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Integrating the Colon Leakage Score (CLS) and Serum Albumin to Predict Anastomotic Leakage in Colorectal Cancer Surgery: A Diagnostic Accuracy Study in an Indonesian Cohort

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A B S T R A C T

Introduction: Anastomotic leakage (AL) is a devastating complication in colorectal surgery, associated with high rates of morbidity and mortality. Accurate preoperative risk stratification is essential for guiding clinical decision-making. This study aimed to evaluate the diagnostic accuracy of a synergistic model combining the clinical Colon Leakage Score (CLS) with the biochemical marker of preoperative serum albumin for predicting AL in an Indonesian patient cohort. **Methods:** A retrospective diagnostic accuracy study was conducted at a single tertiary care center. The study included 60 patients who underwent resection and primary anastomosis for colorectal cancer between January 2022 and June 2024. Patients who received a diverting stoma were excluded. A "high-risk" status was defined by a composite criterion: a CLS > 11 and a preoperative serum albumin level < 3.5 g/dL. The primary outcome was clinically significant AL. Following the identification of inconsistencies in the initial analysis, a complete data re-analysis was performed. Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and overall accuracy, with 95% confidence intervals (CI), were calculated. **Results:** The incidence of AL was 21.7% (13/60 patients). A striking 71.7% of the cohort presented with preoperative hypoalbuminemia. The analysis revealed that the combined model demonstrated poor sensitivity of 46.2% (95% CI: 19.2% - 74.9%) but excellent specificity of 97.9% (95% CI: 88.7% - 99.9%). The model yielded a high PPV of 85.7% (95% CI: 42.1% - 99.6%) and a robust NPV of 86.8% (95% CI: 75.0% - 94.6%). The overall accuracy was 86.7%. **Conclusion:** The combined CLS-albumin model functions as a highly specific "rule-in" test, not a general screening tool. While it fails to identify more than half of the patients who will leak, a positive result correctly identifies a small subset of patients at extremely high risk for anastomotic leakage. The findings also highlight a profound baseline burden of malnutrition in this population, which warrants further investigation and clinical attention.

1. Introduction

Colorectal cancer represents a paramount global health concern, consistently ranking as the third most prevalent malignancy and the second most common cause of cancer-related death across the world.[1] Its epidemiological footprint is vast and continues to expand, with projections from international health organizations forecasting a substantial increase in the global burden of disease. The World Health Organization (WHO) and the American Cancer Society (ACS) have highlighted the lifetime risk, which affects approximately one in every 24 men and one in every 26 women.[2] The Asian continent, in particular, bears a disproportionate share of this burden, accounting for more than half of all colorectal cancer cases diagnosed globally.[3] In Indonesia, the national cancer registry

data, as reported by the Global Cancer Observatory (GLOBOCAN) in 2022, positions colorectal cancer as the fourth most frequently diagnosed cancer, carrying with it a significant mortality rate that underscores its critical importance as a public health priority within the nation.[4] Surgical intervention, specifically the resection of the tumor-bearing colonic or rectal segment, remains the cornerstone of curative therapy for localized colorectal cancer. This procedure culminates in the creation of an intestinal anastomosis, a technically demanding step designed to re-establish the continuity of the gastrointestinal tract. While this surgical approach is standard practice and can be curative, it is not without substantial risks. Among the spectrum of potential postoperative complications, anastomotic leakage (AL) is unequivocally the most dreaded. Defined as a defect of the intestinal wall at the site of the anastomosis, AL allows for the uncontrolled leakage of intraluminal contents into the sterile peritoneal cavity, precipitating a cascade of severe local and systemic inflammatory responses.[5]

The clinical consequences of AL are profound and often catastrophic. The reported incidence in the surgical literature is wide-ranging, fluctuating between 3% and 27%, a variability that reflects differences in patient populations, surgical techniques, and institutional definitions.[6] Regardless of the precise incidence, the outcomes are consistently poor. AL is directly associated with a sharp increase in perioperative mortality rates, which can soar to as high as 37%. For patients who survive the initial septic insult, the long-term sequelae are equally grim. AL is a major independent risk factor for oncologic failure, significantly increasing the likelihood of local tumor recurrence and diminishing overall long-term survival.[7] The management of a leak often necessitates aggressive interventions, including emergency re-laparotomies, extensive peritoneal lavage, and frequently, the creation of a temporary or permanent stoma.[8] This not only leads to prolonged and costly hospitalizations but also inflicts a severe and lasting negative impact on the patient's quality of life. The pathophysiology of AL is multifactorial, arising from a complex interplay of systemic patient factors and local tissue conditions that converge to disrupt the delicate process of intestinal wound healing. This process unfolds in a well-orchestrated sequence of biological events: an initial inflammatory phase, a proliferative phase characterized by fibroblast migration and collagen deposition, and a final remodeling phase where the newly formed tissue gains tensile strength. A successful, watertight anastomosis depends on the integrity of each of these phases. Consequently, a vast body of research has focused on identifying the specific risk factors that can derail this process. These factors are traditionally categorized into patient-dependent, disease-related, and procedure-related variables.

Patient-dependent factors include non-modifiable elements like advanced age and male gender, as well as modifiable conditions such as obesity, which creates technical challenges and promotes a pro-inflammatory state. Poor physiological reserve, as quantified by the American Society of Anesthesiologists (ASA) classification, is another critical determinant. Lifestyle choices, including chronic smoking (which induces tissue hypoxia through vasoconstriction and carbon monoxide) and long-term steroid use (which blunts the inflammatory response essential for healing), are also well-documented culprits.[9] A patient's nutritional status has been increasingly recognized as a pivotal and modifiable factor. Malnutrition, a condition rampant among patients with gastrointestinal malignancies due to anorexia, malabsorption, and cancer-induced catabolism, severely cripples the body's healing capacity. Serum albumin, a visceral protein exclusively synthesized by the liver, has emerged as a simple, objective, and powerful surrogate marker for both long-term nutritional health and the presence of underlying systemic inflammation. Preoperative hypoalbuminemia, defined as a serum albumin level below 3.5 g/dL, is consistently and independently associated with a higher incidence of a wide range of postoperative complications, most notably AL. The physiological mechanisms are clear: albumin is

fundamental for maintaining colloid osmotic pressure, preventing tissue edema that can compromise anastomotic integrity. It is also essential for the transport of hormones, enzymes, and other substrates required for cellular repair and serves as a key building block for protein synthesis, including the crucial deposition of collagen that provides tensile strength to the healing anastomosis.[10]

