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Original Article

Clinical Course of Patients with Intestinal Behçet's Disease According to Consensus-Based Diagnostic Categories

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Background/Aims: There have been few studies regarding the prognosis of intestinal Behçet's disease (iBD) patients according to consensus-based diagnostic categories, which reflects the typicality of intestinal ulcers, the presence of oral ulcers, and the accompanying systemic manifestations.

Methods: The medical records of patients who had ileocolonic ulcers with a clinical impression of iBD were reviewed. The patients were categorized according to the diagnostic algorithm at the time of diagnosis. Adverse events were defined as major surgery or admission related to iBD deterioration.

Results: A total of 163 patients were included in the study. The male-to-female ratio was 1:1.2, and the mean age at the time of diagnosis was 48.9±15.9 years. The numbers of patients who met the definite, probable, suspected, and nondiagnostic iBD criteria were 19 (11.7%), 61 (37.4%), 38 (23.3%), and 45 (27.6%), respectively. The event-free survival of patients with definite, probable, and suspected iBD was significantly shorter than that of patients with nondiagnostic iBD (p=0.026), while there was no significant difference among the definite iBD, probable iBD, and suspected iBD groups (p=0.596). After excluding patients with nondiagnostic iBD, multivariate analysis showed that anemia, fever, colonic involvement other than the ileocecum, and accompanying hematologic disorders at the time of diagnosis were significantly associated with the development of adverse events.

Conclusions: The clinical course of patients with definite, probable, and suspected iBD is distinguished from that of patients with nondiagnostic iBD, but patients with definite, probable, and suspected iBD share similar clinical courses. **(Gut Liver 2022;16:746-753)**

Key Words: Behçet syndrome; Inflammatory bowel disease; Prognosis

INTRODUCTION

Behçet's disease is a chronic, idiopathic, relapsing, and immune-related disease involving multiple organs. It is characterized by recurrent oral ulcers, skin lesions, genital ulcers, ocular inflammation, gastrointestinal ulcers, and vascular lesions. The incidence of Behçet's disease is rare and higher in the Mediterranean area and East Asia than in Western countries.[1]

Approximately 3% to 16% of patients with Behçet's disease have gastrointestinal involvement and the ileocecal area is the most common location.[2,3] The diagnosis of intestinal Behçet's disease (iBD) can be considered when a typical oval-shaped large ulcer in the terminal ileum is

present, or ulcerations in the small or large intestine are present with clinical findings of Behçet's disease.[4]

The diagnosis of iBD is often challenging because of manifestations similar to Crohn's disease or intestinal tuberculosis, infrequent pathologic evidence of vasculitis, and the absence of specific laboratory markers for iBD. Moreover, a considerable number of patients with iBD do not present with systemic manifestations when intestinal ulcers are detected.[5] Therefore, the consensus-based diagnostic criteria for iBD were proposed to reflect the morphology of intestinal ulcers and temporal changes in systemic symptoms. The diagnostic algorithm categorizes patients into four groups of definite, probable, suspected, and nondiagnostic according to the typicality of intestinal ulcers, presence of oral ulcers, and systemic manifestations. The diagnostic accuracy of the first three categories for iBD was proved as 91%.[6,7]

However, few studies have been performed to analyze the prognosis of iBD according to the diagnostic categories. This study was performed to evaluate the prognosis of patients with iBD according to their diagnostic categories and the relevant clinical factors affecting the prognosis.

MATERIALS AND METHODS

1. Patients

We reviewed the medical records and colonoscopic findings of patients who had ileocolonic ulcers and a clinical impression of iBD between March 1986 and August 2019 at Seoul St. Mary's Hospital, the Catholic University of Korea, Seoul, Korea. Patients who had undergone previous intestinal resection or were not followed up at least twice after the colonoscopy were excluded. The patients who were finally diagnosed with intestinal tuberculosis, Crohn's disease, ulcerative colitis, infectious colitis, nonsteroidal anti-inflammatory disease-induced enteropathy, or malignant disorders during the follow-up period were also excluded. The study was approved by the Institutional Review Board of Seoul St. Mary's Hospital (IRB number: KC20WISI0232). The waiver of informed consent was approved.

