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URGENCY INDEX AND PREOPERATIVE INDEX: PREDICTION OF ANASTOMOTIC LEAKAGE IN PATIENTS OPERATED FOR COLORECTAL CANCER TREATMENT

ÍNDICE DE URGÊNCIA E ÍNDICE PRÉ-OPERATÓRIO: PREDIÇÃO DE FÍSTULAS ANASTOMÓTICAS EM PACIENTES OPERADOS PARA TRATAMENTO DE CÂNCER COLORRETAL

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Abstract – Several tools are available for predicting the risk of anastomotic leakage (AL) in patients undergoing colectomy for colorectal cancer (CRC) treatment. However, these prognostic indexes have limitations in applicability and efficiency. **AIM:** Developing validated, efficient and easily applicable tools to help physicians predict the risk of AL. **METHODS:** From a meta-analysis and a retrospective cohort, risk factors associated with the development of AL were used to construct and validate two new indexes (Urgency Index and Preoperative Index) to predict AL risk. Sensitivity, specificity, ROC curve, accuracy, and positive and negative predictive value were calculated. **RESULTS:** The Urgency Index indicated four variables for AL risk prediction and showed sensitivity of 81.24%, specificity of 75.8%, AUC of 0.841 (95% CI: 0.742-0.939), and accuracy of 76.24%. The Preoperative Index revealed 13 variables and showed 86.56% specificity, 50% sensitivity, 0.699 area under the ROC curve, 83.66% accuracy, 24.24% positive predictive value, and 95.27% negative predictive value. **CONCLUSION:** The two new indexes created for AL risk prediction in patients operated for CRC treatment present good results of specificity, accuracy, and reasonable AUC values and could be used in clinical practice.

Keywords: Maximum of five wordsColorectal neoplasms. Fistula. Risk factors

Resumo – Existem algumas ferramentas para predição de risco de fístula anastomótica (FA) em pacientes que serão submetidos a colectomia para tratamento de câncer colorretal (CCR). Entretanto, esses índices prognósticos apresentaram limitações de aplicabilidade e eficiência. **OBJETIVO:** Desenvolver ferramentas validadas, eficientes e facilmente aplicáveis que auxiliem os médicos na predição de risco de FA. **MÉTODOS:** A partir de uma meta-análise e uma coorte retrospectiva foram encontrados fatores de risco associados ao desenvolvimento de FA, esses foram utilizados para construção e validação de dois novos índices (Índice de Urgência e Índice Pré-operatório) com o objetivo de predizer risco de FA, sendo calculado sensibilidade, especificidade, curva ROC, acurácia, valor preditivo positivo e negativo. **RESULTADOS:** O Índice de Urgência conta com 4 variáveis para predição de risco de FA e apresentou sensibilidade de 81,24%, especificidade de 75,8%, AUC de 0,841 (IC 95%: 0,742-0,939) e acurácia de 76,24%. O Índice Pré-operatório conta com 13 variáveis e apresentou 86,56% de especificidade, 50% de sensibilidade, 0,699 de área sob a curva ROC, 83,66% de acurácia, 24,24% de valor preditivo positivo, 95,27% de valor preditivo negativo. **CONCLUSÃO:** Os dois novos índices criados para predição de risco de FA em pacientes operados para tratamento de CCR, apresentam bons resultados de especificidade, acurácia e valores razoáveis de AUC e poderão ser utilizados na prática clínica.

Descritores: Neoplasias colorretais Fístula. Fatores de risco.

Introduction

Anastomotic leakage (AL) is a significant complication of colorectal surgery related to increased local recurrence and decreased survival (Wang; Liu, 2020). According to Wang and Liu (2020), it is a severe surgical complication with rates ranging from 2.2% to 18.6%, related to a more extended hospital stay, increased medical costs, and morbidity and mortality in a short period, becoming the most feared complication.

Previous studies have shown that gender, coronary artery disease, type of surgical method, preoperative serum albumin level, and other factors are predictive of AL (Zhou et al, 2020). However, despite knowledge of these risk factors (RF) and improvements in surgical techniques in recent years, the incidence of AL remains unaffected (Shen et al, 2019).

One means a way of reducing the complications and severity resulting from AL is the creation of a protective stoma. Nevertheless, deciding to perform a protective ostomy is problematic because it can lead to numerous complications and harm to the patient.

