

Predictive Value of the REMIND Endoscopic Score for Clinical Recurrence After Ileocolic Resection in Crohn's Disease

Valeur prédictive du score endoscopique du groupe REMIND sur la récurrence clinique après résection iléocolique dans la maladie de Crohn

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ABSTRACT

Background: This study evaluates the REMIND score's performance in predicting postoperative Crohn's disease recurrence compared to the Rutgeerts score, which has the limitation of grouping anastomotic and neo-terminal ileal lesions together with equal prognostic value.

Methods: We conducted a monocentric, retrospective, evaluative study of patients operated for Crohn's disease. All patients had a follow-up colonoscopy within one year of surgery. Clinical relapse was defined by the Crohn's disease related symptoms or complications, such as intra-abdominal collection or occlusion, or subsequent postoperative surgery. Data analysis was performed using SPSS.25.

Results: Eighty patients were included. Clinical recurrence-free survival was significantly shorter in patients with ileal lesions whatever their severity was I(1,2,3,4)A(x), compared with patients without ileal lesions I(0)A(x): $p < 0,001$ and not significantly different between patients without anastomotic lesions I(x)A(0) and patients with anastomotic lesions whatever their severity was I(x)A(1,2,3): $p = 0,2$. However, patients with at least semicircumferential anastomotic ulcerations A(2,3) had more anastomotic occlusive complications than patients classified A0 or A1: A0 VS A2 $p = 0,01$ A0 VS A3 $p < 0,001$ A0 VS A1 $p = 0,9$. The I(x) score, compared with the Rutgeerts and A(x) scores, had the best values in terms of discriminative capacity (Area under the curve = 0,83 VS 0,73 VS 0,61), monotonicity (linearity test χ^2 of 26,77 VS 12,36 VS 3,89), and homogeneity (likelihood ratio χ^2 of 33,91 vs 18,45 VS 5,49).

Conclusion: The I(x) score outperformed both the Rutgeerts and A(x) scores in predicting postoperative recurrence. Consequently, evaluating ileal and anastomotic lesions separately provides a more accurate assessment of endoscopic recurrence.

Key-words: Crohn's disease, Surgery, Recurrence, Rutgeerts score, Endoscopy, REMIND score

RÉSUMÉ

Contexte: Le score de Rutgeerts est le plus couramment utilisé pour évaluer la récurrence endoscopique après une résection iléocolique dans la maladie de Crohn. Cependant, un inconvénient important de ce score est qu'il combine les lésions localisées à l'anastomose avec celles de l'iléon néo-terminal dans la même catégorie, leur attribuant une signification pronostique égale. L'objectif de cette étude était d'évaluer la performance du score REMIND dans la prédiction de la récurrence postopératoire de la maladie de Crohn et de comparer sa performance avec le score de Rutgeerts.

Méthodes: Nous avons mené une étude monocentrique, rétrospective et évaluative sur des patients opérés pour la maladie de Crohn. Tous les patients ont subi une coloscopie de suivi dans l'année suivant l'opération. Le score REMIND a été obtenu à partir des détails endoscopiques documentés dans les rapports de coloscopie. La rechute clinique était définie par les symptômes ou complications liés à la maladie de Crohn, tels que la collecte ou l'occlusion intra-abdominale, ou une intervention chirurgicale postopératoire ultérieure. L'analyse statistique a été réalisée à l'aide de SPSS.25 pour Windows.

Résultats: Quarante-vingts patients ont été inclus, avec un âge moyen de 35,7 ans, et un ratio hommes-femmes H/F = 2,2. Le suivi médian était de 5 ans après l'opération. La survie clinique sans récurrence était significativement plus courte chez les patients présentant des lésions iléologiques quelle que soit leur gravité I(1,2,3,4)A(x), comparé aux patients sans lésions iléales I(0)A(x) : $p < 0,001$, et pas significativement différent entre les patients sans lésions anastomotiques I(x)A(0) et les patients avec lésions anastomotiques quelle que soit leur gravité I(x)A(1,2,3) : $p = 0,2$. Cependant, les patients présentant au moins des ulcères anastomotiques semi-circumférentiels A(2,3) présentaient plus de complications occlusives anastomotiques que les patients classés A0 ou A1 : A0 VS A2 $p = 0,01$ A0 VS A3 $p < 0,001$ A0 VS A1 $p = 0,9$. Le score I(x), comparé aux scores de Rutgeerts et A(x), présentait les meilleures valeurs en termes de capacité discriminative (Surface sous la courbe = 0,83 VS 0,73 VS 0,61), monotonie (test de linéarité χ^2 de 26,77 VS 12,36 VS 3,89) et homogénéité (rapport de vraisemblance χ^2 de 33,91 contre 18,45 VS 5,49).

