Differentiating Intestinal Tuberculosis from Crohn's Disease

7

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Key Points

1. Differentiating Crohn's disease from intestinal tuberculosis is a difficult clinical problem in countries where tuberculosis is endemic.
2. Certain features like shorter duration, presence of fever or pulmonary complaints, ileocecal involvement, transverse ulcers, short segment involvement, necrotic lymph nodes may favor the diagnosis of intestinal tuberculosis but other than necrotic lymphadenopathy none is specific.
3. Models integrating potential features have been proposed. However, external validation of them is required.
4. Anti-tuberculous therapy helps in differentiating these two diseases because the ulcers of intestinal tuberculosis heal with ATT as early as 2 months of treatment (early mucosal response).

Crohn's disease (CD) has become an important differential diagnosis of intestinal tuberculosis (ITB) in Asia because its incidence and prevalence is increasing in this region [1]. Both diseases share many similar presentations. A definite diagnosis of ITB depends on methods that have unsatisfactorily low sensitivities including 5.3–37.5% for acid-fast bacilli (AFB) tissue staining [2–4], 23–46% for mycobacterial culture [5, 6], and 36.4–67.9% for polymerase chain reaction (PCR) [4, 5, 7–9]. As a result, ITB cannot be confidently excluded—even when all of the above results are negative. A misdiagnosis of intestinal tuberculosis and treating it as Crohn's disease can cause life-threatening complications [10]. On the other hand, delayed CD diagnosis due to misdiagnosis with ITB can lead to exacerbation of disease and

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disease-related complications [11]. There have been multiple reports on the demographic, clinical, endoscopic, pathologic, radiologic, and serologic features and in differentiating CD and ITB, and several predictive models have been developed. This chapter summarizes the data from the studies reporting on differentiating CD and ITB. These features are summarized in Table 7.1.

7.1 Demographic Features

Meta-analysis by Limsrivilai et al. including all studies aiming to differentiate CD from ITB from inception till September 2015 found that ITB and CD patients tend to afflict similar age groups [12]. The mean age of CD patients has been reported from 26.8 to 37.4 years whereas it was 29.3–49.3 years in ITB patients [2–4, 7, 9, 13–22]. Male gender has been reported to be more predominant in CD in the meta-analysis but may not have much discriminative value alone [12]. Living in urban domicile, graduation at high school level or higher, and higher income have been reported to have a trend to be favored CD [23] while immunocompromised status, particularly HIV infection is an important risk factor for ITB [24].

7.2 Clinical Features

Clinical presentations are categorized into 3 groups which include intestinal symptoms, extra-intestinal involvement, and systemic symptoms.

For intestinal symptoms, duration of presentation was reportedly longer in CD. The median and range of presenting duration was 6–53.3 months and 0.3–300 months in CD, and 3–23.4 months and 0–120 months in ITB, respectively [2, 7, 16, 20, 23, 25, 26]. Diarrhea and hematochezia have been reported more in CD patients with the reported prevalence of 33–80% and 20–68%, respectively. The corresponding prevalence in ITB patients was 18–65% and 3–31%, respectively [2–4, 7, 9, 13, 15, 16, 18, 20, 23, 25, 27–36]. Abdominal pain has been reported at high prevalence, 60–90% in both diseases [2–4, 7, 9, 13, 15, 16, 18, 20, 23, 25, 27–31, 34]. For disease complications, intestinal fistula has been reported in 5.6–15% of CD and 0–6.7% of ITB patients while intestinal obstruction has been reported in 21–31% of CD and 10–55% of ITB patients [2, 12, 16, 31].

For extra-intestinal involvement, presence of extra-intestinal immunologic manifestations and perianal involvement are more frequent in CD (7–61% in CD and 0–23% in ITB) [2, 4, 12, 13, 15, 18, 27, 36, 37]. The prevalence of perianal disease was 10–34.7% in CD and 0–14.8% in ITB [2, 7, 9, 15, 16, 18, 25, 27, 28, 31–36]. In contrast, pulmonary involvement was significantly higher in ITB patients with the reported prevalence of 12.7–55.6% while in it was 0–8.8% in CD [4, 13, 15, 16, 18, 27, 33, 34, 36].

