	13,837	31.5	5071	29.9
	Stage IV	4868	11.1	1122	6.6
	Stage X	444	1.0	206	1.2

Table 1: Baseline study population characteristics. SCRT: short-course radiotherapy, CRT: long course/chemoradiotherapy, other RTx scheme: radiotherapy unspecified scheme. *Tumour-related complications include ileus, anaemia, haemorrhage, or abscess at the tumour site. **pTNM-stage: ypT0N0M0 carcinomas are included in the stage I group.

conditional survival if still alive one year postoperative (CS-1). Secondary outcomes were the 1 and 3-year OS and 3-year CS-1. The impact of the different types of complications on OS and CS-1 was assessed for surgical complications (including anastomotic leakage, ileus, abscess, bowel perforation, wound infection, fascial dehiscence, bleeding, urethra/bladder perforation), non-surgical complications (including cardiac, pulmonary, thromboembolic, neurologic, infectious, unspecified complications), or combined complications (i.e., both non-surgical and surgical complications).

2.4. Statistical analysis

Study population characteristics that were categorical or dichotomous variables were reported as absolute numbers with

Table 2
Short-term outcomes after colon and rectal cancer surgery.

	Colon cancer (n = 43,908)		Rectal cancer (n = 16,955)	
	n	%	n	%
No complications	31,353	71.4	10,877	64.2
Surgical complication	4249	9.7	2351	13.9
Non-surgical complication	5062	11.5	2155	12.7
Non-surgical & surgical complication	3148	7.2	1522	9.0

Table 2: Adverse outcomes after colon and rectal cancer surgery. Missing postoperative complications for colon cancer n = 96 and rectal cancer n = 50. Surgical complications include wound infection, bowel perforation, abscess, anastomotic leakage, ureter/bladder perforation, ileus, haemorrhage, fascial dehiscence, without any non-surgical complication. Non-surgical complications include cardiac, pulmonary, thrombotic, neurologic, non-surgical infectious complications without any surgical complications. Non-surgical and surgical complications comprise a combination of at least one complication from each category of complications.

percentages. Analyses were stratified for colon and rectal cancer and for types of complications (surgical, non-surgical, and combined complications). Kaplan–Meier method was used to assess 1, 3, and 5-year OS and CS-1 probabilities and significant differences in survival probabilities were evaluated by log-rank method. A multivariable cox regression analysis was performed to identify the association of complication types with OS and CS-1. The model was risk-adjusted for sex, age, Body Mass Index (BMI), American Society of Anaesthesiologist (ASA) score, Charlson Comorbidity Index (CCI), additional resection for metastasis, multivisceral resection, preoperative tumour complications (including ileus, anaemia, haemorrhage or abscess at the tumour site), pTNM-stage, and for rectal cancer also for neoadjuvant (chemo)radiotherapy. The adjusted Hazard Ratio (HR), 95% Confidence Interval (95%CI), and p-value were reported. A p-value of <0.05 was considered significant. RStudio version 3.1.595 (2020) was used for analyses.

3. Results

3.1. Study population

Of the 60,863 colorectal cancer patients included, 43,908 underwent colon resection, and 16,955 rectal resection (Table 1). Colon cancer patients were most often 70–80 years (35.0%), male (52.8%), with ASA I-II score (73.8%), and frequently underwent laparoscopic resection (64.5%). Rectal cancer patients were most often 60–70 years (34.6%), male (63.3%), with ASA I-II score (82.3%). Treatment caracteristics showed that 68.3% of the rectal cancer patients received neoadjuvant radiotherapy (32.6% short course radiotherapy (SCRT) and 33.2% (chemo)radiotherapy (CRT), and that 72.8% underwent laparoscopic resection.

The overall complication rate after colon cancer resection was 28.6%, with a surgical complication rate of 9.7%, a non-surgical complication rate of 11.5%, and a combined complication rate of 7.2% (Table 2). Overall complication rate after rectal cancer resection was 35.8%, with corresponding rates for the different types 13.9%, 12.7%, and 9.0%, respectively.