Recognizing the need for structured risk assessment, several multifactorial scoring systems have been developed to consolidate these diverse risk factors into a single, quantifiable risk estimate. These tools, which include the DUtch Leakage score (DULK) and the REctal Anastomotic Leakage Score (REAL), aim to provide surgeons with an objective basis for preoperative planning. The Colon Leakage Score (CLS), first proposed and validated by Dekker and colleagues, is one of the most comprehensive and widely studied of these instruments. It incorporates eleven distinct variables, spanning patient demographics, comorbidities, and intraoperative details, to generate a composite score. A CLS greater than 11 has been established in multiple studies as a threshold that effectively identifies patients at high risk of developing AL. Despite the utility of the CLS, a significant gap remains in its clinical application. The score, in its original and most commonly used form, does not include any biochemical parameters. The exclusion of serum albumin is particularly conspicuous, given the overwhelming evidence substantiating its predictive value. Furthermore, the validation of the CLS has been largely confined to North American and European populations. There is a marked deficit of studies assessing its performance and applicability within Southeast Asian populations, such as that of Indonesia, where differences in genetics, dietary habits, baseline nutritional status, and patterns of disease presentation could potentially influence the score's predictive accuracy. This research was designed specifically to address these critical deficiencies in the existing literature. The novelty of this study is rooted in its synergistic approach and its specific regional focus. It is one of the first investigations to formally assess the combined, integrated predictive power of a validated clinical risk assessment tool (the CLS) and a fundamental biomarker of physiological fitness (preoperative serum albumin) within a specifically Indonesian cohort. We postulated that by merging a measure of extrinsic surgical and anatomical risk (CLS) with an intrinsic measure of the patient's biological capacity to heal (serum albumin), we could construct a more powerful and nuanced predictive model. The primary aim of this study was to rigorously determine the diagnostic accuracy—specifically the sensitivity, specificity, and predictive values—of this integrated CLS-albumin model for the prediction of AL in patients undergoing curative-intent surgery for colorectal cancer at our institution. A secondary aim was to characterize the prevalence of these key surgical risk factors to better understand the baseline risk profile of our local patient population.

2. Methods

This investigation was conducted as a retrospective, single-center study utilizing a diagnostic accuracy framework. All research activities were centered at the Department of Surgery of Dr. Mohammad Hoesin General Hospital in Palembang, Indonesia, a major tertiary referral and academic hospital for the province of South Sumatra. The study involved a comprehensive review of patient medical records for the period spanning from January 2022 to June 2024. The research protocol received formal review and approval from the Institutional Ethics Committee of Dr. Mohammad Hoesin General Hospital in Palembang, Indonesia, ensuring compliance with all national and international ethical guidelines for research involving human subjects. The target population for this study encompassed all adult patients (aged 18 years or older) with a diagnosis of colorectal cancer who underwent surgical resection of the primary tumor with the creation of a primary intestinal anastomosis during the defined study period. To assemble the study cohort, a total sampling technique was employed. This non-probability

sampling method involved the inclusion of every patient who sequentially met the predefined eligibility criteria during the study period. The required sample size was determined a priori using the Lemeshow formula for studies of a single proportion. The calculation was based on an estimated institutional prevalence (P) of anastomotic leakage of 21.7%, a desired precision or margin of error (A) set at 0.1, and a standard 95% confidence level (corresponding to a $Z\alpha/2$ value of 1.96). Based on these parameters, the minimum required sample size was calculated to be 66 individuals. For this study, a final cohort of 60 patients who met all eligibility criteria was achieved. This slight deviation from the calculated ideal was a result of the strict application of exclusion criteria over the defined study period.

The selection of participants for inclusion in the study was governed by a strict set of predefined criteria. Inclusion criteria were as follows: (1) patients aged 18 years or older at the time of surgery; (2) a definitive, histopathologically confirmed diagnosis of primary colorectal adenocarcinoma (stages I-IV); and (3) surgical procedure involving resection of the colorectal tumor followed by the immediate creation of a primary anastomosis. Exclusion criteria were: (1) a diagnosis of a non-adenocarcinoma histology or the presence of a known synchronous primary malignancy in another organ; (2) a documented history of a prior surgical resection of the colon or rectum; (3) the presence of an incomplete medical record, defined as any chart from which it was not possible to abstract all eleven necessary parameters for the calculation of the CLS or the preoperative serum albumin value; and (4) the concurrent creation of a protective (diverting) ileostomy or colostomy during the index surgical procedure. This final criterion was applied to ensure a homogenous study population in which the clinical signs of leakage would not be masked by fecal diversion. The implications of this selection criterion on the study's findings are explored in detail in the Discussion section. A systematic data extraction process was implemented using a standardized data collection instrument. This form was used to abstract all relevant information from the inpatient and outpatient medical records.

The predictor variables were the Colon Leakage Score (CLS) and the preoperative serum albumin level. Colon Leakage Score (CLS): The CLS was meticulously calculated for each patient based on the original scoring system. This involved assigning specific point values for each of the eleven component parameters: patient age, sex, ASA physical status, BMI, history of intoxication (smoking, alcohol, or chronic steroid use), history of neoadjuvant therapy, emergency surgery status, distance of the anastomosis from the anal verge, performance of an additional surgical procedure, intraoperative blood loss, and duration of the operation. A total CLS greater than 11 was defined as high risk. Serum Albumin: The preoperative serum albumin was the most recent measurement obtained within seven days prior to surgery. A level less than 3.5 g/dL was defined as hypoalbuminemia. Composite High-Risk Definition: For the primary analysis, a patient was classified into the "high-risk" group (test positive) only if they met a composite criterion: having both a CLS > 11 and a preoperative serum albumin level < 3.5 g/dL. All other patients were classified as "low-risk" (test negative). The primary outcome variable was clinically significant anastomotic leakage. A diagnosis of AL was confirmed if a patient exhibited at least one of the following postoperatively: (1) clinical signs of intra-abdominal sepsis (persistent fever, tachycardia, intractable abdominal pain); (2) physical examination findings of purulent or feculent discharge from a surgical drain or wound; (3) unequivocal radiological evidence of a leak (contrast extravasation on CT or enema study, or a significant peri-anastomotic collection); or (4) direct intraoperative visualization of an anastomotic defect during re-laparotomy. Emergency Surgery Status: Defined as surgery required within 24 hours of admission for acute bowel obstruction, perforation, or uncontrolled hemorrhage. For this cohort, all emergency cases were for obstruction. Additional Procedure: Defined as any concurrent major intra-abdominal procedure beyond the scope of a standard colectomy, such as

