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Rendimiento diagnóstico de la procalcitonina para detectar fuga anastomótica en adultos mayores con
cáncer colorrectal: un estudio transversal de tipo diferido

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**Diagnostic performance of procalcitonin for detecting anastomotic leak in older adults
with colorectal cancer: a delayed type cross-sectional study.**

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Abstract

Background: The utility of procalcitonin for detecting anastomotic leaks after colorectal surgery in older adults has not been well documented. As the immune system undergoes changes with age, procalcitonin levels may differ at baseline, and its diagnostic performance could vary when an anastomotic leak occurs after colorectal surgery in older adult patients with cancer. The aim of this study is to evaluate the diagnostic performance of procalcitonin on postoperative day 3 for detecting anastomotic leaks in older adults with colorectal cancer.

Methods: We conducted a diagnostic test study based on a delayed-type cross-sectional design in older adults (≥ 65 years old) with colorectal cancer. Postoperative day 3 procalcitonin levels were tested. The reference standard was anastomotic leak. We calculated the receiver operating characteristic curve and its area under the curve.

Results: The incidence of anastomotic leak was 7.7%. On postoperative day 3, the ROC demonstrated an AUC of 0.68 (95%CI:0.58–0.78) for the prediction of an anastomotic leak using procalcitonin levels. The cutoff point with the highest diagnostic performance, according to the Youden index, was 0.61 ng/ml, with a sensitivity of 0.69, specificity of 0.62, a LR+ of 1.86, and a LR- of 0.48 for predicting an anastomotic leak. The AUC was 0.78 when ileostomies were excluded and 0.81 when evaluating Grade C leaks.

Conclusion: Our study reveals that procalcitonin levels on postoperative day 3 are a poor diagnostic marker for identifying anastomotic leaks in older adults with colorectal cancer, with an improvement in performance for the Grade C anastomotic leak subgroup.

Keywords: procalcitonin, colorectal cancer, older adults, elderly, anastomotic leak.

Introduction

Procalcitonin is a precursor of calcitonin induced by thyroid C cells. In healthy individuals, only a very small amount is released into systemic circulation (<0.05 ng/L). During bacterial infection, its blood level increases rapidly, produced by other tissues(1). Under specific clinical conditions such as after surgical procedures, trauma, renal dysfunction, or immunosuppression, among others, procalcitonin levels may be also increased due to cytokine-mediated stimulation(2).

One of the documented uses of procalcitonin is as a biomarker for the early detection of anastomotic leaks, particularly in colorectal surgery. The reported incidence of anastomotic leaks in colorectal surgeries ranges between 2.8% and 30%(3). A recent systematic review and meta-analysis, which included 11 studies and 3,393 patients who underwent colorectal surgery, reported an area under the curve (AUC) of 0.87 for procalcitonin on postoperative day 3 was in detecting anastomotic leaks (4).

The utility of procalcitonin for detecting anastomotic leaks after colorectal surgery in older adults has not yet been described. Older adults represent an increasingly significant population group. The global number of individuals aged 65 or older is expected to double, from 761 million in 2021 to 1.6 billion in 2050, with the number of individuals aged 80 or older growing at an even faster rate(5,6). Considering this trend and the United Nations' call for research and program development focusing on the aging population (7), the issue is particularly pertinent.

The immune system undergoes age-related changes, a phenomenon known as immunosenescence and inflammaging. This involves a decline in immune function and defense mechanisms, leading to a reduced ability to trigger effective antibody and cellular responses against infections and vaccines. Moreover, there is an imbalance between pro-inflammatory and anti-inflammatory cytokines, resulting in chronic inflammation even in the absence of infection(8–10). Consequently, baseline procalcitonin levels may differ, and its diagnostic accuracy could vary when an anastomotic leak occurs after colorectal surgery in older adult patients with cancer.

Given these considerations, the aim of this study is to evaluate the diagnostic performance of procalcitonin on postoperative day 3 for detecting anastomotic leaks in older adult patients with colorectal cancer.

Methods

Study design

We conducted a diagnostic test study using a delayed-type cross-sectional design (11). All patients admitted to the institution between 2015 and 2022 who met the eligibility criteria were included in the study. Data for all variables were collected in an anonymous database using REDCap electronic data capture tools (12). The study was reviewed and approved by our institution's ethics committee (approval number 2568-CV1861). Upon admission, patients or their caregivers provided written informed consent for the use of their clinical information in research. The study adhered to the list of essential items for reporting diagnostic accuracy studies (STARD)(13).

Study population

Eligible study participants included older adults (≥ 65 years old) who underwent surgical resection of the colon or rectum for colorectal cancer. The exclusion criteria were as follows: (i) no anastomosis performed during the same surgical procedure, (ii) lack of procalcitonin measurement on postoperative day 3, (iii) insufficient follow-up to determine the presence of an anastomotic leak, (iv) patients with active infection prior to surgery, and (v) inability to provide informed consent.

The following variables were analyzed: demographic characteristics of the patients, body mass index (BMI), ASA Physical Status Classification, presence of diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular disease, chronic kidney disease, preoperative laboratory results, neoadjuvant treatments, including radiotherapy and/or chemotherapy, surgical approach (open or laparoscopic), tumor location, TNM classification, intraoperative bleeding and the need for transfusion, procalcitonin levels on postoperative day 3, surgical complications categorized according to the Clavien-Dindo Classification) and hospital stay duration. During the postoperative period, all patients were examined daily to assess their clinical condition, including assessment of pain, fever, hemodynamic status, abdominal examination, return of bowel function, and any wound drainage.

Index test

Serum procalcitonin levels were analyzed in the institution's clinical laboratory, using a chemiluminescence assay. Baseline procalcitonin values were not available because they are not part of the institutional protocol; however, blood levels were measured on postoperative day 3 for all patients as part of routine care. The procalcitonin values were used by the treating surgeons and informed clinical decision-making for each patient.