Thus, some authors have created tools to predict the risk of AL (Dekker et al., 2011; Frasson et al, 2015; Rojas-Machado et al, 2015). However, according to Sammour et al. (2017), there is currently no reliable way to predict AL risk. Clinically valuable data to inform the decision and solicit patient consent on the need for a protective stoma or whether to avoid an unnecessary anastomosis remains quite limited. Moreover, these tools have limitations in applicability and efficiency. In particular, in the preoperative evaluation, these tools have become useless for the surgeon, not even in assessing the risk of AL or deciding whether to use a protective stoma.

Hence, it is necessary to construct validated, efficient, and easy-to-apply tools that effectively assist the physician in predicting the risk of AL, making an ostomy less arbitrary and more accurate, which is the objective of this study.

Materials and methods

This study was approved by the Research Ethics Committee of Santa Casa from Belo Horizonte. CAAE: 36476320.2.0000.5138. Two new tools were constructed to predict the risk of AL in patients undergoing surgery to treat CRC: Urgency Index and Preoperative Index.

A retrospective cohort was performed to construct and validate the Urgency Index. It is an index with only four variables and is easy to apply. Therefore, this Index is recommended for urgent and emergency surgeries.

To perform the Preoperative Index, we used the result of a meta-analysis (Dias et al, 2022) that studied the preoperative RF for the occurrence of AL in patients operated on to treat CRC (Table 1). The Index, which contains (Papamichael et al, 2015) variables, was applied to the patients of the cohort for its validation. Thus, its use is recommended for elective colectomies, as it is a more robust study (meta-analysis) of the RF for the occurrence of AL, allowing the physician to insert risk reduction measures promptly. In addition, due to the variables, a more in-depth study on the patient will be necessary, ideally occurring in the preoperative period of elective colectomies.

Retrospective cohort and construction of the Urgency Index

A retrospective cohort was carried out by analyzing 207 medical records of patients operated on for the treatment of CRC by the Coloproctology and General

Surgery Service of the Hospital São José do Avaí (Itaperuna - Rio de Janeiro, Brazil) from January 2010 to December 2020. Patients were operated by specialists in general surgery and coloproctology.

Patients were followed up at 3, 7, 15, 30, 90, and 180 days after discharge, being evaluated by a surgeon and/or oncologist in an outpatient setting. In case of any alterations and if necessary, the patient was hospitalized.

The patients were operated by seven surgeons from the clinical staff of the General Surgery Service of the Hospital São José do Avaí. The surgeons had extensive experience in colorectal oncologic surgery, having a large casuistry in these cases, with residency in general surgery and surgical subspecialty (R3). They have more than ten years of experience in general surgery and oncology (coloproctology).

Inclusion Criteria: Patients submitted to laparoscopic colectomy (Right colectomy, Left colectomy, Sigmoidectomy, Rectosigmoidectomy, Anterior rectal resection, Total colectomy) for the treatment of CRC who developed or did not develop AL postoperatively. Patients submitted to a mechanical anastomosis. Patients undergoing elective or emergency surgery.

Non-inclusion criteria: Patients submitted to surgical techniques other than those mentioned above. Patients with other types of cancer, patients submitted to colectomy for benign disease, patients operated on by a surgeon with little experience, and patients submitted to a manual anastomosis were not included.

Surgeons with less than 50 cases of laparoscopic colectomy were excluded from the study because they were not experienced enough (Li et al, 2012), as those who operated less than two laparoscopic colectomies per week.

AL in this study was defined by clinical manifestations as abdominal pain, fever, and discharge of pus or intestinal contents through the abdominal drain, causing peritonitis, confirmed by laparoscopy or imaging studies, such as CT scan and X-ray (Yang et al, 2019). AL diagnosed with radiological criteria alone was also included as asymptomatic AL.

Construction and validation of the Preoperative Index

The FRs from the meta-analysis (Dias et al., 2022) were used to construct the Preoperative Index. The neoadjuvant chemoradiotherapy variable was excluded since the variables neoadjuvant chemotherapy and radiotherapy in isolation achieved statistical difference. The score for each corresponding factor was generated through the natural logarithm of the result estimated by the RR found in the meta-analysis (Table 1).

The retrospective cohort presented above was used to validate the results. The Kruskal-Wallis test, Hosmer-Lemeshow test, ROC curve, and AUC (Area Under Curve) were performed.