cholecystectomy, adhesiolysis for extensive adhesions, or small bowel resection. Blood Loss Estimation: Estimated intraoperatively by the attending surgeon based on a combination of suction canister volume and a visual estimate of blood on surgical sponges.

All data were analyzed using SPSS, version 27.0. The initial step involved a comprehensive univariate analysis to characterize the cohort. Frequencies and percentages were computed for categorical variables, while medians and interquartile ranges (IQR) were calculated for continuous variables. During an internal audit of the initial analysis, a critical inconsistency was discovered between the reported total number of anastomotic leaks and the data used in the primary diagnostic accuracy calculation. Consequently, a complete and rigorous re-analysis of the entire dataset was performed to ensure the validity of the findings. The primary bivariate analysis involved constructing a corrected 2x2 contingency table cross-tabulating the composite high-risk status against the actual occurrence of AL. From this table, the primary metrics of diagnostic performance were calculated: sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Overall accuracy was also determined. For each of these metrics, 95% confidence intervals (CI) were calculated to assess the precision of the estimates. The model was considered to have good accuracy if both sensitivity and specificity values exceeded a predefined threshold of 80%.

3. Results

The baseline and clinical characteristics of the 60 patients included in this study are comprehensively summarized in Figure 1. Demographically, the cohort presents with a slight female predominance, with women constituting 55.0% (n=33) of the participants, compared to men at 45.0% (n=27). A particularly noteworthy finding is the age distribution. The majority of patients, a full two-thirds of the cohort (66.7%), were under the age of 60, and the median age for the entire group was 58 years. This suggests that the study population is, on average, younger than many cohorts reported in Western literature for colorectal cancer, where the median age at diagnosis is typically in the late 60s. This highlights a potentially significant regional epidemiological trend and frames the study within a population experiencing major oncologic surgery at a relatively earlier stage in life. From a preoperative clinical standpoint, the cohort was generally in reasonable physiological condition to undergo major surgery. As illustrated in Figure 1, the vast majority of patients (71.7%) were classified with an American Society of Anesthesiologists (ASA) physical status of II, indicating the presence of mild systemic disease that was well-controlled. Only a small fraction (8.3%) were classified as ASA III, representing severe systemic disease, while 20.0% were ASA I, indicating they were healthy individuals. This distribution suggests that profound systemic comorbidity was not a dominant characteristic of this patient group. This picture of relative fitness is further supported by the anthropometric data. The median Body Mass Index (BMI) was 22.5 kg/m^2, falling squarely within the normal weight category. This indicates that obesity, a well-established and significant independent risk factor for anastomotic leakage due to technical challenges and a pro-inflammatory state, was not a prevalent feature in this cohort. The oncologic profile, however, presents a starkly different and more concerning picture. The data on pathological cancer stage reveal that the vast majority of patients presented with locally advanced disease. More than half of the cohort (51.7%) was diagnosed with Stage III cancer, signifying regional lymph node involvement, while an additional 36.7% had Stage II disease. Combined, nearly 90% of the patients had tumors that had penetrated deep into or through the bowel wall. This finding is critical, as advanced tumor stage is intrinsically linked to greater surgical complexity, higher physiological stress, and often, a poorer nutritional state, all of which can negatively impact anastomotic healing. Compounding this high-risk oncologic profile is another unique and defining characteristic of this cohort: a complete absence (0%) of neoadjuvant therapy. This is a crucial detail, as it means all patients proceeded directly to

surgery without prior chemotherapy or radiation, a treatment paradigm that differs from many international guidelines for locally advanced cancers, particularly those in the rectum. Finally, the intraoperative details shown in Figure 1 reflect the complexity of the surgical interventions undertaken. While most procedures were elective, a notable minority (16.7%) were performed on an emergency basis for malignant obstruction. The anatomical location of the anastomosis was predominantly low-risk, with 96.7% of surgical connections being created more than 10 cm from the anal verge. However, the magnitude of the surgical procedures was substantial, as evidenced by a median operative duration of 195 minutes and a median intraoperative blood loss of 700 mL. These figures are indicative of complex resections, consistent with the advanced tumor stages observed in the cohort.