3.2. Survival after colorectal cancer surgery

Median follow-up time was 66.1 months for colon cancer patients and 66.5 months for rectal cancer atients. The 5-year OS was 68.6%, after colon cancer resection, and 73.6% after rectal cancer resection (Fig. 2A). Corresponding 5-year CS-1 was 76.2% for colon cancer patients and 78.0% for rectal cancer patients (Fig. 2B).

Regarding secondary outcomes, the 1 and 3-year OS was 89.9% and 77.2% for colon cancer, with corresponding rates of 94.4% and 83.2% for rectal cancer, respectively. The 3-year CS-1 was 85.9% for colon cancer and 88.2% for rectal cancer.

3.3. Postoperative complications and survival

The 1, 3 and 5-year OS probability for colon cancer patients without complications were 93.8%, 81.6% and 73.2% respectively, which were significantly higher compared to patients with surgical complications (86.9%, 73.9% and 65.4%), non-surgical complications (78.2%, 63.0% and 52.9%), and combined complications (74.9%, 61.3% and 51.8%) (Fig. 3A). Three and 5-year CS-1 probability were 87.0% and 78.1% in colon patients without complications, 85.0% and 75.3% for surgical complications, 80.5% and 67.7% for non-surgical complications, and 81.8% and 69.2% for combined complications (Fig. 3B).

The 1, 3 and 5-year OS probability after rectal cancer resection was the lowest for patients with combined complications (86.9%, 75.1% and 63.2%), followed by patients with non-surgical complications (88.0%, 74.8% and 64.9%), surgical complications (95.0%, 83.4% and 72.7%) and without complications (96.6%, 86.0% and 76.9%) (Fig. 3C). The 3 and 5-year CS-1 probability were comparable for rectal cancer patients with combined complications (87.8% and 72.7%) and with non-surgical complications (85.0% and 73.8%), but better for no complications (89.0% and 79.7%) or surgical complications (87.7% and 76.6%) (Fig. 3D).

Multivariable cox regression analyses demonstrated that colon and rectal cancer patients who suffered from surgical, non-surgical, and combined complications were at increased risk for a poor OS (Table 3, Suppl. Tables 1 and 2). Besides, colon- and rectal cancer patients with non-surgical or combined complications, were at risk for a worse CS-1. In contrast to rectal cancer patients with surgical complications, colon cancer patients with surgical complications had no increased risk for impaired CS-1.

4. Discussion

This population-based study reveals an independent association between surgical, non-surgical, and combined complications with OS after colon and rectal cancer resection. Rectal cancer patients demonstrated an independent associations between all three groups of complications and an impaired CS-1, while in colon cancer patients only non-surgical and combined types of complications were associated with a worse CS-1. Furthermore, different types of complication have a different impact on survival, with non-surgical and combined types of complications having bigger impact on OS than surgical complications. These findings illustrate the potential improvements in long-term survival can be achieved by optimizing surgery and perioperative colorectal cancer. In addition, these data suggest that detailed assessment of postoperativel complications should probably become an integral part of prospective intervention trials in which resection of the primary tumour is part of new treatment strategies.

