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TOWARDS PATIENT-CENTERED COLORECTAL CANCER SURGERY

FOCUS ON RISKS, DECISIONS AND CLINICAL AUDITING

PROEFSCHRIFT

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door

Heleen Simone Snijders
Geboren te Rotterdam in 1985

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	Prof. Dr. D.M.J. Delnoij	(Universiteit Tilburg)

CONTENTS

Introduction:

GENERAL INTRODUCTION AND OUTLINE OF THIS THESIS

Surgical options, risks and benefits

Colorectal cancer is a major source of morbidity and mortality and has an increasing incidence with more than 12,000 patients diagnosed in the Netherlands in 2013.[1] The treatment of colorectal cancer requires a multidisciplinary approach, although surgical resection is still the cornerstone of treatment. In the Netherlands, yearly approximately 10,000 patients undergo a curative resection because of colorectal cancer.[2]

Nevertheless, curative surgery for colorectal cancer comes at a price. Postoperative complications are frequent, including anastomotic leakage which is a serious complication causing re-operation, a prolonged hospital stay, morbidity, a possibly worse oncological outcome or even mortality.[3-5] Also, functional loss of continence and sexual impairment after rectal cancer surgery cause both short- and long-term morbidity. [6,7]

When in rectosigmoid cancer tumour size, localization, and stage of disease allow a sphincter preserving procedure, an (low) anterior resection is performed. The surgical options after resection include a primary anastomosis, an anastomosis with a defunctioning stoma, and an end-colostomy (Figure 1). Each of these surgical options is associated with specific benefits and risks. Both patients and surgeons seem to have a strong preference to avoid a stoma, under the assumption that it will have negative consequences for quality of life.[8,9] On the other hand, poor functional outcome after a low anastomosis, especially in combination with radiotherapy or chemo radiation, can also lead to an impaired quality of life.

A defunctioning stoma has been proven to diminish chances of anastomotic leakage or its sequelae.[10] Furthermore, anastomotic leakage will not occur when an anastomosis is avoided, e.g. when an end-colostomy is constructed.

The benefits of preventing or minimizing anastomotic leakage should however always be balanced against the risks of the alternatives.

A defunctioning stoma itself carries a substantial risk of becoming permanent.[11,12] Furthermore, stomas may also have significant mid-to long-term morbidity when the patient is discharged from the hospital or after reversal of the stoma.[11-15]

Patient information and Shared Decision Making

The decision on anastomosis or stoma construction after surgical resections for rectosigmoid cancer consists of a trade-off between pros and cons of different treatment options. Therefore, it is an appropriate situation for investigating preoperative information provision and Shared Decision Making (SDM).

In recent years, the concept of SDM has gained widespread appeal to both clinicians and patients.[16,17] In SDM, clinicians and patients make decisions together using the best available information. SDM is considered especially important for patients who present with a serious illness such as cancer, when the outcomes are uncertain, or when different treatment options are available.[18] Previous studies have shown that patients with colorectal cancer prefer to be involved in the decision making process and to be informed on the risks of different treatment options.[19]

Surgical treatment strategies

With a growing demand for public transparency of performance in the last decade, surgeons and hospitals are increasingly accountable for their postoperative complication rates. An awareness of the problem of anastomotic leakage together with surgeons' growing accountability for their outcomes could have led to changes in strategies in colorectal cancer surgery and a more routine use of (defunctioning) stomas after low anterior resection. Not all patients however benefit from a stoma, as there are several drawbacks that counterbalance its advantages.[11,13,20,21]

Clear guidelines on which surgical strategy to use in different groups of patients are not yet available. When there are 2 or more generally accepted and effective treatment options, selection of the appropriate treatment should be based on patient preferences. Previous research however suggests that for many conditions treatment selection depends more on the physician's recommendation than on patient characteristics or preferences.[22] Consequently, differences in professional opinion may lead to variation in treatment patterns, which has been demonstrated for several conditions in various parts of the world.[23-30] The threshold for the decision to construct a stoma to avoid the risk of anastomotic leakage may also vary between surgeons. Some surgeons may be more risk-taking or -averse than others. This may lead to a variation between hospitals in surgical strategy concerning anastomosis and stoma construction.

Quality assessment

Although colorectal surgery is performed often, it is considered high-risk surgery as it brings along a relatively high risk of complications. Therefore, colorectal surgery is focus of different quality enhancement programs.[31-33] In the Netherlands, The Dutch Surgical Colorectal Audit (DSCA) was successfully initiated in 2009 with the objective to evaluate and improve quality of care for primary colorectal cancer surgery. Measurement of outcomes may in itself improve surgical outcomes – as suggested by the so-called "Hawthorne effect": colleagues can learn from each other by addressing specific differences in clinical practice and outcome.[4] In time, specific processes can be recognized that are associated with a high likelihood of good outcomes, the so-called 'best practices'.

Postoperative mortality is frequently used in hospital comparisons as an indicator for quality of care. When comparing mortality rates between hospitals, there is an important role for risk adjustment.[4,5] Observed variations in mortality may partly be caused by differences in patient and tumour characteristics (case-mix). High risk patients may not be evenly distributed between hospitals.[6] However, valid case-mix adjustments require a considerable amount of reliable data collected at the patient level. These data are rarely available and require a substantial registration effort. Therefore, it may be valuable to identify outcome measures that are less influenced by differences in case-mix and represent the actual differences in quality of care processes, such as anastomotic leakage.

The overall aim of this thesis is to investigate several aspects of clinical decision-making and outcome assessment in colorectal cancer surgery

Outline of this thesis

Part I: Risks, benefits, and decision-making

The first part of this thesis studies short and long term risks of a primary anastomosis after colorectal resections, an anastomosis with a defunctioning stoma and an end-colostomy, and investigates how these risks are communicated in surgical practice. In *Chapter 1*, we performed a systematic review of studies describing anastomotic leakage and the associated mortality in comparison to the overall postoperative mortality after low anterior resection for rectal cancer. *Chapter 2* investigates the postoperative and one-year outcomes of anastomosis with and without a defunctioning stoma or end-colostomy after resection of mid rectal cancer in seven Dutch hospitals. *Chapter 3* focusses on surgeons' opinion on necessary preoperative information for rectosigmoid cancer patients and evaluates what is actually communicated in practice. Gastroenterological surgeons' attitudes towards Shared Decision Making were assessed and compared with patient involvement in current practice.

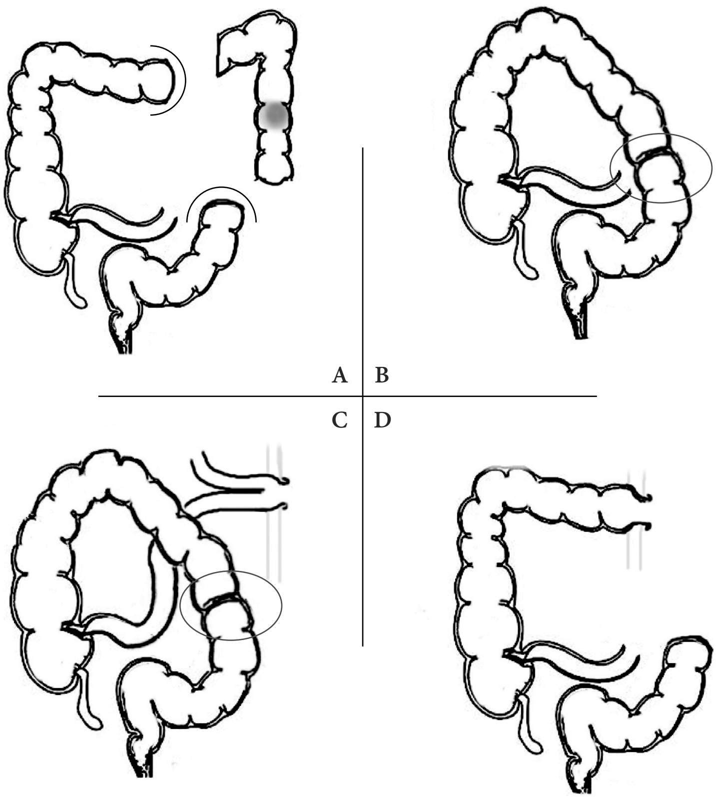
Part II: Surgical treatment strategies

The second part of this thesis mainly focuses on current surgical treatment strategies in colorectal cancer surgery, with regard to stoma and anastomosis construction. In *Chapter 4*, current use of defunctioning stomas after low anterior resection was assessed, and compared with the use of defunctioning stomas at the time of the TME-trial, together with associated outcomes. In *Chapter 5*, differences in professional opinion regarding the use of defunctioning stomas were analyzed, and investigated whether there was variation in treatment patterns between hospitals in the Netherlands. In *Chapter 6*, we assessed whether a tendency to anastomosis or stoma construction was related to postoperative outcomes such as anastomotic leakage and mortality rates.

Part III: Quality assessment of Colorectal Surgery

In the third part of this thesis, different aspects of clinical auditing as a tool for quality assessment of colorectal cancer surgery were studied. *Chapter 7* illustrates the introduction of the Dutch Surgical Colorectal Audit in the Netherlands by describing its main features and presenting the results of three years of auditing. *Chapter 8* describes the role of anastomotic leakage as an outcome measure for quality of colorectal surgery. In this chapter, it was explored whether hospital differences in anastomotic leakage rates were related to differences in case-mix.

Figure 1. Surgical options after resection of the tumour in colorectal cancer (a) include a primary anastomosis (b), an anastomosis with a defunctioning stoma (c), and an end-colostomy (d).



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PART I:
RISKS, BENEFITS, AND DECISION-MAKING

Chapter 1:

META-ANALYSIS OF THE RISK FOR ANASTOMOTIC LEAKAGE, THE POSTOPERATIVE MORTALITY CAUSED BY LEAKAGE IN RELATION TO THE OVERALL POSTOPERATIVE MORTALITY.

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Abstract

Introduction: Availability of anastomotic leakage rates and mortality rates following anastomotic leakage is essential when informing patients with rectal cancer preoperatively. We performed a meta-analysis of studies describing anastomotic leakage and the subsequent postoperative mortality in relation to the overall postoperative mortality after low anterior resection for rectal cancer.

Methods: A systematic search was performed of the published literature. Data on the definition and incidence rate of AL, postoperative mortality caused by AL, and overall postoperative mortality were extracted. Data were pooled and a meta-analysis was performed.

Results: Twenty-two studies with 10343 patients in total were analyzed. Meta-analysis of the data showed an average AL rate of 9%, postoperative mortality caused by leakage of 0.7% and overall postoperative mortality of 2%. The studies showed variation in incidence, definition and measurement of all outcomes.

Conclusion: We found a considerable overall AL rate and a large contribution of AL to the overall postoperative mortality. The variability of definitions and measurement of AL, postoperative mortality caused by leakage and overall postoperative mortality may hinder providing reliable risk information. Large-scale audit programs may provide accurate and valid risk information which can be used for preoperative decision making.

Introduction

When discussing treatment options for rectal cancer with patients preoperatively, difficult considerations can be encountered. Besides tumour and patient related factors, both doctors and patients' preferences play a role in the decisions about treatment options. This is particularly the case in surgical treatment for rectal cancer, when deciding between constructing an anastomosis and/or creating a stoma. Both patients and doctors have a strong preference to avoid a stoma, under the assumption that it will have negative consequences on quality of life.[1]

On the other hand, an anastomosis may not be beneficial to all patients, as a considerable proportion of patients with rectal cancer report defecation problems following a low anastomosis, such as fecal incontinence and urgency.[2] Even more important is considering the risk of anastomotic leakage (AL) following the construction of an anastomosis. AL is the most frequent major complication after surgery for rectal cancer, causing re-operations, prolonged hospital stay, morbidity, mortality and possibly a worse oncological outcome.[3] Recent advances in surgical techniques have increased options for sphincter preservation in rectal cancer. The increasing use of sphincter preserving procedures subsequently exposes more patients to the risk of anastomotic leakage.[4] In order to inform and involve patients in clinical decision-making, clinicians need reliable and accurate information on AL rates and mortality rates following AL. Previous studies have shown that patients with rectal cancer prefer to be involved in the decision making process and to be informed on risks of different treatment options[5].

The aim of this study was to perform a systematic review of studies describing anastomotic leakage and the associated mortality in comparison to the overall postoperative mortality after low anterior resection (LAR) for rectal cancer. Regarding the difference in impact and consequences for a patient, it is important to distinguish clinically relevant anastomotic leakage from radiologic leakage.[1] In this review we assessed clinical anastomotic leakage.

Methods

Literature search

Relevant studies published between January 1990 and August 2011 were identified by searching Medline, Embase and The Cochrane Library databases. The following search terms were used: AL, dehiscence, mortality, anterior resection, mesorectal excision. Both free text search and MeSH search for keywords were employed. Two investigators (HS and BB) independently performed the literature search. To increase the sensitivity of the search strategy, the 'related article' function was used, and reference lists of relevant articles were searched for additional relevant studies. The search was restricted to publications in English.

Study selection and data extraction

All randomized controlled, multi-center and single-center, prospective and retrospective studies describing surgical therapy for rectal cancer were considered for inclusion. Studies were included when describing patients undergoing elective LAR for rectal cancer. The articles had to contain at least data on 1) AL rates 2) mortality following AL and 3) overall mortality. Only articles describing all three outcomes were included. Only original articles were included in order to maintain adequate details on patient selection, study design, methods and outcome, allowing for accurate comparison of the study results. Studies were excluded from analysis when they also described patients that underwent emergency resections, high anterior resections, abdominoperineal resections, procedures other than for rectal cancer and experimental surgical techniques such as robot-assisted surgery. We extracted data on the definition and incidence rate of AL, postoperative mortality caused by AL and overall postoperative mortality. No rating of these studies was performed; al studies were accepted or rejected based on the criteria noted above. Data were extracted independently by two different researchers and compared. Any discrepancies were resolved by discussion.

Statistical analysis

The percentages of AL, postoperative mortality following leakage and overall postoperative mortality were meta-analyzed with a random effects model. Because the numbers were small in most studies, we applied the method of Hamza et al.[6] The standard deviations of the random effect was zero, therefore data could be pooled. The overall percentages of the outcomes were therefore the number of events over studies divided by the total number of patients over studies.
Statistical analyses were carried out in PASW Statistics, Rel. 18.0.2009 (SPSS inc., Chicago, Il, USA) and R 2-14 (The R Project for Statistical Computing and The Comprehensive R Archive Network; http://cran.r-project.org/).

Results

Included studies

We identified 188 studies of which 22 were included.[3,7-26] One hundred and sixty six studies did not meet the inclusion criteria and were excluded from further analysis. The most common reason for exclusion was that the study described also other types of surgery without providing specific data on the outcomes of LAR alone (n=69). Twenty-eight studies were excluded because they did not mention all three outcome measures. Reasons for exclusion are shown in *table 1*.
The included studies had a total population of 10343 patients. Sample sizes of studies varied from 38 to 2726 patients. There were two randomized controlled trials investigating the effect of a defunctioning stoma on AL rates. The other studies were non-randomized (*table 2*).

Anastomotic leakage: incidence and definition.

For the meta-analysis we used the number of ALs as defined in the study. The overall AL rate was 9% (974 out of 10343 patients). There was a large variation in AL rates; the highest reported AL rate was 28% and the lowest reported rate was 3% (*figure 1*).

AL was described in 19 of 22 studies. Three studies gave no definition of AL, fourteen studies gave a detailed description of the definition of AL and the remaining studies gave only a limited definition. Most definitions of AL consisted of a clinical suspicion based on the patient's symptoms. The reported symptoms comprised the signs of localized or generalized peritonitis (10 studies), fecal discharge from the wound and/or drain (9 studies), abscess (10 studies), recto-vaginal fistulas (6 studies), purulent discharge from drain, wound and leukocytosis (1 studies). The need for active intervention was used in some studies to define a clinically relevant AL, whereas others accepted signs of leakage without further intervention. None of the authors provided a grading system to classify the severity of AL (*table 3*).

Overall mortality: incidence and definition

For the meta-analysis we used the number of postoperative deaths as was described in the study. The mean overall postoperative mortality rate was 2% and varied from 0 to 8% (*figure 2*).

The definition of postoperative mortality differed. Two studies specified postoperative mortality as death within 30 days after operation, both in-hospital and after discharge. One study considered all in-hospital deaths as postoperative mortality. Five studies reported postoperative mortality as all patients who died within 30 days after surgery and gave no further specification of the location (in-hospital or after discharge). Three studies included all in-hospital deaths in the postoperative mortality rate, without specification of timing. Nine studies described postoperative mortality without specification of location (in-hospital or after discharge) or timing. Two studies did not specify their definition of mortality.

Postoperative mortality caused by AL: incidence and definition.

For the meta-analysis we used the number of postoperative mortality caused by ALs as defined in the study. In total, 71 out of 10343 patients died as a direct consequence of AL (0.7%), ranging from 0 to 5%. One third of the overall mortality was caused by AL. This ratio ranged from 0 to 100% (*figure 2*).

Nine studies defined postoperative mortality caused by AL as 'death of septic complications secondary to AL'. Five studies defined postoperative mortality caused by AL as 'all deaths after anastomotic leakage'. No study reported details on how causes of death were determined, for example autopsy findings. The remaining studies reported no postoperative deaths in patients with AL (*table 3*).

Discussion

In this thorough overview of studies describing anastomotic leakage and subsequent mortality after low anterior resection for rectal cancer we found that patients have a considerable risk for AL (9%). We found that AL considerably contributed to mortality after rectal cancer surgery, accounting for one third of all postoperative mortality. This finding is supported by, and could well be compared with, the results of a nationwide population based study assessing exclusively patients who died following anterior resection of the rectum[28]. The study describes 140 patients that died following rectal excision with anastomosis, of whom 42% had anastomotic leakage, a result very similar our findings.

The information of the present study may very well be used for counseling patients preoperatively. However, we also found that the definitions of AL and postoperative mortality varied widely. The twenty-two included studies used twelve different definitions to describe AL. The lack of universally accepted definitions for AL has already been described in 2001 by Bruce et al[29]. They described 29 separate definitions for AL after lower gastrointestinal surgery. The author plead for the use of a standard definition that could distinguish between clinical minor and major leaks.

We also found six different definitions of overall postoperative mortality. The timing (30-days or 90-days) or location of death (in-hospital mortality or death after discharge) varied. Recent evidence shows that mortality almost doubles by 90 days when compared with the rate at 30 days in patients undergoing colorectal surgery[30]. This clarifies the importance of a uniform agreement on measurement of postoperative mortality.

Average rates of AL, postoperative mortality and mortality as a result of AL all showed a wide range between the different publications. This may be a reflection of differences in definition, as well as actual differences in performance.

Surgical treatment for rectal cancer is embedded with difficult decision, often subject to both doctors and patients' preferences. The variability of definitions and variance in outcome rates between studies may hinder providing patients with reliable risk information preoperatively.

Obviously, AL and its subsequent mortality will never occur if an anastomosis is avoided, e.g. when a permanent end colostomy is constructed. In the case of choosing the anastomosis there is today strong evidence for adding a defunctioning stoma in order to reduce the risk for clinical leakage.[31] The benefits of preventing or minimizing AL should always be balanced against the disadvantages of the alternatives. A defunctioning stoma itself carries a substantial risk of becoming permanent either as a loop stoma[32] or as a permanent loop ileostomy or a permanent end colostomy.[33,34] Also, different studies report that stomal complications are prevalent, as they are seen in 25 to 50% of patients with a stoma after 8-10 years of follow-up.[35,36] Furthermore, the morbidity and mortality of closure of a defunctioning stoma should be taken into account.[37] On the other hand, if AL occurs in patients without a deviating stoma, it often requires re-operation, and also creation of a secondary stoma. Last, the effect of a treatment on quality of life should be considered. Opposed to the negative influence of a stoma on quality of life, patients with (low) anastomoses also have a risk for functional derangements, incontinence, sexual and bladder functions. All these factors should be balanced against each other and taken into account in the final decision.

This decision would be easier if we could select those patients with a higher risk for AL and subsequent mortality. Predicting AL enhances the possibility to take precautions to prevent it, or diminish its consequences. The percentage of patients developing AL depends on multiple factors. Several patient-, tumour-, and therapy-related parameters have been identified as risk factors for AL in a large amount of studies. A disturbed microcirculation, as seen in nicotine abuse or diabetes mellitus patients, has been said to increase the risk for AL[38,39] Also, height of the anastomosis, preoperative radiation, a malnourished status, steroid use, male gender and peri-operative bleeding are previously described potential risk factors.[40] Unfortunately, despite the vast body of evidence on the potential risk factors, AL remains difficult to predict in an individual patient. As the selection process of high-risk patients remains imperfect, we emphasize that every single patient should be counseled preoperatively on the risk of AL, the consequences including mortality and the possibility of stoma formation.

The available literature however, is insufficient to inform patients on AL and subsequent mortality and make the trade-off between an anastomosis (with or without defunctioning stoma) or a permanent end colostomy.

Ideally, to support clinical decision making in current surgical practice, this meta-analysis would also provide information on AL and the subsequent mortality risk in subgroups of patients, such as patients treated with preoperative radio- or chemotherapy or patients with a defunctioning stoma. However, an important inclusion criterion in our analysis was the availability of data on AL, mortality due to AL and overall mortality. Most articles did not stratify all these three outcomes for individual subgroups; therefore meta-analysis within these subgroups was not possible. The lack of availability of this data further emphasizes the limitation of current evidence on anastomotic leakage rates for the use in daily clinical decision making.

Therefore, more research is needed, one of the most important things being uniformity of definitions. Recent growing public interest in quality and outcome of medical and surgical care has led to the development of audit programs. These guarantee uniformity of definition and measurement of basic outcome parameters such as AL, subsequent postoperative mortality and overall postoperative mortality. Frequent feedback of these outcomes may support clinicians when informing patients about risks of different treatment options and facilitates the decision making process.

Table 1: Studies excluded from the meta-analyses.

Reason for exclusion	***Number of studies (n)***
Other types of surgery included	69
Not all three outcome criteria mentioned	28
Surgical procedures other then for rectal cancer included	14
Only abstract available	13
Review of the literature	13
Described also non-curative resection	6
Also emergency situations included	5
Described new surgical technique to avoid leakage	8
Other	9
Total	**165**

Table 2: Characteristics of the included studies.

Author	***Year***	***Patients (n)***	***Study design***
Swellengrebel et al	2011	47	Prospective single centre
Shiomi et al	2010	329	Retrospective single centre
Fouda	2010	56	Prospective single centre
Den Dulk et al	2009	2726	Retrospective multi centre
Bertelsen et al	2009	1494	Retrospective multi centre
Tsikitis et al	2009	237	Retrospective single centre
Eberl et al	2009	472	Retrospective single centre
Kuroyanagi et al	2008	159	Retrospective single centre
Asteria et al	2008	520	Retrospective single centre
Pugliese et al	2008	157	Retrospective single centre
Matthiessen et al	2007	134	Randomized controlled trial
Lefebure et al	2007	132	Retrospective single centre
Krushewski et al	2007	276	Retrospective single centre
Dulucq et al	2005	218	Retrospective single centre
Eriksen et al	2004	1958	Retrospective single centre
Chaudry et al	2000	69	Retrospective single centre
Poon et al	1999	148	Retrospective single centre
Machado et al	1999	161	Retrospective single centre
Pakkastie et al	1997	38	Randomized controlled trial
Enker et al	1999	681	Retrospective single centre
Memon et al	1996	154	Retrospective single centre
Grabham et al	1995	77	Retrospective single centre
Fick et al	1990	39	Retrospective single centre

Table 3: Definition of AL, overall postoperative mortality and postoperative mortality caused by AL.

Author	***Definition of anastomotic leakage***	***Definition of postoperative mortality caused by anastomotic leakage***	***Definition of overall postoperative mortality***
Swellengrebel et al	Not specified	Not specified	30-day mortality
Shiomi et al	Clinically by the presence of the following: discharge of gas, pus or feces from the drain or wound; discharge of pus per rectum; or rectovaginal fistula	Mortality caused by leakage	Not specified
Fouda et al	Clinically as gas, pus or fecal discharge from the drain, operative wound, pelvic abcess, peritonitis and rectovaginal fistula	Mortality caused by leakage	Not specified
Den Dulk et al	Faecal discharge from pelvic drain or abdominal wound, or radiologically, endoscopically or surgically proven anastomotic leakage in symptomatic patients such as those with peritonitis	All deaths after leakage	30-day mortality
Bertelsen et al	Symptomatic anastomotic leakage defined as peritonitis and a defect in the anastomosis, or discharge of pus from the rectum, or rectovaginal fistula, or the passage of faeces or gas from an abdominal drain	All deaths after leakage	30-day mortality
Tsikitis et al	Pelvic abscess included	Not specified	Postoperative mortality
Eberl et al	Gas, pus or fecal discharge from the pelvic drain, peritonitis, signs of rectovaginal fistula, fever, or leukocytosis	Mortality caused by leakage	30-day mortality or during hospital stay
Kuroyanagi et al	Not specified	Not specified	In-hospital mortality
Asteria et al	Small adjacent absces, adjacent unilocular, abscess, failure of half or more of the circumference of an anastomosis, multilocular abscess or peritonitis	All deaths after leakage	30-day mortality

Pugliese et al	Not specified	Mortality caused by leakage	Postoperative mortality
Matthiessen et al	Peritonitis caused by leakage from any staple line, rectovaginal fistula, and pelvic abscess without radiologically proven leakage mechanism were included	Not specified	30-day mortality
Lefebure et al	Pus or fecal discharge from the drain, pelvic abscess, peritonitis, or discharge of pus per rectum	All deaths after leakage	30 days of operation, both in-hospital and death after discharge
Krushewski et al	Clinically manifest anastomotic leakage: fecal discharge from the drain, surgical wound or vagina or by CT detection	Mortality caused by leakage	Postoperative mortality
Dulucq et al	Leakage requiring operative management with a diverting stoma or treated conservatively with TPN and percutaneous drainage when needed	Not specified	Postoperative mortality
Eriksen et al	Pelvic abscess, faecal discharge from wound, septicaemia, peritonitis, with or without radiologically confirmed leakage.	All deaths after leakage	30 days of operation, both in-hospital and death after discharge
Chaudry et al	Asymptomatic leakage, abcess requiring drainage or reintervention.	Not specified	Postoperative mortality
Poon et al	Clinical anastomotic leakage	Not specified	Postoperative mortality
Machado et al	Pelvic sepsis, which included clinical staple line leaks,infectious collections in the pelvis with or without a proven staple line leak, and enterovaginal fistulas	Mortality caused by leakage	30-day mortality or during hospital stay
Enker et al	Clinically or radiologically apparent leakage, pelvic abscess	Mortality caused by leakage	In-hospital mortality
Memon et al	Clinical anastomotic leakage	Mortality caused by leakage	Operative deaths
Grabham et al	Clinical anastomotic leakage	Not specified	Perioperative deaths
Pakkastie et al	Feacal discharge from the wound or drain, pelvic sepsis, postoperative fever or septicaemia	Mortality caused by leakage	Postoperative mortality

Figure 1. AL rates reported by the included studies ranked by volume.

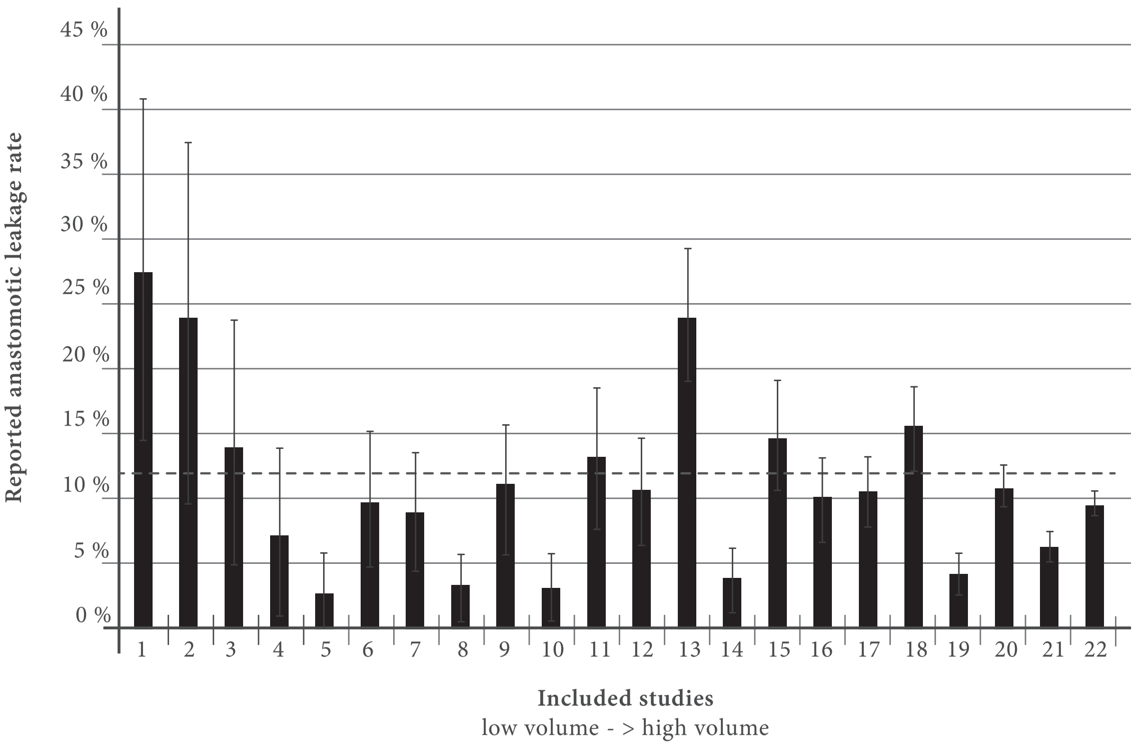
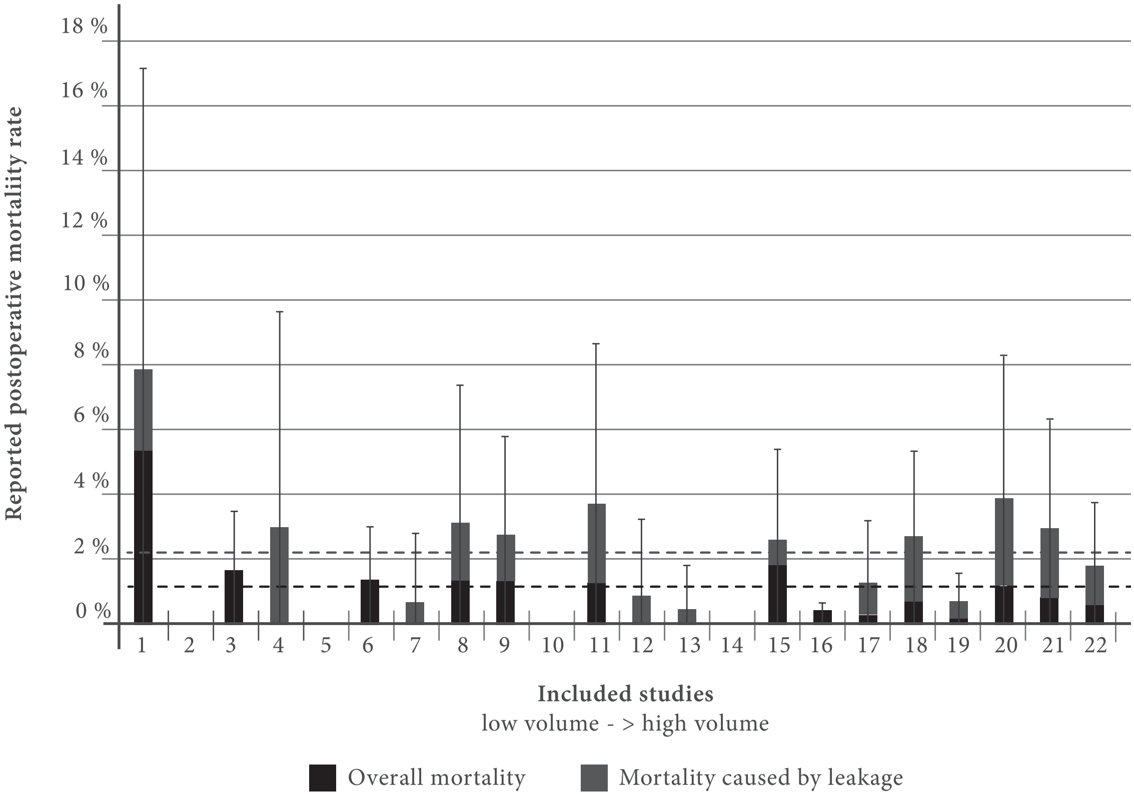


Figure 2. Overall postoperative mortality rates and postoperative mortality caused by AL reported by the included studies. Studies are ranked by volume.