Risk Factor	**Type of Study**	**Number of Studies**	**Number of Participants**	**Relative Risk**	**CI RR (95%)**	**Score (b)**
Gender Chronic Obstructive Pulmonary Disease (male)	Cohort	19	36.284	1,42	(1,07-1,89)	0,351
Smoking	Cohort	5	21.180	1,48	(1,30-1,69)	0,392
Neoadjuvant chemotherapy	Cohort	5	15.610	2,16	(1,17-4,02)	0,770
Neoadjuvant Radiotherapy	Cohort	4	14.426	2,36	(1,33-4,19)	0,859
Previous Abdominal Surgery	Cohort	4	13.417	1,30	(1,04-1,64)	0,262
Diabetes mellitus	Cross-sectional	17	11.871	1,97	(1,44-2,70)	0,678
Pulmonary Disease	Cross-sectional	5	5.260	2,14	(1,21-3,78)	0,761
ASA	Cross-sectional	17	35.727	1,70	(1,37-2,09)	0,531
COPD	Cross-sectional	6	74.459	1,10	(1,04-1,16)	0,095
Coronary Disease	Cross-sectional	6	3.065	1,61	(1,07-2,41)	0,476
Chronic Kidney Failure	Cross-sectional	5	74.819	1,34	(1,22-1,47)	0,300
Emergency Surgery	Cross-sectional	5	29.546	1,61	(1,26-2,07)	0,476
Alcoholism	Cross-sectional	9	77.567	1,35	(1,21-1,52)	0,300

(Source: Dias, et al.[6]) ASA: American Society of Anesthesiologists, COPD: Chronic Obstructive Pulmonary Disease, CI:

95% confidence interval, RR: relative risk.

Table 1 - Risk factors found in the meta-analysis.

Statistical Analysis

In this study, the outcome variable was AL (yes or no), and the explanatory variables were age group, gender, type of anastomosis (colonic or rectal), smoking, neoadjuvant chemotherapy, neoadjuvant radiotherapy, abdominal surgery, diabetes mellitus, pulmonary disease, ASA scale, COPD, coronary disease, chronic kidney failure, emergency surgery.

Statistical software IBM SPSS version 25, Microsoft Excel, and R-STUDIO (version 4.1.0) were used to perform the analyses. Variables were represented as medians and interquartile ranges for quantitative data and absolute and percentage frequency for categorical data. The Chi-square or Fisher's exact test was used to study the association between variables. The non-parametric Kruskal-Wallis or Mann-Whitney test was used to analyze and compare the quantitative variables.

Multivariate logistic regression was used to verify the factors that influenced the occurrence of fistulas. Initially, a bivariate analysis was carried out via the Chi-square test (Agresti A., 2002) to select the potential predictors for the occurrence of fistulas, and a significance level of 25% or less was considered. Subsequently, from the variables selected in the bivariate analysis, a multivariate Logistic Regression model was adjusted using the Backward method (Efroymson M. A., 1960). For the final models, a 0.05 p-value was considered.

To verify if the Urgency Index was adequate and if it had a good predictive capacity, measures of quality of fit were calculated as follows: AUC (area under the ROC curve), sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and the Hosmer-Lemeshow test (Agresti A. , 2002).

Results

Retrospective cohort and Urgency Index

For the retrospective cohort, 207 patients were evaluated, and 203 were included in the study and followed up. Only four patients were excluded (two patients without information about the surgical technique, and two died).

Sixteen patients, representing 7.9% of the sample, had AL. Most patients were older than 66 years old (46.8%) and females (52.5%). The evaluation of comorbidities showed no significant association with AL (p>0.05). It was possible to observe an association between the occurrence of fistula with Chemotherapy, Radiotherapy, and Previous Abdominal Surgery (p<0.05). Most AL patients needed to undergo a Previous Abdominal Surgery (56.3%) (Table 2).