Previous studies found that the impact of postoperative

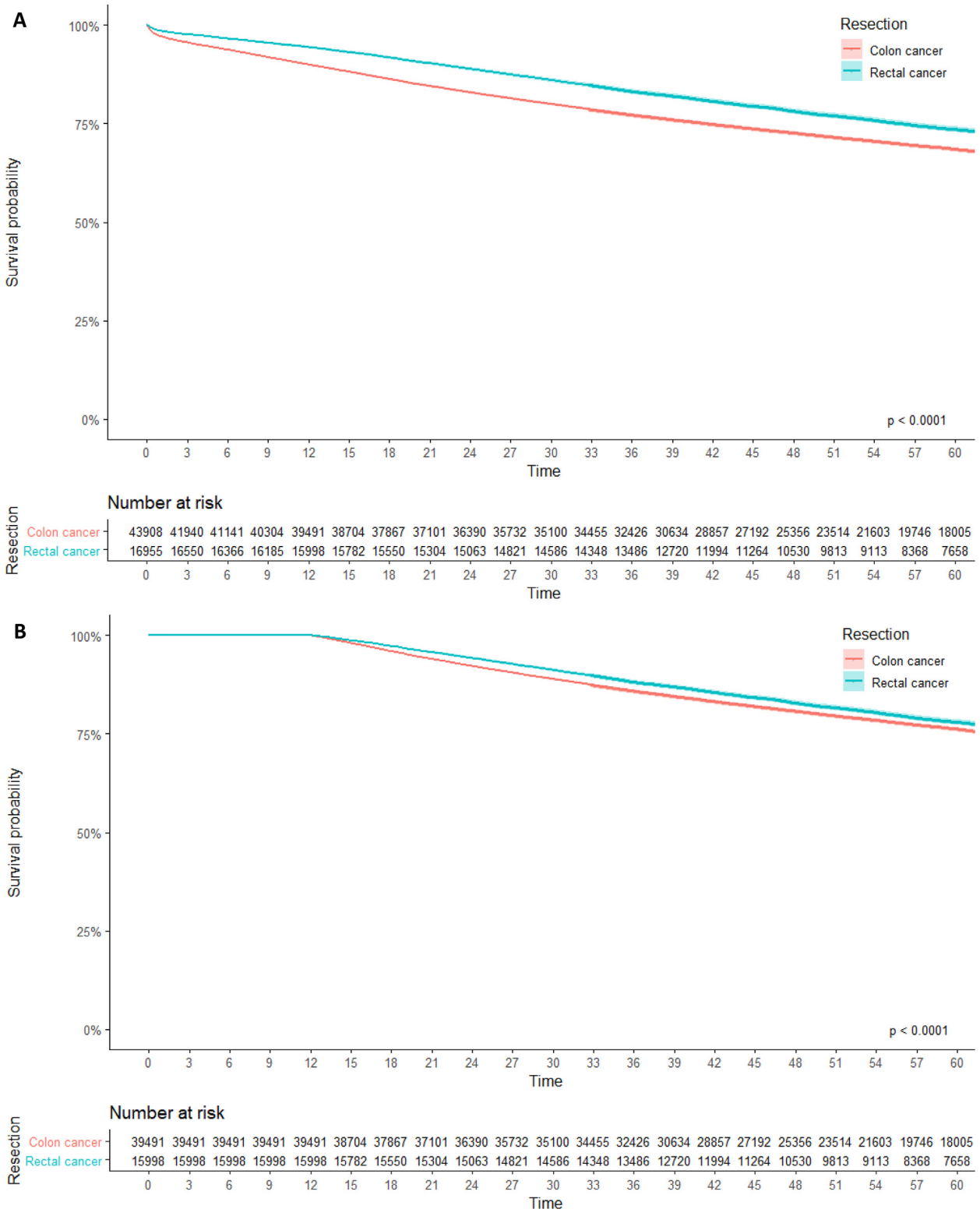