2. Evaluation and definition of clinical variables

We collected the baseline demographics, gastrointestinal symptoms, and systemic manifestations at the time of diagnosis and during the follow-up period. Laboratory findings including hemoglobin, serum C-reactive protein, and albumin levels were also included. All the variables for analysis of prognostic factors were selected as those within 30 days of diagnosis.

Disease activity was assessed using the disease activity index for iBD.[8] All patients underwent a colonoscopy at the time of diagnosis. The shape, location, and typicality of the intestinal ulcers were also reviewed.

3. Categorization of the patients according to the diagnostic criteria of iBD

The diagnostic criteria followed the consensus-based diagnostic algorithm by the Korean Inflammatory Bowel Disease Study Group.[6] The ileocolonic ulcers were classified into "typical" and "atypical" according to the colonoscopic findings. Typical ulcers were defined as round or oval-shaped deep ulcers with discrete borders, which were located at the ileocecal areas and fewer than five in number during the colonoscopic examination. Ulcers that did not fulfill the above characteristics were classified as atypical. The extraintestinal manifestations were defined as the clinical findings by the Behçet's Disease Research Committee of Japan.[9]

Patients with typical ulcers and extraintestinal manifestations were categorized into the definite iBD group. Patients with typical ulcers and recurrent oral ulcers only or those with atypical ulcers and extraintestinal manifestations were assigned to the probable iBD group. Patients with typical ulcers without any extraintestinal manifestations or those with atypical ulcers and recurrent oral ulcers were classified into the suspected iBD group. Patients with atypical ulcers without any extraintestinal manifestations were included in the nondiagnostic iBD group (Fig. 1).

4. Clinical outcomes

The primary outcome of the study was event-free survival (EFS). An event was defined as major surgery such as intestinal resection or admission to manage severe intestinal symptoms, bleeding, or complications such as a fistula, abscess, or perforation. The secondary outcome of the study was disease-specific survival (DSS) which was the period from the time of diagnosis to the time of death due to iBD deterioration.

5. Statistical analysis

The results were analyzed using analysis of variance, Jonckheere trend test, the linear-by-linear association test, and the chi-square test, as appropriate. The data were expressed as the mean±standard deviation. EFS and DSS of the patients were calculated using the Kaplan-Meier analysis and compared by the log-rank test. Univariate and multivariate analyses with the Cox proportional hazard model were used to identify the risk factors for adverse events and disease-specific death. A p-value of less than 0.05 was considered to be statistically significant. Statistical analyses

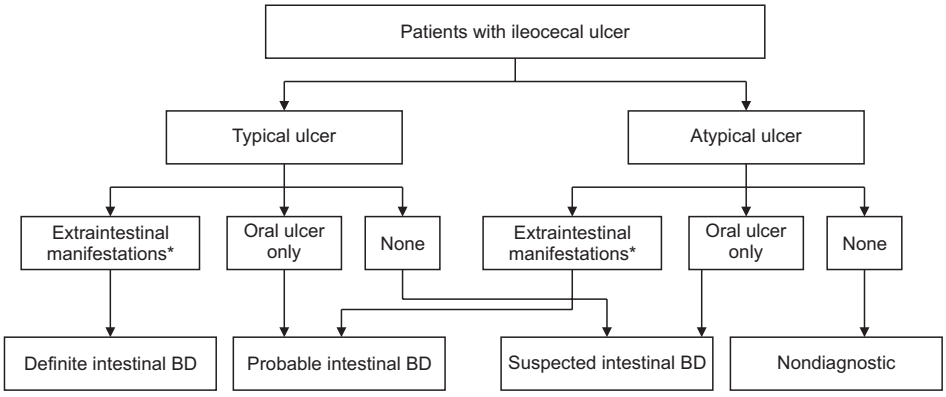

Fig. 1. Diagnostic algorithm for intestinal Behçet's disease (BD). *Extraintestinal manifestations were defined according to the diagnostic criteria of the Behçet's disease Research Committee of Japan. Adapted from Cheon JH, *et al.* Intest Res 2017;15:311-317.[6]

were performed using SAS 9.4 for Windows (SAS Institute, Cary, NC, USA).

