



Review

Intraoperative modifiable risk factors of colorectal anastomotic leakage: Why surgeons and anesthesiologists should act together



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HIGHLIGHTS

- There are many intraoperative risk factors of CAL which are modifiable by improvements in perioperative care.
- Multicenter registration study is necessary to determine the exact contribution of each intraoperative risk factor of CAL.
- Modifiable risk factors are: <36° Celsius, anemia, blood loss and transfusion, events and contamination, duration of surgery.
- Even in non-diabetes patients perioperative hyperglycemia increases the risk of CAL.
- Surgeons and anesthesiologists should cooperate in their continuous effort to reduce the number of CAL.

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ABSTRACT

Background: Colorectal anastomotic leakage (CAL) is a major surgical complication in intestinal surgery. Despite many optimizations in patient care, the incidence of CAL is stable (3–19%) [1]. Previous research mainly focused on determining patient and surgery related risk factors. Intraoperative non-surgery related risk factors for anastomotic healing also contribute to surgical outcome. This review offers an overview of potential modifiable risk factors that may play a role during the operation.

Methods: Two independent literature searches were performed using EMBASE, Pubmed and Cochrane databases. Both clinical and experimental studies published in English from 1985 to August 2015 were included. The main outcome measure was the risk of anastomotic leakage and other postoperative complications during colorectal surgery. Determined risk factors of CAL were stated as strong evidence (level I and II high quality studies), and potential risk factors as either moderate evidence (experimental studies level III), or weak evidence (level IV or V studies).

Results: The final analysis included 117 articles. Independent factors of CAL are diabetes mellitus, hyperglycemia and a high HbA1c, anemia, blood loss, blood transfusions, prolonged operating time, intraoperative events and contamination and a lack of antibiotics. Unequivocal are data on blood pressure, the use of inotropes/vasopressors, oxygen suppletion, type of analgesia and goal directed fluid therapy. No studies could be found identifying the impact of body core temperature or mean arterial pressure on CAL. Subjective factors such as the surgeons' own assessment of local perfusion and visibility of the operating field have not been the subject of relevant studies for occurrence in patients with CAL.

Conclusion: Both surgery related and non-surgery related risk factors that can be modified must be identified to improve colorectal care. Surgeons and anesthesiologists should cooperate on these items in their continuous effort to reduce the number of CAL. A registration study determining individual intraoperative risk factors of CAL is currently performed as a multicenter cohort study in the Netherlands.

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Abbreviations: CAL, Colorectal Anastomotic Leakage; CLS, Colon Leakage Score; MAP, Mean Arterial Pressure; MBP, Mechanical Bowel Preparation; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs.

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1. Introduction

Despite extensive research, the incidence of colorectal anastomotic leakage (CAL) has not decreased (3–19%) over the past decades [1–3]. Research on CAL may focus on the preoperative, intraoperative and postoperative phase.

Research on the *preoperative* period mainly determines patient and surgery related risk factors of CAL. Many of these factors, i.e. age and sex, are non-modifiable. Some are included in the Colon Leakage Score (CLS) that was developed to define the proportion of CAL-risk [4]. The CLS is a list of factors derived from a systematic search that can mainly be consulted prior to colorectal surgery. In addition, prehabilitation programs are being developed to optimize the patient's preoperative condition and nutrition. This promising approach will likely contribute to decrease CAL as many risk factors are related to the patients' lifestyle [5–8].

Many *intraoperative* surgical risk factors of CAL were subject of research projects. For instance, the role of laparoscopy or stapled anastomosis in right colonic resections was determined. Also the role of a defunctioning stoma for reduction of CAL after rectum resections was proposed [9,10]. However, the importance of many of these findings is still under debate. Non-surgical factors influencing the patients' condition during surgery including anesthesiological techniques might also have a large contribution to the risk of CAL. Recently, a multidisciplinary approach to prevent surgical complications is gaining interest. A combination of interventions was found to reduce the superficial surgical wound infection rate and possibly also CAL [11]. This observation warrants a close(r) collaboration of surgical and anesthesiological teams. Although other intraoperative variables such as operation time, blood loss and blood transfusion requirements have been widely accepted as risk factors, other intraoperative potentially modifiable risk factors are to be discovered yet.