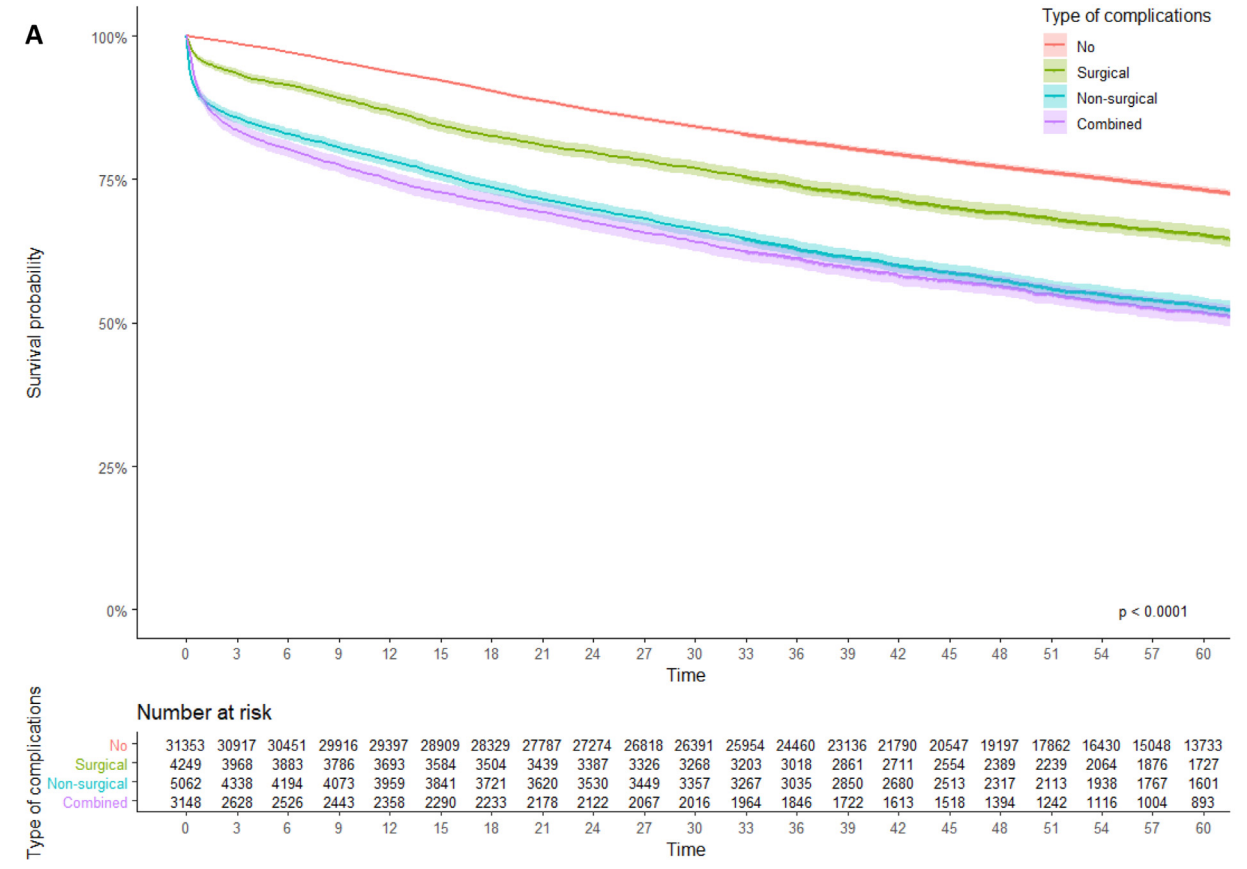
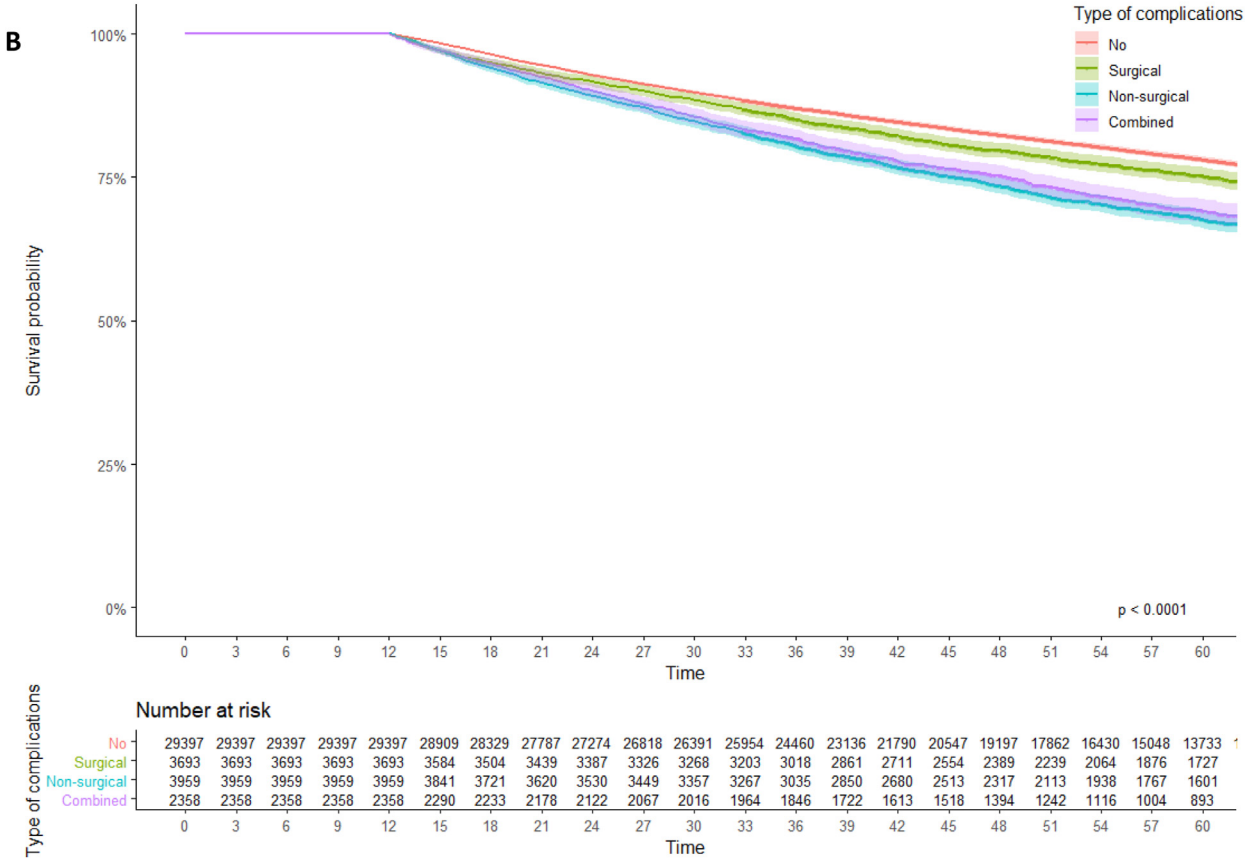