RESULTS

1. Patient characteristics

During the study period, a total of 82,704 patients had undergone colonoscopy in our institution. We selected 202 patients who had ileocolonic ulcers and a clinical impression of iBD at the time of the initial colonoscopy. Among them, 28 patients were excluded because the etiology of their ileocolonic ulcers was proven to be other disorders such as intestinal tuberculosis (n=3), gut graft-versus-host disease (n=1), and asymptomatic isolated terminal ileal ulcerations (n=24).[10] Eleven patients were excluded because of insufficient follow-up (Fig. 2).

Finally, a total of 163 patients were included in the study. Eighty-nine patients (54.6%) were female and the mean age at the time of diagnosis was 48.9±15.9 years. The number of patients with definite, probable, suspected, and nondiagnostic iBD at the time of diagnosis was 19 (11.7%), 61 (37.4%), 38 (23.3%), and 45 (27.6%), respectively (Table 1).

There were no significant differences in age, sex, hemoglobin, C-reactive protein, and albumin levels at the time of diagnosis between the diagnostic categories. However, the disease activity index for iBD score at the time of diagnosis was significantly different according to the diagnostic categories ($p<0.001$) and the Jonckheere trend test showed that the score was gradually decreased in the order of definite, probable, suspected, and nondiagnostic iBD ($p<0.001$). There were also significant differences in the use of steroids, 5-aminosalicylic acid, immunomodulators, and biologics during the follow-up period according to the diagnostic categories.

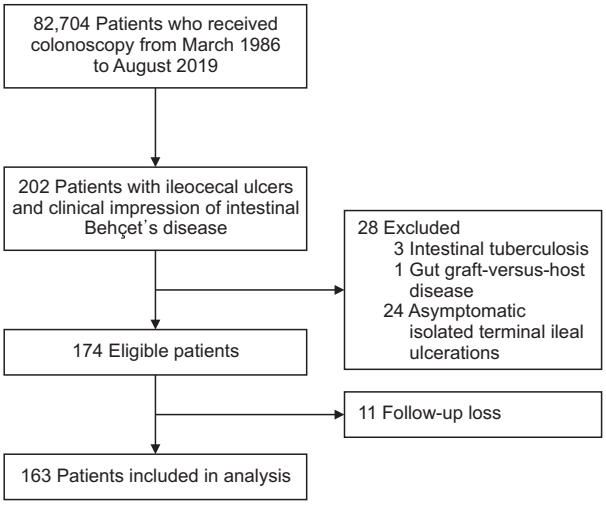

Fig. 2. The study flow diagram.

2. EFS according to disease categories and prognostic factors at the time of diagnosis

Among the total of 118 patients with definite, probable, and suspected iBD, 31 patients (26.2%) were admitted due to iBD-related surgery, severe intestinal symptoms, bleeding, or other complications during the mean follow-up period of 45.0±58.0 months. Six of 19 patients with definite iBD (31.6%) were admitted because of severe intestinal symptoms (n=3) or gastrointestinal bleeding (n=3). None of patients with definite iBD received iBD-related major surgery during the follow-up period. Sixteen of 61 patients with probable iBD (26.2%) were admitted due to severe symptoms (n=6), perforation (n=6) or gastrointestinal bleeding (n=4). All the six patients who underwent surgery were due to perforation. Nine of 39 patients with suspected iBD (23.7%) were admitted because of severe symptoms (n=3), ileus (n=1), perforation (n=2), and bleeding (n=3). Among them, three patients with perforation or ileus received surgery (Table 1).

