

ORIGINAL ARTICLE



Substantial underreporting of anastomotic leakage after anterior resection for rectal cancer in the Swedish Colorectal Cancer Registry

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ABSTRACT

Background: The causes and effects of anastomotic leakage after anterior resection are difficult to study in small samples and have thus been evaluated using large population-based national registries. To assess the accuracy of such research, registries should be validated continuously.

Material and methods: Patients who underwent anterior resection for rectal cancer during 2007–2013 in 15 different hospitals in three healthcare regions in Sweden were included in the study. Registry data and information from patient records were retrieved. Registered anastomotic leakage within 30 postoperative days was evaluated, using all available registry data and using only the main variable anastomotic insufficiency. With the consensus definition of anastomotic leakage developed by the International Study Group on Rectal Cancer as reference, validity measures were calculated.

Results: Some 1507 patients were included in the study. The negative and positive predictive values for registered anastomotic leakage were 96 and 88%, respectively, while the κ -value amounted to 0.76. The false-negative rate was 29%, whereas the false-positive rate reached 1.3% (the vast majority consisting of actual leaks, but occurring after postoperative day 30). Using the main variable anastomotic insufficiency only, the false-negative rate rose to 41%.

Conclusions: There is considerable underreporting of anastomotic leakage after anterior resection for rectal cancer in the Swedish Colorectal Cancer Registry. It is probable that this causes an underestimation of the true effects of leakage on patient outcomes, and further quality control is needed.

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Introduction

Anastomotic leakage after anterior resection for rectal cancer afflicts 10–19% of patients [1–3]. Leakage leads to increased risk of postoperative mortality [3], morbidity [1,4,5] and may also be a risk factor for local and systemic recurrence [6]. Research investigating causes and consequences of anastomotic leakage is therefore vital, and large databases and registries are needed to ensure adequate amounts of data for accurate statistical inference. However, the quality of nationwide clinical registries cannot be taken for granted, and validation of key variables is pivotal to ensure quality of registry-based research. Several definitions of leakage after anterior resection abound, contributing to registration heterogeneity. To remedy this situation, the International Study Group of Rectal Cancer (ISREC) has proposed a consensus definition of anastomotic leakage [7], now acting as a standard in research on the subject.

The Swedish Colorectal Cancer Registry, used nationwide since 1995 for rectal cancer patients, has been used extensively in research [8]. The registry has been validated several times [9,10], but the ISREC leakage definition has hitherto not been used. The goal of this study was to investigate the validity of the variable anastomotic leakage in the

mentioned registry using a retrospective chart review with the ISREC definition as reference.

Material and methods

Study design

Eligible for inclusion in this retrospective cohort study were all patients operated on with anterior resection for rectal cancer during 2007–2013 in 15 hospitals in the Northern, Southern and Western healthcare regions in Sweden. These patients were identified through the Swedish Colorectal Cancer Registry [8], which includes data on patient demographics, the surgical procedure, postoperative course, pathological assessment and pre- and postoperative oncological treatment. The regional ethical review boards at Umeå University and the University of Gothenburg approved the study.

Data collection

In general, all registry data on complications are reported if such complications occur in-hospital or up to 30 days postoperatively if they appear after discharge.

Postoperative complications are identified by the surgical team and reported to the registry electronically. In some hospitals, the latter procedure is delegated to nurses or administrative staff. The registry uses the following variables for possible anastomotic complications: anastomotic insufficiency (checkbox only), reoperation for anastomotic insufficiency (checkbox only), other complications (checkbox, explained in free text), and other reoperations (checkbox, explained in free text). It is notable that there is no formal definition or further explanation of either of the above variables in the registry; moreover, reoperation signifies reintervention ranging from percutaneous drainage to formal laparotomy. Using information from all variables, we assumed the following: a registered anastomotic insufficiency was naturally treated as a registered anastomotic leakage; in case of a registered reoperation for leakage, this always denoted anastomotic leakage although the box for anastomotic insufficiency was not checked; if a complication or reoperation of the 'other' category was specified and the free-text field included the following complications or indications for reoperation, this also denoted leakage: 'pelvic abscess', 'anastomotic insufficiency', or 'rectovaginal fistula'. Therefore, the registry variable anastomotic leakage was derived from all available registry information, emulating a clinical research situation.