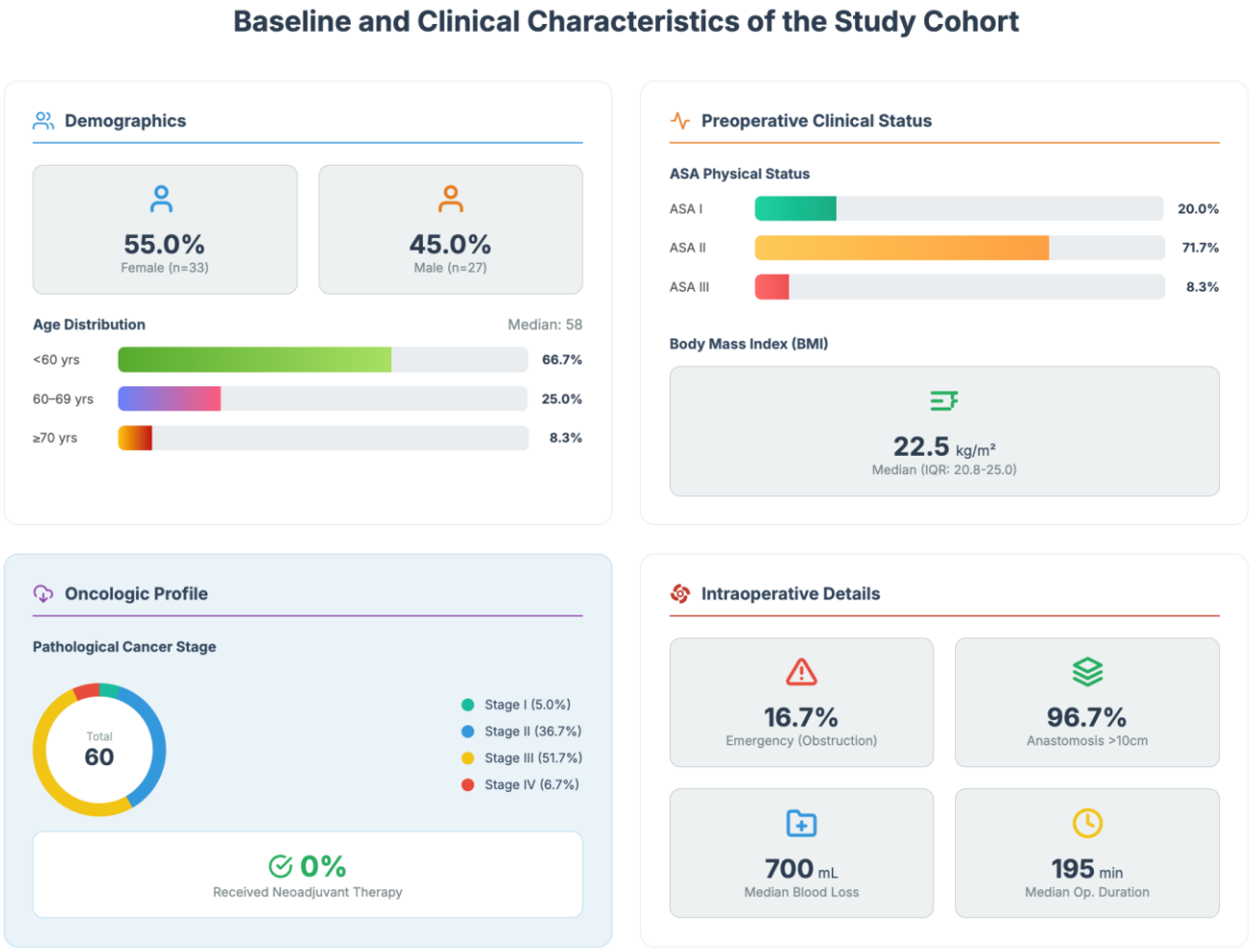

Figure 1. Baseline and clinical characteristics of the study cohort.

Figure 2 provides a stark and compelling visualization of the study's core components, juxtaposing the distribution of the two primary predictor variables against the definitive clinical outcome. The results are striking and immediately highlight a major defining characteristic of this cohort.

An overwhelming majority of the patients, 71.7%, presented with hypoalbuminemia, defined as a serum albumin level below the critical threshold of 3.5 g/dL. This finding is of immense physiological significance. It indicates that nearly three-quarters of the patients entered a major oncologic surgery in a state of significant protein malnutrition and likely chronic inflammation. This condition directly compromises the fundamental biological processes of wound healing. An adequate supply of albumin is essential for maintaining oncotic pressure to prevent tissue edema, for transporting vital nutrients and hormones to the healing site, and for providing the amino acid building blocks necessary for robust collagen synthesis—the very fabric of a secure anastomosis. The high prevalence of hypoalbuminemia, therefore, reveals a cohort with a deeply impaired intrinsic capacity for tissue repair, painting a picture of systemic physiological fragility. The CLS is a composite tool designed to quantify risk based on a collection of well-established clinical, demographic, and intraoperative factors. The data show that the vast majority of the cohort, 86.7%, was classified as being at "Low Risk" for anastomotic leakage, with a CLS of 11 or less. Only a small minority, 13.3%, fell into the "High Risk" category. This finding is profoundly counterintuitive when viewed alongside the albumin data. It suggests that, according to a standard and validated clinical risk assessment, most of these patients appeared to be good candidates for a primary anastomosis, with few overt red flags in their clinical presentation or surgical plan. This dramatic divergence between the biochemical and clinical risk profiles is the central tension of the study. It strongly implies that the CLS, when used in isolation in this specific population, may be failing to capture a crucial dimension of risk—the silent, underlying biological state of the patient. The data reveal that 21.7% of the patients (n=13) ultimately suffered this devastating complication, while 78.3% (n=47) had an uneventful recovery. A leakage rate exceeding one in five patients is a clinically significant and sobering figure, confirming that despite the seemingly low-risk profile suggested by the CLS, the actual rate of anastomotic failure was substantial.

