

Factors Contributing to the Preference of Korean Patients with Crohn's Disease When Selecting an Anti-Tumor Necrosis Factor Agent (CHOICE Study)

Eun Soo Kim*, Kyeong Ok Kim[†], Byung Ik Jang[‡], Chang Kyun Lee[‡], Hyo Jong Kim[‡], Kang-Moon Lee[§], You Sun Kim^{||}, Chang Soo Eun[¶], Sung-Ae Jung[#], Suk-Kyun Yang^{**}, Jun Lee^{††}, Tae-Oh Kim^{††}, Yunho Jung^{§§}, Geom Seog Seo^{|||}, Soon Man Yoon^{††}, and the IBD Study Group of the Korean Association for the Study of the Intestinal Diseases (KASID)

*Department of Internal Medicine, Keimyung University School of Medicine, [†]Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, [‡]Department of Internal Medicine, Kyung Hee University School of Medicine, Seoul, [§]Department of Internal Medicine, The Catholic University of Korea College of Medicine, Suwon, ^{||}Department of Internal Medicine, Inje University College of Medicine, Seoul, [¶]Department of Internal Medicine, Hanyang University College of Medicine, Guri, [#]Department of Internal Medicine, Ewha Womans University School of Medicine, ^{**}Department of Internal Medicine, University of Ulsan College of Medicine, Seoul, ^{††}Department of Internal Medicine, Chosun University School of Medicine, Gwangju, ^{‡‡}Department of Internal Medicine, Inje University College of Medicine, Busan, ^{§§}Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, ^{|||}Department of Internal Medicine, Wonkwang University School of Medicine, Iksan, and ^{†††}Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Korea

See editorial on page 327.

Background/Aims: Two comparable anti-tumor necrosis factor (TNF) agents with different routes of administration (intravenous [iv] infliximab [IFX] vs subcutaneous [sc] adalimumab [ADA]) are available for patients with Crohn's disease (CD) in Korea. This study aimed to identify the preferences of Korean CD patients for a specific anti-TNF agent and the factors contributing to the decision. **Methods:** A prospective survey was performed among anti-TNF-naive CD patients in 10 tertiary referral hospitals. A 16-item questionnaire addressed patient preferences and the factors contributing to the decision in favor of a particular anti-TNF agent. A logistic regression was conducted to assess predictive factors for ADA preference. **Results:** Overall, 189 patients (139 males; mean age, 32.47±11.71 years) completed the questionnaire. IFX and ADA were preferred by 63.5% (120/189) and 36.5% (69/189) of patients, respectively. The most influential reason for choosing IFX was 'doctor's presence' (68.3%, 82/120), and ADA was "easy to use" (34.8%, 24/69). Amid various clinicodemographic data, having a >60-minute travel time to the hospital was a significant independent predictive factor for ADA preference. **Conclusions:** A large number of anti-TNF-naive Korean patients with CD preferred anti-TNFs with an iv route of administration. The reassuring effect of a

doctor's presence might be the main contributing factor for this decision. (*Gut Liver* 2016;10:391-398)

Key Words: Crohn disease; Infliximab; Adalimumab; Preference

INTRODUCTION

Crohn's disease (CD) is characterized by longstanding inflammation in the gastrointestinal tract and often requires life-long medical treatment.¹ Although the exact etiology of the disease has not been fully clarified, tumor necrosis factor (TNF) has been regarded as one of the main pathophysiological mediators involving retractable mucosal inflammation of the gut.² Finally, several anti-TNF agents have been approved for CD treatment in Western countries: adalimumab (ADA), infliximab (IFX), and certolizumab pegol. These drugs are currently regarded as the most effective treatments to achieve sustained clinical remission and mucosal healing.³⁻⁵

Although CD had been considered remarkably rare in Asian countries (including Korea) compared with Western countries, its incidence and prevalence have been soaring recently in the region. Population-based Korean data indicates that the mean annual incidence rates of CD and ulcerative colitis increased from 0.05 and 0.34 per 100,000 persons in 1986–1990 to 1.34 and 3.08 per 100,000 in 2001–2005, respectively.⁶ Accordingly,

Correspondence to: Kang-Moon Lee

Department of Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea College of Medicine, 93 Jungbu-daero, Paldal-gu, Suwon 442-723, Korea

