http://emj.ewhamed.ac.kr

eISSN 2234-2591

EMJ

THE EWHA MEDICAL JOURNAL

April 2022
Vol. 45, No. 2

Ewha Womans University College of Medicine

THE EWHA MEDICAL JOURNAL

Vol.45, No.2, April 2022 (p. 29-54)

Ewha Womans University College of Medicine

EMJ
THE EWHA MEDICAL JOURNAL

eISSN 2234-2591

Aims & Scope

The Ewha Medical Journal (Ewha Med J, http://emj.ewhamed.ac.kr), the official publication of Ewha Womans University College of Medicine and Ewha Medical Research Institute, is published quarterly a year, last day of January, April, July, and October. The first volume was published in March, 1978. It covers all fields of medical science including clinical research and basic medical science. The Journal aims to communicate new medical information between medical personnel and to help development of medicine and propagation of medical knowledges. All manuscripts should be creative, informative and helpful for diagnosis and treatment of the medical diseases and for communication of valuable information about all fields of medicine. Subscripted manuscripts should be written out according to the instructions for the Journal. Topics include original article, case report, images and solution, letter to the editor, invited review article and special issue in the respective field of medicine. The Ewha Medical Journal is indexed/tracked/covered by KoreaMed, KoMCI, KoreaMed Synapse, WPRIM, DOI/CrossRef, EMBASE and Google Scholar.

Copyright & Permissions

The Ewha Medical Journal
Vol. 45 No. 2, April 2022

Publisher Eunhee Ha
Editor-in-Chief Ryung-Ah Lee

Published by Ewha Womans University College of Medicine and Ewha Medical Research Institute
25, Magokdong-ro 2-gil, Gangseo-gu, Seoul 07804, Korea
Tel: 82-2-6986-6013, E-mail: mediewha@ewha.ac.kr, Homepage: http://www.ewhamed.ac.kr

Editorial office Ewha Medical Research Institute
25, Magokdong-ro 2-gil, Gangseo-gu, Seoul 07804, Korea
Tel: 82-2-6986-6092, E-mail: E600091@ewha.ac.kr, Homepage: http://emj.ewhamed.ac.kr

Printing correspondence by Guhmok Publishing Co./Guhmok Info Inc.
#609, Jungang-Deco Plaza, 148, Eulgiro, Jung-gu, Seoul 04549, Korea
Tel: 82-2-2277-3324, Fax: 82-2-2277-3390, E-mail: guhmok@guhmok.com, Homepage: http://www.guhmok.com

· The subscription is free but cost for shipping and handling is charged. The annual shipping and handling rates are 100 US dollars. For inquiry, please contact the editorial office (Tel. 82-2-6986-6054, e-mail E600091@ewha.ac.kr). All the contents are also available at the EMJ website (http://emj.ewhamed.ac.kr).

Editorial Board

EMJ
THE EWHA MEDICAL JOURNAL

eISSN 2234-2591
Vol. 45 No. 2 April 2022

Review Article

Original Articles

EMJ THE EWHA MEDICAL JOURNAL

Review Article

Ewha Med J 2022;45(2):29-34
https://doi.org/10.12771/emj.2022.45.2.29
eISSN 2234-2591

Prevention and Management of Small-for-Size Syndrome of Liver Transplantation

Nam-Joon Yi

Department of Surgery, Seoul National University College of Medicine, Seoul, Korea

Small-for-size syndrome (SFSS) is a critical complication of partial liver transplantation, particularly in adult-to-adult living donor liver transplantation (ALDLT) using a small graft. Minimally required liver graft size for a successful ALDLT is classically 40% of a standard recipient's liver volume or 0.8% of recipient body weight. Recent progress in perioperative care and technical improvement push the lower limit of safe graft size to 25% of the recipient's standard liver volume or 0.6% of the graft versus recipient weight ratio although this is an ongoing debate. The clinical manifestations of SFSS include various symptoms and signs related to graft dysfunction and portal hypertension in patients with small grafts. The risk factors for SFSS include poor preoperative patient condition, including portal pressure, surgical techniques to reduce portal pressure, and graft quality and size. Hence, various approaches have been explored to modulate inflow and pressure to a small graft and to decrease the outflow block to alleviate this SFSS as well as the selection of a patient and graft. Additionally, recent research and efforts to prevent and treat SFSS are reviewed. **(Ewha Med J 2022;45(2):29-34)**

Received February 28, 2022
Revised April 14, 2022
Accepted April 14, 2022

Corresponding author
Nam-Joon Yi
Department of Surgery, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: 82-2-2072-2318, Fax: 82-2-766-3975
E-mail: gsleenj@snu.ac.kr

Key Words
Graft failure; Graft versus recipient weight ratio; Living donor liver transplantation; Small-for-size syndrome

Introduction

Liver transplantation (LT) is a definite and ultimate treatment alternative for end-stage and metabolic liver diseases [1-3]. Donor shortages push the boundaries of marginal donors in deceased donor liver transplantation and living donors worldwide. In living donor liver transplantation (LDLT), the safety of both recipients and donors is in line [4].

Definitions of Small for Size Syndrome

Small-for-size syndrome (SFSS) is a critical complication of LT using a partial graft, particularly in cases of adult-to-adult ALDLT using a small graft (Fig. 1). In general, small-for-size graft (SFSG) corresponds to a graft weight <0.8% of recipient weight or a graft volume <40% of recipient's standard liver volume (SLV) [5-8]. Recent progress in perioperative care and technical improvement in partial LT, minimally required liver graft volume for successful transplantation is an ongoing debate and has decreased to 0.6% graft versus recipient weight ratio (GRWR) (approximately 25% of the recipient's SLV).

The definition of SFSS varies among transplant centers. Persistent portal hypertension and hyperperfusion after SFSG transplantation have been identified as the main factors in this clinical syndrome [9,10]. Nevertheless, the SFSS is a multifaceted event. Typical clinical manifestations of SFSS are consequences of portal hypertension and graft dysfunction, presenting as more than two of the following on 3 consecu-

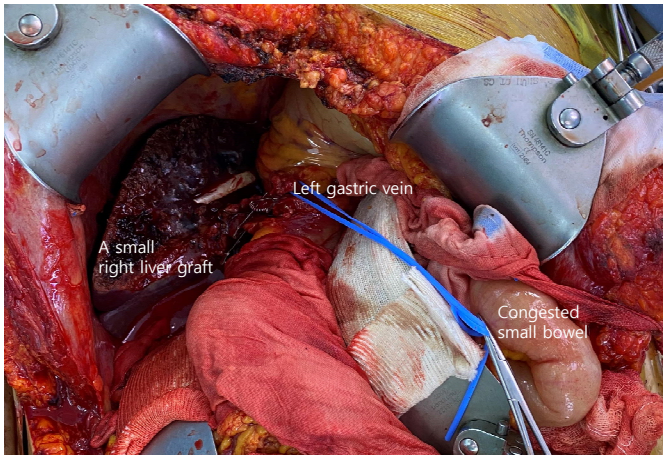

Fig. 1. A small partial graft during adult-to-adult living donor liver transplantation. The patient has undergone a small right liver graft with a 0.7% graft-versus-recipient weight ratio.

tive days: (1) long-standing uncontrolled ascites (>1 L/day), (2) hyperbilirubinemia (total bilirubin >5 mg/dL), (3) coagulopathy (International normalized ratio >2), and (4) encephalopathy (≥grade 3) during the first postoperative week after transplantation and after the exclusion of other causes, such as vascular or biliary complications or rejection. Other symptoms or signs of portal hypertension can also be addressed. These manifestations can disappear or improve compared with the pre-transplantation status after graft functioning.

The factors associated with SFSS include preoperative patient condition, the natural development of varices, medical or surgical efforts to reduce portal pressure, no pressure gradient between the hepatic vein and inferior vena cava (or right atrium), graft quality, and graft size.

