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# Understanding Anastomotic Healing in Colo-Rectal Surgery; a Multicentric 5-Year Analysis of Predictive Factors for Integrity and Fistula Formation

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Article

# Understanding Anastomotic Healing in Colo-Rectal Surgery, a Multicentric 5-Year Analysis of Predictive Factors for Integrity and Fistula Formation

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## Abstract

**Background:** Anastomotic leakage (AL) remains one of the most feared complications after colorectal surgery. This study aims to identify preoperative risk factors for AL using a five-year dataset from two Romanian surgical clinics. **Material and Methods:** A retrospective cohort of 155 patients undergoing colorectal resection with primary anastomosis (105 from "Colentina" Hospital and 50 from "Dr. I. Cantacuzino" Hospital) was analyzed. Preoperative demographic, clinical, and laboratory data were extracted and assessed using univariate and multivariable logistic regression. Statistical analyses were performed using IBM SPSS. **Results:** The overall AL rate was 10.3%. Multivariable analysis identified high ASA class (OR 17.6;  $p = 0.001$ ), emergency surgery (OR 32.2;  $p = 0.0007$ ), and heavy alcohol use (OR 15.3;  $p = 0.004$ ) as independent predictors of leakage. While low preoperative albumin and smoking were associated with leakage in bivariate analysis, these did not remain significant after adjustment. Notably, all laboratory markers were based on preoperative values, distinguishing our approach from prior studies that commonly evaluate postoperative biomarkers. No statistically significant effect was found for neoadjuvant chemotherapy or radiotherapy after controlling for other covariates. **Conclusions:** High ASA score, alcohol abuse, and emergency surgery were the strongest independent predictors of AL in our cohort. The lack of predictive power of certain widely reported factors, such as low albumin, may reflect our dataset's focus on preoperative optimization. These findings support the use of individualized risk assessment and reinforce the role of preoperative preparation in reducing leak incidence in colorectal surgery.

**Keywords:** colorectal surgery; anastomotic leak; ASA score; risk factors; surgical outcomes

## 1. Introduction

Colorectal cancer (CRC) remains a substantial global health burden, highlighting the need for continual medical advances [1]. Anastomotic leakage (AL) is a significant complication following colorectal resection, with reported occurrences typically ranging from 2% to 19%, while some studies indicate a variation from 6% to 30%, with a larger prevalence in low rectal anastomoses compared to colonic resections [2–11]. It is persistently linked to heightened morbidity, mortality, reoperation rates, permanent stoma formation, and poorer oncological outcomes in rectal cancer [12,13]

Recent narrative and systematic reviews categorize risk factors into non-modifiable, modifiable, and technical/surgical categories. Non-modifiable characteristics encompass male sex, substantial

comorbidity burden (cardiovascular, pulmonary, diabetes), and advanced tumor stage; a low rectal tumor placement and minimal distance from the anal margin are consistently associated with elevated leak rates[14–17]

Surgical factors, particularly anastomotic height, are crucial determinants; leak rates can approximate 19% for low rectal (coloanal) anastomoses, in contrast to about 1–3% for more proximal colon anastomoses [18,19]. The choice of surgical method (laparoscopic versus open) has negligible effect on the risk of leaking, as studies indicate comparable incidence rates of leaks across minimally invasive and open resections [20]. Utilization of a protective diverting stoma significantly diminishes anastomotic leakage in low anterior resection, according to research [21] A meta-analysis indicates that clinically significant leaks occur in approximately 6% of diverted patients, compared to around 18% in those without diversion ( $p < 0.00001$ )[22]. Transanal decompression tubes (TDT) have been investigated as a beneficial, safe, prophylactic intervention, yielding conflicting outcomes. TDT is intended to facilitate endo-luminal pressure reduction and fecal diversion, hence providing a protective effect on anastomotic healing. Some analyses indicate a reduction in leak rates, whilst others demonstrate no substantial overall advantage to the routine application of TDT [23–34]

Equally crucial is the establishment of a tension-free, well-perfused anastomosis, as insufficient perfusion or high tension at the site significantly heightens the risk of leakage [35].

Intraoperative perfusion evaluation, such as indocyanine green fluorescence, correlates with markedly reduced leak rates by verifying sufficient blood flow prior to finalizing the anastomosis [35–39].

The anastomotic technique (hand-sewn versus stapled) does not significantly affect leak incidence; recent extensive research and reviews have demonstrated no difference in leak rates between stapled and hand-sutured anastomoses [40–43]

Compliance with ERAS guidelines and the volume of procedures performed by hospitals or surgeons also affect risk, indicating that systemic factors and standardized pathways can reduce patient- and tumor-related risks [16,44,45]

Alterable patient-related factors encompass smoking, excessive alcohol intake, obesity, malnutrition, and immunosuppression (due to steroids and certain biologics), in addition to exposure to preoperative radiation and perioperative blood transfusions [14,46–48]

Extensive cohort studies and meta-analyses validate that male gender, obesity/high BMI, diabetes, pulmonary disease, and elevated ASA class are independent predictors of anastomotic leakage following colon or colorectal cancer surgery [15,44,48]

Reduced blood albumin levels and several indicators of malnutrition are increasingly recognized as significant predictors of leakage in rectal cancer, emphasizing the necessity of prior rehabilitation and nutritional enhancement [47,49]

## 2. Materials and Methods

This study was designed as a retrospective, multicenter analysis conducted at two surgical centers in Bucharest, Romania. These included all the Surgical patients of “Colentina” Clinical Hospital and the patients from General Surgery Clinical Ward I of “Dr. I. Cantacuzino” Clinical Hospital. All adult patients (aged 18 years and older) who underwent an anterior colorectal resection with a primary colorectal anastomosis between January 2020 and December 2024 were identified through hospital databases, operative logs and patients’ charts. This time frame was chosen to provide a 5-year experience from both centers. The study focused on colorectal anastomotic healing and fistula formation (anastomotic leakage-AL).

