Algorithmic Approach to Differentiate Between Non-Specific and Specific Etiologies of Chronic Terminal Ileitis

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Introduction

- Terminal Ileitis (TI) in the form of ulcers, erosions or nodularity is identifiable in numerous patients undergoing ileo-colonoscopy for various clinical presentations.[1,2]

- Patients with acute symptoms frequently have infective etiologies while chronic terminal ileitis like Crohn's disease (CD) and intestinal Tuberculosis (ITB) can pose as a diagnostic dilemma.[3]

- There is an unmet need to identify factors that point towards a specific diagnosis over a nonspecific etiology.

Aims and Objectives

- To develop a revised algorithm and a multi-modality approach that can stratify patients with TI into specific and non-specific etiology.

Methods and Materials

Study design:
Retrospective cohort analysis of patients presenting to IBD clinic between 2007 and 2022 at the All India Institute of Medical Sciences, New Delhi.

Inclusion criteria	Exclusion criteria:
1. Patients whose colonoscopy and biopsy reports were available with a follow up of >6 months.	1. Chronic NSAID intake and other form of terminal ileal involvement such as strictures.
2. Patients with superficial/deep ulcers +/- nodularity or erosions in terminal ileum.	2. Malignancy or infective pathology

Statistical analysis:
- Chi-square test for categorical variables.
- Student's t-test and independent samples Kruskal Wallis test were used for continuous variables with normal distribution and non-normal distribution respectively.
- Univariate and multivariate analysis with bootstrap validation was conducted combining colonoscopic, clinical, laboratory, radiological and histopathological findings to improve diagnostic performance.

Results

- From a database of 3203 patients, 153 patients were followed up.
- Mean age for the cohort was 36±914.6 years with 107 69.9%) males and 46(30.1%) females.
- Validation statistics suggested that based on a combination of clinical (blood in stools, weight loss, hemoglobin), radiological (necrotic lymph nodes, long segment ileal involvement) and colonoscopic findings (presence or absence of deep ulcers), an optimism corrected c-statistic of 0.975 and 0.958 could be obtained, with and without histopathological findings respectively (Figure 1).

N=153	Specific etiology/ treatment (109)	Nonspecific etiology/treatment (44)	P value
Clinical			
Abdominal pain, n(%)	87(79.8)	28(63.6)	0.04*
Fever	31(28.4)	1(2.2)	0.00*
Diarrhea	40(36.7)	12(27.3)	0.35
GI bleed	29(26.6)	0	0.00*
Weight loss	81(74.3)	9(20.5)	0.00*
Hemoglobin (n=142)	11.9±2.2 gm/dl	13.7±1.8 gm/dl	0.00*
Albumin (n=120)	4.2±0.8 gm/dl	4.6±0.6 gm/dl	0.01*
Colonoscopy features			
Superficial ulcers	59(54.1)	44(100)	0.00*
Deep ulcers	50(45.9)	0	0.00*
CT features (n=151)			
Ileal thickening	76/109(69.7)	16/42(38.1)	0.00*
Long segment involvement	22/109(20.2)	0/42	0.00*
Necrotic LN	5/109(4.6)	0/42	0.15
Histological features (n=151)			
Nonspecific inflammation	78/107(72.9)	44/44(100)	0.00*
Specific features (histology and microbiology)	28/107(26.2)	0	0.00*

Table 1: Univariate analysis comparing patients receiving specific treatment versus those receiving symptomatic treatment

Sensitivity	98.2% (95%CI:93.5 - 99.8)
Specificity	75.0% (95%CI:59.7 - 86.8)
Positive predictive value	90.7% (95%CI:85.4 - 94.2
Negative predictive value	94.3% (95%CI:80.5 - 98.5)
Accuracy	91.5% (95%CI:85.9 - 95.4)