For systemic symptoms, fever and night sweat were found predominantly in ITB [12]. Fever was reported at the prevalence of 30–90% in ITB and 0–57% in CD, and night sweat was reported at 31–55% in ITB [2–4, 7, 9, 13, 15, 16, 18, 20, 23, 25,

Table 7.1 Features differentiating Crohn's disease from intestinal tuberculosis

Features	Crohn's disease	Intestinal tuberculosis
Demographic	• Uncommon in extremely old age • High socioeconomic	• Any age • Immunocompromised status
Clinical features		
• Duration of presentation	Longer (median 6–53.3 months)	Shorter (median 3–23.4 months)
• Intestinal symptoms	More common for • Diarrhea (33–80%) • Hematochezia (20–68%)	Less common • Diarrhea (18–65%) • Hematochezia (3–31%)
• Systemic symptoms	Less common for • Fever (0–57%) • Night sweat (2–22%)	More common for • Fever (30–90%) • Night sweat (31–55%)
• Fistula	Not uncommon (5.6–15%)	Rare (0–6.7%)
• Perianal disease	Not uncommon (10–34.7%)	Rare (0–14.8%)
• Extra-intestinal manifestations	Not uncommon (7–61%)	Rare (0–23%)
• Lung involvement	Rare (0–8.8%)	Not uncommon (12.7–55.6%)
Endoscopic features		
• Longitudinal ulcer	More common (10–63%)	Less common (0–33%)
• Transverse ulcer	Less common (4–36%)	More common (25–83%)
• Aphthous ulcer	More common (9–82%)	Less common (0–38%)
• Cobblestone appearance	More common (10–58%)	Less common (0–37%)
• Patulous ileocecal valve	Less common (2–20%)	More common (10–51%)
• Rectal involvement	More common (17–62%)	Less common (2–28%)
• Sigmoid/left-side involvement	More common (31–66%)	Less common (11–37%)
Pathological features		
• Granuloma	Present in 0–63% (small and vague)	Present in 25–100% (confluent, large, multiple, submucosal)
• Focally enhanced colitis	More common (22.5–67.9%)	Less common (20–35.8%)
Imaging features (CTE/MRE)		
• Lymph node >1 cm in size with central necrosis	Not reported found	Very suspicious if present
• Skipped lesions (>3)	Strongly favor	Strongly against

(continued)

Table 7.1 (continued)

Features	Crohn's disease	Intestinal tuberculosis
• Long segment involvement (>3 cm)	Favor	Against
• Comb sign.	Strongly favor	Strongly against
• Fibrofatty proliferation	Favor	Against
• Asymmetrical wall thickening	Favor	Against
• Visceral/subcutaneous fat	Favor	Against
Serological tests		
• Interferon-gamma release assay	Strongly against (0–24.6%)	Strongly favor (66.7–100%)

27–31, 33, 34] and 2–22% in CD [3, 9, 15, 16, 18, 25, 27, 29], respectively. Weight loss was reported nonsignificantly different in the meta-analysis [12]; the reported prevalence was 32.5–92.6% in CD and 51–93.3% in ITB [2, 4, 7, 13, 15, 16, 18, 20, 23, 25, 27, 29–31, 33].

As above, there is overlapping of the reported prevalence in almost clinical presentations. Therefore, clinical presentation along cannot distinguish between these two diseases.

7.3 Endoscopic Features

Endoscopic findings have been reported to differentiate ITB from CD by Lee et al in 2006 [38]. They reported four findings favoring ITB (transverse ulcers, scars or pseudopolyps, a patulous ileocecal (IC) valve, and involvement of less than 4 of 6 segments of the colon, including the ileocecum, ascending colon, transverse colon, descending colon, sigmoid colon, and anorectum), and 4 findings favoring CD (longitudinal ulcers, aphthous ulcers, cobblestone appearance, and anorectal involvement). After this study, many studies relating to differentiation of CD from ITB reported endoscopic findings in these two diseases. Meta-analysis found that aphthous ulcers, longitudinal ulcers, and cobblestone appearance significantly favored CD [12]. The reported prevalence of these findings was 9–82%, 10–63%, and 10–58% in CD, and 0–38, 0–33, and 0–37% in ITB, respectively. On the other hand, transverse ulcers and patulous IC valve were found significantly higher in ITB. The reported prevalence of these findings was 4–36% and 2–20% in CD, and 25–83% and 10–51% in ITB, respectively [2, 3, 7, 9, 13, 15, 16, 20, 23, 25–30, 38]. Figures 7.1 and 7.2 showed longitudinal ulcer in CD and transverse ulcer in ITB, respectively. Difference in location of involvement has also been reported between ITB and CD [12]. The reported prevalence of sigmoid involvement was 31–66% in CD and 11–37% in ITB, and the prevalence of rectum involvement was 17–62% in CD and 2–28% in ITB [7, 13, 15, 16, 20, 25, 27].

