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Preoperative Predictors of Anastomotic Leak Following Digestive Cancer Surgery: A Retrospective Cohort Study

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Rezumat

Predictori preoperatori ai fistulei anastomotice după chirurgia cancerelor digestive: un studiu retrospectiv de cohortă

Introducere: Fistula anastomotică rămâne una dintre cele mai severe complicații ale chirurgiei oncologice digestive, având un impact semnificativ asupra morbidității şi mortalității postoperatorii.
Material şi Metodă: A fost realizat un studiu observațional retrospectiv. Au fost colectate datele pentru 394 de pacienți care au beneficiat de tratament chirurgical pentru neoplazii digestive, din care 248 au beneficiat de rezecție cu anastomoză. Au fost analizați următorii factori de risc: distribuția localizării tumorale, indicele de masă corporală (IMC), sexul, statutul de fumător, stadiul tumoral, scorul American Society of Anesthesiologists (ASA), nivelul hemoglobinei preoperatorii şi intervenția chirurgicală de urgență.
Rezultate: Fistula anastomotică a fost diagnosticată la 38,3% din cazuri. Analiza univariată a evidențiat asocieri semnificative cu ASA ≥3, stadiu tumoral avansat (III-IV), intervenția chirurgicală în urgență, fumatul, IMC subponderal şi severitatea anemiei (riscul crescând proporțional cu severitatea). Analiza multivariată a identificat ASA≥3 (OR 9,60; p<0,001), anemie uşoară (OR 3,11; p=0,005), anemie moderată/severă (OR 7,63; p<0,001) şi stadiu tumoral avansat (OR 2,43; p=0,018) drept predictori independenți asociați fistulei anastomotice.
Concluzii: Numărul şi severitatea comorbidităților (ASA), concentrația hemoglobinei preoperatorii şi stadiile avansate (III-IV) reprezintă factori de risc independeți pentru dehiscența anastomotică la pacienții care beneficiază de tratament chirurgical pentru neoplazii de tub digestiv.

Cuvinte cheie: fistula anastomotică, cancer digestiv, anemie, scor ASA, factori de risc preoperatori, stadiu tumoral avansat

Abstract

Background: Anastomotic leak remains one of the most severe complications in digestive oncologic surgery, significantly impacting postoperative morbidity and mortality.

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Methods: A retrospective observational study was conducted. We collected and analyzed the data for 394 patients with digestive cancer, of which 248 received resection with primary anastomosis. The following variables were analyzed: tumor origin distribution, body mass index (BMI), gender, age, smoking status, tumor stage, American Society of Anesthesiologists score (ASA), hemoglobin levels and surgical indication (elective or emergency).
Results: Anastomotic leakage occurred in 38,4% of cases. Univariate analysis showed significant associations with ASA ≥3, advanced tumor stage, emergency surgery, smoking, underweight BMI, and anemia severity (risk increased in a severity-dependent manner). Multivariate analysis identified ASA ≥3 (OR 9.60; p<0.001), mild anemia (OR 3.11; p=0.005), moderate/severe anemia (OR 7.63; p<0.001), and advanced tumor stage (OR 2.43; p=0.018) as independent predictors.
Conclusions: Preoperative physiological status and anemia severity are independently associated with anastomotic leak following digestive cancer surgery. The graded effect of anemia suggests a potentially modifiable risk factor amenable to preoperative optimization. Advanced malignancy (stages III and IV) plays an independent role in anastomotic leakage incidence.

Keywords: anastomotic leak, digestive cancer, anemia, ASA score, preoperative risk factors, advanced stage tumors

Introduction

Anastomotic leak (AL) remains one of the most serious complications following gastrointestinal surgery, particularly in oncologic resections. Despite advances in perioperative management, surgical technique and recovery protocols, AL is associated with significant morbidity and mortality. The true incidence of anastomotic leak remains uncertain due to variability in definitions that vary according to tumor location, patient characteristics and management strategies (1,2). Nonetheless, it remains a clinically relevant complication that may significantly impact long-term outcomes in patients undergoing surgery for gastrointestinal malignancy.