Fig. 2. Overall and conditional survival after colon and rectal cancer resection

Fig. 2: (A) Overall survival after colon cancer or rectal cancer resection of evaluable patients in the DCRA between 2011 and 2017. (B) Conditional overall survival for those patients who survived the first 365 days postoperative after colon or rectal cancer surgery.


A
Type of complications
No
Surgical
Non-surgical
Combined
Survival probability
100%
75%
50%
25%
0%
p < 0.0001
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time
Number at risk
No 31353 30917 30451 29916 29397 28909 28329 27787 27274 26818 26391 25954 24460 23136 21790 20547 19197 17862 16430 15048 13733
Surgical 4249 3968 3883 3786 3693 3584 3504 3439 3387 3326 3268 3203 3018 2861 2711 2554 2389 2239 2064 1876 1727
Non-surgical 5062 4338 4194 4073 3959 3841 3721 3620 3530 3449 3357 3267 3035 2850 2680 2513 2317 2113 1938 1767 1601
Combined 3148 2628 2526 2443 2358 2290 2233 2178 2122 2067 2016 1964 1846 1722 1613 1518 1394 1242 1116 1004 893
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time
Type of complications


B
Type of complications
No
Surgical
Non-surgical
Combined
Survival probability
100%
75%
50%
25%
0%
p < 0.0001
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time
Number at risk
No 29397 29397 29397 29397 29397 28909 28329 27787 27274 26818 26391 25954 24460 23136 21790 20547 19197 17862 16430 15048 13733
Surgical 3693 3693 3693 3693 3693 3584 3504 3439 3387 3326 3268 3203 3018 2861 2711 2554 2389 2239 2064 1876 1727
Non-surgical 3959 3959 3959 3959 3959 3841 3721 3620 3530 3449 3357 3267 3035 2850 2680 2513 2317 2113 1938 1767 1601
Combined 2358 2358 2358 2358 2358 2290 2233 2178 2122 2067 2016 1964 1846 1722 1613 1518 1394 1242 1116 1004 893
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time
Type of complications

complications on survival and local recurrence depend on the type of complications [1–9]. Surgical complications decrease survival since they might cause an inflammatory microenvironment, with similar inflammation markers contributing to local recurrence and metastases development [6,10–12]. Non-surgical complications are influencing long-term survival through other pathophysiological mechanisms, for example by decreasing cardiorespiratory capacity due to postoperative complications such as myocardial infarction or pulmonary embolism. These non-surgical complications are also more likely to occur in patients with preexisting comorbidities, which makes it difficult to determine the relative contribution of preexisting comorbidities and non-surgical complications to the reduced survival probability. Finally, studies have demonstrated that colon cancer patients who suffered from complications received less frequently or delayed adjuvant chemotherapy [22–24], which might be another reason for the association between complications and survival [23,24].