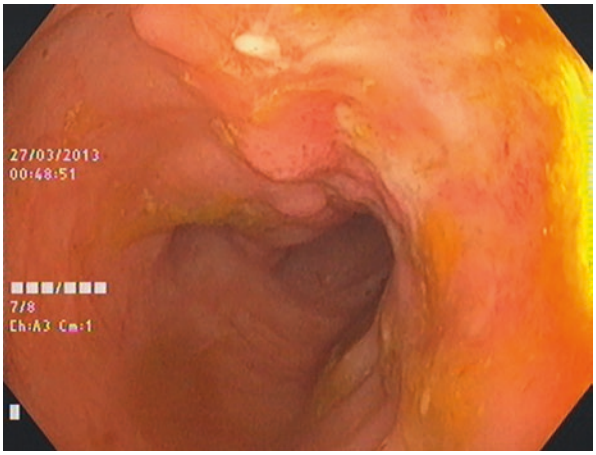

Fig. 7.1 Longitudinal ulcer in Crohn's disease

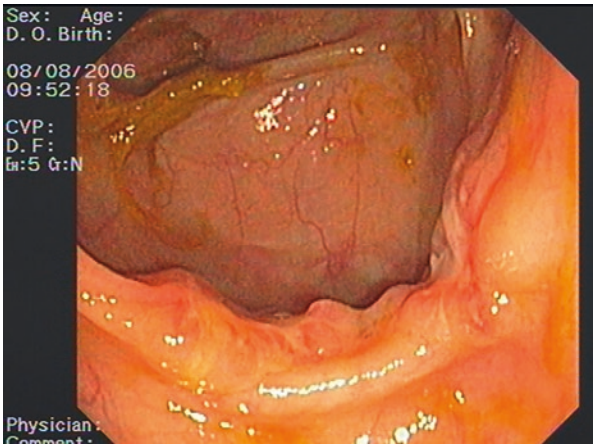

Fig. 7.2 Transverse ulcer in intestinal tuberculosis

As in clinical presentation, overlapping of the prevalence of both endoscopic findings and location of involvement between the two diseases. Endoscopic findings alone, therefore, cannot completely differentiate ITB from CD.

7.4 Pathological Features

In 1972, Tandon and Prakash reported the pathology of intestinal tuberculosis and its distinction from Crohn's disease based on 169 cases (10 CD and 159 ITB) who presented with intestinal obstruction and who underwent intestinal resection. They described that granuloma was present in all ITB, but absent in at least 25% of

CD. The granulomas in TB were often large, usually had caseation, and are often confluent. Furthermore, submucosal widening and fissures were generally present in CD while absent in ITB. Lymph node involvement was found in ITB although no intestinal lesions, but not in CD [39].

Nowadays, most pathological specimens are obtained from colonoscopy. Therefore, some features cannot be evaluated such as fissuring ulcers, transmural inflammation, and granuloma in lymph node. Studies describing microscopic features have been published. Pulimood et al divided the findings into 4 groups including characteristics of granulomatous inflammation, focal crypt-related inflammatory changes such as focally enhanced colitis, other features of mucosal damage such as architectural alteration, deep ulceration, aphthous ulceration, and acute/chronic inflammation, and segmental distribution of changes [40]. These definitions were used by subsequent studies. The meta-analysis found that features more common in ITB included confluent granuloma, large granuloma, multiple granulomas per section, submucosal granuloma, granuloma with surrounding cuffing lymphocytes, and ulcer lined by histiocytes, whereas focally enhanced colitis was found more in CD [12].

Patterns of macrophage polarization may be helpful in differentiating ITB from CD. Proinflammatory M1ϕ polarization was more common in colonic mucosa of CD patients, especially in the presence of mucosal granulomas [41].