There was no significant difference in EFS between

Table 1. Baseline Characteristics

Characteristics	Definite iBD (n=19)	Probable iBD (n=61)	Suspected iBD (n=38)	Nondiagnostic (n=45)	p-value
Age, yr	44.7±14.9	46.6±15.0	49.1±16.5	53.7±16.0	0.082
Sex, M:F	9:10	25:36	16:22	24:21	0.389
Hemoglobin, g/dL	12.0±1.9	12.1±2.5	12.0±2.6	13.3±2.2	0.040
CRP, mg/dL	1.1 (0.6–5.6)	1.1 (0.3–3.7)	1.2 (0.1–3.3)	0.2 (0.1–1.0)	0.010*
Albumin, g/dL	3.9±0.5	3.9±0.6	3.9±0.6	4.1±0.5	0.466
DAIBD score	60.3±29.1	60.2±29.2	49.1±30.7	22.2±19.4	<0.001
Treatment					
Steroid	18 (94.7)	44 (72.1)	17 (44.7)	2 (4.4)	<0.001
5-ASA	16 (84.2)	37 (60.7)	25 (65.8)	1 (2.2)	<0.001
Immunomodulator	3 (15.8)	11 (18.3)	1 (2.6)	1 (2.2)	0.005
Biologics	9 (47.4)	12 (20.0)	5 (13.2)	0	<0.001
Thalidomide	0	1 (1.7)	0	0	
Oral ulcers	19 (100)	60 (98.4)	34 (89.5)	0	<0.001
Systemic Behçet symptoms					
Genital ulcers	12 (63.2)	28 (46.0)	0	0	<0.001
Uveitis	6 (31.6)	9 (14.8)	0	0	<0.001
Skin lesion	8 (42.1)	14 (23.0)	0	0	<0.001
Colonic involvement other than ileocecal area	2 (10.5)	16 (26.2)	11 (28.9)	8 (17.8)	0.739
Adverse event	6 (31.6)	16 (26.2)	12 (31.6)	0	
Operation	0	6 (9.8)	3 (7.9)	0	
Admission	6 (31.6)	10 (16.4)	9 (23.7)	0	
Hematologic disorder	2 (10.5)	10 (16.4)	8 (21.1)	1 (2.2)	
MDS	1 (5.3)	4 (6.6)	4 (10.5)	0	
AA	0	5 (8.2)	1 (2.6)	1 (2.2)	
AML	0	0	1 (2.6)	0	
Lymphoma	1 (5.3)	0	1 (2.6)	0	
Multiple myeloma	0	1 (1.7)	0	0	
ITP	0	0	1 (2.6)	0	
Follow-up, mo	65.6±64.7	54.5±71.5	47.0±51.2	24.3±27.4	
iBD-related admission	6 (31.6)	16 (26.2)	9 (23.7)	0	
iBD-related surgery	0	6 (9.8)	3 (10.5)	0	
iBD-related death	1 (5.3)	2 (3.3)	2 (5.3)	0	

Data are presented as mean±SD, median (interquartile range), or number (%).
iBD, intestinal Behçet's disease; M, male; F, female; CRP, C-reactive protein; DAIBD, disease activity index for intestinal Behçet's disease; 5-ASA, 5-aminosalicylic acid; MDS, myelodysplastic syndrome; AA, aplastic anemia; AML, acute myeloid leukemia; ITP, idiopathic thrombocytopenic purpura.
*Kruskal-Wallis test.

the definite, probable, suspected, and nondiagnostic iBD groups (p=0.087). When the definite, probable, and suspected groups were included in the diagnostic iBD group, there was a significant difference in EFS between the diagnostic iBD group and the nondiagnostic iBD group (p=0.021) (Fig. 3).

Univariate analysis showed that a hemoglobin level of <10.0 g/dL, serum albumin of <3.0 g/dL, fever ≥38.0℃, colonic involvement other than the ileocecal area, and accompanying hematologic disorders at the time of diagnosis were associated with the development of adverse events (Table 2). In multivariate analysis, a hemoglobin level of <10.0 g/dL, fever ≥38.0℃, colonic involvement other than the ileocecal area, and accompanying hematologic disorders at the time of diagnosis were significant factors for development of adverse events (hazard ratio [HR], 4.01; 95% confidence interval [CI], 1.67 to 9.60; HR, 2.54; 95% CI, 1.10 to 5.89; HR, 4.19, 95% CI, 1.77 to 9.92; HR, 2.91; 95% CI, 1.18 to 7.13, respectively).

3. DSS according to disease categories and prognostic factors at the time of diagnosis

Among the 118 patients with definite, probable, and suspected iBD, nine patients (7.6%) died during the follow-up period. Among them, five deaths (4.3%) were associated with iBD progression, and the other four patients expired from lung cancer (n=2) and cerebral hemorrhage (n=2).