Reference standard

An anastomotic leak was defined as any deviation from the expected postoperative recovery associated with the anastomosis. This includes the presence of pus or enteric fluid in surgical drains or wounds, detection of an abdominal or pelvic collection near the anastomosis on a computed tomography (CT) scan, or identification of anastomotic dehiscence during reoperation. This includes anastomotic leakage grade A, B, or C according to The International Study Group of Rectal Cancer (14).

Statistical analysis

A description was made with demographic, clinical and surgical variables. Categorical variables were described as proportions and continuous variables as medians with their respective interquartile range (IQR). A bivariate analysis was performed with Mann-Whitney tests or chi-squared tests, as appropriate, in order to compare differences between the variables according to whether anastomotic leak was present or not. A linear regression analysis was performed to explore the factors that may influence procalcitonin levels.

We calculated the receiver operating characteristic (ROC) curve and its area under the curve (AUC) with the corresponding 95% confidence interval (95% CI). The optimal cutoff point with the highest diagnostic performance was determined using the Youden Index method, and we calculated its sensitivity, specificity and likelihood ratios (LR+ and LR-).

Additionally, we conducted subgroup analyses, excluding patients with a defunctioning ileostomy and those with anastomotic leakage grade A and B. This was done because these patient groups might exhibit a less severe inflammatory response.

The percentages of missing data for the variables were as follows: IMC 0.9%, albumin 16%, approach 0.9%, and intraoperative bleeding 4.4%; these were imputed using multiple imputation by predictive mean matching.

A p-value of <0.05 was considered statistically significant. All analyses were carried out using R (version 2023.12.1+402).

Sample size calculation

All patients who met the selection criteria during the study period were included in the analysis. A *post-hoc* sample power calculation was performed.

Results

A total of 338 patients were included in the study and a flowchart shows the selection process (**figure 1**).

The incidence of anastomotic leak was 7.7%, with 2 cases classified as Grade A, 9 as Grade B, and 15 as Grade C. The median age of the patients was 72.0 years (IQR: 69.0–78.0), with the majority being female (53.8%). Tumors were most commonly located in the right colon, followed by the sigmoid colon and rectum. The most frequent tumor stages were II and III (41.4% and 35.2%, respectively). When comparing characteristics based on the presence or absence of an anastomotic leak, we found that the ASA physical status classification was higher in patients with leaks. Additionally, tumor location in the rectum and the use of neoadjuvant therapy were more common in patients with leaks, with statistically significant differences observed. Further demographic, clinical, and surgical characteristics are detailed in **Table 1**.

The median procalcitonin level was 0.40 ng/mL (IQR: 0.17–0.99). When comparing procalcitonin levels between the groups, patients with anastomotic leaks had significantly higher levels (0.36 ng/mL, IQR: 0.17–0.92 vs. 0.90 ng/mL, IQR: 0.38–1.78; $p = 0.002$).

In terms of surgical outcomes, patients with an anastomotic leak exhibited a significantly higher proportion of major complications and mortality. Similarly, they experienced a longer hospital stay duration (**table 2**).

On postoperative day 3, the ROC curve demonstrated an AUC of 0.68 (95% CI: 0.58–0.78) for the prediction of an anastomotic leak using procalcitonin levels. The cutoff point with the highest diagnostic performance, according to the Youden Index, was 0.61 ng/ml, with a sensitivity of 0.69, specificity of 0.62, a LR+ of 1.86, and a LR- of 0.48 for predicting an anastomotic leak (**figure 2 and 3**).

In the subgroup analysis, we found that excluding patients with a defunctioning ileostomy increased the AUC to 0.78 (95% CI: 0.68–0.88). The optimal cutoff remained the same, with a sensitivity of 0.86, specificity of 0.62, a LR+ of 2.30, and a LR- of 0.21 for predicting an anastomotic leak. In the

other subgroup analysis, excluding patients with Grade A and B anastomotic leaks increased the AUC to 0.81 (95% CI: 0.73–0.89). The optimal cutoff remained unchanged, with a sensitivity of 0.93, specificity of 0.62, an LR+ of 2.51, and an LR- of 0.10 for predicting an anastomotic leak (**figure 2**).

Finally, when analyzing the factors that may influence procalcitonin levels on postoperative day 3, we found that age was significantly associated with higher levels ($p = 0.027$), while a laparoscopic approach was associated with lower procalcitonin levels compared to an open approach ($p < 0.001$). In contrast, neoadjuvant therapy, Charlson comorbidity index, and rectal tumor location were not associated with procalcitonin levels. This indicates that age and surgical approach are independent factors influencing procalcitonin levels, regardless of the presence of anastomotic leakage (**table 3**).

Using the obtained AUC value, the number of cases and controls, and a significance level of 0.05, a *post-hoc* power analysis calculated a power of 0.88 for the sample.

Discussion

The rate of anastomotic leaks after colorectal surgery was 7.7%, consistent with the expected range for such complications. This result is notable given our population's higher risk factors including advanced age and the presence of colorectal cancer in all patients (15,16).

Our findings indicate a poor diagnostic performance (17) of postoperative day 3 procalcitonin levels for predicting anastomotic leaks following colorectal resection in older adults with cancer. With a pre-test probability of 7.7%, the post-test probability for a procalcitonin level above the established cutoff point (0.61 ng/mL) would be 13%, and for a level below the cutoff, it would be 4% (**Figure 3**). These findings demonstrate that procalcitonin at this threshold cannot reliably rule in or rule out the anastomotic leaks.

Despite this, when we conducted a subgroup analysis excluding patients with a defunctioning ileostomy and those with Grade A and B anastomotic leaks, we observed an improvement in the performance of procalcitonin, with an AUC of 0.78 and 0.81, respectively. While this improvement in performance is significant, it is sometimes more important to detect Grade A and B leaks, as they often present with a more insidious clinical course. These findings may be related to the severity of the fistula and, consequently, the intensity of the inflammatory response. It is important to note that among the patients who did not undergo an ileostomy, only one had a Grade B leak, while the rest were Grade C. This means that by excluding patients with an ileostomy, we are also excluding the majority of Grade A and B leaks.

