Surgical challenges in diverticular disease
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2010

document version
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Download date: 25. Apr. 2022
Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial.
Short-term Results of the Sigma-trial

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Abstract

Background
No randomized controlled trial has compared laparoscopic sigmoid resection (LSR) to open sigmoid resection (OSR) for symptomatic diverticulitis of the sigmoid colon. This study tested the hypothesis that LSR is associated with decreased postoperative complication rates as compared to OSR.

Methods
This was a prospective, multi-center, double-blind, parallel-arm, randomized controlled trial. Eligible patients were randomized to either LSR or OSR. Endpoints included postoperative mortality, and complications were classified as major and minor. The generator of the allocation sequence was separated from the executor. Blinding was ensured using an opaque wound dressing to cover the abdomen. Symptomatic diverticulitis of the sigmoid colon was defined recurrent disease Hinchey I, Ila, IIb, symptomatic stricture, or severe rectal bleeding. The decision to discharge patients was made by independent physicians blind to the allocation sequence. Data were analyzed according to the intention to treat principle.

Results
From 2002 to 2006, 104 patients were randomized in five centers. All patients underwent the allocated intervention. 52 LSR patients were comparable to 52 OSR patients for gender, age, BMI, ASA grade, comorbid conditions, previous abdominal surgery, and indication for surgery. LSR took longer (p = .0001), but caused less blood loss (p = .033). Conversion rate was 19.2%. Mortality rate was 1%. There were significantly more major complications in OSR patients (9.6% vs. 25.0%; p =.038). Minor complication rates were similar (LSR 36.5% vs. OSR 38.5%; p =.839). LSR patients had less pain (Visual Analog Scale 1.6 point less; p = .0003), systemic analgesia requirement (p = .029) and returned home earlier (p = .046). The Short Form-36 (SF-36) questionnaire showed significantly better quality of life for LSR.

Conclusions
LSR was associated with a 15.4% reduction in major complication rates, less pain, improved quality of life, and shorter hospitalization at the cost of a longer operating time.

Introduction
Diverticulitis of the sigmoid colon is a common condition in western countries.1 Treatment of diverticulitis is based on the severity of the disease and indications for elective surgery are evolving.2 Open sigmoid resection (OSR) for diverticulitis has been shown to be associated with high postoperative complication rates and a mortality rate of 2 to 5%.3 Laparoscopic sigmoid resection (LSR) for diverticulitis was reported in the mid 1990s mostly with emphasis on improved surrogate endpoints.4-6 Subsequently, non-randomized comparison studies showed that LSR, although invariably associated with a longer operation time, may offer a reduction in postoperative complication rates.7-4 To date the purported beneficial impact of LSR for symptomatic diverticulitis on postoperative complication rates has not been the subject of a randomized controlled trial. The present study was designed as a randomized controlled trial to compare the impact of LSR and OSR on postoperative complication rates in patients with symptomatic diverticulitis.

Patients and methods
Study design and hypothesis
This was a prospective, multi-center, double-blind, parallel-arm, randomized controlled trial. Data were collected daily until discharge via a secured web site and on hardcopy datasheets. Patients and hospital staff were blind to the allocation sequence. The decision to discharge patients was made by independent physicians blind to the allocation sequence. The tested hypothesis was that LSR would be associated with a decreased rate of postoperative complication as compared to OSR in patients for symptomatic diverticulitis of the sigmoid colon.

Study endpoint
The endpoints of the study included: 1) postoperative mortality defined as death from whatever cause occurring within 30 days from surgery in hospital or following discharge; 2) postoperative complications classified as minor and major, the latter including re-operations within 30 days from surgery. Deep venous thrombosis, pneumonia, urinary tract infection, and wound infection were recorded as minor complications. Anastomotic leakage, intra-abdominal abscess, severe postoperative bleeding with requirement for blood transfusion and re-operations were classified as major complications.
Study outcome measures
The study outcome measures included: 1) operating time (minutes) calculated from the first skin incision to the application of dressings; 2) estimated blood loss (ml) recorded by the anaesthesiologist; 3) mobilization of the splenic flexure; 4) conversion rate defined as unplanned laparotomy or conversion to hand-assisted LSR; 5) specimen length (cm) measured by the pathologist after fixation; 6) hospital stay (days) determined by independent physicians blind to the allocation sequence; 7) need for oral and systemic analgesia (days); 8) Visual Analog Scale (VAS) pain score measured preoperatively and daily after surgery up to postoperative day 4; 9) resumption of diet (days); 10) quality of life assessment by the Short Form-36 (SF-36) questionnaire measured preoperatively and 6 weeks after surgery.