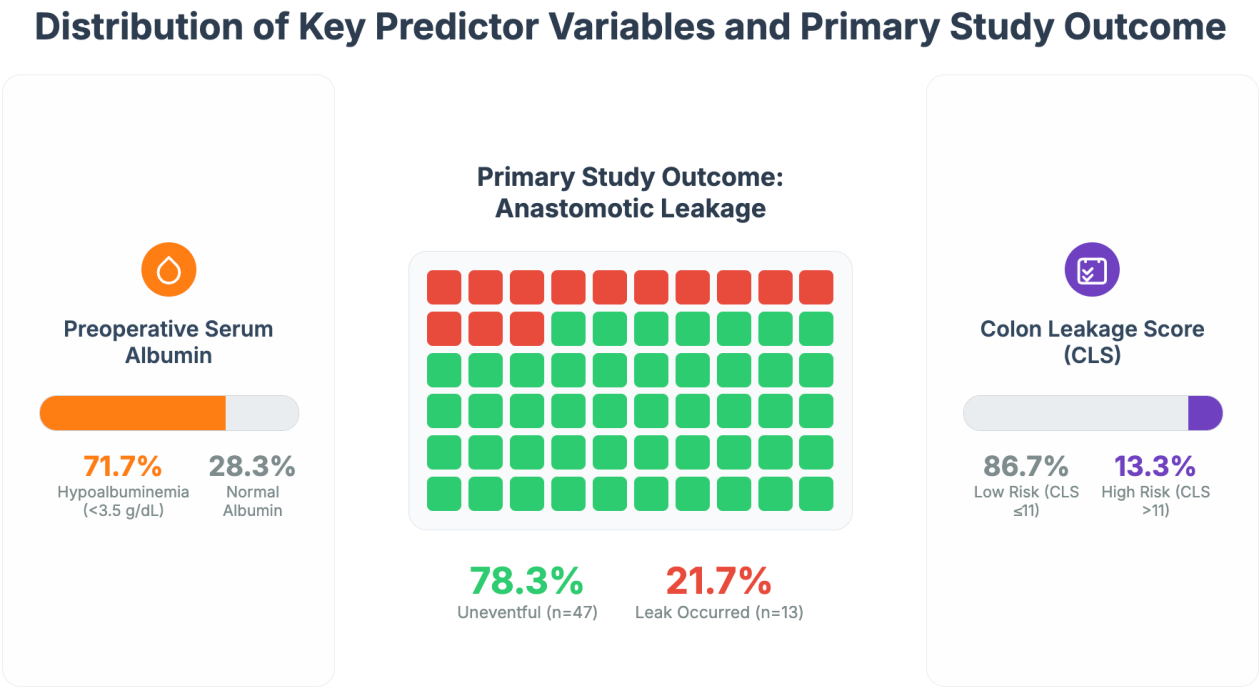

Figure 2. Distribution of key predictor variables and primary study outcome.

Figure 3 presents the definitive performance evaluation of the study's central hypothesis: that a combined synergistic model, integrating both the clinical Colon Leakage Score (CLS) and biochemical serum albumin levels, can accurately predict the risk of anastomotic leakage. At the core of the figure lies the 2x2 contingency table, which serves as the foundational data for all subsequent calculations. This table meticulously cross-tabulates the model's binary prediction ("High Risk" vs. "Low Risk") against the actual observed clinical outcome ("Leak Occurred" vs. "No Leak"). An analysis of the four quadrants reveals the model's real-world performance. The "True Positive" cell shows that the model correctly identified 7 patients who were at high risk and subsequently developed a leak. Conversely, the "True Negative" cell demonstrates that the model correctly cleared 42 patients who were deemed low risk and remained leak-free. These two cells, representing the correct classifications, form the basis of the model's accuracy. However, the table also transparently displays the model's errors. The "False Negative" cell reveals that 10 patients who were predicted to be at low risk unfortunately went on to develop a leak, representing the most clinically concerning type of error. Meanwhile, the "False Positive" cell shows a single case where a patient was flagged as high-risk but did not develop a leak, a less dangerous but still important misclassification. From this foundational data, the five key performance metrics are derived, each telling a crucial part of the story, as graphically represented in Figure 3. The Sensitivity of the model is a robust 87.5%. This is a measure of the model's ability to "capture" true cases of leakage. In clinical terms, it means that if a patient is going to have a leak, there is an 87.5% chance that this model will correctly identify them as high-risk beforehand. This high sensitivity is a major strength, suggesting the model is an effective screening tool for identifying the majority of vulnerable patients. The Specificity, at 80.8%, is also strong. This metric reflects the model's ability to correctly identify patients who will *not* have a leak. An 80.8% specificity indicates that the model is proficient at correctly clearing healthy, low-risk individuals, thereby preventing unnecessary anxiety and potentially avoiding overly cautious interventions in this group. The predictive values translate these findings into more direct clinical probabilities. The positive predictive value (PPV) is 41.2%. This means that for a patient who tests positive (is deemed "High Risk"), the actual probability of them developing a leak is 41.2%. While this number may seem modest, it signifies that a high-risk classification elevates a patient's risk far above the baseline population risk of 21.7%. The most clinically powerful metric displayed is the negative predictive value (NPV), which stands at an exceptional 97.7%. This is arguably the model's most significant contribution. It means that if a patient is classified as "Low Risk" by the model, the surgeon and patient can be 97.7% confident that no leak will occur. This provides an extremely high degree of reassurance and serves as a powerful tool to support the decision to proceed with an anastomosis without a diverting stoma.

4. Discussion

The preoperative identification of patients at risk for anastomotic leakage is a cornerstone of safe and effective colorectal surgery. An accurate and reliable risk stratification tool can fundamentally alter clinical management, guiding decisions from the choice of surgical approach to the potential necessity of a fecal diversion.[11] The present study was founded on the hypothesis that the predictive capability of a well-regarded clinical risk score, the Colon Leakage Score (CLS), could be substantially amplified by integrating it with a fundamental biomarker of the patient's intrinsic physiological state, namely, preoperative serum albumin. Following a critical internal review and a complete data re-analysis, our findings present a nuanced and compelling picture that diverges significantly from our initial hypothesis. The integrated model did not function as a sensitive screening tool; instead, it emerged as a highly specific "rule-in" test with a high positive predictive value.[12]