Small for Size Syndrome Pathophysiology

The main pathophysiology of SFSS is shear stress, which leads to sinusoidal microcirculatory disturbances caused by excessive portal pressure [11]. In the case of a small graft, repair and regeneration cannot overcome the damage and maintain liver function very early after transplantation. If this damage is permanent or severe, the outcome of SFSS is poor, leading to graft failure and patient death.

The early microscopic features of SFSS are ischemia related to arterial vasospasm and/or thrombosis and render hepatocytes vulnerable to the subsequent oxidative stress leading to endothelial damage, cholestasis, hepatocyte ballooning, and ductular reaction, as well as bile duct necrosis. The late features include nodular regenerative hyperplasia [8,12,13].

Outcomes of Small for Size Syndrome

Early reports on SFSS demonstrated poor patient and graft survival outcomes. Patients with both elevated portal pressure (≥20 [range 18-25] mmHg) and SFSG (≤0.8% GRWR) showed significantly worse survival outcomes, bacteremia, and longer hospital stays. If the pre-transplant patient's condition is worse, such as old age and high model for end-stage liver disease (MELD) score, post-transplant outcomes would be much worse [5,8,11,14].

Recent reports regarding the outcomes of SFSG have shown promising results (Table 1). Small grafts are associated with poor short-term outcomes. However, the long-term outcome was not inferior in patients with small grafts [15]. Therefore, prevention, early detection, and interventions to attenuate SFSS are important. Various approaches have been explored to modulate inflow and pressure to a small graft and to decrease the outflow block to alleviate this SFSS. Along with these efforts, strict matching criteria for patient and donor pairs are also important.

Prevention and Management to Improve the Outcome of Small for Size Graft

1. Prevention of small for size syndrome

The management goal of the SFSS is to avoid SFSS. SFSS does not always occur in patients with SFSG. This can be prevented by cautiously matching the donor and recipient and applying surgical or medical modifications. Prevention of damage-related SFSG on portal hypertension is an ideal solution [8,16].

The principles for avoiding SFSS are as follows: First, it does not consider multiple risks of SFSS at once. There are several known factors related to SFSS: aged donor, graft steatosis, longer ischemic time, left small liver than right small liver, and recipient with a high MELD score [8,14,16]. For example, if the patient's condition is poor, sufficient graft volume from a young donor with a short ischemic time rather than a small left liver graft is a better alternative [11,14,17].

Table 1. The outcomes of liver transplantations using a SFSG

Year of study	Study	Country	Definition	Number of SFSG group	Number of control group	Incidence of SFSS (%)	Short-term mortality in SFSG	Long-term mortality (OR, 90% CI)
2008	Yi	Korea	<0.8% GRWR	29	-	-	0% in Right 33% in Left	-
2008	Ikegami	Japan	<35% GV/SLV	33	87	0	12.5% (1 yr)	3.25 (1.29–8.18)
2009	Selzner	Canada	<0.8% GRWR	22	249	9	4.5% (30 days)	0.82 (0.27–2.60)
2010	Moon	Korea	<0.8% GRWR	35	392	5.7	-	1.33 (0.60–2.95)
2014	Lee	Korea	<0.8% GRWR	50	267	8	2% (1 yr)	1.61 (0.72–3.63)*
2015	Au	HongKong	<35% GV/SLV	21	212	-	-	1.61 (0.51–5.15)
2015	Liu	China	<0.8% GRWR	65	181	11	7.7% (30 days)	1.23 (0.65–2.34)
2016	Ikegami	Japan	<35% GV/SLV	88	119	11.4	-	0.69 (0.28–1.72)

SFSG, small for size graft; SFSS, small for size syndrome; OR, odds ratio; CI, confidence interval; GRWR, graft-versus-recipient weight ratio; GV, graft volume; SLV, standard liver volume.
*3-yr follow up.

Second, portal pressure is attenuated after accurate measurement of portal pressure during transplantation [14,16,17–20]. Several surgical procedures can reduce the portal pressure and alleviate potential SFSS. Remaining natural varices or creating transient portosystemic shunts can reduce portal hypertension during the early period of graft regeneration. However, portal steal syndrome can sometimes ruin sufficient inflow to the graft. Accurate measurement of portal pressure and flow via the inferior mesenteric vein or the direct portal puncture technique helps decide whether to proceed with these procedures [18]. After regeneration of a small graft, surgical or interventional shunt occlusion can be performed to improve the long-term graft outcomes and prevent variceal complications. An indirect method to reduce portal pressure is to reduce splenic venous inflow to the portal vein. Splenomegaly and splenic artery hypertrophy are common in patients with end-stage liver disease and portal hypertension. In that case, splenectomy, splenic artery ligation, or splenic devascularization can reduce portal pressure [9,16,21,22].

Third, we used the entire transplanted graft without ischemia or congestion, as possible [9,23,24]. To avoid ischemia of the small graft, the surgeon should reconstruct all the inflows. During hepatectomy and graft implantation, meticulous surgery is mandatory to prevent the use of inotropic agents. To avoid congestion of the small graft, drain all the outflow of the area >20% of the graft, segment 5 veins, segment 8 veins, and right inferior hepatic veins in the right graft, and segment 1 vein in the left graft with the caudate lobe. To improve outflow, the outlet of the hepatic vein should be sufficiently large to transfer the oscillation of the heartbeat. Additionally, physiological obstruction related to hemodynamic changes such as high right atrial pressure or central venous pressure should be properly managed during the reperfusion period.

Finally, dual graft implantation and auxiliary orthotopic partial liver transplantation (APOLT) or heterotopic auxiliary partial liver transplantation (HALT) with future native liver hepatectomy, the so-called resection and partial liver segment 2/3 transplantation with delayed total hepatectomy (RAPID), can be another option to avoid SFSS [24–32]. The APOLT technique was applied to chronic liver disease in the late 90s during ALDLT to avoid SFSS and to protect donor safety using a small graft for sufficient future remnant volume in Asian countries (Fig. 2). Recently, this technique has been applied to patients with colorectal liver-only metastasis without portal hypertension who do not receive an adequate volume of deceased donor graft but can get a split left lateral section.

2. Management after small for size syndrome development

Regardless of these efforts during the operation, the SFSS can develop. Management goals include medical management of portal hypertension and graft support for acute liver failure. The medical reduction of portal pressure is similar to that of the pretransplant management of portal hypertension. Fluid balance and ascites control are basic concepts. Intervention radiology can play a role in splenic artery embolization by reducing portal pressure via flow reduction (Fig. 3).

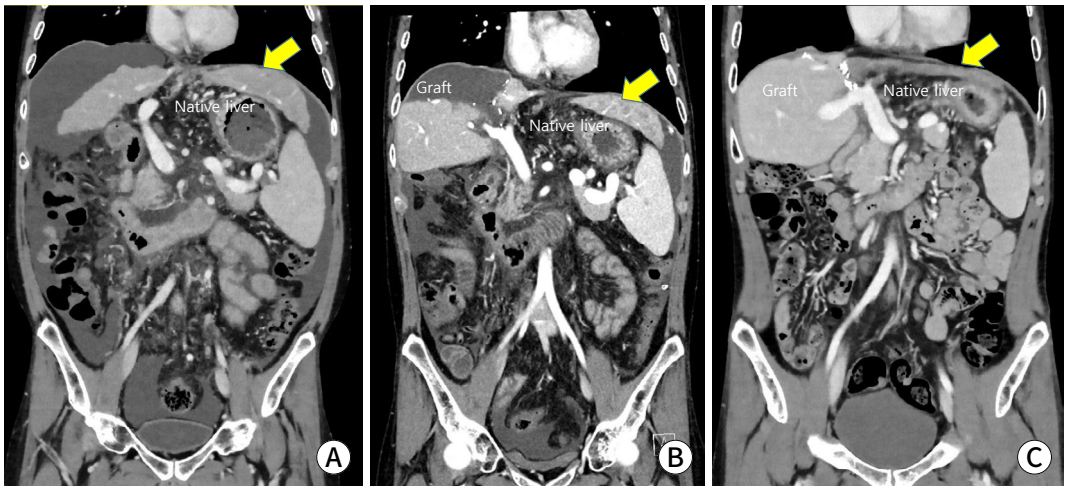

Fig. 2. Auxiliary partial orthotopic liver transplantation to prevent the small-for-size syndrome. A 36-yr-old patient with Wilson's disease has undergone living-donor liver transplantation from a 54-yr-old mother using a right posterior section graft. The graft-versus-recipient weight ratio is 0.64%. He has undergone a native liver hepatectomy 11 mo after transplantation. (A) A preoperative recipient computed tomography (CT) scan. (B) A CT scan of postoperative day 9. (C) A CT scan of postoperative 11 mo.