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Chapter 2:

HIGH ONE-YEAR COMPLICATION RATE AFTER LOW ANTERIOR RESECTION FOR RECTAL CANCER.

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Abstract

Introduction: Surgical options after low anterior resection for rectal cancer include a primary anastomosis, anastomosis with a defunctioning stoma and an end-colostomy. This study describes short-term and one-year outcomes of these different surgical strategies.

Methods: Patients undergoing surgical resection for primary mid and high rectal cancer were retrospectively studied in seven Dutch hospitals with one-year follow up. Short term endpoints were postoperative complications, re-interventions, prolonged hospital stay and mortality. One-year end-points were unplanned readmissions and re-interventions, presence of stoma and mortality.

Results: Nineteen per cent of 388 included patients received a primary anastomosis, 55% an anastomosis with defunctioning stoma, and 27% an end-colostomy. Short-term anastomotic leakage was 10% in patients with a primary anastomosis vs. 7% with a defunctioning stoma (P=0.46). An end-colostomy was associated with less severe re-interventions. One-year outcomes showed low morbidity and mortality rates in patients with an anastomosis. Patients with a defunctioning stoma had high (18%) readmissions and re-intervention (12%) rates, mostly due to anastomotic leakage. An end-colostomy was associated with unplanned re-interventions due to stoma/abscess problems. During follow-up, there was a 30% increase in patients with an end-colostomy.

Conclusion: This study showed a high one-year morbidity rate after low anterior resection for rectal cancer. A defunctioning stoma was associated with a high risk for late complications including anastomotic leakage. An end-colostomy is safe alternative to prevent anastomotic leakage, but stomal problems cannot be ignored. Selecting low-risk patients for an anastomosis may lead to favorable short- and one-year outcomes.

Introduction

Colorectal cancer is a significant source of mortality with more than 12.000 cases diagnosed in the Netherlands each year.[1] The cornerstone of treatment is surgical resection.

When discussing surgical treatment options for rectal cancer with patients preoperatively, difficult considerations can be encountered. When tumor size, stage and location allow a sphincter preserving resection, the surgical options consist of an anastomosis, an anastomosis with a defunctioning stoma and an end-colostomy. Both patients and surgeons seem to have a strong preference to avoid a stoma, under the assumption that it will have negative consequences on quality of life.[2, 3] However, an anastomosis bears the risk of anastomotic leakage, which may cause re-operations, prolonged hospital stay, morbidity, mortality and possibly a worse oncological outcome.[4-6] Furthermore, functional outcome after a low anastomosis, especially in combination with radiotherapy or chemoradiation can also lead to an impaired quality of life.[7, 8] Additionally, a defunctioning stoma has been proven to diminish the sequelae of anastomotic leakage.[9] Anastomotic leakage will not occur when an anastomosis is avoided, e.g. when an end-colostomy is constructed. On the other hand, stomas may also have their own significant mid-to long-term morbidity and complications after reversal of the stoma have been reported.[10-14]

In order to inform and involve patients in preoperative clinical decision-making, surgeons need information on outcomes of different treatment options. The aim of this study is to describe the short-term and one-year outcomes of different surgical treatment options for mid and high rectal cancer patients.

Methods

Study population

We explored short term and one-year outcomes of all consecutive patients who underwent surgical resection for primary rectal cancer between the 1st of January 2009 and 31st of June 2011 in 7 different hospitals in the Netherlands. Surgical resection was performed according total mesorectal excision. In patients with high tumors surgical resection was performed five centimeters below the tumor with the mesorectum optionally left in situ. Patients with a tumor less than 5 cm from the anal verge, patients undergoing abdominoperineal resection, and patients with a T4 tumor were excluded, because these patients represent subgroups with other surgical approaches and subsequent different expected outcomes.

Outcomes

We extracted information on the following patient and tumor characteristics: age, gender, ASA-classification, co-morbidity, abdominal surgical history, preoperative tumor complications, tumor stage, additive resections and distance of tumor to the anal verge.

Short term endpoints, defined as endpoints until 30 days after initial surgery, were postoperative complications, re-interventions, prolonged hospital stay and postoperative mortality. Complications were defined as all postoperative complications, both non-surgical and surgical, during hospital admission; anastomotic leakage was defined as clinically relevant anastomotic leak requiring re-intervention, both radiological and surgical; re-interventions were defined as all additional procedures, both radiological and surgical, performed for the treatment of all postoperative complications; surgical re-interventions were laparotomy or laparoscopy; a prolonged hospital stay was defined as hospital stay longer than 14 days; postoperative mortality was defined as in-hospital mortality or within 30 days after primary surgery.

One-year outcomes were unplanned readmissions and re-interventions after initial admission, presence of a stoma and mortality within one-year. From patients with a defunctioning stoma or end-colostomy, we extracted data on whether a second surgery was performed to restore bowel continuity; post-operative complications and hospital stay of this procedure were also analyzed.

Analyses

The study population was divided in three groups according to their received surgical treatment: anastomosis, anastomosis with defunctioning stoma, or end-colostomy. Whether or not patients with an end-colostomy had a resection of the rectal stump was not taken into account. During the study period, patients switched between these groups, because of re-interventions for complications, or because of elective secondarily stoma reversal. Patient and tumor characteristics and short-term postoperative outcomes were described in relation to the initial received surgical treatment. For analysis of the one-year outcomes, analyses groups were defined according their anastomosis/ stoma status after first hospital admission. A Chi-squared analysis was performed to investigate differences in short-term outcomes.

For one-year outcomes the differences in readmission rate, re-intervention rate and 1-year mortality were statically tested. Statistical significance was defined as $p<0.05$. All statistical analyses were performed in PASW Statistics, Rel. 18.0.2009.

Results

During the period of January 2009 to June 2011, 843 consecutive patients underwent surgical resection for primary rectal cancer in the 7 participating hospitals. A total of 455 patients were excluded (14 urgent resections, 386 patients with low rectum tumors (<5 cm) and/

or undergoing an abdominoperineal resection,), and 45 patients with a T4 tumor). Patients with unknown anastomosis/stoma status were excluded as well (n=10). After selection according the eligibility criteria, 388 patients undergoing low anterior resection for rectal cancer were included in this study.

Short-term outcomes

Table 1 shows patient and treatment characteristics according to initial surgical treatment; seventy-two patients (19%) received a primary anastomosis 214 patients (55%) had an anastomosis with defunctioning stoma, and 102 patients (27%) an end-colostomy. Patients with an end-colostomy were significantly older; and a higher ASA-classification when compared to both other groups; patients with an anastomosis had significantly higher tumors; patients with a defunctioning stoma less often had distant metastases and more often received neoadjuvant chemo-radiation therapy. Fifty-nine per cent of the defunctioning stomas concerned loop ileostomies; 41% were loop transversostomies

Postoperative complications

Table 2 shows the short-term outcomes after initial surgery. One third of all patients developed a postoperative complication; regardless of the type of surgery. Anastomotic leakage rates were 10% (n=7) in patients with an anastomosis; and 7% (n=14) in patients with defunctioning stoma (not statistically significant; p=0.46).

Re-interventions and hospital stay

There were no statistically significant differences between the three treatment groups in overall percentage of re-interventions. In patients with an anastomosis with or without a defunctioning stoma, re-interventions were mainly surgical, while patients with an end-colostomy mainly underwent re-interventions for stoma or wound management. Eighty-six per cent of patients, in which anastomotic leakage occurred, needed a surgical re-intervention. This percentage was similar for patients with and without a defunctioning stoma (respectively 6 out of 7 and 12 out of 14). Patients with a defunctioning stoma and patients with an end-colostomy had a trend towards a longer hospital stay, although this difference was not statistically significant.

Postoperative Mortality

Postoperative 30-day or in-hospital mortality rates were low: 0% in patients with an anastomosis, 1% in patients with an anastomosis with a defunctioning stoma and 2% in patients with an end-colostomy.

One-year outcomes

<u>Unplanned readmissions</u>

Table 3 shows the follow up outcome of the three groups as situated after first hospital admission: 62 patients (16%) with an anastomosis; 209 patients (54%) with an anastomosis with a defunctioning stoma, and 117 patients (30%) with an end-colostomy. Patients with a defunctioning stoma had a readmission rate of 18%, mostly due to (late) anastomotic leakage. Patients with an end-colostomy had a readmission rate of 17%, mostly due to stoma-related problems. Patients with a primary anastomosis had a significantly lower readmission rate than both other groups. Only one patient of the primary anastomosis group was readmitted because of anastomotic leakage, and two patients for other reasons.

Re-interventions

Both patients with a defunctioning stoma and patients with an end-colostomy had a 12% re-intervention rate. In patients with a defunctioning stoma, 5% underwent a surgical re-intervention in which the anastomosis was disconnected and an end-colostomy was created. Five percent of patients underwent a radiological drainage. Revision of the stoma was the most frequent re-intervention in patients with an end-colostomy (7%). Also, in this group, 5% of patients underwent radiological drainage of an abscess. Only one patient with a primary anastomosis underwent a re-intervention because of anastomotic leakage. In this patient, the anastomosis was disconnected and an end-colostomy was created.

Stoma reversal

In the majority of patients with a defunctioning stoma, bowel continuity was restored with a second surgery. In 22% of patients, the stoma was not reversed after one-year. The overall complication rate after stoma closure was 24%; and the anastomotic leakage rate was 4% (*Table 3*). In patients with an end-colostomy, 5% underwent a second surgery to restore bowel continuity. In half of the patients, this secondary surgery was performed within 6 months after the initial surgery. The mean hospital stay after stoma reversal was 6 days for both defunctioning stomas and end-colostomies. There were no deaths after stoma closure.

Mortality

One-year mortality rate was the highest in patients with an end-colostomy; twenty-two patients (19%) in this group died. None of these deaths were surgery-related; all deaths were due to progression of the underlying disease or due to other diseases.

Switching between treatment groups

Due to changes in anastomosis/stoma status, patients switched between the three different treatment groups during the entire study period (*Figure 1*). After initial surgery, 19% of patients had a primary anastomosis, 55% had an anastomosis with defunctioning stoma, and 27% of patients had an end-colostomy. The percentage of patients with an end-colostomy increased with 30% (n=31). This increase consisted mainly of patients with initially a defunctioning stoma, in which anastomotic leakage occurred. Due to unplanned re-interventions and elective stoma reversal, eventually 60% of all patients had an anastomosis, 6% had an anastomosis with defunctioning stoma, and 34% had an end-colostomy.

Discussion

Overview of findings

The present study described short-term and one-year outcomes of different treatment strategies in rectal cancer surgery. Although patients with a defunctioning stoma had a somewhat lower risk for short-term anastomotic leakage, they had a high risk for unplanned readmissions and re-interventions, mostly due to late anastomotic leakage. Furthermore, these patients had an additional high risk for postoperative complications after restoration of bowel continuity, including anastomotic leakage. In contrast, the one-year outcomes of patients with an anastomosis were surprisingly good. Although both groups were not completely comparable, the large difference in one-year outcomes could hardly all be due to lower tumors and a higher use of chemoradiotherapy in patients with a defunctioning stoma.

One expects that patients with an end-colostomy would have worse post-operative outcomes, since these patients were significantly older, and had a higher ASA-classification. Interestingly, these patients had a similar risk for postoperative complications, and even a lower risk for invasive re-interventions. This is probably an over-estimation of the actual risk associated with an end-colostomy. On the long-term however, end-colostomies were associated with stoma problems or pelvic abscesses causing unplanned readmissions.

Comparison with other studies

The value of a defunctioning stoma to diminish the consequences of anastomotic leakage has been the subject of debate for a long time. Earlier randomized studies showed fewer anastomotic leaks and reoperations after low anterior resection with a defunctioning stoma.[9,15,16] A considerable amount of retrospective studies also describes the beneficial effect of a defunctioning stoma on direct postoperative anastomotic leakage rates.[6, 17-19] On the other hand, there studies that support the notion that the routine use of a defunctioning stoma in low anterior resection is not advisable. Fielding et al. observed that there was a higher leakage rate in patients with a defunctioning stoma (18% versus 7%); Enker et al and Matthiessen et al showed that a defunctioning stoma did not reduce the incidence of anastomotic leakage in patients undergoing low or ultralow anterior resection.[20, 21] Furthermore, a study from our own group showed that while during the last decade there was an increase in the use of defunctioning stomas, anastomotic leakage rates remained similar.[22]

Previous studies described the long-term stoma problems of both defunctioning stomas and end-colostomies.[13,14] A study of 163 patients undergoing an extended Hartmann resection, showed pelvic abscesses in 30% of patients, diagnosed on a median of 35 days postoperative (range 7-434).[23] Two studies reported on high readmission rates of patients with defunctioning stomas.[24, 25] In contrast with our findings, patients were mostly readmitted because of dehydration. This might be related to the fact that in our study, 41% of the defunctioning stomas were transversostomies, which are known to have less dehydration problems than ileostomies.[26] Den Dulk et al described the policy of stoma formation in patients entered in the Dutch TME-trial for rectal cancer, and found that 20% of the stomas were never reversed, which is similar to our findings. We found a high overall morbidity and anastomotic leakage rate after stoma reversal, which is confirmed by previous publications; overall morbidity rates of 20-30% and anastomotic leakage rate of 2-9% after closure of defunctioning stomas have been reported.[12, 27, 28]

Strengths and limitations

An important strength of this study is that both the short-term and one-year outcomes were thoroughly evaluated. As far as we are aware, this is the first study to take into account one-year outcomes of all three surgical options. In most studies and audits, only short-term results are reported. As shown in this study, ongoing changes in outcome occur during the first year after surgery for rectal cancer due to complications and stoma reversal. Therefore, it is critical to take these long term outcomes into account when different surgical strategies are considered.

However, some limitations deserve mentioning. There was a possibility of a selection bias, as we randomly selected seven different hospitals. However, comparison of our cohort to the national data of the Dutch Surgical Colorectal Audit, including all patients undergoing surgical resection for colorectal cancer in the Netherlands, showed no significant differences in patient, tumor and treatment characteristics (data not shown).[29] Moreover, due to our small sample size, the outcomes could not be corrected for differences in case-mix since this requires a large amount of cases to prevent over-fitting. A larger study is needed in order to provide a case-mix adjusted comparison in both short- and long-term outcomes between the different groups.

Clinical implications and future research

In this study, we found favorable outcomes in patients with an anastomosis. These are probably caused by adequate identification of high-risk patients. In these patients, an end-colostomy to prevent short-term anastomotic leakage may be the best decision. Although an end-colostomy has the risk for stoma problems or pelvic abscesses on the long term, these are less consequential than immediate postoperative anastomotic leakage. Avoiding or limiting the risk for anastomotic leakage by routine creation of defunctioning stomas is not desirable, especially considering its poor one-year outcomes found in this study.

Scoring systems that could predict a patients' risk for anastomotic leakage pre-operatively should be the focus of future studies to facilitate decision-making.[30] Also, focusing on improvements in intraoperative conditions and surgical techniques rather than routine creation of defunctioning stomas may be the way to go. Previous studies with intraluminal devices showed good results in preventing anastomotic leakage and a multicenter randomized study is currently being performed.[31]

While the decision whether or not to make an anastomosis remains difficult, patients' preferences concerning the risk of morbidity and mortality of anastomotic leakage versus the consequences of stomas should be taken into account. This consideration requires thorough preoperative counselling.

Conclusion

Although a large proportion of patients received defunctioning stomas, these were associated with significant long-term morbidity including late anastomotic leakage. An end-colostomy may be a safe alternative to prevent anastomotic leakage, but long-term problems may also occur. Favorable outcomes in patients with an anastomosis are probably caused by adequate selection of low-risk patients, which should be the focus of future investigation.

Table 1: Characteristics according to type of surgery after initial surgery in 388 rectal cancer patients diagnosed between 01 January 2009 and 31 June 2011.

		Anastomosis		***Anastomosis with defunctioning stoma***		***End-colostomy***	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Total (after initial surgery)		**72**		**214**		**102**	
Age	Mean	64		63		72*	
Gender	Female	38	53	87	41	47	46
ASA classification	ASA 3+	9	13	23	11	17	17*
Charlson	1	13	18	37	17	29	28
	2+	13	18	35	16	17	17
Preoperative complications**		1	1	9	4	1	1
Tumor (T-) stage	pT0	4	6	22	10	8	8
	pT1	5	7	13	6	10	10
	pT2	12	17	64	30	21	21
	pT3	47	65	107	50	62	61
Distant metastases	M1	15	21	7	3*	21	20
Abdominal surgical history		18	25	64	30	22	22
Extensive resection		3	4	25	12	10	10
Distance of tumor to anal verge	Mean	13		10*		10*	
Neoadjuvant therapy	5x5 Gy	27	37	92	43	31	43
	Chemoradiation	13	18	107	50*	17	24

Numbers with an * were statistically significant ($p<0.05$) when compared to patients with an anastomosis.
ASA classification=American Society of Anaesthesiologists classification. ** obstruction, perforation, abscess and bleeding.

Table 2: Short-term outcomes of patients with an anastomosis, an anastomosis with a defunctioning stoma, and an end colostomy.

	Anastomosis		***Anastomosis with defunctioning stoma***		***End-colostomy***	
	Nr	**%**	**Nr**	**%**	**Nr**	**%**
Total (after initial surgery)	**72**		**214**		**102**	
Postoperative complications	21	30	65	31	32	29
Anastomotic leakage	7	10	14	7	n.a.	n.a.
Re-interventions	11	16	27	13	13	12
Radiological drainage	1	1	3	1		
Surgical (laparoscopy/laparotomy)	8	11	20	9	5	5
Stoma/wound management	2	3	4	2	8	8
Prolonged hospital stay	12	18	47	23	23	22
Postoperative mortality	0	0	1	1	2	2

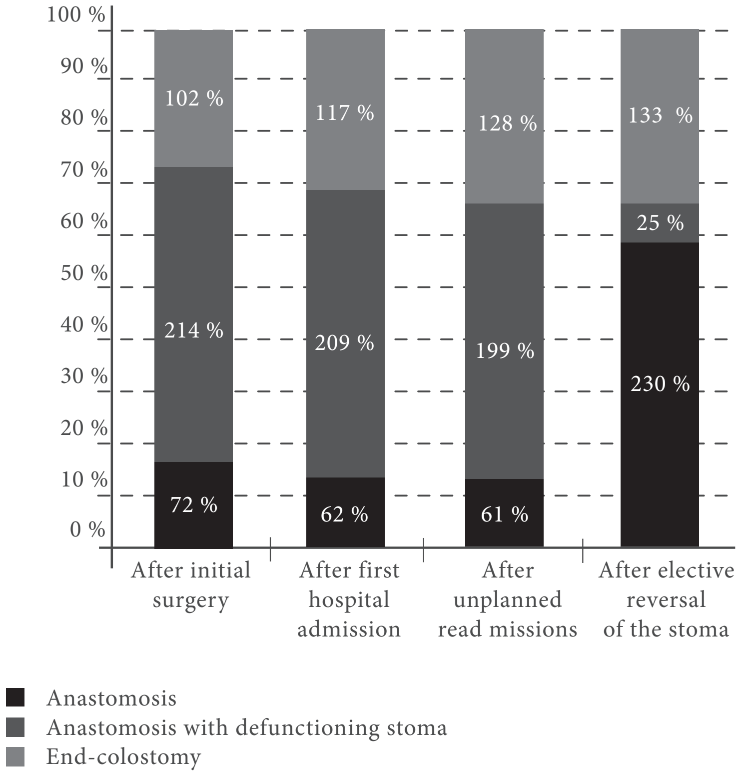
None of the differences were statistically significant

Table 3: One-year outcomes according to type of surgery after first hospital admission.

		Anastomosis		Anastomosis with defunctioning stoma		End-colostomy	
		Nr	%	Nr	%	Nr	%
Total (after first hospital admission)		**62**		**209**		**117**	
Readmissions		3	5	38*	18*	20*	17*
Reason for readmission	Anastomotic leakage	1	2	24	11	n.a.	n.a.
	Ileus	0	0	3	1	3	3
	Stoma problems	n.a.	n.a.	5	2	12	10
	Other**	2	3	6	3	5	4
Re-interventions		1	2	26*	12*	14*	12*
Type of re-intervention	Revision stoma			5	2	8	7
	Disconnect anastomosis + construction stoma	1	2	11	5		
	Drainage			10	5	6	5
Stoma reversal				163	78	6	5
Complications	All			39	24	2	33
	Anastomotic leakage			6	4	0	0
	Other			33	20	2	33
	Hospital stay (mean days)			6		6	
Time to reversal	<3 month			41	25	1	17
	3-6 months			64	39	2	33
	6-9 months			31	19	2	33
	>9 months			26	16	1	17
1-year mortality		2	3	7	3	22*	19*

Differences in readmission rate, reintervention rate and 1-year mortality were analyzed with a Chi-Squared test. Numbers with an * were statistically significant ($p<0.05$) when compared to patients with an anastomosis. ** includes dehydration and infection.

Figure 1. Changes in distribution of patients undergoing resection for mid and high rectal cancer according to stoma or anastomosis construction during the first year.



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Chapter 3:

PREOPERATIVE RISK INFORMATION AND PATIENT INVOLVEMENT IN SURGICAL TREATMENT FOR RECTAL AND SIGMOID

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Abstract

Introduction: Surgery for rectal and sigmoid cancer is an exemplary setting for investigating preoperative information provision and Shared Decision Making (SDM), since the decision consists of a trade-off between the pros and cons of different treatment options. The aim of this study was to explore surgeons' opinion on the preoperative information that should be given to rectal and sigmoid cancer patients and to evaluate what is actually communicated. Seconds, we assessed surgeons' attitudes towards Shared Decision Making and compared these with patient involvement.

Methods: A questionnaire was sent to Dutch surgeons with an interest in gastroenterology. Preoperative consultations were recorded. A check list coded the information surgeons communicated to the patients. The OPTION-scale was used to measure patient involvement.

Results: Questionnaires were sent to 240 surgeons and 103 (43%) responded. They requested information on anastomotic leakage, its consequences, benefits and risks of a defunctioning stoma and impact of a stoma on quality of life necessary preoperative information. In practice, patients were inconsistently informed of these items. Most participants agreed to using SDM in their consultations. In practice, most patients were offered only one treatment option and little SDM was seen. The mean OPTION-score was low. (7/100)

Conclusions: The information given to patients with rectal and sigmoid cancer to decide on which surgical option they would prefer is insufficient. Information should be given on all treatment options with their complications and outcome before any decision is made.

Introduction

In recent years, the concept of Shared Decision Making (SDM) has gained widespread appeal to both clinicians and patients.1, 2 In SDM, clinicians and patients make decisions together using the best available evidence.[2] SDM is considered especially important for patients who present with a serious illness such as cancer, when the outcomes are uncertain, or when different treatment options are available.[3] Since different possible outcomes (benefits and risks) of the treatment options may vary in their impact on the patient's physical and psychological well-being, informing patients on these matters is the cornerstone of decision making about treatment.[4]

The decision on surgical treatment for rectal and sigmoid cancer is a trade-off between benefit and harm, in which, besides tumour and patient related factors, both doctors' and patients' preferences play a role. When tumour size, stage and location allow a sphincter preserving resection, the surgical treatment options consist of an anastomosis, an anastomosis with a defunctioning stoma, or an end-colostomy.

Both patients and surgeons seem to have a strong preference to avoid a stoma, under the assumption that it will have negative consequences for the quality of life.[5, 6] However, an anastomosis bears the risk of anastomotic leakage (AL), which may cause re-operation, prolonged hospital stay, morbidity, a possibly worse oncological outcome and even mortality.[7-9]

The benefits of preventing or minimizing AL should always be balanced against the disadvantages of the alternatives. A defunctioning stoma itself carries a substantial risk of becoming permanent.[10, 11] The morbidity and mortality of closure of a defunctioning stoma should also be taken into account.[12] Different studies report that stomal complications are prevalent, seen in 25 to 50% of patients with a stoma after 8-10 years of follow-up.[13, 14] Finally, as opposed to the negative influence of a stoma on quality of life, patients with a (low) anastomosis also have a risk for functional derangements, such as incontinence, and sexual- and bladder dysfunction.[15]

In order to make this complicated decision, thorough preoperative information provision to patients on these possible outcomes seems essential before a decision is made on the preferred treatment option.

The aim of this study was first to explore gastroenterological surgeons' opinion on the necessary information that should be provided preoperatively on treatment options, including their related benefits and harms and on SDM. We assessed what information surgeons communicated in practice, and to what extent they involved patients in decision making.

Methods

This study consisted of a questionnaire and a clinical encounter study.

Participants

A questionnaire was distributed among all Dutch surgeons with a specialty in the field of colorectal surgery. The questionnaire was sent to all by email; a reminder was sent once.
Moreover, all gastroenterological surgeons of a Dutch university hospital and four regional hospitals were asked to record their consultations with patients with rectal and sigmoid cancer at the outpatient clinic, between May 2011 and March 2012. Patients received information required for each recording. The medical ethics review board agreed on patients giving verbal consent prior to recording.

Questionnaire

The questionnaire first asked surgeons to indicate on a 4-point Likert-scale (1=not important at all to 4=very important) whether they think patients with rectal and sigmoid cancer should be informed about various treatment outcomes of the different options (*table 2*). Next, surgeons were asked to indicate on a 4-points Likert scale (1=not at all to 4 =very much) whether they are familiar with SDM, whether they agree with using SDM in their consultations and whether they think they perform SDM. Also, they were asked to indicate on a 4-points Likert scale (1=not at all to 4=very much) to which extend they experiences each of 8 barriers in practice for implementing SDM .[16, 17] Barriers were subdivided into two groups; practical and attitudinal (see *Figure 1*). Finally, surgeons were asked about their years of experience in their specialization, their institution, and their numbers of rectal and sigmoid cancer cases they see monthly.

Clinical encounter study

Surgeons were equipped with a digital tape recorder and instructions regarding its use. All newly diagnosed patients with rectal and sigmoid cancer with an appointment at the outpatient clinic were eligible for participation. Patients with metastases at the time of primary surgery or resections for multiple synchronous colorectal tumors were excluded because these represent subgroups of patients with other treatment perspectives and different expected outcomes. We excluded patients with lowest 5 cm rectal cancer, since in these patients there is only one option, which is a permanent stoma.

We developed a checklist with a team of members with various backgrounds in medicine, psychology, epidemiology, and communication research to code what information on treatment options, and their related benefits and harms surgeons communicated with their patients. The checklist was based on the literature and following Knops et al. [1]

We coded first whether general information on the procedure and general risks of the procedure were communicated with a patient. Second, we coded whether all therapeutic options (anastomosis with and without a defunctioning stoma and an end-colostomy) with their benefits and side-effects, were explicitly presented to a patient. All items were scored as ‘mentioned’ or ‘not mentioned’. See for items *Table 3*.

For each consultation, the patient's sex, age, and tumour location were registered.

Analyzes

Two raters (HS, MK) independently analyzed and coded the same ten audiotapes. Disagreement was solved in consensus. As substantial agreement between raters was found (Cohen's Kappa = 0.94) the remaining tapes were coded individually.
Spearman correlations were computed to assess the association between the extent to which surgeons experience barriers for using SDM and their age and years of experience. Likert-scale answers were analyzed in two groups (1-2 versus 3-4).

To evaluate patient involvement in the decision about the type of surgery, we used the OPTION-scale. 18 This one-dimensional scale assesses the magnitude of SDM use during the physician–patient consultation by identifying twelve SDM-specific behaviors that clinicians can adopt to promote patients' active participation in decision making. The items are coded on a five-point scale, where "0" indicates the nonperformance of a behavior and "4" indicates the performance of a behavior at high competency. The overall patient involvement score is a value between 0 and 100, with a higher score indicating more frequent and/or higher quality display of clinicians' behaviors to involve patients in the treatment decision.
Data were analyzed using SPSS version 17.0 (SPSS, Chicago, IL, United States of America).

Results

Study population

A total of 103 surgeons responded to the questionnaire (response rate 43%). An average of ten minutes was needed to complete it. Characteristics of participants are shown in *Table 1*. The clinical encounter study consisted of 32 recorded consultations conducted by 11 different gastroenterological surgeons in five different hospitals. The characteristics of participating surgeons, hospitals, and patients are also shown in *Table 1*.

Preoperative information

Surgeons' opinion on necessary preoperative information
Nearly all respondents considered information on the risk of anastomotic leakage after creation of an anastomosis to be essential (99%). Also, the risk of re-operation and the risk of a stoma due to leakage were regarded as important elements of pre-operative counseling, as 93% of respondents considering both items. The majority of the respondents (77%) indicated that the risk of a fecal incontinence should always be mentioned. The risk of death due to leakage should be mentioned "often" according to 27% of the respondents, and always according to 57%. The other results are shown in *Table 2*. The 11 surgeons of whom the consultations were audio-taped did not differ in their opinions when compared to the other respondents.

Information giving in practice

None of the information items were mentioned consistently in every consultation (*Table 3*). Information on the surgical procedure was provided during most of the consultations; information on laparoscopic or open surgery (81%); removal of (a part of) the bowel (72%); remaining of two bowel ends (75%); and duration of hospital stay (69%) were mentioned often.

Three of ten items regarding general risks of surgery were mentioned occasionally: postoperative hemorrhage (47%), wound infection (41%) and pneumonia (13%). Other risk-items were not mentioned.

A primary anastomosis was the surgical treatment option mentioned most often (84%). The advantages of the avoidance of a stoma were mentioned to most of these patients (70%). Also, the risk of anastomotic leakage was mentioned in almost all of these patients (93%). The surgical treatment 'anastomosis with defunctioning stoma' was mentioned to 16 patients (53%). Most of these patients (88%) were informed on the fact that this is a safer option than a primary anastomosis. The advantage of diminishing the consequences of anastomotic leakage was mentioned to half of the patients (44%). A prolonged hospital stay and death due to anastomotic leakage were mentioned in one consultation (6%). Information on re-operation or the risk of a stoma due to leakage were never mentioned. It was often (88%) mentioned that the defunctioning stoma initially is meant to be temporary. The necessity of a second surgery was mentioned to only three (19%) patients. The risks of complications after second surgery and potential stomal complications were never mentioned.

An end-colostomy as a surgical treatment option was mentioned to seven (22%) patients. The fact that there is no risk of anastomotic leakage was mentioned to one of these seven patients (14%). The advantage that fecal incontinence problems are avoided with this option was mentioned to three of seven patients (43%). None of these patients were informed on potential stomal complications.

Shared Decision Making

Surgeons' attitude towards SDM

Forty-one percent of all surgeons indicated to be at least quite a bit familiar with the concept of SDM. Ninety-one percent of the respondents stated to agree at least quite a bit with using SDM in their consultations. At least 37% of the surgeons indicated to use SDM quite a bit in their preoperative consultations with rectal and sigmoid cancer patients. Surgeons perceived various barriers for implementing SDM in their practice and they did not agree to one or more most important barriers (*Figure 1*). The most often cited barrier was the lack of applicability due to perceiving patients as not capable of making treatment decisions (42%). No correlation was found between the extent to which surgeons experienced barriers for using SDM and their age or number of years of experience.

Patient involvement in practice
In more than half (55%) of the consultations, only one treatment option was presented to the patient. In one third (34%), the patient was presented with two options. In three consultations (9%) the patient was informed about three options. The mean OPTION-score of all consultations was 7 points (range 2-25) on a 0-100 scale.

Discussion

This study had a dual objective. Firstly, the aim was first to investigate surgeons' attitude towards essential information provision and SDM. The second aim was to assess what information surgeons actually communicated preoperatively and to what extent they involved patients in decision making.

Although surgeons considered most information on risks and alternative treatment options to be essential for decision making, this was not reflected in practice. We found that patients were insufficiently and inconsistently informed about risks of surgery, alternative treatment options, and their pros and cons, when compared to what surgeons considered as necessary preoperative information. Whilst information was usually given on the surgical treatment option 'an anastomosis', its procedure and the most important risks of surgery such as AL and alternative treatment options were often not mentioned at all. In this way, the patient is directed towards one specific treatment option, which will often be the one preferred by the surgeon.

