

## Early Identification of Anastomotic Leakage following Hand-Sewn Colorectal Anastomoses

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#### Abstract

**Background and Aim:** Anastomotic leaks are among the most dreaded complications after colorectal surgery. A standardized postoperative score, the DULK (Dutch leakage) score, has been demonstrated to be a useful clinical tool in the diagnosis of anastomotic leakage. Author aimed in this study to evaluate the factors used for early diagnosis of anastomotic leakage after Hand-Sewn colorectal anastomoses.

**Material and Methods:** This prospective study was including 100 consecutive patients with colorectal anastomoses using hand sewn technique. Patients were operated at Tertiary care institute of India for the duration of 2 years. Patients follow-up was done to detect postoperative leak, study variables included hospital stay, wound infection, postoperative daily C-reactive protein, parameters of DULK-score and microbiological study of peritoneal fluid.

**Results:** Anastomotic leakage was diagnosed on median day 6 and all occurred before discharge from hospital. The hospital stay for the patients with anastomotic leakage was  $11.94\pm2.8$  days, which took significantly longer than those without AL, at  $7.05\pm0.54$  days (p  $\leq 0.05$ ) C-reactive protein was significantly higher in patients with leakage with a cut-off value of 120 mg/l on 3 rd postoperative day. Intraperitoneal bacterial colonization was significantly higher in patients with clinical evidence of AL. In the postoperative period, it was clearly observed that from POD 2 onwards, the values of serum CRP were significantly higher in anastomotic leakage group.

**Conclusion**: Thus, DULK-score has a major role in risk management and "failure to rescue" reduction. Its value is to improve risk management in GI surgery with the intent of reducing associated mortality by earlier, more reliable diagnosis of AL during early post-operative days. Routine application of DULK-score leads to a diagnosis of AL three days earlier.

Key Words: Anastomotic leak, Colorectal surgery, C-reactive protein, DULK score

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#### Introduction

Intestinal anastomosis as a viable surgical technique came into use after Antoine Lembert's (1802–1851) recognition of the importance of serosal apposition in an intestinal anastomosis, followed by William Stewart Halsted's (1852–1922) canine experiments identifying the mechanical strength and necessity of including the submucosal layer in an anastomosis.<sup>1</sup>Anastomotic leaks place a heavy burden on the patient and surgeon. Major disruptions typically present early and necessitate prompt and aggressive intervention to prevent the development of sepsis and multiorgan failure. Conservative treatment is associated with higher mortality except in minor leaks, which present rather late in the post-operative period and typically require deliberate, thoughtful and individualized management decisions.<sup>2</sup>

The overall incidence of AL after colorectal surgery is reported around 1.6%-16% and widely varies between hospitals and surgery departments depending on many factors linked both to the operator and the comorbidities of the patient.<sup>3</sup> The AL linked mortality ranges between 5%-28% and some authors suggest that the 30-day mortality rate is associated with the length of hospitalization.<sup>4-6</sup> Prediction and early recognition of AL is a challenging task for every surgeon due to the multitude of clinical presentations, which are often indistinguishable from the symptoms caused by the physiological inflammatory response after colorectal surgical procedures.<sup>7</sup> In most cases, these signs and symptoms may vary from mild abdominal pain and fever to ileus, fulminant peritonitis, sepsis and death.<sup>8</sup> Anastomotic leaks usually appear between day 5 to 8 after the surgery, but in some cases it may show a delayed presentation as late as the 13th postoperative day.<sup>9</sup>

The colon leakage score (CLS) can predict the risk of anastomotic leakage following left sided colorectal surgery. After further validation, this score may help the surgeon make a more individualized, safer decision regarding whether to perform an anastomosis or a make a (defunctioning) stoma.<sup>10</sup>

A standardized postoperative score, the DULK (Dutch leakage) score, has been demonstrated to be a useful clinical tool in the diagnosis of anastomotic leakage.<sup>11</sup>E. coli and E. faecalis can be detected in drainage fluid after colorectal surgery by means of culture. Therefore, these bacteria are well suited to serve as indicator organisms for diagnosis of anastomotic leakage on peritoneal drainage fluid.<sup>12</sup>Early and persistent elevation of C-reactive protein after colorectal surgery with anastomosis has been used as a marker of anastomotic leakage.<sup>13</sup> Author aimed in this study to evaluate the factors used for early diagnosis of anastomotic leakage after Hand-Sewn colorectal anastomoses.