Exclusion criteria included surgeries without a primary anastomosis (e.g., those ending in an end stoma); procedures performed solely for palliation (e.g., diversion for advanced disease without an anastomosis); and cases with incomplete perioperative records. These criteria ensured that only cases with complete anastomotic data were analyzed. After applying these criteria, all remaining eligible patients from both institutions were included in the study cohort.

Clinical data were extracted retrospectively from patient medical charts, operative reports, and laboratory records at each hospital. Data collection was standardized between the two centers to ensure consistency. Preoperative variables obtained included patient demographics and health status: age, sex, body mass index (BMI), major comorbidities (such as diabetes and cardiovascular disease), preoperative ASA (American Society of Anesthesiologists) physical status score, smoking status, and alcohol use. In addition, key pre-operative laboratory values were recorded for each patient, all of which were measured within 48 hours prior to surgery. These lab tests included hemoglobin level, white blood cell (WBC) count, serum creatinine, coagulation parameters (including international normalized ratio, INR), C-reactive protein (CRP), serum albumin, and total protein levels.

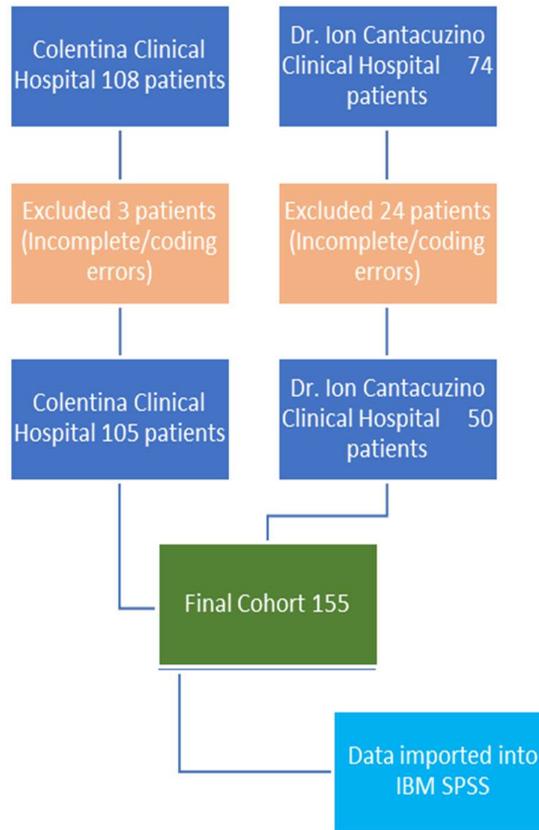
Intraoperative variables were documented based on operative reports. These included the type of resection performed and the anatomical level of the anastomosis (categorized as high, middle, or low rectal anastomosis based on the distance from the anal verge). Surgical urgency was noted as elective or emergency surgery. The surgical approach was recorded as open vs. laparoscopic (both centers do not have access to robotic assisted surgery). The anastomosis technique was classified as hand-sewn (manual suturing) versus stapled anastomosis. We also recorded whether the patient received perioperative blood transfusions and whether a protective stoma was created during the initial surgery. Additionally, at the "Dr. I. Cantacuzino" center it was routine practice to place a transanal decompression tube for low anastomoses; the use of a transanal drainage tube was therefore captured as a variable (yes-1/no-0) for each case.

For each patient, the primary outcome of interest was the occurrence of an AL (anastomotic dehiscence/fistula formation) in the postoperative period. AL was defined as any clinical or radiologic evidence of an anastomotic dehiscence leading to intra-abdominal infection, fecal discharge from drains, or need for re-intervention. The presence or absence of AL was determined from postoperative clinical notes, imaging reports, and intervention records. For cases of leakage, we also noted the timing of leak detection (categorized as early, within 7 days post-operatively, or late, after 7 days) as documented in the charts.

All data were entered into a secure database and analyzed using IBM SPSS Statistics software. Descriptive statistics were used to summarize the patient cohort and operative details. Categorical variables were expressed as frequencies or percentages, while continuous variables were summarized by their mean and standard deviation or median and interquartile range, as appropriate. Office Excel was used for visual representation of the statistical analysis.