There are some limitations of using pathological findings. First, most features are required to characterize granuloma features; however, granuloma was reportedly present in 0–63% in CD and 25–100% in ITB [7–9, 13, 16, 19, 23, 28, 30, 31, 36, 38, 40, 42]. Furthermore, the definition of each finding may not be well known. Many pathologists may not be able to accurately describe these findings.

7.5 Imaging Features

Cross-sectional imaging such as computed tomography enterography (CTE) and magnetic resonance imaging enterography (MRE) have been increasingly used at present. Many studies using CTE in differentiating ITB from CD including two meta-analyses by Kedia et al and Limsrivilai et al have been published recently [12, 18, 20, 26, 43, 44]. Useful features can be grouped into 3 groups including bowel wall changes, mesenteric changes, and pattern of involvement.

The findings at bowel wall include bowel wall thickness and mural stratification. Asymmetrical bowel wall thickening was reported in both meta-analyses that it was significantly associated with CD. However, the performance in differentiating CD from ITB was fair; the area under the curve for summary receiver operating characteristic curve (AUCSROC) was 0.68, sensitivity was 41%, and specificity was 90% [44]. Mural stratification, which is defined as visualization of a two- or three-layer appearance within the small bowel wall, was not a significant finding in one meta-analysis [44]. The other meta-analysis found that it was significant finding favoring CD with an odds ratio of 2.3, but with the lower bound of 95% confident interval close to 1 (1.04–5.17) [12].

Mesenteric changes included comb sign, fibrofatty proliferation, and necrotic lymph node. Fibrofatty proliferation and comb sign were significant findings associated with CD in both meta-analyses [12, 44]. Comb sign had a good performance in differentiating ITB from CD. Its AUCSROC was 0.89 with the sensitivity and specificity of 82% and 81% in one meta-analysis [44], while the other meta-analysis reported its odds ratio favoring CD of 19.8 [12]. Fibrofatty proliferation had an AUCSROC of 0.69, and its sensitivity and specificity were 41% and 89%, respectively, in one meta-analysis [44], and its odds ratio favoring CD was 4.05 in the other [12]. Lymph node necrosis was found only in ITB, not in CD in one meta-analysis [44], and because of this, the other meta-analysis did not do analysis for this finding [12].

The pattern of involvement includes long- or short segmental involvement (> or < 3 cm) and skip involvement (>3 areas). Short segmental involvement was found to be significantly associated with ITB with an odds ratio favoring CD of 0.11 [12], whereas it was not significant in the other meta-analysis [44]. Skip involvement favored CD and had a good performance in one meta-analysis with an AUCSROC of 0.87, sensitivity of 86, and specificity of 74 [44].

More recently, visceral fat/subcutaneous fat ratio of more than 0.63 was reported to be favored the diagnosis of CD with a sensitivity and specificity of 81% and 78%, respectively [45]. Then this parameter had been integrated in a model together with long segmental involvement and lymph node necrosis. The model had been shown to have a specificity of 100% in diagnosis of CD [46].

Based on the above findings, the Indian Society of Gastroenterology and Indian Radiological and Imaging Association recommends that CTE/MRE complements other modalities in differentiation between ITB and CD. The presence of lymph nodes greater than 1 cm in size with central necrosis favors a diagnosis of ITB over CD. On the other hand, the presence of skip lesions (>3), long segment involvement (>3 cm), comb sign, fibrofatty proliferation, left colonic involvement, and asymmetric thickening favor the diagnosis of CD over ITB [47].

7.6 Serological and Other Blood Tests

Interferon-gamma release assays (IGRA) is a marker for latent tuberculosis. Several studies including 3 meta-analyses have been published [12, 48, 49]. Meta-analysis by Ng et al found that the pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of IGRA for the diagnosis of ITB were 81% (95% CI, 75–86%), 85% (95% CI, 81–89%), 6.02 (95% CI: 4.62–7.83), and 0.19 (95% CI: 0.10–0.36), respectively. The AUC was 0.92 [49]. The results went in the same direction in the more recent meta-analysis, which showed that the odds ratio of diagnosis of CD was only 0.02 (0.01–0.04) of IGRA was positive [12].