#### **Material and Methods**

This prospective study was including 100 consecutive patients with colorectal anastomoses using hand sewn technique. Patients were operated at Tertiary care institute of India for the duration of 2 years. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. All operations were carried out by a consultant of surgery who guaranteed adequate exposure and access, gentle handling of the bowel, adequate hemostasis, approximation of well-vascularized bowel, absence of tension at anastomosis, good surgical technique and avoidance of fecal contamination.

Intraoperative testing of anastomosis was done. In addition to the demographic data, other risk factors were collected, such as age, sex, body mass index (BMI), toxic habits, The American Society of Anesthesia (ASA) scale, need for perioperative transfusion, neoadjuvant therapy, indication for surgery, surgical procedure performed, intention of the surgery, surgical technique, type of anastomosis, complications during surgery, operating time, use of drain tubes, distance to anal margin and tumor stage.

Patients underwent colorectal surgery including emergency and elective surgeries, and both sexes and all ages were included. Hemodynamically unstable patients e.g., patients with septic shock, sever polytraumatized patient with multiple abdominal organ affection were excluded. All patients were subjected to preoperative assessment in the form of history taking, general and local clinical examination and investigations in the form of laboratory and radiological, operation where all patients were operated after performing the definitive therapeutic surgery which requires resection, hand sewn intestinal anastomosis using Vicryl 2/0 was done in double layer interrupted anastomosis.

Intraoperative leak test to confirm adequacy of anastomosis and post-operative follow up in which all patients were evaluated daily at the first 5 days postoperative regarding fever, heart rate, blood pressure, respiratory rate, urine output, mental status, nutritional status, signs of ileus (abdominal distention, vomiting, constipation), abdominal pain, signs of infection (increased leukocytic count), kidney function (increased urea and creatinine), frank anastomotic leak, surgical site infection, wound dehiscence and burst abdomen. Daily CRP postoperative for 5 days. Microbiological study of peritoneal fluid (aerobic and anaerobic cultures were done from the drain fluid on days 1, 3 and 5 postoperative).

#### Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

#### Results

Present study included 100 patients, who underwent large intestinal anastomosis for the duration of 2 year, 60 of them were performing elective surgery and 40 from emergency, clinically evident AL occurred in fifteen patients (15%). Six of those were admitted from emergency while nine of them were performing elective surgery (Table 1). Author performed this study at 62 male and 38 female patients. From 62 male patients, 10 patients developed AL, while five female patients from 38 developed AL.

Anastomotic leakage was diagnosed on median day 6 and all occurred before discharge from hospital. Fifteen patients were urgently re-operated on 8 patients had simple loop ileostomy, other 7 patients had double barrel colostomy. Wound infection was significantly higher in anastomotic leakage group 12 from 15 patients (83.3%) versus 11 from 85 patients in patients without anastomotic leakage ( $p \le 0.05$ ).

The hospital stay for the patients with anastomotic leakage was  $11.94\pm2.8$  days, which took significantly longer than those without AL, at  $7.05\pm0.54$  days (p  $\le 0.05$ ) (Table 1).

In this study, colon leakage score was considered positive when a score of more than 11 points was recorded during the primary admission (preoperative and intraoperative). Number of patients with positive score 17 about 17% while there were 83 patients with negative score of 83%. Total sensitivity was 67%, total specificity was 90.5%, accuracy about 88%, total positive predictive value was 56.5%, and total negative predictive value was 94.5%. In this study, DULK score was considered positive when a score of more than three points was recorded on any time during the primary admission. Number of patients with positive score was 23 about 23% while there were 77 patients with negative score about 77% ( $p \le 0.05$ ).