Comorbidities increase with age, making elderly patients at increased risk for postoperative mortality and poor survival [7,13,25]. Latkausas et al. showed that elderly patients who underwent colorectal cancer surgery had a comparable surgical complication rate but a higher non-surgical complication rate and postoperative mortality rate [26]. Furthermore, Slankamenac et al. found that non-surgical complications have the strongest association with poor survival [27]. Similarly, we found that non-surgical and combined complications after colon and rectal cancer surgery had a higher risk of poor OS and CS-1 compared to patients with surgical complications, suggesting that non-surgical complications are most predictive for survival. However, the question remains whether the observed decreased survival is caused by non-surgical complications per se or that these complications are associated with other factors (e.g., preexisting comorbidities/poor physical condition) that might also decrease survival [25].

Colon cancer and rectal cancer patients who had a surgical complication showed a different risk for CS-1, which might be explained by the higher prolonged inflammatory state after complications in rectal cancer surgery. Colonic anastomoses permit free leakage into the peritoneal cavity causing a more generalized peritonitis than anastomotic leakage after rectal cancer surgery [28,29]. One might suggest that anastomotic leakage after rectal cancer surgery results in a sustained inflammatory microenvironment (i.e., higher risk of tumour cell spreading) due to a contained low grade pelvic sepsis with less severe symptoms and later diagnosis and treatment. As a result, this might lead to a higher cancer-related mortality in the long run, as well as mortality from chronic pelvic sepsis with severe late complications that might still occur several years after rectal cancer resection.

Whether the risks of postoperative complications can be modified, thereby potentially improving OS, is an important question for the clinical implications of the present study. It has been demonstrated that laparoscopy can reduce the surgical stress response, thereby improving the postoperative course (e.g., less postoperative morbidity and mortality) [30–32]. Also compliance with the Enhanced Recovery After Surgery Program (ERAS) after colorectal cancer surgery has shown to be associated with a better long-term survival [33,34] by decreasing the surgical stress response [35]. Curtis et al. demonstrated that only two factors related to long-term survival were modifiable factors in colorectal cancer surgery, which were the use of a laparoscopic approach and following the ERAS program [36].

Preoperative optimization of a patients' physical condition seems promising for reducing complications [37–39]. Recently de Klerk et al. showed that a multimodal prehabilitation program before elective colorectal cancer surgery in high-risk patients reduces postoperative complications, unplanned readmissions, and shortens the median hospital stay when compared to standard care [38]. Van der Hulst et al. demonstrated that older frail colorectal cancer patient who attended a prehabilitation had a comparable complication rate to less frail patients [37]. A study by Niemeläinen et al. suggested that preoperative evaluation of patient's physical and cognitive performance could potentially improve long-term survival [40].

Clinical audits monitor developments and changes in colorectal cancer care making it an essential tool for quality assessment and improvement on a short cycle base [18]. The DCRA-data has contributed to improvement in postoperative complications and mortality [18], and we now have the ability to use survival as an outcome parameter in the DCRA. This provides additional opportunities to identify areas for improvement, although plan-do-check-act cycles are more challenging using survival related to the delay of several years after which implemented quality improvement measures can be evaluated. However, our results showed that short-term outcomes were strongly associated with survival, indicating that these short-term outcomes can be used in auditing as surrogate markers for survival.