The anti-*Saccharomyces cerevisiae* antibody (ASCA) has been recognized as a specific serologic marker of CD. ASCA was reported to be positive in about 50% of CD patients [50]. However, the results of studies using ASCA for differentiating

ITB from CD are conflicting [35, 51, 52]. In meta-analysis by Limsrivilai et al., ASCA had a trend to favor the diagnosis of CD, but not statistically significant [12].

Serum proteomic profiles have been shown in a study by Zhang et al. (30 CD, 21 ITB) that a differential diagnostic model comprising three potential biomarkers protein peaks (M/Z 4267, 4223, 1541) can well distinguish CD patients and ITB patients, with a specificity and sensitivity of 76.2% and 80.0%, respectively [53].

Frequency of CD4 + CD25 + FOXP3+ Treg cells in peripheral blood was significantly increased in ITB as compared to CD in a prospective study of 124 patients (32 CD, 16 ITB, 38 ulcerative colitis, and 33 controls). FOXP3+ cells in peripheral blood showed an AUROC curve of 0.908 in differentiating ITB from CD. At a cut-off value of>32.5%, a sensitivity of 75% and a specificity of 90.6% had been demonstrated [54].

7.7 Models Differentiating Intestinal Tuberculosis from Crohn's Disease

Many clinical, endoscopic, pathologic, imaging, and serological features have been shown to be significantly different between ITB and CD, but none of those features are exclusive to either ITB or CD. Many models integrating significant features have been proposed to differentiate ITB from CD to help decrease the rate of incorrect empirical therapy [55]. The early models included diagnostic parameters routinely available and used in clinical practice, such as clinical features, endoscopic findings, and pathologic findings [7, 15, 16, 21, 38]. The diagnostic models developed later included more advanced diagnostic parameters, such as high-resolution imaging [18, 20, 26, 46] and serological testing [12, 19, 22, 56, 57]. The published models are summarized in Tables 7.2, 7.3, and 7.4. These models are required to be validated by external populations. For the models using clinical, endoscopic, and pathological features, the model with more significant parameters seems to be more accurate [58].

7.8 Anti-Tuberculous Therapeutic (ATT) Trial

In 2008, Park et al prospectively analyzed the colonoscopic findings before and after short-term antituberculosis treatment in 18 patients with nonspecific ulcers on the ileocecal area and compared them with 7 patients of confirmed tuberculous colitis by acid-fast bacilli or caseating granuloma on colonic biopsy [59]. This study found that endoscopic mucosal healing after short-term ATT could differentiate ITB from CD.

In 2016, Pratap Mouli et al studied in 131 patients who received anti-tubercular therapy before being diagnosed as CD and in 157 ITB patients. In ITB patients, 94% showed global symptomatic response by 3 months, and all had endoscopic mucosal healing at 6 months. In CD patients, global symptomatic response with ATT was seen in 38% at 3 months and in 37% who completed 6 months of ATT, but

Table 7.2 Models integrating clinical, endoscopic, and pathological findings

Authors	Country	Study Design	Model type	Parameters	Model detail		Performance	
Lee YJ et al. Endoscopy 2006	Korea	Prospective CD 44, ITB 44	Scoring system	8 endoscopic findings	Favor CD (+1/each): Longitudinal ulcer, aphthous ulcer, cobblestone appearance, anorectal involvement Favor ITB (−1/each): Transverse ulcer, scars or pseudopolyps, a patulous ileocecal valve, involvement <4 segments Final score: 1–4: Crohn's disease 0: Indeterminate (−1) – (−4): ITB		Correct diagnosis: 87.5% Incorrect diagnosis: 8% Indeterminate: 4.5%	
Makharia et al. Am J Gastroenterol 2010	India	Prospective CD 53, ITB 53 (training) CD 20, ITB 20 (validation)	LR model	4 (2 clinical, 1 endoscopic, 1 pathological findings)	+ 2.3 × weight loss – 2.1 × blood in stool – 2.5 × involvement of sigmoid colon – 2.1 × focally enhanced colitis + 7		AUROC Training 0.906 Validation 0.893	
Li X et al. Dig Dis Sci 2011	China	Retrospective CD 130, ITB 122	LR model	6 clinical, 6 endoscopic findings	*Clinical score* Hematochezia Surgery history Perianal disease Pulmonary TB Ascites PPD skin test	*Endosc. Score* Rectum Long. Ulcers Cobblestone IC valve Tran. Ulcers Rodent-like ulcer	*Clinical* Se 90% Sp 77% Acc 84%	*Endoscopy* Se 83% Sp 82% Acc 83%
Yu H et al. Digestion 2012	China	Retrospective CD 53, ITB 43	LR model	3 (1 clinical, 1 endoscopic, 1 pathological findings)	– 2.0 × night sweat + 3.6 × longitudinal ulcer – 3.8 × granuloma		AUROC 0.864	