Conclusion: Contrairement aux scores de Rutgeerts et A(x), le score I(x) semble présenter une performance supérieure à la prédiction de la récurrence postopératoire. Par conséquent, l'utilisation d'un score décrivant séparément les lésions iléales et anastomotiques pourrait être plus appropriée pour définir la récurrence endoscopique postopératoire.

Mots clés: Maladie de Crohn, chirurgie, récurrence, score de Rutgeerts, endoscopie, score REMIND

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INTRODUCTION

Despite significant advances in the medical treatment of Crohn's disease (CD), surgery is often necessary. The cumulative risk of surgery after diagnosis is 16.3% at 1 year, 33.3% at 5 years, and 46.6% at 10 years (1,2). After ileocolic resection of the macroscopically pathological segment, the disease relapses in nearly half of the patients at 10 years (3). Postoperative management is therefore a major challenge. This clinical relapse is preceded by endoscopic recurrence, mainly at the level of the neo-terminal ileum and/or the anastomosis (4). Endoscopic recurrence helps predict clinical recurrence (5). Thus, an ileocolonoscopy in the year following resection serves as a reference examination that allows subsequent management to be adjusted. The Rutgeerts score is the reference score for evaluating endoscopic recurrence in several countries. It classifies recurrence into five grades based on the presence of lesions in the anastomosis and/or neo-terminal ileum (5). However, this score has some limitations. Mainly at stage i2, it does not take the location of the involvement into account. Indeed, it groups lesions confined to the anastomosis and those of the neo-terminal ileum into the same category, giving them the same prognostic value. From a pathophysiological point of view, ileal lesions, regardless of their severity, are associated with worse clinical outcomes and more rapid disease progression, independently of anastomotic lesions (6). Conversely, mild and isolated anastomotic lesions classified as i2 may simply be related to other injury mechanisms, including local ischemia secondary to the creation of the anastomosis. In fact, anastomotic ulcers in patients without Crohn's disease have been reported in the literature (7,8). Therefore, it is important to distinguish between lesions confined to the anastomosis and those in the neo-terminal ileum to better identify patients at high risk of recurrence and complications. Recently, a new modified score, A(x) I(x), has been proposed by the REMIND group, separately describing anastomotic and ileal lesions to address this limitation (6). This score has not yet been validated by large-scale studies worldwide. Moreover, no Tunisian study has evaluated it. The objective of our study was to evaluate the performance of the REMIND score compared to the Rutgeerts score in predicting postoperative recurrence of CD.

METHODS

Study Design

The present work was undertaken on a bicentric retrospective evaluative study involving a series of patients followed for Crohn's disease (CD) who underwent surgery and were treated from January 2011 to December 2021. The inclusion criteria were as follows: age 18 years or older, confirmed diagnosis of CD, and ileal or ileocolic disease requiring a first surgical resection. Patients who did not undergo a follow-up endoscopy to assess endoscopic recurrence after ileocolic resection

were not included. Exclusion criteria were unexploitable or missing hospitalization records, patients lost to follow-up after less than 18 months, presence of dysplastic lesions in biopsies, or patients whose endoscopy reports did not provide sufficient description of elementary lesions to allow evaluation of the Rutgeerts score and/or REMIND group classification.