The definition of anastomotic leak has historically been nebulous. The non-uniformity in diagnostic criteria and reporting standards was evaluated in earlier literature (3). Efforts have been made to standardize definitions and grading systems to improve comparability between studies and optimize clinical management (1,4-6). Anastomotic leak is currently understood as a defect of intestinal wall integrity at the anastomotic site resulting in a communication between intraluminal and extraluminal compartments, with potential clinical manifestations ranging from localized abscess to generalized peritonitis and sepsis (1,4,7).

Given that AL consequences have substantial patient and economic impact, greater attention should be directed toward modifiable perioperative risk factors. Leaks are associated with prolonged length of stay, higher healthcare costs, increased need for reintervention and delayed initiation of oncologic therapy. Evidence suggests that AL may adversely affect long-term oncologic results, particularly in colorectal malignancies (2,4)

While surgical technique, vascular supply and tension at the anastomotic site play dominant roles, a variety of patient related factors have been associated with anastomotic leakage, making pathogenesis multifactorial (8). Thus, systemic conditions that impair wound healing, including anemia, nutritional status, male sex, high American Society of Anesthesiologists (ASA) scores, smoking and advanced stage malignancy have been strongly associated with an increased risk of anastomotic dehiscence (1,4,9).

In the First Surgical Clinic of Pius Brînzeu Timiş County Emergency Clinical Hospital, a progressive and concerning increase in clinically significant anastomotic leaks was observed over recent years, especially immediately after COVID-19. The coronavirus pandemic has put significant strain on the healthcare systems, resulting in the need for managing patients with more advanced disease and comorbidities. We have observed an increase in advanced stage tumors and patient comorbidities in both prevalence and severity that eventually led to a higher number of postoperative complications and greater mortality rates. This observation motivated a systematic evaluation of potential preoperative predictors that could justify the rise in anastomotic failure and, more importantly, identify potential targets for risk reduction by means of improving perioperative management.

The present study focused on identifying independent preoperative predictors of anastomotic leak in patients undergoing surgery for digestive malignancies.

Materials and Methods

Study Design and Data Collection

Out of a total of 8125 cases that underwent surgical treatment between Jan 2020 and Dec 2024 in the First Clinic of Surgery of Pius Brînzeu Timiş County Emergency Hospital, 394 represented digestive tract malignancies. Of the 394 patients, 248 met eligibility criteria for resection with anastomosis. A retrospective observational study regarding risk factor analysis for anastomotic leak was conducted for patients who underwent resection with primary anastomosis during this period (n=248). Primary tumor origin (*Table 1*) was recorded for all 394 patients and categorized as esophageal, gastric, small bowel, colorectal (right colon, transverse colon, left colon and sigmoid, rectum and anal canal), pancreatic and other (complex/ synchronous / recurrent tumors / pelvic mass). The "other" category included multivisceral resections for locally advanced or recurrent malignancies of gastrointestinal origin or that required individualized surgical strategies. Only 2 patients in this subgroup underwent primary anastomosis.

Collected data including clinical data, laboratory blood tests results, Computed Tomography scans results and pathology reports were extracted from patient records. For the purpose of identifying global risk factors for anastomotic leakage the following pre-operative variables were analyzed: age continuous and categorical (<50; 50-70; >70 years old); Sex (male/ female); Body mass index (BMI), analyzed both as continuous variable and categorized (<18.5; 18.5–25; >25 kg/m²); American Society of Anesthesiologists (ASA) score (dichotomized as < 3 and ≥3); Smoking status (yes/no); Emergency surgery (yes/no); Tumor Node Metastasis (TNM) stage (Early: Stage 0–II; Advanced: Stage III–IV); Preoperative anemia status (none, mild, moderate, severe). Anemia was classified according to institutional laboratory reference values detailed in *Table 2*. Moderate and severe categories were merged in multivariate analysis due to small numbers.