Eligibility criteria for patients
All patients presenting at the participating centers with symptomatic diverticulitis of the sigmoid colon were candidates for inclusion in the study. Diagnosis of diverticulitis was established by CT-scan and/or barium enema, and colonoscopy. Symptomatic diverticulitis of the sigmoid colon was defined as one of the following: previous two or more recurrent attacks of acute diverticulitis with (Hinchey I) or without pericolic abscess necessitating hospitalization with intravenous antibiotics and nil per os; previous recurrent attacks of acute diverticulitis with percutaneously drainable distant abscess necessitating CT-guided drainage (Hinchey IIa); presence of internal fistula between the sigmoid colon and a hollow organ with abscess (Hinchey IIb) or without; presence of symptomatic stricture of the sigmoid colon with no evidence of cancer; recurrent severe diverticular bleeding requiring blood transfusions verified at colonoscopy and/or arteriogram. Surgery was performed at least three months following the last attack of diverticulitis.

Patients were not admitted to the study if any of the following criteria were present: 1) failure to sign informed consent, 2) previous colorectal resectional surgery, 3) previous laparotomy other than for gynecological or obstetrical surgery, 4) perforated diverticulitis with peritonitis (Hinchey III or IV).

Enrollment of patients
Patients were referred to participating centers by primary care physicians, secondary care hospitals, or gastroenterologists. The external validity of the study was addressed by using no advertisement as method of patient recruitment.
Chapter 6
Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial. Short-term results of the Sigma-trial

Surgical field. All wounds were closed layer by layer.

OSR was carried out through a midline laparotomy. The splenic flexure was mobilized if needed. The sigmoid colon was mobilized. The left ureter was identified. The sigmoid vessels were divided. The rectosigmoid junction was identified by the absence of taenia coli and transected at the level of the promontory with a stapler. The proximal resection margin was placed on supple, normal appearing descending colon with no signs of inflammation or induration of the mesentery and serosal surface. The specimen was retrieved and a purse string suture was fashioned at the oral bowel end. A double-stapled anastomosis was performed. Care was taken to achieve a truly tension-free anastomosis. The midline wound was closed layer by layer.

Postoperative management
The decision to discharge patients was made by independent physicians blind to the allocation sequence. Following surgery all patients were started on intravenous patient controlled analgesia (PCA-pump, B. Braun Medical, Melsungen, Germany) with morphine (0.02 mg/kg, max. 6 times / hour) up to maximum postoperative day 3. Oral analgesia (Paracetamol 1 gram / 24 hours qid) was started on postoperative day 2. Nasogastric tubes were removed at the end of the operation. Bladder catheters were removed on postoperative day 1. Non-carbonated liquids were offered the evening after the surgery. If oral liquids were tolerated, diet was advanced to soft, and thereafter solid food was given. Early mobilization was encouraged and implemented starting on postoperative day 1. Patients were discharged after having had a bowel movement, tolerating solid food, able to walk properly and feeling comfortable with oral analgesia. Follow-up was scheduled at 6 weeks and 6 months after surgery.

Definition of variables
The American Society of Anesthesiology (ASA) classification was used as part of the preoperative assessment, but did not provide a prediction of risk for a particular patient. Body Mass Index (BMI) was used as part of the preoperative assessment. Hinchey classification is a staging system that helps categorize the findings associated with symptomatic diverticulitis of the sigmoid colon.

Ethics
This study was conducted in accordance to the principles of the Declaration of Helsinki and ‘good clinical practice’ guidelines. The study protocol was approved by the Institutional Review Boards of all participating institutions. Prior to randomization, written informed consent was obtained from all patients.

Study interventions
Eligible patients were randomized to either LSR or OSR. Regardless of study arm, patients were given bowel preparation and prophylactic intravenous antibiotics prior to surgery. LSR was performed through four or five ports. The splenic flexure was mobilized if needed. The sigmoid colon was mobilized. The left ureter was identified. The sigmoid vessels were divided. The rectosigmoid junction was identified by the absence of taenia coli and transected at the level of the promontory using a laparoscopic stapler. The oral end of the transacted bowel was exteriorized through a suprapubic incision. The proximal resection margin was placed on supple, normal appearing descending colon with no signs of inflammation or induration of the mesentery and serosal surface. The specimen was retrieved and a purse string suture was fashioned at the oral bowel end. An intracorporeal double-stapled anastomosis was created following closure of the suprapubic wound and reestablishment of the pneumoperitoneum. Care was taken to achieve a truly tension-free anastomosis. If conversion was necessary, LSR was converted to a hand-assisted LSR or to OSR. The hand-port device was placed at the suprapubic incision site. The left hand of the surgeon was introduced through the hand-port and assisted in improving exposure of the surgical field.
Sample size
Software (Power and Precision, BioStat, Englewood, NJ) was used for sample size calculation. Available data from the literature suggested a 23% difference in postoperative complication rates between LSR (12%, range 8–18%) and OSR (35%, range 24–50%). To demonstrate a 0.23 difference in proportions, two groups of 52 patients were required. The study had a power of 80% to yield a statistically significant result with alpha = 0.05 and beta = 0.2.