A recent meta-analysis including patients of all ages and with both benign and malignant conditions, reported a pooled AUC of 0.81 for postoperative day 3 procalcitonin levels, with a cutoff value of 0.75 ng/mL (4). This study found a pooled LR+ of 3.27 and a LR- of 0.34, suggesting that procalcitonin levels below this threshold might potentially rule out anastomotic leaks after colorectal surgery. However, the wide confidence intervals raised concerns about the reliability of these results. Specifically, they showed that a pre-test probability of 8% would decrease to a post-test probability of 3% with procalcitonin levels below 0.75 ng/mL, which is not compelling for ruling out leaks (4). Similarly, another meta-analysis, including different age groups and with both benign and malignant conditions, found a pooled AUC of 0.87 for postoperative day 3 procalcitonin levels, suggesting better diagnostic performance than our findings (16). The discrepancy between our findings and

those of these systematic reviews could be attributed to multiple factors, including differences in patient populations, methodologies, and cutoff thresholds. However, when performing the subgroup analysis, the results are more similar to those reported in the literature.

Firstly, we exclusively included older adult patients, who have distinct characteristics compared to other age groups. In this population, the balance between pro-inflammatory and anti-inflammatory responses is often disrupted, potentially causing variations in procalcitonin levels (18). In other infectious conditions, where prior studies have demonstrated good diagnostic performance of procalcitonin, this effect has been less consistent in older adults (19), although some studies still report reliable performance (20,21). For example, a study by Ying Yang et al., which evaluated older adults with and without infection, including pneumonia, based on frailty status, found a positive association between procalcitonin levels and frailty, independent of infection status. Secondly, all included patients had colorectal cancer, with no cases of benign disease. Baseline procalcitonin levels may differ in colorectal cancer patients, which could limit its diagnostic performance for predicting anastomotic leaks in this population (22,23).

Immunosenescence is closely linked to inflammaging, a process associated with aging. This phenomenon involves the secretion of various molecules, including proteases, chemokines, angiogenic factors, proinflammatory cytokines, matrix metalloproteinases, and extracellular matrix components. These changes can alter the inflammatory response in older adults and lead to variations in the baseline and infection-induced levels of several inflammatory biomarkers, such as procalcitonin, C-reactive protein, and leukocytosis, among others (24,25).

A model was developed to predict procalcitonin levels on postoperative day 3 and to explore plausible explanatory variables for these levels. As previously mentioned, age can influence procalcitonin levels, and surgical approach has also been shown to affect them, as well as the trauma associated with open surgery may elevate procalcitonin levels. Finally, the variable of interest— anastomotic leak—was also included in the model. The variables age, laparoscopic approach and anastomotic leak were statistically significant. Notably, laparoscopic surgery was inversely associated with procalcitonin levels, consistent with prior studies suggesting that minimally invasive approaches lead to reduced surgical trauma and inflammatory response (4). Also, the variables neoadjuvant therapy, Charlson comorbidity index, and rectal tumor location were included in the model, but they were not statistically significant.

More recently, combined markers such as C-reactive protein, procalcitonin, and leukocyte count have been evaluated to improve predictive performance. Additionally, clinical variables like ASA classification status and comorbidities have been integrated into predictive models. These approaches may offer enhanced diagnostic accuracy, particularly in older adults with colorectal cancer, by accounting for the unique physiological and clinical characteristics of this population (26,27).

This study has several notable strengths. To our knowledge, it is the only study evaluating the performance of procalcitonin as a diagnostic marker for anastomotic leaks in older adults. Although we did not conduct an a priori sample size calculation, we performed a post-hoc power analysis, which demonstrated a power greater than 80% with a significance level of 0.05. The missing data was minimal (less than 5%), except for albumin, which was only a descriptive variable. However, this study also has several limitations. First, a major limitation is the lack of a definitive gold standard for diagnosing anastomotic leaks. It is possible that under-diagnosis of anastomotic leak occurred in our

study due to asymptomatic or mildly symptomatic leaks that did not warrant further investigation. Second, this study was conducted at a single center with a selected patient sample, which may limit the generalizability of the findings. Third, incorporation bias is present, as the treating surgeons were aware of the procalcitonin levels (the result of the index test), which could have influenced clinical decision-making. Lastly, we did not have baseline procalcitonin levels, which could provide critical context, as elevated levels might indicate pre-existing inflammatory conditions (inflammaging) or malignancies.

Future studies should explore additional biomarkers or integrate procalcitonin with clinical parameters to enhance diagnostic accuracy in this population. They should also measure baseline procalcitonin levels preoperatively and evaluate their correlation with postoperative levels.

Conclusion

Our study indicates that procalcitonin levels on postoperative day 3 are a poor diagnostic marker for identifying anastomotic leaks in older adults with colorectal cancer, with an improvement in performance for Grade C anastomotic leak subgroup. Surgeons should be cautious using procalcitonin for the early detection of anastomotic leak in this patient population. Further research is needed to better define the role of procalcitonin in predicting anastomotic leaks in older adults.

Declarations

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Availability of data and material: The data and statistical analysis are available in the supplementary material.

Author contribution

Camilo Ramírez-Giraldo: Study conception and design, analysis and interpretation of data, drafting of manuscript, critical revision of manuscript.

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Andrés Isaza-Restrepo: Study conception and design, analysis and interpretation of data, drafting of manuscript, critical revision of manuscript.

All authors and approved the final version of the manuscript.

Ethical Standards

Ethical compliance with the Helsinki Declaration, current legislation on research Res. 008430-1993 and Res. 2378-2008 (Colombia) and the International Committee of Medical Journal Editors (ICMJE) were ensured under our Ethics and Research Institutional Committee (IRB) approval. Informed consent was filled out as required for the execution of this study.