Data collection

Clinical, surgical, endoscopic and imaging data were collected retrospectively from hospital records and observation books. All patients had a follow-up colonoscopy. The description of elementary lesions was documented at the level of the ileocolic anastomosis as well as in the neoterminal ileum. The Rutgeerts score was recorded when reported. When it was not specified, it was calculated based on the endoscopic findings described in the colonoscopy reports. For anastomotic lesions (less than 1 cm in length after the anastomosis), four grades were defined: A(0): no lesion, A(1): ulcerations covering less than 50% of the anastomosis circumference, A(2): ulcerations covering more than 50% of the anastomosis circumference, and A(3): anastomotic stenosis. For ileal lesions, five grades were defined according to the Rutgeerts score (RS) (11): I(0): no lesion, I(1): fewer than 5 aphthous ulcers, I(2): more than 5 aphthous lesions with normal intervening mucosa or skip areas of larger lesions, I(3): diffuse aphthous ileitis with diffusely inflamed mucosa, and I(4): diffuse inflammation with larger ulcers. Thus, each patient had a separate evaluation of the anastomosis and ileum, with an overall score reported as A(x)I(x). The postoperative follow-up duration for each patient was specified as the period between the date of surgery and the date of the latest contact, the date of death, or the study end date. Clinical recurrence was defined by the reappearance of symptoms related to CD, the occurrence of a complication such as an intra-abdominal collection or obstruction, or the need for a second surgery. Anastomotic occlusive complications were defined by obstructive clinical symptoms, confirmed by imaging or endoscopy.

Data Analysis

Descriptive statistics were calculated for all quantitative variables as means and standard deviations. For qualitative variables, we calculated simple frequencies and relative frequencies.

For the analysis of clinical outcomes, recurrence-free survival curves were constructed for each stage of the two scores using the Kaplan-Meier method, and crude log-rank tests were calculated. The performance of the two scores was assessed using three criteria: homogeneity (the most similar prognosis within the same stage), which was evaluated by the χ^2 likelihood ratio, monotonicity (lower recurrence risk in patients in early stages compared to those in late stages), which was assessed by the χ^2 linear trend test, and discriminative ability (significant difference in recurrence between different stages of a score), which was evaluated by the

analysis of the area under the ROC curve. Indeed, the ROC curve analysis allows the assessment of the sensitivity and specificity of each score in predicting postoperative recurrence.

Data entry was performed using SPSS version 25. In all statistical tests, the significance threshold was set at 0.05.

Ethical considerations

The strict anonymity of individual data was maintained throughout the study. Only the case identification number was recorded for future verification. No data related to ethnicity, customs, or sexual life were collected.

RESULTS

Patient characteristics

Eighty patients (mean age 35.7 years; M/F=2.2) were included; 41.2% were smokers, 21.25% had inaugural surgery, with a mean delay of 41 months and 5-year median follow-up (Table 1).

Table 1. Patients' characteristics at the time of surgery

	Patients n=80 (%)
Median age, yr	35,7
Men	55 (68,8%)
Active smoking	33 (41,2%)
Disease location	
ileocecal	63 (78,8%)
ileal	10 (12,5%)
ileocolonic	7 (8,8%)
Behavior	
stricturing	34 (42,5%)
penetrating	15 (18,8%)
Stricturing and penetrating	31 (38,8%)
Non-structuring non-penetrating	0
Anoperineal lesion	16 (20%)
Upper GI involvement	3 (3,8%)
Extradigestive symptoms	
Joint manifestations	15 (18,8%)
Hepatobiliary manifestations	1 (1,25%)
Previous exposure to medical treatment	
Thiopurines	5 (6,25%)
Anti-TNF therapy	6 (7,5%)
Combination therapy	1 (1,25%)
Median time between diagnosis and resection, mo	41
Surgical indication	
Stricturing complication	46 (57,7%)
Penetrating complication	33 (41,25%)
Severe acute colitis	1 (1,25%)
Surgical intervention	
Ileocaecal resection	73 (91,25%)
Ileocolic resection	5 (6,25%)
Right colectomy with terminal ileal resection	1 (1,25%)
Total colectomy (including ileal segment)	1 (1,25%)
Ileal resection ≥50 cm	10 (12,5%)
Type of anastomosis	
End-to-side	54 (67,5%)
Side-to-side	26 (32,5%)

Scoring of postoperative recurrence

The postoperative follow-up colonoscopy was performed on average at 11.21 months after the surgery, with a range of 5 to 32 months.