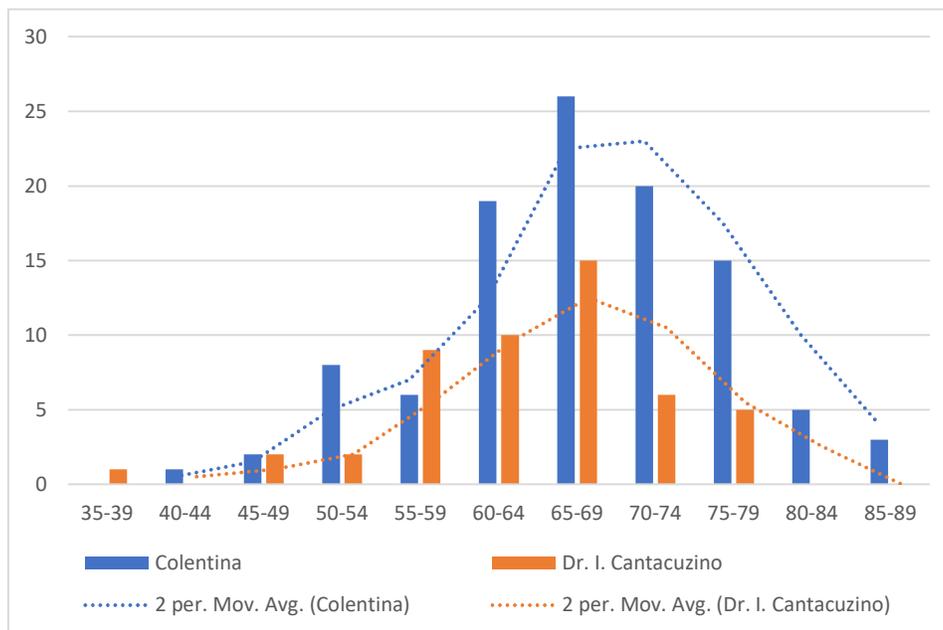
### 3. Results

After the initial hospital database patient search, we identified 108 potential patients from "Colentina" Clinical Hospital and 74 potential patients from "Dr. I. Cantacuzino" Clinical Hospital. After data collection, charts and operation logs review 3 patients from "Colentina" were excluded for incomplete records and coding error and 24 patients were excluded from "Dr. I. Cantacuzino" database for coding inconsistencies and incomplete data. (Figure 1)



**Figure 1.** Patients’ inclusion process.

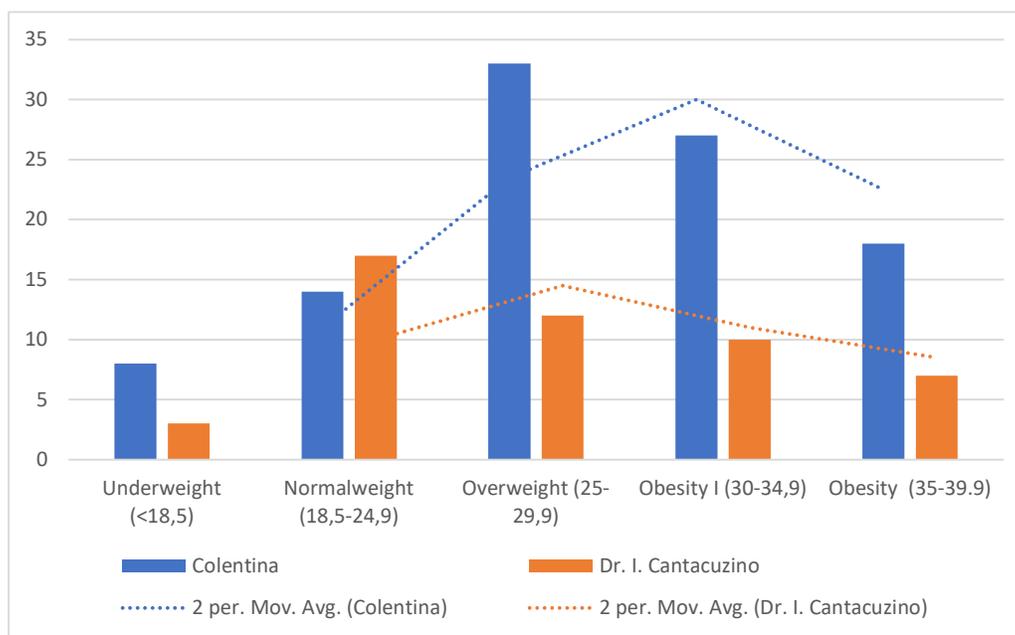
“Colentina” patients were slightly older (mean  $67.4 \pm 9.0$  vs  $64.0 \pm 8.2$  years,  $p \approx 0.021$ ) (Figure 2) and had more laparoscopic procedures (38.5% vs 6.1% laparoscopic,  $p < 0.001$ ). “Dr. I. Cantacuzino” patients more often received neoadjuvant therapy (chemotherapy: 33% vs 15%,  $p \approx 0.025$ ; radiotherapy: 40.8% vs 15.4%,  $p \approx 0.001$ ).



**Figure 2.** Distribution of Age by Center.

Sex distribution and rates of comorbidities were similar, across both centers.

The “Colentina” center demonstrates a higher concentration of patients with BMIs above the population median (especially in the 30–35 kg/m<sup>2</sup> range), reflecting a higher prevalence of overweight and potentially obese patients (Figure 3). By contrast, “Dr. I. Cantacuzino” BMI distribution shows a wider variance and a heavier tail toward lower BMI categories (<25 kg/m<sup>2</sup>), including several outliers below 20 kg/m<sup>2</sup>. These findings suggest demographic or referral pattern differences between centers.