Tel: +82-31-249-8151, Fax: +82-31-253-8898, E-mail: drmaloman@catholic.ac.kr

Received on March 11, 2015. Revised on May 3, 2015. Accepted on May 3, 2015. Published online September 9, 2015

pISSN 1976-2283 eISSN 2005-1212 <http://dx.doi.org/10.5009/gnl15126>

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

anti-TNF agents have been increasingly used since they were approved for CD treatment in the mid-2000s in Korea; IFX was the first anti-TNF (approved in 2005) followed by ADA (2010).⁷⁻⁹

Until now, the use of only two types of biologics (ADA and IFX) is reimbursed for CD treatment by the Korean National Insurance Service.¹⁰ The mode (subcutaneous [sc] vs intravenous [iv]) and interval of administration (2 weeks vs 2 months) are the primary differences. Large clinical trials comparing these two agents found similar efficacy in induction and maintenance of remission for patients with moderate to severe CD.¹¹⁻¹⁴ Adverse effects of these drugs are also comparable.

Rigorous patient involvement in decision making has emerged as an important issue in the management of chronic diseases because patients with more active roles in decisions for their care may be more satisfied and may have better clinical outcomes.¹⁵⁻¹⁷ Most inflammatory bowel disease (IBD) patients think that active involvement in the decision making process is "very important."¹⁸ In fact, there are many issues that are appropriate for shared decision making during IBD treatment (i.e., for selection among various anti-TNFs).¹⁹ A recent study demonstrated that patients with CD living in Switzerland preferred an anti-TNF agent with a sc mode of administration mainly due to its convenience for use.²⁰ This preference for a sc administration mode of anti-TNFs was also found in patients with rheumatoid arthritis (RA) from Western countries.^{21,22} These patients preferred to receive treatment at home.²² However, no study has been conducted to address this issue for Asian patients with CD. Historically, there has been a long list of differences between the East and West.²³ The East Asian culture is likely to be interdependent, whereas the Western culture is more independent.²⁴ Additionally, it has been reported that there are racial disparities in treatment preferences for patients with RA.^{25,26} Considering these substantial cultural and ethnical differences, it is clinically relevant to evaluate the preferences concerning anti-TNFs in Asian patients with CD. Therefore, we determined the preferences for anti-TNF agents (ADA and IFX) and identified the contributing factors for this preference in Korean patients with CD.

MATERIALS AND METHODS

1. Study design and patients

This was a cross-sectional, multicenter study using a questionnaire survey conducted by the IBD Study Group of the Korean Association for the Study of the Intestinal Diseases (KASID) and was conducted between Jan 2014 and May 2014. Ten tertiary referral hospitals in South Korea participated in the study. CD patients over 18 years old that had received treatment for at least 6 months were eligible for inclusion. CD was diagnosed based on a detailed history, physical examination, endoscopic findings, histology, radiological findings, and laboratory investigations.²⁷ We excluded patients who had previously received

an anti-TNF or who had previously been regularly treated with self-administered sc injection therapies, such as insulin or heparin. Patients who were admitted to the hospital, were in critical condition where anti-TNF therapy was really necessary, or were not able to read the questionnaires were also excluded from the study. During the outpatient visit, all eligible participants were provided the questionnaire to determine their preference, if they needed anti-TNF therapy in the future, after reading a brief description on both anti-TNF agents (ADA and IFX). The description of the drugs included the mode; time, place, and interval of administration; cost; approval date in Korea; efficacy; and adverse effects (Appendix 1). Informed consent was obtained from each participant, and this study was approved by the ethics review committee of the Institutional Review Board of all hospitals.

2. Questionnaires

The questions consisted of seven items, which could be completed by the patients within 10 minutes. First, the patients were asked about their knowledge of each anti-TNF agent and the source of information (if any). After reading the short description of the two anti-TNFs, their preference and reasons contributing to the choice of a specific drug over the other were evaluated. The answer lists of reasons in questionnaire were "easy to use," "self-care," "dislike of needles," "frequency of administration," "time of administration," "place of administration," "doctor's presence," "interference with everyday life," and "cost." We asked the patients to select all of the reasons they regarded as important for their decision (multiple answers). Then, the next question asked patients to choose a single best answer, which was considered the most essential reason for their preference. We also assessed the patients' options for the ideal conditions of anti-TNF, such as administration mode (iv vs sc), place (patient's home vs hospital), frequency (2 weeks vs 2 months), and person who administered the drugs (myself or family member vs health care personnel), regardless of the specific anti-TNF agents (IFX or ADA). The patient's decision could have been influenced by the order in which the anti-TNF agents appeared in the questionnaire or description. To avoid this potential bias, we provided two types of questionnaires and descriptions according to the order of appearance of the anti-TNF agents. One questionnaire and information presented IFX first, while the others presented ADA first. The patients were randomly provided each type of survey (IFX first questionnaire and description or ADA first ones).