Medical charts were reviewed by four independent investigators, using a predefined clinical record form to identify anastomotic leakage, as defined by ISREC [7]. In summary, this definition proposes anastomotic leakage as a leak from any staple or suture line, pelvic abscess (even without radiologically proven leakage) or rectovaginal fistula. Leaks are also graded: type A leaks result in no change in patients' management, type B leaks require treatment other than laparotomy, and type C leaks require laparotomy [7].

To ensure that the registered leaks did indeed occur in-hospital or within 30 days of surgery per the registry, registry information concerning discharge data was used; this variable contained no missing data and, for the purpose of this study, was assumed to be correct.

Statistical analyses

The negative and positive predictive values for the registry variable anastomotic leakage were calculated, using the variable derived from the medical charts as reference. We also calculated agreement and analyzed κ -values. The latter is a measure of inter-observer agreement, commonly used in validity studies. By convention, values 0–0.20 suggest slight agreement, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, while 0.81–1 indicate almost perfect agreement [11]. In addition, false-negative and false-positive registrations were visualized using a Venn diagram. In sensitivity analyses, we evaluated whether leaks in university versus non-university hospitals were registered differently; for comparison purposes, we also analyzed registered leaks using only the anastomotic insufficiency registry variable, thus excluding information from auxiliary variables.

Statistical calculations and graphics were performed with STATA version 13.1 (StataCorp, Houston, TX, USA).

Results

Study participants

A total of 1568 patients were identified via the Swedish Colorectal Cancer Registry as potentially eligible for inclusion (Figure 1). Of these, 61 patients (4%) were excluded at chart review: 55 patients were excluded due to other procedure than anterior resection (abdominoperineal excision or Hartmann's procedure), while six more patients were excluded as charts could not be retrieved. Three (4.9%) of these excluded patients had registered anastomotic leaks. Some 1507 patients remained for analysis.

Patient demography and clinical details

Demographic and clinical data in Table 1 were derived from the registry, with the exception of type of mesorectal excision and anastomotic leakage. Most patients were male, had some comorbidity and had preoperative therapy. Laparoscopic surgery was uncommon. About a quarter of patients underwent partial mesorectal excision, while the vast majority of all patients had a diverting stoma fashioned before or during surgery.

Anastomotic leakage and registry validity

According to chart review, 180 (11.9%) patients had an anastomotic leakage. Three patients (1.7%) had an A leak, 123 patients (68.3%) had a B leak, while 54 patients (30.0%) sustained a grade C leak. The registry indicated that 145 patients (9.6%) suffered a leakage. Thirteen of these leaks met the ISREC criteria but occurred after 30 days postoperatively according to chart review and were therefore deemed to be non-leaks, while four leaks did not meet the definition at all.

Using the ISREC definition as reference, validity measures are presented in Table 2. The negative predictive value was high at 96%, while the positive predictive value was slightly lower at 88%. Agreement amounted to 95%, whereas the kappa value reached 0.76. Figure 2 displays a Venn diagram, visualizing the false-positive and false-negative registrations. There was a substantial false-negative rate of 29% (52/180), while the false-positive rate amounted to 1.3% (17/1327).

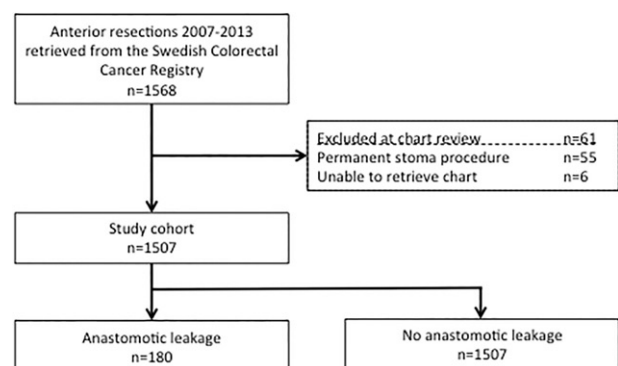


Figure 1. Study flowchart. Anastomotic leakage is defined according to the International Study Group for Rectal Cancer, within 30 days after surgery or in-hospital.