There was no significant difference in DSS between the definite, probable, suspected, and nondiagnostic iBD

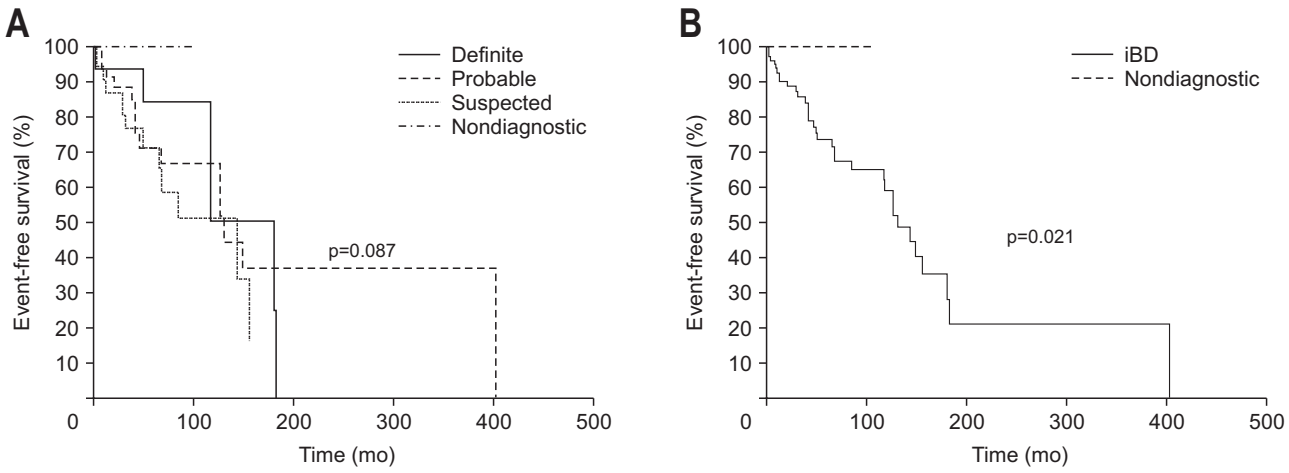

Fig. 3. Event-free survival (EFS) according to the diagnostic categories. (A) EFS of the definite, probable, suspected, and nondiagnostic intestinal Behçet's disease (iBD) groups. (B) EFS of diagnostic iBD (definite+probable+suspected iBD) and nondiagnostic iBD.

Table 2. Analysis of Prognostic Factors of Intestinal Behçet's Disease for the Development of Adverse Events

Characteristics	Category	Univariate analysis			Multivariate analysis		
		HR	95% CI	p-value	HR	95% CI	p-value
Age	≥40 yr <40 yr	1.67	0.79–3.56	0.182			
Sex	Male Female	1.18	0.58–2.39	0.655			
Typicality of ulcer	Typical Atypical	1.10	0.54–2.19	0.804			
Histology-proven vasculitis	Yes No	1.50	0.51–4.40	0.924			
Systemic Behçet's disease symptoms	Yes No	1.33	0.18–9.91	0.780			
Abdominal pain	Yes No	1.58	0.73–3.44	0.245			
Hemoglobin	<10.0 g/dL ≥10.0 g/dL	4.53	2.16–9.50	<0.001	4.01	1.67–9.60	0.002
C-reactive protein	≥2.5 mg/dL <2.5 mg/dL	1.89	0.92–3.87	0.082			
Albumin	<3.0 g/dL ≥3.0 g/dL	10.65	3.16–35.90	<0.001	2.17	0.57–8.21	0.253
Fever	≥38.0℃ <38.0℃	2.64	1.21–5.74	0.013	2.54	1.10–5.89	0.030
DAIBD	≥40 <40	3.20	0.76–13.41	0.112			
Colonic involvement other than ileocecal area	Yes No	5.78	2.67–12.48	<0.001	4.19	1.77–9.92	0.001
Hematologic disorders	Yes No	5.54	2.30–13.33	<0.001	2.91	1.18–7.13	0.019

HR, hazard ratio; CI, confidence interval; DAIBD, disease activity index for intestinal Behçet's disease.

groups (p=0.714). There also was no significant difference in DSS between the diagnostic iBD (definite, probable, and suspected iBD) and nondiagnostic iBD group (p=0.584).

The Cox proportional hazard model revealed that lower hemoglobin levels (<10.0 g/dL) at the time of diagnosis were the only significant factor associated with poor DSS in univariate (HR, 6.41; 95% CI, 1.03 to 40.07) and multivariate analysis (HR, 6.41; 95% CI, 1.03 to 40.07) (Table 3).