3. Statistical analysis

The variables for factors associated with the choice of a specific drug were age, sex, marriage, level of education, occupation, time taken to the hospital, disease duration, disease location, disease behavior, medication for CD, smoking history, and surgical history. A logistic regression analysis was conducted

to determine the independent predictive factors of ADA choice. For comparisons of categorical variables between groups, chi-square or Fisher exact test were used. Differences in continuous

variables were examined by a Student t-test, and the results were presented as means±standard deviations.

Table 1. Baseline Characteristics of Anti-Tumor Necrosis Factor Agent-Naive Patients with Crohn's Disease

Characteristic	Value
No. of patients	189
Age, yr	32.47±11.71
Age at diagnosis, yr	28.59±11.39
A1: ≤16 yr old	11 (5.8)
A2: 17–40 yr old	148 (78.3)
A3: >40 yr old	30 (15.9)
Sex, male:female	139:50
Follow-up duration, yr	3.94±3.89
Occupation	
Currently employed	156 (82.5)
Jobs in charge	31 (16.4)
No limit for leave	42 (22.2)
Marriage	70 (37.0)
Active smoker	22 (11.6)
Education degree, ≥university or college	113 (59.8)
CD location	
L1: ileum	57 (30.2)
L1+L4: ileum+upper GIT	6 (3.2)
L2: colon	19 (10.1)
L2+L4: colon+upper GIT	1 (0.5)
L3: ileocolonic	96 (50.8)
L3+L4: ileocolonic+upper GIT	10 (5.3)
CD behavior	
B1: nonstricturing, nonpenetrating	114 (60.3)
B2: stricturing	46 (24.3)
B3: penetrating	29 (15.3)
Perianal disease	73 (38.6)
CDAI score (range)	90.5±67.1 (12 to 358)
CD related surgery	66 (34.9)
Medication	
5-ASA	184 (97.4)
Azathioprine/6-MP	166 (87.8)
Exposure to corticosteroid	107 (56.6)
Previous knowledge of anti-TNFs	105 (55.6)
ADA	60 (31.7)
IFX	87 (46.0)
Both	47 (24.9)
Could not remember which one	5 (2.6)

Data are presented as mean±SD or number (%).

GIT, gastrointestinal tract; CDAI, Crohn's disease activity index; CD, Crohn's disease; ASA, aminosalicic acid; MP, mercaptopurine; TNF, tumor necrosis factor; ADA, adalimumab; IFX, infliximab.

RESULTS

Overall, 189 anti-TNF naive patients with CD were included in the study (male, 139 [73.5%]; mean age, 32.47±11.71 years). The mean age at diagnosis and follow-up duration were 28.59±11.39 years and 3.94±3.89 years, respectively. Most patients had a college education (59.8%). At the time of the survey, 17.5% of patients were unemployed. L3 (ileocolonic) was the most common location of CD followed by L1 (ileum). B1 (nonstricturing, nonpenetrating) was the most common CD behavior. The mean Crohn's disease activity index (CDAI) score was 90.5±67.1. Most patients were taking 5-ASA (184, 97.4%) and azathioprine (166, 87.8%). In total, 107 patients (56.6%) had previously taken corticosteroids. None had previously taken methotrexate or cyclosporine. More than half of the patients (105, 55.6%) had heard of anti-TNF agents before participating in the survey (60 patients [31.7%] had heard of ADA, 87 [46%] had heard of IFX, and 47 [24.9%] had heard of both). Five patients could not remember which one, although they were sure that they had received information on anti-TNFs. The source of information was primarily from doctors (64/105, 60.9%) followed by internet sites (46/105, 43.8%) and other patients (14/105, 13.3%) (Supplementary Fig. 1). The baseline characteristics of the patients are described in Table 1.