Variables analyzed		Anastomotic Leakage				p*
		No (n=187)		Yes (n=16)		
		n	%	n	%	
Age Group						
	Up to 35 yrs. old	6	3,2	1	6,3	0,235
	36 to 45 yrs. old	8	4,3	1	6,3	
	From 46 to 55 yrs. old	36	19,3	5	31,3	
	From 56 to 65 yrs. old	45	24,1	6	37,5	
	Aged 66 or over	92	49,2	3	18,8	
Gender						
	Female	97	51,9	9	56,3	0,736
	Male	90	48,1	7	43,8	
Anastomosis type						
	Colonic	95	51,6	6	40	0,386
	Rectal	89	48,4	9	60	
Smoking						
	No	161	86,1	12	7,0	0,230
	Yes	18	13,9	4	25,0	
Neoadjuvant chemotherapy						
	No	169	90,4	9	56,3	0,000

Yes	18	9,6	7	43,8	
Neoadjuvant radiotherapy					
No	171	91,4	10	62,5	0,000
Yes	16	8,6	6	37,5	
Previous abdominal surgery					
No	147	79,0	7	43,8	0,001
Yes	39	21,0	9	56,3	
Diabetes mellitus					
No	163	87,2	14	87,5	0,969
Yes	24	12,8	2	12,5	
Pulmonary disease					
No	179	95,7	15	93,8	0,713
Yes	8	4,3	1	6,3	
ASA 3/4					
No	180	96,3	16	100	0,431
Yes	7	3,7	0	0	
COPD					
No	178	95,2	15	93,8	0,799
Yes	9	4,8	1	6,3	
Coronary heart disease					
No	173	92,5	15	93,8	0,856
Yes	14	7,5	1	6,3	
Chronic Kidney failure					
No	175	93,6	15	93,8	0,979
Yes	12	6,4	1	6,3	
Emergency surgery					
No	180	96,3	14	87,5	0,102
Yes	7	3,7	2	12,5	

ASA: American Society of Anesthesiologists, COPD: Chronic Obstructive Pulmonary Disease. *Pearson's Chi-square test.

Table 2 - Anastomotic leakage evaluation according to patients' demographic characteristics.

The variables age group, smoking, neoadjuvant chemotherapy, neoadjuvant radiotherapy, previous surgery, and emergency surgery showed p-value <0.250 and were selected for multivariate analysis. In general, patients with AL had no previous history for most of the comorbidities evaluated. However, it can be pointed out that the most common risk factors were smoking (25%), diabetes (12.5%), and alcoholism (12.5%).

Table 3 shows the final model, where it is possible to state that there was a significant difference in the fistula occurrence between patients younger than 35 yrs. old and older than 65 yrs. old (p=0.038). An individual over 65 years old has a lower chance of having a fistula when compared to an individual up to 35 years old.

There was a significant influence of the chemotherapy variable (p<0.001) on the occurrence of fistula, and individuals who received chemotherapy were 11.19 (2.95-42.49) times more likely to have fistula when compared to individuals who did not receive chemotherapy. The previous abdominal surgery variable also had a significant influence (p=0.003) on the occurrence of fistula, and individuals with previous surgery were 6.50 (1.89-22.36) times more likely than individuals without previous surgery.

Emergency surgery had a significant influence (p=0.030) on the occurrence of fistula. Individuals who had emergency surgery were more likely to have a fistula (OR: 9.43; 1.24-71.51) than individuals who had not had this procedure.

Variables	***Odds Ratio***	**CI – 95%**	**p**
Age Group			
Up to 35 yrs. old	1,00	---	---
36 to 45 yrs. old	0,20	0,01 - 6,88	0,376
From 46 to 55 yrs. old	0,33	0,03 - 4,28	0,398
From 56 to 65 yrs. old	0,25	0,02 - 3,04	0,274
Aged 66 or older	0,06	(0,00-0,86)	0,038
Neoadjuvant Chemotherapy			
No	1,00	---	---
Yes	11,19	2,95 - 42,49	<0,001
Previous Abdominal Surgery			
No	1,00	---	---
Yes	6,50	1,89 - 22,36	0,003
Emergency Surgery			
No	1,00	---	---
Yes	9,43	1,24 - 71,51	0,030

CI: 95% confidence interval.

Table 3 - Multivariate analysis - factors influencing the occurrence of fistula.

Table 4 shows the measures of the quality prediction model. The index accuracy was 76.24%, indicating that the model could correctly predict 76.24% of AL cases. This model showed good sensitivity and specificity indexes (81.25% and 75.81%), demonstrating an excellent ability to predict the cases in which AL did and did not occur.