This phenomenon has been previously described in some studies investigating information provision to patients undergoing surgical treatment.[19] Knops et al. studied preoperative information communicated to patients about to undergo surgery for an abdominal aneurysm.[20] They found that although surgeons informed patients about the disorder and about their individual prognosis, alternative treatment options were not discussed. Also, Vohra et al. investigated whether patients were informed about risks of cardiac surgery and found that the surgeons did not discuss more then one treatment option with patients.[21]

Some limitations of this study deserve attention. We audio taped only the first consultation of patients with rectal and sigmoid cancer at the outpatient clinic. Therefore, we may have missed information that was discussed during other related consultations. It is however important to realize, that most decision-making takes place in the first encounter with the surgeon, and at that point all information on treatment options and risks should have been addressed at least to some extent.[31] Also, participating surgeons knew they were audio taped, which may have biased their information provision and caused them to be more comprehensive that they would otherwise be. This would lead to an overestimation of the information provided. However, research has shown that this effect fades within minutes as the surgeon returns to his or hers standard routine.[32]

Last, the inclusion of both rectal and sigmoid cancer patients may have caused a somewhat heterogeneous study population, and subgroups of patients could differ in their treatment perspectives or outcomes. We excluded patients with lowest 5 cm rectal cancer to attempt to create a homogeneous cohort with respect to preoperative sphincter dysfunction. Considerable leakage rates in patients with high rectal and sigmoid cancer have been described. [33] We therefore considered items related to anastomotic leakage, and the need for defunctioning stomas relevant in all subgroups.

Surgeons agreed on the importance of providing information but seemingly did not manage to do so during the first visit. The major aim of the first visit is possibly not to address the large amount of issues required for SDM in rectal and sigmoid cancer surgery, but to gain the trust of the patient and family and to establish a relationship of truth-telling. Ideally, the moment of decision making would be postponed from the first consultation to a second consultation at which the patient has had the time to consider his/her options. Details of consent, including complications and alternative procedures can then be discussed in the meantime by nurses or other members of the surgical team. In practice however, there may not be the possibility to have a second preoperative encounter, due to economic reasons. A less expensive solution would be to inform the patient before the first consultation with the surgeon, for example with printed or web-based materials describing the therapeutic options and their most important pros and cons, or with decision aids with additional values clarification methods. [34] These decision aids may support patients in forming preferences for the different options and treatment outcomes. Decision aids have proven to be particularly useful in situations of equipoise, where the surgeon is comfortable in providing the patient a choice between two medically equivalent options.[35] The use of multimedia-based programs such as film or animation may be of additional value.[36-38] Patient navigation by nurse practitioners or physician assistants is another suggested approach to addressing informational needs and facilitate the decision making process. [39]

These methods serve to empower the patient for a consultation with the surgeon, in which the information can subsequently be individualized to that patient.

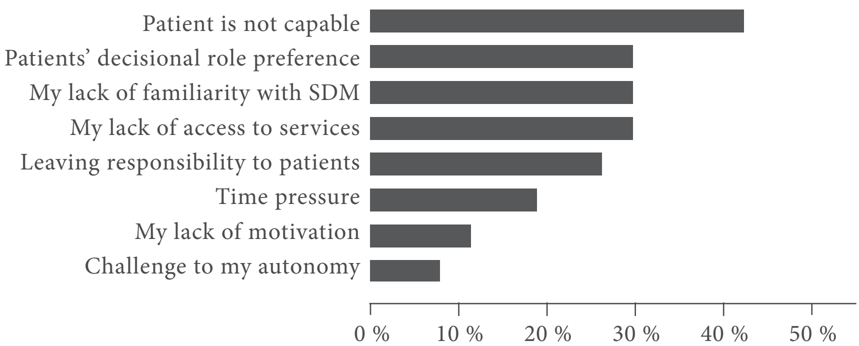
In our study, the majority of the responding surgeons had a positive attitude towards SDM. The discrepancy between the positive attitude and the absence of putting SDM into clinical practice suggests that barriers exist, which was confirmed in our study. We found that almost half of the surgeons experienced the fact that patients are unable to participate in decision making in rectal and sigmoid cancer treatment as a barrier for SDM. This inability could be related to the patients' characteristics, as well as to the difficulty of the clinical situation, which both have been nominated as important barriers for SDM by physicians in multiple settings.[22-26]

Stiggelbout et al provide some simple steps for clinicians, to enable the process of SDM.2 The first and most important step is creating awareness that there are different options, that there is no best choice and that a decision has to be made. If patients are not made aware that more than one option is available, they will not realize a decision is to be made. Next, the benefits and harms of each option need to be laid out as well as their respective probabilities. Exact probabilities are not always needed, but in most preference-sensitive decisions the patient will need numbers to be able to weigh the pros and cons. 3 Finally, patients' ideas, concerns, and expectations about the options should be elicited, and the patient should be supported in the process of deliberation. With these steps, patients will not only receive all necessary information on their possible treatments, but will become more involved in deciding about their treatment, and will experience a more tailored treatment decision making process.

Conclusion

The information necessary for patients with rectal and sigmoid cancer in order to decide on which surgical option they prefer seems far from complete in clinical practice. We recommend giving information on at least all treatment options and their most important consequences before decision making takes place. Alternative methods to enhance information giving such as improved printed materials, multimedia-based programs, or patient navigators should be explored and developed.

Figure 1. Perceived barriers for implementing Shared Decision Making into their own practice (n=85).



Percentage of participants is displayed which stated to agree at least quite a bit on the different items.

Table 1. Characteristics of the participants of the questionnaire (n=101) and the clinical encounter study (n=32).

Participants of questionnaire (n=103)	
Surgeon	
Mean age of surgeons	46 years (33-64)
Mean years of experience as a gastro-enterological surgeon	11.2 years (1-30)
Mean number of new patients with rectosigmoid cancer/month	3 patients (1-30)13
Hospital	
Academic hospital	15 (15%)
Non-academic teaching hospital	55 (54%)
Non-teaching hospital	32 (31%)
Participants of clinical encounter study (n=32)	
Surgeon	
Mean age of surgeons	43.7 years (35-60)
Mean years of experience as a gastro-enterological surgeon	8.7 years (1-25)
Mean number of new patients with rectosigmoid cancer per month	2,8 patients (1-5)
Hospital	
Academic hospital	9 (28%)
Non-academic teaching hospital	13 (41%)
Non-teaching hospital	10 (32%)
Patient	
Male patients	20 (63%)
Mean age of patients	64 years (38-87)
Rectal cancer	16 (50%)

Table 2. Surgeons' (N=101) opinion on importance of preoperative information items for patients with rectosigmoid cancer.

Frequency with which patients should receive various information items preoperatively (%)	***Never***	***Sometimes***	***Often***	***Always***
The risk for anastomotic leakage following construction of an anastomosis			1	99
The risk of re-operation due to anastomotic leakage			8	93
The risk of a stoma due leakage	2		5	93
The risk of death due to anastomotic leakage	4	11	27	57
The risk for faecal incontinence after construction of an anastomosis		3	20	77
Dimished consequences of anastomotic leakage after construction of a defunctioning stoma	15	12	16	57
Morbidity after closure of defunctioning stoma	5	25	16	54
Mortality after closure of a defunctioning stoma	38	26	17	19
The risk that a diverting stoma becomes permanent	13	44	19	24
No risk for anastomotic leakage following a permanent stoma	8	20	22	50
The impact of a stoma on quality of life	3	9	28	60

Table 3. Actual information on procedure, general risks, different options and their pros and cons communicated in consultations (n=32)

Surgeons	1	2			3		4			5						6		7			8					9		10				#
Patients	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
1. General information on procedure and risks of surgery																																
Open and laparoscopically	■	■	■	■	■	■	■	■	■	■	■	■	■			■		■	■	■	■		■	■		■	■		■	■	■	■
Remove bowel with lymph nodes	■	■	■		■		■	■	■	■	■		■		■	■	■	■	■	■	■	■	■	■	■	■						■
Two bowel ends remain	■	■	■		■	■	■	■		■			■	■	■	■	■	■	■	■	■	■		■	■	■		■		■		■
Duration of surgery	■	■			■					■	■		■	■	■			■	■	■			■				■		■	■		■
Duration of hospital stay	■	■			■	■	■	■		■	■		■	■					■	■	■			■	■	■	■	■	■	■	■	■
Period duration of illness	■														■				■				■			■		■	■			■
Myocardial infarction																																
Cardiac arrhythmia																																
Heart failure																																
Stroke																																
Postoperative hemorrhage	■	■	■			■	■		■	■	■				■		■	■					■			■	■					■
Pulmonary embolism																																
ARDS																																
Pneumonia	■						■	■	■	■								■				■	■									
Wound infection		■				■	■		■	■	■				■		■	■				■				■	■					■
Death																																
2. Pro's and cons of different treatment options																																
2.1 option 1: primairy anastomosis																																
Option mentioned	■	■			■							■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■
Pro: no stoma					■					■		■	■		■	■	■	■	■	■	■	■		■	■		■	■	■	■	■	
Con: anastomotic leakage (AL)	■	■			■		■	■	■	■		■	■		■	■	■	■	■	■	■			■	■	■	■	■	■	■	■	■
Con: re-operation due to AL	■	■			■				■	■			■		■		■	■	■	■	■			■	■	■		■		■	■	
Con: stoma due to AL	■	■			■		■			■			■		■		■	■	■	■	■				■	■	■			■	■	■
Con: prolonged hospital stay due to AL		■						■																								
Con: longterm illness due to AL	■	■								■			■		■	■	■	■	■	■	■					■		■		■		■
Con: death due to AL		■								■			■		■	■	■															
Con: faecal incontinence																■													■			

Surgeons	1	2			3		4			5						6		7			8					9		10				
Patients	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
2.2 option 2: primairy anastomosis with defunctioning stoma																																
Option mentioned			■			■	■				■	■		■		■			■	■	■	■						■	■	■	■	■
Pro: (implicit) safer otion then option 1			■			■	■				■	■				■			■	■	■	■						■		■	■	■
Pro: diminishes consequences of AL			■			■	■									■			■											■	■	■
Pro: stoma is temporary			■			■	■				■	■				■				■	■	■						■	■	■	■	■
Con: still risk for AL			■				■																									
Con: re-operation due to AL																																
Con: stoma due to AL																																
Con: prolonged hospital stay due to AL																													■			
Con: longterm illness due to AL																																
Con: death due to AL			■																													
Con: faecal incontinence			■																													
Con: second surgery is neccesary			■				■																					■				
Con: complications after second surgery																																
Con: stomal complications																																
2.3 option 3: end-colostomy																																
Option mentioned			■	■							■	■		■						■			■									
Pro: no risk for AL												■																				
Pro: no problems with feacal incontinence			■	■																			■									
Pro: no consequences of AL																																
Con: stomal complications																																

■ mentioned □ not mentioned

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PART II:
SURGICAL TREATMENT STRATEGIES

Chapter 4:

AN INCREASING USE OF DEFUNCTIONING STOMAS AFTER LOW ANTERIOR RESECTION FOR RECTAL CANCER. IS THIS THE WAY TO GO?

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Abstract

Introduction: The last decade there has been an increased awareness of the problem of anastomotic leakage after low anterior resection for rectal cancer, which may have led to more defunctioning stomas. In this study, current use of defunctioning stomas was assessed and compared to the use of defunctioning stomas at the time of the TME-trial together with associated outcomes.

Methods: Eligible patients with rectal cancer undergoing low anterior resection were selected from the Dutch Surgical Colorectal Audit (DSCA, n=988).Similar patients were selected from the TME-trial (n=891). The percentages of patients with a defunctioning stoma, anastomotic leakage and postoperative mortality rates were studied. Multivariable models were used to study possible confounding on the outcomes.

Results: At the time of the TME-trial, 57% of patients received a defunctioning stoma. At the time of the DSCA, 70% of all patients received a defunctioning stoma ($p<0.001$). Anastomotic leakage rates were similar (11.4% and 12.1%; $p=0.640$). The postoperative mortality rate differed (3.9% in the TME-trial vs. 1.1% in the DSCA; $p<0.001$), but was not associated with a more frequent use of a stoma (OR 1.80, 95% CI 0.91-3.58).

Conclusion: In current surgical practice, 70% of patients undergoing LAR for rectal cancer receives a defunctioning stomas. This percentage seems increased when compared to data from the TME-trial. Clinically relevant anastomotic leakage rates remained similar. Therefore, current routine use of defunctioning stomas should be questioned.

Introduction

During the past decades the strategy for surgery in rectal cancer has changed considerably. With the introduction of total mesorectal excision (TME) there has been an improvement in surgical techniques which enabled low anterior resections where previously abdominoperineal resections were performed[1-3]. Concurrently, radio-chemotherapy has become a more common neo-adjuvant therapy[4,5]. However, with an increasing number of primary anastomoses there are more patients at risk for possible anastomotic leakage[6,7]. The last decade, the problem of anastomotic leakage has been widely addressed in multiple symposia and many publications[8]. Leakage rates from 3% to >20% leading to substantial postoperative morbidity and mortality have been reported[9-12]. Anastomotic leaks may also be associated with decreased local control and long term survival[13-17]. Many solutions have been sought to prevent or diminish anastomotic leakage and its sequelae, such as mechanical bowel preparation, drains and intra-luminal devices. The only strategy that has proven to be effective is the use of a defunctioning stoma[18]. Matthiessen et al showed that patients with a defunctioning stoma have a risk of 10.3% compared to 28% in the group with no stoma. The outcome of this study combined with an increasing awareness of the problem of anastomotic leakage could have led to a change in surgical strategy and a more routinely use of a defunctioning stoma after low anterior resection (LAR) for rectal cancer. The purpose of this study was to investigate current use of defunctioning stomas in patients undergoing LAR for rectal cancer by using data from the Dutch Surgical Colorectal Audit. We assessed whether there has been an increase in the use of defunctioning stomas in the last decade. Furthermore, postoperative outcomes were analysed.

Methods

Patients

All surgically treated patients from the DSCA in 2010 were included. The DSCA is a national audit including patients with colorectal cancer in the Netherlands in which all hospitals participate. For using data from the DSCA, no ethical approval or informed consent was required under Dutch law. On a national and hospital level, data are annually checked for completeness and accuracy with the independent data registration of the National Cancer Registry (NCR)[19]. The dataset shows a nearly 100% completeness on most items, including anastomotic leakage on validation against the NCR. Furthermore, we analysed surgically treated Dutch patients with rectal cancer from the TME-trial database (January 1996 until December 1999). This randomised multicentre trial assessed TME surgery with or without preoperative 5×5 Gy radiotherapy.

Patients aged 18 years or over with clinically resectable adenocarcinoma of the rectum were randomly assigned to either radiotherapy followed by TME, or TME alone. Almost every hospital in the Netherlands participated. There was no age limitation in the trial. The trial was approved by the medical ethics committees of all the participating hospitals. The trial design and the calculation of the sample size have been described in detail elsewhere.[2]

From both datasets only patients without distant metastases at time of surgery that underwent low anterior resection (LAR) with a primary anastomosis were selected for inclusion. Since emergency patients in the TME-trial were excluded, the same strategy was applied to patients from the DSCA. The decision to construct a defunctioning stoma was at the discretion of the surgeon. In both datasets anastomotic leakage was defined as clinically apparent leakage, for which a re-intervention (radiological or surgical) was necessary.

Endpoints, variables and statistical analyses

The use of a defunctioning stoma, the occurrence of anastomotic leakage and the 30-day/in hospital mortality were compared between both datasets using the chi-squared test. Patient, tumor and treatment characteristics were derived from the two databases. Univariable and multivariable logistic regression analyses were performed with the following variables to study their association with these outcomes: time-period, gender, age at time of diagnosis, distance of tumor from anal verge, T-stage and use of neo adjuvant treatment. For age; patients were divided into two age groups; younger than 75 years and 75 years and older. The use of neo adjuvant treatment was divided into three groups; none, short course radiotherapy (5x5 Gy), and long course radiotherapy (25x2 Gy)/chemo radiation therapy (CRT). Postoperative mortality was defined as in-hospital mortality or mortality within 30 days after surgery. All analyses were performed in STATA 10. Statistical significance was defined as $p<0.05$.

Results

In total, 2434 patients were registered in the DSCA; 1530 patients were included in the TME-trial. For the analyses of this study, 988 patients from the DSCA and 891 patients from the TME-trial were included. Reasons for exclusion are shown in *Figure 1*. In the DSCA, 644 (26%) were treated with an abdominoperineal resection (APR), 370 (15%) with a low Hartmann's procedure. In the TME-trial, 484 patients were treated with another procedure then low anterior resection, 419 patients (27%) underwent APR and 65 (4%) underwent a Hartmann's procedure. While the APR rates remained similar, the increase in Hartmann's procedure was statistically significant ($p<0.01$). Patient and disease characteristics of included patients are shown in *Table 1*. There were no differences between both groups in age, gender, and tumor stage. In the DSCA, three patients underwent a low anterior resection for tumor located at 0 cm from the anal verge, but there was no difference in mean distance between datasets. The use of chemo radiation differed between both groups; at the time of the TME-trial no patients received this type of treatment since the trial randomized patients to receiving 5x5 radiotherapy.

The use of a defunctioning stoma.

In the DSCA, 70% of all patients received a defunctioning stoma (692 of 988). At the time of the TME-trial, in total 507 patients (57%) received a defunctioning stoma. This increase was statistically significant (p<0001). To assess possible confounders in this comparison, we performed a multivariable analysis. *Table 2* shows the odds ratios for factors associated with a defunctioning stoma. The variable 'time-period' was entered into the analyses to investigate the difference in defunctioning stomas between the DSCA en the TME-trial. The odds for receiving a defunctioning stoma was 1.28 at the time of the DSCA when compared to the TME-trial (95% CI 1.01-1.62). There was a strong association between the use of chemo radiation and the use of a defunctioning stoma (OR 4.21 95% CI 2.73-6.48). Also, gender, and tumor distance to the anal verge were independently associated with a more often creation of a defunctioning stoma.

Anastomotic leakage

The clinically relevant anastomotic leakage rate was 12% (120 out of 988 patients) in the DSCA. This was similar to the anastomotic leakage rate at the time of the TME-trial; clinically relevant leakage occurred in 102 of 981 patients (11%, p=0.60). The multivariable analyses for anastomotic leakage showed that time-period was still not significant after correcting for other factors (*Table 3*). A defunctioning stoma, female gender, lower T-stage and higher distance from the tumor to the anal verge were independently associated with a reduced risk of anastomotic leakage.

Postoperative mortality.

The overall postoperative mortality rates was 1.1% in the DSCA; 11 out of 988 patients died during hospital stay or within 30 days after surgery. At the time of the TME-trial, postoperative mortality rates was 3.9% (35 out of 891 patients, $p<0.001$). In multivariable analysis, the DSCA-time period remained associated with a reduced risk for postoperative mortality (*Table 4*). The decrease in postoperative mortality could not be attributed to the use of a defunctioning stoma; the use of a defunctioning stoma was not significantly associated with a lower risk for postoperative mortality (OR 1.81; 95% CI 0.91 – 3.58). The occurrence of anastomotic leakage, age and gender were independent risk factors for postoperative mortality.

Discussion

This study assessed whether there has been an increase in the use of defunctioning stomas after low anterior resection for rectal cancer in the last decade since the TME-trial. We found that the substantial percentage of patients that received a defunctioning stoma at times of the TME-trial (57%) seemed to have further increased in recent years. In current surgical practice, 70% of patients receive a defunctioning stoma after LAR. Interestingly, clinically relevant anastomotic leakage rates remained similar.

Our study showed that nowadays almost one third of all patients received chemo radio therapy (CRT), which is an important change in the treatment of rectal cancer since the TME-trial.[5] The association between CRT and the use of a defunctioning stoma was probably due to the fact that todays' surgeons have the assumption that CRT is associated with the risk for anastomotic leakage. However, this is contradicted by a randomized controlled trial evaluating radiotherapy or CRT, as they found leakage rates of 7% in the CRT group, compared to 9% in the radiotherapy group, while the use defunctioning stomas was comparable in both groups.[4] The association of leakage and CRT was also not found in our study.

Possibly, the higher defunctioning stoma rate may have led to the lower postoperative mortality rate in the later period, as it is often stated that a defunctioning stoma protects from the clinical consequences of the anastomotic leak instead of lowering the incidence. Results of the multivariable analysis however did not show a significant relation between a more frequent use of a defunctioning stoma and lower postoperative mortality rates. Moreover, the percentage of anastomotic leakage requiring a re-intervention was similar in both time-periods. The substantial decrease in postoperative mortality rate over time could therefore be more due to general advances in perioperative care in the Netherlands such as better postoperative monitoring, better ICU facilities and quality of surgery in the latter period.[20-25] Moreover, there has been increased specialization and centralization of rectal cancer surgery[26] as well as more standardized postoperative surveillance[27] for symptoms of anastomotic leakage. Furthermore, the higher percentage of low Hartmann's procedures in the DSCA group ($p<0.01$) implies a more defensive strategy and a different patient selection. This could also be an explanation for the lower postoperative mortality in the DSCA group.

Limitations

The datasets may not be completely comparable due to the differences in the intent and purpose and area of both groups. Therefore, some limitations deserve attention. First, in randomised trials, there is always a risk for selection bias, as older patients with more co morbidities are more often excluded from randomization.[28-30] We had no information on co morbidity status of patients in the TME-trial. Therefore, outcomes may have been influenced by this confounder. However, when we repeated our analysis selecting only patients with ASA I and II from the DSCA, this revealed similar results. Moreover, there was no difference in age between both groups, suggesting that the selection of only young

and vital patients in the TME-trial was limited. Second, the patient group in the TME-trial may have been subject to inclusion bias based on clinical T classification. It is very well possible that some patients were ineligible for resection because of a cT4 tumor, because downsizing options were more limited before the introduction of neoadjuvant chemo radiotherapy. However, in the DSCA, 83% of patients with chemo radiotherapy have another indication than cT4. Therefore we decided not to exclude these patients from our analysis.
Arguably, although we attempted to correct for the most important differences with multivariable analysis, the groups may not be perfectly comparable regarding purpose and period of treatment. However, the important point that needs to be addressed here is that the current percentage of patients in which a defunctioning stoma is constructed seems rather high, especially since has there has been no additional benefit on reducing anastomotic leakage rates when compared to the TME-trial.

Appropriate use of defunctioning stoma

There are obvious advantages of a defunctioning stoma, as multiple studies have shown that it can decrease the incidence of anastomotic leakage rates.[6,18] Moreover, a defunctioning stoma can mitigate its consequences.[31,32] However, there are several drawbacks to a defunctioning stoma that counterbalance its advantages. It is known that stomas can induce morbidity, hospital re-admission, discomfort, and prolonged hospital stay.[33-36] In addition, in certain cases the stoma may not be closed, or closure itself can lead to significant morbidity and (rarely) mortality.[37,38] Furthermore, even when a defunctioning stoma is constructed there is still is a considerable risk of anastomotic leakage.[6,18,31,39]

Finally, a defunctioning stoma is not free of costs. A cost-effectiveness analysis reviewed 70 consecutive patients undergoing LAR with and without a defunctioning stoma.[40] It was estimated that to balance the extra cost of a stoma, the anastomotic leak rate for LAR would have to be 16.5%. Their suggested goal was to limit the stoma rate to less than 10% of LARs performed to limit the costs.

Patient selection

The previously described protective effect of a defunctioning stoma on the risk of anastomotic leakage could be confirmed in this study. However, the observed an increase in stomas did not seem to result in lower anastomotic leakage rates when both datasets are compared. The protective effect of a defunctioning stoma is probably most apparent in high-risk patients, while the additional benefit for the rest of the population is limited. The risk for anastomotic leakage of 28% which was found in the study from Mathiessen et al[18] suggests a cohort of high-risk patients. In these patients ,a defunctioning stoma led to a relative risk reduction of 60%, and an absolute risk reduction of 18% which implies a Number Needed to Treat of 5.5. The NNT however increases in low-risk patients with an a priori leakage risk of, say, 3%. In these patients, the 60% risk reduction of a defunctioning stoma leads to an absolute risk reduction of 1.8%, and a subsequent NNT of 55. Therefore, identification of high-risk patients is essential to guide appropriate use of defunctioning stomas.

Scoring systems that could predict a patient's risk for anastomotic leakage pre-operatively have been developed, but not yet validated in larger multi-centre series.[41] Further focused research on this matter is warranted. While the decision whether or not to construct a defunctioning stoma remains difficult, patients' preferences concerning the risk of morbidity and mortality of anastomotic leakage versus the consequences of a defunctioning stoma should be taken into account preoperatively.

Conclusion

In conclusion, while current use of defunctioning stomas has increased, there has been no benefit in reducing clinically relevant anastomotic leakage rates. The 70% defunctioning stoma rate in this study suggest routine use in current surgical practice which should be questioned since defunctioning stomas have clear disadvantages. Identification high-risk patients and involvement of patient preferences in the decision should guide the appropriate use defunctioning stomas in the future.

Table 1: patient and tumor characteristics of patients with rectal cancer undergoing low anterior resection.

		DSCA (n=988)	***TME-trial (n=891)***	***p-value***
Age	<75 years	782 (79.1%)	727 (81.6%)	0.2
	> 75 years	206 (20.9%)	164 (18.4%)	
Gender	Male	601 (60.8%)	544 (61.1%)	0.9
	Female	387 (39.2%)	347 (38.9%)	
Tumor (T) stage	T0-2	419 (42.4%)	371 (41.6%)	0.062
	T3	480 (48.6%)	496 (55.7%)	
	T4	39 (3.9%)	24 (2.7%)	
	Tx	50 (5.1%)	0	
Nodal (N)-stage	N0	644 (65.2%)	542 (60.8%)	0.015
	N+	328 (33.2%)	349 (39.2%)	
	Nx	16 (1.6%)	0	
Tumor distance	Median cm(range)	9 (0-12)	9 (0-10)	0.3
Preoperative radiotherapy	None	169 (17.1%)	453 (50.8%)	<0.001
	5x5 Gy	532 (53.8%)	438 (49.2%)	
	chemo radiation	287 (29.0%)	0	

Bold printed numbers are significant differences (p<0.05).

Table 2: multivariable analyses for the use of a defunctioning stoma with adjustment for patient and tumor characteristics.

		OR (95% CI)	***p-value***
Time-period	TME-trial	**1.0 (ref)**	**0.,41**
	DSCA	**1.28 (1.01 - 1.62)**	
Age	<75	1.0 (ref)	0.4
	≥ 75	1.14 (0.863 - 1.43)	
Gender	Female	**1.0 (ref)**	**0.001**
	Male	**1.44 (1.17 - 1.77)**	
T-stage	0-2	1.0 (ref)	0.06
	3	1.13 (0.92 - 1.39)	
	4	2.06 (1.10 - 3.88)	
Tumor distance		**0.92 (0.89-0.95)**	**<0.0011**
Preoperative radiotherapy	None	**1.0 (ref)**	**<0.001**
	5x5	**1.84 (1.47 - 2.30)**	
	Chemo radiation	**4.21 (2.73 - 6.48)**	

OR = Odds ratio CI = Confidence interval Bold printed numbers are significant odds ratios (p<0.05).

Table 3: multivariable analyses for anastomotic leakage with adjustment for patient and tumor characteristics.

		OR (95% CI)	***p-value***
Time-period	TME-trial DSCA	1.0 (ref) 1.33 (0.94 - 1.89)	0.112
Defunctioning stoma	None Yes	**1.0 (ref)** **0.42 (0.30 – 0.57)**	**<0.001**
Age	<75 ≥ 75	1.0 (ref) 1.00 (0.68 – 1.47)	0.9
Gender	Female Male	**1.0 (ref)** **1.59 (1.16 - 2.18)**	**0.004**
Tumor (T) stage	0-2 3 4	1.0 (ref) 0.98 (0.72 - 1.33) 2.29 (1.12 - 4.70)	0.06
Tumor distance		**0.91 (0.87 - 0.95)**	**<0.001**
Preoperative radiotherapy	None 5x5 Gy Chemo radiation	1.0 (ref) 0.94 (0.53 - 1.65) 1.01 (0.619 - 1.65)	0.9

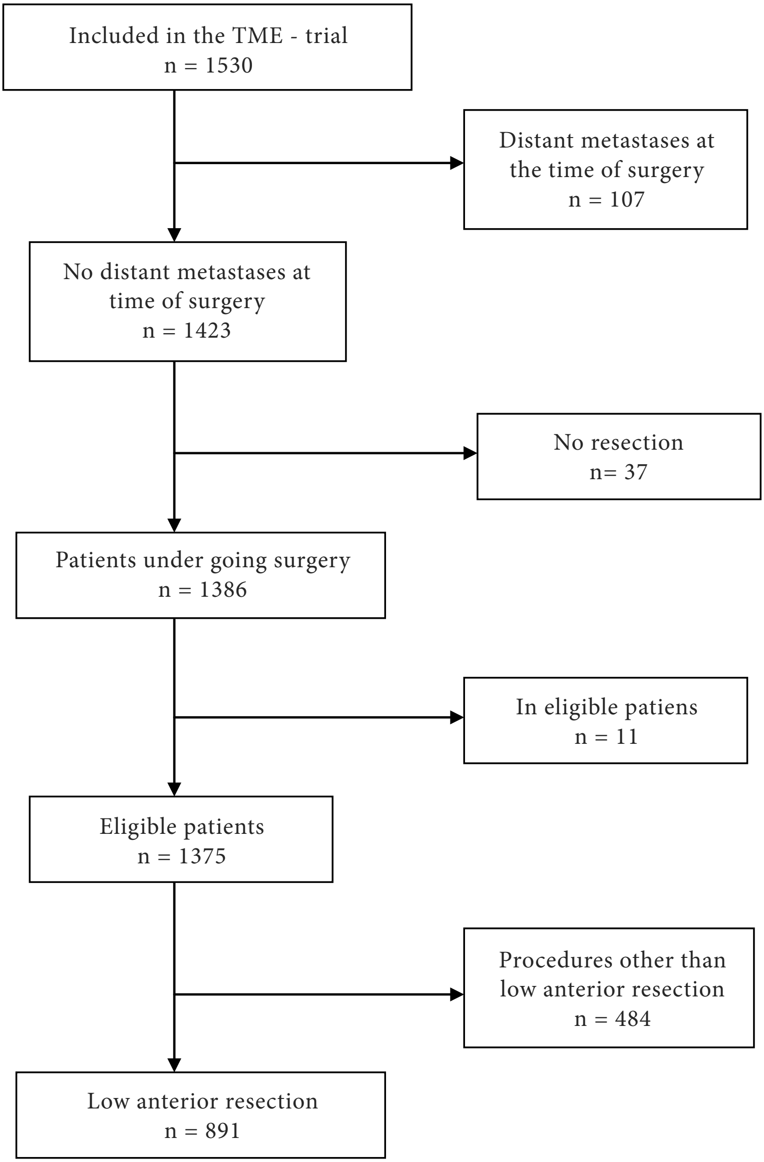
OR = Odds ratio CI = Confidence interval Bold printed numbers are significant odds ratios (p<0.05).

Table 4: multivariable analyses for postoperative mortality with adjustment for patient and tumor characteristics.