Statistical methods
Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Study arms were compared using an independent samples t-test for continuous variables with normal distribution. Converted patients were kept in the LSR arm in accordance with the intention to treat principle. Wilcoxon W test was employed for continuous variables, which were not normally distributed. Pearson chi-square test was used for discrete variables. Pain scores were analysed using repeated measures analysis. A database (SPSS 15.0.1, SPSS Inc., Chicago, IL) was created for statistical calculations.

Results
A total of 104 consecutive patients who underwent elective surgery for symptomatic diverticulitis of the sigmoid colon were randomized in five centers from February 2002 to December 2006. Pathology confirmed preoperative diagnosis in all cases. Table 1 outlines the breakdown of patients by center. All patients underwent the allocated intervention. Data on eligibility, enrollment, follow-up, and analysis are shown in a flow-diagram (Figure 2). 52 LSR patients were comparable to 52 OSR patients for gender, age, BMI, ASA classification, prevalence of comorbid conditions, previous abdominal surgery, preoperative workup, and indication for surgery (Table 2). The diagnosis was confirmed by colonoscopy in 70.2% of the cases, water soluble contrast enema in 61.5% and/or CT-scan in 51.9% of the cases.

Except for operating time, there were no significant differences in intra-operative data in the two study arms (Table 3). Conversion rate was 19.2% (10 patients). Five LSR cases were converted to hand-assisted LSR, and five other cases were converted to OSR. Reasons for conversion included extensive adhesions (five patients), bleeding (one patient), ureter lesion (one patient), and obesity (three patients). There were no significant differences between converted patients and LSR or OSR patients in terms of outcomes, VAS-pain score, overall morbidity, minor and major complications. Three patients (two LSR versus one OSR) received loop ileostomy due to extensive inflammation or compromised blood supply.

The postoperative outcomes are shown in Table 4. Based on the repeated measures analysis of the VAS, LSR patients had significantly less pain than OSR patients (daily on average 1.6 point less; p = .003). The duration of systemic analgesia was significantly decreased in LSR patients as compared to OSR patients (Table 4). Moreover, 87 patients received a PCA pump, whereas 17 patients had epidural analgesia. The latter was a protocol violation as PCA was warranted. There were no differences in violations among the centers. Patients who underwent epidural analgesia were equally distributed in the study arms (9 LSR versus 8 OSR; p = .278). There were no differences in the use of oral analgesia between the study arms. LSR patients were discharged on average 2 days earlier than OSR patients (Table 4). To test ascertainment biases of the allocation concealment, patients were asked to guess the type of operation they had undergone.
The proportions of patients guessing correctly were 32% in the LSR arm and 58% in the OSR arm (p = .427).

Postoperative complications are shown in Table 5. There were no significant differences in overall morbidity rates. When classified as minor and major complications, no significant differences in minor complication rates were found. LSR patients developed significantly fewer major complications than OSR patients (5 LSR versus 13 OSR). Re-operations were performed within 30 days after surgery in 11 patients (4 LSR versus 7 OSR). Percutaneous drainage of intra-abdominal abscesses was performed in 3 patients (LSR 1 versus OSR 2). Anastomotic leakages and abscesses occurred in different patients. A postmortem confirmed myocardial infarction accounted for one postoperative death.

SF-36 data showed no preoperative inter-group differences (Figure 3). Postoperative SF-36 data were significantly better in LSR patients for role limitations due to physical and emotional problems, social functioning and pain-level (Figure 3).