The model showed a good fit (p=0.994), so the probabilities predicted by the test did not deviate from the observed probabilities. Thus, the proposed model explains well what is observed. Regarding the ROC curve, satisfactory measurements were also achieved (AUC=0.841; 95% CI=0.742-0.939), demonstrating the Index's ability to discriminate between patients who did and did not develop AL (Table 4).

Quality measures		**Real**	
		No	**Yes**
Predict	No	141	3
	Yes	45	13
Sensitivity		81,25%	
Specificity		75,81%	
Positive predictive value		22,41%	
Negative predictive value		97,92%	
Accuracy		76,24%	
AUC (Aurea Under Curve)		0,841	
P-value*		0,994	
Cut-off Point (Probability)		0,054	

* Hosmer-Lemeshow test.

Table 4 - Measures of quality prediction model.

Figure 1 shows the ROC curve, with an area under the ROC curve of 0.841 (95% CI: 0.742-0.939).

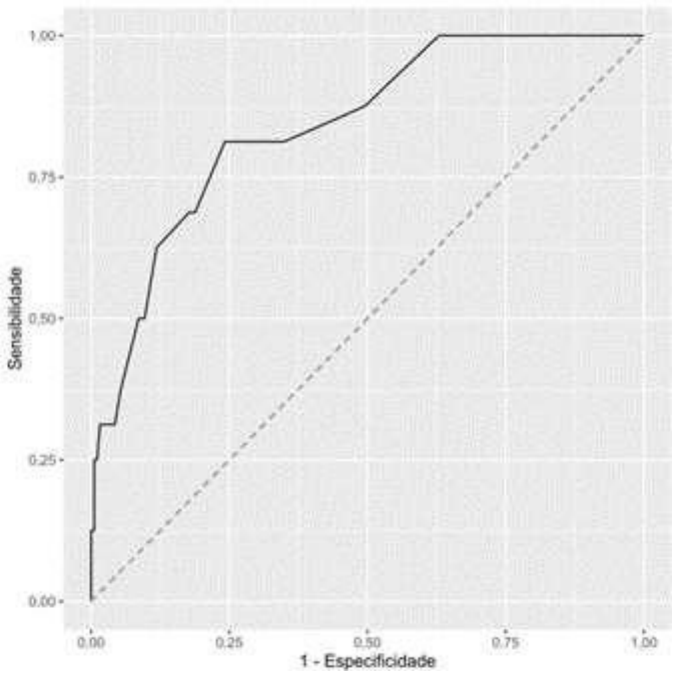

Figure 1 - ROC Curve.

Construction of the Preoperative Index

Table 5 compares the preoperative Index results, and a statistically significant difference was found in the following items: women with fistulas have a higher preoperative Index score (p=0.006); patients who do not use tobacco have a higher preoperative Index when they have fistulas (p=0.047); patients who have had previous abdominal surgery have a higher preoperative Index score when they present fistulas (p=0.023); patients who do not have any pulmonary disease have a higher preoperative Index score when they present fistulas (p=0.008); patients who are not ASA 3 and 4 have a higher preoperative Index score when they present fistulas (p=0.004); patients who do not have COPD have a higher preoperative Index when they present fistulas (p=0.007); patients who do not have any coronary artery disease have a higher preoperative Index when they present fistulas (p=0.009); patients who do not have any chronic renal disease present a higher preoperative Index when presenting fistulas (p=0.011); patients who did not undergo urgent surgery have a higher preoperative Index when presenting fistulas (p=0.014) and patients who are not alcoholics have a higher Index when presenting fistulas (p=0.018).