**Figure 3.** Distribution of BMI by Center.

While both distributions peak around 27–30 kg/m<sup>2</sup>, the Gaussian kernel density estimate (KDE) for “Colentina” is unimodal and sharper, indicating tighter clustering around the mean, whereas “Dr. I. Cantacuzino” KDE is flatter, suggesting more heterogeneity in body habitus.

Other preoperative factors (anemia, leukocytosis, platelet count, CRP, albumin, protein, creatinine, INR abnormalities) were similar in both patient cohorts.

Overall AL rates were comparable (Colentina 10.6%, Cantacuzino 10.2%,  $p \approx 1.00$ ).

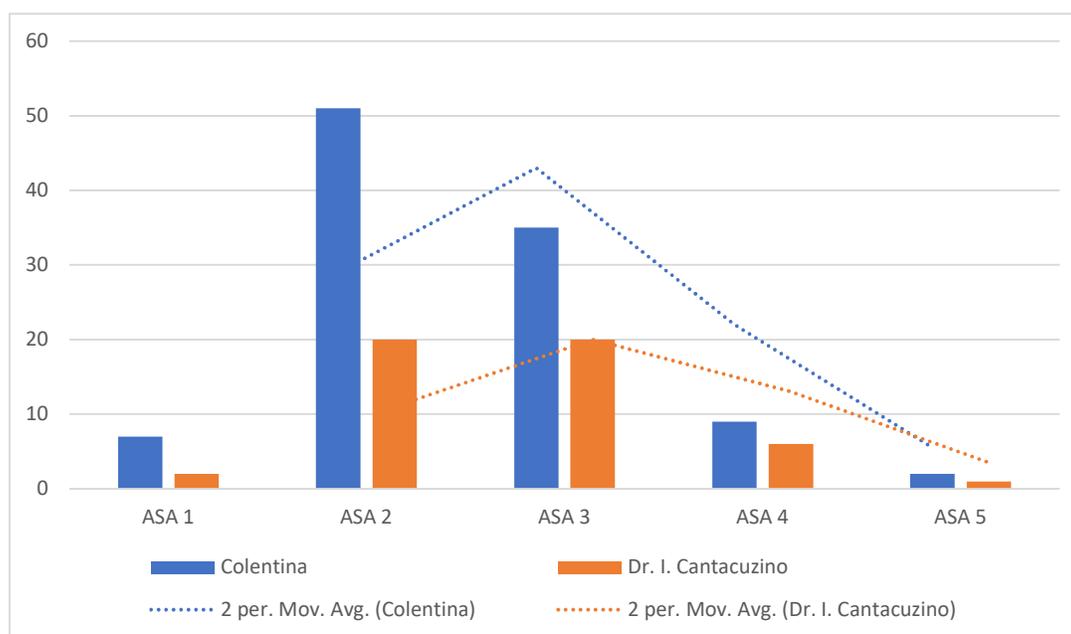
As seen in Table 1, the prevalence of key comorbidities like diabetes, cardiovascular disease, and other systemic illnesses, was comparable between the two centers. Diabetes was present in 22.1% of patients at “Colentina” and 18.4% at “Dr. I. Cantacuzino” ( $p = 0.75$ ), while cardiovascular comorbidities affected 60.6% and 65.3% of patients, respectively ( $p = 0.70$ ). Other comorbidities were evenly distributed (58.7% vs. 57.1%,  $p = 1.00$ ). None of these differences reached statistical significance, suggesting a broadly similar baseline health status across the two institutional cohorts.

**Table 1.** Baseline Clinical and Treatment Characteristics of Patients by Surgical Center.

Characteristic	Colentina (n=104)	Dr. I. Cantacuzino (n=49)	p-value
Age, years (mean±SD)	67.4±9.0	64.0±8.2	0.021
Female sex, n (%)	42 (40.4%)	22 (44.9%)	0.72
Diabetes (yes), n (%)	23 (22.1%)	9 (18.4%)	0.75

Cardio - Vascular comorbidity (yes), n (%)	63 (60.6%)	32 (65.3%)	0.70
Other comorbidity (yes), n (%)	61 (58.7%)	28 (57.1%)	1.00
Neoadjuvant chemotherapy (yes), n (%)	16 (15.4%)	16 (32.7%)	0.025
Neoadjuvant radiotherapy (yes), n (%)	16 (15.4%)	20 (40.8%)	0.001
Laparoscopic surgery, n (%)	40 (38.5%)	4 (6.1%)	<0.001
Emergency surgery, n (%)	5 (4.8%)	0 (0%)	0.28
Protective stoma (yes), n (%)	3 (2.9%)	1 (2.0%)	1.00
Anastomotic leak, n (%)	11 (10.6%)	5 (10.2%)	1.00

“Colentina” center’s case mix is skewed toward lower-risk patients, with the majority of cases classified as ASA I–II (Figure 4). Specifically, ASA I and II collectively account for nearly 70% of “Colentina” cohort. In contrast, “Dr. I. Cantacuzino” presents a more even distribution across ASA classes I–III, with notably higher proportions of ASA III patients and a small but visible representation of ASA IV. ASA V appears rarely in either group but is not absent.

