〔原著〕 CLINICAL COURSE, COMPLICATIONS, SURGERY
AND PROGNOSIS OF 220 TURKISH PATIENTS
WITH INFLAMMATORY BOWEL DISEASE
BETWEEN 1981 AND 1992

Hasan Özkan, Ahmet Erten, Negüz Sümer,
A. Kadir Dökmeci, Ali Özden, Nihat Sipahi,
Erol Kesim, Necati Örmeci, Kadir Bahar,
Selim Karayalcin, Ali Resit Beyler and Özden Uzunalimoglu

SUMMARY

We analyzed the clinical course, complications, surgery and prognosis of 220 patients with inflammatory bowel disease seen at Medical Faculty Hospital and Ibni Sina Hospital of Ankara University between 1981 and 1992. Of these, 166 had ulcerative colitis and 54 had Crohn's disease. Mean age was 35.8 ± 3.7 years for patients with ulcerative colitis, 36.2 ± 2.7 years for Crohn's disease at the time of onset.

In the patients with ulcerative colitis, the majority of patients (53.6) had leftsided colitis. Complications were highest among patients with pancolitis. Fulminate colitis occurred in 4.2 %. 3 patients had primary sclerosing cholangitis. Surgery was required for 14.4 % of the patients in whom there was poor response to medical treatment. Total colectomy was necessary in only 4 patients. No patient with ulcerative colitis had carcinoma of the colon. During follow-up period, 7 patients died from causes related to ulcerative colitis.

As for the patients with Crohn's disease, the most encountered pattern was predominantly terminal ileal involvement (25.9 %). Surgical resection had been performed in 33.3 % of patients and 27.7 % of these had had two or more resections. No malignancies were found in the patients with Crohn's disease. 6 death occurred (11.1 %), 4 of which related directly to Crohn's disease.

In conclusion, in our series, the spectrum of inflammatory bowel disease concerning the average age at onset and diagnosis, joint symptoms, the frequency of primary sclerosing cholangitis, and progression are somewhat different from those of Western countries and Japan.

Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey.
トルコにおける過去12年間の炎症性腸疾患220例の臨床経過, 合併症, 外科治療および予後に関する検討
アンカラ大学 (トルコ) 消化器科
(平成6年11月18日受付, 平成6年11月28日受理)

I. Introduction

Inflammatory bowel disease (IBD) includes basi-cally two chronic disorder which are ulcerative coli-tis (UC) and Crohn's disease (CD). They may lead to lifelong ill health, often requiring drugs and sometimes surgery. The prognosis of IBD today is very different from over the past years, when many patients died early in the disease course. Early diagnosis, the introduction of safe and effective me-dications and better surgical procedures have altered the clinical course of the disease[1].

IBD is generally believed to be more frequent in Western Europe especially in the UK and in Scan-dinavia[2,3], but to be relatively infrequent in Sou-theastern Europe, such as Greece[4] and Turkey[5]. However, IBD is extremely rare in Asian and in under developed countries[6-8]. In Japan, IBD was reported to be less common than in the West[9].

In this context, the aim of this report is to analyze the clinical course, complications, surgery and prognosis in 220 patients with IBD in Ankara, Turkey and to compare with those reported from other countries.

II. Materials and Methods

Case records of all 220 inpatients and outpatients with IBD treated at Medical Faculty Hospital and Ibni Sina Hospital of Ankara University between 1981 and 1992 were studied. Data before 1990 were obtained retrospectively. Gender, family history, age at the time of onset and at diagnosis, extent of disease at first diagnosis, complications (disease-related and systemic manifestations), treatment, in-dication for surgery were analyzed. The diagnosis of UC and CD confirmed by clinical, radiological, endoscopic, and histologic examinations. Infecti-ous colitis and other forms of IBD were excluded. The complexity of these disorders was obvious, and in another 8 patients, it was impossible to establish a diagnosis of either UC or CD. These patients were classified as having indeterminate colitis.

The standardized diagnostic criteria by Binder[10] for UC and by Gallop and Phillips[11] for CD were adopted in this study. The grading of severity of diseases was measured according to the criteria of Truelove and Witts[12]. Details of the operations and histological findings in operative specimens were obtained from the surgeon concerned.