According to the RS, 8 patients had no lesions (i0), 7 patients (8.75%) were classified as i1, 47 patients (58.75%) were classified as i2, 7 patients (8.75%) as i3 and 11 patients (13.75%) as i4.

According to the REMIND group's scoring, in the neoterminal ileum, 22 patients had no lesions (I0), 12 patients (15%) had fewer than 5 aphthous ulcers (I1), and more severe endoscopic recurrence (I2, I3, and I4) was found in 32 patients (40%), 8 patients (10%), and 6 patients (7.5%) respectively. At the anastomosis site, 32 patients (40%) had no lesions (A0), while more severe ulcerations (A1 and A2) were found in 29 patients (36.25%) and 11 patients (13.75%), respectively. Finally, an anastomotic stricture (A3) was observed in 8 patients (10%). Twenty-one percent of the patients (n=10) classified as i2 according to the Rutgeerts score only had anastomotic lesions (IOA1 or IOA2).

Postoperative recurrence

The median follow-up duration was 5 years [2-35 years]. Clinical recurrence was observed in 46 patients (57.5%) with a median delay of 75 months after the surgery date [1-323 months].

Clinical recurrence-free survival according to RS

For the RS, clinical recurrence-free survival was significantly longer in patients with no endoscopic lesions on follow-up colonoscopy i0 compared to patients with endoscopic lesions of any severity i1, 2, 3, 4. The median clinical recurrence-free survival was not reached for i0 patients, versus 140, 125, 18, and 55 months, respectively, for i1, i2, i3, and i4 ($p < 0.0001$). Severe endoscopic lesions i3, i4 were clearly correlated with poorer clinical outcomes shown in Figure 1.

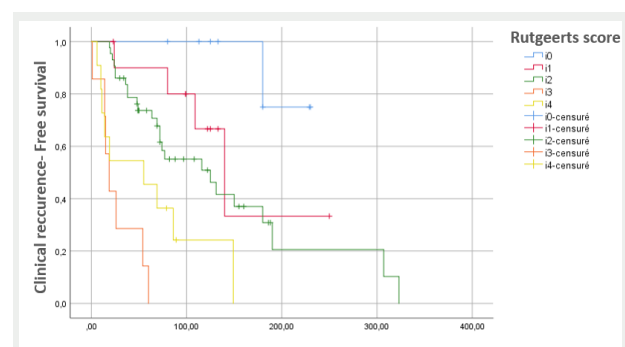


Figure 1. Recurrence-free survival according to Rutgeerts score

For the REMIND score: When analyzing ileal and anastomotic lesions separately, the median clinical recurrence-free survival was significantly shorter in patients with ileal lesions on follow-up endoscopy, regardless of the severity (I1, 2, 3, 4 A(x)), compared to patients without ileal lesions (I0 A(x)): 329 months for

I0 A(x) versus 207, 112, 46, and 40 months for I1 A(x), I2 A(x), I3 A(x), and I4 A(x), respectively, with $p < 0.0001$ shown in Figure 2.

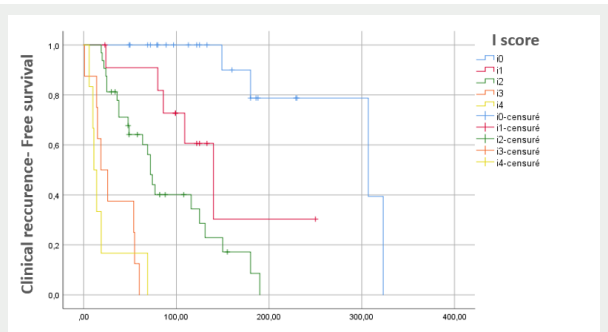


Figure 2. Recurrence-free survival according to I score

The median clinical recurrence-free survival was not significantly different between patients without anastomotic lesions (I(x) A0) and those with anastomotic lesions of any severity (I(x) A1, 2, 3): 150 months for I(x) A0 versus 116, 77, and 69 months for I(x) A1, A2, and A3, respectively, with $p = 0.2$ shown in Figure 3.