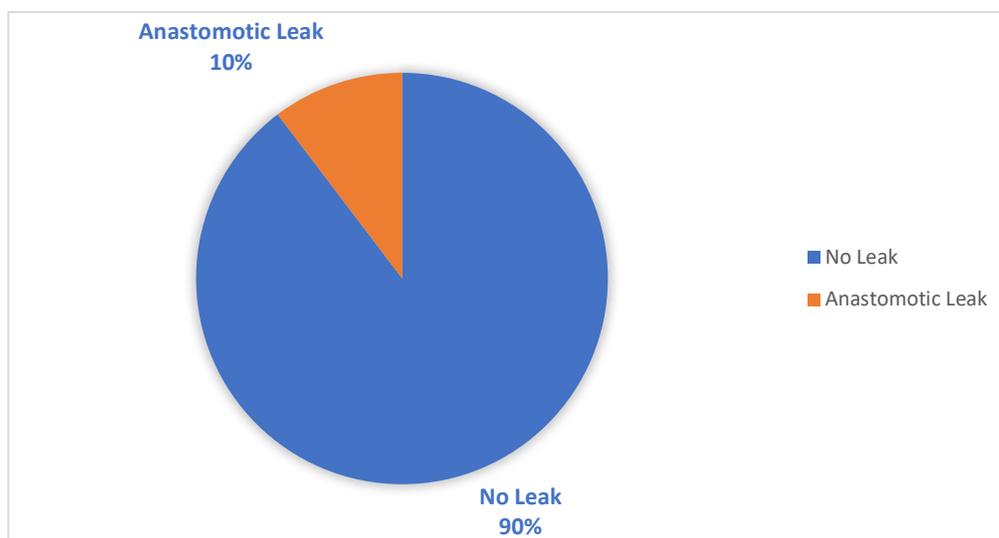


**Figure 4.** Distribution of ASA by Center.

The kernel density estimate (KDE) curves further emphasize the divergence in patient complexity: “Colentina” curve is left-shifted and peaks at ASA II, while “Dr. I. Cantacuzino”’s is flatter, with greater density at ASA III and a longer tail extending toward higher-risk strata.

This finding is consistent with previous inter-center comparisons and reflects a differing case profile between the two institutions. The higher rates of open surgical approaches and neoadjuvant treatments observed at “Dr. I. Cantacuzino” may be influenced by a greater proportion of lower rectal tumors and tailored treatment strategies, rather than necessarily indicating a higher overall case complexity.

Across both centers, the overall AL rate was 10.3% (16/155). Of these, 12 cases (75%) were identified as early leaks (within 7 days postoperatively), while 4 cases (25%) occurred later. (Figure 5)



**Figure 5.** Overall incidence of AL. Out of 155 colorectal anastomoses, 16 (10.3%) developed an anastomotic leak.

We analyzed the datasets to assess each blood marker’s association with leak risk. For each variable (hemoglobin, WBC, CRP, albumin, total protein, creatinine, INR), we fit a univariate logistic regression (outcome=leak yes/no) to estimate the odds ratio (OR) and p-value (Table 3).

**Table 3.** Univariate Analysis of Preoperative Laboratory Markers as Predictors of Anastomotic Leakage.

Variable	Odds Ratio (OR)	95% CI	p-value
Hemoglobin (g/dL)	1.58	0.41–6.12	0.51
WBC ( $10^3/\mu\text{L}$ )	1.68	0.43–6.54	0.45
CRP (mg/L)	1.17	0.14–10.0	0.89
Albumin (g/dL)	2.41	0.25–23.1	0.45
Total Protein (g/dL)	1.03	0.12–8.75	0.98
Creatinine (mg/dL)	1.66	0.49–5.64	0.42
INR	4.89	0.42–57.4	0.21

Of the eight markers, none showed a statistically significant association in our data, but the point estimates suggest possible trends. Hemoglobin had OR $\approx$ 1.58 (95% CI 0.41–6.12, p=0.51), indicating a non-significant trend toward higher leak risk with higher hemoglobin. WBC had OR $\approx$ 1.68 (95% CI 0.43–6.54, p=0.45), also non-significant; however, elevated preoperative (Table 2).

CRP had an estimated OR $\approx$ 1.17 (95% CI 0.14–10.0, p=0.89) for each unit increase, i.e., a negligible effect. In our data, preoperative CRP did not significantly predict leak.

Albumin showed OR $\approx$ 2.41 (95% CI 0.25–23.1, p=0.45). Although this effect was not significant, on AL prediction.

Our data trend hints to the suggestion that poorer nutritional status (lower albumin or total protein) may impair anastomotic healing. Total Protein had  $OR \approx 1.03$  (95% CI 0.12–8.75,  $p=0.98$ ), showing no effect.

Creatinine gave  $OR \approx 1.66$  (95% CI 0.49–5.64,  $p=0.42$ ) per unit; elevated creatinine may reflect comorbidity or poor perfusion, but no association was found here.