(continued)

Table 7.2 (continued)

Authors	Country	Study Design	Model type	Parameters	Model detail	Performance
Jung Y et al. Am J Gastroenterol 2016	Korea	Retrospective CD 79, ITB 49 for training CD 79, ITB 49 for validation	LR model	7 (4 clinical, 3 endoscopic findings)	Diarrhea Longitudinal ulcers Involvement of sigmoid colon Age Female gender Ring shape ulcers Suspicious of pulmonary TB	AUROC Training 0.979 Validation 0.978

AUROC area under receiver operating characteristic curve, *LR* logistic regression
(Adapted from Limsrivilai J, Pausawasdi N. Intestinal tuberculosis or Crohn's disease: a review of the diagnostic models designed to differentiate between these two gastrointestinal diseases. Intest Res 2020 with permission)

Table 7.3 Model integrating computed tomography enterography

Authors	Country	Study Design	Model type	Parameters	Model detail		Performance
Zhao HS et al. Inflamm Bowel Dis 2014	China	Retrospective CD 141, ITB 47	LR model	6 clinical 8 CTE findings	*Clinical model* Hematochezia Perianal disease PPD test Ascites Pulmonary TB Night sweat	*CTE model* Left colon Asymmetrical wall Abscess Comb sign LN along rt. colic artery. Contracted IC Fixed patulous IC LN with necrosis	*AUROC* Clinical model 0.916 CTE model 0.986
Kedia S et al. Indian J Gastroenterol 2015	India	Retrospective CD 54, ITB 50	Scoring system	3 CT/CTE findings	Long segment involvement+ (1–ileocecal region involvement)+ (1–LN ≥1 cm)		Risk score for CD 3: Se 37, Sp 90 Risk score for ITB 0: Se 14, Sp 100
Mao R et al. Endoscopy 2015	China	Prospective, consecutive 67 CD, 38 ITB for training 40 CD, 20 ITB for validation	Algorithm (combining Lee's endoscopic score)	2 CTE findings 8 endoscopic findings	Presence of comb sign or/and Segmental small bowel lesion		Increase accuracy of endoscopic score alone 71.6% − > 88.3%
Kedia S et al. J Gastroenterol Hepatol 2018	India	Retrospective 32 CD, 27 ITB for training 38 CD, 31 ITB for validation	Scoring system	2 CT/CTE findings	VF/SC ratio > 0.63 + long segment involvement		Validation set Risk score for CD 2: Se 50, Sp 97 Risk score for ITB 0: Se 61, Sp 84

AUROC area under receiver operating characteristic curve, *CD* Crohn's disease, *CTE* computed tomography enterography, *IC* ileocecal valve, *LN* lymph node, *LR* logistic regression, *Se* sensitivity, *Sp* specificity, *TB* tuberculosis

(Adapted from Limsrivilai J, Pausawasdi N. Intestinal tuberculosis or Crohn's disease: a review of the diagnostic models designed to differentiate between these two gastrointestinal diseases. Intest Res 2020 with permission)

Table 7.4 Models integrating clinical, endoscopy, pathology, imaging study, and laboratory tests

Authors	Country	Study Design	Model type	Parameters	Model detail		Performance
Huang X et al. World J Gastroenterol 2015	China	Prospective CD 25, ITB 40	Scoring system	12 findings (2 clinical, 5 endoscopic, 4 CTE, 1 IGRA)	*Favor CD (+1)* Longitudinal ulcers Nodular hyperplasia Cobblestone Intestinal diseases Intestinal fistulas Target signs Comb signs	*Favor ITB (−1)* Night sweats Positive PPD tests Positive T-SPOT.TB Ring ulcers Ulcer scars	AUROC 0.997
Bae JH et al. Inflamm Bowel Dis 2017	Korea	Prospective CD 40, ITB 40 for training CD 14, ITB 23 for validation	Scoring system	8 endoscopic findings 2 images (CXR, SBFT) 2 laboratory tests (ASCA, IGRA)	*Endosc. Score* (8 findings)	*Lab-radio score* *Favor CD (+1)* - proximal SB (SBFT) - ASCA *Favor ITB (−1)* - pulmonary TB (CXR) - IGRA	AUROC Training 0.990 Validation 0.981
					(+)➔1, 0➔0, (−)➔(−1)	(+)➔1, 0➔0, (−)➔(−1)	
					Summation (−2, −1) = > ITB, (0,1,2) = > CD		