Table 1. Demographic and clinical data on 1507 patients operated with anterior resection for rectal cancer in 15 Swedish hospitals during 2007–2013.

Variables	
Age (years: median/range)	67 (23–93) N (%)
Sex	
Male	890 (59.1)
Female	617 (40.9)
ASA classification	
I	381 (26.1)
II	882 (60.5)
III–IV	195 (13.4)
Tumour stage	
I	384 (26.3)
II	439 (30.1)
III	523 (35.8)
IV	115 (7.9)
Preoperative radiotherapy	
No	617 (41.0)
Yes	887 (59.0)
Laparoscopic operation	
No	1318 (88.3)
Yes	175 (11.7)
Type of mesorectal excision	
Total	1059 (72.1)
Partial	409 (27.9)
Diverting stoma	
No	274 (18.2)
Yes	1230 (81.8)
Anastomotic leakage ^a	
No	1327 (88.1)
Yes	180 (11.9)

^aDefinition used by the International Study Group for Rectal Cancer; N: number; ASA: American Society of Anesthesiologists; percentages may not add up due to missing data.

Table 2. Validity of registry leakage, using chart leakage as reference, in a cohort of 1507 patients operated with anterior resection for rectal cancer in 15 Swedish hospitals during the period 2007–2013.

Measure	Estimate (%)	95% CI
NPV	96.2	95.0–97.1
PPV	88.3	81.9–93.0
Agreement	95.2	94.2–96.4
κ	0.76	0.71–0.82

NPV: negative predictive value; PPV: positive predictive value; CI: confidence interval.

In a sensitivity analysis, we analyzed whether a university or non-university setting affected the results, but this did not prove to be important (data not shown). Using only the information from the registry variable denoting anastomotic insufficiency, the frequency of anastomotic leakage was reduced to 7.8%, the false-negative rate increased from 29 to 41%, while the false-positive rate was similar at 1%.

Discussion

We discovered a considerable underreporting of anastomotic leakage after anterior resection for rectal cancer diagnosed during the first 30 postoperative days, as over a quarter of true leaks were not recorded in the Swedish Colorectal Cancer Registry. False-positive registrations were uncommon and most of them represented true leaks, although diagnosed after the first month after surgery. However, the

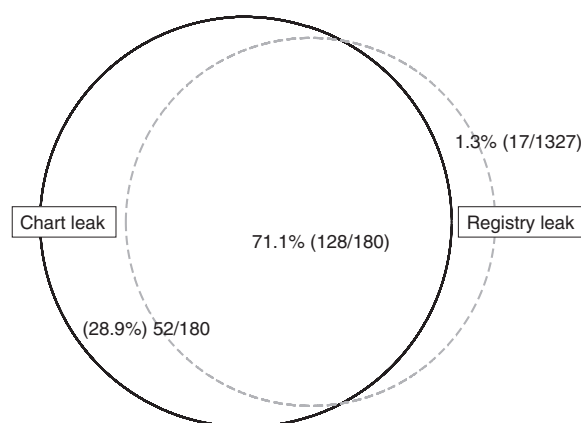


Figure 2. Venn diagram showing the proportion of false-negative and false-positive registrations. Chart leaks are denoted by the solid circle, while registry leaks are represented by the dashed circle.

negative predictive value especially, but also the positive predictive value, proved to be quite high, using the chart review and the ISREC definition as reference. The κ -value of 0.76 also indicated good validity, according to convention [11].