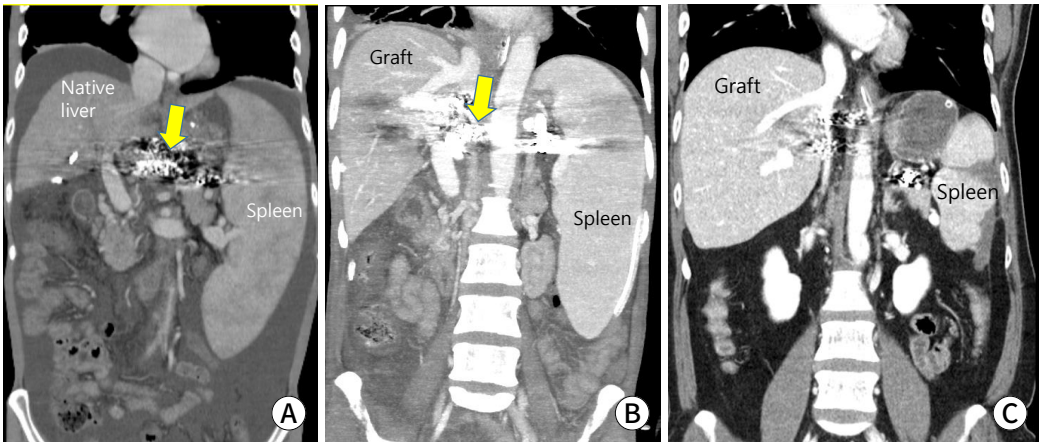

Fig. 3. Post-transplant splenic arterial embolization to reduce portal hypertension. A 40-yr-old woman with hepatitis B-related liver cirrhosis with the hepatorenal syndrome and uncontrolled ascites underwent living-donor liver transplantation from his 35-yr-old wife using a right liver graft. He underwent gastrorenal shunt occlusion before transplantation to control variceal bleeding and encephalopathy. One mo after transplantation, the patient underwent partial occlusion of the splenic artery because of uncontrolled ascites related to small-for-size syndrome (arrow, material for gastrorenal shunt occlusion). (A) A preoperative recipient computed tomography (CT) scan. (B) A CT scan of postoperative day 7. (C) A CT scan 2 yrs after transplantation.

The SFSS can be overcome after the early period of graft regeneration. If varices or shunt flow remains, we should wait for a minimum of 2 weeks (10–21 days after transplantation) for graft regeneration. Delayed closure would be helpful for the restoration of graft function. Delayed native liver hepatectomy in cases of APOLT (or HALT, RAPID) can be performed during this period [25–31].

Conclusion

SFSS can occur in any case when using a small partial graft. However, a better understanding of SFSS and the recent progress in perioperative management and surgical techniques can push the boundary of a small graft. Before permanent damage of a small graft, prevention and early detection of SFSS can save patients with only the alternative for a small graft.

References

1. Chen CL, Fan ST, Lee SG, Makuuchi M, Tanaka K. Living-donor liver transplantation: 12 years of experience in Asia. *Transplantation* 2003;75:S6-S11.
2. Hashikura Y, Makuuchi M, Kawasaki S, Matsunami H, Ikegami T, Nakazawa Y, et al. Successful living-related partial liver transplantation to an adult patient. *Lancet* 1994;343:1233-1234.
3. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, et al. Surgical techniques and innovations in living related liver transplantation. *Ann Surg* 1993;217:82-91.
4. Hong SK, Choe S, Yi NJ, Shin A, Choe EK, Yoon KC, et al. Long-term survival of 10,116 Korean live liver donors. *Ann Surg* 2021;274:375-382.
5. Kiuchi T, Kasahara M, Uryuhara K, Inomata Y, Uemoto S, Asonuma K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. *Transplantation* 1999;67:321-327.
6. Kiuchi T, Tanaka K, Ito T, Oike F, Ogura Y, Fujimoto Y, et al. Small-for-size graft in living donor liver transplantation: how far should we go? *Liver Transpl* 2003;9:S29-S35.
7. Lo CM, Fan ST, Liu CL, Chan JK, Lam BK, Lau GK, et al. Minimum graft size for successful living donor liver transplantation. *Transplantation* 1999;68:1112-1116.
8. Masuda Y, Yoshizawa K, Ohno Y, Mita A, Shimizu A, Soejima Y. Small-for-size syndrome in liver transplantation: definition, pathophysiology and management. *Hepatobiliary Pancreat Dis Int* 2020;19:334-341.
9. Ben-Haim M, Emre S, Fishbein TM, Sheiner PA, Bodian CA, Kim-Schluger L, et al. Critical graft size in adult-to-adult living donor liver transplantation: impact of the recipient's disease. *Liver Transpl* 2001;7:948-953.
10. Dahm F, Georgiev P, Clavien PA. Small-for-size syndrome after partial liver transplantation: definition, mechanisms of disease and clinical implications. *Am J Transplant* 2005;5:2605-2610.
11. Yi NJ, Suh KS, Cho YB, Lee HW, Cho EH, Cho JY, et al. The right small-for-size graft results in better outcomes than the left small-for-size graft in adult-to-adult living donor liver transplantation. *World J Surg* 2008;32:1722-1730.
12. Emond JC, Renz JF, Ferrell LD, Rosenthal P, Lim RC, Roberts JP, et al. Functional analysis of grafts from living donors: implications for the treatment of older recipients. *Ann Surg* 1996;224:544-554.
13. Demetris AJ, Kelly DM, Eghtesad B, Fontes P, Wallis Marsh J, Tom K, et al. Pathophysiologic observations and histopathologic recognition of the portal hyperperfusion or small-for-size syndrome. *Am J Surg Pathol* 2006;30:986-993.
14. Yi NJ, Suh KS, Lee HW, Shin WY, Kim J, Kim W, et al. Improved outcome of adult recipients with a high model for end-stage liver disease score and a small-for-size graft. *Liver Transpl* 2009;15:496-503.
15. Ma KW, Wong KHC, Chan ACY, Cheung TT, Dai WC, Fung JYY, et al. Impact of small-for-size liver grafts on medium-term and long-term graft survival in living donor liver transplantation: a meta-analysis. *World J Gastroenterol* 2019;25:5559-5568.
16. Ikegami T, Balci D, Jung DH, Kim JM, Quintini C. Living donor liver transplantation in small-for-size setting. *Int J Surg* 2020;82:134-137.
17. Chan SC, Fan ST, Lo CM, Liu CL. Effect of side and size of graft on surgical outcomes of adult-to-adult live donor liver transplantation. *Liver Transpl* 2007;13:91-98.
18. Ito T, Kiuchi T, Yamamoto H, Oike F, Ogura Y, Fujimoto Y, et al. Changes in portal venous pressure in the early phase after living donor liver transplantation: pathogenesis and clinical implications. *Transplantation* 2003;75:1313-1317.
19. Troisi R, Cammu G, Militerno G, De Baerdemaeker L, Decruyenaere J, Hoste E, et al. Modulation of portal graft inflow: a necessity in adult living-donor liver transplantation? *Ann Surg* 2003;237:429-436.
20. Botha JF, Langnas AN, Campos BD, Grant WJ, Freise CE, Ascher NL, et al. Left lobe adult-to-adult living donor liver transplantation: small grafts and hemiportocaval shunts in the prevention of small-for-size syndrome. *Liver Transpl* 2010;16:649-657.
21. Moon DB, Lee SG, Hwang S, Ahn CS, Kim KH, Ha TY, et al. Splenic devascularization can replace splenectomy during adult living donor liver transplantation: a historical cohort study. *Transpl Int* 2019;32:535-545.
22. Ito K, Akamatsu N, Ichida A, Ito D, Kaneko J, Arita J, et al. Splenectomy is not indicated in living donor liver transplantation. *Liver Transpl* 2016;22:1526-1535.
23. Yi NJ, Suh KS, Lee HW, Cho EH, Shin WY, Cho JY, et al. An artificial vascular graft is a useful interpositional material for drainage of the right anterior section in living donor liver transplantation. *Liver Transpl* 2007;13:1159-1167.
24. Lee SG. A complete treatment of adult living donor liver transplantation: a review of surgical technique and current challenges to expand indication of patients. *Am J Transplant* 2015;15:17-38.
25. Kasahara M, Kiuchi T, Uryuhara K, Takakura K, Egawa H, Asonuma K, et al. Auxiliary partial orthotopic liver transplantation as a rescue for small-for-size grafts harvested from living donors. *Transpl Proc* 1998;30:132-133.
26. Kasahara M, Takada Y, Egawa H, Fujimoto Y, Ogura Y, Ogawa K, et al. Auxiliary partial orthotopic living donor liver transplantation: Kyoto University experience. *Am J Transplant* 2005;5:558-565.
27. Lee SG, Hwang S, Park KM, Kim KH, Ahn CS, Lee YJ, et al. Seventeen adult-to-adult living donor liver transplantations using dual grafts. *Transpl Proc* 2001;33:3461-3463.
28. Soejima Y, Taketomi A, Ikegami T, Yoshizumi T, Uchiyama H, Yamashita Y, et al. Living donor liver transplantation using dual grafts from two donors: a feasible option to overcome small-for-size graft problems? *Am J Transplant* 2008;8:887-892.
29. Konigsrainer A, Templin S, Capobianco I, Konigsrainer I, Bitzer M,