References

1. Davies J. Procalcitonin. *J Clin Pathol*. 2015;68(9):675–9.
2. Smith SE, Muir J, Kalabalik-Hoganson J. Procalcitonin in special patient populations: Guidance for antimicrobial therapy. *Am J Heal Pharm*. 2021;77(10):745–57.
3. Chiarello MM, Fransvea P, Cariati M, Adams NJ, Bianchi V, Brisinda G. Anastomotic leakage in colorectal cancer surgery. *Surg Oncol* [Internet]. 2022;40(January):101708. Available from: <https://doi.org/10.1016/j.suronc.2022.101708>
4. Xu Z, Zong R, Zhang Y, Chen J, Liu W. Diagnostic accuracy of procalcitonin on POD3 for the early diagnosis of anastomotic leakage after colorectal surgery: A meta-analysis and systematic review. *Int J Surg* [Internet]. 2022;100(February):106592. Available from: <https://doi.org/10.1016/j.ijso.2022.106592>
5. United Nations Department of Economic and Social Affairs. World Social Report 2023: Leaving No One Behind in an Ageing World. United Nations [Internet]. 2023. Available from: <https://www.un-ilibrary.org/content/books/9789210019682>.
6. Isaza-restrepo A, Ramírez-giraldo C, Venegas-sanabria LC, Rojas-lópez S. Hacia la formalización de programas para la atención quirúrgica integral del paciente anciano. *Rev Colomb Cir*. 2025;40(1):474–82.
7. Lozada-martinez ID, Sebastian J, Castelblanco-toro SM, Sarmiento M, Mazonett-granados EA, Fredy J, et al. Demographics and clinical characteristics of a new population of centenarians in Colombia . The COOLCEN cohort. *Arch Gerontol Geriatr Plus*. 2024;1(October 2023).
8. Quiros-Roldan E, Sottini A, Natali PG, Imberti L. The Impact of Immune System Aging on Infectious Diseases. *Microorganisms*. 2024;12(4):1–30.
9. Miki C, Kusunoki M, Inoue Y, Uchida K, Mohri Y, Buckels JAC, et al. Remodeling of the immunoinflammatory network system in elderly cancer patients: Implications of inflamm-aging and tumor-specific hyperinflammation. *Surg Today*. 2008;38(10):873–8.
10. Fulop T, Larbi A, Dupuis G, Page A Le, Frost EH, Cohen AA, et al. Immunosenescence and inflamm-aging as two sides of the same coin: Friends or Foes? *Front Immunol*. 2018;8(JAN).
11. Knottnerus JA, Muris JW. Assessment of the accuracy of diagnostic tests: The cross-sectional study. *J Clin Epidemiol*. 2003;56(11):1118–28.
12. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O’Neal L, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* [Internet]. 2019;95(May):103208. Available from: <https://doi.org/10.1016/j.jbi.2019.103208>
13. Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: Explanation and elaboration. *BMJ*

- Open. 2016;6(11):1–17.
14. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: A proposal by the International Study Group of Rectal Cancer. *Surgery*. 2010;147(3):339–51.
 15. Litchinko A, Buchs N, Balaphas A, Toso C, Liot E, Meurette G, et al. Score prediction of anastomotic leak in colorectal surgery: a systematic review. *Surg Endosc*. 2024;38(4):1723–30.
 16. Bona D, Danelli P, Sozzi A, Sanzi M, Cayre L, Lombardo F, et al. C-reactive Protein and Procalcitonin Levels to Predict Anastomotic Leak After Colorectal Surgery: Systematic Review and Meta-analysis. *J Gastrointest Surg*. 2023;27(1):166–79.
 17. Nahm FS. Receiver operating characteristic curve: overview and practical use for clinicians. *Korean J Anesthesiol*. 2022;75(1):25–36.
 18. Koo EGY, Lai LML, Choi GYS, Chan MTV. Systemic inflammation in the elderly. *Best Pract Res Clin Anaesthesiol*. 2011;25(3):413–25.
 19. Choi JJ, McCarthy MW, Meltzer KK, Cornelius-Schecter A, Jabri A, Reshetnyak E, et al. The Diagnostic Accuracy Of Procalcitonin for Urinary Tract Infection in Hospitalized Older Adults: a Prospective Study. *J Gen Intern Med [Internet]*. 2022;37(14):3663–9. Available from: <https://doi.org/10.1007/s11606-021-07265-8>
 20. Lin XY, Lin YZ, Lin SH, Lian JJ. Effect of procalcitonin on the severity and prognostic value of elderly patients with a severe infection of oral and maxillofacial space. *Med (United States)*. 2022;101(34):E30158.
 21. Zincircioğlu Ç, Rollas K, Güldoğan IK, Saritaş A, Özkarakaş H, Ersan G, et al. Diagnostic value of procalcitonin and c reactive protein for infection and sepsis in elderly patients. *Turkish J Med Sci*. 2021;51(5):2649–56.
 22. Miyake T, Iida H, Shimizu T, Ueki T, Kojima M, Ohta H, et al. The Elevation in Preoperative Procalcitonin Is Associated with a Poor Prognosis for Patients Undergoing Resection for Colorectal Cancer. *Dig Surg*. 2021;38(1):80–6.
 23. Villegas-Coronado L, Villegas-Coronado K, Urrea-Quezada A, Villegas-Coronado D. Procalcitonin as an Early Marker of Colorectal Anastomotic Leakage in Postoperative Colorectal Cancer Patients : A Systematic Review and Meta- Analysis. *Cureus*. 2024;16(10):1–17.
 24. Liu Z, Liang Q, Ren Y, Guo C, Ge X, Wang L, et al. Immunosenescence: molecular mechanisms and diseases. *Signal Transduct Target Ther*. 2023;8(1).
 25. Santoro A, Bientinesi E, Monti D. Immunosenescence and inflammaging in the aging process: age-related diseases or longevity? *Ageing Res Rev*. 2021;71(August).
 26. El Zaher HA, Ghareeb WM, Fouad AM, Madbouly K, Fathy H, Vedin T, et al. Role of the triad of procalcitonin, C-reactive protein, and white blood cell count in the prediction of anastomotic leak following colorectal resections. *World J Surg Oncol [Internet]*. 2022;20(1):1–10. Available from: <https://doi.org/10.1186/s12957-022-02506-4>
 27. Yang L, Zhang P, Yang W, Huang Y, Lv J, Du Y, et al. Development and Validation of a Novel Nomogram Model for Early Diagnosis of Anastomotic Leakage After Laparoscopic Colorectal Cancer Surgery. *Surg Infect (Larchmt)*. 2024;

Figure 1. Flowchart selection process.