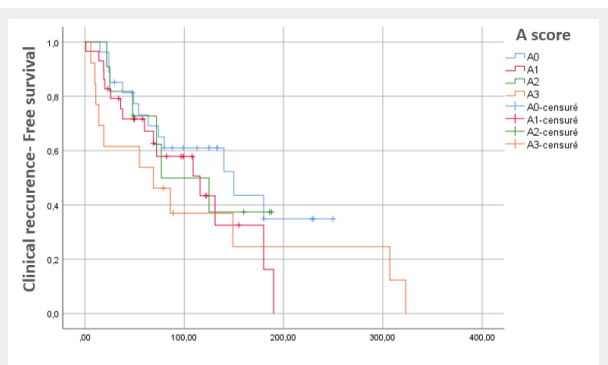


Figure 3. Recurrence-free survival according to A score

Patients with exclusively ileal lesions (I1, 2, 3, 4 A0) had shorter recurrence-free survival than those with exclusively anastomotic lesions (I0 A1, 2, 3), with median recurrence-free survival of 68 months for I1, 2, 3, 4 A0 versus 109 months for I0 A1, 2, 3.

Patients with at least semicircumferential anastomotic lesions (A2, 3) experienced more anastomotic obstructive complications than patients with A0 or A1 lesions, with p-values of: A0 vs A2 ($p = 0.01$), A0 vs A3 ($p < 0.001$), and A0 vs A1 ($p = 0.9$).

However, anastomotic obstructive complications were not significantly different across stages for patients with ileal lesions (I0 vs I2, 3, 4 $p = 0.83$, I0 vs I1 $p = 0.99$).

Study of the performance of scores in predicting postoperative recurrence

The Rutgeerts score and the I(x) score from the REMIND group predict postoperative recurrence (POR) with $p < 0.0001$, while the A(x) score appears less effective in predicting POR, with a non-significant p-value of 0.078. However, the A(x) score appears effective in predicting obstructive complications with $p < 0.0001$. The I(x) score

and the Rutgeerts score are less effective in predicting obstructive complications, with p-values of 0.03 and 0.01, respectively.

The I(x) score, compared with the Rutgeerts and A(x) scores, had the best values in terms of discriminative capacity (Area under the curve respectively 0,83 VS 0,73 VS 0,61) shown in Figure 4, monotonicity (linearity test χ^2 respectively 26,77 VS 12,36 VS 3,89), and homogeneity (likelihood ratio χ^2 respectively 33,91 vs 18,45 VS 5,49) shown in table 2.

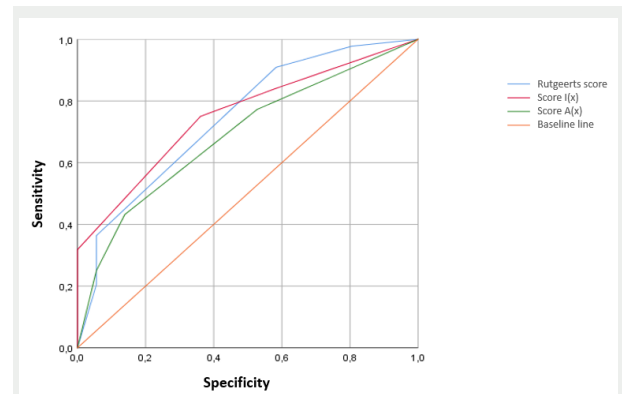


Figure 4. ROC Curves of Endoscopic Scores

Table 2. Study of the performance of scores in predicting postoperative recurrence

Score	likelihood ratio χ^2	linearity test χ^2	Area under the curve	IC 95% Upper limit	Lower limit	p
RS	18,45	12,36	0,730	0,619	0,841	<0,0001
I(x)	33,91	26,77	0,830	0,741	0,919	<0,0001
A(x)	5,49	3,89	0,613	0,490	0,736	0,085

DISCUSSION

This retrospective study compared the REMIND score against the traditional Rutgeerts score for predicting postoperative recurrence in Crohn's Disease (CD). While the RS is the global standard (4), its management of i2 lesions is debated because it conflates anastomotic-confined lesions with those in the neoterminal ileum. Pathophysiologically, ileal lesions indicate more aggressive disease progression (6), whereas isolated anastomotic lesions may simply reflect local ischemia (7,8). Therefore, it appears rational to separate anastomotic-confined lesions from those in the neoterminal ileum to better identify patients at high risk for recurrence and anastomotic complications.