INR had  $OR \approx 4.89$  (95% CI 0.42–57.4,  $p=0.21$ ) per unit increase, with very wide confidence limits. A higher INR (coagulopathy) might theoretically impair healing or signal liver disease, but our CI spanned unity due to limited sample size, so this was not statistically significant.

We found no blood marker with a significant predictive effect on leak risk, likely reflecting small event numbers.

These results suggest that in this cohort none of the individual preoperative blood tests were strong standalone predictors of leakage. For clinical interpretation, markers of inflammation (WBC, CRP) and nutrition (albumin, total protein) remain important.

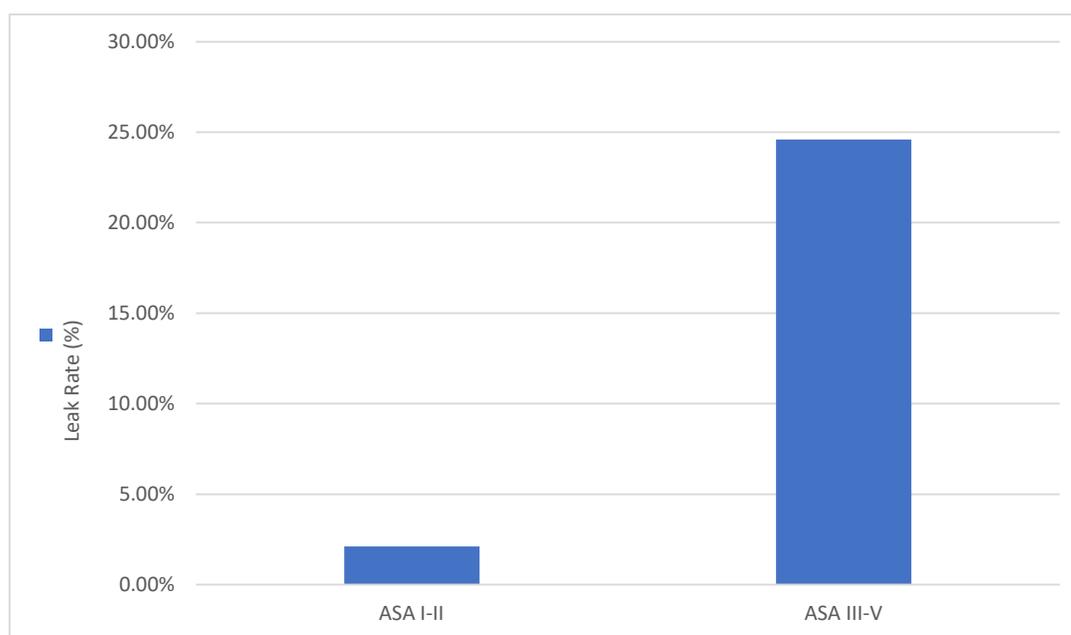
These findings suggest that in our cohort of elective colorectal cases, no single preoperative blood parameter was a significant univariate predictor of anastomotic leak.

In univariate logistic regression, emergent surgery and neoadjuvant therapies were associated with leak. Emergency (vs elective) surgery had an odds ratio (OR)  $\approx 17.0$  ( $p=0.003$ ), and neoadjuvant radiotherapy showed  $OR \approx 3.29$  ( $p=0.033$ ). Neoadjuvant chemotherapy trended higher ( $OR \approx 2.87$ ,  $p=0.064$ ).

Other factors (age, sex, comorbidities, lab abnormalities, laparoscopic approach, stoma) were not significant predictors.

In univariate logistic regression analysis, emergency surgery emerged as a strong and statistically significant predictor of anastomotic leakage, with an estimated odds ratio (OR) of approximately 17.0 (95% CI: 2.58–111.9,  $p \approx 0.003$ ), indicating a markedly elevated risk compared to elective procedures. Neoadjuvant radiotherapy was also significantly associated with increased leak risk ( $OR \approx 3.29$ , 95% CI: 1.10–9.82,  $p \approx 0.033$ ), while neoadjuvant chemotherapy showed a positive trend toward higher leakage but did not reach statistical significance ( $OR \approx 2.87$ , 95% CI: 0.94–8.78,  $p \approx 0.064$ ). Other examined variables—including sex, comorbidity burden, and preoperative anemia—did not demonstrate significant associations with leakage (all  $p > 0.1$ ).

Figure 6 depicts the sharp contrast in leak incidence by ASA class, reaffirming previous findings that high ASA status correlates with poor healing capacity. Higher ASA status (III–V) was associated with significantly greater AL incidence ( $\sim 24.6\%$ ) compared to ASA I–II ( $\sim 2.1\%$ ).



**Figure 6.** AL rate by ASA physical status.

In the multivariable model, only emergency surgery remained a significant independent predictor of leakage (adjusted OR  $\approx$ 32.2, 95% CI 4.34–238.0,  $p=0.0007$ ).

In our multivariate analysis, neither neoadjuvant radiotherapy (nRT) nor neoadjuvant chemotherapy (nCT) was a significant independent predictor of colorectal AL. We observed an OR  $\approx$ 4.80 for nRT ( $p = 0.15$ ) and OR  $\approx$ 1.09 for nCT ( $p = 0.93$ ), indicating no statistically reliable effect (Table 4).