Zender L, et al. Paradigm shift in the management of irresectable colorectal liver metastases: living donor auxiliary partial orthotopic liver transplantation in combination with two-stage hepatectomy (LD-RAPID). *Ann Surg* 2019;270:327-332.
30. Lim C, Turco C, Balci D, Savier E, Goumard C, Perdigao F, et al. Auxiliary liver transplantation for cirrhosis: from APOLT to RAPID: a scoping review. *Ann Surg* 2022;275:551-559.
31. Ravaioli M, Brandi G, Siniscalchi A, Renzulli M, Bonatti C, Fallani G, et al. Heterotopic segmental liver transplantation on splenic vessels after splenectomy with delayed native hepatectomy after graft regeneration: a new technique to enhance liver transplantation. *Am J Transplant* 2021;21:870-875.
32. Cho JY, Suh KS, Kwon CH, Yi NJ, Kim MA, Jang JJ, et al. Auxiliary partial orthotopic living donor liver transplantation in a patient with alcoholic liver cirrhosis to overcome donor steatosis. *Transpl Int* 2006;19:424-429.

EMJ THE EWHA MEDICAL JOURNAL

Original Article

Ewha Med J 2022;45(2):35-45
https://doi.org/10.12771/emj.2022.45.2.35
eISSN 2234-2591

Medication Adherence in Korean Patients with Inflammatory Bowel Disease and Its Associated Factors

Kyunghwan Oh*, Eun Ja Kwon[1,*], Jeong Hye Kim[2], Kyuwon Kim, Jae Yong Lee, Hee Seung Hong, Seung Wook Hong, Jin Hwa Park, Sung Wook Hwang, Dong-Hoon Yang, Byong Duk Ye, Jeong-Sik Byeon, Seung-Jae Myung, Suk-Kyun Yang, Jeong Yun Park[2], Sang Hyoung Park

Department of Gastroenterology and [1]Nursing, Asan Medical Center, University of Ulsan College of Medicine, [2]Department of Clinical Nursing, University of Ulsan, Seoul, Korea

Objectives: It is important that inflammatory bowel disease (IBD) patients adhere to their prescribed medication regimens to avoid the repeat exacerbations, complications, or surgeries associated with this disorder. However, there are few studies on medication adherence in patients with IBD, especially in Asian populations. So, we analyzed the factors associated with medication adherence in Korean IBD patients.

Methods: Patients who had been diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) more than 6 months previously and receiving oral medications for IBD were enrolled. Medication adherence was measured using the Medical Adherence Reporting Scale (MARS-5), a self-reported medication adherence measurement tool.

Results: Among 207 patients in the final study population, 125 (60.4%) had CD and 134 (64.7%) were men. The mean age was 39.63 years (SD, 13.16 years) and the mean disease duration was 10.09 years (SD, 6.33 years). The mean medication adherence score was 22.46 (SD, 2.86) out of 25, and 181 (87.4%) patients had score of 20 or higher. In multiple linear regression analysis, self-efficacy (β=0.341, P<0.001) and ≥3 dosing per day (β=−0.192 P=0.016) were revealed to be significant factors associated with medication adherence. Additionally, there was a positive correlation between self-efficacy and medication adherence (r=0.312, P<0.001). However, disease related knowledge, depression, and anxiety were not significantly associated with medication adherence.

Conclusion: To improve medication adherence among patients with IBD, a reduction in the number of doses per day and an improved self-efficacy will be helpful.

(Ewha Med J 2022;45(2):35-45)

Received February 28, 2022
Revised April 1, 2022
Accepted April 3, 2022

Corresponding author
Sang Hyoung Park
Department of Gastroenterology and Inflammatory Bowel Disease Center, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: 82-2-3010-5768, Fax: 82-2-476-0824
E-mail: umdalpin@hanmail.net

Jeong Yun Park
Department of Clinical Nursing, University of Ulsan, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: 82-2-3010-5333, Fax: 82-2-3010-5332
E-mail: pjyun@ulsan.ac.kr

*These authors contributed equally to this work.

Key Words
Inflammatory bowel diseases; Medication adherence; Self efficacy; Korea

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disease that occurs in the gastrointestinal tract that includes Crohn's disease (CD) and ulcerative colitis (UC), and that may sometimes present with extraintestinal manifestations [1,2]. The prevalence of IBD is increasing in Asian countries including Korea [3−5]. Symptoms such as ab−

dominal pain, diarrhea, weight loss, and a bloody stool are common to IBD. If the inflammation is not well controlled in affected patients, complications including intestinal stricture, fistula, perforation, and cancer can occur [6–8]. IBD is also a progressive disease, and it is important therefore to maintain appropriate medical interventions to prevent disease progression and reduce complications [9,10]. Adherence to medication regimens is thus vital and several studies have indicated in this regard that the prognosis is poorer in non-adherent IBD patients [11].

Medication adherence indicates that patients are taking their medications as prescribed [12]. Tae et al. [13] reported previously in patients with IBD that the risk of recurrence was 2.9-times higher in patients with low medication adherence. Despite its importance, medication adherence in patients with IBD has been reported to be only 55%–70% in a prior Western study [14], and to range from 63.8%–77.7% in Korean IBD populations [13,15]. By contrast, medication adherence in patients with hypertension, which is representative of a highly prevalent chronic disease in Korea, is reported to be much higher at 85% [16].