Wu X et al. Inflamm Bowel Dis 2018	China	Prospective CD 107, ITB 60 for training CD 46, ITB 26 for validation	LR model	5 (2 clinical, 2 endoscopic, 1 IGRA)	Perianal disease Longitudinal ulcer Left colon Pulmonary TB-specific Ag to phytohemagglutinin	AUROC Training 0.975 Validation 0.950
He Y et al. Am J Gastroenterol 2019	China	Prospective CD 143, ITB 69 for training CD 76, ITB 22 for validation	Step1: Select variable from a random forest regression model Step2: LR model	2 models 8 (1 clinical, 2 endoscopic, 3 CTE, 2 IGRA/PPD)	*Model 1* Age Rectum involvement Transverse ulcer Skipped involvement of small bowel Comb sign IGRAs	AUROC Training 0.977 Validation (cut-off $p = 0.5$) Se 86.8% Sp 90.9% Accuracy 87.8%
					Model 2 Age Rectum involvement Transverse ulcer Skipped involvement of small bowel Target sign PPD	AUROC Training 0.930 Validation (cut-off p = 0.5) Se 84.2% Sp 100% Accuracy 87.8%

(continued)

Table 7.4 (continued)

Limsrivilai et al. Am J Gastroenterol 2017		Meta-analysis Validation cohort 29 CD, 22 ITB	Step 1: Select significant variables with low heterogeneity based on meta-analytic results Step 2: Integrate the variables to Bayesian model	9 clinical, 8 endoscopic, 5 pathological, 5 CTE, and 1 IGRA (can select only available parameters)	bit.ly/ITBvsCD	AUROC Clinical + endoscopy 0.920 Clinical + endoscopy + pathological findings 0.943

ASCA Anti-*Saccharomyces cerevisiae* antibody, *AUROC* area under receiver operating characteristic curve, *CD* Crohn's disease, *CTE* computed tomography enterography, *CXR* chest X-ray, *IC* ileocecal valve, *IGRA* interferon-gamma release assay, *LN* lymph node, *LR* logistic regression, *SBFT* small bowel follow through, *Se* sensitivity, *Sp* specificity, *TB* tuberculosis

(Adapted from Limsrivilai J, Pausawasdi N. Intestinal tuberculosis or Crohn's disease: a review of the diagnostic models designed to differentiate between these two gastrointestinal diseases. Intest Res 2020 with permission)

only 5% had endoscopic mucosal healing at 6 months. The same response pattern was observed in a validation cohort of 55 patients who were prospectively recruited. This study suggested that symptom persistence after a therapeutic trial of 3 months of ATT may indicate the diagnosis of Crohn's disease, and emphasizing a need for repeat colonoscopy for diagnosing CD [60]. Healing of ulcers has been reported as early as 2 months after initiation of ATT and this early mucosal response may discriminate ITB and CD [61].

Sharma et al did a retrospective study in 112 patients suspected abdominal tuberculosis (105 TB, 3 CD, 7 other diagnoses). This study found that lack of decline in CRP may suggest alternative diagnosis or drug-resistant TB [62].

In summary, response to ATT trial is reliable for differentiating ITB from CD, and the Asia-Pacific guidelines recommend 8–12 weeks of empirical antituberculosis treatment (ATT) for patients with diagnostic uncertainty due to the possible onset of potentially fatal complications if immunosuppressive agents are inappropriately prescribed to ITB patients [63].

7.9 Conclusion

Crohn's disease is very difficult to be distinguished from intestinal tuberculosis. The tools we have in hand currently help us to improve diagnostic capability. However, the problem has not been solved. ATT is still required in some situations. Future research is warranted.

Conflict of Interest None.

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