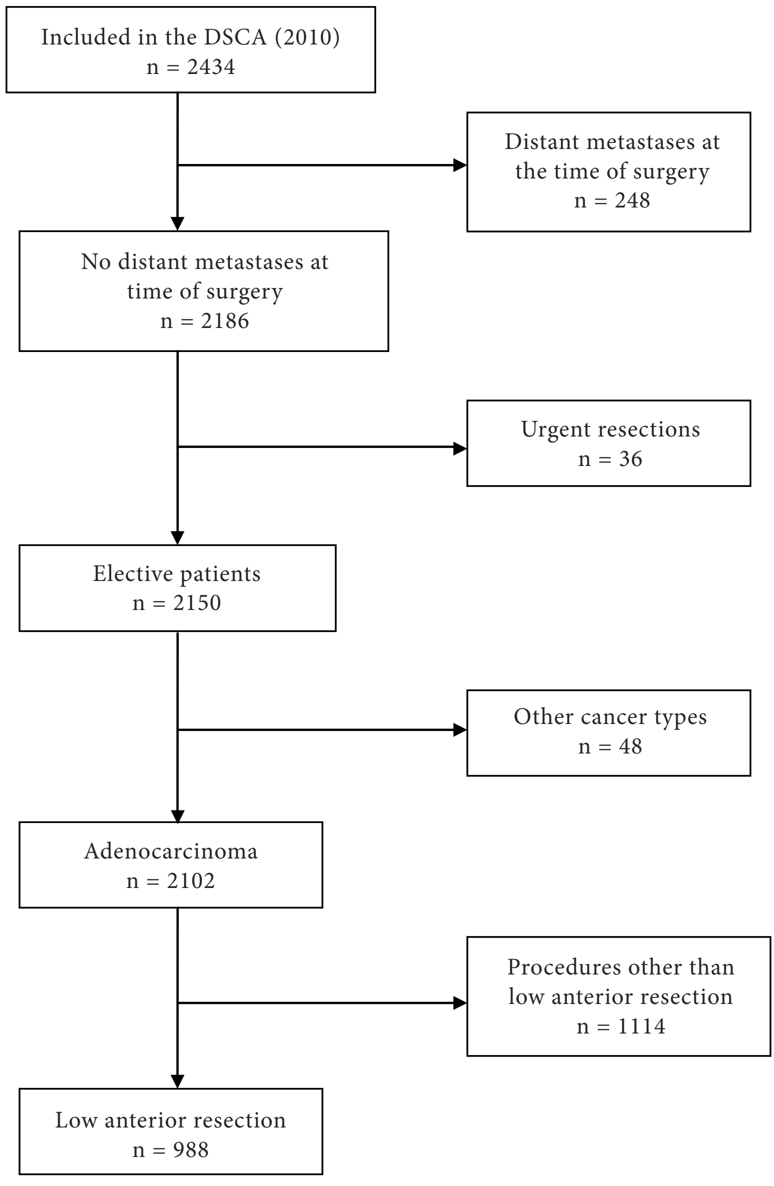
		OR (95% CI)	***p-value***
Time-period	TME-trial DSCA	1.0 (ref) 0.26 (0.12 – 0.60)	**0.002**
Defunctioning stoma	None Yes	1.0 (ref) 1.80 (0.91 - 3.58)	0.09
Anastomotic leakage	None Yes	1.0 (ref) **4.78 (2.38 - 9.60)**	**<0.001**
Age	<75 ≥ 75	1.0 (ref) **3.39 (1.75 - 6.55)**	<0.001
Gender	Female Male	1.0 (ref) **2.42 (1.13- 5.21)**	**0.023**
T-stage	0-2 3 4	1.0 (ref) 1.14 (0.60 - 2.16) 0.99 (0.00 - ∞)	0.9
Tumor distance		1.01 (0.97 - 1.05)	0.8
Preoperative radiotherapy	None 5x5 Chemo radiation	1.0 (ref) 1.07 (0.55 - 2.08) 0.99 (0.00 - ∞)	0.9

OR = Odds ratio CI = Confidence interval Bold printed numbers are significant odds ratios (p<0.05).

Figure 1. Flow diagram of selected and excluded patients.



DSCA = Dutch Surgical Colorectal Audit; TME = Total Mesorectal Excision


Included in the DSCA (2010)
n = 2434
Distant metastases at
the time of surgery
n = 248
No distant metastases at
time of surgery
n = 2186
Urgent resections
n = 36
Elective patients
n = 2150
Other cancer types
n = 48
Adenocarcinoma
n = 2102
Procedures other than
low anterior resection
n = 1114
Low anterior resection
n = 988

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Chapter 5:

LARGE VARIATION IN THE USE OF DEFUNCTIONING STOMAS AFTER RECTAL CANCER SURGERY. A LACK OF CONSENSUS.

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Abstract

Introduction: The use of a defunctioning stoma in rectal cancer surgery is an exemplary setting to investigate clinical decision making, since choosing the ideal surgical treatment consists of a trade-off between benefits and risks. This study investigated 1a) factors associated with the use of defunctioning stomas, 1b) hospital variation and 2) surgeons' perceptions regarding factors that determine this decision.

Methods: Population based data from the Dutch Surgical Colorectal Audit (DSCA) were used. Factors for receiving a defunctioning stoma were analyzed with multivariate logistic regression analysis. Hospital variation was assessed before and after case-mix adjustment. A survey was performed among gastroenterological surgeons on the importance of factors for the decision to construct a defunctioning stoma or not.

Results: Male gender, higher BMI, lower tumors, preoperative radiotherapy, and treatment in a teaching or university hospital increased the odds for a defunctioning stoma. Unadjusted hospital ranged from 0 to 98%. Variation remained after case-mix adjustment (0-100%). There was also a large variation in factors considered important for the decision; almost all factors were ranked as 'most important' by at least one surgeon.

Conclusion: There is large variation in the use of defunctioning stomas for patients with rectal cancer in the Netherlands, and a lack in uniformity of the selection criteria. These results underline the need to further improve current decision making and identification of high risk patients.

Introduction

Rectal cancer surgery is an exemplary setting to investigate clinical decision making, since choosing the ideal surgical treatment consists of a trade-off between benefits and risks of different surgical treatment options. Constructing a defunctioning stoma has proven to mitigate the sequelae of anastomotic leakage, which is a serious complication causing re-operation, prolonged hospital stay, morbidity, a possibly worse oncological outcome and even mortality. [17-9] Not all patients however benefit from a defunctioning stoma, as there are several drawbacks that counterbalance its advantages.[2-5] When there is more than one generally accepted and equally effective treatment option, selection of the appropriate treatment should be informed by patient preferences. Previous research suggests that for many conditions treatment selection depends more on the physician's recommendation than on patient characteristics or preferences.[6] Consequently, differences in professional opinion may lead to variation in treatment patterns, which has been demonstrated for several conditions in various parts of the world.[7-14]

The aim of this study was 1a) to assess whether patient, tumor, and hospital related factors were associated with a higher likelihood of receiving a defunctioning stoma 1b) to measure variation in the use of a defunctioning stoma across hospitals treating patients with rectal cancer; 2) to assess surgeons' perceptions regarding factors that determine this decision.

Methods

To investigate these research questions we performed two studies, a hospital practice study and a survey among surgeons treating rectal cancer patients.

Hospital data study

Dataset

To assess practice variation and determinants of constructing a defunctioning stoma we derived data from the Dutch Surgical Colorectal Audit (DSCA), a prospectively collected clinical database in which over 200 variables concerning the patient, co-morbidity, diagnostics, disease-specific details, treatment, and outcomes are registered. The DSCA contains data registered by all hospitals performing colorectal cancer surgery in the Netherlands (n=92).[15] The data set is disease-specific for colorectal cancer and shows a nearly 100% accordance on most items on validation against the National Cancer Registry (NKR) data set.[14,16-18]

Patients

All patients undergoing low anterior resection for rectal cancer and in whom a primary anastomosis was constructed between January 1, 2009 and December 31 2012 were evaluated. Patients with metastases at the time of primary surgery or resections for multiple synchronous colorectal tumors were excluded because these represent subgroups of patients with other treatment perspectives and different expected outcomes.

Hospitals

Hospital-specific factors like procedural volume, type of hospital, and geographic region were assessed. Hospital type was categorized into general, teaching, or university hospital. Hospital volume was categorized into <25, 25–50 and >50 resections per year. Hospitals were categorized into four regions based on their topographic location. Each region comprises an area covered by 15-40 hospitals.

Surgeon survey

To assess surgeons' perceptions regarding factors that determine constructing a defunctioning stoma or not, a questionnaire was distributed among all Dutch surgeons with an interest in the field of colorectal surgery (n=232). First, socio-demographic and work-related details were assessed. Next, surgeons were offered sixteen patient and tumor related factors relevant for the decision to construct a defunctioning stoma or not after rectal resection with primary anastomosis. Eleven of these factors were similar to those available for analysis in the hospital data study. Five additional factors were added: the patient's acceptance of a stoma, patient's acceptance of the risk of anastomotic leakage, lifestyle (smoking; alcohol consumption), perioperative factors (duration of the operation, blood loss) and perioperative judgment of the anastomosis. The latter three factors were potential risk factors for anastomotic leakage reported in literature that were not available in the DSCA.[19-23]

Surgeons were asked to rate all factors on a 0-100 Visual Analog Scale (VAS) ranging from not at all important to very important for their decision. Using the VAS, it was possible to calculate the relative importance of these factors. Descriptive analyses were used to present the relative importance scores of the factors.

Statistics

The association of patient, tumor and hospital factors with receiving a defunctioning stoma or not was assessed using a Chi-squared test. All variables with $p<0.10$ were next entered in a multivariate logistic regression analysis. A p-value < 0.05 was considered statistically significant for further case-mix adjustment.

To compare the adjusted percentage of defunctioning stomas per hospital, a funnel plot was made using 95% control limits calculated around the mean of all hospitals.[24] In the funnel plot, each hospital is displayed as a scatter point presenting the (adjusted) rate of patients receiving a defunctioning stoma by volume rate. The observed defunctioning stoma rate was adjusted by multiplying observed/expected ratios by overall average defunctioning stoma rates of the total study population. Hospitals' expected defunctioning stoma rates were obtained using coefficients from the multivariate logistic regression analyses.

Results

Hospital data study

On December 31st 2012, 92 hospitals had registered a total of 11.093 eligible primary rectal cancer patients in de the DSCA since 2009. After exclusion of patients without an anastomosis (n=5.500), patients with synchronous tumors (n=943), and distant metastases (n=282), a total of 4.368 patients were included in the analyses.

The mean percentage of patients in whom a defunctioning stoma was constructed was 67% (n=2945/4368). Characteristics of patients with and without a defunctioning stoma are shown in Table 1. Patients with a defunctioning stoma were slightly younger, were more often male, more often had an abdominal surgical history, higher tumor stage, more often a tumor closer to the anal verge, and more often preoperative radiation therapy when compared to patients with an anastomosis without a defunctioning stoma ($p<0.10$).

Results from the multivariate analysis are presented in *Table 2*. Age, abdominal surgical history, and tumor stage were not significant anymore. Male patients had higher odds of receiving a defunctioning stoma compared to female patients. Patients with a higher Body Mass Index (>30 kg/m2) were more likely to receive a defunctioning stoma. The OR increased with shorter distance of the tumor to the anal verge compared to those with a higher tumor. Patients receiving preoperative radiotherapy and patients receiving chemo radiation had higher odds of receiving a defunctioning stoma compared to patients receiving no preoperative radiation therapy. Patients diagnosed in teaching or university hospitals had higher odds of receiving a defunctioning stoma compared to patients diagnosed in general hospitals. A higher hospital volume was associated with a lower odds of receiving a stoma. There was variation between regions in the odds of receiving a defunctioning stoma with the highest having a 3.5 higher odds than the lowest.

Unadjusted hospital variation was large: the two hospitals with the lowest percentage had a defunctioning stoma rate of 0% (n=0/6) and 12% (5/41); the hospital with the highest percentage had a defunctioning stoma rate of 98% (n=41/42).

The obtained patient and tumor related coefficients from the multivariate analysis were used to perform case-mix adjustment for the percentage of defunctioning stomas per hospital. After case-mix adjustment, there still was a large variation between hospitals: the adjusted proportion of patients in which a defunctioning stoma was constructed ranged from 0 to 100% (*Figure 1*).

In the funnel plot, the adjusted proportion of patients in which a defunctioning stoma was constructed is depicted for each hospital by hospital type and hospital volume. A large variation in percentage of defunctioning stomas remained within each type of hospital and within each volume category.

Surgeon survey

One hundred and three replies (43%) were received from a single mailing of the questionnaire.

They needed an average of ten minutes to complete it. The majority of the respondents were male (84%), mean age was 46 years (range, 33-64). The respondents had an average of 11 years of experience since their specialization (range, 1-30) and the majority had their specialty in the field of colorectal surgery (93%). Most of them were practicing in a teaching hospital or in a general hospital (respectively 54 and 31%). The average number of new patients with rectal cancer that the respondents reported to encounter in the outpatient clinic was three per month (range, 1-30).

Figure 2 shows VAS scores for the 16 factors, ordered by mean score. There was large variation in how the respondents scored the importance of factors in determining the construction of defunctioning stoma. Almost all factors were ranked as 'most important' by at least one surgeon, except for gender. 'Preoperative complications' was the factor with the highest average score (mean 78, SD 21) followed by co morbidity, tumor location and ASA-score. Gender was given the lowest value (mean 19, SD 22), followed by tumor-stage, abdominal surgical history, patients' fear for anastomotic leakage and patients' acceptance of a defunctioning stoma.

Discussion

This nationwide population-based study showed that even after correction for differences in case-mix there was a substantial variation between individual hospitals and regions in the proportion of patients receiving a defunctioning stoma. Furthermore, although hospital type and volume had an effect on the odds of receiving a defunctioning stoma, also a large variation was observed within hospital types and volume categories. Further, there was a large variation in the factors that were considered important by surgeons when deciding to construct a defunctioning stoma or not. These factors were different from those shown to be associated with the use of a defunctioning stoma in the hospital data study.

Comparison with other studies

Previous studies have demonstrated differences between hospitals for other aspects of colorectal cancer treatment. Elferink et al found that treatment patterns for radiation therapy in rectal cancer patients varied considerably between hospitals in the Netherlands. In their study, patients treated in a teaching or university hospital had lower odds and patients treated in a high-volume hospital had higher odds of receiving preoperative radiotherapy. [25] A study from Kolfschoten et al found substantial differences between hospitals in the use of laparoscopic surgery for the treatment of colorectal cancer in the Netherlands, with percentages varying between 0 and 96%.[26] That study reported no information on the relation between hospital type or volume and the use of laparoscopy. Morris et al studied the use of abdominal perineal excisions (APE) in hospitals in Great-Britain and found statistically significant variations in the odds of receiving an APE between individual surgeons, hospital trusts and cancer networks.[27] Patients treated in hospitals with a lower surgical volume were significantly more likely to receive an APE. No differences were found for hospital type.

Strengths and limitations

Our study has several strengths. It used a comprehensive national database, which reduces the risk of selection bias. Also, the combination of results of the hospital data study with those of the survey allowed us to explore possible mechanisms for the observed variation in defunctioning stomas between hospitals. This could never have be done when looking at the database alone.

Although much detailed information about patient and tumor demographics is available in the dataset of the DSCA, some limitations remain. First, some potentially important data points may be missing. For example, detailed information on smoking, alcohol consumption, nutrition status, and preoperative sphincter function were not available. We have no reason to believe that some hospitals have disproportionate numbers of smoking patients or patients with a higher consumption of alcohol or lower nutrition status necessitating higher rates of defunctioning stomas. Moreover, high risk patients, according to the surgeons' preoperative risk judgment, may not have been selected for a primary anastomosis, and therefore excluded which may have caused a potential selection bias. Last, although the response rate was not optimal, it is comparable to prior reported surveys to professionals.[28-30]

Clinical implications and future research

The results from the survey corroborated our expectations: that the variation in defunctioning stomas may be caused by a variation in surgeons' opinion and perceptions regarding factors that are important for this decision. These findings suggest that there is no generally accepted strategy to select patients for a defunctioning stoma. Male gender increased the odds of a stoma in our hospital data study but were found to be the least important by surgeons in the survey, whereas ASA-score, urgency of surgery and age on the contrary were considered important, but did not explain the variation in stoma rates. The latter might be explained by confounding, with surgeons attributing their choice to .e.g. age or ASA-score whereas in fact it should have been gender. Further, the factors we added that were not available in the hospital dataset (lifestyle, preoperative factors, and judgment of the anastomosis) had mean scores of above 50, so might explain some of the residual variation in the hospital data study.

Our study did not focus on whether hospitals with higher defunctioning stoma rates had better outcomes. Another investigation performed by our study group however describes the lack of a significant correlation between hospitals' percentage of defunctioning stomas and their anastomotic leakage rate (data to be published). Possibly, there are patients receiving a defunctioning stoma that would have had good outcomes without a stoma. In our study, nearly all hospitals constructed a defunctioning stoma in more than 10% of patients; the majority (80%) constructed a defunctioning stoma in even more than 50% of patients. Koperna et al performed a cost-effectiveness analysis, and estimated that to balance the extra cost of a stoma the anastomotic leak rate would have 16.5%.[5] A suggested benchmark following that study was a rate of less than 10% defunctioning stomas. The authors stated that a stoma rate of more than 50% has no supplementary effect on reducing anastomotic leakage.[37] A study from our own group showed that while during the last decade there was an increase in the use of defunctioning stomas, anastomotic leakage rates remained similar.[31] These findings suggest that protective effect of a defunctioning stoma is most apparent in high-risk patients, while the additional benefit for the rest of the population is limited. Identification of high-risk patients therefore seems essential to guide appropriate use of defunctioning stomas. An algorithm with which surgeons can select high-risk patients has been developed, but not yet validated in larger multi-center series.[19]

Further focused research on this matter is warranted since, obviously, a lack of agreement on which treatment strategy to use in different groups of patients, leads to differences between patients depending on surgeons' perceptions. As a result, patients receive the care preferred by their physician, instead of making their own informed choice. Not all patients benefit from a defunctioning stoma, as there are several drawbacks that counterbalance its advantages. It is known that stomas can induce morbidity, hospital re-admission, discomfort, and prolonged hospital stay.[32-35] In addition, in certain cases the stoma may not be closed, or closure itself can lead to significant morbidity and (rarely) mortality.[2,3] Furthermore, even when a defunctioning stoma is constructed there is still is a considerable risk of anastomotic leakage.1, [23, 36, 37] We advocate that patients' preferences regarding the morbidity and mortality of anastomotic leakage versus the consequences of a defunctioning stoma should be taken into account preoperatively.

Conclusion

In conclusion, there is a considerable variation in the use of defunctioning stomas for patients with rectal cancer in the Netherlands. There is a need for uniformity of selection criteria for defunctioning stomas between surgeons. Future research should focus on an algorithm selecting high-risk patients to guide the appropriate use defunctioning stomas.selecting high-risk patients to guide the appropriate use defunctioning stomas.selecting high-risk patients to guide the appropriate use defunctioning stomas.selecting high-risk patients to guide the appropriate use defunctioning stomas.

Figure 1. Funnel plot of proportion of patients in which a defunctioning stoma was constructed by mean number of patients and hospital type. The proportion for each hospital was adjusted for gender, body mass index, tumor height, and preoperative radiotherapy. 95% CL=95% Confidence Limit.

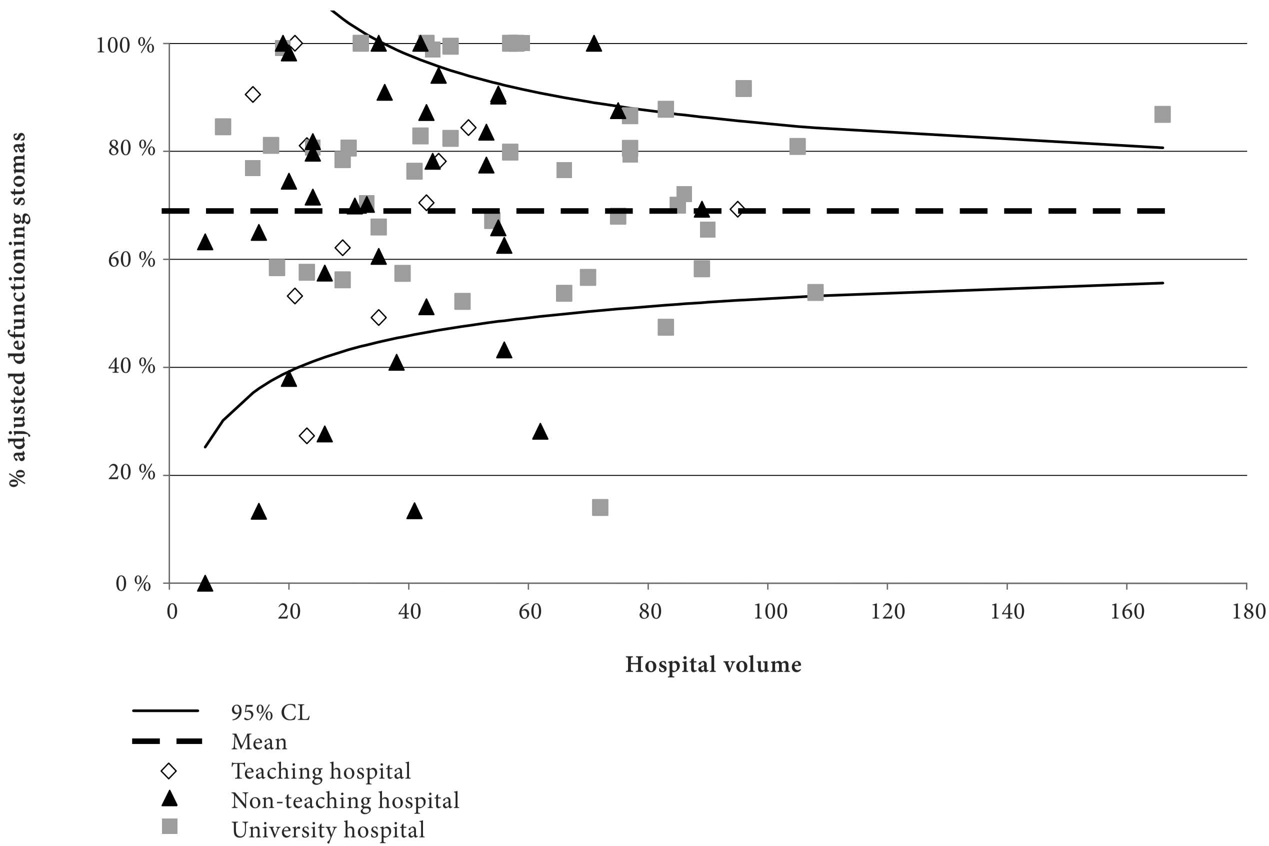


Table 1. Patient and hospital characteristics of patients with and without a defunctioning stoma included in the sample drawn from the DSCA (Chi-Square analyses). ASA classification= American Society of Anesthesiologists classification, BMI=Body Mass Index.

		No defunctioning stoma		**Defunctioning stoma**		**P-value**
Age	<75 years	1098	77%	2412	82%	
	> 75 years	324	23%	532	18%	<0.01
Gender	Male	743	52%	1908	65%	
	Female	680	48%	1037	35%	<0.01
ASA-classification	ASA I	431	30%	860	29%	
	ASA II	807	57%	1691	57%	
	ASA III+	166	12%	357	12%	
	Unknown	19	1%	37	1%	0.88
Co-morbidity	None	579	41%	1134	39%	
	1	413	29%	855	29%	
	2 or more	431	30%	956	32%	0,27
BMI	25-30	426	30%	762	26%	
	<25	473	33%	970	33%	
	>30	166	12%	373	13%	
	Unknown	358	25%	840	29%	0,01
Abdominal surgical history	Yes	429	30%	793	27%	0,03
TNM-pT	pT0/1/2/x	631	50%	1001	36%	
	pT3	583	46%	1662	59%	
	pT4	46	4%	155	6%	<0.01
Urgency of the resection	Elective	1396	98%	2902	99%	
	Urgent	25	2%	36	1%	0,16
Distance of tumor to the anal verge	< 10 cm	617	48%	2070	74%	
	> 10 cm	678	52%	725	26%	<0.01

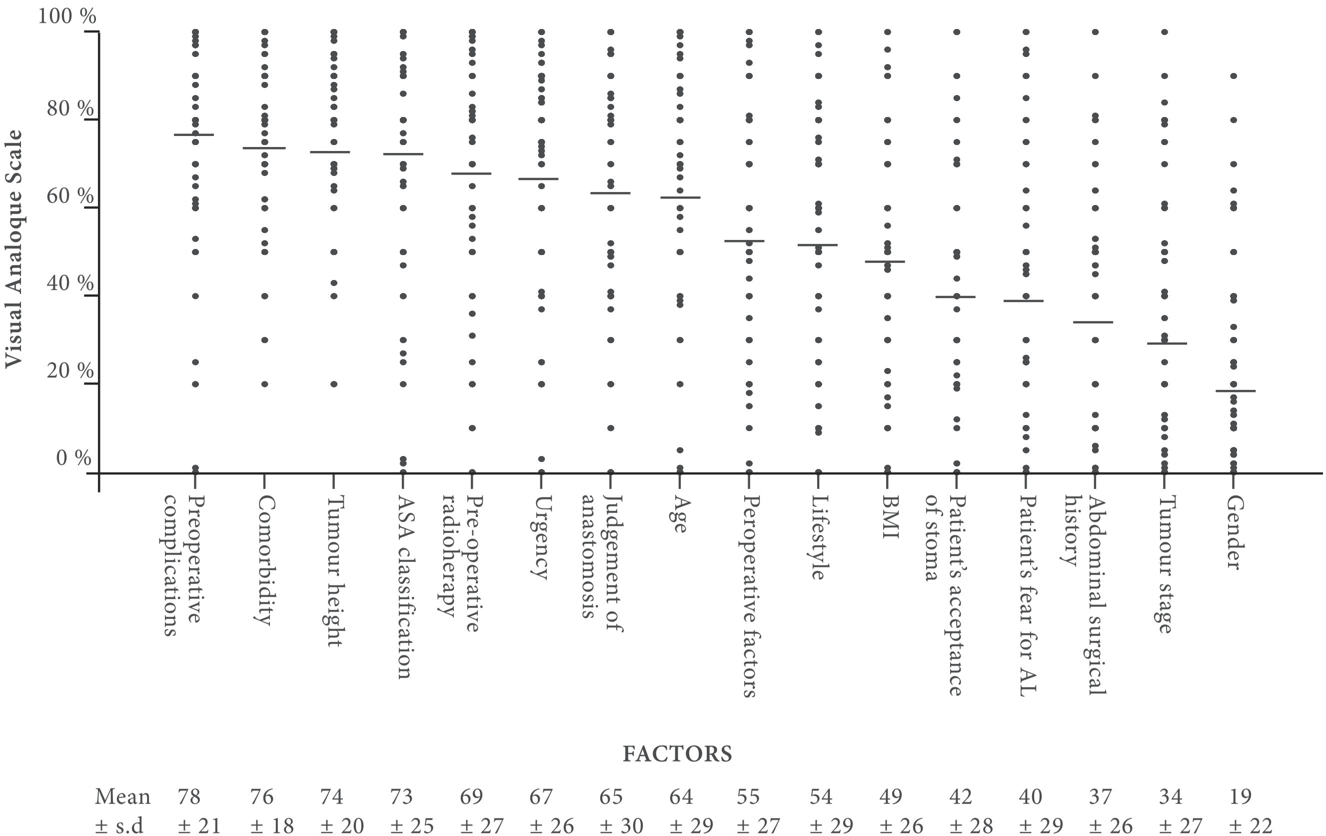
Preoperative radiotherapy	None	507	36%	280	10%	
	5x5 Gy	665	47%	1568	53%	
	Chemoradiation	251	18%	1097	37%	<0.01
Type of hospital	General hospital	436	31%	800	27%	
	Teaching hospital for surgery	915	64%	1905	65%	
	University hospital	72	5%	240	8%	<0.01
Hospital volume	Low volume (< 25/year)	310	22%	660	22%	
	Medium volume (25-50 /year)	706	50%	1474	50%	
	High volume (>50/year)	407	29%	811	28%	0,74
Region	1	248	17%	310	11%	
	2	602	42%	1074	36%	
	3	267	19%	814	28%	
	4	306	22%	747	25%	<0.01

Table 2. Odds ratio of receiving a defunctioning stoma in patients undergoing surgery for rectal cancer in the period 2009-2012 (multivariate analysis). ASA classification= American Society of Anesthesiologists classification, BMI=Body Mass Index. CI=confidence interval; Ref=reference category. Bold printed numbers are statistically significant ($p<0.05$).

		OR	***95% CI***	
			Lower	***Upper***
Age	<75 years	1.00	Ref	
	>75 years	.95	.78	1.16
Gender	Female	1.00	Ref	
	Male	1.71	**1.45**	**2.00**
ASA-classification	1	1.00	Ref	
	2	1.02	.83	1.24
	3+	1.20	.88	1.65
Co-morbidity	None	1.00	Ref	
	1 organ system involved	1.06	.86	1.30
	2 or more organ systems involved	1.14	.91	1.43
BMI	20-30	1.00	Ref	
	<20	.95	.78	1.15
	>30	**1.29**	**.99**	**1.68**
Abdominal surgical history	Yes	1.08	.91	1.29
TNM-pT	pT0/1/2/x	1.00	Ref	
	pT3	1.16	.99	1.37
	pT4	.95	.63	1.44
Urgency of the resection	Urgent resection	1.21	.61	2.40
Distance of tumor to the anal verge	>10 cm	1.00	Ref	
	<10 cm	**2.58**	**2.21**	**3.03**
Preoperative radiotherapy	None	1.00	Ref	
	5x5 Gy	**3.54**	**2.88**	**4.34**
	Chemo radiation	**6.35**	**4.91**	**8.21**

Type of hospital	General hospital			
	Teaching hospital for surgery	1.56	1.25	1.94
	University hospital	1.64	1.16	2.33
Hospital volume	Low volume (< 25/year)	1.00	Ref	
	Medium volume (25-50 /year)	**.72**	**.58**	**.91**
	High volume (>50/year)	**.71**	**.53**	**.96**
Region	1	1.00	Ref	
	2	**1.28**	**1.00**	**1.62**
	3	**3.53**	**2.70**	**4.61**
	4	**2.30**	**1.78**	**2.98**

Figure 2. Surgeons' score (range 0-100) for factors determining the construction of a defunctioning stoma. (n=103). SD=standard deviation; ASA classification= American Society of Anesthesiologists classification; BMI = Body Mass Index; AL= Anastomotic Leakage.



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Chapter 6:

OPTIMAL TREATMENT STRATEGY IN RECTAL CANCER SURGERY; SHOULD WE BE COWBOYS OR CHICKENS?

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Abstract

Introduction: Surgeons and hospitals are increasingly accountable for their postoperative complication rates. This may lead to risk-averse treatment strategies. It is not known whether a risk-averse strategy leads to providing better care. The aim of this population-based study was to determine the association between hospitals' strategy regarding defunctioning stoma construction and postoperative outcomes in rectal cancer surgery.

Methods: Data of the Dutch Surgical Colorectal Audit including 3104 patients undergoing rectal cancer resection and receiving an anastomosis between January 2009 to July 2012 in 92 hospitals were used. Hospital variation in defunctioning stoma rates was calculated as an observed (O) versus expected (E) rate, adjusted for relevant case-mix factors. Anastomotic leakage and 30-day mortality rates were compared in hospitals with high and low tendency towards stoma construction.

Results: Seventy-six percent of all patients received a defunctioning stoma; 9.6% of all patients developed anastomotic leakage. Postoperative mortality was 1.8%. Hospitals' adjusted proportion of defunctioning stomas varied from 0-100%. There was no significant correlation between hospitals' adjusted stoma O/E rate and anastomotic leakage rate. Severe anastomotic leakage rates were similar (7.0 versus 7.1%, p=0.95) in hospitals with the lowest and highest stoma rates. Mild leakage and postoperative mortality rates were higher in hospitals with high stoma rates.

Conclusion: A high tendency towards stoma construction in rectal cancer surgery did not result in lower overall anastomotic leakage or mortality rates. It seems that not a risk averse strategy, but the ability to select patients for stoma construction is the key towards preferable outcomes.

Introduction

Surgical resection is the cornerstone of rectal cancer treatment. If tumour size, stage and location allow for a sphincter preserving resection, and bowel continuity is restored, the surgeon has to decide whether or not to defunction the anastomosis. This decision concerns the trade-off between benefit and harm. The advantage of a defunctioning stoma can be that it decreases the consequences of anastomotic leakage, and may also decrease its incidence.[1;2] Anastomotic leakage is a serious complication causing re-operation, prolonged hospital stay, morbidity, mortality, and possibly worse oncological outcome.[3-5] On the other hand a stoma has evident disadvantages; defunctioning stomas can induce morbidity, discomfort (decreased quality of life), higher costs[6], longer hospitalisation[7] and even mortality from surgery to close the stoma. [8-12] Furthermore, 80% of defunctioning stomas is only reversed after 4 months and 20 % is never reversed.[13]

Nowadays quality of care has become a major topic and surgeons and hospitals are increasingly accountable for their postoperative complication rates. This may lead to risk averse treatment strategies. Previous research suggests that differences in professional opinion may lead to variation in health care delivery.[14-21] The threshold for the decision to construct a stoma to avoid the risk for anastomotic leakage may also vary between surgeons. Some surgeons may be more risk-taking or risk-averse than others. However, the attempt to avoid or limit the risk for anastomotic leakage after colorectal surgery by frequent use of stomas is only in patients' interest if it in fact lowers clinically relevant anastomotic leakage and mortality rates.