Table 1. Primary Tumor Origin in the Study Cohort (n = 394)

Primary Tumor Origin	n	%
Esophagus	6	1.5
Stomach	28	7.1
Small bowel	6	1.5
Right colon	60	15.2
Transverse colon	12	3.0
Left colon and sigmoid	85	21.6
Rectum and anal canal	88	22.3
Pancreas	2	0.5
Complex / synchronous / recurrent tumors	107	27.2
Total	394	100

Percentages are calculated relative to the total study cohort (n = 394).
The "Complex / synchronous / recurrent tumors" category includes multivisceral resections for locally advanced or recurrent malignancies of gastrointestinal and gynecologic origin, as well as tumors without clearly identifiable primary origin at presentation. Only 2 patients in this subgroup underwent primary anastomosis.

Outcomes

Surgical procedures for the study population were represented by: Oesophago-gastrectomy (1.5%), Total and subtotal Gastrectomy (7.1%), Segmentary enteral resections (1.5%), Right hemicolectomy (15,2%), Segmentary transverse colon resections (3%), Left Hemicolectomy and Segmentary Sigmoid Resection (21.6%), Anterior rectal resections (22.3%), other procedures that include stomas (colostomy, ileostomy), digestive diversions, multivisceral resections or individualized procedures for synchronous, recurrent or locally advanced tumors (27,8%).

The primary outcome was anastomotic leak, which was established clinically and radiologically.

Given the heterogeneity of anastomotic locations included in the study, no unified severity grading system was applied to anastomotic leaks, as currently available classifications are location-specific and not universally validated across all gastrointestinal anastomoses. Therefore, all clinically and radiologically diagnosed leaks were included in the analysis to capture the full spectrum of this complication.

Clinical criteria for positive diagnostic of dehiscence relies upon one of the following: presence of pus or enteric content drainage from surgical drains or wound sites, or confirmation by means of surgical exploration for patients with need for reintervention for peritonitis, sepsis with an abdominal origin including parietal defects i.e. evisceration. For descriptive purposes, the need for reintervention was recorded as an indicator of clinically severe anastomotic leak (13.3%).

Table 2. Institutional Hemoglobin Reference Values for Anemia Classification

Category	Women (g/dL)	Men (g/dL)
No anemia	≥ 11.5	≥ 12.5
Mild anemia	10–11.4	10–12.4
Moderate anemia	8–9.9	8–9.9
Severe anemia	<8	<8

Values represent institutional laboratory reference ranges used for anemia classification

Imagistically confirmed leaks, using computed tomography with contrast agent, identified the presence of, free fluid, free gas, perianastomotic inflammation or collections, intraabdominal abscesses or contrast agent leaking from anastomotic partners.

Enrolment Criteria and Study Groups

The study group is comprised of 248 patients that received a surgical resection with primary anastomosis for digestive tract malignancy, based on the following inclusion and exclusion criteria:

Inclusion criteria:

- Adult patients (≥18 years);
- Histologically confirmed digestive tract malignancy;
- Surgical treatment performed within the study period;
- Resection with primary anastomosis.

Exclusion criteria:

- Patients undergoing non-resectional procedures;
- Patients without intestinal continuity reconstruction;
- Incomplete clinical or laboratory data (≥2 monitored criteria).

Data Analysis

Statistical analyses were performed using JASP version 0.95.4.0 computer software. Continuous variables are expressed as mean ± standard deviation and were compared using Student's t-test. Categorical variables were compared using Pearson's χ^2 test. Univariate logistic regression was performed to evaluate associations between preoperative variables and anastomotic leak. Variables with clinical relevance and/or statistical significance in univariate analysis were entered into a multivariate logistic regression model using the enter method. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. A p-value < 0.05 was considered statistically significant. Multivariate analyses were performed using complete-case data; patients with missing values in any of the included variables were excluded from regression models. Given the heterogeneity of tumor locations and surgical procedures, subgroup analyses were performed to assess the consistency of identified risk factors across different clinical contexts.

Results

A total of 394 patients underwent surgery for digestive malignancies during the study period. Of these, 248 patients underwent resection with primary anastomosis and were included in the leak risk analysis. Anastomotic leak occurred in 95 cases (38.3%) (*Table 1*). Among these, 33 cases required reintervention, identifying a subgroup of clinically severe anastomotic leaks.