Factors associated with medication adherence in patients with IBD include symptoms, multiple concomitant medications, and doctor–patient relationships [17]. Selinger et al. [18] reported that poor patient knowledge could lead to the aggravation of IBD or a delay in treatment as it can reduce medication adherence. The concept of self-efficacy, i.e., a personal belief in disease management, has also been found to be related to medication adherence in patients with IBD [19]. In addition, Jackson et al. [14] reported that psychological distress is associated with non-adherence.

To date, few studies have analyzed the factors associated with medication adherence in patients with IBD, especially in an Asian context [13,15,20,21]. It is difficult to apply the results of previous studies on medication adherence that have been conducted in Western patients with IBD [14,17,22,23] or in Korean patients with other chronic diseases [24]. Hence, in our present study we analyzed the factors associated with medication adherence in Korean patients with IBD using a structured questionnaire.

Methods

1. Study population

Adult patients (aged 18 years and older) who had been visiting Asan Medical Center for more than 6 months after being diagnosed with CD or UC, and who were receiving oral medications for these conditions, were enrolled. Patients who were taking psychotropic agents were excluded. The study sample size was calculated using G-Power [25,26] (Version 3.1.9, Heinrich-Heine-Universitat Dusseldorf, Dusseldorf, Germany), based on multiple regression analysis, a two-sided test significance level of 0.05, a median effect size of 0.15, power of 0.95, and 14 predictors. The minimum number of subjects was calculated as 199. As the dropout rate was assumed to be 10%, we distributed the questionnaire to 218 patients.

2. Data collection

Patient data were collected from 14–28 April 2021 through the use of a structured questionnaire. Information on disease activity and medications among the IBD cohort were collected from the electronic medical records. Information on these patients including age, gender, marital status, family living arrangements, education level, religion, socioeconomic status, and smoking history were collected as general characteristics. Other factors such as duration of disease, previous IBD-related hospitalizations, previous IBD-related surgeries, active disease history, number of medications, outpatient visit period, education experience on IBD, and disease activity information were collected as disease-related characteristics. Disease activity was evaluated using the Crohn's disease activity index (CDAI) in patients with CD and the partial Mayo score in patients with UC.

Medication adherence was evaluated using Medication Adherence Report Scale-5 (MARS-5) developed by Horne et al. [22] with permission from the original author. The tool was translated into Korean with verification of language accuracy. It was then translated back into English and again verified. Since this was the first use of this tool in Korea, the validity of the questionnaire translated into Korean was verified by 10 experts (3 gastroenterologists, 2 nursing professors, 3 IBD specialist nurses, and 2 nurses working in the gastroenterology department for more than 10 years). As a result of this further review, a content validity index of 0.8 or higher was

calculated. Finally, both the Korean and retranslated English versions of the MARS-5 tool were sent to the original author at his request for approval. The scores calculated by this questionnaire range from 5 to 25, with higher scores indicating a higher degree of medication adherence. A score of 20 points or less, i.e., 80% or below, was defined as low medication adherence [23].

The IBD knowledge measurement tool (IBD-KNOW, Inflammatory Bowel Disease Knowledge) which was previously developed by Yoon et al. [27], was used to evaluate disease-related knowledge among the cases in our current series. Permission to use this system was also obtained from the original author. The IBD-KNOW questionnaire consists of a total of 24 items which reflect various aspects of a patient's knowledge about IBD, such as anatomy, function, epidemiology, diet/lifestyle, general knowledge, medications, complications, surgery, reproduction, and vaccination. The responses can be "yes", "no", or "don't know". A correct answer is assigned 1 point, and an incorrect or "don't know" is scored as 0. The total score can range from 0 to 24, with a higher score indicating higher disease-related knowledge. IBD-KNOW was validated with a Cronbach α of 0.952 at the time of its development.

Self-efficacy was evaluated using the inflammatory bowel disease self-efficacy scale (IBD-SES) developed originally by Keefer et al. [19] and previously translated into Korean by Lee et al. [28] We used this questionnaire with permission from the original author and translator. The IBD-SES consists of a total of 29 questions that cover managing stress and emotions, managing medical care, managing symptoms and disease, and maintaining remission. Each question is assessed on a 10-point Likert scale with 10 being "totally sure"; 5, "somewhat sure"; and 1, "not sure at all." The total score can thus range from 29 to 290, with a higher score indicating higher self-efficacy. At the time of its development, the IBD-SES received a 0.96 using Cronbach α, which was calculated as 0.97 by Lee et al. [28].

Anxiety and depression was evaluated using the hospital anxiety and depression scale (HADS) which has mainly been used in patients with cancer, and was developed by Zigmond et al. [29] and translated into Korean by Oh et al. [30] HADS was used with permission from GL Assessment (London, UK). The 7 even-numbered questions in this tool comprise the depression subscale (HADS-D), and the 7 odd-numbered questions the anxiety subscale (HADS-A). Each question is scored from 0 to 3 points, with a total possible score of 21 points on each subscale. Higher scores indicate higher levels of depression and anxiety. A score of 0 to 7 was defined as normal, 8 to 10 as indicating mild anxiety or depression, and 11 or higher as indicative of severe anxiety or depression.

3. Statistical analysis

The general characteristics, disease-related characteristics, disease-related knowledge, self-efficacy, depression and anxiety, and medication adherence of the current study subjects were analyzed in terms of frequency and percentage, or by mean values with SD. An independent t-test and one way ANOVA were used to analyze differences in medication adherence in accordance with the general characteristics and disease-related characteristics of the IBD patients, and a Scheffe test was used for post hoc analysis. Multiple linear regression analysis was used to identify factors affecting medication adherence. The variance inflation factor (VIF) ranged from 1.151-1.898 with no cases exceeding 10, and the tolerance limit ranged from 0.527-0.869, with all cases larger than 0.1 confirming that there was no multicollinearity problem. The multiple linear regression analysis model was suitable for the regression analyses with $F=4.337$, $P<0.001$, and adjusted $R^2=0.127$, indicating an explanatory power of 12.7%. The correlation between the disease-related knowledge, self-efficacy, depression and anxiety and medication adherence variables was analyzed using Pearson's correlation analysis. Statistical significance was defined as $P<0.05$. All collected data were analyzed using IBM SPSS statistics for Windows, version 25.0 (IBM, Armonk, NY, USA).

4. Ethical considerations

The current study protocol was approved by the Institutional Review Board of Asan Medical Center, Seoul, Korea (IRB No. 2021-0452).

Results

1. General and disease-related characteristics of the study subjects

The study questionnaire was distributed to all 218 enrolled IBD patients, with 207 of these cases (95.0%) responding ad-

equately to enable further analysis. Among these 207 patients, 134 (64.7%) were male, and the mean age at enrollment was 39.63 years (SD, 13.16 years), with the 30–39 year age group representing the largest sub-population (30.4%). One hundred and thirteen (54.6%) patients were married and 182 (87.9%) were living with their family. In terms of educational attainment, 159 (76.8%) patients had a university degree or higher, 119 patients (57.5%) were non-religion, 67 (32.4%) had no occupation, and 179 (86.5%) patients were never smokers (Table 1).