III. Results

Of total group of 220 patients, 104 were women and 116 were men. Of these, 166 (75 %) had UC and 54 (25 %) had Crohn's disease. The distribu-tion for sex and age of UC and CD patients is shown in Table 1.

Table 1. · Age and sex distribution of UC and CD patients

Age	UC*		CD**	
(years)	Male	Female	Male	Female
10-19	7	10	1	1
20-29	15	20	4	2
30-39	12	22	12	6
40-49	20	17	8	7
50-59	12	6	6	3
60-69	14	6	1	1
≧ 70	3	2	1	1
Total	83	83	33	21

  * UC : Ulcerative colitis
 ** CD : Crohn's diease

Ulcerative colitis

There were 83 men and 83 women patients. At the time of onset, mean age for men was 38.5± 1.6 years. It was 33.1±5.8 years for women. Fif-ty-two patients (31.3 %) were younger than 25 years old. The mean interval of time between onset and diagnosis was 25.4±4.4 months. The majority of patients (68.3 %) belonged to the age group 20-49 years, with the male/female ratio being 1 ∶ 1. The distribution of the disease when first diagnosed was similar in the different population groups.

Twelve patients (7.2 %) had proctitis (disease li-mited to the rectum). There were eighty-nine pati-ents (53.6 %) with left-sided colitis (disease up to the splenic flexure), and sixty-five patients (39.2 %) with pancolitis (colitis of entire large intestine).

The predominant symptoms and common com-

Table 2. The presenting symptoms in patients with UC

Symptoms*	No**	(%)
Bloody diarrhea	135	81
Abdominal pain	124	74
Passage of mucus	83	50
Weight loss	74	44
Fever	12	7.2

* Patients may have more than one symptom
** No : Number of patients

Table 3. Associated features and complications in UC

Previous stress-induced diarrhea	7.2%
Pseudopoliposis	6.6%
Anal fissure	5.0%
Colonic strictuce	3.6%
Overt liver disease	3.0%
Arthralgia/arthritis	1.8%
Family history	1.8%
Sclerosing cholangitis	1.8%
Toxic megacolon	1.2%

Table 4. Indications for surgery in the patients with UC

Indications	No*
Free perforation	6
Colonic stricture	5
Perianal disease	7
Acute Medical failure	3
Bleeding	2
Colonic dilatation	1

* No : Number of patients

plaints at presentation were abdominal pain, weight loss, and diarrhea (Table 2). Regarding severity of symptoms, 51.2 % of patients has mild disease, 27.8 % moderate disease, and 21 % severe disease at presentation. The severity of symptoms at the time of diagnosis was related to the extent of disease.

As for laboratories data, the hematocrit level, erythroryte sedimentation rate (ESR), and albumin level were found as 35.7±3.2 %, 26.4±2.1 mm/hour, and 3.1±0.1 g/dl, respectively. Hemoglobin level was less than 10 gr/dl in 15 patients (9 %).

Associated features and complications are presented in Table 3.

42 patients (25.3 %) were given only sulphasalazine compounds to maintain the remission. 112 patients (67.5 %) received either oral, topical or parental corticosteroids for getting relief in addition to sulfasalazine compounds. There was poor response to medical management in 24 patients (14.4 %) in whom disease-related surgical procedure were performed between the initial diagnosis and the present time. In all the 24 patients with UC, the indications for surgery are shown Table 4. Four patients underwent an ileal-anal pouch operation without ileostomy, two patients underwent right-sided colectomy and other exghteen patients underwent complication-related operation. No malignancies were observed in patient with UC.

During this follow-up period, 7 patients died from causes related to the UC; three patients had an acute fulminating course, 2 toxic magacolon, 2 massive colonic hemorrhage, and 2 patients died from a myocardial infarction.

Crohn's disease

Fifty four patients, 25 % of the total, were classified as having CD. Of these, thirty-three patients were men and twenty-one were women. Mean age for men was 35.4±2.2 years and 37.0±3.2 years for women at the time of onset. The delay between onset of symptoms and diagnosis was 30.6± 7.0 months. 7 patients (13 %) were younger than 25 years old. The majority of patients (61 %) belonged to the age group 20–49 years, with the male/female ratio 11 : 7.

