High complication rate after low anterior resection for mid and high rectal cancer; results of a population-based study

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Accepted 18 February 2014
Available online 28 February 2014

Abstract

Background: Surgical resection is the cornerstone of treatment for rectal cancer patients. Treatment options consist of a primary anastomosis, anastomosis with defunctioning stoma or end-colostomy with closure of the distal rectal stump. This study aimed to compare postoperative outcome of these three surgical options.

Methods: Data was derived from the national database of the Dutch Surgical Colorectal Audit. Mid and high rectal cancer patients who underwent rectal cancer resection between January 2011 and December 2012 were included. Endpoints were postoperative complications including anastomotic leakage, reinterventions, hospital stay and mortality within 30 days postoperative.

Results: In total, 2585 patients were included. Twenty-five per cent of all patients received a primary anastomosis; 51% an anastomosis with defunctioning stoma, and 24% an end-colostomy. More than one third of patients developed postoperative complications, the lowest rate being in the primary anastomosis group. Anastomotic leakage rates were 12% in patients with a primary anastomosis, and 9% in patients with an anastomosis with defunctioning stoma (p < 0.05). Multivariate analysis showed more postoperative complications, prolonged hospital stay, and increased mortality rates in patients with a defunctioning stoma or end-colostomy. The latter had proportionally less invasive reinterventions when compared to the other two groups.

Conclusions: Patients with a primary anastomosis had the best postoperative outcome. A defunctioning stoma leads to a lower anastomotic leakage rate, though is associated with higher rates of complications, prolonged hospital stay and mortality. The decision to create a defunctioning stoma should be focus of future studies.

Introduction

Colorectal cancer is the third most common malignancy worldwide, with in the Netherlands more than 12 000 new cases each year.1 The treatment for colorectal cancer requires a multidisciplinary approach with surgical resection as cornerstone of treatment. In the Netherlands, approximately 10 000 patients per year undergo a resection for colorectal cancer, from which 2,500 patients are operated on for rectal cancer.2
When in patients with rectal cancer the patient’s preference, tumour size, tumour location and stage of disease, allow a sphincter preserving procedure, a low anterior resection of the rectum is performed. A low anterior resection comes with three surgical options: a primary anastomosis, an anastomosis with a defunctioning stoma and an end-colostomy with closure of the distal rectal stump. Each of these options has specific advantages and disadvantages and a corresponding outcome. The creation of an anastomosis bears the risk of anastomotic leakage leading to reinterventions, morbidity, longer hospital stay and sometimes mortality.\textsuperscript{3–5} The fashioning of a temporary defunctioning stoma decreases the leakage rate and its sequelae\textsuperscript{4,6} and the creation of an end-colostomy even avoids anastomotic leakage. However, stoma formation is associated with other disadvantages. Creation of a stoma leads to the burden of stoma care and possibly stoma-related complications like parastomal hernias, re-admission for dehydration, stoma revisions, abscesses and postoperative complications after stoma reversal.\textsuperscript{7–10} Moreover, a large amount of temporary stomas is never reversed and becomes permanent.\textsuperscript{11,12} To select the best surgical strategy for individual patients it is important to balance the patient’s preference and the outcome of different surgical strategies.

In the Netherlands, public interest in quality and outcome of medical and surgical care led to the initiation of a national audit program, the Dutch Surgical Colorectal Audit (DSCA), founded in 2009.\textsuperscript{13} The DSCA was developed to evaluate and improve quality of care for colorectal cancer surgery in the Netherlands. The audit strives for uniformity of definition and measurement of basic outcome parameters such as complication rates, anastomotic leakage, reinterventions and postoperative mortality. These outcomes may support clinicians when informing patients about risks of different surgical strategies.

The aim of this study is to compare the postoperative outcomes of three different surgical strategies for completion of the operation after a radical mid or high rectal cancer resection over the last two years in the Netherlands.

\textbf{Methods}

\textit{Study population}

For analysis of surgical outcome, data was derived from the DSCA, a database in which variables concerning patient factors, co-morbidity, diagnostics, disease-specific details, performed treatments, and outcomes, are collected prospectively. The DSCA contains data registered by 92 hospitals (all hospitals performing colorectal cancer surgery, 99\% of all hospitals in the Netherlands). The dataset is disease-specific for colorectal cancer and shows a nearly 100\% concordance on validation against the National Cancer Registry dataset.\textsuperscript{2} All information concerning individual patients and hospitals are made anonymous, therefore no ethical approval from the medical ethics committee was required for this study.