1. Choice of anti-TNF agent and contributing factors

IFX was chosen by 120 patients (63.5%), and ADA was chosen by 69 patients (36.5%) (Fig. 1). When asked with multiple choices, the patients attributed "doctor's presence" (90/189, 47.6%) as the most common reason followed by "place of administration" (65/189, 34.4%) and "easy to use" (60/189, 31.7%) (Fig. 2A). For the single best answer, patients who favored IFX

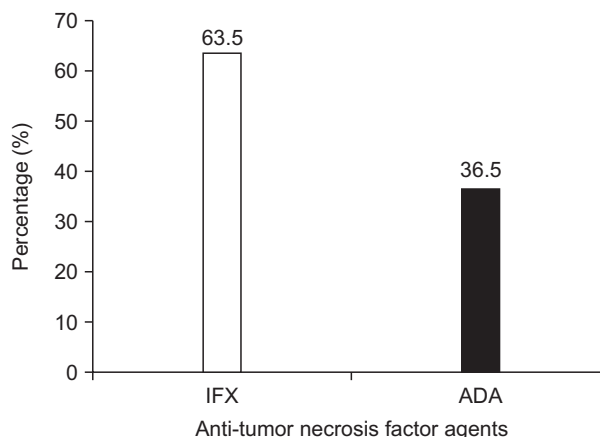


Fig. 1. Anti-tumor necrosis factor-naive patient choices for specific medicines. ADA, adalimumab; IFX, infliximab.

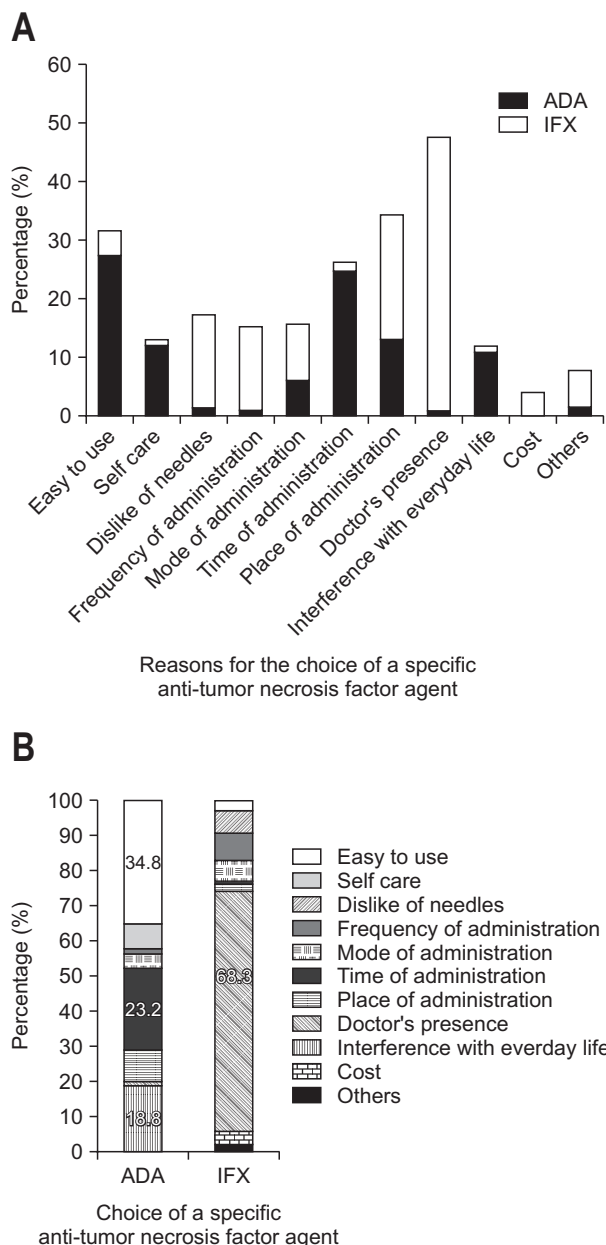


Fig. 2. Answer lists of reasons influencing the decision of a patient for a specific anti-tumor necrosis factor agent. (A) Multichoice answers. (B) Single best answers. ADA, adalimumab; IFX, infliximab.

considered “doctor’s presence” as the most important factor. Patients who selected ADA considered “easy to use” as the most crucial contributing factor followed by “mode of administration” and “interference with everyday life” (Fig. 2B).