Baseline comparison between patients with and without leak is presented in *Table 3*. Significant differences were observed regarding ASA score ($p < 0.001$), anemia severity ($p < 0.001$), tumor stage

Table 3. Baseline characteristics of patients with and Without Anastomotic Leak (n = 248)

Variable	No Leak (n=153)	Leak (n=95)	p-value
Age (years)	68.08 ± 10.82	67.86 ± 11.02	0.880
BMI (kg/m^2)	27.33 ± 5.56	27.91 ± 6.26	0.455
Male sex	94 (61.4%)	53 (55.8%)	0.379
ASA ≥3	38 (24.8%)	79 (83.2%)	<0.001
Stage			<0.001
Early	72 (47.1%)	21 (22.1%)	
Advanced	81 (52.9%)	74 (77.9%)	
Emergency surgery	25 (16.4%)	40 (42.1%)	<0.001
Smoking	60 (39.2%)	50 (52.6%)	0.039
BMI category			0.062
18.5–25 kg/m^2	66 (44.6%)	34 (35.8%)	
<18.5 kg/m^2	2 (1.4%)	6 (6.3%)	
>25 kg/m^2	80 (54.1%)	55 (57.9%)	
Anemia			<0.001
None	98 (68.1%)	27 (28.7%)	
Mild	32 (22.2%)	28 (29.8%)	
Moderate/Severe	14 (9.7%)	39 (41.5%)	

Continuous variables are expressed as mean ± standard deviation and were compared using Student's t-test. Categorical variables were compared using Pearson's χ^2 test. BMI = body mass index; ASA = American Society of Anesthesiologists physical status classification. Stage: Early (Stage 0–II); Advanced (Stage III–IV). Anemia defined according to institutional laboratory reference values (*Table 2*). Cases with missing data were excluded from specific analyses.

(p < 0.001), emergency surgery (p < 0.001), and smoking status (p < 0.039). No statistically significant differences were observed with respect to age (p = 0.880), sex distribution (p = 0.379), or continuous BMI values (p = 0.455).

Anastomotic technique was explored descriptively in a subset of patients with available data. Hand-sewn anastomoses were associated with a higher crude leak rate compared to mechanical anastomoses (53.7% vs 32.8%). Due to the lack of standardization, this comparison was not included in multivariate analysis.

Univariate logistic regression analysis (*Table 4*) demonstrated that ASA ≥3 (OR 14,94), advanced tumor stage (OR 3.13), emergency surgery (OR 3.70), smoking (OR 1.72), and anemia severity (mild OR 3.18; moderate/severe OR 10.11) were significantly associated with an increased risk of anastomotic leak. A graded effect was observed for anemia, with higher odds ratios corresponding to increasing severity. Age reached statistical significance (p <0.001, OR 0.993); however, the effect size was negligible, indicating limited clinical relevance.

In multivariate analysis (*Table 5*), ASA ≥ 3 (adjusted OR 9.60), anemia severity (mild adjusted OR 3.11, p = 0.005; moderate/severe adjusted OR 7.63, p <0.001) and advanced tumor stage (adjusted OR 2.43, p = 0.018) remain independent predictors of leak. Smoking did not retain statistical significance after adjustment. ASA ≥3 was identified as the strongest independent predictor. The magnitude of association observed for anemia suggests a clinically relevant and potentially modifiable risk factor.

To address cohort heterogeneity, subgroup analyses were performed stratified by surgical setting (elective vs emergency), tumor location (colorectal vs non-colorectal), and tumor stage (early vs advanced).

Subgroup Analysis – Elective vs Emergency

In the elective subgroup, ASA ≥3 (OR 10.26; p < 0.001), moderate and severe anemia (OR 5.64; p = 0.002), and advanced tumor stage (OR 2.92; p = 0.012) remained independently associated with an increased risk of anastomotic leak, while mild anemia showed a borderline association (OR 2.34; p = 0.078). The emergency subgroup represents a selected population, as a significant proportion of patients with bowel obstruction or advanced disease underwent stoma formation without primary anastomosis.