All patients undergoing a radical resection (total of partial mesorectal excision) for mid or high rectal cancer (tumour between 5 and 15 cm from the anal verge) between the 1st of January 2011 and 31st of December 2012 were evaluated. Minimal data requirements for inclusion in analyses were information on tumour location, type of surgical resection, date of surgery and mortality. Patients with a double tumour, urgent resections, patients with a T4 tumour, patients undergoing an abdominoperineal resection and patients with an unknown anastomosis/stoma status were excluded, because these patients represent subgroups of patients with other treatment options and subsequent different expected outcomes.

\textbf{Outcomes}

Information on the following patient and tumour characteristics: age, gender, ASA-classification co-morbidity reflected in Charlson score,\textsuperscript{14,15} abdominal surgical history, preoperative tumour complications, tumour stage, extensive resections (resection of other organs during surgery) and distance from the anal verge, were extracted from the dataset of the DSCA.

Study endpoints, defined as endpoints within 30 days after initial surgery, were postoperative complications, reinterventions, prolonged hospital stay and mortality. Complications were defined as all postoperative complications, both surgical and non-surgical. Surgical complications were defined as anastomotic leakage, abscesses, stoma or wound problems, bleeding, wound dehiscence, ileus or iatrogenic lesions. Non-surgical complications were defined as cardiac, thrombo-embolic, pulmonary, infectious, neurological or other. Anastomotic leakage was defined as clinically relevant anastomotic leakage requiring a reintervention. Reinterventions were defined as all additional procedures performed for the treatment of all postoperative complications, both radiological and surgical. 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.

\textbf{Analyses}

Patient and tumour characteristics were described according to performed surgical strategy (primary anastomosis, anastomosis with defunctioning stoma, end-colostomy). Univariate analyses were performed to investigate differences in postoperative outcome between the different groups. Logistic regression analyses were performed to correct for case-mix factors between the three groups. Case-mix consisted of patient and tumour factors as age, gender, ASA classification, Charlson score, preoperative complications, tumour stage, abdominal surgical history, neoadjuvant therapy, additive resections and tumour distance from the anal verge. Results were
displayed in odds ratios and 95% confidence intervals; the surgical option of a primary anastomosis without a defunctioning stoma was used as reference group. 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 2011 to December 2012 data from 6030 patients with rectal cancer were collected from the dataset of the DSCA. A total of 3,445 patients were excluded (2,243 patients with tumour <5 cm from the anal verge, or unknown tumour height, 730 patients with a double tumour, 221 abdominoperineal resections, 123 patients with a T4 tumour and 65 patients with unknown anastomosis/stoma status). After selection according the eligibility criteria, 2,585 patients undergoing low anterior resection for mid or high rectal cancer were included in the study. Table 1 shows the patient and tumour characteristics for the three groups of patients.

In 657 patients, a primary anastomosis was constructed (25%), 1,319 patients (51%) received an anastomosis with a defunctioning stoma and an end-colostomy was constructed in 609 patients (24%, Table 1). Patients with a defunctioning stoma were more often male, and more often received neoadjuvant chemoradiation therapy when compared to patients with a primary anastomosis ($p < 0.05$). Patients with an end-colostomy were significantly older, had a higher ASA classification, more often had a higher Charlson score, more frequently had extensive tumour resections and more often received neoadjuvant chemoradiation therapy. Fifty per cent of all patients received short term chemoradiation therapy and 30% of included patients underwent long scheme neoadjuvant chemoradiation therapy.