2. Predictive factors for the preference of ADA

A univariate analysis indicated that currently employed or students (89.9% vs 78.3%, $p=0.048$); disease duration >5 years (37.7% vs 23.3%, $p=0.036$); and time taken to a hospital >60 minutes (46.4% vs 28.3%, $p=0.012$) were significantly associated with ADA preference over IFX (Table 2). Patients who were

exposed to corticosteroid treatment (65.2% vs 51.7%, $p=0.07$) and had previous knowledge of ADA (13% vs 3.3%, $p=0.054$) were more likely to choose ADA rather than IFX although there was no statistical significance. In a multivariate analysis, time taken to a hospital >60 minutes was found to be the single independent predictive factor for ADA preference (odds ratio [OR], 1.995; 95% confidence interval [CI], 1.057 to 3.764; $p=0.033$) (Table 3). However, age, sex, marital status, education level, smoking, and the clinical characteristics of the patients were not different between the ADA and IFX group.

3. Conditions for ideal medicine

The next question asked patients to choose their ideal medicine based on four aspects (mode, frequency, place, and person who administers) without considering the specific anti-TNF (IFX or ADA). More patients favored an iv mode of administration compared to sc (55.1% vs 44.9%). Not surprisingly, most patients (93.1%) preferred less frequent administration (every 2 months), and this was true even for patients who had selected ADA (30.5% for 2 months vs 6.4% for 2 weeks). Interestingly, more patients wanted to have their medicine administered by health care personnel than by a family member or themselves (79.3% vs 20.7%) and at a hospital rather than at home (70.2% vs 29.8%) (Fig. 3).

DISCUSSION

The results of this cross-sectional study using a questionnaire-based survey demonstrated that anti-TNF naive Korean patients with CD were more likely to favor an anti-TNF with an iv route of administration rather than a sc mode of administration (63.5% vs 36.5%). “Doctors’ presence during administration” was a dominant reason for choosing IFX. “Easy to use” was an important factor for selecting ADA. Among various clinico-demographic factors, a longer time taken to the hospital was significantly associated with the choice of ADA. In addition, more patients chose an iv mode, longer intervals, hospital as the place of administration, and doctors/nurses as the person who administers the medicine as the optimal conditions of an ideal anti-TNF. To the best of our knowledge, this is the first study to investigate the preference of patients with CD for anti-TNFs in Asia.

Interestingly, the results of this study (preference of iv mode compared to sc) completely contrasted the results of several recent Western studies. Western anti-TNF naive patients with RA or CD preferred a sc mode of anti-TNF agent over one with an iv route (51%–52.5% vs 17.5%–25%).²⁰⁻²² Although a sc mode in these Western studies included etanercept or certolizumab pegol, the patients who favored ADA still outnumbered those who chose IFX (36%–47% vs 17.5%–25%).^{20,21} Even though the cause for the disparity between the present study and Western studies is unclear, the substantial cultural difference between

Table 2. Univariate Analysis of Predictive Factors for Preference toward Adalimumab

Variable	ADA (n=69)	IFX (n=120)	p-value
Age	32.0±9.7	32.7±12.8	0.705
Male	55 (79.7)	84 (70.0)	0.145
Marriage	25 (36.2)	45 (37.5)	0.862
Education degree, ≥university or college	44 (63.8)	69 (57.5)	0.397
Currently employed or students	62 (89.9)	94 (78.3)	0.048*
Active smoker	7 (10.1)	15 (12.5)	0.811
Time to a hospital, >60 min	32 (46.4)	34 (28.3)	0.012*
Disease duration, >5 yr	26 (37.7)	28 (23.3)	0.036*
Disease location			0.405
Ileum	20 (29.0)	37 (30.8)	
Ileum+upper GIT	1 (1.4)	5 (4.2)	
Colon	4 (5.8)	15 (12.5)	
Colon+upper GIT	0	1 (0.8)	
Ileocolonic	39 (56.5)	57 (47.5)	
Ileocolonic+upper GIT	5 (7.2)	5 (4.2)	
Disease behavior			0.819
Nonstricturing nonpenetrating	43 (62.3)	71 (59.2)	
Stricturing	15 (21.7)	31 (25.8)	
Penetrating	11 (15.9)	18 (15.0)	
Perianal disease	22 (31.9)	51 (42.5)	0.149
CDAI score	90.2±64.1	90.7±69.1	0.963
Medications			
5-ASA	68 (98.6)	116 (96.7)	0.654
Azathioprine/6-MP	60 (87.0)	106 (88.3)	0.819
Exposure to corticosteroids	45 (65.2)	62 (51.7)	0.071
Previous knowledge of anti-TNFs			0.054
ADA	9 (13.0)	4 (3.3)	
IFX	10 (14.5)	30 (25.0)	
Both	16 (23.2)	31 (25.8)	
Yes, but could not remember	1 (1.4)	4 (3.3)	
None	33 (47.8)	51 (42.5)	
CD related surgery	37 (53.6)	77 (64.2)	0.154