Several limitations of the study need to be addressed. Although, the Dutch law for privacy allows registration of citizen service number (CSN) by hospitals for clinical audits, hospitals have their own local privacy policy that might prohibit CSN registration. Patients from which this number was not registered could not be linked with the Vektis dataset. Besides a mismatch was found in date of death between the DCRA-Vektis likely caused by registration errors in one of the registries. The impossibility to link patients and the mismatch in date of death in the dataset caused a substantial number of patients who could not be included in the study. Consequently, patient selection cannot be ruled out completely. Secondly, until 2017 the 30-day follow-up period was registered in the DCRA (from 2018 on 90-day follow-up is registered), causing an underestimation of the total number of postoperative complications since complication after colorectal cancer surgery also occur after the initial postoperative period. Although we were able to account for many variables that might influence survival in our cox-regression analyses, there might be other confounding variables for which survival could not be accounted, e.g. steroid use, sarcopenia, and weight loss. Therefore, a strong correlation between postoperative complications and long-term survival is demonstrated, but causality could not be proven.

5. Conclusion

This population-based study demonstrates that non-surgical and surgical complications after colorectal cancer surgery have a different impact on survival. Non-surgical complications have a much stronger association with OS and CS-1 than surgical

Fig. 3. Overall and conditional survival after colon and rectal cancer resection per type of complications
Fig. 3: *(A) Overall survival after colon cancer resection depending on the occurrence of complications and stratified for type of complications. (B) Conditional overall survival for patients who survived the first 365 days after colon cancer resection with or without postoperative complications and stratified for type of complications. (C) Overall survival after rectal cancer resection depending on the occurrence of complications, and stratified for type of complications. (D) Conditional overall survival for patients who survived the first 365 days after rectal cancer resection with or without complications and stratified for type of complications.*