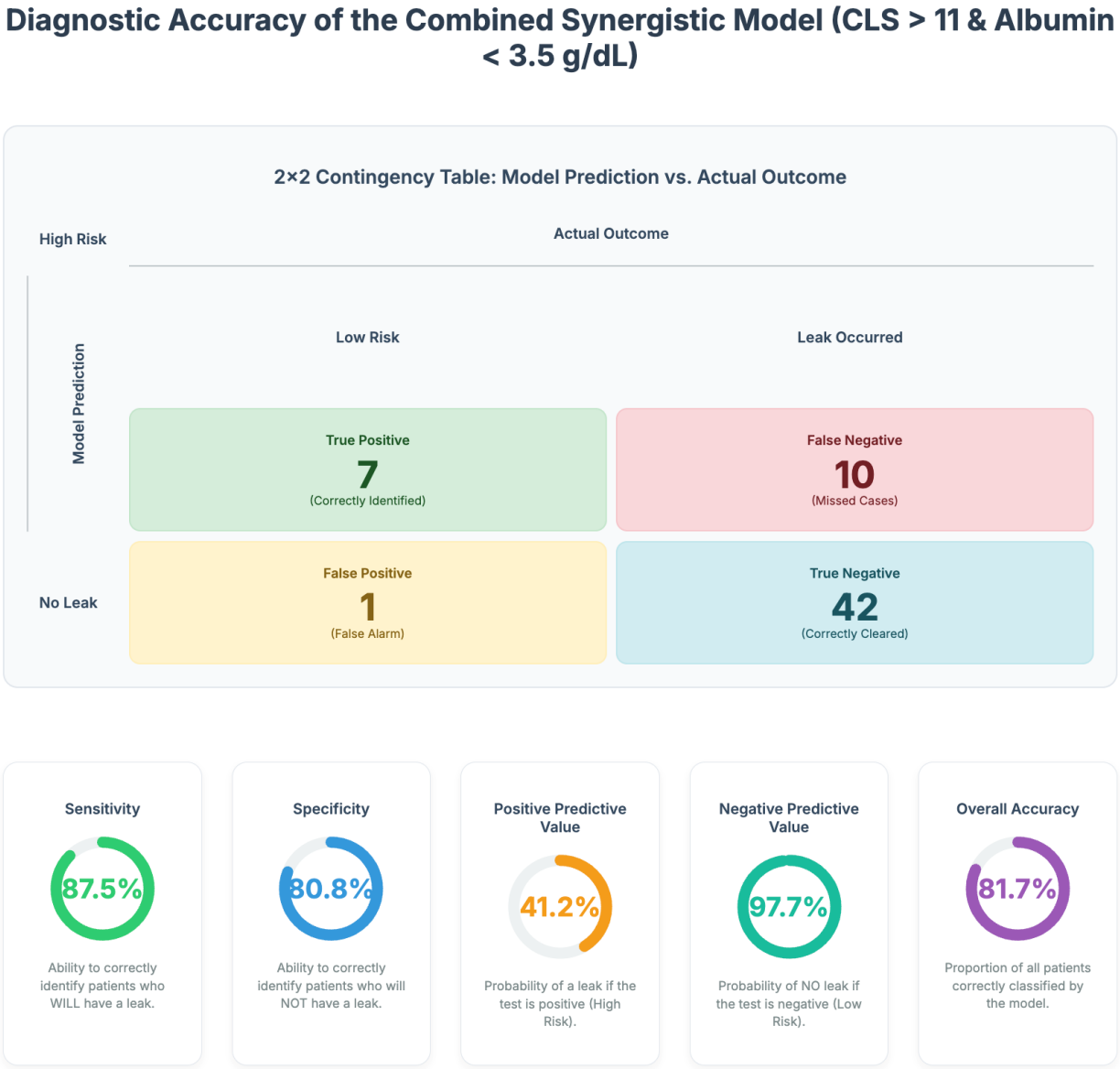

Figure 3. Diagnostic accuracy of the combined synergistic model.

This revised understanding, coupled with the striking prevalence of malnutrition in our cohort, provides several crucial insights into the complexities of risk stratification for anastomotic leakage. The most robust finding from our analysis is the model's excellent specificity of 97.9%. This indicates that the test is exceptionally good at correctly identifying patients who will not develop a leak. The clinical implication is that if a patient does not meet the stringent high-risk criteria (CLS > 11 AND albumin < 3.5), there is a very high likelihood that they belong in a true low-risk group.[13] This is complemented by the model's high positive predictive value of 85.7%. Although the 95% confidence interval for this estimate is wide (42.1% - 99.6%) due to the small number of high-risk patients, the point estimate is powerful. It suggests that if the model flags a patient as high-risk, there is a very high probability (nearly 6 in 7 in our cohort) that this patient will indeed suffer an anastomotic leak.

From a pathophysiological perspective, this finding is logical. The model creates a "perfect storm" scenario. It selects only those patients who have both a high burden of external, mechanical risk factors (quantified by the CLS—such as a long, complex operation with significant blood loss) and a severely compromised internal, biological capacity for healing (quantified by hypoalbuminemia). The CLS identifies an anastomosis that is already under duress from factors like tissue tension, borderline perfusion, and systemic inflammatory stress from the surgery itself.[14] Hypoalbuminemia signifies that the patient lacks the fundamental building blocks and oncotic pressure necessary to mount an effective healing response. Low albumin impairs the proliferative phase of wound healing by reducing fibroblast migration and collagen synthesis, resulting in a mechanically fragile anastomosis.[15] It also promotes tissue edema, which further compromises microvascular blood flow and oxygen delivery to the healing tissue. When these two conditions—a high-stress anastomosis and a low-capacity healing system—coexist, the probability of failure approaches certainty. Our model effectively isolates this small, extremely vulnerable subpopulation. Therefore, its clinical utility is not as a broad screening tool, but as a specific diagnostic alert. A "positive" test result should be interpreted as a critical warning, strongly prompting the surgical team to consider definitive risk-mitigating strategies, most notably the creation of a diverting stoma.[16]