The objective of this study was to investigate whether hospitals differ in their treatment strategy regarding construction of defunctioning stomas in rectal cancer surgery, and to assess if a hospital's treatment strategy is related to its postoperative outcomes such as clinically relevant anastomotic leakage and mortality rates.

Methods

Study cohort

Data was derived from the Dutch Surgical Colorectal Audit (DSCA), a national quality improvement project in which over 200 variables concerning the patient, co-morbidity, diagnostics, disease-specific details, treatment, and outcomes are collected prospectively. The DSCA contains data registered by 92 hospitals (representing all hospitals performing colorectal cancer surgery in the Netherlands). Over 90% of all eligible patients are included. The dataset is disease-specific for colorectal cancer and has shown a nearly 100% concordance on most items upon validation against the Netherlands Cancer Registry dataset.22 All patients having undergone anterior resection for primary rectal cancer between the 1st of January 2009 and 31st of July 2012 were evaluated. Minimal data requirements for inclusion in the analysis were: information on tumour location, date of surgery, and mortality. Patients without an anastomosis, with metastasis at time of primary surgery, resections for multiple synchronous colorectal tumours, and patients with a tumour less than 5 cm from the anal verge were excluded, because these represent subgroups of patients with specific treatment perspectives and subsequent different expected outcomes.

Definitions

Overall anastomotic leakage, as used in the hospital comparisons, was defined as 'clinically relevant anastomotic leak requiring a re-intervention, either radiological (mild) or surgical (severe)'. Postoperative mortality was defined as 'in-hospital mortality or all deaths within 30 days after primary surgery'.

The following casemix factors were considered: age, gender, ASA-classification, abdominal surgical history, tumour height, preoperative tumour complications, and urgency of the resection.

Considered treatment factors were surgical procedure (laparoscopic or open), and the use of neoadjuvant treatment.

Hospitals were stratified into two categories: non-teaching and teaching hospitals. A teaching hospital is a hospital, which provides medical training to surgical residents. Procedural volume in rectal cancer resections was calculated for each hospital before the aforementioned exclusion of patients. Hospital volume was categorized into <25, 25–50 and >50 resections per year.

Statistical considerations

As patient and tumour related case-mix factors may be responsible for a large part of the hospital variation in the number and proportion of patients with a defunctioning stoma, we adjusted for these differences by calculating the Observed/Expected (O/E) stoma rate. For this calculation, the observed outcome was the number of patients with a defunctioning stoma in a hospital and the expected outcome is the sum of all patients' estimated probabilities for a defunctioning stoma. Patients' probability estimates were derived from a backwards-stepwise multivariate logistic regression model, fitted on the data of all included hospitals, and using all case-mix factors mentioned above. For an average performing hospital, the observed outcome will be equal to the expected outcome, resulting in an O/E outcome ratio of 1. Hospitals that construct more defunctioning stomas than average have an O/E outcome ratio higher than 1, while this ratio is lower than 1 in hospitals with lower than average stoma rates.
Next, the adjusted hospitals O/E ratios for strategy (stoma use) were plotted against their anastomotic leakage rates.

The relation between the hospitals' strategy and its outcomes was analyzed by two methods. First, to evaluate whether stoma rates were related to (lower) anastomotic leakage rates on a hospital level, a linear correlation was calculated using Pearson's correlation coefficient R. Second, to evaluate whether a risk averse strategy (high stoma rates) is related to better postoperative outcomes on a hospital level, hospitals were grouped into equally-sized groups based on quintiles of their case-mix adjusted rate of defunctioning stomas. Differences between groups in outcomes (mild and severe anastomotic leakage and mortality rates) were analyzed using a chi-square test.

The association of patient and tumour related case-mix factors, hospital factors (teaching status, volume) and treatment factors (neoadjuvant therapy, laparoscopic surgery) with being in the high stoma group was assessed with a chi-squared test and multivariate logistic regression analysis, considering the same case-mix factors as mentioned above All statistical analyses were performed in PASW Statistics, Rel. 18.0.2009. Chicago.

Results

Between January 1 2009 and July 31 2012, 92 hospitals registered all rectal cancer patients in de the DSCA. After exclusion of ineligible patients, a total of 3104 patients were included in the analysis. Characteristics of the included patients and hospitals are shown in Table 1.Of all patients, 67% (n=2080) received an anastomosis with a defunctioning stoma.

In total, 302 patients (9.6%) developed anastomotic leakage. The majority (187 of 302, 62%) were severe leakages requiring a surgical reintervention. Anastomotic leakage rates were somewhat higher in patients with a defunctioning stoma (9.3 versus 10.4%), but this difference was not statistically significant (p=0.35). Fifteen of 302 patients that developed anastomotic leakage, died during hospital stay or within 30 days after surgery (5%). Overall postoperative mortality rate was 1.8% (n=187); anastomotic leakage caused one-fourth of overall mortality.

Hospitals

Relevant casemix factors were selected by backward stepwise logistic regression analysis. Relevant factors for the proportion of defunctioning stomas were gender, preoperative complications, tumour location, and laparoscopic surgery.

Hospitals' unadjusted proportion of defunctioning stomas varied considerably: percentages ranged from 0-100% (*figure 1*). *Figure 2* shows the relation between the hospitals' adjusted proportion (O/E ratio) of defunctioning stomas and the hospitals' overall anastomotic leakage rate. Hospitals varied in anastomotic leakage rates (3-18%). There was a weak positive correlation between hospitals' adjusted O/E stoma ratio and anastomotic leakage rates (r=0.032), this was not statistically significant (p=0.76).

Low versus high stoma rate

Eighteen hospitals with a total number of 604 patients were identified as the group of low stoma rates. This group had a mean percentage of 26% of patients with a defunctioning stoma. The group of high stoma rates consisted of 18 hospitals, which treated 521 patients in total, had a 88% mean defunctioning stoma rate (*Figure 3*). A slight difference in overall anastomotic leak rates was found between groups, although not statistically significant (8.4 vs11.3%, p=0.11). Severe anastomotic leakage rates were similar in both groups; 7.1 versus 7.5% (p=0.95). Mild anastomotic leakage rates were significantly higher in the group with high stoma rates: 1.5 versus 3.8% (p<0.001). Postoperative mortality rates were significantly higher in the group with high stoma rates; 2.9 versus 1.0% (P=0.02). The remaining hospitals formed a group with intermediate stoma rates (67%), and had outcomes in between the low and high stoma groups (9.7% anastomotic leakage, 1.7% mortality).

Table 2 shows the results of univariate and multivariate analysis for factors contributing to the odds of being in the group of high stoma rates. The percentage of patients treated with short course radiation therapy (SCRT) was higher in the group with high stoma rates, as well as the percentage of patients treated in teaching hospitals. Also in multivariate analysis, these patients had higher odds of being in the group of high stoma rates. Urgent resections and volume were associated with a lower risk of being treated in a high stoma rate hospital in both univariate and multivariate analysis (*Table 2*). Other case-mix factors, as age, ASA score and tumor characteristics, were not statistically different in both groups.

Discussion

Overview of findings

This study demonstrates a large hospital variation in treatment strategy concerning defunctioning stoma construction after surgical resection of rectal cancer, even after adjustment for relevant casemix factors. Hospitals with a low threshold for defunctioning stoma construction after rectal cancer resection did not have lower anastomotic leakage rates in comparison with hospitals with an opposite strategy. Interestingly, mortality and anastomotic leakage rates requiring radiological drainage were even higher in hospitals with a high stoma rate. The latter may be partly due to the slight difference in short course radiation therapy (SCRT) between both groups. Although a direct correlation between clinically apparent anastomotic leakage and neoadjuvant therapy has not been demonstrated,[4;23-26] den Dulk et al showed SCRT to be a limiting factor for reversal of a (secondary) constructed stoma suggesting that it increases the risk for subclinical, or mild anastomotic leakage.[27]
An explanation for the remarkable correlation between a risk averse strategy and low hospital volume or teaching status cannot be provided within the scope of this article. Possibly, these hospitals may use other selection criteria for defunctioning stomas, or treat patients with an

impaired condition for which could not be adjusted in this study.

Comparison with other studies

There is an on-going debate on differences in treatment approach despite ample data describing the direct correlation between the rate of both defunctioning stomas on the one hand, and anastomotic leakage and postoperative mortality on the other hand. The discussion focuses mainly on whether defunctioning stomas should be used routinely after low anterior resection to decrease anastomotic leakage rates. A meta-analysis from Hüser et al1, mainly based on the results of a randomized controlled trial from Mathiessen et al2 clarifies the advantage of a defunctioning stoma on lowering anastomotic leakage rates. This is confirmed by a considerable amount of retrospective studies.[4;28-30] On the contrary, a study from Fielding et al. observed a higher leakage rate in patients with a defunctioning stoma (18% versus 7%) and suggested that surgeons with an individual anastomotic leakage rate less than 5% do not need to create a defunctioning stoma at all. Both Enker et al, and Matthiessen et al. showed that a defunctioning stoma did not reduce the incidence of anastomotic leakage in patients undergoing low or ultralow anterior resection.[7;31] Nevertheless, it has been agreed previously that there is a need for a benchmark on hospitals' defunctioning stoma and anastomotic leakage rates.

Strengths and limitations of study

We retrospectively evaluated a prospectively maintained, population-based database to determine the association between hospitals' strategy regarding defunctioning stoma construction and postoperative outcome in rectal cancer. It could be argued that comparing patient outcomes for patients with and without a stoma is not valid, because of confounding by indication: patients may have received a stoma because they were considered to be high risk patients and are therefore not comparable to patients that did not receive a defunctioning stoma. This bias could also explain the relatively high mortality in the group with high stoma rates. However, in our study this bias is largely overcome by comparing hospitals at both ends of the spectrum (either very high or very low defunctioning stoma rates). Defunctioning stoma rates of 88% and 26% respectively, reflect a strategic approach (standard a stoma or standard no stoma), that is only slightly based on individual decision making concerning patient characteristics. It is likely that only very high risk patients received a stoma in both groups, and very low risk patients in both groups did not. For other patients, the decision was mainly based on the hospitals strategic approach. Therefore the method we used in our study resembles a “pseudorandomisation”. This is supported by the fact that baseline characteristics were similar for both groups in our study.

The findings of this study are very useful for clinical practice because they strengthen the concept that the decision of stoma formation after anterior rectal resection cannot be standardized but require a careful evaluation of individual risk factors. Data represent current surgical practice at a population level, since all hospitals participate in the DSCA and the percentage of eligible patients registered is over 90%.

A limitation of this study is that analyses were performed at a hospital level, while the surgical strategy may differ between surgeons within a hospital. Information on a surgeons’ level is not available in the DSCA and individual volumes may be low, introducing more impact of chance variation in the analyses.

Clinical implications

Should we then be cowboys or chickens; if the latter does not necessarily result in better outcomes? The results confirm that the protective effect of a defunctioning stoma is probably most apparent in high-risk patients, while the additional benefit for the rest of the population is limited or even non-existent. There have been numerous studies identifying risk factors for anastomotic leakage. [9-13] Dekker et al developed and tested the Colon Leakage Score (CLS) in which multiple risk factors were used to provide an objective prediction of the risk for anastomotic leakage.[32] They found that only 20% of their population could be considered as high risk. If we take into account the relative risk reduction of 64% that was found in the randomized trial of Matthiessen et al. (reduction in AL from 28% to 10%) for high-risk patients with lets say an a priori risk of anastomotic leakage of 20%, this would mean an absolute risk reduction of 12.8% and so 8 defunctioning stomas would have to be constructed in order to prevent one anastomotic leak. In contrast, for patients with an a priori risk of 5%, (ARR 3.2%) 31 defunctioning stomas would have to be created to prevent one leak.

It should thereby kept in mind that stomas can induce morbidity, discomfort (quality of life), costs and even mortality. Stomal complications cause re-admission within two months after initial surgery in up to 17% of all patients, mostly due to de-hydratation[9;11;33;34]. Even when a defunctioning stoma is constructed, there is still is a considerable risk of (late) anastomotic leakage [2;4;35-37] It is also recognized that 15-30% of defunctioning stoma's are never closed, resulting in a permanent stoma[10;38]

Future multicentre randomised trials are important to gain more evidence on the possible benefits of defunctioning stomas. However, in our opinion they can be only useful if they discriminate between high and low risk patients. Therefore, future studies should first focus on adequately identifying these patients, to prevent the creation of non-beneficial defunctioning stomas in low risk patients.

Finally, we advocate that patients' preferences concerning the risk of morbidity and mortality of anastomotic leakage versus the consequences of a defunctioning stoma should be taken into account preoperatively. This requires thorough preoperative counselling.

Conclusion

In conclusion, a high tendency towards defunctioning stoma construction in rectal cancer surgery did not result in lower overall anastomotic leakage or mortality rates. The optimal treatment strategy can probably be found in hospitals with both low stoma rates and favourable postoperative outcomes. It seems that hospitals with low stoma rates were better in selecting high-risk patients, and that stoma formation in more patients does not lead to better outcomes. Adequate identification of high-risk patients should be focus of future studies to facilitate decision-making.

Table 1. Patient, tumour and treatment characteristics of included patients. ASA: American Society of Anaesthesiologists risk score.

		N	**%**
Total			
Age	Mean (range)	66	(15-97)
Gender	Male	1850	60%
ASA classification	I-II	2567	83%
	III+	369	12%
	Missing	168	5%
Abominal surgical history	Yes	808	26%
Tumor location	>=10 cm	1149	14%
	<10 cm	1660	20%
Urgency	Acute/urgent	57	2%
Tumour stage	(Y) pT0/X	207	7%
	pT1	269	9%
	pT2	990	32%
	pT3	1533	49%
	pT4	105	3%
Surgical preoperative treatment	Stoma	162	5%
	Stent	8	0,30%
	Other	51	3%
Neoadjuvant treatment	5x5 Gy	1623	52%
	Chemoradiation	825	27%
Surgical procedure	Laparoscopic resection	1393	45%
Hospitals: type	Teaching hospital	2175	70%
	Non-teaching hospital	929	30%
Hospitals: volume	High volume (>50/year)	875	28%
	Medium volume (25-50 /year)	1490	48%
	Low volume (< 25/year)	739	24%

*Table 2: Univariate and multivariate analysis for factors contributing to being in the group of high stoma rates, *Odds ratios display the odds for being in the group of high stoma rates.*

Factor		***Univariate***		***Multivariate***	
		Cowboys n (%)	***Chickens n (%)***	***OR****	***95 % CI***
Age	mean	66	66	0.99	0,98 - 1.01
Gender	female	247 (41)	210 (40)	0.88	0,68 - 1.14
Asa	1	157 (30)	149 (30)	1.0	ref
	2	297 (56)	307 (60)	1.13	0.76 – 1.36
	3+	79 (15)	52 (10)	0.81	0.55 - 1.30
Urgency	urgent operation	**18 (4)**	**4 (0.8)**	**0.29**	**0.09 - 0.89**
Preopeative surgery	Yes	24 (4)	25 (5)	1.19	0.64 - 2.24
Tstage (p)	T0	22 (4)	32 (7)	1.0	Ref
	T1	53 (9)	55 (11)	1.35	0.36 - 5.00
	T2	193 (32)	165 (32)	1.02	0.29 - 3.61
	T3	314 (52)	260 (50)	1.08	0.31 - 3.78
	T4	22 (4)	9 (2)	0.62	0.14 - 2.74
Abdominal surgical history	yes	135 (22)	144 (28)	1.26	0.94 1.70
Tumour distance - anal verge	>10 cm	225 (37)	137 (33)	0.87	0.66 - 1.14
Neoadjuvant therapy	none	**171 (28)**	**100 (19)**	1.0	ref
5x5	5x5 gy	**301 (50)**	**308 (60)**	**1.67**	**1.20 - 2.31**
	chemoradiation	132 (22)	133 (22)	1.13	0.72 - 1.69
Surgical treatment	laparoscopy	291 (50)	286 (55)	1.09	0.84 - 1.41
Hospital type	teaching	**259 (43)**	**269 (52)**	**2.88**	**2.04 - 4.10**
Volume	<25	191 (32)	141 (27)	1.0	ref
	25-50	222 (36)	274 (53)	1.18	0.86 - 1.62
	>50	**191 (32)**	**106 (20)**	**0.27**	**0.17 - 0.43**

Bold printed numbers are statistically significant (p<0.05).

Figure 1. Hospitals ranked by their case-mix adjusted defunctioning stoma rate. Based on quintiles a group of low (left) and high (right) stoma rates was identified.

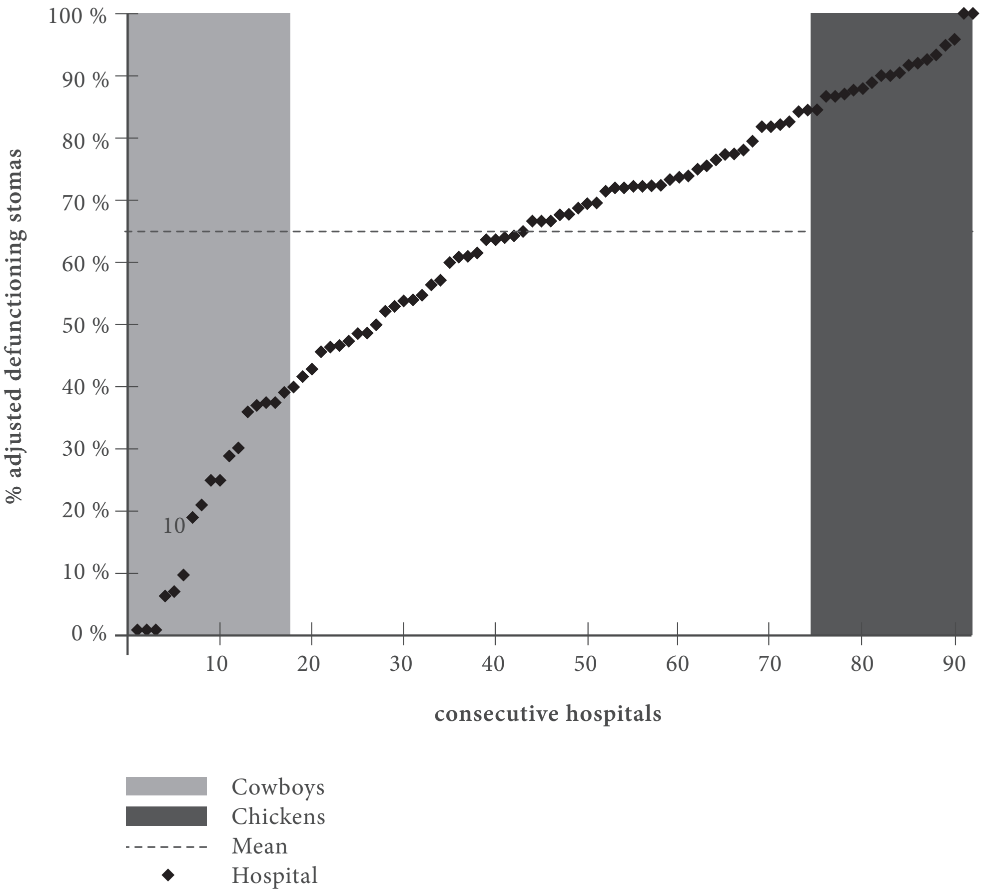


Figure 2. Hospitals' adjusted defunctioning stoma rates plotted against their anastomotic leakage rates.

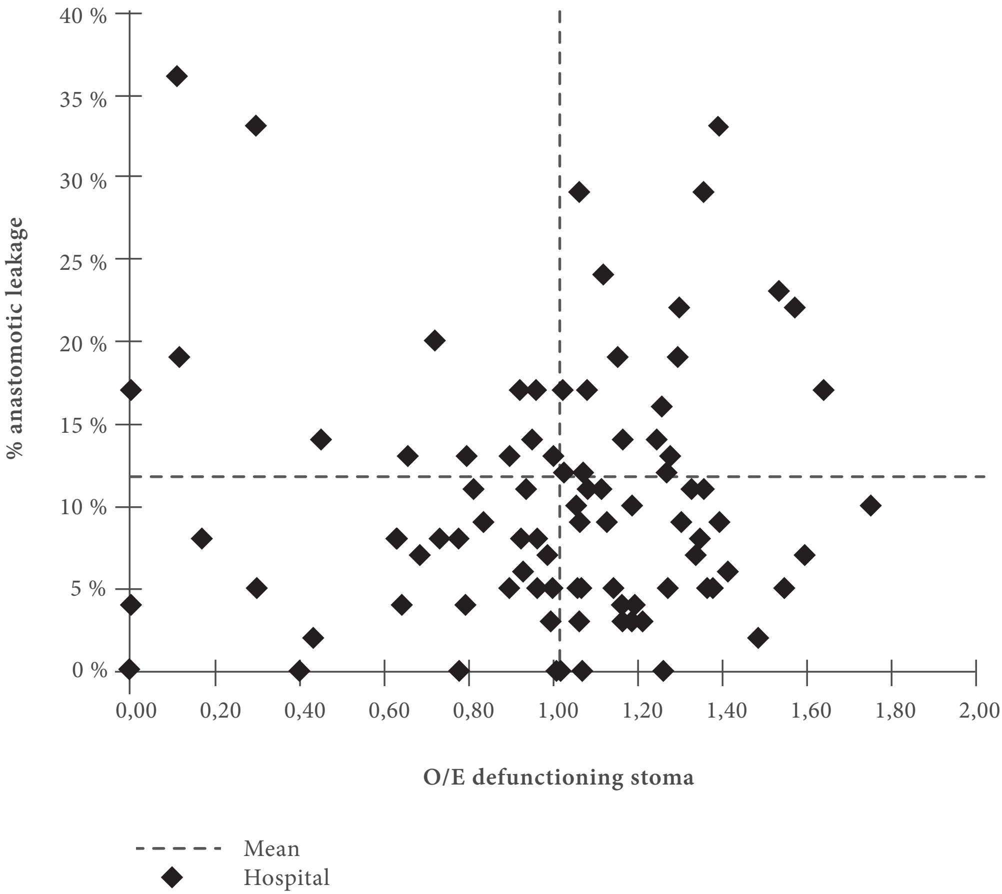
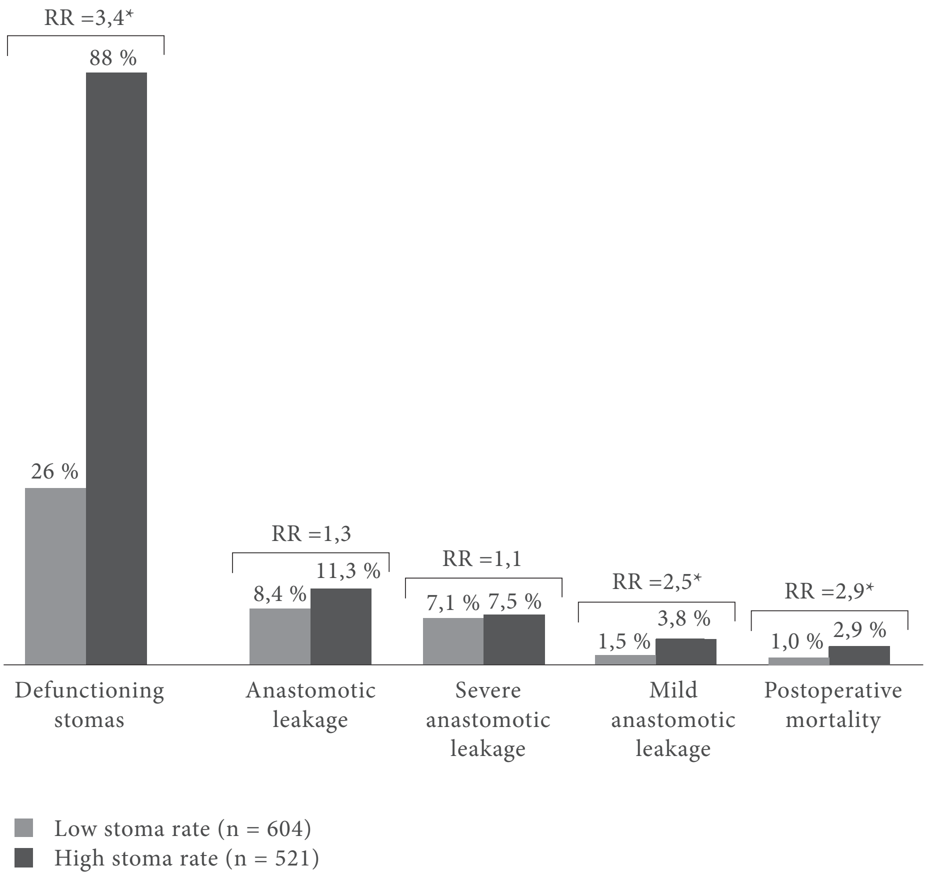


*Figure 3. Comparison of outcomes between groups identified as low and high stoma rates. Results with an * are considered statistically significant (P<0.05).*



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PART III:
QUALITY ASSESSMENT OF COLORECTAL SURGERY

Chapter 7:

THE DUTCH SURGICAL COLORECTAL AUDIT

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Abstract

Introduction: In 2009, the nationwide Dutch Surgical Colorectal Audit (DSCA) was initiated by the Association of Surgeons of the Netherlands (ASN) to monitor, evaluate and improve colorectal cancer care. The DSCA is currently widely used as a blueprint for the initiation of other audits, coordinated by the Dutch Institute for Clinical Auditing (DICA). This article illustrates key elements of the DSCA and results of three years of auditing.

Methods: Key elements include: a leading role of the professional association with integration of the audit in the national quality assurance policy; web-based registration by medical specialists; weekly updated online feedback to participants; annual external data verification with other data sources; improvement projects.

Results: In two years, all Dutch hospitals participated in the audit. Case-ascertainment was 92% in 2010 and 95% in 2011. External data verification by comparison with the Netherlands Cancer Registry (NCR) showed high concordance of data items. Within three years, guideline compliance for diagnostics, preoperative multidisciplinary meetings and standardised reporting increased; complication-, re-intervention and postoperative mortality rates decreased significantly.

Discussion: The success of the DSCA is the result of effective surgical collaboration. The leading role of the ASN in conducting the audit resulted in full participation of all colorectal surgeons in the Netherlands. By integrating the audit into the ASNs' quality assurance policy, it could be used to set national quality standards. Future challenges include reduction of administrative burden; expansion to a multidisciplinary registration; and addition of financial information and patient reported outcomes to the audit data.

Introduction

Several clinical audits have been initiated internationally, acknowledging the importance of reliable and valid quality information in health care. Clinical auditing has been recognised as an important tool for quality assessment and improvement, consequently leading to demonstrable improvements in patient outcome[1-4] Moreover, clinical audits are increasingly appreciated as a source of information for research on evidence based medicine as they provide 'real world' data on patients often not eligible for clinical trials.[5] However, the voluntary nature of existing audits may unintentionally lead to participation of mainly dedicated hospitals and underrepresentation of underperforming hospitals. Also, audit data are seldom transparent to other stakeholders involved in health care.

In 2009, the Dutch Surgical Colorectal Audit (DSCA) was initiated by the Association of Surgeons of the Netherlands (ASN) in collaboration with the Dutch Association for Surgical Oncology (NVCO), the Dutch Association for Gastrointestinal Surgery (NVGIC) and the Dutch Colorectal Cancer Group (DCCG). Their main goal was to evaluate and improve quality of care for primary colorectal cancer surgery in the Netherlands.

After one year of registration, participation in the audit had become a national performance indicator. Full participation of Dutch hospitals was realised within two years. Subsequent to this success, the Dutch Institute of Clinical Auditing (DICA) was founded in 2011 with the objective to facilitate and organise the start-up of new nation-wide audits. This article illustrates the introduction of the DSCA in the Netherlands by describing its main features and presenting the results of three years of auditing.

Methods

Main features of the DSCA

This section describes the organisational and structural key elements of the DSCA.

1. The initiator: the professional organisation of surgeons

All surgeons in the Netherlands are united in a professional organisation, the Association of Surgeons in the Netherlands (ASN). The ASN serves as a central protector of common interests of surgeons. Membership of the ASN is compulsory to all surgeons in the Netherlands. One of its main objectives is to assure that every surgical patient in the Netherlands receives high quality care. Furthermore, ASN continuously attempts to improve the quality of surgical care. The ASN uses different instruments to accomplish this, for example the development of evidence-based guidelines, surgical training programs and accreditation of surgeons in their surgical specialty. The initiation of clinical audits was necessary to facilitate the uniform measurement of quality of care and enhance the Association's quality improvement efforts.

2. Dataset: involvement of all experts in the field

The ASN formed a scientific committee of mandated clinical experts in colorectal cancer care (surgeons, oncologists, pathologists, epidemiologists) to initiate the first clinical audit. The scientific committee defined performance indicators and outcome measures, based on pre-existing evidence based guidelines, to highlight potential quality concerns, identify areas that need further investigation, and track changes over time. The committee defined a dataset using a Delphi method6. The dataset generally covers three aspects: case-mix variables (e.g. age, gender, co morbidity) necessary for hospital comparison; process variables (e.g. wait times and number of patients discussed in a multidisciplinary team); and outcomes of care (e.g. morbidity and mortality).

3. Organizational structure

In accordance with the format of the DSCA, the Dutch Institute of Clinical Auditing (DICA) was founded to enhance other clinical audit initiatives in the Netherlands. The main goal of the DICA was to support other clinical audits by facilitating on legal, technical, methodological and logistic issues. Three new audits have been initiated since the introduction of the DSCA: the breast cancer audit (NBCA), the upper GI cancer audit (DUCA) and the lung surgery audit (DLSA). The organization structure of the DICA is graphically presented in Figure 1.

4. Funding

The onset of the DSCA was funded by quality improvement grants donated by a health care insurance company. Since 2013, hospitals pay a subscription fee for participating in the DSCA. The subscription costs are returned to the hospitals as they are enclosed in the payments of treating patients with colorectal cancer. Costs of the data registration itself are not compensated and are borne by the hospitals.

5. Online data is self-registered in a secured web form

Each participating hospital appoints a surgeon responsible for (supervising) the data registration. The majority of the colorectal surgeons record the data themselves. The DSCA uses a generic internet based program to enable data entry in a secured web environment[7]. Depending on the complexity of the patient and perioperative course, a number of 56 to 179 variables have to be completed; registration time is approximately 20 to 30 minutes per patient. Data-entry can be entered either throughout patient's management or at the end of each admission. Data can be updated when necessary; for example when follow-up data is available. A third trusted party anonymises data regarding patient identification directly after data entry8. Definitions and helping texts are appointed to each variable in the dataset and are available during data entry. These guarantee that registration is performed uniformly. Also, frequently asked questions (FAQs) are available on the website and a front office can be contacted by data registrants for questions on both technical and content issues.

6. Internal and external data verification

Data validity is achieved and verified in various ways. The surgeon receives direct feedback on erroneous, missing or improbable data items during data entry through quality control tools that are built in the program. Hospitals receive feedback information on the number of patients and completeness of the data to encourage the participants to correct them when needed.
Data are annually compared with an external data registration, the National Cancer Registry (NCR), on completeness and accuracy.[1] The NCR registers all newly diagnosed malignancies in the Netherlands. Information on patient characteristics (e.g. age, gender) tumour characteristics (TNM stage, localization, histology) treatment (surgical procedure, chemo and/or radiation therapy, laparoscopy, urgency of procedure) hospital of diagnosis, hospital of treatment and outcomes (30-day mortality, anastomotic leakage, CRM, lymph nodes), are collected from the medical records by specially trained registrars

9 months after diagnosis[9,10]. The NCR has an automatic linkage to many important and solid databases, among which the Municipal Administration (GBA), which allow the full enrolment of patients eligible for registration and notification for postoperative mortality. Quality of the NCR data is high; completeness is estimated to be at least 95%.[11] The registration of the NCR is linked to the Municipal Administration, which by law receives notification on all patients that decease in the Netherlands. The quality of the data in comparison to the NCR is described elsewhere[12].

7. Online feedback is provided on a weekly basis

Information regarding volume, performance indicators and outcomes of care are presented online to individual hospitals. Each participating hospital has access to its own secured website. Data are weekly updated. Results of the hospital are presented in relation to the national average and in relation to results of other anonymised hospitals.