4. Chronological changes in the diagnostic category during the follow-up period

During the follow-up period, each of the two patients

Table 3. Analysis of Prognostic Factors of Intestinal Behçet's Disease for Disease-Specific Survival

Characteristics	Category	Univariate analysis			Multivariate analysis		
		HR	95% CI	p-value	HR	95% CI	p-value
Age	≥40 yr <40 yr	2.45	0.27–22.55	0.430			
Sex	Male Female	1.79	0.30–10.72	0.524			
Typicality of ulcer	Typical Atypical	2.32	0.39–13.88	0.359			
Histology-proven vasculitis	Yes No	4.95	0.50–48.70	0.170			
Systemic Behçet's disease symptoms	Yes No	20.87	0.00–3.498E+13	0.832			
Abdominal pain	Yes No	1.11	0.18–6.67	0.911			
Hemoglobin	<10 g/dL ≥10 g/dL	6.41	1.03–40.07	0.047	6.41	1.03–40.07	0.047
C-reactive protein	≥2.5 mg/dL <2.5 mg/dL	1.53	0.21–10.87	0.673			
Albumin	<3.0 g/dL ≥3.0 g/dL	21.68	0.00–1.260E+10	0.765			
Fever	≥38.0℃ <38.0℃	1.98	0.22–17.73	0.543			
DAIBD	≥40 <40	1.12	0.12–10.16	0.922			
Colonic involvement other than ileocecal area	Yes No	6.15	0.98–38.57	0.053			
Hematologic disorders	Yes No	29,322.19	0.00–2.773E+31	0.746			

HR, hazard ratio; CI, confidence interval; DAIBD, disease activity index for intestinal Behçet's disease.

with suspected iBD at the time of the initial diagnosis became compatible with probable iBD by the development of typical ulcers and uveitis, respectively. One patient with probable iBD became compatible with definite iBD by the development of typical ulcers (Fig. 4). None of the patients with nondiagnostic iBD changed their diagnostic category during the follow-up period.

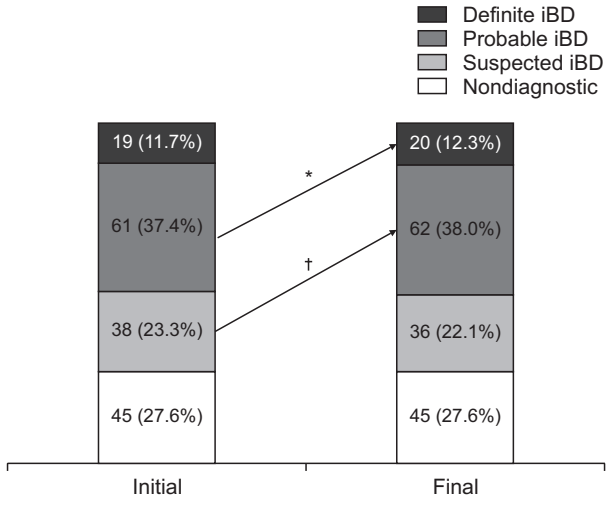

Fig. 4. Chronological changes in the diagnostic categories. *The initial diagnosis of patients with probable intestinal Behçet's disease (iBD) was changed into definite iBD at the end of the follow-up by the development of typical ulcers; †The initial diagnosis of two patients with suspected iBD was changed into probable iBD at the end of the follow-up by the development of typical ulcers and uveitis, respectively.

DISCUSSION

Our study showed for the first time that the clinical course of patients with definite, probable, and suspected iBD was clearly distinguished from that of patients with nondiagnostic iBD. In contrast, the clinical course between patients with definite, probable, and suspected iBD was not significantly different, which suggests that the former three categories belong to a single disease entity called iBD.

The diagnostic algorithm of iBD is mainly dependent upon the typicality of intestinal ulcers, presence of oral ulcers, and accompanying systemic manifestations, and our univariate and multivariate analyses showed that those factors were not significantly associated with the development of adverse events or poor DSS. A previous retrospective study also did not find any difference in clinical charac-

teristics between iBD patients who fulfilled the systemic manifestations and those with few systemic manifestations.[5] These findings are consistent with our results that no significant differences were found in the clinical courses of patients with definite, probable, and suspected iBD.