Table 1 Patients inclusion by center

<table>
<thead>
<tr>
<th>Center</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>57 (54.8%)</td>
<td>13 (12.5%)</td>
<td>12 (11.5%)</td>
<td>15 (14.4%)</td>
<td>7 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 (32 – 84)</td>
<td>54 (38 – 85)</td>
<td>64 (30 – 84)</td>
<td>58 (36 – 72)</td>
<td>62 (46 – 74)</td>
<td>.127</td>
</tr>
<tr>
<td>Gender (f : m)</td>
<td>37 : 20</td>
<td>7 : 6</td>
<td>7 : 5</td>
<td>6 : 9</td>
<td>2 : 5</td>
<td>.233</td>
</tr>
<tr>
<td>BMI (kg / m²)</td>
<td>26 (17 – 45)</td>
<td>29 (24 – 33)</td>
<td>27 (20 – 39)</td>
<td>28 (23 – 33)</td>
<td>28 (24 – 35)</td>
<td>.475</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>32 (56.1%)</td>
<td>8 (16.1%)</td>
<td>5 (41.6%)</td>
<td>9 (60.0%)</td>
<td>2 (28.6%)</td>
<td>.529</td>
</tr>
</tbody>
</table>

Participating centers, number of patients per clinic (%), age in years, gender (female : male), Body Mass Index (kg / m²) and presence of comorbidity (%). Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Independent Samples T-test was used for continuous variables with normal distribution, otherwise Willcoxon W test was used. Pearson Chi-square test was used for discrete variables.

Table 2 Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>LSR (n=52)</th>
<th>OSR (n=52)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male 23 (44.2%)</td>
<td>Male 21 (40.4%)</td>
<td>.689</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62 (32 – 85)</td>
<td>63 (30 – 84)</td>
<td>.571</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 (17.2 – 45.2)</td>
<td>25.9 (19.1 – 39.0)</td>
<td>.332</td>
</tr>
<tr>
<td>ASA grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>25 (50.0%)</td>
<td>29 (58.0%)</td>
<td>.341</td>
</tr>
<tr>
<td>II</td>
<td>24 (46.2%)</td>
<td>18 (36.0%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1 (2.0%)</td>
<td>3 (6.0%)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Ankyrhisms</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Valve diseases</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ischemic diseases</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Previous abdominal surgery</td>
<td>24 (46.2%)</td>
<td>25 (48.1%)</td>
<td>.844</td>
</tr>
<tr>
<td>Indications for surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent diverticulitis</td>
<td>30 (57.8%)</td>
<td>31 (59.6%)</td>
<td>.627</td>
</tr>
<tr>
<td>Sigmoid stricture</td>
<td>19 (36.5%)</td>
<td>14 (26.9%)</td>
<td>.258</td>
</tr>
<tr>
<td>Fistula</td>
<td>1 (1.9%)</td>
<td>4 (7.7%)</td>
<td>.169</td>
</tr>
<tr>
<td>Recurrent rectal bleeding</td>
<td>2 (3.8%)</td>
<td>3 (5.8%)</td>
<td>.647</td>
</tr>
<tr>
<td>Abscess drainage in previous episode</td>
<td>5 (9.6%)</td>
<td>2 (3.8%)</td>
<td>.229</td>
</tr>
</tbody>
</table>

LSR = Laparoscopic Sigmoid Resection; OSR = Open Sigmoid Resection; BMI = Body Mass Index; ASA = American Society of Anesthesiologists. Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Independent Samples T-test was used for continuous variables with normal distribution, otherwise Willcoxon W test was used. Pearson Chi-square test was used for discrete variables.
**Table 3** Operative results

<table>
<thead>
<tr>
<th></th>
<th>LSR (n=52)</th>
<th>OSR (n=52)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating time (minutes)</td>
<td>183 (85 – 271)</td>
<td>127 (75 – 243)</td>
<td>.0001</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>100 (0 – 2000)</td>
<td>200 (10 – 2500)</td>
<td>.033</td>
</tr>
<tr>
<td>Transfusion requirement</td>
<td>2 (3.8%)</td>
<td>6 (11.5%)</td>
<td>.374</td>
</tr>
<tr>
<td>Conversions</td>
<td>Hand-assisted</td>
<td>5 (9.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Laparotomy</td>
<td>5 (9.6%)</td>
<td></td>
</tr>
<tr>
<td>Splenic flexure mobilization</td>
<td>31 (59.6%)</td>
<td>36 (69.2%)</td>
<td>.432</td>
</tr>
<tr>
<td>Loop ileostomy</td>
<td>2 (3.8%)</td>
<td>1 (1.9%)</td>
<td>.558</td>
</tr>
<tr>
<td>Specimen length (cm)</td>
<td>19 (11 – 50)</td>
<td>19 (8 – 37)</td>
<td>.949</td>
</tr>
</tbody>
</table>

LSR = Laparoscopic Sigmoid Resection; OSR = Open Sigmoid Resection. Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Independent Samples T-test was used for continuous variables with normal distribution, otherwise Wilcoxon W test was used. Pearson Chi-square test was used for discrete variables.