The registry has been validated previously on two occasions regarding postoperative complications [9,10]. First, Gunnarsson et al. [9] performed a validation study of surgical complications following colorectal cancer surgery, comparing national, regional and hospital registers to chart review of 511 patients. Although anastomotic leakage was not studied exclusively, it was found that surgical complications necessitating reoperation were missed at an alarmingly high rate of 45% on the national level, hinting that even Grade C leaks were not registered accurately, as leakage is a major cause of reoperation. However, this study was performed in the healthcare region of Uppsala/Örebro using data from 1997 and 1999, and was thus geographically and temporally apart from the current study. Moreover, the ISREC definition was not used at the time, making comparisons even more difficult. In addition, it is difficult to assess the impact of false-positive registrations, as these were not calculated. Secondly, Jörgren et al. [10] validated national registry data on several variables, including anastomotic leakage, from the period 1995–1997. The authors analyzed 592 charts and found a good κ -value of 0.82, while false-negative and false-positive registrations amounted to 2.6 and 16.2%, respectively; interestingly, the leak rate in this early study was very high at 29%, possibly reflecting less use of diverting stomas in this time period. Both the low false-negative and high false-positive rates are also at stark odds with the present study, which again might be a consequence of the introduction of the ISREC definition of anastomotic leakage. Some 70% of false-positives were due to late registrations (>30 days after surgery), which correspond to the current study findings, although it is unclear whether in-hospital leaks after the first postoperative months were considered erroneously registered. The ISREC definition includes not only anastomotic insufficiency, denoted by a communication between intra- and extraluminal compartments, but also perianastomotic abscesses. The latter might not have been considered as a leakage by the registrars during the study period, possibly

leading to misclassification. We included pelvic abscesses if indicated in free text fields used to specify 'other' complications or reoperations, but the degree to which these free text fields are used is also unknown. However, there is a registry variable termed intra-abdominal infection, which presumably comprises abscesses; adding information from this variable to the registry data on leaks reduced the false-negative rate only slightly to 24%, while the false-positive rate rose to 5%. Thus, it is unlikely that this element of the ISREC definition contributed significantly to the observed underascertainment. On the contrary, only using the registry variable denoting anastomotic insufficiency led to a substantial increase in underreporting to 41%, implying that investigators of anastomotic leakage after anterior resection using this particular registry are advised to use all available registry data, including free text fields and reoperation data.

One strength of this study is the large cohort size—compared to the two previous validation studies this cohort is three times as large. Another advantage is the clinical record form that was used with the ISREC classification, reducing the risk of bias and misclassification, as this form was developed and its definitions discussed with all researchers prior to chart review.

A weakness of this study is that about 50 hospitals performed procedures for rectal cancer during the study period, and were thus recording data in the registry; this study uses data from less than a third of these hospitals, and the study results may therefore not be fully generalizable. We included data from major hospitals in three healthcare regions, while units with only a few cases per year were excluded from data collection due to practical issues; this may lead to some selection bias, although unlikely to affect the results significantly as numbers were small. Another limitation of this study is due to the fact that the medical charts were not examined by a single investigator, thus possibly introducing interpretation discrepancies. The participating hospitals also did not use a uniform method of suspecting and diagnosing leakage, which may lead to under-diagnosis of true leaks; however, this reflects real-world surgical practice, which is the context in which registry-based research is employed. It is also important to appreciate that the use of diverting stoma was very frequent in this cohort, reflecting the common opinion in the Swedish surgical community, as well as in other countries, that anterior resection performed with total mesorectal excision necessitates such a stoma [12,13]. As a diverting stoma reduces symptomatic leaks and reoperation for leakage, such widespread use would probably decrease leak rates and, therefore, the results of this study may not be generalized to other settings.

The ISREC definition of anastomotic leakage is gaining acceptance among colorectal surgeons, but is not so far included in the instructions for the registrars in the Swedish Colorectal Registry. This definition has been validated against clinical presentations and found to be relevant, readily identifying groups with distinct clinical courses [14]. However, it is currently used more in research than in clinical work and quality control; the findings in the present study do not necessarily imply that the registry quality is substandard,

although registration quality might still be improved by providing clear definitions, e.g. the ISREC definition.

The current study shows that there is considerable underreporting of anastomotic leakage, as defined by ISREC, after anterior resection for rectal cancer in the Swedish Colorectal Cancer Registry. Such misclassification, or incorrect reporting, may lead to underestimation of the true effect of anastomotic leakage on research outcomes. Implementation of the ISREC definition in the registry as well as further validation is needed to facilitate research on anastomotic leakage after anterior resection.

Disclosure statement

No potential conflict of interest was reported by the authors.

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