The diagnostic algorithm was developed because the diagnosis of iBD using the previous criteria was not easy due to systemic symptoms emerging at different times during the disease course.[6] Likewise in our study, a total of three patients with probable or suspected iBD were assigned to higher diagnostic categories due to the development of extraintestinal manifestations during the follow-up period. However, none of the patients with nondiagnostic iBD were diagnosed with definite, probable, or suspected iBD during the follow-up period, indicating again that the three categories were distinguished as a single disease entity from nondiagnostic iBD.

The disease course of iBD is frequently unpredictable with relapse and remission and related to adverse outcomes including significant morbidity and mortality. According to a Korean nationwide population-based study,[11] the cumulative rates of surgery and hospitalization at 1 and 4 years after diagnosis were 11% and 32%, respectively. In our study, the rates surgery and hospitalization of for patients with definite, probable, and suspected iBD at 1 and 4 years was 7.3% and 22.6%, respectively. Anti-tumor necrosis factor agents are proven to be effective for inducing and maintaining the clinical remission of iBD,[12-14] and proactive management of patients with higher risk in the early stage may decrease disease-specific morbidity and mortality.[7] Thus, the identification of iBD with a higher risk in the early stage is very important.

Previous studies reported that younger age at the time of diagnosis, higher initial disease activity, and the presence of volcano-type ulcers were risk factors for surgery.[15,16] In our study, age under 40 at the time of diagnosis was not associated with a higher risk of major surgery or admission (HR, 0.60; 95% CI, 0.28 to 1.26). The HR of disease activity index for intestinal Behçet's disease score at the time of diagnosis ≥40 was 3.20 (95% CI, 0.76 to 13.41) in the univariate analysis, which was not significant. The presence of typical ulcers was also not associated with the development of adverse events.

Our study showed that anemia, fever, colonic involvement other than the ileocecum, and accompanying hematologic disorders at the time of diagnosis were poor prognostic factors of iBD. It is known that Behçet's disease is associated with hematologic disorders, especially bone marrow failure such as myelodysplastic syndrome or aplastic anemia.[17-19] Patients with Behçet's disease and bone marrow failure showed more frequent intestinal involvement and refractoriness to steroids and immunomodulators[16] and the proportion of trisomy 8 was reported in up to 64%–86% of patients with Behçet's disease and bone marrow failure.[20-22] In our study, accompanying hematologic disorders at the time of diagnosis were associated with a higher risk of major surgery or admission related to iBD (HR, 2.91; 95% CI, 1.18 to 7.13). Of the 118 patients with definite, probable, and suspected iBD, hematologic disorders were present in 20 (16.9%) and there were seven patients with trisomy 8 among the 15 patients with bone marrow failure (46.7%).

This study had some limitations. First, this was a single-center retrospective study based on the review of medical records. However, a relatively large number of patients with iBD were included and followed up for considerable periods. Second, the mean follow-up period of the patients with nondiagnostic iBD was shorter. However, we believe that the follow-up of those patients was stopped by their doctors or patients themselves because of minimal clinical symptoms or a favorable clinical course.

In conclusion, our study demonstrated that the clinical course of patients with definite, probable, and suspected iBD was clearly distinguished from that of the patients with nondiagnostic iBD and the consensus-based diagnostic algorithm could diagnose patients with iBD at the early stage of the disease. Patients with definite, probable, and suspected iBD share similar clinical courses, and active treatments should be considered regardless of their diagnostic subtypes. Anemia, fever, colonic involvement other than the ileocecum, and accompanying hematologic disorders at the time of diagnosis are poor prognostic factors of iBD. Further studies are required to evaluate whether advanced treatment at the early stage can change the clinical course of iBD patients with risk factors.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: B.I.L. Data curation: Y.Y.J. Formal analyses and investigation: Y.Y.J., B.I.L. Resources: S.J.K., H.H.L., J.S.K., J.M.P., Y.S.C., K.M.L., S.W.K., H.C., M.G.C. Supervision: B.I.L., K.M.L., S.W.K., H.C., M.G.C. Writing - original draft: Y.Y.J. Writing - review and editing: B.I.L. All authors read and approved the final manuscript.