Figure 2. ROC curve of procalcitonin levels on postoperative day 3.

Figure 3. Fagan's nomogram with cut-off de 0.61 ng/ml of procalcitonin levels on postoperative day 3.

Table 1. Demographic and clinical characteristics based on the presence or absence of an anastomotic leak.

	N (%)	No anastomotic leak(n=312)	Anastomotic leak (n=26)	p value
Age(median)(IQR)(years)	72.00 (69.00 – 78.00)	72.00 (69.00 - 78.00)	76.50 (71.25 - 79.00)	0.096*
Sex				0.065
Female	182 (53.8)	173 (55.4)	9 (34.6)	
Male	156 (46.2)	139 (44.6)	17 (65.4)	
Body mass index (median)(IQR)(kg/m ²)	25.05(22.40 – 27.50)	25.15 (22.65 - 27.52)	23.30 (21.40 - 25.97)	0.081*
ASA				0.022
I	0 (0.0)	0 (0.0)	0 (0.0)	
II	131 (38.8)	127 (40.7)	4 (15.4)	
III	203 (60.1)	182 (58.3)	21 (80.8)	
IV	4 (1.2)	3 (1.0)	1 (3.8)	
Co-morbidity				
Arterial hypertension	206 (60.9)	194 (62.2)	12 (46.2)	0.162
Diabetes mellitus	53 (17.7)	49 (15.7)	4 (15.4)	1.000
Chronic obstructive pulmonary disease	19 (5.6)	18 (5.8)	1 (3.8)	1.000
Chronic kidney disease	10 (3.0)	8 (2.6)	2 (7.7)	0.379
Cardiovascular disease	37 (10.9)	34 (10.9)	3 (11.5)	1.000
Charlson comorbidity index (median)(IQR)(points)	5.00 (4.00 – 6.00)	5.00 (4.00 - 6.00]	5.00 (5.00 - 6.00)	0.913*
Albumin (median)(IQR)(mg/dL)	3.89 (3.42 – 4.20)	3.89 (3.46 - 4.20)	3.75 (3.22 - 4.35)	0.606*
Tumor location				0.028
Right-sided	132 (39.1)	123 (39.4)	9 (34.6)	
Left-sided	16 (4.7)	15 (4.8)	1 (3.8)	
Transverse	9 (2.7)	8 (2.6)	1 (3.8)	
Sigmoid	94 (27.8)	92 (29.5)	2 (7.7)	
Rectum	87 (25.7)	74 (23.7)	13 (50.0)	
Defunctioning ileostomy				0.015
No	265 (78.4)	250 (80.1)	15 (57.7)	
Yes	73 (21.6)	62 (19.9)	11 (42.3)	
Neoadjuvant				0.043
No	296 (87.6)	277 (88.8)	19 (73.1)	
Yes	42 (12.4)	35 (11.2)	7 (26.9)	
Stage				0.958
I	66 (19.5)	61 (19.6)	5 (19.2)	
II	140 (41.4)	128 (41.0)	12 (46.2)	
III	119 (35.2)	111 (35.6)	8 (30.8)	
IV	13 (3.8)	12 (3.8)	1 (3.8)	

Lymphovascular invasion				0.886
No	197 (58.3)	181 (58.0)	16 (61.5)	
Yes	141 (41.7)	131 (42.0)	10 (38.5)	
Perineural invasion				0.075
No	293 (86.7)	267 (85.6)	26 (100.0)	
Yes	45 (13.3)	45 (14.4)	0 (0.0)	
Resection margin				0.558
R0	335 (99.1)	310 (99.4)	25 (96.2)	
R+	3 (0.9)	2 (0.6)	1 (3.8)	
Approach				0.306
Open	9 (2.7)	7 (2.2)	2 (7.7)	
Laparoscopic	329 (97.3)	305 (97.8)	24 (92.3)	
Transfusion				0.844
No	309 (91.4)	286 (91.7)	23 (88.5)	
Yes	29 (8.6)	26 (8.3)	3 (11.5)	
Intraoperative bleeding (median)(IQR)(ml)	30.00 (15.00 – 100.0)	30.00 (15.00 - 100.00)	50.00 (20.00 - 115.00)	0.232
p values were obtained using the chi-squared test.				
*p values were obtained using the Mann–Whitney test.				
Bold values indicate statistically significant p values (p < 0.05)				

Table 2. Surgical outcomes based on the presence or absence of an anastomotic leak.

	N (%)	No anastomotic leak(n=312)	Anastomotic leak (n=26)	p value
Procalcitonin on postoperative day 3 (median)(IQR)(ng/ml)	0.40 (0.17 – 0.99)	0.36 (0.17 - 0.92)	0.90 (0.38 - 1.78)	0.002*
Hospital stay (median)(IQR)(days)	4.00 (3.00 – 6.00)	4.00 (3.00 - 5.00)	15.00 (5.25 - 19.50)	<0.001*
Major complication (Clavien-Dindo ≥ III)				<0.001
No	305 (90.2)	298 (95.5)	7 (26.9)	
Yes	33 (9.8)	14 (4.5)	19 (73.1)	
Mortality				0.002
No	332 (98.2)	309 (99.0)	23 (88.5)	
Yes	6 (1.8)	3 (1.0)	3 (11.5)	
p values were obtained using the Chi-squared test				
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Bold values indicate statistically significant p values (p < 0.05)				

Table 3. Linear regression model to predict procalcitonin levels on postoperative day 3.