Risk Factors		Anastomotic Leakage No Median (IQR)	Anastomotic Leakage Yes Median (IQR)	p*
Gender	Female	0,26 (0,35-1,29)	1,50 (0,59-2,23)	0,006
	Male	0,65 (0,00-0,68)	1,12 (0,26-1,89)	0,226
Smoking	No	0,35 (0,00-0,81)	0,93 (0,33-1,89)	0,047
	Yes	1,10 (0,77-1,49)	2,23 (1,55-2,67)	0,134
Neoadjuvant Chemotherapy	No	0,35 (0,00-0,76)	0,35 (0,26-0,84)	0,530
	Yes	1,98 (1,63-2,23)	2,57 (1,89-2,62)	0,248
Neoadjuvant Radiotherapy	No	0,35 (0,00-0,80)	0,54 (0,28-1,05)	0,356
	Yes	1,94 (1,63-2,05)	2,57 (2,06-2,65)	0,102
Previous Abdominal Surgery	No	0,35 (0,00-1,04)	0,84 (0,35-1,90)	0,211
	Yes	0,61 (0,26-0,94)	1,78 (0,74-1,89)	0,023
Diabetes Mellitus	No	0,35 (0,00-0,79)	0,98 (0,35-1,86)	0,015
	Yes	1,27 (0,94-1,51)	2,57 (2,57-2,57)	0,033
Pulmonary Disease	No	0,35 (0,07-0,94)	1,12 (0,35-2,23)	0,008
	Yes	1,58 (1,05-2,09)	1,50 (1,50-1,50)	0,697
ASA 3/4	No	0,35 (0,10-0,94)	1,31 (0,35-2,06)	0,004
	Yes	1,75 (1,18-2,53)	-	-
COPD	No	0,35 (0,13-0,94)	1,50 (0,35-2,23)	0,007
	Yes	1,17 (0,49-1,53)	0,84 (0,84-0,84)	0,726
Coronary Heart Disease	No	0,35 (0,00-0,94)	1,12 (0,35-2,23)	0,009
	Yes	1,07 (0,83-1,52)	1,78 (1,78-1,78)	0,245
Chronic Kidney Failure	No	0,35 (0,00-0,92)	1,12 (0,35-1,89)	0,011
	Yes	1,38 (0,65-1,94)	2,67 (2,67-2,67)	0,180
Emergency Surgery	No	0,35 (0,10-1,03)	1,45 (0,35-2,40)	0,014
	Yes	0,74 (0,61-1,09)	1,12 (0,93-1,31)	0,453
Alcoholism	No	0,35 (0,00-0,83)	0,98 (0,35-1,89)	0,018

	Yes	1,31 (1,04-1,52)	2,23 (2,00-2,45)	0,109

IQR: Interquartile range, ASA: American Society of anesthesiologists, COPD: Chronic obstructive pulmonary disease. * Kruskal-Wallis test.

Table 5 - Comparative analysis of the Preoperative Index according to risk factors.

Table 6 presents a logistic regression model with the explanatory variable "Preoperative Index." It is possible to state that there was a significant influence (p=0.001) of the Preoperative Index on the occurrence of fistula.

Source	OR.	CI - 95%	p*
Preoperative Index	2,79	[1,52; 5,11]	0,001

CI: 95% confidence interval, * Kruskal-Wallis test.

Table 6 - Influence of preoperative Index on fistulas.

A new tool was created for AL risk prediction, with 13 variables. Table 7 presents the quality measures of the "Preoperative index" model that was carried out from its application to the patients of the retrospective cohort.

The proposed model also presented good values of accuracy and specificity. The accuracy of the Index was 83.66%, indicating that the model could correctly predict 83.66% of AL cases. This model showed good specificity indexes (86.56%), which reveals a satisfactory ability to predict the cases in which AL did not occur and presented a good fit (p=0.802). The proposed model explains well what is observed. Regarding the ROC curve, it also reached AUC=0.699, showing almost a 70% chance of correct classification between patients who developed and did not develop AL.

The cut-off point of the preoperative Index was 1.421 (probability=0.120). Thus, patients with a sum of scale greater than 1.421, or more than a 12% chance of AL, are classified as high risk for AL. Those with lower results are considered low risk.

Quality measures		Real No	Real Yes
Predict	No	161	8
	Yes	25	8
Sensitivity		50,00%	
Specificity		86,56%	
Positive Predictive Value		24,24%	
Negative Predictive Value		95,27%	
Accuracy		83,66%	
AUC (Area Under Curve)		0,699	
P-value*		0,802	
Cut-off point (Probability)		0,120	
Cut-off point (Preoperative Index)		1,421	

* Hosmer-Lemeshow test.

Table 7 - Quality model measures.

Figure 2 shows the ROC curve, in which an area under the curve of 0.699 was recorded.