Data are presented as mean±SD or number (%).

ADA, adalimumab; IFX, infliximab; GIT, gastrointestinal tract; CDAI, Crohn's disease activity index; ASA, aminosalicic acid; MP, mercaptopurine; TNF, tumor necrosis factor; CD, Crohn's disease.

*Variables with p<0.05 which were included for multivariate analysis.

Table 3. Multivariate Analysis of Predictive Factors for Preference toward Adalimumab

Variable	OR	95% CI	p-value
Currently employed or students	2.468	0.992–6.143	0.052
Disease duration, >5 yr	1.854	0.949–3.620	0.071
Time to a hospital, >60 min	1.995	1.057–3.764	0.033

OR, odds ratio; CI, confidence interval.

Asia and the West might be the probable explanation. The East Asian culture is known to be more interdependent, while the Western culture is recognized to be more independent.^{24,28} Kitayama *et al.*²⁸ noted that this cultural difference can also be linked to well-being and health in the United States and Japan. Americans regarded “personal control” (independence) as a more reliable and significant predictor of the well-being and health compared to Japanese. Scales of interdependence, which are strongly valued by Japanese, includes “seeking of

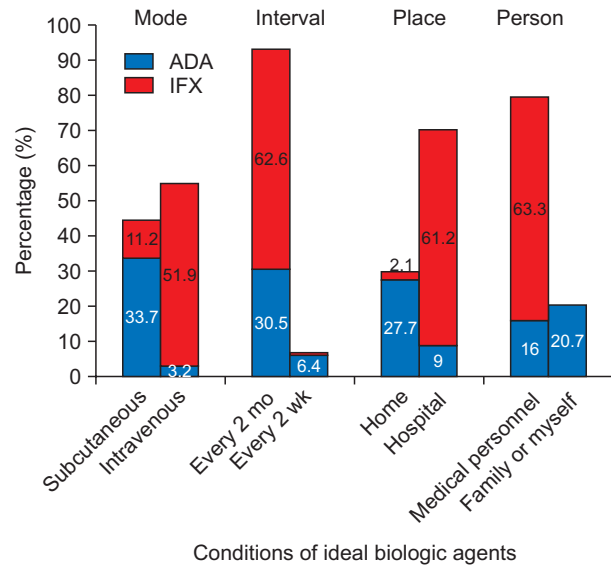


Fig. 3. Conditions that Crohn's disease patients think are ideal for future biologics with respect to the administration mode, interval, place and person. ADA, adalimumab; IFX, infliximab.

other's advice" and "related to others."²⁹ In this context, a sc mode of anti-TNF administration appears to be more suited for the Western culture, and the iv mode of anti-TNF administration is more suited for the Eastern culture. Indeed, patients who chose a sc delivered anti-TNF appeared to be more independent because they considered "convenience of self-administration" and "treatment at home" as important factors that determined their choice of therapy.²⁰⁻²² Meanwhile, patients who preferred an iv administration route appeared to be more reliant because they regarded "contact with other patients" and "staff available if problems arose" as crucial factors influencing their treatment choice.²¹ These findings are consistent with the results of the present study demonstrating that "easy to use" and "interference with everyday life" were important factors for choosing ADA, and a "doctor's presence" was main factor for selecting IFX. Therefore, the cultural background of patients should be considered when establishing a strategy of anti-TNF treatment.