8. Outcomes are adjusted for differences in case-mix

The methods to measure quality of care are described in detail elsewhere.[12,13] When comparing hospital outcomes differences in case-mix must be taken into account.[14] Therefore, a set of relevant case-mix variables specific for each outcome measure is embedded in the database. A standardised co morbidity module was developed using the Delphi method with incorporation of the Charlson Co morbidity Index.[15, 16] Case-mix adjusted hospital outcomes are presented in funnel plots using 95% confidence limits that vary in relation to the hospital volume.[17]

9. Results and targets for quality improvement are presented in an annual report.

An extensive national report presenting the results of the audit is published annually.[12] This report focuses on various themes for improvements in the scope of recent literature. The results are presented in a yearly conference accessible to clinicians, patients, patient advocates, health insurers and policy makers, politicians. The conference functions as a platform for all parties to address their (common) interests and to discuss diverse health care topics.

Analysis of results of the DSCA

The completeness of the data on a national level is described by the percentage of participating hospitals and case ascertainment for each audit year. Patient, tumour and treatment characteristics are shown separately for patients with colon and rectal cancer. Then, the results of performance indicators on both process and outcomes of care were evaluated using a Chi square trend test was used to analyse changes over time. Last, hospital variation for preoperative multidisciplinary team discussions for rectal cancer surgery are presented in a scatter plot, illustrating changes in variation over time.

Results

Dataset

From 2009 to 2011, 26,511 patients undergoing surgical resection for colorectal carcinoma were registered by all 92 hospitals providing colorectal cancer care in the Netherlands (8 university, 47 teaching and 37 non-teaching hospitals). The national case ascertainment and completeness of the data per patient record was high. Compared with the data collected by the NCR, the DSCA included 80% of all eligible patients in 2009, 92% in 2010, and 95% in 2011. External data verification with the NCR showed nearly 100% completeness and high correspondence on almost all items of the dataset[12].

Patients

Information on tumour localisation, date of surgery and mortality are minimal requirements for analysis of patient records. In total, 752 patients (2.8%) were excluded for this reason. Hospitals that failed to register more than 10 patients were excluded to minimise selection bias. In 2009, this concerned 5 hospitals registering a total of 37 patients. In 2010 and 2011, none were excluded. In the results presented in this article, patients with multiple synchronous tumours (n=894) were excluded as well. A total of 24,828 patients were included in the analysis. Patient, tumour and treatment characteristics are shown in Table 1, stratified by tumour location: colon (n=17,729) and rectal cancer (n=7,099). Patients in both groups differ in age, prevalence of preoperative complications, urgency of the resection and tumour stage. Treatment patterns differ as well. For example, the percentage of diverting stomas is 4% in colon cancer surgery compared to 33% in rectal resections. Preoperative radiation therapy is applied in 84% of rectal cancer patients, which is very high from an international perspective.[17]

Performance indicators

A number of noticeable improvements on pre-defined performance indicators occurred since the introduction of the audit in 2009. These improvements concerned both processes as well as outcomes of care. Table 2 shows the results. Definitions of the various variables are provided in *table 3*.

Process

From 2009 to 2011, the percentage of patients discussed in a preoperative multidisciplinary team increased significantly both in colon (46 to 68%, P<0.01) and rectal cancer surgery (80 to 96%, p<0.01). Moreover, the in-between hospital variation decreased during this time period (*Figure 2*). There was a significant increase in the implementation of guideline-recommended preoperative MR-imaging for rectal cancer surgery (80 to 83%, p<0.001), as well as an improved standard of pathological reporting of the circumferential resection margins (48% to 80%, p<0.01).

Outcomes

Postoperative morbidity, length of hospital stay and postoperative mortality decreased significantly from 2009 to 2011 both for colon and rectal cancer surgery. The incidence of any postoperative complication decreased from 33 to 31% (p<0.01) after colon resections and from 40 to 38% (p<0.01) after rectal resections. The re-intervention rate decreased from 15 to 13% (p<0.001) after colon resections and from 17 to 14% (p<0.01) after rectal resections. Duration of hospital stay regressed with 2 days (both after colon and rectal resections). Postoperative mortality rates (both in-hospital and 30-day mortality) decreased from 5.8 to 4.0% (p=0.012) after colon resections and from 3.8 to 2.7% after rectal resections.

The percentage of patients with a positive circumferential resection margin (CRM) after rectal cancer surgery (≤1 mm distance tumour to CRM) decreased from 14% to 8.5% (p<0.001).

Discussion

This paper reports the key elements of the Dutch Surgical Colorectal Audit that have been crucial for its success. Quality of care regarding guideline compliance and clinical outcomes for colorectal cancer patients in the Netherlands improved significantly.

Numerous international audit projects leading to substantial improvements in quality of care have preceded the DSCA. Many examples of successful clinical audits have been described in detail. [2,3,18-20] Often, the main goal of the audit is to generate valuable information for clinicians to receive feedback on the quality of care.

A unique feature of the DSCA is the use of the audit data to support the effectuation of the national quality assurance policy of the surgical professional association, the ASN. There is a common need for evidence based, professionally supported consensus on what high quality care means in order to set standards of care. Benchmarking hospital performances can support surgeons in determining the minimal requirements of the provided care. On a national level, outliers can be identified. The ASN initiated an independent audit committee to provide consultative advice to hospitals identified as negative outliers in the DSCA. Furthermore, the ASN can use the data for board certification of surgeons, accreditation of hospitals, national and local improvement projects and the provisioning of valid quality information for patients, health care insurers and policy makers.

The engagement of colorectal surgeons to participate was mainly achieved by a strong plea for auditing in national meetings and conferences. The ASN strongly believed that for a valid measurement of quality of care, quality measures should be designed, registered, and interpreted by surgeons themselves. From the onset, the initiative was supported by the majority of Dutch colorectal surgeons, despite the investment in time and costs. One year later, participation became a quality indicator for the health care inspectorate, which ensured an almost 100% participation rate.

The contents of the DSCA dataset as well as the pre-defined process and outcome measures are generally supported by colorectal surgeons in the Netherlands, since they are based on evidence based guidelines and developed by representatives of their own professional organization, who are experts in the field. The leading role of the professional association and its expert members in the design, development and conduct of the audit has important advantages. It produces meaningful and feasible quality information, valid in the face of participating surgeons. This may also have led to the high participation rate among colorectal surgeons and their tremendous efforts to enter high quality data in the registry.

In three years, a trend towards better performance indicator results was objectified. A significant reduction in postoperative morbidity and mortality was observed, as well as a reduced duration of hospital stay. Although promising, the continuation of these trends needs a longer period of registration to be confirmed.

Also, as was presented in *Figure 2*, the variation in guideline compliance between hospitals was reduced. Although, these improvements may have multifactorial causes, the active and integrated approach of the DSCA has at least resulted in increased awareness of surgeons for quality aspects of their practice and provided insight in areas of improvement. The potential of clinical registries to improve health care outcomes and lowering related costs was recently demonstrated in a study by Larsson et al. [21]

An important feature that supports the audit to function as a quality improvement tool, is the web based data collection system. This system facilitates timely registration of patients and automated feedback of benchmarked performance information on a weekly basis. These features may have contributed to the demonstrable improvements in quality of care presented here.

In recent years there has been an increasing demand for valuable and reliable information on the performance of health care providers from various perspectives. The ASN aimed at developing a system that responds to the exigencies of all major stakeholders in hospital care: patients, clinicians, managers, policy makers and insurance companies. Dutch surgeons have recently agreed to gradually publish publicly their hospital-specific audit results to provide transparency to all parties concerned. For the ASN, an important condition for external transparency is the validity and reliability of the data. This is assured by consistent quality checks on the registered data in the online system and the annual external validation with the National Cancer Registry.

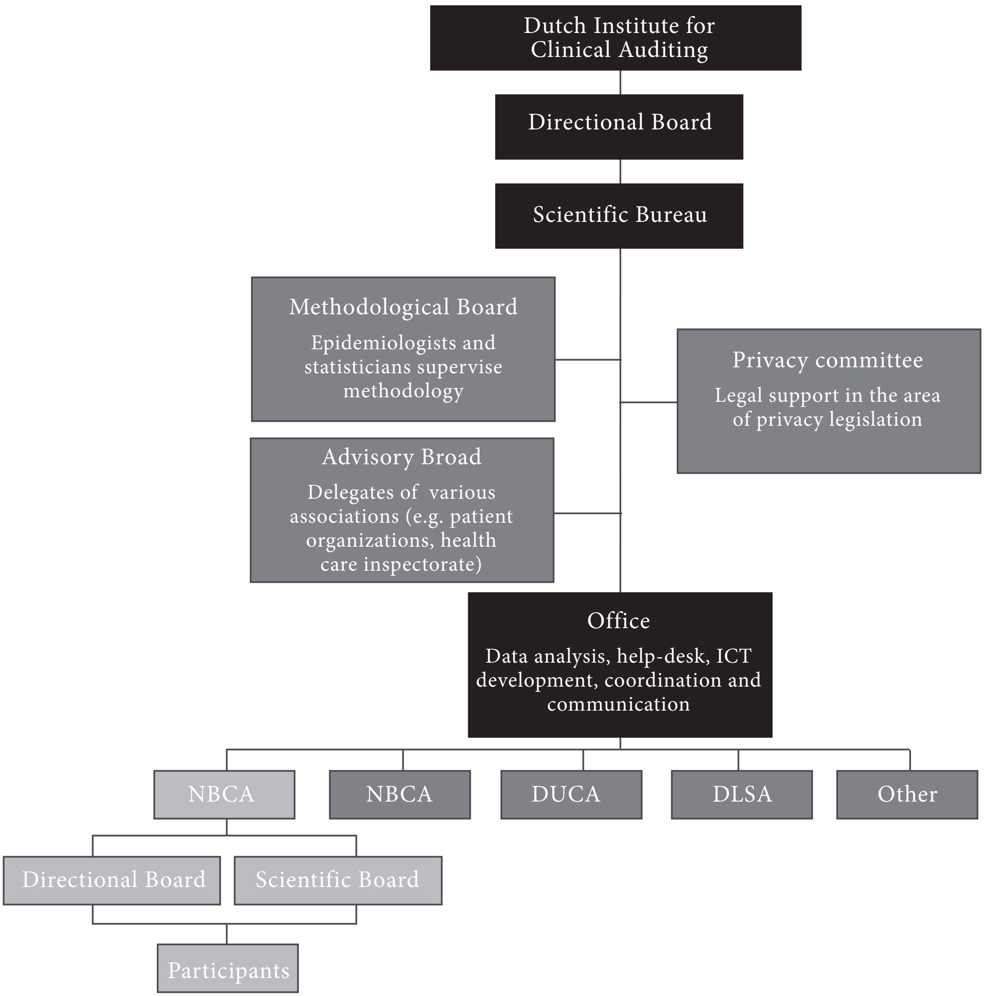
A limitation of the DSCA concept is the administrative burden that is associated with data collection. The measurement of quality of care is complex, and requires the collection of multiple data points from different phases of the care process. The dataset is limited, but still entails detailed information to perform case-mix adjustment and in-depth analysis of observed variation in care processes. Structural data management support for the health care professionals is essential for a sustainable auditing process. Automated retrieval of data from electronic patient files is the logical next step. However, apart from the technical difficulties that have to be solved to extract data from the varying electronic systems in Dutch hospitals, it is essential that synoptic reporting is implemented in the administrative process of hospitals. Links between other databases like the Dutch Pathological Anatomical District Automatized Archives (PALGA) are being established to minimise the registration burden and to automate as much as possible.

In the future, to reach full potential of the audit, information on outcomes of care should be linked to patient reported outcomes and financial information. Feedback to clinicians on patients' satisfaction and quality of life enables them to improve their practice, attitude, facilities and outcomes. Cancer patient organizations in the Netherlands have already committed themselves to collaborate in providing the clinical audits with patient reported outcomes in the near future.

Conclusion

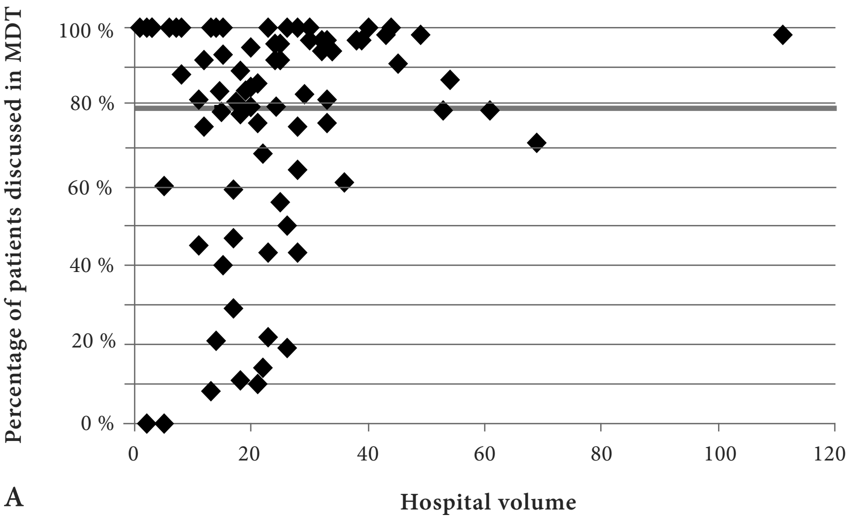
We demonstrated the feasibility of nationwide surgical audit programs, with national coverage and high case-ascertainment, accomplished in a relatively short period of time. The Dutch Surgical Colorectal Audit shows that substantial improvements can be realized within a time period of 3 years. Success factors include: a leading role for medical specialists, external data verification, weekly updated online feedback of benchmarked and meaningful quality information, and embedded in the quality assurance program of the professional association. In the Netherlands, this has been the recipe for the initiation of several other clinical audits, with a generic format consistent with the blueprint of the DSCA.

Figure 1. Organisational structure of the Dutch Institute for Clinical Auditing (DICA).



DSCA: Dutch Surgical Colorectal Audit; NBCA: Nabon Breast Cancer Audit; DUCA: Dutch Upper GI Audit; DLSA: Dutch Lung Surgery Audit.

Figure 2. Variation between hospitals in the percentage of patients with rectal cancer that was preoperatively discussed in a multidisciplinary team; a) 2009; b) 2010; c) 2011.



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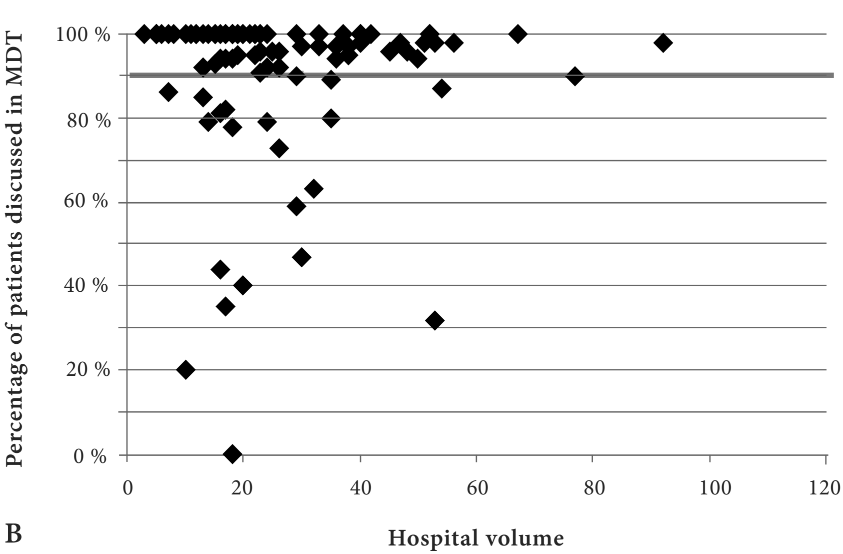

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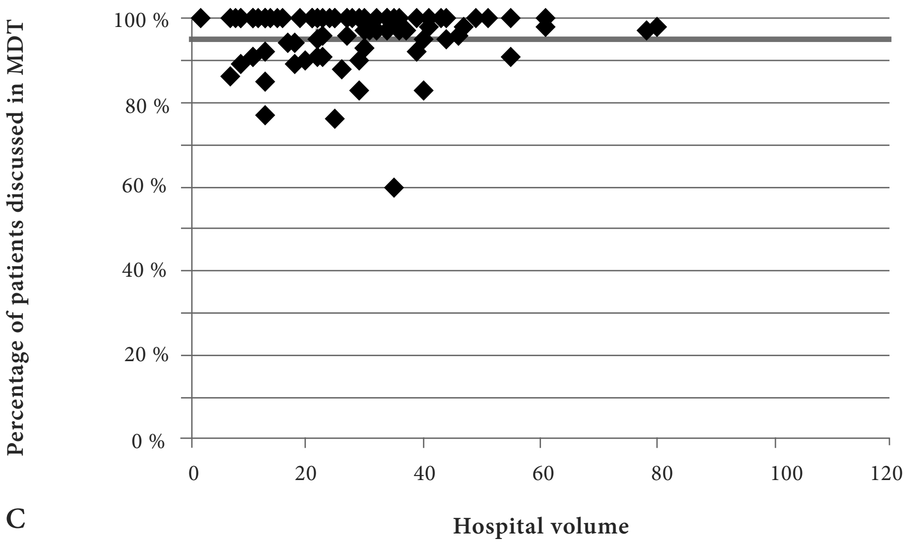

C

The black line represents the average percentage of patients.

Table 1. Patient, tumour and treatment characteristics of patients included in the DSCA, stratified by colon and rectum.

		Colon		***Rectum***	
		N	**%**	***N***	**%**
Total		**17729**		**7099**	
Age	>70	10192	57.5%	3155	44.4%
Gender	Male	9212	52.0%	4394	61.9%
ASA classification	III	4064	22.9%	1133	16.0%
	IV-V	410	2.3%	65	.9%
	Missing	426	2.4%	168	2.4%
Charlson score	1	3965	22.4%	1409	19.8%
	≥ 2	4313	24.3%	1327	18.7%
Body mass index	25-30 kg/m^2	4701	26.5%	1935	27.3%
	>30 kg/m^2	4752	26.8%	2204	31.0%
	Missing	5982	33.7%	2073	29.2%
Abominal surgical history	Yes	6009	34.6%	2094	30.1%
Tumour location	Right colon	7917	44.7%	-	-
-	Transversum/left colon	2884	16.3%	-	-
	Sigmoid	6928	39.1%	-	-
Distance of tumour from anal verge	< 5 cm	-	-	2379	37.1%
	5 - 10 cm	-	-	2613	40.8%
	> 10 cm	-	-	1417	22.1%
	Missing	-	-	697	9.9%
Urgency of resection	Acute/urgent	3567	20.1%	199	2.8%
Preoperative tumour complications	Tumour perforation	354	2.0%	41	.6%
	Abces	262	1.5%	33	.5%
	Ileus	2290	12.9%	176	2.5%
	Bleeding	983	5.5%	383	5.4%

Tumour stage	I	2974	16.8%	2054	28.9%
	II	6410	36.2%	1804	25.4%
	III	5500	31.0%	2030	28.6%
	IV	2319	13.1%	566	8.0%
	X	365	2.1%	259	3.6%
Surgical preoperative treatment	Stoma	182	9.6%	560	9.8%
	Stent	157	8.3%	16	.3%
	Metastasectomy/RFA	35	1.8%	96	1.7%
	Other	24	1.3%	34	.6%
Preoperative radiotherapy	5x5 Gy	-	-	3312	46.7%
	Long course isolated radiotherapy			595	7.9%
	Chemoradiation	-	-	2033	28.6%
Surgical procedure	Ileocoecal resection	258	1.5%	-	-
	Right hemicolectomy	7785	43.9%	-	-
	Transversal resection	553	3.1%	-	-
	Left hemicolectomy	1762	9.9%	-	-
	Sigmoid/Low anterior resection	6489	36.6%	4371	61.6%
	Abdominoperineal resection	-	-	2168	30.5%
	Laparoscopical	6606	37.4%	2690	38.1%
	Primairy anastomosis	14845	86.2%	1146	17.0%
	With diverting stoma	698	4.1%	2208	32.7%
	End colostomy	1684	9.8%	3405	50.4%
	Minimal local extended resection	1036	6.2%	258	3.9%
	Maximal local extended resection	810	4.8%	280	4.2%
	Metastasectomy	591	3.5%	202	3.0%

ASA: American Society of Anaesthesiologists risk score. RFA: radiofrequent ablation. *Includes abdominoperineal resections; **percentage is related to the performed anastomoses.

Table 2. Results of performance indicators for colorectal cancer care from 2009 – 2011.

	Colon						
	2009		***2010***		***2011***		***P-value***
Process							
Cases discussed in preoperative MDT	2286	**46%**	3504	**56%**	4255	**68%**	<0.01
Total colonoscopy	2931	**61%**	3816	**62%**	4149	**67%**	<0.01
Preoperative MRI							
CRM reported in pathology rapport							
>10 lymph nodes in sample	3623	**73%**	4902	**78%**	5423	**84%**	<0.01
Outcomes							
All complications	1595	**33%**	2062	**33%**	1918	**31%**	<0.01
Reinterventions	706	**15%**	917	**15%**	699	**13%**	<0.01
Anastomotic leakage	352	**7,4%**	456	**7,5%**	370	**6,1%**	<0.01
Hospital stay (mean in days)	13		12		11		<0.01
CRM positive margin							
30-day mortality	223	**4,5%**	255	**4,1%**	210	**3,4%**	<0.01
In-hospital mortality	232	**4,7%**	276	**4,4%**	230	**3,6%**	0.02
In-hospital mortality/30 day mortality	289	**5,8%**	300	**4,8%**	256	**4,0%**	<0.01
Total	**4960**		**6293**		**6263**		

MDT: Multidisciplinary Team; MRI: Magnetic Resonance Imaging; CRM: Circumferential Resection Margin * only for patients with a primary anastomosis.

Rectum

2009		*2010*		*2011*		*P-value*
1625	**80%**	2249	**91%**	2400	**96%**	<0.01
1467	**76%**	1858	**77%**	2016	**83%**	<0.01
1625	**80%**	2016	**81%**	2129	**85%**	<0.01
980	**48%**	1472	**59%**	2066	**80%**	<0.01
1182	**58%**	1520	**61%**	1700	**68%**	<0.01
793	**40%**	1007	**41%**	945	**38%**	<0.01
351	**17%**	435	**18%**	352	**14%**	<0.01
159	**7,9%**	217	**8,8%**	175	**7,1%**	<0.01
16		14		14		<0.01
138	**14,0%**	175	**12,0%**	168	**8,5%**	<0.01
48	**2,4%**	48	**1,9%**	54	**2,2%**	<0.01
55	**2,7%**	55	**2,2%**	64	**2,5%**	0.663
77	**3,8%**	58	**2,3%**	69	**2,7%**	0.035
2035		**2484**		**2494**		

Table 3. Definitions used in the DSCA.

Term	***Definition***
Tumour perforation	Preoperative tumour perforation with clinical signs of faecal peritonitis.
Abscess	Preoperative abscess formation in the intraperitoneal or extraperitoneal spaces.
Ileus	Preoperatieve presence of (partial) mechanical bowel obstruction with symptoms of abdominal cramping, abdominal distention, nausea, vomiting or failure to pass gas or stool.
Bleeding	Preoperative tumour related blood loss that requires an intervention (transfusion, urgent operation) or leads to anemia (Hb <7 mmol/L in male patients and <6.5 mmol/L in female patients).
Total colonoscopy	Preoperative visualization of the entire colon including the ascending colon by colonoscopy or CT colonography.
(Low) anterior resection	Rectosigmoid or rectal resection according to the TME principle with anastomosis of the colon to the intra- or extraperitoneal rectum or anal canal.
Multidisciplinary team	A team that consists of all mentioned specialists: a surgeon, an oncologist, a radiologist, a radiotherapist, and a gastroenterologist.
Urgent procedure	Non-elective colorectal resection that was required and performed within 24 hours of admission.
Anastomotic leakage	Clinically relevant anastomotic leak requiring a radiological or surgical reintervention.
Reintervention	An invasive (surgical, radiological or endoscopical) measure to treat a complication (excluding superficial drainage abscess of a wound abscess on the patient ward; introduction of a nasogastric tube; a central venous catheter; or tracheostomy).
Positive CRM	A circumferential resection margin of 1 mm or less.
Negative outlier	A hospital with a significantly worse (adjusted) outcome than the population average of all hospitals in the registration.

Hb=haemoglobin. CT=computed tomography. TME=total mesorectal excision. CRM=circumferential resection margin.

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Chapter 8:

THE DUTCH SURGICAL COLORECTAL ANASTOMOTIC LEAKAGE AS AN OUTCOME MEASURE FOR QUALITY OF COLORECTAL CANCER SURGERY

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Abstract

Introduction: When comparing mortality rates between hospitals to explore hospital performance, there is an important role for adjustment for differences in case-mix. Identifying outcome measures that are less influenced by differences in case-mix may be valuable. The main goal of this study was to explore whether hospital differences in anastomotic leakage (AL) and postoperative mortality are due to differences in case-mix, or to differences in treatment factors.

Methods: Data of the Dutch Surgical Colorectal Audit were used. Case-mix factors and treatment related factors were identified from the literature, and their association with anastomotic leakage and mortality were analyzed with logistic regression. Hospital differences in observed anastomotic leakage and mortality rates; and adjusted rates based on the logistic regression models were shown. The reduction in hospital variance after was adjustment was analyzed with a Levene's test for equality of variances.

Results: 17 out of 22 case-mix factors and 4 out of 11 treatment factors related to anastomotic leakage derived from literature were available in the database. Variation in observed AL rates between hospitals was large with a maximum rate of 17%. This variation could not be attributed to differences in case-mix, but more to differences in treatment factors. Hospital variation in observed mortality rates was significantly reduced after adjustment for differences in case-mix.

Discussion: Hospital variation in anastomotic leakage is relatively independent of differences in case-mix. In contrast to 'postoperative mortality' the observed anastomotic leakage rates of hospitals evaluated in our study were only slightly affected after adjustment for case-mix factors. Therefore, anastomotic leakage rates may be suitable as an outcome indicator for measurement of surgical quality of care.

Introduction

Nowadays there's a growing public interest in quality of medical and surgical care, with an increasing urge for outcome measures that represent hospital performance. The outcome measure postoperative mortality is often used to benchmark surgical performance.[1-3] When comparing mortality rates between hospitals, there is an important role for risk adjustment.[4, 5] Observed variations in mortality may be caused by differences in patient and tumor characteristics (case-mix), and high risk patients may not be evenly distributed between hospitals.[6]

However, valid case-mix adjustments require a substantial amount of reliable data collected on a patient level. These data are rarely available and require a substantial registration effort. Therefore, it may be valuable to identify outcome measures that are less influenced by differences in case-mix and represent the actual differences in quality of care processes.

Colorectal cancer is a significant source of mortality with nearly 10,000 new cases diagnosed in the Netherlands each year.[7] The cornerstone of this treatment is surgical resection. Patients undergoing surgical resection have a considerable risk for postoperative complications, which can lead to significant morbidity, mortality and large costs. Internationally, several quality improvement programs have therefore been initiated to reduce postoperative complications after colorectal surgery.

Anastomotic leakage is one of the most feared complications after colorectal surgery, often causing prolonged hospital stay, morbidity, mortality and possibly worse oncological outcomes.8 The percentage of patients developing anastomotic leakage depends on multiple factors. In literature, several elements have been identified as risk factors. These can be patient- or tumor-related, often referred to as case-mix, such as height of the anastomosis, a malnourished status, steroid use and male gender.[9-13] Treatment related factors such as surgeons' experience, operative duration, blood loss, preoperative radiation and a defunctioning stoma have also demonstrated to be associated with the occurrence of anastomotic leakage.[9-13]

The aim of this study was to explore whether hospital differences in anastomotic leakage rates are related to differences in case-mix. We compared the role of case-mix adjustment for anastomotic leakage and postoperative mortality. With this objective, the following research questions were drawn:

1. Which case-mix and treatment related risk factors are associated with anastomotic leakage and postoperative mortality after colorectal surgery?
2. What are differences in anastomotic leakage and mortality rates between hospitals and are these due to differences in case-mix or due to differences in treatment-patterns?

Methods

Patients

Data was derived from the Dutch Surgical Colorectal Audit (DSCA), a national quality improvement project in which over 200 variables concerning the patient, co-morbidity, diagnostics, disease-specific details, treatment, and outcomes are collected prospectively. The DSCA contains data of patients registered by 92 hospitals (all hospitals performing colorectal cancer surgery). The data set is disease-specific for colorectal cancer and shows a nearly 100% accordance on most items, including anastomotic leakage on validation against the National Cancer Registry (NKR) data set.[14]

All patients undergoing resection for primary colorectal cancer between the 1st of January 2009 and 31st of December 2011 and registered in the DSCA before March 15th 2012 were evaluated. Minimal data requirements for inclusion in analyses were information on tumor location, date of surgery and mortality. Patients with metastases at time of primary surgery and resections for multiple synchronous colorectal tumours were excluded, because these represent subgroups of patients with other treatment perspectives and subsequent different expected outcomes. Also, patients in which a primary end-colostomy was constructed were excluded form analysis.

Risk Factors

Since part of the dataset of the DSCA was designed with the objective of performing case-mix adjustment particularly for postoperative mortality, variables have been determined as risk factors for postoperative mortality in an early stage of conduction of the dataset. These factors were based on existing evidence on potential risk factors for mortality and determined by an expert panel using a Delphi method.6

To assess whether there are additional case-mix and treatment related risk factors that need to be taken into account when adjusting for anastomotic leakage, we performed a systematic search for literature published between 1990 and 2012 on biomedical bibliographical databases Pubmed and the Cochrane Library. The search headings "anastomotic leak and colorectal surgery" were used in combination with the keyword "risk factor". The "related articles" function was used to expand the search. References from the articles were also used when appropriate. Letters, reviews without original data, non-English language papers, overlapping patient populations and animal studies were excluded.

From the articles retrieved from the literature search, different risk factors for anastomotic leakage were selected. A distinction was made between patient and tumor related factors (case-mix factors) and treatment related factors. We selected risk factors with a statistical significance of $p < 0.05$, which were analyzed with multivariate logistic regression.

Outcomes

Various definitions of AL have been previously presented.15 The definition of anastomotic leakage in this study was 'a clinically relevant anastomotic leak requiring a re-intervention'. Both radiological and surgical re-interventions were included. Postoperative mortality was defined as 'death during postoperative hospital stay or within 30 days after the date of surgery'.

Analyses

The association of case-mix and treatment factors and both anastomotic leakage and mortality were tested with multivariate logistic regression models. Separate models were used for each outcome.

To analyze the differences in anastomotic leakage and mortality between hospitals and investigate whether these were due to differences in case-mix or due to differences in treatment-patterns we applied 3 different models. model 1: unadjusted (observed) variation in outcome; model 2: adjusted for patient (case-mix) characteristics; model 3: 'adjusted' for case-mix and treatment characteristics. Adjustment was performed by calculating expected outcomes (E) using case-mix (model 2) and both case-mix and treatment (model 3) coefficients from the regression analysis. Next, for each hospital, the observed percentage (O) was divided by the expected value (E) and multiplied by the overall mean (observed/E * mean) to obtain the adjusted percentages.

Hospital differences in anastomotic leakage and mortality rates before and after adjustment were plotted in a graph; a summary measure of the between hospital variance was given with ranges and standard deviations. The reduction in between center variance after adjustment for (model 2) case-mix and (model 3)case-mix and treatment factors was analyzed with a Levene's test for equality of variances. A p-value <0,05 was considered statistically significant.

Furthermore, a mixed logistic regression model with hospitals as random effects was performed A likelihood ratio test was used to test whether the variance of the random effects was statistically significant after adjustment for case-mix and treatment factors.
Hospitals with more than 15% missing case-mix factors were excluded from multivariate analyses. All statistical analyses were performed in PASW Statistics, Rel. 18.0.2009. Chicago: SPSS and R version 2.14.16

Results

On March 15th 2012, 92 hospitals (8 university, 47 teaching and 37 non-teaching hospitals) registered a total of 25,555 eligible primary colorectal cancer patients with a date of surgery between January 1st 2009 and December 31 2011 in the DSCA. Nine hospitals had more than 15% missing case-mix factors in total, and were therefore excluded (n=1,460). After additional exclusion of patients with multiple synchronous tumors (n=598), distant metastases (n=2,032) and without an anastomosis (n=5,480), a total of 15,236 patients were included in the analysis. Characteristics of the included patients are shown in Table 1.