Subgroup Analysis – Colorectal vs Non-colorectal

In the colorectal subgroup, ASA ≥3 (OR 5.26; p<0.001), anemia severity (mild OR 4.17; p=0.008; moderate

Table 4. Univariate logistic regression analysis of risk factors for anastomotic leak

Variable	OR	95% CI	p-value
Age (per year)	0.993	0.989–0.997	<0.001
Male sex	0.79	0.47–1.33	0.379
ASA ≥3	14.94	7.80–28.64	<0.001
Advanced stage	3.13	1.76–5.59	<0.001
Emergency surgery	3.70	2.05–6.67	<0.001
Smoking	1.72	1.03–2.89	0.039
BMI <18.5 kg/m^2	5.82	1.12–30.41	0.037
BMI >25 kg/m^2	1.34	0.78–2.29	0.293
Mild anemia	3.18	1.64–6.16	<0.001
Moderate/Severe anemia	10.11	4.80–21.29	<0.001

Univariate binary logistic regression analysis. OR = odds ratio; CI = confidence interval.
Reference categories: • Sex: Female; • ASA: <3; • Tumor stage: Early (Stage 0–II); • Surgery: Elective; • Smoking: Non-smoker; • BMI: 18.5–25 kg/m^2; • Anemia: None.
BMI categories were defined according to World Health Organization criteria: Underweight (<18.5 kg/m^2), Normal (18.5–25 kg/m^2), Overweight (>25 kg/m^2). Anemia was classified according to institutional laboratory reference values (*Table 2*).

Table 5. Multivariate logistic regression analysis of independent predictors of anastomotic leak

Variable	Adjusted OR	95% CI	p-value
ASA ≥3	9.60	4.74–19.42	<0.001
Mild anemia	3.11	1.40–6.90	0.005
Moderate/Severe anemia	7.63	3.14–18.53	<0.001
Advanced stage	2.43	1.16–5.07	0.018
Smoking	1.74	0.87–3.49	0.117

Multivariate binary logistic regression using enter method. Variables included based on clinical relevance and univariate significance. Reference categories: ASA <3; Early stage; Non-smoker; No anemia. OR = odds ratio; CI = confidence interval.

/severe OR 9.68; p<0.001), advanced tumor stage (OR 3.37; p=0.012), and emergency surgery (OR 6.85; p=0.040) were independently associated with anastomotic leak.

In the non-colorectal subgroup, ASA ≥3 and moderate-to-severe anemia remained significant predictors, while emergency surgery also emerged as a relevant factor. Tumor stage did not retain statistical significance, likely due to smaller sample size and increased heterogeneity.

Subgroup Analysis – Early vs Advanced Stage

Stratified analysis by tumor stage demonstrated that in the early-stage subgroup, ASA ≥3 (OR 13.24; p<0.001), mild anemia (OR 3.03; p=0.038), and moderate/severe anemia (OR 5.37; p=0.003) were independently associated with an increased risk of anastomotic leak.

Similarly, in the advanced-stage subgroup, ASA ≥ 3 (OR 13.47; p < 0.001), mild anemia (OR 2.90; p= 0.048), and moderate / severe anemia (OR 5.59; p=0.002) remained significant predictors.

Emergency surgery and other covariates did not retain statistical significance in either subgroup.

Discussion

The present study focused on identifying independent preoperative predictors of anastomotic leak across patients operated for digestive malignancies, and several important observations were made. Physiological status represented by ASA ≥3, anemia severity, advanced stage (III and IV) demonstrated strong and independent associations with leak development. Furthermore, these findings were consistent across multiple subgroup analyses, including stratification by surgical setting, tumor location and tumor stage.