Another notable finding of the present study was that a logistic challenge to the hospital was the single independent predictive factor for choice of ADA (OR, 1.995; 95% CI, 1.057 to 3.764; $p=0.033$) among the various clinical and sociodemographic characteristics, which has never been explored before. This result is understandable considering the beneficial aspects of ADA, such as no need to travel to the hospital. Although we also investigated whether there were differences according to a means of transportation to the hospital (such as one's own car, bus, subway, train, or walking), we did not find any between the ADA and IFX (data not shown) groups.

Given that most promising new biologics waiting for approval in the management of IBD are designed to be administered parenterally or subcutaneously with variable intervals,^{30,31} which

might influence a patient's preference, it is crucial to elucidate the optimal conditions of administration for ideal biologics for IBD patients. More participants in the present study selected an anti-TNF that was administered via an "iv route" by "health care providers" at "a hospital", with "longer intervals" as the ideal drug for their treatment. We assumed that this finding might also be attributed to Asian cultural contexts, which are characterized by more interdependence. In contrast, the majority of Western patients with RA would rather receive treatment at home indicating the influence from Western cultural circumstances (independent).²² The drug manufacturing industry for biologic therapies should understand different patients' preferences for specific types of new drugs based on diverse cultural backgrounds.

More patients are engaged in the decision process of treatment in this digital age where patients become more educated and more sophisticated researchers on the benefits and risks of their therapy.^{15,19,32} In particular, there is a lot of room for patient involvement during IBD treatment due to the uncertainty of the evidence regarding many clinical questions and the heterogeneity of the disease course.¹⁹ Because shared decision making with a patient is key to improved clinical outcomes resulting from a better adherence to the therapy,¹⁷ doctors should discuss the therapy with the patients before prescribing a particular therapy. We believe that our results can facilitate individual decisions for specific anti-TNFs for Asian patients with CD.

There are limitations to the present study. Because this study was only conducted in Korea, it is difficult to generalize and extrapolate the results to other Asian countries. Because there were variable costs and accessibility regarding outpatient-based intravenous administration in each hospital, we could not exclude the potential influence of this aspect on the patients' preferences. Finally, as IFX was approved earlier than ADA in Korea (2005 vs 2010), patients might be more familiar with IFX. This awareness might have affected patients' preference to this anti-TNF. More researches investigating the preference of anti-TNFs in other Asian countries are needed to confirm the results of the present study.

In conclusion, a large number of anti-TNF naive Korean patients with CD preferred anti-TNFs delivered via iv (over sc), and the reassuring effect of a doctor's presence might be the primary contributing factor for this decision. Logistical challenges, such as length of time to the hospital, were significantly related to the choice of a sc mode of anti-TNF administration. The treatment choice should be discussed with patients because individual preferences are determined by diverse factors.