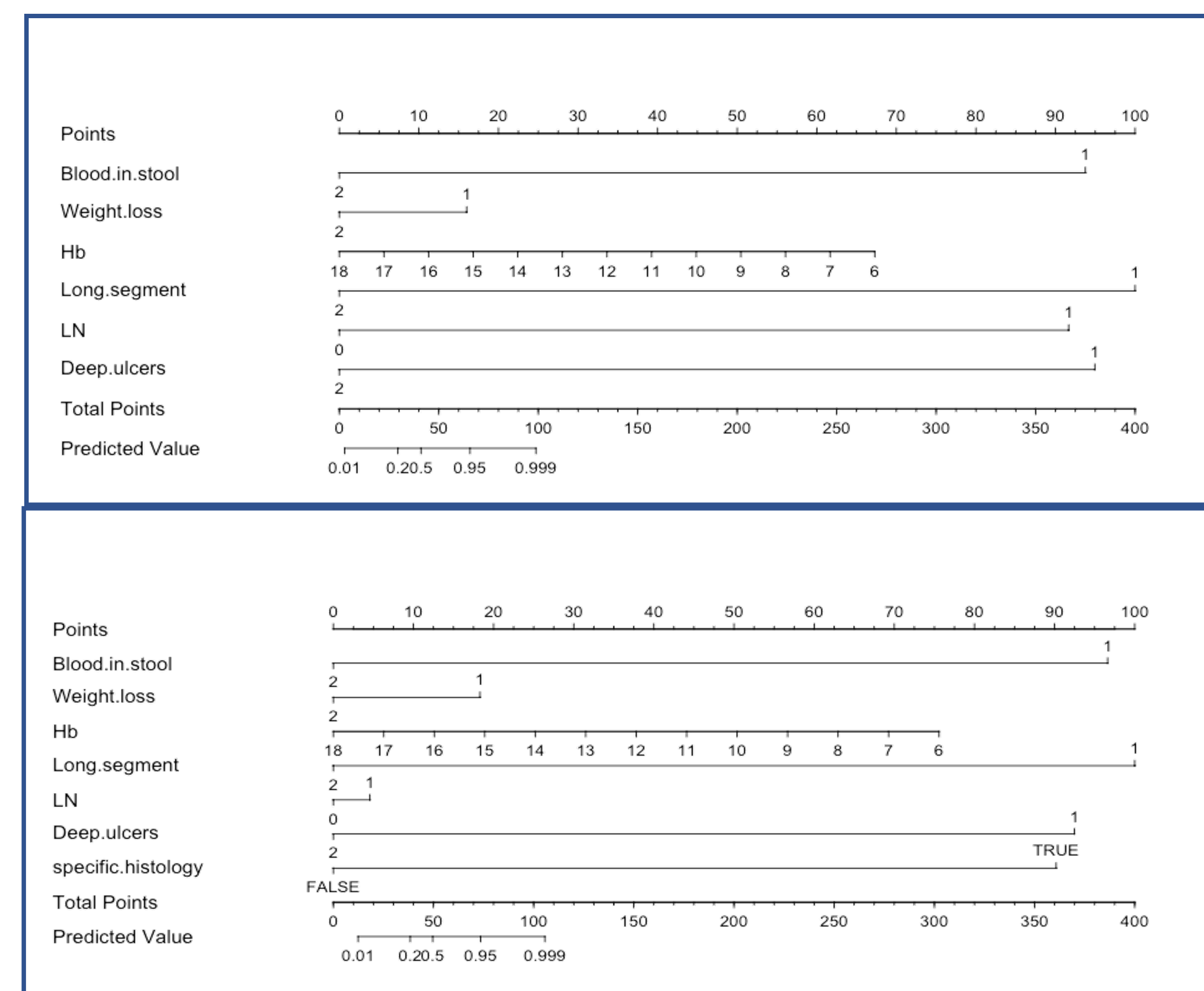Table-2: Sensitivity, specificity, PPV,NPV of the Algorithm