Variables in the model	Regression coefficient β	standard error	p-value
Intercept, β_0	1.394	0.234	<0.001
Mean Age, β_1	0.012	0.005	0.027
Anastomotic leak, β_2	0.457	0.121	<0.001
Laparoscopic approach, β_3	-0.947	0.198	<0.001
Neoadjuvant therapy, β_4	0.133	0.112	0.234

Charlson comorbidity index, β_5	0.020	0.024	0.402
Rectal tumor, β_6	-0.147	0.086	0.087
Bold values indicate statistically significant p values ($p < 0.05$)			

Adults with Colorectal Cancer

Anastomotic leaks increase morbidity/mortality after colorectal surgery.



Procalcitonin (PCT) is used for infection detection, but its reliability for leaks in older adults (≥ 65 years) is unclear.



Leak incidence: 7.7%

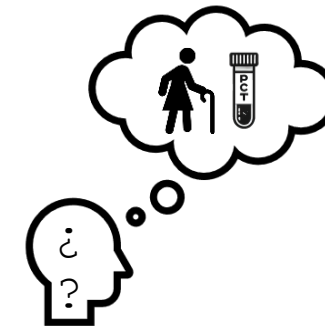
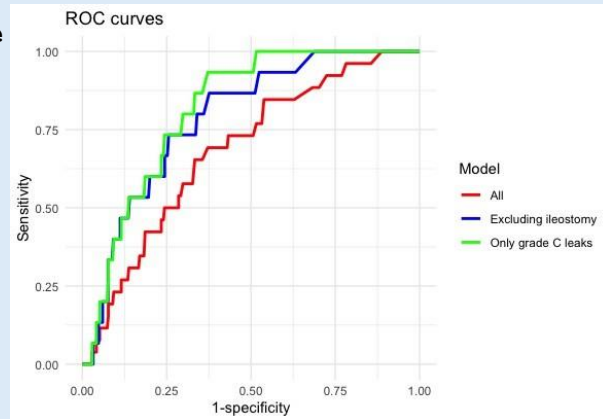
Optimal PCT cutoff: 0.61 ng/mL

Diagnostic Performance: AUC: 0.68 (95% CI: 0.58-0.78) Sensitivity: 0.69 | Specificity: 0.62

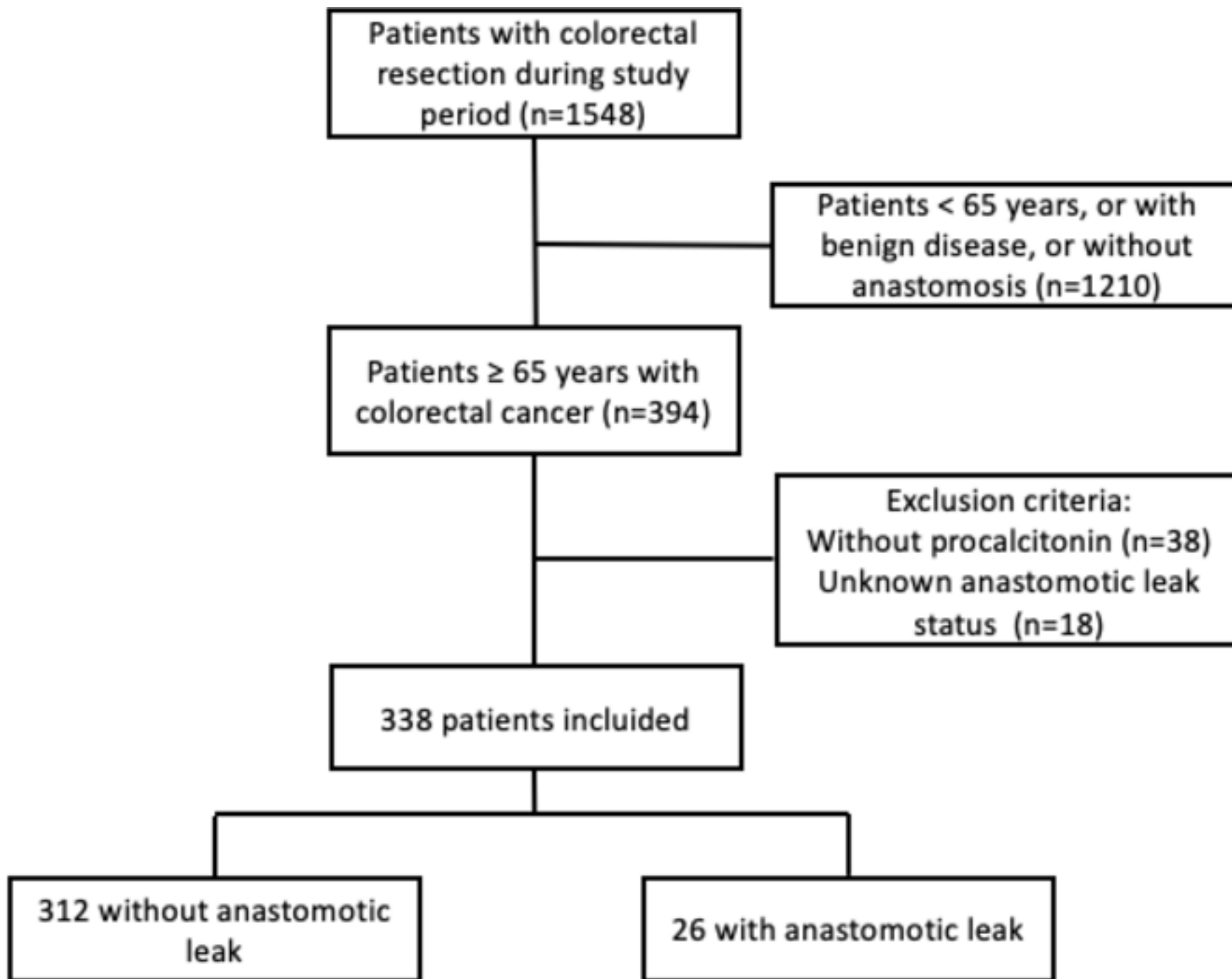
Delayed-type cross-sectional diagnostic study

Population: Older adults (≥ 65 years) with colorectal cancer

Test



Procalcitonin is a poor diagnostic marker for leaks in older adults, with an improvement in performance for the Grade C anastomotic leak subgroup.