**Table 4** Postoperative results

<table>
<thead>
<tr>
<th></th>
<th>LSR (n=52)</th>
<th>OSR (n=52)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NG tube postoperative (number of patients)</td>
<td>23 (44.2%)</td>
<td>30 (57.7%)</td>
<td>.305</td>
</tr>
<tr>
<td>Duration of tube (days)</td>
<td>0 (0 – 5)</td>
<td>1 (0 – 40)</td>
<td>.091</td>
</tr>
<tr>
<td>Re-insertion tube (number of patients)</td>
<td>4 (7.7%)</td>
<td>5 (9.6%)</td>
<td>.727</td>
</tr>
<tr>
<td>Diet (days)</td>
<td>Liquid</td>
<td>1 (0 – 4)</td>
<td>.802</td>
</tr>
<tr>
<td></td>
<td>Soft</td>
<td>2 (0 – 6)</td>
<td>.333</td>
</tr>
<tr>
<td></td>
<td>Solid</td>
<td>4 (1 – 12)</td>
<td>.084</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>5 (3 – 66)</td>
<td>7 (3 – 128)</td>
<td>.046</td>
</tr>
<tr>
<td>Systemic analgesia (days)</td>
<td>2 (0 – 5)</td>
<td>2 (0 – 5)</td>
<td>.029</td>
</tr>
</tbody>
</table>

LSR = Laparoscopic Sigmoid Resection; OSR = Open Sigmoid Resection; NG = Nasogastric. Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Independent Samples T-test was used for continuous variables with normal distribution, otherwise Wilcoxon W test was used. Pearson Chi-square test was used for discrete variables.

**Table 5** Postoperative morbidity

<table>
<thead>
<tr>
<th></th>
<th>LSR (n=52)</th>
<th>OSR (n=52)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall morbidity</td>
<td>22 (42.3%)</td>
<td>28 (53.8%)</td>
<td>.239</td>
</tr>
<tr>
<td>Minor complications</td>
<td>19 (36.5%)</td>
<td>20 (38.5%)</td>
<td>.839</td>
</tr>
<tr>
<td>Urine tract infection</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Major complications</td>
<td>5 (9.6%)</td>
<td>13 (25.0%)</td>
<td>.038</td>
</tr>
<tr>
<td>Anastomotic leakage⁠</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal bleeding⁠</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal abscess⁠</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Evisceration⁠</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Small bowel perforation⁠</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Richter hernia⁠</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0%)</td>
<td>1 (19%)</td>
<td>.315</td>
</tr>
</tbody>
</table>

1 = Re-operation; 2 = Blood transfusion; 3 = Percutaneous drainage. Morbidity and complications are reported per patient.

LSR = Laparoscopic Sigmoid Resection; OSR = Open Sigmoid Resection. Values were expressed as median and range for continuous variables. The distributions of dichotomous data were given in percentages. Independent Samples T-test was used for continuous variables with normal distribution, otherwise Wilcoxon W test was used. Pearson Chi-square test was used for discrete variables.

**Discussion**

The main finding demonstrated by this randomized controlled trial was that LSR patients had significantly decreased major postoperative complication rates as compared to OSR for symptomatic diverticulitis. Additional findings in the LSR study arm included...
In order to simulate clinical practice as closely as possible, data were analyzed on an intention to treat basis, which entailed that converted cases were analyzed within the LSR study arm. In the present study, the overall conversion rate was 19.2% (10 patients), which is higher than other series. \(^6\) This may be due to the definition of conversion used in this trial. In fact, 10 converted patients were converted to hand-assisted LSR. That makes conversion rate to OSR 9.6%.

A learning curve effect on conversions was unlikely, because all participating surgeons met the entry requirements. Nonetheless, the random order operations design is always biased in favor of interventions in wide use at pretrial routine.

Previous non-randomized studies have shown a reduction in minor complication rates, earlier resumption of food, shorter hospital stay, and better quality of life following LSR. \(^7\) \(^9\) In the present study, some of these improvements were confirmed, some were not. There were no differences in rates of minor complications in the study arms. The timing for resumption of food was comparable in both groups. Subjectively, patients who underwent LSR scored significantly better than OSR patients on VAS-pain score and SF-36 questionnaire. Several items of the latter showed improved role limitations due to physical health, role limitations due to emotional problems, social functioning, and pain. LSR patients left the hospital two days sooner than OSR patients. Although the average hospital stay may seem somewhat long, this was a reflection of the European health care system.