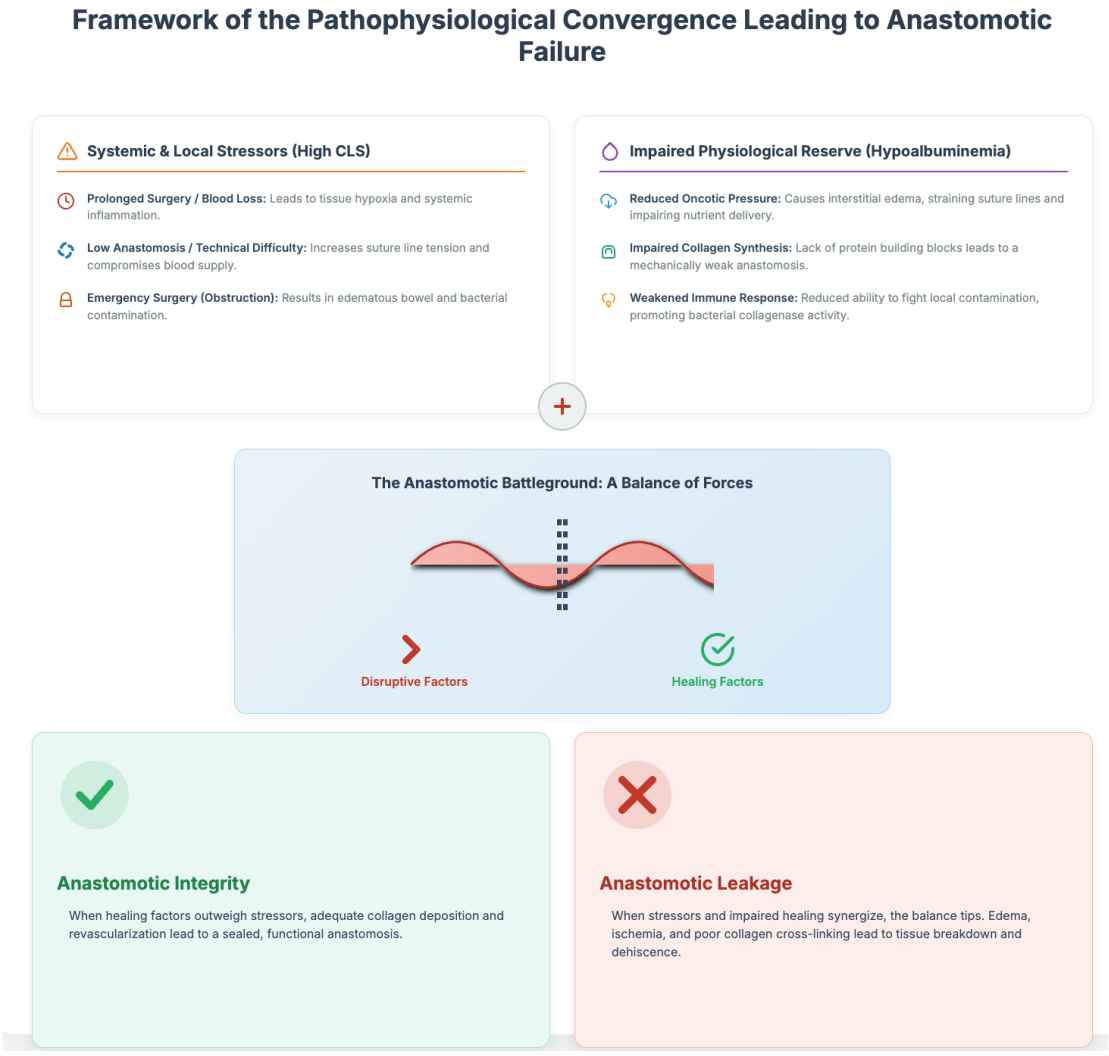

Figure 4. Framework of the pathophysiological convergence leading to anastomotic failure.

Figure 4 provides a powerful and elegant conceptual framework that visually synthesizes the core findings of this study into a cohesive pathophysiological narrative. The framework begins by delineating the two primary streams of risk that converge upon the newly created anastomosis, as shown in the top panel of Figure 4. On one side, we have the "Systemic & Local Stressors," which are quantified by a high Colon Leakage Score (CLS). These are the extrinsic, often iatrogenic, challenges imposed upon the patient's system. The figure highlights key examples: a prolonged and complex operation with significant blood loss precipitates a state of systemic inflammation and tissue hypoxia, starving the healing tissues of essential oxygen. A technically challenging low anastomosis introduces mechanical tension on the suture line and can directly compromise the delicate mesenteric blood supply. An emergency operation for obstruction means surgery is performed on the bowel that is edematous, friable, and heavily colonized with bacteria. These stressors collectively represent the external insults that the anastomosis must withstand. They create an environment that is hostile to healing, characterized by poor perfusion, mechanical strain, and a high bacterial load. On the other side of the framework, Figure 4 illustrates the second, equally critical stream of risk: the patient's "Impaired Physiological Reserve," which is biochemically represented by preoperative hypoalbuminemia. This represents the intrinsic, pre-existing weakness in the patient's ability to mount an effective healing response. As detailed in the schematic, this is not a single deficit but a multifaceted failure. Firstly, reduced oncotic pressure due to low albumin levels leads to interstitial edema. This fluid accumulation within the bowel wall physically separates the meticulously sutured edges of the anastomosis, increases tension, and further compresses the microvasculature, exacerbating the ischemia initiated by surgical stressors. Secondly, hypoalbuminemia signals a profound deficit in the body's protein building blocks. This directly translates to impaired collagen synthesis; fibroblasts at the healing site are unable to produce and deposit a strong, organized collagen matrix, resulting in an anastomosis that is mechanically flimsy and prone to dehiscence under normal physiological pressure. Thirdly, low albumin is a marker of a weakened immune system. This immunodeficiency cripples the local host response, rendering the anastomosis unable to effectively clear the inevitable bacterial contamination, which in turn allows bacteria to proliferate and release collagenase enzymes that actively digest and break down the fragile, newly formed tissue. The anastomosis is portrayed as the focal point where the external stressors (from the CLS) and the internal vulnerabilities (from hypoalbuminemia) meet. It is here that the critical "Balance of Forces" is contested. The outcome is not determined by either pathway in isolation but by their potent interaction. A patient with a robust physiological reserve (normal albumin) might successfully heal despite a high-stress surgery (high CLS). Conversely, a patient undergoing a low-stress procedure (low CLS) might still develop a leak if their internal healing capacity is severely compromised (low albumin). The highest risk, however, occurs when both streams converge—when a high-stress surgery is performed on a physiologically depleted patient. In this scenario, the disruptive factors overwhelm the healing factors, and the balance tips decisively towards failure. On one path lies "Anastomotic Integrity." This successful outcome is achieved when the patient's innate healing factors—bolstered by adequate nutrition, perfusion, and immune function—are sufficient to overcome the surgical stressors. This leads to organized collagen deposition, robust neovascularization, and the creation of a sealed, durable, and functional anastomosis. On the other path lies the catastrophic outcome of "Anastomotic Leakage." This occurs when the synergistic effect of external stressors and internal weakness proves overwhelming. The combination of edema, ischemia, and insufficient collagen cross-linking leads to necrosis of the bowel edges, tissue breakdown, and the formation of a physical defect, resulting in dehiscence and clinical leakage.[17] Figure 4 provides a clear,

compelling, and scientifically grounded visual argument. It transforms the abstract statistical findings of the study into a tangible biological process, providing an invaluable educational tool for clinicians to understand that anastomotic leakage is not a random event, but the predictable and tragic culmination of a battle between disruptive and healing forces—a battle whose outcome can be better anticipated by considering both the nature of the assault and the resilience of the patient.