Of all patients, 1207 patients (8%) developed anastomotic leakage and 525 patients (3.4%) died within 30 days or during hospital admission.

Risk factors

The literature search gave a total of 39 studies describing risk factors for anastomotic leakage.8, 10-13, 17-49 In total, 22 case-mix factors and 11 treatment related factors for were identified. Table 1 shows the results.

Case-mix factors described most frequently were gender, American Society of Anesthesiologists (ASA) score and location of the tumor and/or anastomosis. Treatment factors often described were blood loss/transfusion, duration of the operation and the use of a defunctioning stoma.

Of the 22 case-mix factors for anastomotic leakage identified in literature, 17 were available in the DSCA. The database had no information on the factors weight loss, nutrition status, alcohol abuse, smoking and leukocytosis. Treatment factors were less often available; 4 out of 11 were available in the dataset.

The case-mix and treatment related risk factors that were found for anastomotic leakage in literature were similar to those that have been used for risk adjustment for postoperative mortality in the DSCA dataset.

A multivariate analysis has been performed to investigate the association of case-mix and treatment factors with anastomotic leakage and postoperative mortality; results of the analysis are shown in *table 2*.

Individual case-mix factors predicting anastomotic leakage were male gender, urgency of the resection, renal disease and tumor location. Treatment related factors associated with anastomotic leakage were short preoperative radiotherapy, the absence of a defunctioning stoma and postoperative blood transfusion. For postoperative mortality the case-mix factors age, gender, ASA score, pulmonary disease, tumor location sigmoid, urgency of the resection were individual predicting factors. Treatment related factors were chemo-radiotherapy and blood transfusion.

Hospital variation

Anastomotic leakage

Unadjusted hospital variation in anastomotic leakage rates was large: the hospital with the lowest percentage had an anastomotic leakage rate of 0% (n=0/166); the hospital with the highest percentage had an anastomotic leakage rate of 18% (n=12/70) (SD 0.036,, *Figure 1a*). After adjustment for case-mix, there was still a large variation between hospitals: the adjusted anastomotic leakage rates per hospital ranged from 0 to 17% (SD 0.033). The reduction in variation after adjustment for case-mix was not statistically significant (p=0.52).

The variance in anastomotic leakage rates significantly decreased after including treatment factors in the adjustment model (p<0.01). Case-mix and treatment adjusted anastomotic leakage rates varied from 0 to 12% (SD 0.024).

For 60% of the hospitals (50/83), the unadjusted anastomotic leakage rate was similar to the case-mix adjusted anastomotic leakage rate. In 36% of the hospitals, anastomotic leakage rates slightly in-or decreased with 1%, and in 4% of the hospitals with 2% (*Figure 2a*).
For 75% of the hospitals (63/83), unadjusted anastomotic leakage rate altered after adjustment for treatment factors with at least 1%; for 32% of the hospitals, the unadjusted rate altered with more than 3% and for 10% with more than 5%.

Although hospital variance decreased after adjustment for case-mix and treatment factors, there was still variability between hospitals as a likelihood ratio test showed that the variance of the random effects was statistically significant in all models.

Postoperative mortality

Hospitals' unadjusted mortality rates ranges from 0 to 10% (SD 0.017). The variance in postoperative mortality significantly decreased after case-mix adjustment (p<0.01) (range 0-6%, SD 0.012, Figure 1b).
The variance in postoperative mortality rates slightly increased (range 0-6%, SD 0.013) after including treatment factors in the adjustment model, although not statistically significant (p=0.81).

For 84% of the hospitals (70/83), the unadjusted postoperative mortality rate altered after adjustment for treatment factors with at least 1%; for 24% of the hospitals, the unadjusted rate altered with more than 3% and for 6% with more than 5% (*Figure 2b*).
Adjustment for treatment factors had a slight effect on two hospitals when compared to the case-mix adjusted mortality rate. In these hospitals, case-mix adjusted mortality rate altered with 1% after adjustment for treatment factors.
Hospital variability in postoperative mortality was still significant after adjustment for case-mix and treatment factors, as a likelihood ratio test showed that the variance of the random effects was statistically significant in all models.

Discussion

The present study suggests that 'anastomotic leakage rate' is an outcome indicator for measurement of surgical quality of care that is relatively independent of differences in case-mix between hospitals. We found a large variation in anastomotic leakage rates between Dutch hospitals, which confirm the ability of this outcome indicator to be discriminative. In contrast to 'postoperative mortality' the observed anastomotic leakage rates of hospitals evaluated in our study could not be explained by differences in case-mix. In addition, we found that the influence of treatment factors on the variation in anastomotic leakage rates was substantial. These findings imply that anastomotic leakage rates may be much more related to treatment factors and in hospital care processes, than to characteristics of the patient population treated in a certain hospital. Anastomotic leakage rates may therefore be a good reflection of the quality of care provided.

Outcome measures

Optimizing surgical outcomes can be seen as 'the bottom line' of what surgeons do, and outcome indicators have the advantage that they have 'face validity' for surgeons as well as there patients. Also, measurement in itself may improve surgical outcomes – as suggested by the so-called Hawthorne effect. 4 As shown in our study, outcome indicators can present meaningful differences between hospitals. However, there was still significant variability in both anastomotic leakage and mortality rates, after adjustment for case mix factors and treatment factors in our study. This suggests that there are other characteristics of the hospital, its staff and the care they deliver, that may explain the observed differences. Although outcomes of care are important, process and structure information is essential to identify which area is susceptible for innovation. Therefore, adopting to the Donabedian paradigm50, a balanced indicator set needs to include information on structures, processes and outcomes.

Limitations

The results presented in this study should be interpreted in the light of some important limitations. First, despite the fact that most patient-related risk factors were available in the database of the DSCA, it lacked data on some important host-related factors, such as smoking, alcohol consumption, nutrition status and preoperative leukocytosis. Although unlikely, it is possible that a strong case-mix adjustment model for AL could have been made when exactly those four missing factors would have been available from the data set. Also, high risk patients according to the surgeons' preoperative risk judgment or patients with impaired continence at baseline may not have been selected for a primary anastomosis, and therefore excluded which may have caused a potential selection bias. It is not exactly clear how these differences in patient selection might affect the between hospital comparisons. Moreover, due to a lack of clear agreements on definitions, the factors we used may not have been identical to the ones we found in literature.

Although we found that case-mix adjustment does not seem to play a large role when comparing hospitals' anastomotic leakage rates, there are some limitations of using it as an outcome indicator that deserve mentioning. It may unintentionally lead to the perverse incentive of aiming for the lowest possible anastomotic leakage rate by constructing more end-colostomies or defunctioning stomas. This defensive attitude would not immediately contribute to a higher quality of care, as a surgeon or clinic that has zero AL rates at the cost of constructing defunctioning stomas or end-colostomies in all patients will not be regarded as the best practice. Obviously, anastomotic leakage rates are only calculated over patients in whom an anastomosis has been created. Therefore hospitals, with lower rates of patients with anastomoses could automatically have better scores, without immediately better quality of care, as the stoma itself may cause morbidity, lead to a higher need for readmissions[51, 52] and may be associated with morbidity at the time of surgical removal of the stoma.[53] In reality, there is probably an optimum percentage of defunctioning stoma's and end-colostomies to be created, and AL rates should always be seen in the light of these percentages. However, the exact optimum is unclear and it may vary between different surgeons or clinics. Auditing programs like the DSCA may help to clarify in what range this optimum should be. A composite quality measure might be a solution, that is a metric which includes whether or not AL occurred, creation of a defunctioning stoma or end-colostomy, readmissions or mortality. Patient reported outcomes are of additive value in this context. The choice between an anastomosis with or without a defunctioning stoma or an end-colostomy can and should always be influenced by patient preferences.

Improvement of outcomes

When anastomotic leakage is used in hospital comparisons, it should be under the condition that practices with higher anastomotic leakage rates have the opportunity to improve their performance. Unfortunately, the actual cascade of factors resulting in anastomotic leakage still remains a 'black box'. Our findings suggest that this black box consists of factors that represent multiple elements of the care processes taking place within a hospital. Per-operative factors, such as blood loss and duration of the operation have been described as important predictors for AL by several authors.[9-13] Longer duration, more blood loss than anticipated, an increased anastomotic strain and limited vascular supply at the anastomotic sites may be a proxy of a more complicated procedure, suggesting that anastomotic leakage rates might be related to surgical technical skill and experience. Additionally, factors more related to perioperative care than to surgical skill, such as oliguria during the operation, are are also said to enhance the risk for leakage.[54]

The ultimate challenge for outcome researchers is to understand the complex clinical mechanisms that lead to success or failure, so that the excellence of best practices can be transferred to all hospitals performing these procedures.

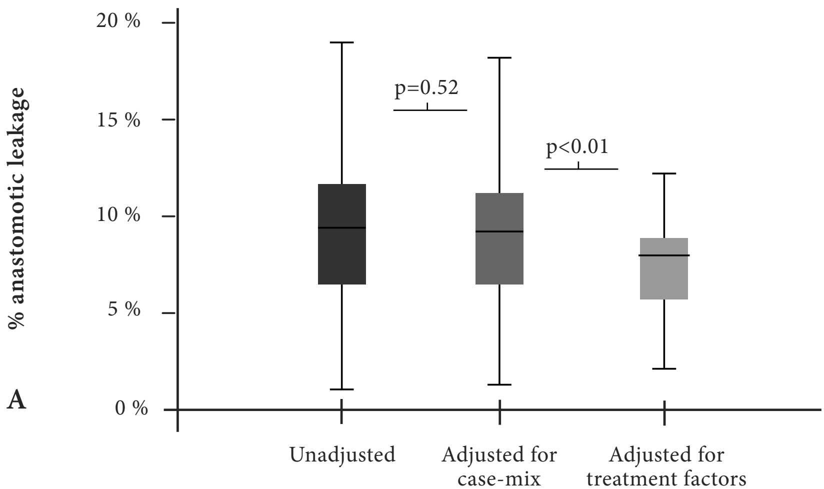
Definition of AL

Comparison of AL between hospitals also requires the use of standard definitions and methods of measurement of AL. It has however been stated before that the definition of AL varies; a systematic review done by Bruce et al found 56 separate definitions for AL used in literature.[15] A valuable feature of an audit registration system is that it applies one definition that is used by all participants. In the DSCA; only clinical apparent leaks requiring re-intervention have been registered, and a distinction has been made between radiological and surgical re-intervention. Further (international) agreement on a standard definition that is valid and reliable, and can distinguish between clinical minor and major anastomotic leaks are explicitly important when using anastomotic leakage as an outcome indicator.

Conclusion

Hospital variation in anastomotic leakage rates is relatively independent of differences in case-mix. Differences in treatment factors contributed more to the variation of anastomotic leakage rates. Further exploration of in-hospital factors may give insight in further improvement possibilities and understanding the multifactorial process that underlies anastomotic leakage. Audit programs may provide data for targeted visitation of clinics with bad outcomes, as well as best practices, aiding in identification of the most important areas for improvement.

Figure 1. Boxplots presenting the range in hospitals' anastomotic leakage rates (A) and mortality rates (B). The unadjusted range (left), the range after adjustment for case-mix (centre), and the range after adjustment for case-mix and treatment factors (right) are shown. p Values describe the statistical significance of the reduction in variance (Levene's test); a p value <0.05 was considered statistically significant.



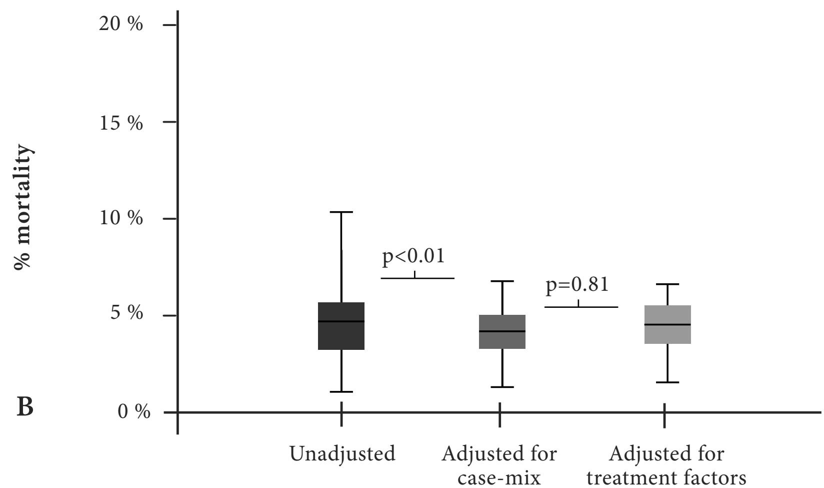
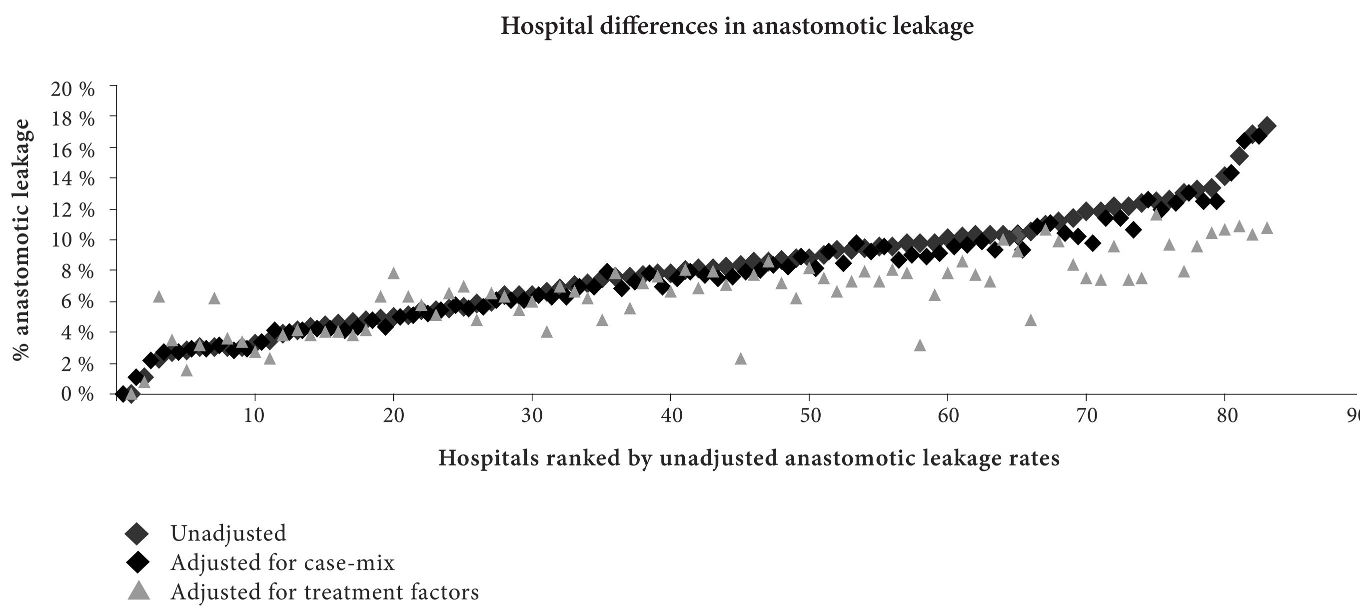


Figure 2a & 2b. Scatterplots showing the effect of adjustment for case-mix (model 2) and case-mix and treatment factors (model 3) for anastomotic leakage (A) and mortality (B) on an individual hospital level. Each scatter represents a single hospital's unadjusted, case-mix adjusted, and case-mix and treatment adjusted rate. On the x-axis, hospitals are ranked according to their unadjusted anastomotic leakage or mortality rate.



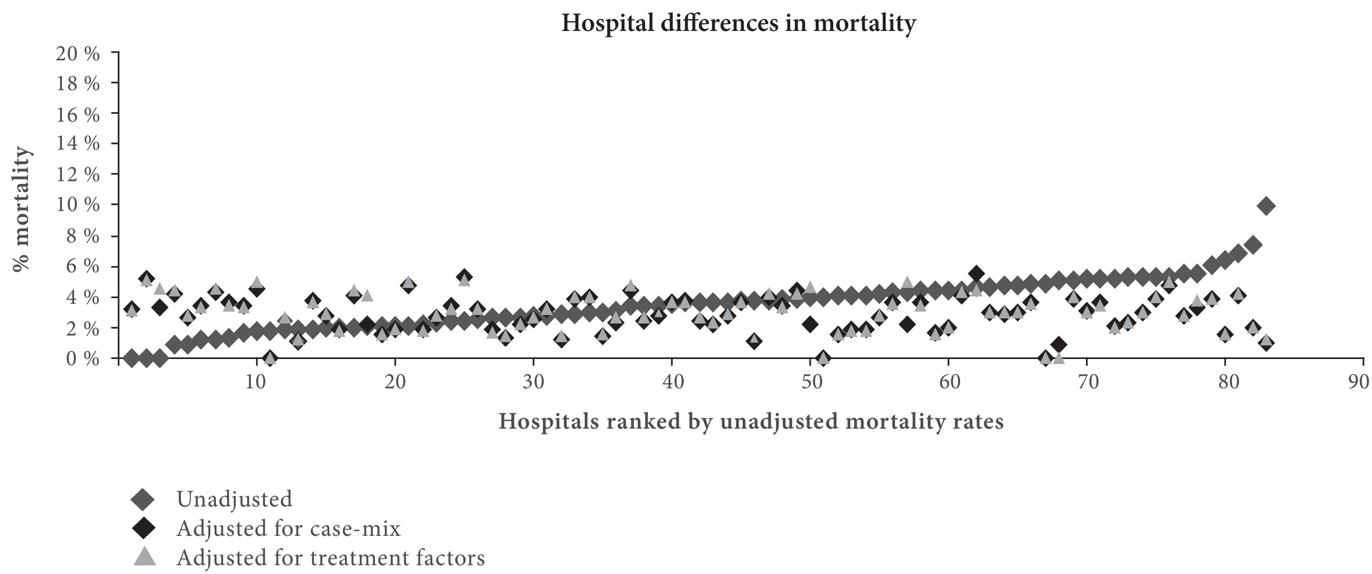

Hospital differences in mortality
% mortality
20 %
18 %
16 %
14 %
12 %
10 %
8 %
6 %
4 %
2 %
0 %
10
20
30
40
50
60
70
80
90
Hospitals ranked by unadjusted mortality rates
Unadjusted
Adjusted for case-mix
Adjusted for treatment factors

Table 1. Risk factors for AL described in literature and available patient and treatment characteristics of included patients in the DSCA.

FACTOR		***DSCA (n=15.236)*** ***N***	***%***
CASE-MIX FACTORS			
Age	>75	5464	38%
Gender	Male	8034	53%
ASA score	3+	3268	21%
BMI	<25	4048	27%
	25-30	4327	28%
	>30	1964	13%
	Unknown	4897	32%
2 or more comorbidities	Yes	6456	42%
Cardiovascular disease	Yes	6408	42%
Pulmonary disease	Yes	1858	12%
Diabetes	Yes	2186	14%
Crohn's disease	Yes	107	1%
Preoperative anemia	Yes	846	6%
Renal failure	Yes	461	3%
Steroid treatment	Yes	1174	8%
Previous abdominal surgery	Yes	5037	33%
Weight loss	N.a.		
Hypoproteinemia/nutritial status	N.a.		
Alcohol abusis	N.a.		
Smoking	N.a.		
Leukocytosis	N.a.		
Tumor stage	Stage 0/I	1156	8%
	Stage II	3068	20%
	Stage III	8940	59%
	Stage IV	1588	10%
Additional resection	Locally	1126	7%
Tumor location	Right-sided	5966	12%
	Transverse/descending	2003	39%
	Sigmoid	4468	13%
	Rectum	2799	29%
Urgent resection	Acute	1799	12%

Literature (n=39) ***Author***
Hun Yung et al (2006)
Van ‘t Sant (2010); Bertelsen (2010); Peng (2010); Lee (2008); Jestin (2008); Hun Yung (2006); Lipska (2006); Yuh Yeh (2005); Rudinskaite (2005); Peeters (2005); Law (2004); Mathiessen (2003); Poon (1999); Rulier (1998).
Van ‘t Sant (2010); Wang (2010); Eberl (2008); Bucher (2007); Jestin (2008); Choi (2006); Makela (2003); Alves (2002); Tang (2001)
Kim (2009); Biondo (2005); Makela (2003);
Iancu (2008); Makela (2003)
Iancu (2008); kruschewski (2007); Makela (2003); Tang (2001)
Akasu (2009); Iancu (2008); Makela (2003)
Iancu (2008); kruschewski (2007); Benoist (2000); Vignali (1997)
Lipska (2006)
Iancu (2008);
Alves (2002)
Konoshi (2006); Alves (2002)
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Iancu (2008); Makela (2003)
Iancu (2008); Makela (2003)
Nickelsen (2005); Makela (2003)
Bertelsen (2010); Iancu (2008); Kruschewksi (2007)
Iancu (2008); Alves (2002)
Eberl (2008)
Yuh Yeh (2005)
Bertelsen (2010); Peng (2010); Cong (2009); Kim (2009); Lee (2008); Eberl (2008); Bucher (2008); Jestin (2008); Hun Yung (2006); Lipska (2006); Yuh Yeh (2005); Rudinskaite (2005); Law (2004); Matthiessen (2003); Marush (2002); Rulier (1998); Vignali (1997)
Choi (2006)

FACTOR		DSCA (n=15.236) N	%
TREATMENT FACTORS			
Neoadjuvant therapy	5x5 GY Chemoradiation	1508 830	18% 10%
Defunctioning stoma	Yes	2467	16%
Blood loss/transfusion	Yes	2042	13%
Intra-operative contamination	N.a.		
Intra-operative adverse events	N.a.		
Pelvic drain	N.a.		
Incomplete donut	N.a.		
Stapling device	N.a.		
Duration of operation	N.a.		
Specialization surgeon	N.a.		
After-hours' surgery	N.a.		

ASA= American Society of Anesthesiologists score. BMI= Body Mass Index.

Literature (n=39) ***Author***
Eriksen (2005); Alves (2002);
Matthiessen (2007); Rullier (1998); Peeters (2005); Pakkastie (1997); Cong (2009)
Alves (2002); Sorensen (1999); Law (2004); Yuh Yeh (2005); Nesbakken (2002); Tang (2001); Akasu (2009); Boccola (2009); Telem (2010);
Alves (2002); Makela (2003); Konishi (2006)
Matthiessen (2003)
Peeters (2005); Tang (2001); Yuh Yeh (2005); Boccola (2010); Cong (2009)
Makela (2003); Schmidt (2003)
Boccola (2010)
Vignali (1997); Marusch (2002); Alves (2002);Konishi (2006); Bucher (2007); Choi (2010); Telem (2010)
Cong (2009)
Komen (2009)

ASA= American Society of Anesthesiologists score. BMI= Body Mass Index.

Table 2. Case-mix and treatment factors included in the multivariate logistic regression model for AL and mortality after colon and rectal carcinoma resections. Age and BMI were analyzed as continuous variables.

		AL			Mortality		
		OR	95% C.I.		OR	95% C.I.	
CASE-MIX FACTORS							
Age		0.99	0.98	1.02	2.65	2.33	3.04
Gender	male	1.31	1.11	1.55	1.82	1.39	2.37
ASA	2	1.01	.84	1.22	3.09	1.54	6.17
	3+	1.00	.80	1.24	6.44	3.46	13.12
BMI		.91	.74	1.13	.99	.97	1.02
2 or more comorbidities		.88	.70	1.10	1.17	.82	1.67
Cardiovascular disease		.85	.70	1.04	1.21	.90	1.62
Pulmonary disease		.92	.71	1.20	1.44	1.06	1.97
Diabetes		.99	.77	1.28	1.12	.81	1.55
Crohn's disease		1.06	.43	2.60	1.35	.36	4.98
Preoperative blood loss		.72	.42	1.25	.68	.23	2.00
Steriod treatment		1.27	.81	2.00	1.25	.72	2.15
Renal disease		1.34	1.01	1.78	.91	.62	1.34
Abdominal surgical history		1.03	.87	1.22	.87	.67	1.14
T-stage	T3	1.03	.87	1.21	1.05	.81	1.36
	T4	1.13	.78	1.64	1.22	.71	2.10
Additional resection		1.20	.88	1.64	.96	.59	1.55
Urgent resection		1.32	1.01	1.73	2.18	1.60	2.98
Tumor location	Transverse colon	1.93	1.49	2.50	1.25	.89	1.76
	Sigmoid	1.68	1.33	2.11	.70	.50	1.00
	Rectum	2.22	1.49	3.29	1.04	.52	2.04
TREATMENT FACTORS							
Neo-adjuvant therapy	5x5	1.70	1.13	2.54	.88	.42	1.85
	Chemoradiotherapy	1.33	.84	2.09	.30	.09	.98
Defunctioning Stoma		.54	.42	.70	1.15	.69	1.89
Transfusion		4.27	3.56	5.12	4.06	3.14	5.25

AL= anastomotic leakage; CI= confidence interval; OR= odds ratio; ASA= American Society of Anesthesiologists score; BMI = Body Mass Index. Bold printed numbers are significant odds ratios ($p < 0.05$).

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PART IV:
DISCUSSION AND APPENDICES

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

General discussion and future perspectives

The health care industry is undergoing tremendous transformations. The extent of needed care is rapidly growing due to the aging of the population, and to an increase in patients with chronic diseases and multi-morbidity. As a consequence of rising health costs, health care insurers request a greater effectiveness and efficiency in health care organization. Methods are being sought to ensure sustainability of health systems, to promote quality improvement and to shorten waiting times. Subsequently, the Ministry of Health and the Health Inspectorate place high demands on quality and safety of care provided. They request an increased transparency of quality of healthcare, with the ultimate goal to improve patient outcomes. Simultaneously, patients are becoming more and more empowered and knowledgeable. Internationally, initiatives have been taken to extend patients' ability to choose their health care provider, to encourage them to make an active choice in treatment decisions, and to support them in the process of making these choices.[1-4]
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These ongoing developments inevitably affect daily surgical practice. Surgeons are increasingly accountable for their postoperative complication rates, since quality of care has become a major topic. Quality enhancement programs, like nation-wide clinical audits, have been initiated internationally. The clinical audit contains information of different phases of treatment, such as diagnostics, treatment and outcomes. Auditing has shown to provide meaningful information to healthcare providers, who can actually for improve their quality of care with the feedback on their performance compared to other hospitals. Frequent feedback of this information can diminish the risks for postoperative complications, and subsequently reduce significant morbidity, mortality and costs.[5-7]
Simultaneously, from various angles there has been an increased demand for valid and reliable information on performance and outcomes of

care. The public reporting of outcomes may however influence surgical decision-making, since it may lead to a more risk-averse treatment strategy - with the objective to lower postoperative complication rates. Also, surgeons need reliable and accurate information on the risks and benefits of surgical treatment options to inform their patients and involve them in the treatment decision.

Colorectal cancer surgery is considered high-risk, since it brings along a relatively high number of postoperative complications. Choosing the ideal surgical treatment consists of a trade-off between benefits and risks of different surgical treatment options, which subsequently calls for preoperative information provision and the incorporation of patient preferences. Further, its high-risk nature has led to being the focus of several quality improvement initiatives, including the Dutch Surgical Colorectal Audit in the Netherlands. Therefore, colorectal cancer surgery is an exemplary setting to investigate postoperative risks, clinical decision-making and clinical auditing.

Risks and Benefits

The results in this thesis, together with existing evidence, emphasize that both doctors and patients should be aware that the surgical options for colorectal cancer have different risks and benefits to consider.
It is commonly known that creating an anastomosis bears the risk of anastomotic leakage, a serious complication contributing to one third of all postoperative deaths after rectal cancer surgery (*chapter 1*). Obviously, patients with an end-colostomy have no risk of anastomotic leakage. Although these patients run risks of stoma problems, or abscess complications (*chapter 2*), these may be less consequential than immediate postoperative anastomotic leakage. An end-colostomy may therefore be a safe short-term solution, specifically in frail patients.

A defunctioning stoma seems beneficial, since earlier randomized studies have proven that a defunctioning stoma diminishes the clinical consequences of anastomotic leakage [8-10], but there are drawbacks that argue against its use. First, a residual risk of clinically relevant anastomotic leakage of 7% in these patients should not be ignored (*chapter 2*). Furthermore, a defunctioning stoma reduces the consequences of short-term generalized anastomotic leakage, but does not protect from the risk for late anastomotic leakage (*chapter 2*); if anastomotic leakage is present for more than one year, secondary complications may occur including fistula formation, peri-ureteric fibrosis and infection of adjacent tissues.[11,12] Moreover, a second surgery in which bowel continuity is restored causes an additional risk of complications including anastomotic leakage (*chapter 2*), which is confirmed by findings in previous research.[13,14] As ongoing changes in outcome occur during the first year after surgery, it is essential to include long-term complications in the initial decision making process.

Informing and involving the patient

The outcomes of the different treatment of reconstructive options in colorectal cancer surgery mentioned previously may vary in their impact on a patient's physical and psychological well being. Therefore, involving a patient in the decision seems essential, since preferences towards the different options may also vary between patients. Involving a patient, or performing Shared Decision Making (SDM), starts with thorough preoperative information provision on all relevant options, their consequent benefits and risks.[15] Although informing a patient preoperatively seems self-evident in the decision making process for colorectal cancer surgery, at present, patients are sub optimally informed about risks and alternative treatment options (*chapter 3*). Previous studies have also underlined the need for improvement of the process of informed consent in other domains of care.[16,16,17]

Benefit

Providing risk information has additional valuable consequences; it encourages patients to be more aware of the limits of medical treatment in general; it enables the doctor to educate the patient or to discourage possible medical consumerism, and it may be easier for a doctor to maintain a constructive relationship with the patient in case a complication arises. Patients generally seem to appreciate to be informed on the risks of interventions.18 In two studies, the majority of patients expected to be informed of all known complications, even if the rates were smaller than 1%.[19,20,20]

Improving patient information

An often raised argument for withholding information on surgical risks, is doctors' perception that patients do not understand the concept of risks, and have a poor memory of the disclosed information.21 Possibly, the great number of issues to be addressed in colorectal cancer surgery acts as a complicating factor. In today's multi-disciplinary, rapid-throughput ambulatory care, in which patients may not even meet their operating surgeon until the day of the operation, such detailed information with comprehensive discussion of risks may be difficult to realize. A systematic review by Schenker et al. found a wide range of communication interventions that improve patient comprehension in informed consent, such as written information, audio-visual/multimedia programs, patient navigation by a nurse practitioner, extended discussions, and test/feedback techniques.[22] These methods serve to empower a patient before a consultation with the surgeon in which the information can subsequently be individualized to that patient. Then, the surgeon can explore the patient's preferences and tailor the final decision to what fits the patient best, which forms the basis of SDM.[15]

Improving SDM

Although in our survey Dutch surgeons underlined the necessity of SDM in the decision on surgical treatment for colorectal cancer, an absence was seen in clinical practice (*chapter 3*). An important reported barrier towards using SDM concerns surgeons' lack of familiarity with the concept (*chapter 3*), which confirms prior research in other domains.[23-26] SDM is considered especially important for patients who present with a serious illness, such as colorectal cancer, or when different treatment options are available.[3] Not only is it essential for respecting autonomy (enabling individuals to make reasoned informed choices), but it is also needed for beneficence (the balancing of benefits of treatment against the risks and costs) and non-maleficence (avoiding harm).[27] Moreover, evidence suggests that patients tend to make more conservative decisions than their doctors, thus SDM may also reduce unwarranted hospital variation in treatment patterns.[28] Finally, it has been suggested that SDM may lead to better health outcomes and lower litigation rates, although this evidence remains limited.[29] Dutch gastroenterological surgeons need to be made aware of the fact that patients with colorectal cancer are currently not informed nor involved appropriately. As stated by Stiggelbout et al, and expressed in the Salzburg Statement, the implementation of SDM in (surgical) practice will need a culture change and enhanced awareness among doctors, their professional societies, and patients.[27,30]

Patient selection

The fact that nowadays 70% of patients undergoing low anterior resection for rectal cancer receive a defunctioning stoma, suggests routine use in current surgical practice. As stomas also cause morbidity and discomfort to patients, and are very costly in the long run, frequent use is only justifiable when it in fact lowers anastomotic leakage rates. The previously described protective effect of a defunctioning stoma on the risk of anastomotic leakage could be confirmed in this thesis (*chapter 2, chapter 4*). However, this effect may be most apparent in high-risk patients, while there is a limited effect in low-risk patients. The beneficial effect of a defunctioning stoma was proven in a randomized controlled trial from Matthiessen et al. However, they studied a cohort with a risk of anastomotic leakage of 28%, which is high when compared to an average risk of anastomotic leakage of 9% found in literature (*chapter 1*). In these high-risk patients, a defunctioning stoma had a Number Needed to Treat of 5.5. In low-risk patients however, the NNT may increase to 55. The fact that last decade's increase in defunctioning stomas from 57 to 70% did not lower anastomotic leakage rates (*chapter 5*) even further suggests that the effect is most apparent in high-risk patients only.