Figure 1: Nomograms without and with histology for bootstrap validation
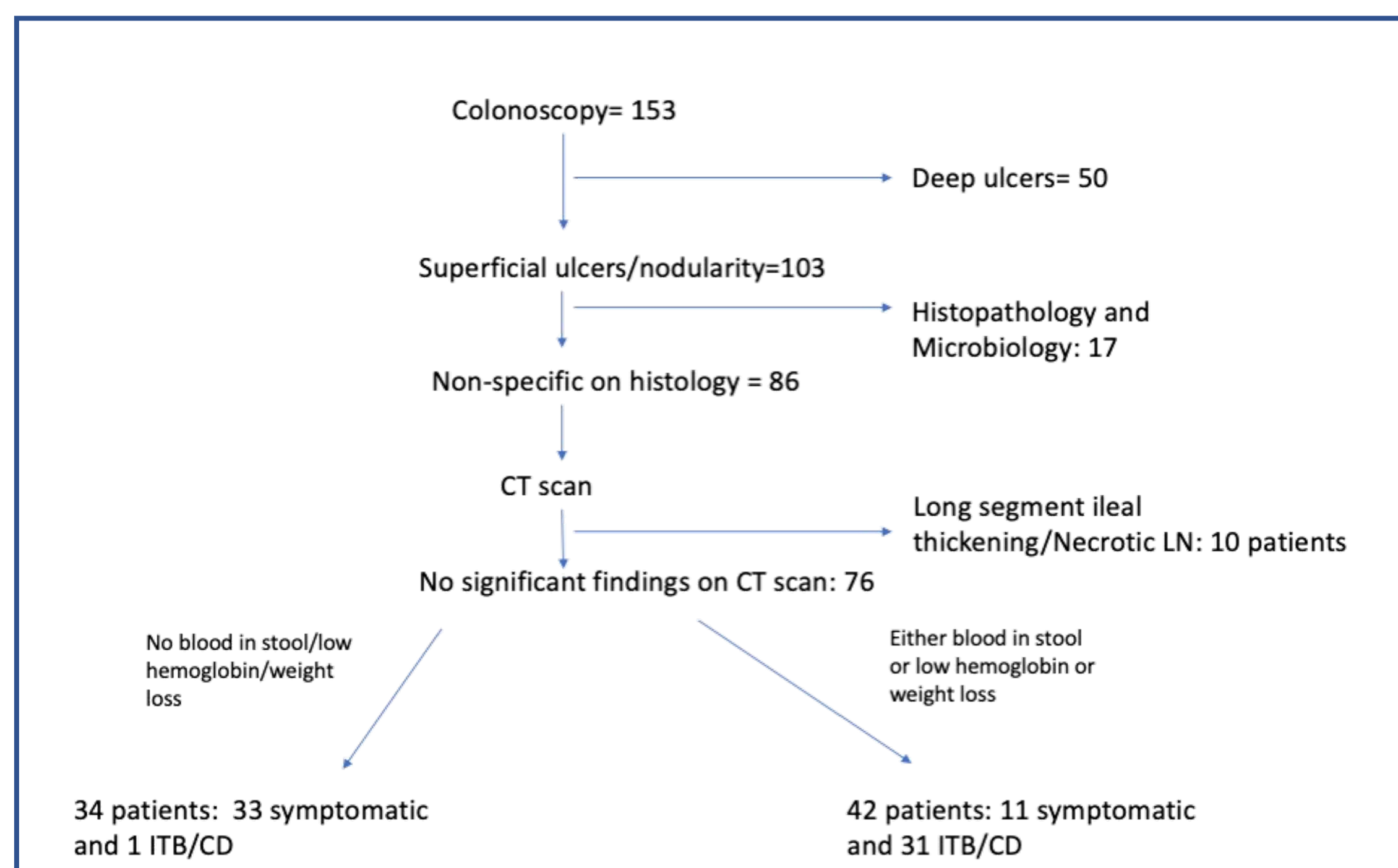