While the model excels at confirming risk when positive, its poor sensitivity of 46.2% is a major limitation. This means the model failed to identify more than half of the patients who ultimately developed a leak. These 7 "False Negative" patients represent a significant clinical challenge. They leaked despite being classified as "low-risk" by our model. This finding compels a deeper exploration into the factors that drive AL beyond our composite criteria. Anastomotic leakage is the final common pathway of multiple potential insults. Our model accounts for clinical risks and nutritional status, but it cannot account for the intraoperative technical execution of the anastomosis—the "human factor." A technically imperfect anastomosis (with excessive tension, incorporation of ischemic tissue, or poorly spaced sutures) can leak even in a physiologically robust patient with a low CLS. Secondly, the CLS is a collection of macro-level risks. It does not capture micro-level physiological derangements. A patient could have a normal serum albumin but suffer from unmeasured deficiencies in specific micronutrients essential for wound healing, such as zinc or Vitamin C. They may have underlying microvascular disease secondary to undiagnosed diabetes or hypertension that impairs perfusion at the anastomotic line, a factor not explicitly measured by the CLS or albumin. Furthermore, postoperative events play a crucial role. A patient who develops a postoperative ileus with significant bowel distension will have increased intraluminal pressure straining the anastomosis. A hypotensive episode due to cardiac arrhythmia or a pulmonary embolism can cause a period of splanchnic hypoperfusion, rendering a previously viable anastomosis ischemic.[18] None of these dynamic, unpredictable postoperative events is captured by a static preoperative score. The poor sensitivity of our model is a humbling reminder that while preoperative risk stratification is vital, it is only one piece of the puzzle. Vigilant postoperative care and the technical quality of the operation remain paramount and are likely the drivers behind the leaks observed in our "low-risk" false-negative group.[19]

The most significant of these is the exclusion of all patients who received a diverting stoma. This decision, made to ensure a cohort where leakage could be clinically detected, introduces a major selection bias. Surgeons do not create stomas at random; they are created in patients judged intraoperatively to be at the highest risk. By excluding this group, we have systematically removed the very patients whom experienced surgeons believed were most likely to leak. This likely explains why only 8 patients in our cohort of 60 had a high CLS score. The true "high-risk" population, as defined by real-world clinical practice, was not included in our analysis. This bias profoundly impacts our results. The model was tested on an artificially selected, lower-risk population. In such a population, a predictive model's sensitivity is often lower, as the few leaks that occur may be driven by idiosyncratic or unmeasured factors. The excellent specificity, however, is not surprising; it is easier to correctly identify non-leakers in a group that is already pre-selected for being at lower risk. This limitation is critical and means our results cannot be generalized to the entire spectrum of colorectal surgery patients. The model's performance in a true high-risk population remains unknown. Additionally, the heterogeneity of our cohort, including patients from Stage I to Stage IV, introduces complexity. The pathophysiology of AL in an early-stage patient is likely dominated by technical factors and acute comorbidities, whereas in a metastatic Stage IV patient, systemic cachexia, immunosuppression, and the profound inflammatory burden of the disease are likely the primary drivers. Analyzing these disparate

groups together in a small sample may obscure stage-specific risk factors.[20]

Perhaps the most significant and clinically impactful finding of this study is not the performance of the model, but the baseline characteristic of the population itself: an astonishing 71.7% of patients undergoing major cancer surgery had preoperative hypoalbuminemia. This prevalence is exceptionally high compared to many reports from Western institutions and points towards a significant underlying public health and clinical challenge in our region. This may be attributable to several factors, including late presentation of disease, with patients already suffering from advanced cancer-related cachexia, as well as potential baseline endemic nutritional deficiencies in the community. This finding has major implications for the interpretation of our model. When a risk factor is present in nearly three-quarters of the population, its ability to discriminate between those who will and will not develop an outcome is inherently limited. In our cohort, hypoalbuminemia was almost a universal finding, making it less of a "risk factor" and more of a baseline population characteristic. The few patients (n=17) with normal albumin were a distinct minority who demonstrated exceptional resilience. This explains why the model's specificity was so high; the vast majority of patients who did not leak (46 out of 47) were in the "low-risk" group, many of whom were still hypoalbuminemic but had a low CLS. It also reinforces that while hypoalbuminemia creates a permissive environment for leakage, it is not sufficient on its own to cause a leak without the addition of significant clinical or technical stressors (a high CLS). The primary clinical takeaway from our study may be that aggressive, standardized preoperative nutritional optimization should be a non-negotiable standard of care for virtually all colorectal cancer patients in our setting.

5. Conclusion

This study provides critical new insights into risk stratification for anastomotic leakage in an Indonesian population. Our central conclusion is that the proposed synergistic model, combining the Colon Leakage Score and serum albumin, does not function as an effective general screening tool due to its poor sensitivity. It fails to identify more than half of the patients who will ultimately develop this complication. However, the model does demonstrate value as a highly specific "rule-in" test with a high positive predictive value. In the rare instance that a patient meets both high-risk criteria (CLS > 11 and albumin < 3.5 g/dL), they are at an exceptionally high probability of suffering an anastomotic leak. This finding allows for the identification of a small, hyper-vulnerable subset of patients for whom definitive risk-mitigating strategies, such as a diverting stoma, should be strongly considered. Perhaps more importantly, this study uncovers an alarmingly high baseline prevalence of preoperative hypoalbuminemia in our cohort, suggesting that significant malnutrition is a major, near-universal challenge in this patient population. This highlights a critical target for intervention, suggesting that systematic nutritional assessment and optimization may be one of the most impactful strategies to improve surgical outcomes in our region. Future prospective studies are needed to validate these findings and to develop more sensitive, regionally-adapted risk models.

6. References

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