Univariate analysis

Fig. 1 shows the short-term postoperative outcomes of the three treatment groups, without adjustments for differences in patient- and tumour characteristics. The percentage of patients developing a postoperative complication of any kind was significantly lower in patients with a primary anastomosis compared to patients with an anastomosis with defunctioning stoma and patients with an end-colostomy (31 vs. 39 and 40%, $p < 0.05$). Anastomotic leakage rates were significantly higher in patients with a primary anastomosis compared to patients with an anastomosis with defunctioning stoma and patients with an end-colostomy (12 vs. 9% $p < 0.05$). Patients with an anastomosis with defunctioning stoma and patients with an end-colostomy had significantly more

| Table 1 Patient and tumour characteristics according to type of surgery in rectal cancer patients diagnosed between January 1st 2011—December 31st 2012. |
|-------------------------------------|-----------------|-----------------|-----------------|
| Age (mean)                          | 67              | 66              | 75              |
| Gender                              | Male            | Male            | Male            |
| ASA classification                  | ASA I/II        | ASA III+        | ASA III+        |
| Charlson score                      | 445             | 827             | 255             |
| Charlson score 1                    | 118             | 218             | 194             |
| Charlson score 2+                   | 94              | 218             | 194             |
| Preoperative complications          | 152             | 132             | 132             |
| T-stage                             | ypT0            | ypT2            | ypT3            |
| Radiotherapy                        | 73              | 202             | 354             |
| Long course Chemoradiation          | 116             | 456             | 663             |
| Extensive resection of the tumour   | 13              | 23              | 39              |
| Distance of tumour from anal verge  | 8               | 8               | 8               |

Bold printed numbers are statistically significant ($p < 0.05$) when compared to patients with a primary anastomosis.
often a prolonged hospital stay compared to patients with an anastomosis. Postoperative mortality rates were significantly higher for patients with a defunctioning stoma and patients with an end-colostomy, 2 and 3% respectively, compared to 1% in patients with a primary anastomosis.

Postoperative complications consisted of surgical and non-surgical complications. Proportionally more surgical complications occurred in the primary anastomosis group, followed by the group with a defunctioning stoma, 19 and 17% respectively, compared to 14% in the end-colostomy group. The most common surgical complications were anastomotic leakage and abscesses. There were proportionally more non-surgical complications in the group with an end-colostomy 16%, followed by the patients with a defunctioning stoma 13%, compared to 8% in the patients with a primary anastomosis. Non-surgical complications were mostly thrombo-embolic, cardiac or pulmonary adverse events.

In 44% per cent of all postoperative complications, a reintervention was performed. There were no significant

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**Table 2**

Reason for reinterventions in patients with a primary anastomosis, an anastomosis with a defunctioning stoma and an end-colostomy.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Anastomosis (n = 657)</th>
<th>Anastomosis with defunctioning stoma (n = 1319)</th>
<th>End-colostomy (n = 609)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Anastomotic leakage</td>
<td>66</td>
<td>10%</td>
<td>95</td>
</tr>
<tr>
<td>Abcess</td>
<td>0</td>
<td>0%</td>
<td>5</td>
</tr>
<tr>
<td>Bleeding</td>
<td>7</td>
<td>1.1%</td>
<td>8</td>
</tr>
<tr>
<td>Ileus</td>
<td>10</td>
<td>1.5%</td>
<td>35</td>
</tr>
<tr>
<td>Iatrogenic lesion</td>
<td>6</td>
<td>0.9%</td>
<td>17</td>
</tr>
<tr>
<td>Wound/stomal problems</td>
<td>14</td>
<td>2.1%</td>
<td>58</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>103</strong></td>
<td><strong>16%</strong></td>
<td><strong>218</strong></td>
</tr>
</tbody>
</table>

**Table 3**

Multivariate differences in postoperative outcomes between patients with an anastomosis, an anastomosis with a defunctioning stoma and an end-colostomy. The for case-mix adjusted odds ratios display outcomes of defunctioning stomas and end-colostomies when compared to a primary anastomosis (reference 1.0).

<table>
<thead>
<tr>
<th></th>
<th>Anastomosis</th>
<th>Anastomosis with defunctioning stoma</th>
<th>End-colostomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>OR&lt;sup&gt;a&lt;/sup&gt; 95% CI</td>
<td>OR&lt;sup&gt;a&lt;/sup&gt; 95% CI</td>
</tr>
<tr>
<td>All postoperative</td>
<td>1.0 (ref)</td>
<td>1.39 1.19–1.62</td>
<td>1.20 1.02–1.42</td>
</tr>
<tr>
<td>complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anastomotic leakage</td>
<td>1.0 (ref)</td>
<td>0.67 0.53–0.85</td>
<td>n.a. n.a.</td>
</tr>
<tr>
<td>Reinterventions</td>
<td>1.0 (ref)</td>
<td>0.95 0.78–1.16</td>
<td>0.78 0.64–0.96</td>
</tr>
<tr>
<td>Prolonged hospital stay</td>
<td>1.0 (ref)</td>
<td>1.62 1.73–2.52</td>
<td>1.48 1.22–1.80</td>
</tr>
<tr>
<td>Postoperative mortality</td>
<td>1.0 (ref)</td>
<td>3.59 1.52–8.52</td>
<td>3.97 1.70–9.29</td>
</tr>
</tbody>
</table>