The relatively high anastomotic leak rate observed in this study (38.3%) should be interpreted in the context of several factors. First, the definition used included both clinically manifest and radiologically detected leaks, capturing a broader spectrum of this complication. Second, the study period encompassed the COVID-19 pandemic, during which a shift toward more advanced-stage disease and increased comorbidity burden was observed. This period was marked by a significant reallocation of healthcare resources required to manage SARS-CoV-2 patients, resulting in reduced availability of specialized personnel, redistribution of surgical teams, and changes in operating room logistics. In addition, supply chain disruptions led to inconsistent availability of stapling devices and advanced energy systems, which may have influenced intraoperative decision-making. Notably, prior to the pandemic, the institutional anastomotic leak rate was approximately 16.8% (unpublished data), suggesting that the current findings reflect increased case complexity rather than a deviation in surgical performance. Furthermore, only 33 of the 95 leaks required reintervention, identifying a subgroup of clinically severe cases that may be more comparable to clinically relevant leak rates reported in the literature (10,11).

Our findings identify ASA ≥3 as the strongest independent predictor for AL, suggesting that global physiological reserve may outweigh isolated AL risk factors. Previous studies have demonstrated that a higher ASA score is consistent with a higher leakage rate across gastrointestinal surgical procedures and determines higher postoperative morbidity and mortality. Increased number and severity of comorbidities impair physiological reserve, leading to loss of tissue perfusion and diminished wound healing, which may contribute to anastomotic dehiscence (12–15).

A graded association between anemia severity and AL incidence was observed, highlighting the value of correcting hemoglobin levels preoperatively via iron supplementation or blood transfusion. Anemia is associated with oxygen delivery to healing tissues, directly disrupting collagen synthesis and fibroblast activity. Several studies have identified anemia as a major perioperative risk factor (14,16–21). Yamada et al. demonstrated that even mild presurgical anemia can increase postoperative complications for rectal cancer patients (17). Hassin et al. found that ferritin-related mechanisms affect inflammatory response and tissue healing (16). Dumitriu et al. demonstrated that perioperative anemia is associated with increased risk of postoperative complications in gastric cancer patients (21).

Subgroup analyses confirmed the robustness of these associations. In the colorectal subgroup, all key predictors remained significant, supporting their role in a relatively homogeneous surgical population. In contrast, the non-colorectal subgroup showed greater variability, likely reflecting smaller sample size and increased heterogeneity of tumor types and procedures.

Stratification by tumor stage further demonstrated that ASA score and anemia severity remain significant predictors regardless of disease stage, suggesting that systemic physiological reserve plays a dominant role in anastomotic healing.

Advanced tumor stage was independently associated with increased risk of AL in this cohort. Advanced tumor stage is generally linked to poor patient nutritional status and psychological reserve, longer and more challenging surgical interventions. Several studies reported that tumors larger than 5 cm and advanced TNM stages have a greater risk of anastomotic leak for patients that had surgery for rectal cancer (22,23). Numata et al. concluded that bulky tumors, larger than 5 cm and advanced stages were predictors for AL in patients undergoing surgery for rectal cancer (24). Van Kooten et al. found that higher TNM stage required more extensive resections and technically more demanding surgery thus increasing the risk of postoperative complications for upper gastrointestinal malignancy (25). Recognition of tumor stage and its relation to risks for complications should influence intraoperative decision making, including protective stoma and postoperative patient monitoring.

Emergency surgery was correlated with leak in the univariate analysis, but lost significance in the multivariate regression model, suggesting that its effect might be mediated through other variables such as advanced disease, greater ASA score, lower hemoglobin levels. Several studies reported that emergency surgery was an important risk factor for anastomotic leakage due to improper bowel preparation and hemodynamic instability (18,26). Similarly, Chiarello et al. and Zhao et all. found that emergency resections with anastomosis represent an independent risk factor for anastomotic dehiscence (15,27). In contrast, Parthasarathy et al. reported that emergency surgery was not a significant predictor for anastomotic complications (28).

Regression analysis concluded that smoking is not an independent predictor for leakage in this study population. Some authors suggest that by vascular ischemia from nicotine-induced vasoconstriction and microthromboses, coupled with carbon monoxide-induced cellular hypoxia, anastomotic circulation is inhibited and a greater risk of dehiscence was observed (29,30). In accordance with our findings, Awad et al reported that smoking was not an independent predictor for AL, suggesting that it may act synergistically with other risk factors (18).