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REFERENCES

1. Suzuki Kurokawa M, Suzuki N. Behcet's disease. Clin Exp Med 2004;4:10-20.
2. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. N Engl J Med 1999;341:1284-1291.
3. Hisamatsu T, Ueno F, Matsumoto T, et al. The 2nd edition of consensus statements for the diagnosis and management of intestinal Behçet's disease: indication of anti-TNFα monoclonal antibodies. J Gastroenterol 2014;49:156-162.
4. Kobayashi K, Ueno F, Bito S, et al. Development of consensus statements for the diagnosis and management of intestinal Behçet's disease using a modified Delphi approach. J Gastroenterol 2007;42:737-745.
5. Lee CR, Kim WH, Cho YS, et al. Colonoscopic findings in intestinal Behçet's disease. Inflamm Bowel Dis 2001;7:243-249.
6. Cheon JH, Lee HJ. Optimal diagnosis and disease activity monitoring of intestinal Behcet's disease. Intest Res 2017;15:311-317.
7. Cheon JH, Kim WH. An update on the diagnosis, treatment, and prognosis of intestinal Behçet's disease. Curr Opin Rheumatol 2015;27:24-31.
8. Cheon JH, Han DS, Park JY, et al. Development, validation, and responsiveness of a novel disease activity index for intestinal Behçet's disease. Inflamm Bowel Dis 2011;17:605-613.
9. Kurokawa MS, Yoshikawa H, Suzuki N. Behçet's disease. Semin Respir Crit Care Med 2004;25:557-568.
10. Chang HS, Lee D, Kim JC, et al. Isolated terminal ileal ulcerations in asymptomatic individuals: natural course and clinical significance. Gastrointest Endosc 2010;72:1226-1232.
11. Han M, Jung YS, Kim WH, Cheon JH, Park S. Incidence and clinical outcomes of intestinal Behçet's disease in Korea, 2011-2014: a nationwide population-based study. J Gastroenterol 2017;52:920-928.
12. Naganuma M, Sakuraba A, Hisamatsu T, et al. Efficacy of infliximab for induction and maintenance of remission in intestinal Behçet's disease. Inflamm Bowel Dis 2008;14:1259-1264.
13. Ariyachaipanich A, Berkelhammer C, Nicola H. Intestinal Behçet's disease: maintenance of remission with adalimumab monotherapy. Inflamm Bowel Dis 2009;15:1769-1771.
14. Suzuki Y, Hagiwara T, Kobayashi M, Morita K, Shimamoto T, Hibi T. Is adalimumab safe and effective in patients with intestinal Behcet's disease in real-world practice? Intest Res 2021;19:301-312.
15. Jung YS, Yoon JY, Hong SP, Kim TI, Kim WH, Cheon JH. Influence of age at diagnosis and sex on clinical course and long-term prognosis of intestinal Behcet's disease. Inflamm Bowel Dis 2012;18:1064-1071.
16. Park JJ, Kim WH, Cheon JH. Outcome predictors for intestinal Behçet's disease. Yonsei Med J 2013;54:1084-1090.
17. Ahn JK, Cha HS, Koh EM, et al. Behcet's disease associated with bone marrow failure in Korean patients: clinical characteristics and the association of intestinal ulceration and trisomy 8. Rheumatology (Oxford) 2008;47:1228-1230.
18. Soysal T, Salihoğlu A, Esatoğlu SN, et al. Bone marrow transplantation for Behçet's disease: a case report and systematic review of the literature. Rheumatology (Oxford) 2014;53:1136-1141.
19. Shen Y, Ma HF, Luo D, Cai JF, Zou J, Guan JL. High incidence of gastrointestinal ulceration and cytogenetic aberration of trisomy 8 as typical features of Behçet's disease associated with myelodysplastic syndrome: a series of 16 consecutive Chinese patients from the Shanghai Behçet's disease database and comparison with the literature. Biomed Res Int 2018;2018:8535091.
20. Tada Y, Koarada S, Haruta Y, Mitamura M, Ohta A, Nagasawa K. The association of Behçet's disease with myelodysplastic syndrome in Japan: a review of the literature. Clin Exp Rheumatol 2006;24(5 Suppl 42):S115-S119.
21. Kawabata H, Sawaki T, Kawanami T, et al. Myelodysplastic syndrome complicated with inflammatory intestinal ulcers: significance of trisomy 8. Intern Med 2006;45:1309-1314.
22. Mori Y, Iwamoto F, Ishida Y, et al. Long-term outcome after surgery in a patient with intestinal Behçet's disease complicated by myelodysplastic syndrome and trisomy 8. Intest Res 2020;18:469-475.