The disease-related characteristics of our study participants are also presented in Table 1. There were 125 CD cases (60.4%) with a mean disease duration of 10.09 years (SD, 6.33 years). Ninety-four (45.4%) of the patients were receiving bi-

Table 1. General and disease-related characteristics of the current study population (n=207)

Characteristics	n (%)	Characteristics	n (%)
Gender (male)	134 (64.7)	Previous IBD-related hospitalization	131 (63.3)
Age (yr), mean±SD	39.63±13.16	Previous IBD-related surgery	76 (36.7)
Age range (yr)		Previous relapse	178 (86.0)
≤29	52 (25.1)	Medications	
30–39	63 (30.4)	5-ASA	162 (78.3)
40–49	46 (22.2)	Immunomodulators	128 (61.8)
50–59	28 (13.5)	Biologics	94 (45.4)
≥60	18 (8.7)	Steroids	11 (5.3)
Married	113 (54.6)	Route of medications	
Living status		PO only	121 (58.5)
With family member(s)	182 (87.9)	PO and parenteral	86 (41.5)
Alone	22 (10.6)	Number of medications	
With others	3 (1.5)	One	104 (50.2)
Education level		More than two	103 (49.8)
≤High school	48 (23.2)	Number of pills (per day), mean±SD	6.21±3.97
≥Bachelor's degree	159 (76.8)	Number of pills (per day)	
Religion		<5	73 (35.3)
Yes	88 (42.5)	≥5	134 (64.7)
No	119 (57.5)	Number of doses (per day)	
Occupation		Once	66 (31.9)
Yes	140 (67.6)	Twice	66 (31.9)
No	67 (32.4)	Three or more times	75 (36.2)
Monthly household income (Korean won)		Outpatient visit interval (days), mean±SD	73.77±35.66
<3 million	86 (41.5)	Outpatient visit interval (days)	
≥3 million	121 (58.5)	<28	31 (15.0)
Smoking		28–56	65 (31.4)
Yes	28 (13.5)	57–84	40 (19.3)
No	179 (86.5)	≥85	71 (34.3)
Disease		IBD education experience	170 (82.1)
Crohn's disease	125 (60.4)	Disease activity	
Ulcerative colitis	82 (39.6)	Remission	158 (76.3)
Disease duration (yr), mean±SD	10.09±6.33	Mild	34 (16.4)
Disease duration (yr)		Moderate	13 (6.3)
<5	50 (24.2)	Severe	2 (1.0)
5–9	52 (25.1)		
10–14	64 (30.9)		
≥15	41 (19.8)		

IBD, inflammatory bowel disease; 5-ASA, 5-aminosalicylic acid; PO, per oral.

ologic agents and 11 (5.3%) patients were on a corticosteroid regimen. There were 121 (58.5%) patients in the series taking only oral medications and 104 (50.2%) taking only one kind of oral medication. The mean number of pills being taken per day was 6.21 (SD, 3.97), and the mean outpatient visit interval was 73.77 days (SD, 35.66 days).

2. Medication adherence, disease-related knowledge, self-efficacy, and anxiety and depression scores

The mean medication adherence score was 22.46 (SD, 2.86) out of 25, with 26 (12.6%) patients showing low adherence, defined as a score of 20 points or less. The mean disease-related knowledge score was 14.46 (SD, 4.63) out of 24, and the mean self-efficacy score in relation to IBD management was 203.21 (SD, 40.86) out of 290. With regard to the HADS responses, the mean depression score was 6.36 (SD, 3.36), with 24 (11.6%) patients indicating severe depression. The anxiety scores determined by the HADS responses had a mean of 5.85 (SD 3.64), with 23 (11.1%) patients showing severe anxiety (Table 2).

3. Medication adherence in accordance with general and disease-related characteristics

The observed differences in medication adherence among the study patients, in accordance with their general characteristics, did not show statistical significance (Table 3). In terms of the disease-related characteristics of the study subjects, the patients with CD (P=0.015) had a lower medication adherence than the patients with UC, and the patients with a previous IBD-related surgery (P=0.035) also showed a lower medication adherence (Table 4). The patients who were taking steroids (P<0.001) showed higher medication adherence, as did the patients who were taking only oral medications (P=0.040), compared with the patients who were taking both oral and parenteral medications. There was no significant difference found in the medication adherence between the patients taking one medication and those on a regimen of two or more drugs. The medication adherence was lower in the patients who were taking medicines three or more times a day regimen, compared with those on a once per day regimen (P=0.008).

4. Factors associated with medication adherence and correlations between disease-related knowledge, self-efficacy, depression, anxiety and medication adherence

Multiple linear regression analysis was performed to identify factors affecting medication adherence. Self-efficacy (β =0.341, P<0.001), and three or more daily doses (β=−0.192, P=0.016, compared with a single daily dosage) were significant factors associated with medication adherence (Table 5).

Table 2. Disease-related knowledge, self-efficacy, depression, anxiety, and medication adherence in patients with IBD (n=207)

Variables	Score range	n (%)	Mean±SD
Disease related knowledge	0–24		14.46±4.63
Self-efficacy	29–290		203.21±40.86
Stress & emotions	9–90		61.41±16.56
Medical care	8–80		65.26±12.39
Symptoms and disease	7–70		43.89±12.88
Remission	5–50		32.78±8.69
Depression	0–21		6.36±3.36
Normal	0–7	131 (63.3)	
Mild	8–10	52 (25.1)	
Severe	>11	24 (11.6)	
Anxiety	0–21		5.85±3.64
Normal	0–7	149 (72.0)	
Mild	8–10	35 (16.9)	
Severe	>11	23 (11.1)	
Medication adherence	5–25		22.46±2.86
Low adherence	<20 (80%)	26 (12.6)	

IBD, inflammatory bowel disease.

Table 3. Differences in medication adherence by general characteristics

Variable	Mean±SD	t or F-value	P-value
Sex		1.456	0.147
Male	22.67±2.65		
Female	22.07±3.18		
Age range (yr)		1.176	0.323
≤29	22.23±3.01		
30–39	22.30±3.02		
40–49	22.24±3.09		
50–59	22.79±2.35		
≥60	23.72±1.45		
Married		0.188	0.851
Yes	22.42±2.99		
No	22.50±2.70		
Living status		0.085	0.919
With family member	22.43±2.82		
Living alone	22.68±3.26		
Others	22.67±3.22		
Education level		1.386	0.167
≤High school	22.96±2.33		
≥Bachelor	22.31±2.99		
Religion		−1.363	0.175
Yes	22.77±2.72		
No	22.23±2.94		
Occupation		−1.738	0.084
Yes	22.22±2.96		
No	22.96±2.58		
Monthly household income (Korean won)		−0.072	0.942
<3 million	22.44±2.88		
≥3 million	22.47±2.85		
Smoking		−0.772	0.441
Yes	22.07±3.19		
No	22.52±2.81		

Self–efficacy (r=0.312, P<0.001) showed a positive correlation with medication adherence, whereas disease–related knowledge, depression, and anxiety had no significant correlation with medication adherence (Table 6).

Discussion

We have here investigated medication adherence among Korean patients with IBD, and analyzed factors that associated with medication adherence, including disease–related knowledge, depression, and anxiety. Our findings indicated that 26 cases among our final study subjects of 207 (12.6%) patients had low medication adherence, defined as a score on the self–administered questionnaire 20 points or less (80% or lower), and that the factors contributing to this low adherence were a reduced self–efficacy and a drug regimen of three or more daily doses. With another analysis, a positive correlation was evident between self–efficacy and medication adherence. Our current results for Korean patients with IBD indicated a better level of medication adherence compared to previously studied populations [13,15]. For example, Kim et al. [15] reported that 49.3% (32/67) of their CD patients and 48.0% (36/75) of their UC patients showed a low medication adherence. Tae et al. [13] reported that 36.2% (50/138) of the IBD patients in their study cohort were non–adherent to their drug regimens. In prior Western studies [14,17,22], the low adherence was reported to range from 29%–45% which is also higher than the rate found in our present study. The mean

Table 4. Differences in medication adherence by disease-related characteristics

Variable	Mean±SD	t or F-value	P-value
Disease		−2.450	0.015
CD	22.10±3.16		
UC	23.01±2.21		
Disease duration (yr)		2.557	0.056
<5	22.84±2.99		
5–9	22.92±2.23		
10–14	22.44±2.33		
≥15	21.44±3.83		
Previous IBD-related hospitalization		0.864	0.389
Yes	22.33±3.08		
No	22.68±2.42		
Previous IBD-related surgery		2.126	0.035
Yes	21.87±3.32		
No	22.80±2.50		
Previous relapse history		0.749	0.455
Yes	22.40±2.97		
No	22.83±2.00		
Concomitant steroid use		−5.039	<0.001
Yes	24.18±0.98		
No	22.36±2.90		
Route of medications		2.065	0.040
PO only	22.80±2.40		
PO and parenteral	21.98±3.34		
Number of medications		1.478	0.141
One	22.75±2.52		
More than two	22.17±3.15		
Number of pills (per day)		1.198	0.232
<5	22.70±2.59		
≥5	22.28±2.98		
Number of doses (per day)		4.950	0.008
Once[a]	23.12±2.06		a>c*
Twice[b]	22.68±2.99		
Three or more times[c]	21.68±3.17		
Outpatient visit interval (days)		2.300	0.079
<28	23.23±2.13		
28–56	21.77±3.44		
57–84	22.83±3.00		
≥85	22.55±2.34		
IBD education experience		−0.952	0.342
Yes	22.55±2.85		
No	22.05±2.90		
Disease activity		0.307	0.821
Remission	22.41±2.91		
Mild	22.68±2.88		
Moderate	22.77±2.46		
Severe	21.00±0.00		

CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; PO, per oral.
*Scheffe test.