**Table 4.** Multivariate logistic regression for AL.

Variable	Odds Ratio (95% CI)	p-value
Emergency surgery (vs elective)	32.2 (4.34–238.0)	0.0007
Neoadjuvant radiotherapy (yes)	4.80 (0.57–40.55)	0.15
Neoadjuvant chemotherapy (yes)	1.09 (0.13–9.24)	0.93

When comparing outcomes by institution, no significant difference in AL rates was found: “Colentina” (10.6%) vs “Dr. I. Cantacuzino” (10.2%),  $p = 1.00$ . This suggests that, despite differences in surgical approach and protective strategies, overall anastomotic integrity was comparable between centers.

#### 4. Discussion

Recent thorough studies and evaluations indicate that anastomotic leak rates in colorectal surgery typically vary from approximately 2% to 19% overall [2–11]. This broad spectrum indicates variations in patient demographics, surgical circumstances (elective versus emergency), and particularly the site of anastomosis [50–54]. Our data falls in this wide range offered by previous studies regarding overall AL rates.

Preoperative anemia has been recognized as an independent risk factor for colorectal anastomotic leak (AL). Patients with low preoperative hemoglobin exhibit significantly elevated rates of anastomotic leakage, with one study indicating around a 5-fold increase in odds of leakage and another finding a roughly 6.5-fold increased risk when hemoglobin levels are below 11 g/dL [55–57].

Our study examined the prognostic capacity of preoperative blood tests on AL rates. Hemoglobin exhibited an odds ratio (OR) of around 1.58 (95% confidence interval [CI] 0.41–6.12,  $p=0.51$ ), while white blood cell (WBC) count shown an OR of approximately 1.68 (95% CI 0.43–6.54,  $p=0.45$ ), both findings being non-significant; although, increased preoperative WBC has been identified as an independent risk factor in other studies [58].

In our study, CRP had a minimal impact on AL. CRP is an acute-phase inflammatory marker frequently enhanced in the context of a potential leak; for instance, significantly higher postoperative CRP levels ( $>180$  mg/L on day 4) are recognized as predictors of leaks [59]. In our data, preoperative CRP did not significantly predict leak, possibly because post-op trends are more informative.

Total Protein had OR  $\approx$ 1.03 (95% CI 0.12–8.75,  $p=0.98$ ), showing no effect.

The literature evaluation indicates that chronic renal illness, characterized by creatinine levels exceeding 3.5 mg/dl, correlates with poorer postoperative outcomes [50,60,61]. Creatinine gave OR  $\approx$ 1.66 (95% CI 0.49–5.64,  $p=0.42$ ) per unit; but no association was found in our study.

Coagulopathy (elevated INR or other coagulation abnormalities) has been identified as a systemic risk factor for anastomotic failure [62–64]. INR had OR  $\approx$ 4.89 (95% CI 0.42–57.4,  $p=0.21$ ) per unit increase, with very wide confidence limits.

Preoperative serum albumin level – a marker of nutritional status – did not predict leaks in our cohort [OR  $\approx$ 2.41 (95% CI 0.25–23.1,  $p=0.45$ )]. Initially, this appears to contradict a significant portion of the surgical literature, which frequently identifies hypoalbuminemia as a risk factor for anastomotic dehiscence and inadequate healing [50,65–71].

Our study measured albumin only preoperatively, and importantly, the patient population in both Romanian centers was thoroughly optimized before elective surgery, by optimizing nutrition preoperatively, our institutions may have neutralized hypoalbuminemia as a risk factor. Notably, compared to international studies that mostly describe a link between postoperative hypoalbuminemia and AL. By comparison, our negative result regarding albumin can be explained by when and in whom the albumin was measured.

Our experience is supported by at least one recent study: Shimura et al. indicated that preoperative albumin levels were not significantly different between patients who had leaks and those who did not, however a decrease in albumin during the initial postoperative days was strongly correlated with AL [68]

No blood measure demonstrated a significant predictive effect on leak risk, perhaps due to the limited number of events. The impact direction for WBC and albumin aligns with established risk patterns in the literature [58,67]

These results suggest that in this cohort none of the individual preoperative blood tests were strong standalone predictors of leakage. In clinical interpretation, inflammatory markers (WBC, CRP) and nutritional indicators (albumin, total protein) are significant: elevated WBC and diminished albumin have been associated with leaks in bigger studies, however this specific dataset lacked sufficient power to validate this association [58,67]

These findings suggest that in our cohort of elective colorectal cases, no single preoperative blood parameter was a significant univariate predictor of anastomotic leak.

Clinically, these results reinforce that risk stratification for leaks must integrate multiple factors (patient health, operative factors, etc.) rather than rely on any single lab value. The wide confidence intervals highlight the need for larger studies to determine if subtle effects of these blood markers truly exist. Both institutions are clinical hospitals equipped to provide comprehensive preoperative optimization, thereby enhancing patients' physiological status prior to surgery. This capacity for preoperative preparation may influence postoperative outcomes and distinguishes them from emergency care hospitals, where such optimization is often limited.