Whom to select?

Adequate patient selection may therefore be the key towards better outcomes. Several attempts to identify possible risk factors for anastomotic leakage have been published in recent years (*chapter 8*). However, studies found that surgeons lack accurate prediction of anastomotic leakage in a single patient.[31,32] The clinical judgment of the operating surgeon (denominated as 'gut feeling') seems to localize a subset of patients at risk of developing complications in general, whereas many patients with no risk factors at all may develop anastomotic leakage. Apparently, the actual cascade leading to anastomotic leakage remains a black box.

Although patient-related risk factors such as height of the anastomosis, a malnourished status, steroid use and male gender have often been described as important risk factors in literature, hospital differences in anastomotic leakage rates could not be explained by

these factors (*chapter 8*). We found that the influence of treatment factors on the variation in anastomotic leakage rates was substantial. These findings imply that anastomotic leakage rates may be much more related to treatment factors and in hospital care processes, than to characteristics of the patient population treated in a certain hospital. An important note is that the database lacked data on some important host-related factors, such as smoking, alcohol consumption, nutrition status and preoperative leukocytosis.
Previous studies have also found an association of hospital- or surgeon-related factors with the occurrence of anastomotic leakage: several authors have described per-operative factors, such as blood loss and duration of the operation as important predictors for anastomotic leakage. [33-37] Longer duration and more blood loss than anticipated may be a proxy of a more difficult procedure, suggesting that anastomotic leakage rates might be related to surgical technical skills. Also, an increased strain and limited vascular supply at the anastomotic sites have been considered to contribute to the pathophysiology of leakage33. This, again, would be more related to technical aspects than patient-factors. The ultimate challenge for outcome researchers is to understand the complex clinical mechanisms that lead to success or failure, so that the excellence of best practices can be transferred to all hospitals performing these procedures.

Hospital variation

The lack of clear guidelines on 'whom to select' for an anastomosis with or without defunctioning stoma may partly explain the variation we found in this thesis in the use of defunctioning stomas between hospitals in the Netherlands (*chapter 5, chapter 6*). Another possible explanation may be found in differences in the threshold to construct a defunctioning stoma (to avoid the risk of anastomotic leakage) between surgeons. Some surgeons may be 'cowboys', others 'chickens'.

Interestingly, neither at a hospital level nor at a national level, correlation exists between a risk averse strategy (high stoma rate) and favourable outcomes (*chapter 6*).

Feedback of information on stoma and anastomotic leakage rates, relative to those of peers (benchmarking), provides clinicians an insight in the efficiency of their current treatment strategy. Sharing knowledge between clinicians on the optimal selection strategy, which probably can be found in hospitals with both low stoma rates and favourable postoperative outcomes, should be promoted.

Clinical auditing

The Dutch Surgical Colorectal Audit has proven to be a robust system to measure, report and enhance quality of colorectal cancer surgery in the Netherlands. It has led to a remarkable reduction of hospital variation in guideline adherence within a time period of three years only (*chapter 7*). In addition, significant improvements in outcome were shown, with a more than 20 per cent drop in the risk of postoperative mortality and a 14 per cent reduction in the risk of severe postoperative morbidity (*chapter 7*).

In the USA, a similar reduction in surgical morbidity and mortality was seen in the Veteran Affairs hospitals, after introduction of the National Surgical Quality Improvement Program (NSQIP).[38] In Norway, local recurrence rates after rectal cancer surgery decreased from 28 to 7% after introduction of a national audit program.[39] A systematic review performed by our study group confirmed the positive effect of audit and feedback on the quality of surgical care. [40]

The surgical Hawthorne effect - measurement and feedback in itself may improve surgical outcomes – may underlie these trends towards improvement, as was also shown in a study from O'Connor et al, where postoperative mortality rates after CABG decreased directly after surgeons were provided with feedback.[41] It has also been stated that when feedback is accompanied with benchmark information and meaningful suggestions for improvement, the effect is even stronger.[42] In accordance with the format of the DSCA, the Dutch Institute of Clinical Auditing (DICA) was founded to enhance other clinical audit initiatives in the Netherlands. The main goal of the DICA is to support other clinical audits by facilitating legal, technical, methodological and logistic issues. Several new audits have been initiated since the introduction of the DSCA: the breast cancer audit (NBCA), the upper GI cancer audit (DUCA), the lung surgery audit (DLSA), the aneurysm audit (DSAA), the carotid audit (DACI), the pancreatic cancer audit (DPCA), the lung radiation audit (DLRA), the cerebrovascular audit (CVBA),the hepatobiliary audit (DHBA), the melanoma treatment audit (DMTR), the european pediadric surgical audit (EPSA), and the obesity treatment audit (DATO).

Outcome measures

Determining outcomes that measure and represent actual quality of care remains challenging. Each medical condition or population of patients will need their own specific set of outcome measures. Quality of care for procedures that are both common and relatively high-risk, as is the case with colorectal surgery, may be assessed using outcome measures such as anastomotic leakage or mortality. Postoperative mortality is the most often used outcome measure to benchmark surgical performance.[43-45]

Case-mix adjustment

When comparing mortality rates between hospitals, there is the necessity of case-mix adjustment, as some hospitals treat more severely ill patients than others. A study from Kolfschoten et al showed that case-mix significantly varies among hospitals in the Netherlands.11 To adjust for these differences in case-mix, the DSCA has included baseline characteristics in its dataset, such as age, ASA-classification, emergency surgery, and tumour stage (*chapter 8*). These 'case-mix factors' however add to registration burden, which at this moment may hinder a sustainable auditing process.

Therefore, future automated retrieval of data from electronic patient files, or structural data management support for health care professionals is essential. Identifying outcome measures that are influenced to a smaller extent by case-mix, and more by treatment and hospital related factors, may be useful (*chapter 8*). First, it will decrease the necessity of collecting data on case-mix factors and thereby lower registration burden. Second, instead of measuring variation due to chance or differences in case-mix, the outcome indicator discriminates hospitals based on their actual performance. Anastomotic leakage may be such an indicator.

Structure and process outcomes

After adjustment for case-mix and treatment factors, Dutch hospitals still vary in both anastomotic leakage and mortality rates, (*chapter 8*), which makes both outcome measures suitable for discrimination. This however also suggests that other unknown characteristics of the hospital, its staff and the care they deliver may contribute to the observed differences. Adopting the Donabedian paradigm50, a balanced indicator set needs to include information on structures, processes and outcomes. Process components refer to the interactions between the doctor and the patient, for example the delivery of adequate staging investigations to detect distant metastases. Structural factors describe the setting in which the care is delivered. These structural variables, for instance, availability of a high-level ICU, or on-site radiotherapy department, can be related to patient outcomes, especially by the influence they have on the process of care.

International developments

Outcome measures can indicate meaningful differences between hospitals nationally, which may help identifying relevant areas of improvement. The next step would be to standardize health outcomes data globally, so that internationally doctors can learn from another and apply new solutions to treating patients. The International Consortium for Health Outcomes Measurement (ICHOM) has recently launched standardized sets for different conditions with the purpose to transform health care systems worldwide by measuring and reporting patient outcomes in a standardized way.[46]

Composite measures

Although an individual outcome or process indicator may give useful information for targeted quality improvement programs, a hospital may have a high score on one indicator, but a low score on another indicator. For example, a surgeon or clinic that has zero anastomotic leakage rates at the cost of constructing defunctioning stomas or end-colostomies in all patients will not be regarded as the best practice. In reality, there is probably an optimum percentage of defunctioning stoma's and end-colostomies to be created, and leakage rates should always be seen in the light of these percentages.

More comprehensive measures including both processes and outcomes, or the use of composite measures are needed for true assessment of hospital performance. Several studies have investigated the relation between process and outcome measures to determine whether a good score on composite process measures is associated with favourable short-term outcomes, however with inconsistent results.[47,48] Kolfschoten et al. investigated the validity of a composite measure, combining process and outcome measures using the database of the Dutch Surgical Colorectal Audit.[49] They found that a hospital's good score on the composite measures based on process indicators was correlated with more favourable risk-adjusted short-term outcomes. Additional studies with empirical testing of different composite measures to better understand their ability to discriminate quality of care are warranted.

Patient reported outcomes

The choice between an anastomosis with or without a defunctioning stoma or an end-colostomy can and should always be influenced by patient preferences. Therefore, patient reported outcomes measures (PROMs) are of additive value in this context. PROMs may provide a means of gaining an insight into the way patients perceive their health and the impact that treatments or adjustments to lifestyle have on their quality of life.

Although PROM-research has proved to be highly wanted for current modern research on clinical outcomes[50], it is important that this be performed in a standardized manner and based on valid, reliable and clinically useful measures.51Moreover, methods of communicating patient-reported outcomes to patients should be investigated, in order to increase their clinical use for the benefit of both doctors and patients.[52] Also, response rates are an issue. Systems to increase patient participation in the evaluation of their health care process should be developed, such as web based patient logs or compensating on insurance fees.

Cancer patient organizations in the Netherlands have already committed themselves to collaborate in integrating PROMS in the clinical audits in the near future. A transparent view on true value of hospitals in the Netherlands however calls for an even more integrated approach, as Porter et al. defined value in health care as outcomes relative to costs.[53] The next step would be to guarantee availability of medical and patient reported outcomes, so that these can be weighed against cost.

Audits for patient choice

While the main aim of audit systems is to encourage doctors to improve the quality of care they provide, the comprehensive set of information can be well used to promote patients' involvement in choosing their hospital or provider, and in deciding on their course of treatment.
In the Netherlands, implementation of two acts on regulated competition in 2006 assigned the responsibility to well-informed patients to 'vote with their feet' by selecting the healthcare providers they preferred.[54,55] Ideally, patients can use the comparative information available in the audit, to choosing only those healthcare providers that offer 'best' care. Unfortunately there still is a scarcity of public available meaningful information, even though performance indicators introduced by the Healthcare Inspectorate and Zichtbare Zorg Ziekenhuizen are publicly reported since 2003. 56 Steps towards true transparency of reliable audit data have however been taken. The Association of Surgeons of the Netherlands (ASN) has introduced a roadmap towards transparency in 2011, starting with public reporting of process indicators, followed by hospital specific outcome measures such as (case-mix adjusted) morbidity and mortality rates. An important condition for external transparency is the validity and reliability of the data in the audit, which is insured by the consistent quality checks on the registered data in the online system of the audits and the annual external validation with the National Cancer Registry (*chapter 8*).

Audit data can also be used to enhance patient involvement in treatment decisions. Providers can use the information to inform patients of their risks of medical and surgical complications. Since the dataset contains 200 variables concerning the patient, co-morbidity, diagnostics, disease-specific details, treatment, and outcomes (*chapter 7*), the data might be used to calculate an individual patient's risk of outcomes, and subsequently help patients to make informed choices and their treatment.[57] Such risk prediction models have been developed to predict the outcomes of treatment in other domains of care using specific clinical parameters.[58] A well-known model is 'Adjuvant! Online' for patients with early breast cancer, which predicts survival after surgery with and without adjuvant therapy.[59,60] The program gives the estimated prognosis and expected treatment benefit in a comprehensive format and can help to inform patients and to involve them in decision making about therapeutic options.[61] Similarly, patients undergoing surgery for colorectal cancer can be supported in the decision concerning stoma or anastomosis construction, by estimating their risks of unfavorable outcomes. The possibility of developing such a tool, by using the rich and detailed information from the DSCA, should be investigated. Furthermore, although these prediction models are increasingly used in the clinical consultation for breast cancer patients, little is known about the frequency and way in which risks are communicated in the consultation. Future studies should focus on the understanding of patients of such risk communication and the effect of its use on decision making and treatment choice.[62]

Conclusions

The findings in this thesis may form the basis for some important statements on decision-making and quality improvement in colorectal cancer surgery. First, Dutch surgeons should be made aware of the fact that, at present, patients are not informed nor involved appropriately in surgical treatment decision making. Patients' preferences concerning different aspects of treatment, such as mortality, morbidity, discomfort, long-lasting functional effects, cure of disease, and hospital readmission rates should be taken into account. The risk of anastomotic leakage versus the consequences of a stoma seems of critical importance in decision-making. Methods to enhance thorough preoperative counselling should be developed. Surgeons can use short-term risk information provided by audit systems, such as the DSCA, although long-term outcomes need to be taken into account as well. Furthermore, not a risk averse strategy per se, but optimal patient selection may be the key towards preferable outcomes in colorectal cancer surgery. In high-risk patients, an end-colostomy may be the best decision to prevent short-term anastomotic leakage. Routine creation of defunctioning stomas to limit the risk of anastomotic leakage is not desirable, especially considering its unfavourable one-year outcomes. The next step in order to improve quality of colorectal cancer care is to identify best practices, or better even, algorithms for adequate patient selection, and to share this knowledge between different doctors and hospitals.

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SUMMARY / SAMENVATTING

Summary

The aim of this thesis was to explore several aspects of both clinical decision making and quality assessment in colorectal cancer surgery. Part one focusses on benefits and risks of treatment options, preoperative information provision and Shared Decision Making (SDM); part two investigates changes and hospital differences in surgical treatment strategies regarding anastomosis and stoma construction, and their relation with postoperative outcomes; part three describes features of clinical aud

Part I: Risks, benefits and decision making

In chapter 1, a systematic search was performed for studies describing anastomotic leakage and the subsequent postoperative mortality in relation to the overall postoperative mortality after low anterior resection. Twenty-two studies with 10,343 patients in total were analyzed. The results showed a considerable overall anastomotic leakage rate and a large contribution of anastomotic leakage to the overall postoperative mortality. There was considerable variation in incidence, definition, and measurement of all outcomes in literature, which may hinder providing accurate and reliable risk information.

In chapter 2, we described both short-term postoperative and one-year outcomes of a primary anastomosis, an anastomosis with a defunctioning stoma, and an end-colostomy, after surgery for rectal cancer. We retrospectively analyzed 388 patients in 7 different hospitals with one year of follow-up. In this study, patients with an anastomosis had a risk of 11% for anastomotic leakage. Although a defunctioning stoma resulted in a somewhat lower short-term anastomotic leakage rate (9%, not significant), we found a high (18%) unplanned readmission rate and a high (12%) re-intervention rate due to anastomotic leakage

in these patients during one year after initial surgery. Furthermore, we found a high risk of postoperative complications (24%), and an additional risk of anastomotic leakage (4%) in patients undergoing reversal surgery to restore bowel continuity. Although patients with an end-colostomy had no risk of anastomotic leakage, they had high readmission rates in the long term, mostly due to stoma or abscess complications. Furthermore, in one-fourth of all patients with a defunctioning stoma, bowel continuity was not restored one year after surgery. Due to these results, it seems critical to also take these long-term outcomes into account when different surgical strategies are considered and patients are informed.

In Chapter 3 we investigated whether patients with rectosigmoid cancer were adequately informed preoperatively about the options, their risks, and benefits, , and whether patients were involved in the decision making. The opinion of Dutch gastroenterological surgeons' regarding preoperative information, and their attitudes towards SDM were investigated by means of a questionnaire. Next, it was assessed what was actually communicated in practice and whether patients were involved in the decision by recording preoperative consultations. Surgeons considered most information on risks and alternative treatment options to be essential. However, the information provided in clinical practice did not meet these criteria. Alternative treatment options were often not mentioned at all, and patients were not involved appropriately. Despite the clear benefits of SDM, it is not a routine in surgical practice, and its implementation will need an increased awareness amongst surgeons. Furthermore, methods to empower the patient before a consultation with the surgeon need to be developed.

Part II: surgical treatment strategies

The possibilities for sphincter saving surgery for rectal cancer have increased, partly due to the improvement in surgical techniques. Inevitably, this has led to an increased focus on the problem of anastomotic leakage. The role of a defunctioning stoma to minimize the risks of anastomotic leakage and its sequelae has been discussed repeatedly. In daily practice, this decision remains difficult, as a defunctioning stoma also has its drawbacks and it may not be beneficial for all patients. With the introduction of the Dutch Surgical Colorectal Audit (DSCA) in the Netherlands, there has been a growing demand for transparency of performance. Surgeons and hospitals are increasingly accountable for their postoperative complication rates, which may have led to a change of strategy in colorectal cancer surgery and a more routinely use of (defunctioning) stomas after low anterior resection.

In chapter 4 we assessed whether there has been an increase in the use of defunctioning stomas after low anterior resection in the last decade (since the TME-trial). Related postoperative outcomes such as anastomotic leakage and mortality were analysed. We found that the substantial percentage of patients who received a defunctioning stoma at times of the TME-trial (57%) further increased in recent years; in current surgical practice, 70% of patients receive a defunctioning stoma after LAR. Interestingly, clinically relevant anastomotic leakage rates remained similar. Arguably, the groups may not be perfectly comparable regarding purpose and period of treatment. Therefore, we attempted to correct for the most important differences with multivariable analyses. Nevertheless, current percentage of patients in whom a defunctioning stoma is constructed seems rather high, especially since has there has been no additional benefit of reducing anastomotic leakage rates when compared to the TME-trial. The results of this study underline the necessity for surgeons to determine whether an increase in the use of defunctioning stoma is justified. It is important to focus on further identification high-risk patients and involvement of patient preferences in the decision, instead of constructing defunctioning stomas in the majority of patients.

Chapter 5 had a dual objective: we first evaluated current hospital practice and assessed whether patient, tumour and hospital factors were associated with the rate of construction of defunctioning stomas, and whether there was variation in this rate between hospitals treating rectosigmoid cancer patients. Second, we surveyed all gastroenterological surgeons in the Netherlands to investigate their perceptions regarding factors that determine the construction of a defunctioning stoma or not. There was a considerable variation in the use of defunctioning stomas between hospitals. Furthermore, there was a lack in uniformity of selection criteria for defunctioning stomas between surgeons. The results of this study underline the need to further improve current decision making.

In chapter 6 we compared hospitals with regard to a risk taking or – averse surgical strategy. We assessed whether a hospital's defunctioning stoma rate was related to anastomotic leakage and mortality rates. Hospitals varied in their treatment strategy; even after adjustment for relevant case-mix factors, there are hospitals with a significantly higher tendency to construct a stoma. Interestingly, risk-adjusted anastomotic leakage and mortality rates were not lower in hospitals with a higher stoma rate. Probably, hospitals with low stoma rates and favourable outcomes were better able to select high risk patients, and stoma construction in more patients has no additional benefit.

Part III: quality assessment in colorectal surgery.

The DSCA was initiated by the Association of Surgeons of the Netherlands (NVvH) to monitor, evaluate, and improve colorectal cancer care in the Netherlands. Chapter 7 illustrates key elements of the DSCA and shows the results of three years of auditing. The article focuses specifically on the key elements of the audit that contributed to this success and how the DSCA has a central role in the national quality improvement policy defined by the NVvH. The format of the Dutch Surgical Colorectal Audit has quickly lead to robust data with full national coverage: in two years, all Dutch hospitals participated in the audit. Data quality is high; comparison with the Dutch Cancer Registry shows that both datasets correspond well. Within three years, guideline compliance for diagnostics, preoperative multidisciplinary meetings and standardised reporting significantly increased; and complication-, re-intervention and postoperative mortality rates significantly decreased. The combination of "how we do it" and our results so far could stimulate audit initiatives in other countries.

In chapter 8 we explored whether hospital differences in anastomotic leakage and postoperative mortality are due to differences in case-mix, or to differences in treatment factors. Identifying outcome measures that are less influenced by differences in case-mix between hospitals, and more by treatment- and hospital-related factors may be useful, since it makes such a measure a suitable indicator for discriminating hospitals based on their performance. We found that hospital variation in anastomotic leakage was large, and, in contrast to postoperative mortality, relatively independent of differences in case-mix. We also found that treatment factors played a larger role. Likely, in-hospital factors are more related to anastomotic leakage than patient and tumour factors. Both findings make anastomotic leakage suitable as an outcome indicator for measurement of quality of care.

Samenvatting

Bij de ingewikkelde keuze van een bepaald type operatie voor darmkanker spelen verschillende afwegingen een rol. Niet alleen het type resectie maar ook eventueel continuïteitsherstel moet worden bepaald. De keuze bestaat uit het aanleggen van een eindstandig stoma en een anastomose mét of zonder ontlastend stoma.
Dit proefschrift richt zich op verschillende aspecten van deze klinische besluitvorming, alsmede op kwaliteitsmeting en verbetering van darmkankerchirurgie in Nederland. Deel I focust op de voor-en nadelen van de verschillende behandelingsopties, de huidige preoperatieve informatieverschaffing en Shared Decision Making (SDM) in de praktijk; deel II onderzoekt veranderingen in behandelingsstrategieën over de tijd, alsmede huidige verschillen tussen chirurgen en ziekenhuizen, in relatie tot postoperatieve uitkomsten; deel III beschrijft de implementatie en resultaten van 'the Dutch Surgical Clinical Audit' als een instrument voor kwaliteitsmeting en verbetering van darmkankerchirurgie, en onderzoekt het gebruik van naadlekkage als uitkomstmaat voor kwaliteit.

Deel I : Kosten, baten en klinische besluitvorming

Hoofdstuk 1 beschrijft de resultaten van een systematische review van de beschikbare literatuur over naadlekkage en de daardoor veroorzaakte postoperatieve sterfte in relatie tot de totale sterfte na een Laag Anterieure Resectie (LAR) vanwege rectumcarcinoom. In totaal werden 22 studies met 10.343 patiënten geïncludeerd. De resultaten toonden een gemiddeld naadlekkage percentage van 9%, alsmede een grote bijdrage van naadlekkage aan de totale postoperatieve sterfte. Er bestonden echter grote verschillen in incidentie, definitie en meting van de in de literatuur gerapporteerde uitkomsten. De huidige literatuur lijkt derhalve ongeschikt voor het geven van nauwkeurige en betrouwbare risico-informatie aan de patiënt.

Hoofdstuk 2 beschrijft de korte termijn en 1-jaars uitkomsten van de verschillende behandelopties na sfincter-sparende rectumchirurgie (anastomose, anastomose met ontlastend stoma, eindstandig stoma). Er werden 388 patiënten geopereerd in 7 verschillende ziekenhuizen retrospectief onderzocht met een follow-up van 1 jaar. Eén-jaars uitkomsten toonden lage morbiditeit bij patiënten met een anastomose. Patiënten met een ontlastend stoma hadden een hoog percentage heropnames (18%) en reinterventies (12%), voornamelijk als gevolg van (late) naadlekkage. Ongeplande reinterventies bij een eindstandig stoma vonden veelal plaats wegens stoma-of abces problematiek. Tijdens follow-up was er een 25% toename van patiënten met een eindstandig stoma. Deze resultaten kunnen worden gebruikt in de klinische besluitvorming rond de behandeling en bij het preoperatief voorlichten van de patiënt.

In hoofdstuk 3 werd door middel van audiotapes van preoperatieve consulten onderzocht in hoeverre patiënten met rectosigmoid carcinoom adequaat werden geïnformeerd over de chirurgische mogelijkheden, kosten en baten, en hun betrokkenheid bij de besluitvorming. Middels een vragenlijst werd vervolgens de houding van Nederlandse GE-chirurgen ten aanzien van preoperatieve informatie verschaffing en SDM onderzocht en vergeleken met de klinische praktijk. Ondanks het feit dat chirurgen de meeste informatie over risico's en alternatieve behandelingsopties van essentieel belang beschouwden, werd in klinische praktijk informatie niet voldaan aan deze criteria. Alternatieve behandelingen werden vaak niet genoemd en patiënten nauwelijks betrokken bij de besluitvorming. Deze resultaten laten zien dat SDM nog niet of nauwelijks routine is in de dagelijkse chirurgische praktijk. Verdere bewustwording hiervan is noodzakelijk. Methoden die de rol van de patiënt kunnen versterken in het preoperatief gesprek dienen te worden onderzocht en ontwikkeld.

Deel II : chirurgische behandelstrategieën

De laatste tien jaar, zijn mede door verbetering van chirurgische technieken, de mogelijkheden voor sfinctersparende chirurgie bij rectumkanker aanzienlijk toegenomen. Deze ontwikkeling heeft, naast een kwaliteitsverbetering, onvermijdelijk geleid tot een toegenomen aandacht voor het probleem van naadlekkage. Multipele oplossingen werden in de loop der tijd onderzocht, echter van het ontlastende stoma werd als enige een wetenschappelijk bewezen gunstig effect gevonden, met name door de gevolgen van naadlekkage te beperken.

In de dagelijkse praktijk blijft deze beslissing echter moeilijk; een ontlastend stoma heeft ook zijn nadelen, en is derhalve niet voor alle patiënten een ideale oplossing. Tegelijkertijd is er vanuit meerdere partijen een groeiende vraag naar transparantie van zorguitkomsten. Het feit dat chirurgen en ziekenhuizen steeds vaker verantwoordelijk worden gehouden voor hun postoperatieve complicaties zou mogelijkerwijs geleid hebben tot veranderingen in van chirurgische strategie bij rectumcarcinoom. In hoofdstuk 4 werd een eventuele stijging in het percentage ontlastende stomata na een LAR de afgelopen tien jaar onderzocht, alsmede diens relatie met postoperatieve uitkomsten. Er bleek inderdaad een stijging in het percentage ontlastende stomata van 57% naar 70% te zijn geweest, echter zonder dat dit gepaard ging met een verwachtte daling in het percentage klinisch relevante naadlekkage. In de analyse werd gecorrigeerd voor de belangrijkste patiënt-en tumorkarakteristieken. Het huidige percentage ontlastende stomata suggereert een hedendaags routinematig gebruik, welke niet gerechtvaardigd kan worden gezien het uitblijven van een gunstig effect op naadlekkage percentage sinds de TME trial. Toekomstige onderzoeken dienen zich te focussen op het identificeren van hoog-risico patiënten, om een verdere stijging in overbodige ontlastende stomata te voorkomen.

Het doel van hoofdstuk 5 was tweeledig: ten eerste het beoordelen van ziekenhuisverschillen in diens percentage ontlastende stomata na rectumchirurgie, ten tweede het onderzoeken van de perceptie van Nederlandse GE-chirurgen ten aanzien van bepalende factoren in de aanleg van een ontlastend stoma. Er bleek een aanzienlijke variatie tussen ziekenhuizen te bestaan, ondanks correctie voor patient- en tumorfactoren. Tevens was er een gebrek aan uniformiteit van selectiecriteria tussen chirurgen, en kwamen deze niet overeen met de factoren die in werkelijkheid bepalend waren.
Interessant genoeg werden factoren gerelateerd aan patiënt-voorkeur gemiddeld door chirurgen als minder belangrijk beschouwd. De resultaten van dit onderzoek tonen een duidelijke inconsistentie onder chirurgen, en onderstrepen de noodzaak van verdere verbetering van de huidige besluitvorming rondom de aanleg van het ontlastend stoma, om de praktijkvariatie te reduceren.

In hoofdstuk 6 werd onderzocht of het percentage ontlastend stoma per ziekenhuis gerelateerd waren aan diens percentage naadlekkage. Er bleek geen duidelijke correlatie te bestaan. We vonden vergelijkbare percentages naadlekkage in geclusterde ziekenhuizen met een laag (10%) en een hoog (85%) percentage ontlastende stomata. Wellicht zijn deze eerste ziekenhuizen beter in het selecteren van de hoog-risico patiënt. Het heeft de voorkeur de selectieprocedures in deze ziekenhuizen te onderzoeken, zodat het gebruik van overbodige ontlastende stomata kan worden gereduceerd.

Deel III : kwaliteitstoetsing van darmkankerchirurgie

Om de kwaliteit van colorectale chirurgische zorg in Nederland te monitoren, te evalueren en te verbeteren werd op initiatief van de Nederlandse Vereniging voor Heelkunde (NVvH) de DSCA opgericht. Hoofdstuk 7 geeft de belangrijkste elementen van de DSCA weer en toont de resultaten van drie jaar clinical auditing. Het artikel richt zich specifiek op de elementen die hebben bijgedragen aan de succesvolle implementatie, en de centrale rol van de audit in de kwaliteitsbewaking van de beroepsgroep. Het format van de DSCA heeft al snel geleid tot het genereren van betrouwbare gegevens met volledige landelijke dekking binnen twee jaar. De datakwaliteit is hoog; dataverificatie met de Nederlandse Kankerregistratie toont een hoog percentage overeenkomstige gegevens. In drie jaar vond een aanzienlijke stijging plaats in de percentages richtlijnnaleving op het gebied van diagnostiek, preoperatief MDO en gestandaardiseerde rapportage gedurende drie jaar; het aantal complicaties , re- interventies en postoperatieve sterfte nam af. Dit artikel toont dat de 'blueprint' van de DSCA kan bijdragen aan kwaliteitsverbetering van postoperatieve uitkomsten, en kan dienen als voorbeeld voor (internationale) audit-initiatieven.

Bij meten van kwaliteit spelen uitkomstindicatoren een cruciale rol. Een uitkomstindicator onderscheidt ziekenhuizen bij voorkeur op basis van hun prestaties. Het is derhalve nuttig uitkomstindicatoren te identificeren die vooral afhankelijk zijn van behandelings- en ziekenhuisfactoren, en in mindere mate worden veroorzaakt door verschillen in case-mix. In hoofdstuk 8 werd onderzocht of ziekenhuisverschillen in percentage naadlekkage en mortaliteit worden veroorzaakt door verschillen in case-mix, of door ziekenhuis en behandelingsfactoren. We vonden een ziekenhuisvariatie in zowel percentage naadlekkage als mortaliteit. In tegenstelling tot mortaliteit was naadlekkage relatief onafhankelijk van verschillen in case- mix. Behandelingsfactoren speelden een grotere rol. Beide bevindingen maken naadlekkage geschikt als uitkomstindicator voor het meten van kwaliteit van zorg.

LIST OF PUBLICATIONS, CURRICULUM VITAE & ACKNOWLEDGEMENTS

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Curriculum vitae

Heleen Snijders werd geboren op 23 januari 1985 te Rotterdam. Na het behalen van haar Gymnasiumdiploma aan het Erasmiaans Gymnasium begon zijn in 2003 met de studie geneeskunde aan de Universiteit van Amsterdam. In 2008 startte ze naar idee en onder begeleiding van dr. Alexander de Vries in het kader van haar wetenschappelijke stage een onderzoek naar besluitvorming voor darmkankerchirurgie dat uiteindelijk de basis vormde voor dit proefschrift.

Zij volgde coschappen in de regio Amsterdam, een keuzecoschap oncologische chirurgie in het LUMC, waarna zij eind 2010 haar artsexamen behaalde. In het LUMC vond zij de inhoudelijke begeleiding voor het voortzetten van haar reeds verrichtte onderzoek bij Prof. dr Anne Stiggelbout en klinische begeleiding bij dr. Bert Bonsing. In mei 2011 werd ze door Prof. dr Rob Tollenaar aangenomen als arts-onderzoeker bij de Dutch Institute for Clinical Auditing (DICA). Daar combineerde zij gedurende 2 jaar haar promotie-onderzoek op het gebied van darmkankerchirurgie met dagelijkse werkzaamheden voor de DICA in het algemeen, en de oncologische registraties voor de Dutch Surgical Colorectal Audit (DSCA) en de Nabon Breast Cancer Audit (NBCA) in het bijzonder. In mei 2013 begon zij als arts-assistent heelkunde in het Groene Hart Ziekenhuis te Gouda, waarna zij na een jaar klinische ervaring te hebben opgedaan werd aangenomen voor de opleiding tot chirurg. Op1 juli 2014 is zij gestart in het LUMC met als opleider prof. dr. J.F. Hamming.

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