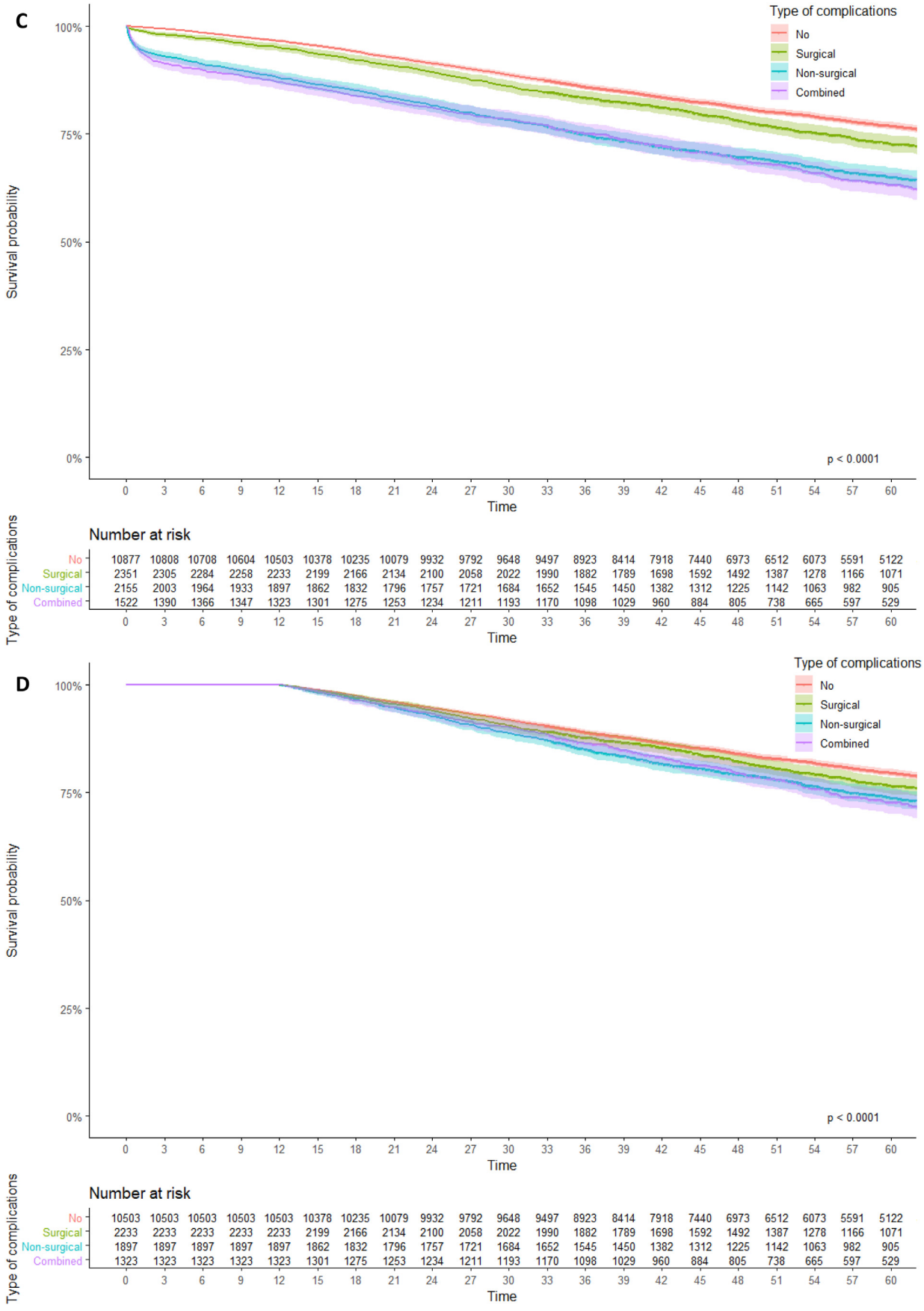


Fig. 3. (*continued*).

Table 3
Multivariable Cox Regression Analyses of the association between complications and Overall Survival and Conditional Survival after surviving the first 365 days postoperative following colon cancer and rectal cancer resection.

Colon cancer					
Adjusted for: sex, age, CCI, ASA score, BMI, preoperative tumour complications, the urgency of surgery, pTNM-stage, multivisceral resection, and additional resection for metastases					
Overall survival:	Total (n)	Events (n)	HR	95% CI	p-value
No complications	42,863	14,757	Ref.	Ref.	Ref.
Surgical complications			1.198	1.136–1.264	<0.001
Non-surgical complications			1.489	1.423–1.558	<0.001
Non-surgical & surgical complications			1.590	1.505–1.681	<0.001
Conditional overall survival when surviving 365 days postoperative:	Total (n)	Events (n)	HR	95% CI	p-value
No complications	38,591	10,485	Ref.	Ref.	Ref.
Surgical complications			1.007	0.943–1.075	0.845
Non-surgical complications			1.155	1.090–1.224	<0.001
Non-surgical & surgical complications			1.117	1.036–1.204	0.004
Rectal cancer					
Adjusted for: sex, age, CCI, ASA score, BMI, preoperative tumour complications, the urgency of surgery, pTNM-stage, multivisceral resection, additional resection for metastases, and neoadjuvant (chemo)radiotherapy					
Overall survival:	Total (n)	Events (n)	HR	95% CI	p-value
No complications	16,538	4840	Ref.	Ref.	Ref.
Surgical complications			1.193	1.097–1.297	<0.001
Non-surgical complications			1.456	1.346–1.576	<0.001
Non-surgical & surgical complications			1.489	1.357–1.633	<0.001
Conditional overall survival when surviving 365 days postoperative:	Total (n)	Events (n)	HR	95% CI	p-value
No complications	15,622	3924	Ref.	Ref.	Ref.
Surgical complications			1.150	1.050–1.260	0.003
Non-surgical complications			1.212	1.105–1.329	<0.001
Non-surgical & surgical complications			1.178	1.053–1.317	0.004

Table 3: Multivariable Cox Regression Analyses of the association between complications and overall survival and conditional survival after surviving the first 365 days postoperative following colon cancer and rectal cancer resection.

complications. In contrast with colon cancer patients, surgical complications after rectal cancer resection still had a measurable impact on long-term survival beyond the first postoperative year. Future research should focus on how to modify the risk of postoperative complications. Minimally invasive surgery, optimizing the patient's physical condition by prehabilitation and ERAS could be helpful to improve not only short-term outcomes but also long-term survival.

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

CRediT authorship contribution statement

A.K. Warps: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – review & editing. **R.A.E.M. Tollenaar:** Conceptualization, Methodology, Supervision, Validation, Writing – original draft. **P.J. Tanis:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft. **J.W.T. Dekker:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft.

Declaration of competing interest

All authors have no conflicts of interests to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2021.10.035.

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