In this retrospective cohort from two Romanian hospitals, a higher ASA (American Society of Anesthesiologists) score and emergency surgical presentation emerged as the most significant predictors of colorectal AL. These findings are strongly corroborated by recent international studies. A 2023 meta-analysis of more than 115,000 colon cancer cases revealed that patients with ASA class  $\geq$ III had considerably elevated odds of anastomotic leakage (about 1.3-fold higher), and that urgent (non-elective) surgery similarly heightened the probability of leakage by approximately 30% [14]. The ASA classification adequately represents a patient's comorbidities and physiological reserve, making its correlation with leak risk understandable; patients who are more ill and weak endure surgical stress and recover from wounds less efficiently [14,15,25,72–77]

Emergency colorectal resections are significantly associated with an increased risk of anastomotic leakage compared to elective procedures [77–79] A study by the American College of Surgeons NSQIP involving about 150,000 colectomy patients (2013–2017) revealed that emergency and urgent cases had greater leak rates compared to elective cases. After controlling for additional variables, urgent colectomies exhibited almost 30% increased probabilities of anastomotic leakage (adjusted OR  $\approx$ 1.3, 95% CI 1.2–1.4), whereas emergency colectomies shown about 20% heightened odds (OR  $\approx$ 1.2, 95% CI 1.1–1.3) in comparison to elective procedures [80] The outcome is corroborated by our data, indicating that emergency surgery is a strong independent predictor of leakage. The urgent or emergency surgical context, frequently associated with blockage, perforation, or peritonitis, exacerbates risk by limiting preoperative optimization for surgeons and introducing complications such as contamination and hemodynamic instability [48,74,81]

In alignment with our findings, Choi et al. indicated that the conjunction of emergency surgery and elevated ASA (III–V) poses significant risks, recommending protective strategies such as a diverting stoma or the avoidance of primary anastomosis for patients exhibiting these risk factors [81]

In our multivariate analysis, neither neoadjuvant radiotherapy (nRT) nor neoadjuvant chemotherapy (nCT) was a significant independent predictor of colorectal AL. To provide context, we analyze recent literature investigating the influence of neoadjuvant therapy on the risk of AL. In summary, recent evidence suggests that neoadjuvant radiation is not a conclusive independent predictor of anastomotic leakage following rectal surgery [50,82,83]. The impact of neoadjuvant chemotherapy (excluding radiation) on anastomotic leakage has been examined, particularly in cases with locally advanced colon or rectal cancer treated with comprehensive neoadjuvant therapy. Numerous studies indicate that neoadjuvant chemotherapy does not substantially increase AL rates [60,61,70,84].

This does not contradict the broader literature on nutrition and healing, but rather highlights the value of preoperative optimization: it turns a once-risky patient (e.g., with low albumin) into a better prepared surgical candidate.

## 5. Conclusions

Surgeons should continue to incorporate systemic risk factors – particularly patient frailty (ASA score) and the urgency of the case – into decision-making for colorectal anastomoses. Our data support an individualized approach: for a patient with multiple comorbidities or an emergency indication, a guarded strategy (elective stoma, delayed anastomosis, or enhanced postoperative monitoring) is warranted to mitigate the well-documented leak risk.

Conversely, the lack of association between pre-op albumin and leaks in this optimized cohort is a testament to the effectiveness of preoperative interventions in a chronic hospital. It underscores that modifiable factors like nutrition, anemia, and overall fitness should be addressed whenever possible before undertaking elective colorectal resections. The two hospitals contributing data to this study routinely implement such pre-habilitative measures, and the results suggest tangible benefits: when patients enter surgery in optimal condition, certain classical risk factors can be blunted.

These insights support a proactive, tailored approach to colorectal surgical planning and highlight the continuing importance of optimizing patients before they ever enter the operating room, thereby improving the chances of uneventful anastomotic healing.

Finally, we acknowledge the limitations of our analysis. The study is retrospective and observational, which introduces inherent biases in data capture and cannot prove causation. The sample size, spanning five years but limited to two institutions, is modest. This may reduce our power to detect subtler risk factors and could explain why some known contributors (e.g., smoking or BMI) did not reach statistical significance in our model.

Additionally, our cohort's composition – predominantly elective cases – may limit generalizability. Not all healthcare settings will have the resources or time to optimize patients preoperatively, and outcomes can differ in emergency-heavy or resource-limited environments.

Future research, ideally large prospective cohorts or pooled international data, is needed to confirm these risk factor trends and to explore interventions for high-risk groups.

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**Informed Consent Statement:** Given the retrospective design and use of existing records, a waiver of informed consent was obtained from the ethics committees.

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**Conflicts of Interest:** : The first author is conducting a doctoral thesis on innovative techniques for securing digestive anastomoses in colorectal surgery, which is related to the scope of this study. We report no other conflicts of interest..

## Abbreviations

The following abbreviations are used in this manuscript:

AL	Anastomotic leakage
DM	Diabetes Mellitus
CV	Cardiovascular
ASA	American Society of Anesthesiologists (physical status classification)
BMI	Body Mass Index
INR	International Normalized Ratio
KDE	Kernel Density Estimation
nCRT	Neoadjuvant Chemoradiotherapy
OR	Odds Ratio
SD	Standard Deviation
WBC	White Blood Cells
INR	International normalized ratio
CRP	C-Reactive Protein

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