The present study has a number of limitations. The power calculation was based on a 23% reduction in postoperative complication rates. Although the source of this difference in favor of LSR was non-randomized data on diverticulitis, a similar reduction in complication rates had been reported in a randomized study on colon cancer. \(^10\) The hypothesis that LSR leads to a 23% reduction in postoperative complication rates in patients with symptomatic diverticulitis was not proven. However, the 15.4% difference in major complications in favor of LSR was statistically significant. A second drawback of the present study was that only 75% of all eligible patients were included for the reasons outlined in the flow diagram (Figure 2). The third limitation regarded the ascertainment bias of the allocation concealment. Despite the absence of any known blinding violations, the proportions of patients guessing correctly were 32% in the LSR arm, and 58% in the OSR arm.

In conclusion, LSR was associated with a 15.4% reduction in major complication rates, less pain, shorter hospitalization, and improved quality of life at the cost of a longer operating time. Elective LSR may well be the procedure of choice for patients presenting with symptomatic diverticulitis of the sigmoid colon.

![Pre-operative vs. 6 weeks post-operative SF-36 questionnaire results](image-url)

**Figure 3** Results of SF-36 questionnaire

**Figure 3** Results of SF-36 questionnaire. The arrows indicate significantly different data between LSR and OSR for PRF (p = .039), ERF (p = .024), SF (p = .015) and PN (p = .032). A higher score resembles a better outcome. PF = Physical functioning, PRF = Role limitations due to physical health, ERF = Role limitations due to emotional problems, VT = Energy/fatigue, MH = Emotional well-being, SF = Social functioning, PN = Pain, GHP = General health, HC = Health change.
Chapter 6

Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial. Short-term results of the Sigma-trial

References


Chapter | 6.1

Letter to the editor:
Laparoscopic vs. open colonic resection – better design and result presentation required for sufficient interpretation

Henrik Kehlet

Reaction on the letter to the editor

Bastiaan R. Klarenbeek
Donald L. van der Peet
Miguel A. Cuesta

Annals of Surgery 2009, 250 (3): 495-496
Letter to the editor

Klarenbeek et al. recently presented a double-blind trial comparing laparoscopic vs. open colonic resection for elective diverticulitis surgery. Although the authors should be congratulated for undertaking such a double-blinded trial, and where the primary endpoints were morbidity, it is unfortunate that the design and data presentation are made with many inadequacies that hinder sufficient interpretation. Thus, the duration of hospital stay was with no clear-cut discharge definitions, or analyses on why the patients stayed in hospital, although in the discussion it is mentioned that the long hospital stay (5-7 days) reflected the European health care system. So, are the authors studying traditions or the effect of laparoscopic vs. open surgery?

Also, pain scores were not presented (measured at rest or function?) and neither duration and opioid requirements during PCA as well as the overall pain management was not in accordance with current evidence (www.postoppain.org). Some patients received epidural analgesia, but there is no information on the type and content. There is no information about nausea and vomiting or why the patients did not tolerate early solid food or when defecation occurred. In the method section, it is mentioned that nasogastric tubes were removed at the end of operation but in table 4 between 44-58% had a nasogastric tube which is difficult to understand since the tube reinsertion rate was only between 8-10%.

Finally, it is a little surprising that the discussion does not refer to the concept of fast-track surgery where several trials (randomized and non-randomized as well as double-blind trials in elderly patients) have demonstrated much faster achievement of discharge criteria and shorter hospital stay – all evidence-based and with a positive effect on morbidity. Therefore, comparison of postoperative outcomes in relation to surgical technique needs to be combined with updated evidence-based care principles in order to allow sufficient interpretation. We hope that such methodological issues will be considered in future trials, also to achieve the optimal potential for minimal invasive colorectal surgery.

Reaction on the letter to the editor

We would like to thank Professor Kehlet for his useful comments in his letter to the editor about the Sigma-trial. His questions concern to which extent comparison of postoperative outcomes in relation to surgical techniques (laparoscopic versus open sigmoid resection in elective diverticulitis) need to be combined with updated evidence based care principles.

This randomized study was performed as a multicentric trial between 2002 and 2006. During this period, progressive implementation of fast-track principles have been adopted. Moreover the primary aim of the study was not to demonstrate the advantages of the perioperative care, in terms of the length of nasogastric tube, pain management and hospital stay, but the differences in major morbidity, in a double blindered way, after laparoscopic or open surgery.

The obtained hospital stay in our study reflects the European standards of laparoscopic and open surgery at the start of the trial in 2002 and probably even today. In the Sigma-trial clear discharge criteria were established. Patients were discharged after having had a bowel movement, tolerating solid food, able to walk properly, and feeling comfortable with oral analgesia. Our results, five versus seven days (statistically significant in favor of laparoscopic group) is clearly longer than the data obtained by Basse et al and Kehlet et al of two days, but quite comparable with the five and seven days obtained by King et al, comparing laparoscopic and open colonic resection within an enhanced recovery program.