The REMIND score was recently developed by the French Research Group for Inflammatory Bowel Diseases (REMIND group). It divides ileal and anastomotic lesions into two sub-scores: Score I(x) for ileal lesions and Score A(x) for anastomotic lesions (6). However, this score has not been evaluated in other studies worldwide.

The REMIND group conducted a prospective, multicenter study including 225 patients to evaluate the association between anastomotic and ileal lesions during postoperative ileocolonoscopy and long-term outcomes using their new I(x)A(x) score (6). Recurrence-free survival after surgery was significantly shorter for patients with ileal lesions, regardless of severity, compared to those without such lesions. Ileal lesions, regardless of severity, were associated with a significant reduction in recurrence-free survival. In contrast, severe anastomotic lesions primarily predicted occlusive complications rather than overall clinical recurrence.

In our study, we reached similar conclusions. By analyzing ileal and anastomotic lesions separately, we found that median recurrence-free survival was significantly shorter for patients with ileal lesions at follow-up endoscopy, regardless of severity I(1,2,3,4) A(x), compared to patients without ileal lesions I(0) A(x): 329 months vs. 207, 112, 46, and 40 months, respectively, for I(0) A(x) vs. I(1) A(x), I(2) A(x), I(3) A(x), I(4) A(x), with $p < 0.0001$.

Median recurrence-free survival was not significantly different between patients without anastomotic lesions I(x) A(0) and those with anastomotic lesions, regardless of severity I(x) A(1,2,3): 150 months vs. 116, 77, and 69 months, respectively, for I(x) A(0) vs. I(x) A(1,2,3), with $p = 0.2$.

Patients with exclusively ileal lesions I(1,2,3,4) A(0) had a shorter median recurrence-free survival than those with exclusively anastomotic lesions I(0) A(1,2,3): 68 months vs. 109 months, respectively, for I(1,2,3,4) A(0) vs. I(0) A(1,2,3).

Patients with at least semi-circumferential anastomotic lesions A(2,3) had more occlusive anastomotic complications than patients with A0 or A1 lesions: A0 vs. A2 $p = 0.01$, A0 vs. A3 $p < 0.001$, A0 vs. A1 $p = 0.9$. Occlusive anastomotic complications were not significantly different between patients with ileal lesions (I0 vs. I2,3,4 $p = 0.83$; I0 vs. I1 $p = 0.99$).

Homogeneity, monotonicity, and discriminatory ability are three criteria for evaluating and comparing prognostic score performance. Homogeneity (most similar prognosis within the same stage) is assessed by the χ^2 likelihood ratio. Monotonicity (lower recurrence risk for patients in early stages compared to those in later stages) is evaluated by the χ^2 linearity test. Finally, discriminatory ability (significant recurrence differences across score stages) is evaluated by the area under the ROC curve analysis, as ROC curves help assess each score's sensitivity and specificity in predicting postoperative recurrence.

In our series, the I(x) score, compared to the Rutgeerts and A(x) scores, had the best values for discriminatory ability (Area under the curve = 0.83 vs. 0.73 vs. 0.61), monotonicity (χ^2 linearity test of 26.77 vs. 12.36 vs. 3.89), and homogeneity (χ^2 likelihood ratio of 33.91 vs. 18.45 vs. 5.49).

The main limitation of our study was inter-observer variability, which may have led to discrepancies in classifying endoscopic lesions. The lack of a consensus on the timeframe after surgery for distinguishing between surgery-related complications and true postoperative recurrence, as well as the study's retrospective nature and small sample size, are additional limitations.

CONCLUSION

In conclusion, our results reinforce the findings of Hammoudi et al. (6). We therefore suggest separating anastomotic and ileal lesions to obtain a more precise characterization of patients at high risk of recurrence and postoperative complications. Therapeutic intensification is suggested when I score is ≥ 1 to prevent general postoperative recurrence. When A score is ≥ 2 a special attention must be paid to prevent occlusive complications. Larger-scale, prospective studies are needed to validate these results.

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