The distribution of disease on first diagnosis was similar in the different population groups. The ileocolic involvement (25.9 %) was the frequently encountered pattern that the impact of the disease was more on the terminal ileum or the ascending colon. The small intestine alone was involved in 9.2 % of the patients and the colon in 22.2 %. The colon and the small intestine together were involved in 24.2 % of patients. One patient had involvement of the duodenum in addition to involvement of the ileum and colon. Perianal-rectal

Table 5.   Presenting symptoms in the
patients with CD

Symptoms*	No**	(%)
Abdominal pain	42	77.0
Diarrhea	28	51.8
Weightloss	21	38.8
Right lower quadrant tenderness	10	18.5
Fever	8	14.8

 * Patients may have more than one symptom
** No : Number of patients

Table 6.   Associated features in CD patients

Previous appendectomy	22.2%
Malabsorbsion	7.4%
Renal stones	7.4%
Behçet's disease	1.8%
Gallstones	1.8%
Urinary bladder stone	1.8%
Ankylosing spondylitis	1.8%

Table 7.   Indications for initial surgery
in the patients with CD

Indications*	No**	(%)
Obstruction	13	24.0
Internal fistulea	7	12.9
Medical failure	6	11.1
Perianal disease	5	9.2
Free perforation	4	7.4
Bleeding	1	1.8

 * Patients may have more than one indication
** No : Number of patients

disease was present in nine patients. The most common symptoms were diarrhea, abdominal pain, rectal bleeding and weight loss (Table 5). At presentation 56.3 % of patients had mild disease, 32.7 % moderate disease, and 11.9 % severe disease. The severity of symptoms at the time of diagnosis was related to the extent of the disease.

The hematocrit level, ESR, and albumin level were found 36.1 ± 1.8 %, 33.4 ± 5.1 mm/hour, 3.3 ± 0.1 g/dl, respectively. Hemoglobin level was less than 10 gr/dl in 6 patients. The majority of patients (72.2 %) received sulphasalazine as maintenance therapy. The remaining patients required steroids or immunosuppressive. During follow-up

period, some of patients were given hyperalimantation. Other associat-d conditions are shown in Table 6.

Eighteen patients (33.3 %) with CD had been performed at least one disease-related surgical procedure between the time of the initial diagnosis of the disease and the present time. 5 of these (28 %) underwent two or more resections. The indications for operation are documented in Table 7. Generally, indications reflected complications that had occurred in the course of the disease. No malignancies were found. During follow-up period 6 patients died; 2 perforated megacolon, 2 from ongoing sepsis, and 2 from unrelated causes.

IV.   Discussion

In Turkey, IBD is uncommon less than in Western Europe despite one of the frequently encountered chronic digestive diseases[5]. It is probably related to current Western diets and lifestyles. The exact incidence of IBD in our country is difficult to determine, mainly because of the decentralized health care system and tendency for referral of more complicated cases to tertiary care centers. Therefore, there have been no reports on the epi demiological characteritics of IBD so far.

The age at onset was 21.1 years, and the age at diagnosis was 23.6 years in CD patients in the study by Tominaga et al[13]. In our series, those were 36.2 ± 2.7 years and 38.8 ± 3.3 years, respectively. However, in the patients with UC, there was slight differences between our study and the study by Farmer et al[14].

According to the results, there was a good correlation between clinical severity of colitis and colonoscopic findings, histology, serum albumin, hemoglobin level, and elevated ESR.

Joint symptoms occurred less frequently in our series. Eleven patients (5 %) with IBD had joint disease in our group. In the study by Wright et al, joints were involved in 30 %[8].

As for the association between primary sclerosing cholangitis (PSC) and UC, the frequency of PSC is about 3 %[15,16]. In our series, 1.8 % of the patients with UC had PSC. On the other hand, there

was no case in CD patients.