Nevertheless some questions concerning the use of nasogastric tubes and pain management need explanation. Professor Kehlet addresses the high percentage of nasogastric tubes postoperatively. This may be considered, indeed, as a protocol violation since our study stressed its removal at the end of the procedure. An explanation might be a liberal policy of non-removal and re-insertion of nasogastric tubes at the recovery room by the anesthesiologists. Furthermore the “erroneous” nasogastric tubes were removed very soon after return from the recovery room, median duration of zero days in the laparoscopic group versus one day in the open group.

Concerning pain score presentation, VAS-pain scores were analyzed by repeated measures analysis, showing a significant lower level of pain in the laparoscopic group over the five day postoperative period (1.6 points on average; p .003). This significant
reduction in VAS-pain score is presented in the results section. Moreover duration of systemic analgesia is given in table 4, indicating some benefit of the laparoscopic approach. On the other hand opioid requirements, which would have been helpful in adequate pain assessment, were not registered. Furthermore, in our study, 16% of the included patients received epidural analgesia instead patient controlled analgesia and this may be also considered as violation of the protocol. To date thoracic epidural analgesia is favored over patient controlled analgesia, even though this technique seems to offer no advantages in combination with fast-track programs and there is no reduction of major morbidity rates in patients undergoing colorectal surgery. Moreover the current recommendations of the PROSPECT-workgroup were not clear at the start of the trial in 2002. Since then, several studies on enhanced postoperative recovery programs have been published, showing improvements in terms of pain, mobilization and hospital stay. In contrast no significant reduction in major morbidity has been proven.

In conclusion, trying to answer the main question of this letter: “Are the authors studying traditions or the effect of laparoscopic versus open surgery?”. The aim of this study was to demonstrate the possible benefits of the laparoscopic approach in terms of major morbidity. The Sigma-trial has shown a significant reduction in major morbidity if elective diverticulitis is approached laparoscopically instead of open. Moreover Professor Kehlet is right that the fast-track perioperative principles have contributed to a great extent the enhancement of the quality of life of our patients and the shorter hospital stay. Probably the combination of different factors of the fast-track treatment and the laparoscopic approach will provide the best outcome for our patients. Soon the LAFA-trial will define the role of laparoscopic surgery as part of the fast-track principles.

References

Letter to the Editor:
Re: Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial.

Pascal H.E. Teeuwen
Marieke G.J. Schouten
Andre J.A. Bremers
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Reaction on the letter to the editor
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Letter to the editor

We read with great interest the article on laparoscopic versus open sigmoid resection (LSR vs. OSR) in the January issue of Annals of Surgery. In this report, Klarenbeek et al. analyzed the outcome of 104 patients undergoing a laparoscopic or open procedure for Hinchey I, IIa and IIb diverticulitis. Patients having open surgery were more likely to develop major complications. Although laparoscopic surgery took longer to perform, blood loss was reduced, patients had less pain, experienced an improved quality of life, and were hospitalized for a shorter time.

It is our opinion that this study is of accurate methodological quality and we would like to congratulate the authors. However, we feel some issues need to be clarified before the conclusion that laparoscopic surgery decreases major morbidity in patients with diverticulitis can be justified.

First, the eligibility criteria state that patients having previous colorectal resection or median laparotomy (except for gynecologic or obstetrical reasons) were excluded from analysis. These criteria seem to be in contrast with the characteristics of patients given. Table 1 shows that 46.2% of the patients in the laparoscopic group and 48.1% of patients in the open group had previous abdominal surgery.

Second, the authors reduced surgeon bias to perform all procedures by surgeons skilled in both techniques stating that 15 laparoscopic sigmoid resections indicate the end of a learning curve. However, the referred literature uses total operative time as an indication of learning. More recent literature reports the assessment of a learning curve should not be limited to measurement of a decrease in operation time, but should also include the conversion and complication rates. Steady states are then reached at 70-80 laparoscopic interventions. All surgery was done in teaching hospitals where residents often do this kind of surgery. It is of interest to know if surgery was performed by residents as well and if their representation was equally distributed in both groups.

Third, overall morbidity in the open group was higher than in the laparoscopic group. How many complications were found in how many patients remains unclear. Many patients having a complicated postoperative course have more than one complication. Therefore it is essential to report on the number of patients with a complicated postoperative course to see whether the difference still reaches significance.