CONFLICTS OF INTEREST

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

REFERENCES

1. Vermeire S, van Assche G, Rutgeerts P. Review article: altering the natural history of Crohn's disease: evidence for and against current therapies. *Aliment Pharmacol Ther* 2007;25:3-12.
2. Reinecker HC, Steffen M, Witthoef T, et al. Enhanced secretion of tumour necrosis factor-alpha, IL-6, and IL-1 beta by isolated lamina propria mononuclear cells from patients with ulcerative colitis and Crohn's disease. *Clin Exp Immunol* 1993;94:174-181.
3. van Assche G, Vermeire S, Rutgeerts P. Mucosal healing and anti TNFs in IBD. *Curr Drug Targets* 2010;11:227-233.
4. Chang CW, Wei SC, Chou JW, et al. Safety and efficacy of adalimumab for patients with moderate to severe Crohn's disease: the Taiwan society of inflammatory bowel disease (TSIBS) study. *Intest Res* 2014;12:287-292.
5. Kim NH, Jung YS, Moon CM, et al. Long-term clinical outcomes of Korean patient with Crohn's disease following early use of infliximab. *Intest Res* 2014;12:281-286.
6. Yang SK, Yun S, Kim JH, et al. Epidemiology of inflammatory bowel disease in the Songpa-Kangdong district, Seoul, Korea, 1986-2005: a KASID study. *Inflamm Bowel Dis* 2008;14:542-549.
7. Lee KM, Jeon YT, Cho JY, et al. Efficacy, safety, and predictors of response to infliximab therapy for ulcerative colitis: a Korean multicenter retrospective study. *J Gastroenterol Hepatol* 2013;28:1829-1833.
8. Ye BD, Yang SK, Shin SJ, et al. Guidelines for the management of Crohn's disease. *Korean J Gastroenterol* 2012;59:141-179.
9. Choi CH, Kim YH, Kim YS, et al. Guidelines for the management of ulcerative colitis. *Korean J Gastroenterol* 2012;59:118-140.
10. Lee KM, Lee JM. Crohn's disease in Korea: past, present, and future. *Korean J Intern Med* 2014;29:558-570.
11. Rutgeerts P, D'Haens G, Targan S, et al. Efficacy and safety of retreatment with anti-tumor necrosis factor antibody (infliximab) to maintain remission in Crohn's disease. *Gastroenterology* 1999;117:761-769.
12. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. *Lancet* 2002;359:1541-1549.
13. Hanauer SB, Sandborn WJ, Rutgeerts P, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. *Gastroenterology* 2006;130:323-333.
14. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. *Gastroenterology* 2007;132:52-65.
15. Guadagnoli E, Ward P. Patient participation in decision-making. *Soc Sci Med* 1998;47:329-339.
16. Silliman RA, Dukes KA, Sullivan LM, Kaplan SH. Breast cancer care in older women: sources of information, social support, and emotional health outcomes. *Cancer* 1998;83:706-711.
17. van den Bemt BJ, van Lankveld WG. How can we improve adherence to therapy by patients with rheumatoid arthritis? *Nat Clin Pract Rheumatol* 2007;3:681.
18. Baars JE, Markus T, Kuipers EJ, van der Woude CJ. Patients' preferences regarding shared decision-making in the treatment of inflammatory bowel disease: results from a patient-empowerment study. *Digestion* 2010;81:113-119.
19. Siegel CA. Shared decision making in inflammatory bowel disease: helping patients understand the tradeoffs between treatment options. *Gut* 2012;61:459-465.
20. Vavricka SR, Bentele N, Scharl M, et al. Systematic assessment of factors influencing preferences of Crohn's disease patients in selecting an anti-tumor necrosis factor agent (CHOOSE TNF TRIAL). *Inflamm Bowel Dis* 2012;18:1523-1530.
21. Chilton F, Collett RA. Treatment choices, preferences and decision-making by patients with rheumatoid arthritis. *Musculoskeletal Care* 2008;6:1-14.
22. Williams EL, Edwards CJ. Patient preferences in choosing anti-TNF therapies-R1. *Rheumatology (Oxford)* 2006;45:1575-1576.
23. Nisbett RE, Peng K, Choi I, Norenzayan A. Culture and systems of thought: holistic versus analytic cognition. *Psychol Rev* 2001;108:291-310.
24. Talhelm T, Zhang X, Oishi S, et al. Large-scale psychological differences within China explained by rice versus wheat agriculture. *Science* 2014;344:603-608.
25. Constantinescu F, Goucher S, Weinstein A, Fraenkel L. Racial disparities in treatment preferences for rheumatoid arthritis. *Med Care* 2009;47:350-355.
26. Constantinescu F, Goucher S, Weinstein A, Smith W, Fraenkel L. Understanding why rheumatoid arthritis patient treatment preferences differ by race. *Arthritis Rheum* 2009;61:413-418.
27. Ye BD, Jang BI, Jeon YT, et al. Diagnostic guideline of Crohn's disease. *Korean J Gastroenterol* 2009;53:161-176.
28. Kitayama S, Karasawa M, Curhan KB, Ryff CD, Markus HR. Independence and interdependence predict health and wellbeing: divergent patterns in the United States and Japan. *Front Psychol* 2010;1:163.
29. Oyserman D, Coon HM, Kimmelmeier M. Rethinking individualism and collectivism: evaluation of theoretical assumptions and meta-analyses. *Psychol Bull* 2002;128:3-72.
30. Scharl M, Vavricka SR, Rogler G. Review: new anti-cytokines for IBD. What is in the pipeline? *Curr Drug Targets* 2013;14:1405-1420.
31. Lobatón T, Vermeire S, Van Assche G, Rutgeerts P. Review article: anti-adhesion therapies for inflammatory bowel disease. *Aliment Pharmacol Ther* 2014;39:579-594.
32. Street RL Jr, Voigt B. Patient participation in deciding breast cancer treatment and subsequent quality of life. *Med Decis Making* 1997;17:298-306.