There is no longer doubt that an increased risk for colon cancer exists in patients with UC. In one study, more than 25 % of patients who had had disease for more than 25 years developed colorectal carcinoma[17]. However, the risk of a CD patient developing colon carcinoma is lower than the risk in UC patients[18]. In the report by Farmer et al, all patients had chronic UC in whom no cancer was diagnosed within five years of the intial diagnosis of UC[14]. Among our patients with UC, no case was seen having colon cancer and also there was no malignant case in the patients with CD as well. We believe that the follow-up time in this study was not long enough to give figure for the risk of developing carcinoma of colon.

In the study by Nakahara et al, cumulative probability of surgery ten years after onset of symptoms were reported 39.1 % in the patients with CD[19]. It was 33.3 % in the present series. On the other hand, several studies have emphasized the importance of the problem of dealing with recurrence in a patient with CD after ablative surgery. In these series, reoperation rate varied between 18 and 23 %[20]. In our group, 27.7 % of the patients with CD underwent two or more operations related to CD.

An ileal-anal aouch operation without ileostomy had been performed in the majority of patients with UC who sought surgical intergention as a one-time cure of their disease. This type operation had the added advantage of doing away with the ileostomy bag. In addition to this, the quality of life for patients with ileal-anal pouch operation appeared to be as good as that for patients with medically treated colitis.

Early age of diagnosis, persistent joint symptoms, bleeding, toxic colitis, and pancolitis were associated with a poorer prognosis in patients with UC. Further, limited colitis that occurs at a relatively older age carries with it a more benign prognosis, according to our results.

The major long-term concern for patients with CD is that of mortality. In our series, 11.1 % of patients died from all causes (6 out of 54) but 4 (7.4

%) of the deaths were directly related to CD. This percentage is less than that reported by Trnka et al[21]. However, it is almost similar to that observed (9.9 %) in Japanese study[19]. The predominant underlying factors in mortality in CD were sepsis because of an internal fistula and perforated megacolon in our study. 7 out of 166 patients (4.2 %) died from causes related to the UC. This figure is a little higher than that reported previously by O'Keefe et al in which 3 deaths out of 114 patients were disease-related during 11 year-follow up period[22].

Consequently, although there are some differences as discussed above, most of our IBD patients bear a close resemblance to the clinical aspects described from major academic centers of the other Western countries and Japan.

要　旨

1981年から1992年までにアンカラ大学付属病院（トルコ）にて経験された炎症性腸疾患220例の臨床経過，合併症，外科治療および予後について検討した。疾患の内訳は潰瘍性大腸炎166例，クローン病54例で，発症時の平均年齢は潰瘍性大腸炎で35.8±3.7歳，クローン病で36.2±2.7歳であった。

潰瘍性大腸炎の半数以上（53.6%）は左側結腸型であった。合併症は全結腸型で最も多く認められた。急性電撃型は4.2%にみられ，また原発性硬化性胆管炎は3例で認められた。薬物治療にて効果のなかった14.4%に外科的治療を行った。そのうち結腸全摘出術が必要となったのは4例のみであった。大腸癌の合併は1例もなかった。経過観察中7例は合併症が原因で死亡した。

クローン病では病変が回盲部に限局した症例が25.9%と最も多かった。外科的切除は33.3%の症例で行われ，そのうち27.7%は2回以上の切除術が施行された。大腸癌の合併は1例もなかった。4例は経過観察中合併症にて死亡した。

以上より，トルコにおける炎症性腸疾患の平均年齢，関節症状，原発性硬化性胆管炎の頻度および臨床経過は欧米あるいは日本の報告と異なることが明らかとなった。

REFERENECES

1) Langholz E, Munkholm P, Davidsen M and Binder V: Course of ulcerative colitis: Analysis of changes in disease activity over

years. Gastroenterology 107 : 3-11, 1994.

2) Devlin HB, Datta D and Dellipiani AW : The incidence and prevalence of inflammatory bowel disease in North Tees Healt District. World J Surg 4 : 183-193, 1980.

3) Ekbom A, Helmic C, Zack M and Adami HO : The epidemiology of inflammatory bowel disease : A large population-based study in Sweden. Gastroenterology 100 : 350-358, 1991.