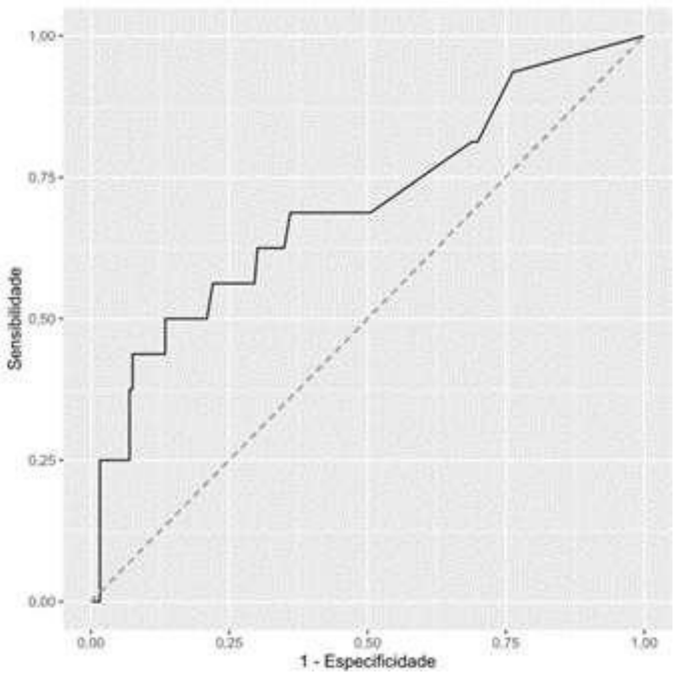

Figure 2 - ROC Curve.

Discussion

Analyzing the study results, it could be observed that neoadjuvant chemotherapy, previous abdominal surgery, and emergency surgery were FR for AL. The influence of neoadjuvant chemotherapy on the occurrence of AL was significant, with OR of 11.19 (95% CI: 2.95-42.49), which is confirmed by previous studies (Altin O.; Alkan M., 2019; Kwak et al, 2017; Qu et al, 2015). A study by Park et al. (2013) suggested that chemoradiotherapy is RF for the development of AL when analyzing a subgroup of patients without a protective stoma.

Previous abdominal surgery was also considered an RF for AL in this study, confirmed by Park et al. (2016). Previous surgeries may be responsible for technical difficulties, impairing the performance of the surgery, which may increase the risk of AL.

Another factor for fistula occurrence was emergency surgery in this and other previous studies (Altin O.; Alkan M., 2019; Bakker et al, 2014; Choi et al, 2016, Frasson et al, 2015; Reilly et al, 2014). Several factors may be related to the increased risk of AL in emergency colectomy. Blood loss, comorbidities, a worse clinical picture of the patient, and greater technical difficulty can coexist in the same patient. It is known that the risk of AL is cumulative based on the patient's RF. Thus, in an emergency resection, with significant blood loss and transfusion, in a patient with comorbidities and the need for vasoactive drugs, the risk of AL is so high that performing an anastomosis is contraindicated (Mcdermott et al, 2015).

Several studies have reported excellent outcomes in older patients, advanced age is no longer considered a contraindication for colorectal surgery (Mamidanna R.; Almoudaris A. M., 2012; Papamichael et al, 2015). However, this study showed older age (patients older than 66 yrs. old) as a protective factor for AL occurrence. Older patients are better prepared to perform the colectomy from the preoperative point of view, which could explain this result. Thus, it is possible to infer that reducing or at least controlling the RF for AL effectively reduces the risk of occurrence of AL by emphasizing the need for good preoperative care, focusing on controlling RF for AL, and aiming to perform a safer anastomosis with a better prognosis for the patient.

Patients operated on for CRC treatment undergo colectomy either electively or in cases of urgency, such as intestinal obstruction and bleeding, for example. The preoperative Index is recommended for the first case, and the urgency index is advised for urgent surgeries.

According to Sammour et al. (2017), currently, there is no reliable way to predict the risk of AL, nor even clinically valuable data to inform the decision and request the patient's consent as to whether or not a protective stoma is necessary.

Considering the tools built in this study and their respective cut-off points, both indexes can stratify outcomes into low and high risks of developing AL. The tools can help the surgeon decide whether or not to perform a protection ostomy on the colectomized patient.

If the patient is at high risk of fistula, although the detour cannot reduce the risk of fistula occurrence, it can reduce the severity of fistula-induced complications (Shiome et al, 2015). However, performing stoma may have numerous complications by increasing the postoperative morbidity of its carriers. In this case, patients with high risk should be submitted to a protective ostomy, and those with low risk should not, in case the surgery is performed without significant complications.