Fourth, our most important concern regards the open technique. One should not ignore that both open and laparoscopic surgery are developing and we doubt if the open group received state of art perioperative care. Enhanced recovery programs combine individual evidence-based elements in the care of patients receiving colorectal resection. The use of colonic lavages, nasogastric tubes and delayed diet after colorectal resection is proven obsolete and specifically applied to open surgery patients in this trial. Colonic lavage is proven to be harmful in patients undergoing open colorectal resection.6-6 Nasogastric tubes were frequently used although there is evidence that they are disadvantageous in patient undergoing abdominal surgery. A step up diet delays restoration of GI-function while restoring a normal diet as soon as possible and the use of prokinetic drugs enhances gastro-intestinal function.7

Furthermore, all patients received a patient controlled analgesia pump. Epidural analgesia is known to provide better pain relief, reduce the surgical stress response and may further reduce postoperative mortality and morbidity. Using epidural anesthesia not only reduces the stress response, but also diminishes the use of morphimetics that hamper GI function.8 The choice for midline laparotomy instead of a transverse incision in the lower abdomen facilitates pain management and is less likely to reduce pulmonary function.9 Enhanced recovery programs imply guideline to prevent excessive fluid administration, which is thought to contribute to an increased complication rate.10 In our centre, we reduced the incidence of complications after open colorectal resection to a third by applying enhanced recovery after surgery. Almost all patients received epidural anesthesia and had significantly less fluid intake. Regarding the major complication rate, there was a reduction from 30% to 16%. Hospital stay was significantly reduced from 9 to 6 days.

Reaction on the letter to the editor

We appreciate the ‘letter to the editor’ from dr. Teeuwen et al. responding to our manuscript entitled ‘Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial’. In this reaction we will attempt to clarify the issues mentioned by the authors.

First of all, the authors address the high percentage of patients included with previous abdominal operations despite the fact that previous colorectal surgery was one of the exclusion criteria. Similar numbers of previous abdominal surgery were present in both
groups (laparoscopic 46.2% and open 48.1%), these were interventions such as cholecystectomies, appendicectomies and gynecological operations.

During the design of the study in 2002, the available evidence suggested fifteen laparoscopic sigmoid resections to be the minimum experience for surgeons to participate in the trial. Moreover, all surgeons participating in our study at that time already exceeded this number and thus would also have met the more recent requirements. It is also mentioned that some bias might have been introduced by an unbalanced number of procedures performed by residents. Suggesting that more open surgery was performed by residents and more laparoscopic procedures by experienced staff. Accomplishing the study, all procedures were performed by surgeons who had met the requirements of our protocol.

Concerning the analysis and presentation of the complications, we agree that you should not count complications, but patients with a complicated course. Therefore the complications in this trial were reported per patient instead of per complication. If more than one complication per patient was present, we reported only the main complication that was thought to be at the basis of the complicated course, and not all accumulative complications. Our major morbidity rates of five in the laparoscopic group and thirteen in the open group represent five patients and thirteen patients respectively with major complications.

The Sigma-trial was performed as a multicentric study (five centers in three countries) between 2002 and 2006. During this period, implementation of fast track principles have been progressively adopted. Moreover the primary aim of the study was not to demonstrate the advantages of the perioperative care in terms of the length of nasogastric drainage, pain management and hospital stay, but the differences in major morbidity, in a double blinded way, after laparoscopic or open surgery.

The fourth comment in the letter is made about the development of open surgery and perioperative fast-track care. A few statements are made on obsolete or inadequate care, that were actually standard procedures at the start of the trial. And even though the referred literature shows no benefit of step-up diet, bowel preparation or nasogastric tubes, it is not to be expected that there is a negative or harmful effect on our primary endpoints. The same can be taken into account concerning epidural versus patient controlled analgesia (PCA). Nowadays we also prefer epidural analgesia in colorectal surgery, yet this does not result in a reduction in adverse morbidity outcomes. The use of epidural analgesia instead of PCA in 16% of the included patients could be considered as a protocol violation. In concordance with the authors we support the superiority of transverse incisions instead of longitudinal incisions, but also the superiority of the use of laparoscopic over open approaches. This has been established in the short term outcomes of all randomized studies on colon cancer and the here discussed Sigma-trial.

Moreover, in open elective sigmoid resection after diverticulitis, we have no experience with mobilization of the splenic flexure through a transverse incision.

Many questions were about the possible benefits of perioperative fast-track care in this study. The Sigma-trial has proven that major morbidity is less if elective diverticulitis is approached laparoscopically. Moreover, the progressive introduction of fast-track aspects in perioperative care will contribute to enhance the quality of life of our patients and shorten the hospital stay.
References