Figure 2: Algorithm for patients presenting with isolated chronic terminal ileum involvement
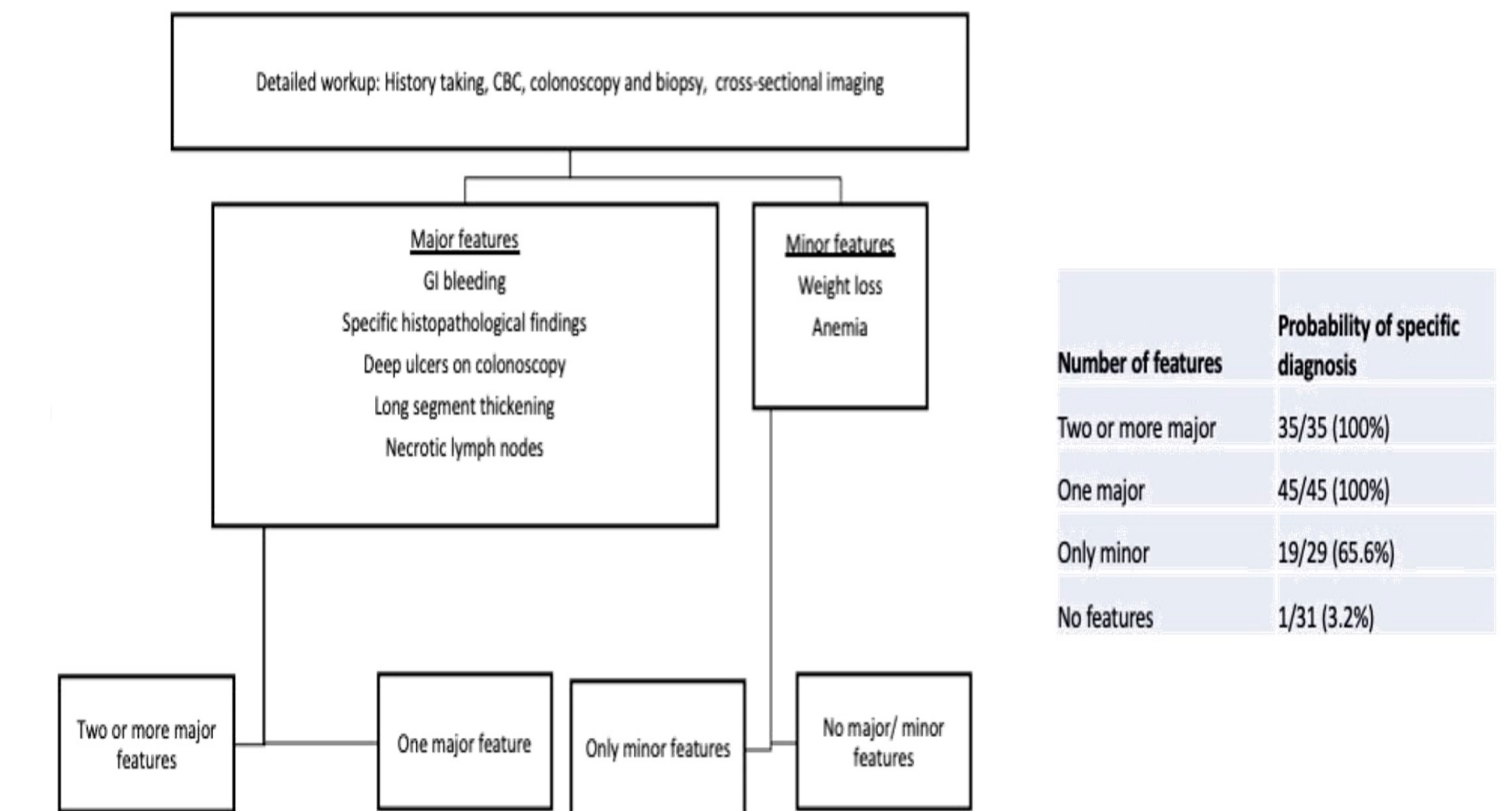

Figure 3: Approach to patients presenting with isolated TI involvement on colonoscopy based on major/minor features

Discussion

- The algorithm achieved an accuracy of 91.5%, sensitivity of 98.2% and specificity of 75.0%.

- Lower specificity could be accounted by coincidental weight loss or low hemoglobin due to other reasons. Most of these patients regained weight without intervention and had borderline low hemoglobin.

- In comparison to previous studies, we used a larger number of features and multivariate regression with bootstrap validation and a large and diverse cohort to strengthen the results.

Conclusions

- Our study is amongst the handful that have attempted to stratify patients with chronic terminal ileitis.

- The algorithmic approach based on a multivariate regression analysis has been developed by keeping clinicians in a variety of clinical practices in mind.

- These can be used in any kind of clinical scenario based on the investigative modalities available.

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