
Management of Anastomotic Leakage in a Nationwide Cohort of Colonic Cancer Patients

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BACKGROUND: The mortality associated with anastomotic leakage (AL) after colonic cancer surgery is high and management often results in permanent fecal diversion. Preservation of bowel continuity in combination with proximal loop diversion (salvage) may reduce the number of permanent ostomies without jeopardizing safety.

STUDY DESIGN: This nationwide study used prospective data from the database of the Danish Colorectal Cancer Group, the National Patient Registry, and patient files. Patients with AL requiring surgery (grade C) were categorized according to the type of surgical treatment as anastomotic takedown with an end-ostomy or salvage. Thirty-day mortality, long-term mortality, and permanent ostomy rates were analyzed using multivariable logistic and Cox regression analyses.

RESULTS: Anastomotic leakage occurred in 593 of 9,333 patients (6.4%), of whom 507 with grade C were included. Takedown and salvage were undertaken in 433 (85.4%) and 74 (14.6%) patients, respectively. Salvage was performed more frequently for Hinchey I-II or minor anastomotic defects and resulted in increased likelihood of stoma reversal (adjusted hazard ratio 3.24, 95% CI 2.04 to 5.16, $p < 0.001$), corresponding to a risk of permanent fecal diversion of 16.8%, compared with 54.5% after takedown. Adjusted mortality rates were comparable between the groups. A second episode of AL after stoma reversal occurred more frequently in patients with end-ileostomies (10 of 64) than in patients with end-colostomies (1 of 64) or loop-ileostomies (3 of 36), $p = 0.017$.

CONCLUSIONS: Patients with Hinchey I-II and small anastomotic defect were safely managed by anastomotic salvage, which reduced the risk of permanent fecal diversion. Anastomotic salvage is a viable option for this subset of patients. (J Am Coll Surg 2014;218:940–949. © 2014 by the American College of Surgeons)

Anastomotic leakage (AL) after colonic surgery occurs in 3% to 10% of patients, depending on the location of the anastomosis.^{1,2} The consequences of AL are devastating, illustrated by a short-term mortality rate of 19% to 33%.^{1–4} In addition, AL contributes to an inferior oncologic outcome leading to decreased long-term survival.^{1,4,5}

Surgical management of AL is technically demanding and is associated with high postoperative morbidity,⁶ yet the choice of rescue procedure is predominantly based on the attending surgeon's personal experience rather

than solid evidence. There are only a few studies investigating the outcomes after different treatment strategies, and the small patient series preclude valid statistical analyses. Furthermore, the lack of a universally used definition of AL makes it difficult to compare outcomes between studies. The definition proposed by Rahbari and colleagues⁷ consists of a 3-grade scale based on the following clinical consequences of AL: no therapeutic intervention required (grade A), active therapeutic intervention without a laparotomy (grade B), and laparotomy (grade C). Stratification of AL has proven useful, as the clinical course in patients with major leakage is more severe.⁸ Most patients with AL require emergency surgical intervention, categorizing them into grade C.⁹

Various surgical strategies for management of AL are available. Takedown of the anastomosis with creation of an end-ostomy is the most frequently applied approach.¹⁰ This strategy, however, is associated with excessive numbers of patients with permanent fecal diversion^{11,12} and reduced quality of life because of ostomy-associated

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Abbreviations and Acronyms

AL	= anastomotic leakage
CCI	= Charlson comorbidity index
DCCG	= Danish Colorectal Cancer Group
HR	= hazard ratio
ICD-10	= International Classification of Disease
IQR	= interquartile range
OR	= odds ratio
reAL	= reanastomotic leakage

complications such as leakage, dermatitis, peristomal hernia, and sexual dysfunction.¹³ Another viable option includes salvage of the large bowel continuity using a loop-ostomy either alone or in combination with anastomotic repair or redo of the anastomosis.^{11,14,15}

In a questionnaire on management of AL sent to 350 members of the Dutch Society of Gastrointestinal Surgery, the answers demonstrated heterogeneous surgical strategies with a tendency toward preservation of left-sided anastomoses in physically fit patients.¹⁶ Recently, anastomotic salvage in 93 patients was associated with lower mortality and an increased likelihood of stoma reversal compared with takedown.¹⁷ However, control for confounding factors was not undertaken, raising the risk that patient selection, in part, could explain the observed benefits of anastomotic salvage.

There is therefore a need for large-scale studies to define the optimal management of AL. The aim of this nationwide study was to investigate the outcomes of anastomotic takedown compared with salvage in a large unselected cohort of patients with grade C AL after curative colonic cancer surgery.

METHODS

Study population and variables

This study was based on prospectively collected nationwide data from 2 population-based Danish registers; the database of the Danish Colorectal Cancer Group (DCCG) and the National Patient Registry. Information from the reoperations for AL extracted from patient records were merged with the 2 databases using the unique personal identification number given all Danish citizens. The primary outcome was 30-day mortality and secondary outcomes were long-term mortality and rate of permanent ostomies in patients subjected to anastomotic takedown or salvage for grade C anastomotic leakage.

Takedown of the anastomosis was defined as interruption of the bowel continuity with resection or transection of the anastomosis in combination with formation of an end-ileostomy, end-colostomy, or both. Anastomotic salvage was defined as preservation of the large bowel

continuity with repair or redo-anastomosis either alone or in combination with a proximal loop-ostomy.

Data from patients with a first-time diagnosis of colonic adenocarcinoma were prospectively entered into the DCCG database between May 2001 and December 2008. The DCCG database was approved by The Danish Data Protection Agency (Ref. no. 2000-53-0073) and includes at least 95% of all Danish patients with colorectal cancer.¹⁸ All patients included in the study underwent a curative colonic resection with a primary intraperitoneal anastomosis without a protecting stoma. The curative resection criteria required a colonic excisional specimen with at least 2 mm between the deepest tumor growth and the nonperitonealized resection margin and no tumor growth or distant disease left after completed surgery.

Patients with AL were identified in both the DCCG database and the National Patient Registry using the codes of the International Classification of Disease (ICD-10) for diagnosis and reoperation associated with AL (DT813A, KJWF00). Anastomotic leakage was defined as clinical symptoms suggesting AL and confirmed by contrast enema, CT, or surgery. The AL was then graded according to Rahbari and associates.⁷ Information on management of AL was obtained from ICD-10 codes in the National Patient Registry and from the original description of the reoperation in the patient records. Patients dying before treatment or with grade A or B AL were excluded, leaving patients with grade C AL for inclusion. The included patients were subdivided according to the surgical strategy into anastomotic takedown or salvage. The decision to perform a takedown or salvage procedure was taken exclusively by the local surgical staff members. The time to AL was calculated as the duration between the index operation and the primary reoperation for AL.

Short-term mortality was defined as any deaths within 30 days after the reoperation for AL. Long-term mortality encompassed all-cause mortality in patients surviving at least 30 days after the index operation. Information on vital status and complete restoration of bowel continuity was extracted from the National Patient Registry using the ICD-10 codes for stoma reversal (KJFG00-37). The rate of AL after reversal of a temporary ostomy (re-AL) was defined and analyzed as mentioned above.

Potential confounding covariates were extracted from the DCCG database or the National Patient Registry and included age, sex, tumor stage (Union for International Cancer Control, UICC), anastomotic location, surgical priority, surgeon specialization level, surgical approach (open or laparoscopic) at the index operation, time to AL, discharge before detection of AL, and comorbidity as assessed by the Charlson Comorbidity Index (CCI). This parameter reflects the cumulative likelihood

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