The *postoperative* status of the patient is closely monitored to detect CAL as early as possible [12]. To date, many studies have been performed, and the Enhanced Recovery After Surgery program (ERAS) has been introduced to improve surgical outcome [13]. CAL due to a technical failure will most probably occur within the first few days after surgery. CAL due to other reasons will become evident within 3–6 days post surgery. Consequences of CAL such as peritonitis and intra-abdominal sepsis might be limited if treated promptly. Several studies trying to identify CAL at the earliest stage have met with limited success [12,14–19]. Imaging using radiological techniques has a disappointingly low sensitivity. An evidence-based algorithm is required for early detection of CAL.

Some modifiable risk factors possibly influencing the *perioperative* period such as medication (i.e. corticosteroids and non-steroidal anti-inflammatory drugs), poor nutritional status (i.e. body composition, albumin level) and other lifestyle related factors were not included in this review since these factors are considered as an integrated part of prehabilitation. The present review therefore systematically identified existing and modifiable *intraoperative* risk factors of CAL allowing for recommendations aimed at improving the quality of care for colorectal patients. Collaboration between surgeons and anesthesiologists on improving these items may be the key in the continuous effort to reduce the number of CAL.

2. Material and methods

A complete search was conducted on August 20th, 2015 using the PubMed version of MEDLINE, the OvidSP version of Embase and the Cochrane library (January 1970 to August 2015). Articles were

restricted to the English language. Reference lists were checked for additional studies. Both clinical and experimental studies were included. The main outcome measure was the risk of anastomotic leakage and other postoperative complications during colorectal surgery. Letters and papers omitting CAL as outcome were excluded. Determined risk factors of CAL were stated as strong evidence (level I and II high quality studies), and potential risk factors as either moderate evidence (experimental studies level III), or weak evidence (level IV or V studies) [20].

2.1. Search strategy

Two searches were performed separately by two independent researchers (SJ van Rooijen, D Huisman) with support from the clinical library of Máxima Medical Center (MMC) and VU Medical Center (VUmc). The search headings 'anastomotic leakage' and 'colorectal surgery' were used in combination with predefined keywords as established by colorectal surgeons of MMC and VUmc (hyperglycemia, glucose level, temperature, anemia, blood loss, tissue oxygen tension, inotropes, vasopressors, blood pressure, mean arterial pressure, hypotension, fluid administration, goal directed therapy, blood transfusion, antibiotics, analgesia, epidural, operation duration, intraoperative events, conversion, contamination and surgical experience; Fig. 1). If disagreement existed between the two researchers, a third author (F Daams) aimed at reaching consensus.

3. Results

The existing evidence regarding intraoperative modifiable parameters was classified into 3 categories, the general status of the patient, tissue perfusion and a surgery related section (Table 1).

3.1. General patient status and CAL

3.1.1. Hyperglycemia

Eight studies (human/experimental/retrospective/Cochrane review and 2 recent multicenter RCT's) showed a negative influence of a high preoperative HbA1C on the onset of CAL [19–26]. In general, hyperglycemia is regarded as a predictor of complications of any type in colorectal surgical procedures [27]. Diabetes mellitus, hyperglycemia and a high preoperative HbA1c are all independent risk factors of CAL [28–35]. Risk rates depend on level of hyperglycemia and starts at levels of >140 mg/dL with odds ratio's varying from 1.2 to 4.3. An observational study concluded a higher risk on adverse events due to intraoperative hyperglycemia (>180 mg/dL) in non diabetic versus diabetic patients (OR 5.1) [36]. However, other observational studies found that non diabetic patients sustained a significantly higher risk of postoperative adverse events compared to diabetic patients, probably as a result of perioperative hyperglycemia [21–26].

3.1.2. Temperature

Body core temperature below 36 °C beyond 60 min induces vasoconstriction and is associated with increased surgical site infection (SSI) rates [32,37]. Unfortunately, no studies indicating the relation of body temperature and CAL were identified. One animal study showed multidirectional changes in perioperative temperature on early stage tissue regeneration after small bowel resection [38].

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