4) Tsianos EV, Masalas CN, Merkouropoulos M, Dalekos GN and Logan RFA : Incidence of inflammatory bowel disease in nortwest Greece : rarity of Crohn's disease in an area where ulcerative colitis is common. Gut 35 : 369-372, 1994.

5) Aktan Hamdi : iltihabi barsak hastaligi. Gastroenteroloji. Makro yayincilik, Ankara, pp : 173-191, 1988 (in Turkish)

6) Tan CC, Kang JY, Guan R, Yap I and Tay H : Inflammatory bowel disease : An uncommon problem in Singapore. J. Gastroterol Hepatol 7 : 360-362, 1992.

7) Odes HS, Fraser D, Krugliak P, Fenyves D, Fraser GM and Sperber AD : Inflammatory bowel disease in the Bedouin Arabs of southern Israel : Rarity of diagnosis and clinical features. Gut 32 : 1024-1026, 1991.

8) Wright JP, Marks IN, Jameson C, Garisch JAM, Burns DG and Kottler RE : Inflammatory bowel disease in Cape Town, 1975-matory bowel disease in Cape Town, 1975-1980. S Afr Med J 63 : 223-228, 1983.

9) Higashi A, Watanabe Y, Ozawa T, Hayashi K, Akaike A and Kawai K : Prevalence and mortality of ulcerative colitis and Crohn's disease in Japan. Gastroenterologia Japonica 23 : 521-526, 1988 (in Japanese)

10) Binder V : Incidence and prevalence of ulcerative colitis and Crohn's disease in the county of Copenhagen, 1962 to 1978. Gastroenterology 83 : 563-568, 1982.

11) Gallop JH and Phillips SF : Epidemiologic aspects of Crohn's disease : A population based study in Olmest County, Minnesota, 1943-1982. Gut 29 : 49-56, 1988.

12) Truelove SC and Witts IJ : Cortisone in ulcerative colitis. Report on threpeutic trial.

BMJ 2 : 1041-1048, 1955.

13) Tominaga M : Clinical features of Crohn's disease : relationship of disease type and severity to clinical findings at the time of diagnosis in 166 cases. Fukuokaigaku-Zasshi 83 : 6-20, 1992.

14) Farmer RG, Easley KA and Rankin GB : Clinical patterns, natural history and progression of ulcerative colitis. Dig Dis Sci 38 : 1137-1146, 1993.

15) Hashimoto E, Ideta M, Tanai M, Watanabe U, Okuda H, Nagasako K, Hisamitsu T and Obata H : Prevalence of primary sclerosing chlangitis and other liver disease in Japanese patients with chronic ulcerative colitis. J. Gastroenterol Hepatol 8 : 146-149, 1993.

16) Tobias R, Wright JP, Kottler RE, Bornman PC, Price SK, Hatfield A and Marks IN : Primary sclerosing cholangitis associated with inflammatory bowel disease in Cape Town, 1975-1981. S Afr Med J 63 : 229-235, 1983.

17) Lashner B : Recommondations for colorectal cancer screening ulcerative colitis. Gastroenterology 103 : 431-434, 1992.

18) Munkholm P, Langholz E, Davidsen M. and Binder V : Intestinal cancer risk and mortality in patients with Crohn's disease. Gastroenterology 105 : 1716-1723, 1993.

19) Nakahara Y, Yao T, Sakurai T, Okada M, Iida M, Fuchigami T, Tanaka K, Akasa Y, Sakamoto K, Sata M and Date H : Long-term prognosis of Crohn's disease. Nippon-Shokakibyo-Gakkai-Zasshi 88 : 1305-1312, 1991 (in Japanese)

20) Whelan G, Farmer RG, Fazio VW and Woormastic M : Recurrence after surgery in Crohn's disease. Gastroenterology 88 : 1826-1833, 1985.

21) Trnka YM, Glotzer DJ, Kasdon EJ, Goldman H, Steer ML and Goldman LD : The long-term outcome of restorative operation in Crohn's disease. Ann Surg 196 : 345-354, 1982.

22) O'Keefe EA, Wright JP, Froggatt J, Cuming L and Eliiot M : Medium-term follow-up of ulcerative colitis in Cape Town. S Afr Med J 76 : 142-145, 1989.