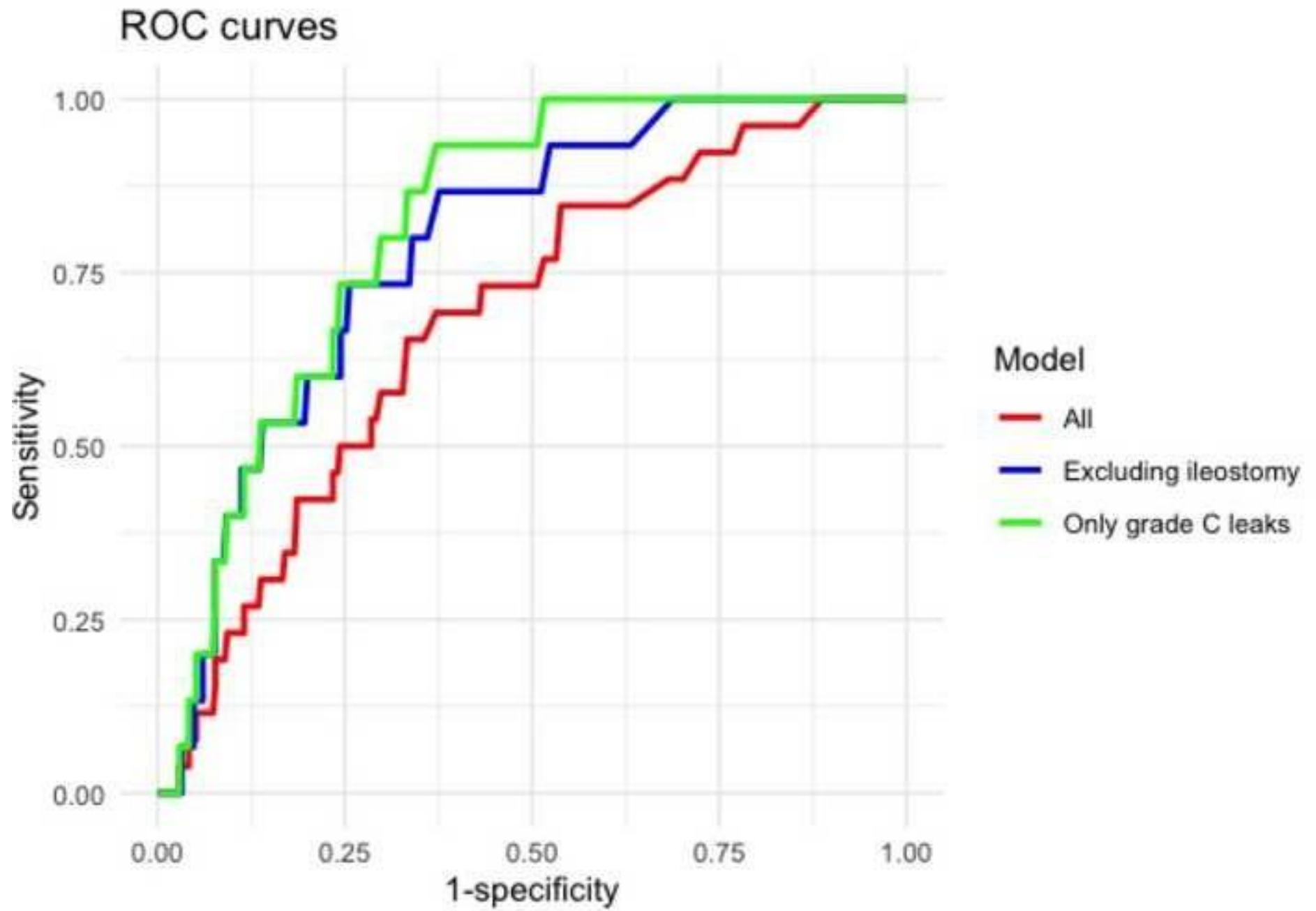


Figure 3

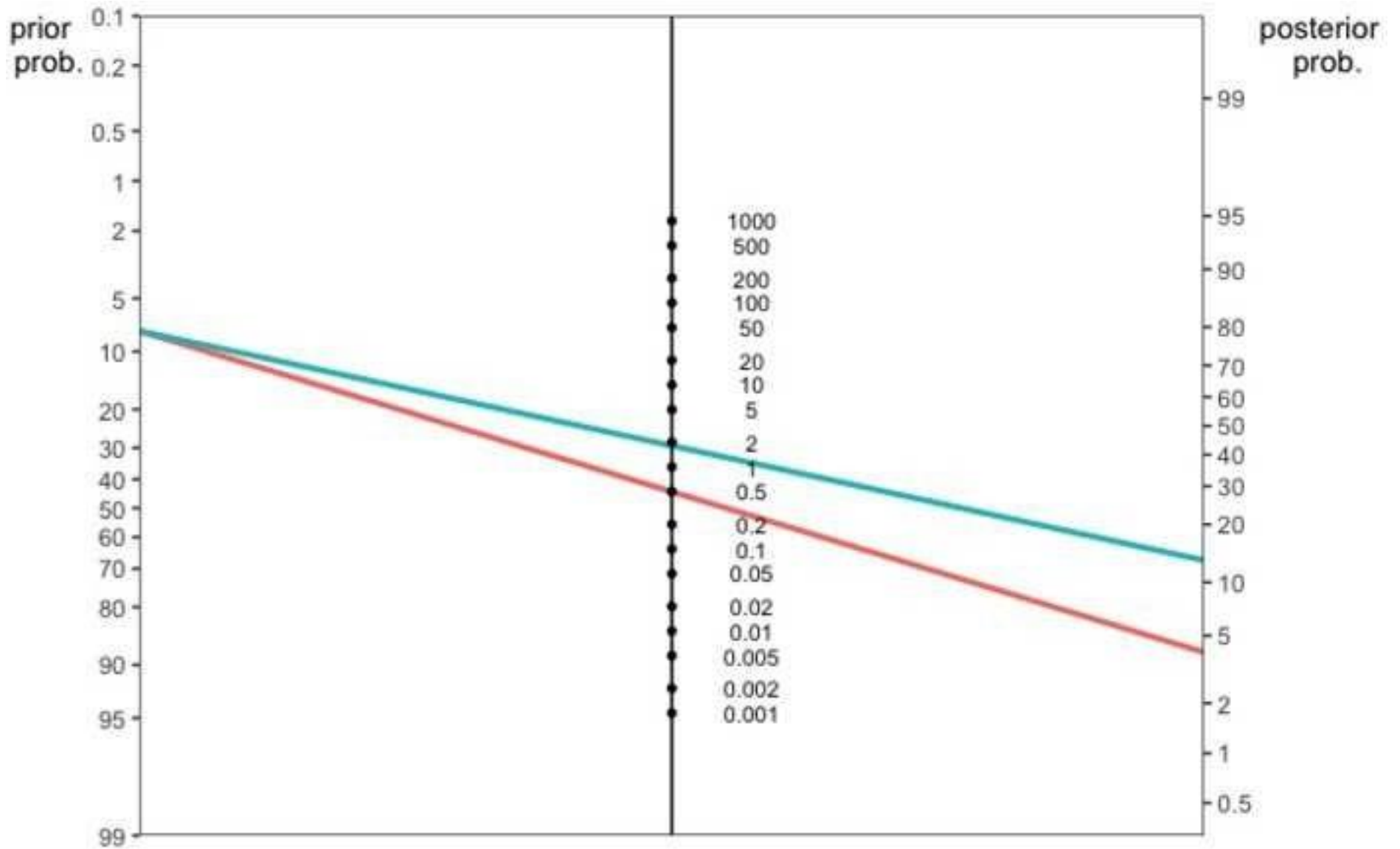


Table 1. Demographic and clinical characteristics based on the presence or absence of an anastomotic leak.

	N (%)	No anastomotic leak(n=312)	Anastomotic leak (n=26)	p value
Age(median)(IQR)(years)	72.00 (69.00 – 78.00)	72.00 (69.00 - 78.00)	76.50 (71.25 - 79.00)	0.096*
Sex				0.065
Female	182 (53.8)	173 (55.4)	9 (34.6)	
Male	156 (46.2)	139 (44.6)	17 (65.4)	
Body mass index (median)(IQR)(kg/m ²)	25.05(22.40 – 27.50)	25.15 (22.65 - 27.52)	23.30 (21.40 - 25.97)	0.081*
ASA				0.022
I	0 (0.0)	0 (0.0)	0 (0.0)	
II	131 (38.8)	127 (40.7)	4 (15.4)	
III	203 (60.1)	182 (58.3)	21 (80.8)	
IV	4 (1.2)	3 (1.0)	1 (3.8)	
Co-morbidity				
Arterial hypertension	206 (60.9)	194 (62.2)	12 (46.2)	0.162
Diabetes mellitus	53 (17.7)	49 (15.7)	4 (15.4)	1.000
Chronic obstructive pulmonary disease	19 (5.6)	18 (5.8)	1 (3.8)	1.000
Chronic kidney disease	10 (3.0)	8 (2.6)	2 (7.7)	0.379
Cardiovascular disease	37 (10.9)	34 (10.9)	3 (11.5)	1.000
Charlson comorbidity index (median)(IQR)(points)	5.00 (4.00 – 6.00)	5.00 (4.00 - 6.00]	5.00 (5.00 - 6.00)	0.913*
Albumin (median)(IQR)(mg/dL)	3.89 (3.42 – 4.20)	3.89 (3.46 - 4.20)	3.75 (3.22 - 4.35)	0.606*
Tumor location				0.028
Right-sided	132 (39.1)	123 (39.4)	9 (34.6)	