Total sensitivity was 84%, total specificity was 88%, accuracy about 87%, total positive predictive value was 55% and total negative predictive value was 97%. E. coli, E. faecalis, Klebsiella, and Bacteroid microorganism were significantly more in AL group in first, third, fifth days postoperatively. E. coli was the most common micro-organism detected in patients with AL. In this study, a cut-off value of 120 mg/l on POD, 3 maximized the sensitivity (82.5%) and specificity (93.5%) and a positive predictive value (71.1%) and a negative predictive value (96.8%) of serum CRP in predicting the risk of leakage. In the postoperative period, it was clearly observed that from POD 2 onwards, the values of serum CRP were significantly higher in

anastomotic leakage group. In group without anastomotic leakage, mean serum CRP reached a peak on POD 2, followed by a rapid decline thereafter  $(p \le 0.05)$  (Table 2).

Table 1. Demographic Distribution of study participants										
Variable	No anastomotic leakage N=85		With anastomotic leakage N–15		P value					
	47 45+14 12		61 98+7 54		0.03*					
Age	47.45±14.12		01.96±7.54		0.05					
BMI	28.30±4.50		30.12±3.45		0.34					
Gender										
Male	52	61.17	10	66.66						
female	33	38.82	5	33.33	0.2					
ASA										
Ι	35	41.17	1	6.6						
II	40	47.05	7	46.66	0.03*					
III	10	11.76	7	46.66						
Wound infection										
No	74	87.05	3	20						
yes	11	12.94	12	80	0.02*					

<b>Fable 1: Demographic</b>	Distribution of study	participants
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\* indicates statistically significance at  $p \le 0.05$ 

Table 2: Comparison between the studied groups according to C-reactive protein at third
postoperative day

C-RP (POD3)	No anastomotic leakage N=85		With anastomotic leakage N=15		P value
Negative	79	92.94	3	20	
positive	6	7.05	12	80	0.002*

\* indicates statistically significance at  $p \le 0.05$ 

#### Discussion

Surgeons are all too familiar with the potentially devastating consequences of an anastomotic leak. Patients classically develop agonizing abdominal pain, tachycardia, high fevers, and a rigid abdomen, often accompanied by hemodynamic instability. In these cases, urgent return to the operating room for peritoneal washout and fecal diversion is generally required; prolonged stays in the intensive care unit and death are not uncommon. The mortality rate for an anastomotic leak in the literature typically is in the 10% to 15% range.<sup>14-17</sup> Further, anastomotic leakage has been associated with increased local recurrence and diminished survival after colorectal cancer surgery.<sup>18,19</sup> However, a large number of patients ultimately found to have an anastomotic leak develop a more insidious presentation, often with low-grade fever, prolonged ileus, or failure to thrive.<sup>20</sup> In these patients, making the diagnosis may be much more difficult as the clinical course is often similar to other postoperative infectious complications. Radiologic imaging is usually required; even then, the diagnosis may be elusive or at least uncertain.

The overall percentage of leakage in this study was 15%. Other studies showed wide difference in leakage rate. The original study of Dulk et al, showed 9.4% AL rate less than this tudy.<sup>11</sup> The study of Kostas et al, showed anastomotic leaks occur as same as this study in approximately 15% of patients undergoing colorectal surgery.<sup>21</sup> Buchs et al, study showed that leak rate higher than this study reached up to (39%).<sup>22</sup> Konishi and his colleagues reported that the overall incidence of colorectal AL, ranging from 0.5% to 30%.<sup>23</sup> Komen et al, reported that leakage rate varying between 2 and 24%.<sup>1</sup>