* Adjusted in multivariate analysis for differences between groups (age, gender, ASA classification, Charlson score, preoperative complications, tumour stage, abdominal surgical history, neoadjuvant therapy, additive tumour resection, tumour distance).

Bold printed numbers are statistically significant (p < 0.05).
differences in the number of reinterventions between the three groups (Fig. 1). Anastomotic leakage was the most causative factor leading to a reintervention in both anastomoses groups. Ten per cent of the patients with a primary anastomosis and 7% of the patients with an anastomosis with a defunctioning stoma, underwent a reintervention for anastomotic leakage (Table 2). In the end-colostomy group, most of the reinterventions were performed because of presacral and abdominal abscesses (40%). In the groups with a defunctioning stoma or an end-colostomy also frequent reinterventions were performed because of stoma and wound related complications (19%).

In the primary anastomosis group proportionally more surgical reinterventions were performed than radiological drainages, compared to both groups with a stoma. From the reinterventions for anastomotic leakage and abscesses, 80% were surgical compared to 20% radiological drainages in the primary anastomosis group. In the defunctioning stoma group 50% were surgical and 50% radiological. In the end-colostomy group 40% of the reinterventions for abscesses were surgical compared to 60% of radiological drainages.

**Multivariate analysis**

Logistic multivariate regression analysis was performed to adjust for differences in patient and tumour characteristics between the three groups. The adjusted odds ratios of different outcomes are shown in Table 3.

The risk factors for postoperative complications, prolonged hospital stay and postoperative mortality in patients with a defunctioning stoma or end-colostomy, found in the univariate analyses, were confirmed in the multivariate analyses. The lower risk for the occurrence of anastomotic leakage in patients with an anastomosis with defunctioning stoma compared to patients with a primary anastomosis, also remained after multivariate analysis. Patients with an end-colostomy had a significant lower risk for reinterventions (OR 0.78, 95% CI 0.64–0.96).

**Discussion**

The present study on postoperative outcome of radical resections in patients with mid and high rectal cancer showed a high overall postoperative complication rate; as more than one third of all patients developed postoperative complications. In half of the study population a defunctioning stoma was created. Although creation of a defunctioning stoma resulted in a 3% lower leakage rate, patients with a defunctioning stoma had more overall postoperative complications, a prolonged hospital stay, and a higher postoperative mortality rate when compared to the primary anastomosis group. Even after case-mix adjustment, the outcomes of the primary anastomosis group were surprisingly favourable.

Patients with an end-colostomy had a lower risk for reinterventions, and proportionally less invasive reinterventions compared to the other two groups, even after case-mix adjustment. However, the risk for overall complications, prolonged hospital stay and mortality, was high in these patients. Although we adjusted for differences in case-mix, this group consisted of significantly older patients, with more co-morbidity, and therefore, adjustments may not have been sufficient.

One of the strengths of this nationwide study on low anterior resection for mid and high rectal cancer resection, is that results are based on a large, disease specific database in which all hospitals performing colorectal surgery in the Netherlands participated. Completeness is validated against the National Cancer Registry. However, some limitations remain. Firstly, the present study is a retrospective analysis of data collected in a prospective database, and therefore results cannot be compared to conclusions following randomized clinical trials. Randomization between the three surgical strategies however, is practically impossible for ethical reasons. Moreover, there could be a bias due to inaccuracies in the definition of variables because data is extracted from a large database. However, ambiguities in definitions are minimized by the clear definitions that are given in the web-based data-collection program of the DSCA. Additionally, in the database of the DSCA, only data of patients diagnosed with a colorectal malignancy are collected, while these surgical strategies are also performed in patients with a benign operation indication. Finally, the present study evaluates only short-term outcomes within 30 days after the resection, although long-term outcomes are also important in the comparison between the three different surgical strategies.