Single variable analysis revealed that underweight patients were at risk of anastomotic leak, but BMI categories did not reach statistical significance in the multivariate logistical regression. Obesity has been reported in several articles as a risk factor for postoperative complications, including anastomotic leakage due to technical dissection difficulties and higher tension between anastomotic partners (22,27). Suding et al. concludes that a BMI $\geq$30 does not influence anastomotic healing (31). Other studies highlight that a BMI lower than 18,5 alongside other nutritional makers such as hypoproteinemia and hypoalbuminemia lead to a greater risk of dehiscence (32-34).

The impact of anastomotic technique should be interpreted with caution. The choice between hand-sewn and mechanical anastomosis was not standardized and was influenced by intraoperative conditions, tumor location, and logistical constraints. The inclusion period overlapped with the COVID-19 pandemic, during which supply chain disruptions and limited availability of stapling devices may have influenced surgical decision-making. In addition, the lack of detailed data regarding stapler type further limits interpretation.

In our study, although age showed a statistically significant association in univariate analysis, the effect size was negligible, indicating limited clinical relevance. In multivariate analysis, age did not remain an independent predictor, suggesting that frailty is better captured by ASA classification. In addition, elderly patients are more likely to receive a stoma, potentially reducing leak incidence. Recent literature is less consistent regarding the impact of age in anastomotic failure. Several studies have identified that advanced age impairs wound healing, thereby increasing the risk of anastomotic failure(25,35), while others consider age to be a risk factor for greater mortality after surgical treatment and not necessarily a predictor for leaks (18,36).

Given that the study population included multiple tumor locations, gender related differences might be diluted. Data analysis showed that gender did not retain statistical significance in the multivariate analysis, in accordance with the results of other researchers, who reported that gender was not a risk factor for AL for broader gastrointestinal surgery (18,26,37). Female sex seems to be a protective factor regarding AL, especially for colorectal cancer surgery (31). Multiple studies associate higher leakage rate with narrow pelvis anatomy specific for males, especially when coupled with large tumors (14,27).

Limitations

This study has several limitations that should be acknowledged. The study was conducted in a single tertiary referral center, where institutional surgical practices or patient selection strategy and management protocols may influence outcomes, thus limiting generalizability of the findings. The retrospective design limits the ability to establish a causal relationship between the selected preoperative predictors and anastomotic leakage. Several clinically relevant variables known to influence anastomotic healing, including nutritional status, neoadjuvant therapy, technical aspects of the anastomosis, and use of protective stoma, were not included due to the retrospective design and incomplete data availability.

Residual confounding cannot be completely excluded, even though multivariate logistic regression was performed to adjust for potential covariates.

Tumor locations were pooled across the digestive tract to evaluate global preoperative predictors independent of anatomical site, introducing heterogeneity in surgical techniques and anatomical conditions that may influence anastomotic healing.

A proportion of cases had missing data regarding anastomotic technique, which limited the ability to include this variable in multivariate analysis and may introduce selection bias.

Although the results provide clinically significant insights into anastomotic leakage risk factors, further research is needed. Future prospective studies across multiple centers, involving a larger and more diverse database, are required to confirm the results.

Conclusion

The present study supports a model in which systemic physiological reserve (ASA score), anemia severity and tumor staging play central roles in anastomotic healing.

ASA ≥ 3 was associated with a 9.5-fold increase in risk of anastomotic failure, supporting the need for perioperative patient optimization.

The observed anemia gradient is noteworthy, suggesting that even mild deviations from normal hemoglobin values may significantly influence healing outcomes. Incorporating structured preoperative anemia management protocols may represent a tangible strategy for reducing leak incidence.

Although advanced malignancy offers limited opportunities for optimization, it should also be considered from an anastomotic failure perspective, when performing resections with anastomosis for gastrointestinal cancers.

Conflicts of Interest

The authors report no conflict of interest.

Ethical Statement

The principles of the Declaration of Helsinki were respected, and the study was approved by the Ethics Committee of the University of Medicine and Pharmacy Victor Babes Timisoara, Romania No: 24/ 02.03.2026.

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