Table 5. Factors associated with medication adherence

Variable	B	SE	β	t-value	P-value	Tolerance	VIF
Disease	0.423	0.485	0.073	0.870	0.385	0.610	1.640
Previous IBD-related surgery	−0.452	0.495	−0.076	−0.911	0.363	0.603	1.659
Route of medications	−0.383	0.404	−0.066	−0.948	0.344	0.869	1.151
Number of doses (per day) (Reference : Once)							
Twice	−0.154	0.470	−0.025	−0.327	0.744	0.715	1.398
Three or more times	−1.136	0.466	−0.192	−2.441	0.016	0.687	1.457
Disease-related knowledge	−0.002	0.044	−0.003	−0.043	0.966	0.816	1.225
Self-efficacy	0.024	0.006	0.341	4.017	<0.001	0.589	1.699
Depression	0.078	0.076	0.092	1.026	0.306	0.527	1.898
Anxiety	0.007	0.068	0.009	0.102	0.919	0.569	1.756
F(P)=4.337 (<0.001), R^2=0.165, adjusted R^2=0.127, Durbin-Watson=2.108							

VIF, variance inflation factor; IBD, inflammatory bowel disease.

Table 6. Correlations between disease-related knowledge, self-efficacy, depression, anxiety and medication adherence

Variable	Disease-related knowledge	Self-efficacy	Depression	Anxiety	Medication adherence
Disease-related knowledge	1				
Self-efficacy	0.003 (0.970)	1			
Depression	0.048 (0.495)	−0.586 (<0.001)	1		
Anxiety	0.106 (0.130)	−0.535 (<0.001)	0.603 (<0.001)	1	
Medication adherence	−0.090 (0.195)	0.312 (<0.001)	−0.121 (0.082)	−0.135 (0.052)	1

Values are presented as r (P).

MARS-5 score was 22.46 (SD, 2.86) in our current study, which is similar to that reported previously by Stone et al. [23] of 22.5 (SD, 2.2).

We found from our present analyses that self-efficacy (P<0.001) and regimens requiring three or more dosages per day (P=0.016) were associated with medication adherence, respectively. These results are consistent with the findings of a previous study [31] in which a requirement for three or more doses per day was also reported to be associated with poor medication adherence. Jackson et al. [14] reported that psychological distress and patient beliefs regarding medications were associated with non-adherence. Notably however, depression and anxiety were not associated with medication adherence in our present study series. Patient beliefs and attitudes about treatment were reported to be related to medication adherence in other previous studies [22,32], but we did not investigate these factors in our current investigations.

No significant correlation was found in our present study between disease-related knowledge and medication adherence. Previously, Lim et al. [33] had reported that the patients with higher level of IBD knowledge showed better adherence among Korean pediatric patients with IBD. In addition, Ashok et al. [34] reported that a higher disease-related knowledge led to a higher degree of medication compliance among patients with IBD. However, other studies [18,35] reported no correlation between disease-related knowledge and medication adherence, which is consistent with our present study results. Hence, the relationship between disease-related knowledge and medication adherence is not yet fully clear. The tool we used herein to assess disease-related knowledge (IBD-KNOW) [27] includes questions on anatomy, function, epidemiology, diet/lifestyle, general knowledge, medication, complications, surgery, reproduction, and vaccination. However, the ages of our current IBD subjects had a wide range, which led to differences in the proportion of correct answers by field of interest. We contend therefore that it is necessary to educate patients after confirming their knowledge level in each of these fields.

We found no correlation between anxiety, depression and medication adherence in our present analyses, consistent with the prior study results of Selinger et al. [18] However, Jackson et al. [14] reported that depression and anxiety do affect medication adherence, and Nahon et al. [36] found that higher anxiety correlated with a lower medication adherence among the patients with IBD. In addition, Park et al. [37] reported that patients with chronic disease such as hypertension, diabetes, and dyslipidemia have higher rates of depression and lower medication adherence. As the effects of different variables on medication adherence have been reported in a variety of ways, further studies are needed to identify the factors that link depression/anxiety with medication adherence in IBD.

The mean score for disease-related knowledge in our study was 14.46 out of 24. This is higher score that that described in previous studies. Kim et al. [15] reported a mean disease-related knowledge score of 9.0 in patients with CD and 8.2 in patients with UC using the same knowledge measurement tool [38]. Yoon et al. [27] reported a disease-related knowledge score of 13.3 in patients with IBD at the time in which the IBD-KNOW tool was developed. Our present study had more frequent histories of IBD-related hospitalizations (63.3% vs. 36.6%) and surgeries (36.7% vs. 4.9%) than was reported in a previous study [15]. We speculate that patients who experienced an IBD-related hospitalization or an IBD-related surgery would take a greater interest in their condition and thus make more of an effort to acquire disease-related knowledge. This may underlie our current findings for this variable. In a previous study from the United States, the disease-related knowledge score for patients with IBD was 14.8 [39], which is similar to the score in our current study. The overall low disease-related knowledge scores in Korea for IBD may be due to a lower prevalence of this disorder compared to other chronic disease such as hypertension and diabetes. As a result of this however, even medical staff in local community hospitals are commonly transferring IBD patients to tertiary hospitals due to their lack of knowledge and experience, leading to an insufficient amount of publicity and awareness of IBD among many Korean medical institutions.

The measure of self-efficacy in our present study (209 points out of 290 points) was slightly higher than hat obtained by Keefer et al. [19] (194.9 points out of 290 points) using the same measurement tool (IBD-SES). The IBD-SES can evaluate 4 areas, the scores of which can then be expressed as a percentage. In our present study, managing medical care was 81.53%, managing stress and emotions was 68.23%, maintaining remission was 65.52%, and managing symptoms and disease was 62.7%. This suggests that strategies are needed in Korean patients with IBD to improve the management of symptoms and disease and to maintain remission.

The mean scores for depression and anxiety in this study were 6.37 and 5.85, respectively, with 77 of our patients (37.2%) showing mild to severe depression, and 58 (28.0%) displaying mild to severe anxiety. In a previous IBD cohort study [15], the prevalence of depression and anxiety were measured at 19.7% and 42.9%, respectively, using the same tool. Hence, more patients experienced depression and fewer experienced anxiety among our study population. Of note in particular, 24 (11.6%) of our current IBD patients had severe depression. In a previous Western study, Graff et al. [40] reported that the rate of depression within 1 year of the diagnosis of IBD was about twice as high as in patients without IBD, whereas anxiety did not show a difference, and that about 17% of their IBD cases experienced a major depressive disorder. Depression was less frequent in our current study, but it must be noted that we excluded patients receiving psychotropic drugs.