According to the literature anastomotic height is an independent risk factor for the occurrence of anastomotic leakage, with a lower anastomosis leading to higher leakage rates. Our results did not confirm this finding. Possibly because in our study the anastomotic height was comparable for the different groups. In order to overcome bias we corrected for anastomotic height in multivariate analysis. From the literature is also known that creation of a defunctioning stoma can diminish the incidence of anastomotic leakage and its subsequent clinical consequences, as is also confirmed in the present study. However, anastomotic leakage still occurs, and the creation of a defunctioning stoma has problems of its own. Patients with a defunctioning stoma are known to have more postoperative morbidity, more reinterventions and more hospital re-admissions. In literature, most studies on stoma complications describe short-term outcomes. Recent results from our own group showed also on the long term a higher reintervention rate and more hospital re-admissions in patients with a defunctioning stoma. Patients with a defunctioning stoma require secondary surgery to reverse the stoma, which is associated with postoperative complications in 20–30% of the patients and 2–9% of patients develop anastomotic leakage after
Stoma reversal.\textsuperscript{20,21} Furthermore, it must be taken into account that a high proportion of defunctioning stomas is not reversed at all and become permanent.\textsuperscript{11,12} Despite these well-known drawbacks of the construction of a defunctioning stoma, previous research showed an increase in the use of defunctioning stomas during the last decade, without the benefit of a reduction of clinical anastomotic leakage rates.\textsuperscript{22} Snijders et al. concluded that routine use of defunctioning stomas should be questioned, but preoperative high risk patients selection should be encouraged. For high risk patients avoidance of an anastomosis, and thus construction of an end-colostomy with closure of the distal rectal stump, could be considered as well. In our study twenty-four per cent of patients received an end-colostomy. This relative high percentage is also reported in recent literature\textsuperscript{22,23} and might be due to a current trend of defensive surgery preventing postoperative complications including anastomotic leakage. The latter surgical option not only prevents anastomotic leakage, it also leads to better functional outcome especially in patients with a low anastomosis and patients with a preoperative poor sphincter function.\textsuperscript{23} Overall quality of life is not different for patients with or without an end-colostomy.\textsuperscript{25} An end-colostomy may be a safe alternative to prevent anastomotic leakage, but these patients have the risk to develop stoma problems and pelvic abscesses on the long term due to stump necrosis.\textsuperscript{10} An intersphincteric resection, in which the existence of a stump is avoided, could be an alternative.

The results in this study, together with data from the literature, accentuate that both doctors and patients should be aware that different surgical strategies are accompanied with different risks and benefits to consider. To select the best option for a specific patient is not always easy. It is important to know the trade-offs of each surgical strategy, and these should be discussed with the patient so his or her preferences can be taken into account.

In the present study, patients with an end-colostomy were consistently older and had more co-morbidity. Nonetheless they had had a lower risk for reinterventions, and proportionally less invasive reinterventions when compared to the other two groups. Therefore, an end-colostomy seems a safe alternative to an anastomosis in high risk patients.

Considering the results from the present study, apparently patients with a primary anastomosis were well selected and had most favourable postoperative outcomes. Based on patient- and tumour characteristics collected in the DSCA, the patients in the group with a primary anastomosis were comparable to the patients with an anastomosis and a defunctioning stoma, except for more males and more patients receiving neoadjuvant chemoradiation therapy in the defunctioning stoma group. The latter had a lower risk for anastomotic leakage, though also had a higher percentage of postoperative complications, more reinterventions and more often a prolonged hospital stay.

Results from this study emphasize the fact that it remains unclear with patients with an anastomosis benefit from creation of a defunctioning stoma. To facilitate optimal decision-making, and guide the appropriate use of defunctioning stomas, identification of high-risk patients should be focus of future studies. Possibly less defunctioning stomas, together with intensive postoperative follow-up and early intervention in case of an anastomotic leakage might be a better alternative.

\textbf{Disclaimers}

\textbf{None.}

\textbf{Source of funding}

\textbf{None.}

\textbf{Conflict of interest}

\textbf{None.}

\textbf{References}