Left-sided	16 (4.7)	15 (4.8)	1 (3.8)	
Transverse	9 (2.7)	8 (2.6)	1 (3.8)	
Sigmoid	94 (27.8)	92 (29.5)	2 (7.7)	
Rectum	87 (25.7)	74 (23.7)	13 (50.0)	
Defunctioning ileostomy				0.015
No	265 (78.4)	250 (80.1)	15 (57.7)	
Yes	73 (21.6)	62 (19.9)	11 (42.3)	
Neoadjuvant				0.043
No	296 (87.6)	277 (88.8)	19 (73.1)	
Yes	42 (12.4)	35 (11.2)	7 (26.9)	
Stage				0.958
I	66 (19.5)	61 (19.6)	5 (19.2)	
II	140 (41.4)	128 (41.0)	12 (46.2)	
III	119 (35.2)	111 (35.6)	8 (30.8)	
IV	13 (3.8)	12 (3.8)	1 (3.8)	
Lymphovascular invasion				0.886
No	197 (58.3)	181 (58.0)	16 (61.5)	

Yes	141 (41.7)	131 (42.0)	10 (38.5)	
Perineural invasion				0.075
No	293 (86.7)	267 (85.6)	26 (100.0)	
Yes	45 (13.3)	45 (14.4)	0 (0.0)	
Resection margin				0.558
R0	335 (99.1)	310 (99.4)	25 (96.2)	
R+	3 (0.9)	2 (0.6)	1 (3.8)	
Approach				0.306
Open	9 (2.7)	7 (2.2)	2 (7.7)	
Laparoscopic	329 (97.3)	305 (97.8)	24 (92.3)	
Transfusion				0.844
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Two-Sentence Article Summary

- To evaluate the diagnostic performance of procalcitonin on postoperative day 3 for detecting anastomotic leaks in older adults with colorectal cancer.
- The importance of this is that surgeons should be cautious when using procalcitonin for the early detection of anastomotic leak in this patient population.