With these tools, the physician can go into surgery knowing that he will need or not to perform an ostomy. If there are no major surgical eventualities since both do not use intraoperative variables, or require previous exams, increasing their applicability, in contrast to what occurs in the already-mentioned tools (Dekker et al., 2011; Rojas et al., 2015). In addition, it will be possible with greater accuracy to inform the patient about the need for a protective ostomy and to request his or her consent.

Frasson et al. (2015) created a risk calculator. However, this model has a variable called "intraoperative complications," which, besides being imprecise, makes it impossible to apply the scale preoperatively. In addition, the variable "serum protein level," which needs a previous laboratory test, is challenging to use in emergency surgeries.

The new Urgency Index can be applied through a simple anamnesis because the information required is simple to obtain in a dialogue with the patient (age, previous chemotherapy, previous abdominal surgery, and urgent surgery). In urgent surgery, using a prognostic Index with only four variables can significantly help due to its applicability and ease of use.

For elective colectomies, using the preoperative Index can better plan the surgery when there is a high risk of AL, to eliminate or at least reduce modifiable RF, with a consequent reduction in the risk of AL, in case of elective surgeries.

According to Dekker et al. (2011), the importance of predicting AL risk is based on prevention and early detection, and prevention can be achieved by correcting existing RF prior to surgery. Strategies such as reinforcing anastomosis with a suture or other material can be adopted in high-risk patients. Early detection and treatment are critical to decreasing morbidity and mortality when AL does occur.

Other authors have already built tools for AL risk prediction in patients with CRC (Dekker et al., 2011; Frasson et al., 2015; Rojas et al., 2015). However, they did not show good applicability and efficiency. The study by Dekker et al.5 was carried out using a systematic review, and the authors decided which FRs would be used based on their accessibility. Thus, the criteria for selecting the RF were subjective, as well as the determination of their respective scores. However, our study used the results of a meta-analysis to choose the RF and their respective scores. Moreover, this study used a more significant number of patients compared to previous studies to validate the tool created.

Despite the good results of Rojas-Machado et al. (2015), the tool created for AL risk prediction has very low applicability because there are many variables (n=23). Also, the model created presents a division of surgeries into ultra-low anterior resection, low anterior resection, and intraperitoneal resection, making its use even more difficult for doctors because frequently, only during the intraoperative period will the size of the anastomosis be known.

A possible limitation of this study would be the low number of patients for the tool validation (203 patients and 16 AL). However, previous studies with a similar methodology used smaller absolute numbers of patients and AL: Dekker et al. (2011) studied 139 patients and 12 AL, and Sammour et al. (2017) used 83 patients and 8 AL. Rojas-Machado et al.18 also had lower total numbers of patients (123), with a higher number of AL (41) than the present study.

The Urgency Index was shown to be effective and to have good indices. It is a robust tool for assessing the risk of developing fistulas. Another limitation of this study was the low sensitivity found in the Preoperative Index. However, it should be noted that intraoperative variables were excluded from achieving greater applicability of the tool and for its use in the preoperative period, which reduced sensitivity. The use of intraoperative variables makes the Index unfeasible because it is impossible to predict before the moment of surgery. Consequently, it helps little or nothing in the decision about the protection ostomy, in the dialogue with the patient, and the preoperative treatment of modifiable RF.

In addition, tools for predicting the risk of AL should only be auxiliary in the surgeon's decision about ostomy or other protective measures intraoperative because the surgeon's experience at the time of surgery is and will continue to be of fundamental importance. Moreover, there are neither quantifiable nor modifiable variables, such as the patient's anatomy and eventual technical difficulties, endorsing that the decision will always remain in the hands of the experienced surgeon.

Further research is needed to evaluate the indices found using different multicenter. A prospective study with this Index is also suggested to evaluate its efficacy better, comparing the results with the surgeon's decision arbitrarily and with the tools presented here.

Conclusion

Two new indexes were suggested for predicting AL risk in patients treated for CRC. The Urgency Index showed good sensitivity, specificity, and accuracy results, proving a valuable tool due to its easy applicability. The Preoperative Index, in turn, showed good accuracy, specificity, and negative predictive value, besides reasonable AUC values. Its use is suggested for elective colectomies, as it may greatly help surgical programming regarding the performance of protective ostomy. Additionally, implementing possible measures could eliminate or at least reduce the RF for fistulas, possibly reducing the prevalence of AL and achieving a better prognosis.

Declarations

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