This study showed that the incidence of AL was correlated with higher age, with mean age of leak group 61.98 years and (p value 0.02). These results are in keeping with a study by survey of the Italian Society of Colorectal Surgery that included a group of 520 patients who had undergone a low anterior resection were evaluated. The incidence of AL was correlated with higher age, with mean age of leak group 69 years and (p value 0.02).<sup>24</sup> Similar results obtained from a study by Jung et al, old age was significant risk factor (p value 0.021).<sup>25</sup> This study found that male gender was a risk factor for leakage. Most likely, gender only influences low anastomoses, where the narrower male pelvis makes dissection and anastomoses more challenging.<sup>26</sup> In a prospectively evaluated cohort of male patients, Branagan et al, noted that there was a substantially higher rate of leakage in male (5.6%) compared with female patients (2.4%) throughout the colon and rectum.<sup>27</sup> Lipska et al, found the same result, as regard male sex being a risk factor.<sup>28</sup>

Distinguishing an "anastomotic leak" from a postoperative abscess, especially retrospectively, can be very difficult. Unless concomitant review is undertaken of patients classified as having a postoperative abscess, some leaks will be missed. In many cases in our database, we were able to show that a postoperative abscess was caused by a small anastomotic leak. Although the literature is replete with studies that specify a rate of anastomotic leakage, it is seldom possible to know what constitutes a "leak." Bruce et al performed a systematic review of studies measuring the incidence of anastomotic leaks after gastrointestinal surgery; in the 97 studies reviewed, there were a total of 56 separate definitions of anastomotic leak.<sup>28</sup> A leak may be defined by the need for reoperation, clinical findings, or radiologic criteria, making comparisons between studies difficult or impossible. Further, there is typically a "cutoff" at 30 days postoperatively and/or hospital discharge for diagnosis, which will fail to capture many leaks, as our study clearly shows.

This study showed no statistical difference between elective and emergent anastomosis as regard leakage development. However, Choy et al, identified emergency procedures as a significant risk factor for anastomotic leak.<sup>29</sup> Also Choi et al, advocated that the emergency intervention was the most significant factor associated with anastomotic leakage as surgery performed in an emergency setting, on debilitated patients without adequate preoperative preparation and stabilization, has an increased risk for anastomotic dehiscence.<sup>30</sup>

This study had a specificity of 88.5% which is higher than specificity at Martin G et al. study which was 55.6% and both of them are higher than specificity of Dulk et al, which is 53.6%. At this study, the median interval between appearance of the initial signs of clinical deterioration i.e. a DULK-score >3 and the confirmation of AL was three days While at the study of Martin G et al, it was more helpful as it permitted diagnosis of anastomotic leak three and half days earlier.<sup>31</sup> In the study of Warchkow et al, concluded that the cut-off point that they established on the fourth day of the postoperative period was 135 mg/l, with an NPV of 89%, 68% sensitivity and 83% specificity.<sup>32</sup> Platt et al observed that, on post-op day 3 and with a cut-off point of 190 mg/l, sensitivity was 77% and specificity 76%.<sup>33</sup> Singh et al, concluded that the best day is the POD4 with a cut-off point of 124 mg/l, which obtained an NPV of 97%, a PPV of 21%.<sup>34</sup> Fernandez et al, observed that CRP was useful on postoperative days 4 with cut-off point of 159.2 mg/l, sensitivity 75%, specificity 89% and NPP 96%.<sup>35</sup>

#### Conclusion

Thus, DULK-score has a major role in risk management and "failure to rescue" reduction. Its value is to improve risk management in GI surgery with the intent of reducing associated mortality by earlier, more reliable diagnosis of AL during early post-operative days. Routine application of DULK-score leads to a diagnosis of AL three days earlier. C-reactive protein is a simple way to ensure a safe discharge from hospital after colorectal surgery. Patients with CRP values >120 mg/l on the third postoperative day should not be discharged.

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Conflict of interest: None declared.

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