This study had several limitations of note. First, the study subjects were enrolled from a single tertiary center within a short period of time, which will likely have caused some selection bias. Second, there is a possibility that medication adherence was overestimated due to the use of a self-reported questionnaire. Third, although valid questionnaires used in previous studies were used, there is no gold standard for evaluating disease-related knowledge, depression and anxiety, or medication adherence. It remains necessary to analyze a larger number of IBD patients over a sufficient period in the future using more accurate measurement tools.

In conclusion, our present study is the first to investigate the relationship between medication adherence and self-efficacy in Korean patients with IBD using previously verified measurement tools [19,22,27-30] that enhanced the reliability and validity of the data. Our findings indicate that reducing the number of medication doses per day and improving self-ef-

ficacy will help to improve medication adherence among patients with IBD. Our current results thus provide useful basic data for the development of nursing interventions that can improve medication adherence in this patient population.

References

1. Mizoguchi E, Low D, Ezaki Y, Okada T. Recent updates on the basic mechanisms and pathogenesis of inflammatory bowel diseases in experimental animal models. *Intest Res* 2020;18:151-167.
2. Kim JM, Cheon JH. Pathogenesis and clinical perspectives of extraintestinal manifestations in inflammatory bowel diseases. *Intest Res* 2020;18:249-264.
3. Sood A, Kaur K, Singh A, Midha V, Mahajan R, Bansal N, et al. Trends of inflammatory bowel disease at a tertiary care center in northern India. *Intest Res* 2021;19:282-290.
4. Kaibullayeva J, Ualiyeva A, Oshibayeva A, Dushpanova A, Marshall JK. Prevalence and patient awareness of inflammatory bowel disease in Kazakhstan: a cross-sectional study. *Intest Res* 2020;18:430-437.
5. Park SH, Kim YJ, Rhee KH, Kim YH, Hong SN, Kim KH, et al. A 30-year trend analysis in the epidemiology of inflammatory bowel disease in the Songpa-Kangdong district of Seoul, Korea in 1986–2015. *J Crohns Colitis* 2019;13:1410-1417.
6. Baumgart DC, Sandborn WJ. Crohn's disease. *Lancet* 2012;380:1590-1605.
7. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. *Lancet* 2017;389:1756-1770.
8. Yoo JH, Holubar S, Rieder F. Fibrostenotic strictures in Crohn's disease. *Intest Res* 2020;18:379-401.
9. Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T, et al. ECCO guidelines on therapeutics in Crohn's disease: medical treatment. *J Crohns Colitis* 2020;14:4-22.
10. Harbord M, Eliakim R, Bettenworth D, Karmiris K, Katsanos K, Kopylov U, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 2: current management. *J Crohns Colitis* 2017;11:769-784.
11. Bassi A, Dodd S, Williamson P, Bodger K. Cost of illness of inflammatory bowel disease in the UK: a single centre retrospective study. *Gut* 2004;53:1471-1478.
12. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol* 2012;73:691-705.
13. Tae CH, Jung SA, Moon HS, Seo JA, Song HK, Moon CM, et al. Importance of patients' knowledge of their prescribed medication in improving treatment adherence in inflammatory bowel disease. *J Clin Gastroenterol* 2016;50:157-162.
14. Jackson CA, Clatworthy J, Robinson A, Horne R. Factors associated with non-adherence to oral medication for inflammatory bowel disease: a systematic review. *Am J Gastroenterol* 2010;105:525-539.
15. Kim MC, Jung YS, Song YS, Lee JI, Park JH, Sohn CI, et al. Factors associated with anxiety and depression in Korean patients with inactive inflammatory bowel disease. *Gut Liver* 2016;10:399-405.
16. Son YJ, Won MH. Depression and medication adherence among older Korean patients with hypertension: mediating role of self-efficacy. *Int J Nurs Pract* 2017;23:e12525.
17. Sewitch MJ, Abrahamowicz M, Barkun A, Bitton A, Wild GE, Cohen A, et al. Patient nonadherence to medication in inflammatory bowel disease. *Am J Gastroenterol* 2003;98:1535-1544.
18. Selinger CP, Eaden J, Selby W, Jones DB, Katelaris P, Chapman G, et al. Inflammatory bowel disease and pregnancy: lack of knowledge is associated with negative views. *J Crohns Colitis* 2013;7:e206-e213.
19. Keefer L, Kiebles JL, Taft TH. The role of self-efficacy in inflammatory bowel disease management: preliminary validation of a disease-specific measure. *Inflamm Bowel Dis* 2011;17:614-620.
20. Banerjee R, Pal P, Adigopula B, Reddy DN. Impact of demographic, clinical and psychosocial variables on drug adherence and outcomes in Indian patients with inflammatory bowel disease: cost is not the only factor! *J Clin Gastroenterol* 2021;55:e92-e99.
21. Lee J, Jee SR, Kim HW, Baek DH, Song GA, Moon W, et al. Factors associated with low adherence to oral 5-aminosalicylic acid in patients with ulcerative colitis. *PLoS One* 2019;14:e0214129.
22. Horne R, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. *Inflamm Bowel Dis* 2008;15:837-844.
23. Stone JK, Shafer LA, Graff LA, Lix L, Witges K, Targownik LE, et al. Utility of the MARS-5 in assessing medication adherence in IBD. *Inflamm Bowel Dis* 2021;27:317-324.
24. Kim JA, Kim ES, Lee EK. Evaluation of the chronic disease management program for appropriateness of medication adherence and persistence in hypertension and type-2 diabetes patients in Korea. *Medicine* 2017;96:e6577.
25. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39:175-191.
26. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 2009;41:1149-1160.
27. Yoon H, Yang SK, So H, Lee KE, Park SH, Jung SA, et al. Development, validation, and application of a novel tool to measure disease-related knowledge in patients with inflammatory bowel disease. *Korean J Intern Med* 2019;34:81-89.
28. Lee YJ, Kim YH, Kim HW. Preconception care program for women with inflammatory bowel disease using intervention mapping: a protocol for program development. *Int J Environ Res Public Health*

2020;17:9365.
29. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-370.
30. Oh SM Min KJ, Park DB. A study on the standardization of the hospital anxiety and depression scale for Koreans: a comparison of normal, depressed and anxious groups. *J Korean Neuropsychiatr Assoc* 1999;38:289-296.
31. Kane SV. Systematic review: adherence issues in the treatment of ulcerative colitis. *Aliment Pharmacol Ther* 2006;23:577-585.
32. Kim SB, Kim KO, Jang BI, Kim ES, Cho KB, Park KS, et al. Patients' beliefs and attitudes about their treatment for inflammatory bowel disease in Korea. *J Gastroenterol Hepatol* 2016;31:575-580.
33. Lim JK, Lee YJ, Park JH. Medication-related knowledge and medication adherence in pediatric and adolescent patients with inflammatory bowel disease. *J Korean Med Sci* 2020;35:e92.
34. Ashok K, Mathew AA, Thomas A, Mohan D, Gopalakrishna R, Reghu R. Clinical pharmacist's interventions on medication adherence and knowledge of inflammatory bowel disease patients. *J Young Pharm* 2017;9:381-385.
35. Moradkhani A, Kerwin L, Dudley-Brown S, Tabibian JH. Disease-specific knowledge, coping, and adherence in patients with inflammatory bowel disease. *Dig Dis Sci* 2011;56:2972-2977.
36. Nahon S, Lahmek P, Durance C, Olympie A, Lesgourgues B, Colombel JF, et al. Risk factors of anxiety and depression in inflammatory bowel disease. *Inflamm Bowel Dis* 2012;18:2086-2091.
37. Park JW Kim DH, Suh YS, Kim JB, Lee GH. Drug compliance according to severity of depressive symptoms in medically ill outpatients. *Korean J Health Promot* 2007;7:39-44.
38. Eaden JA, Abrams K, Mayberry JF. The Crohn's and Colitis Knowledge Score: a test for measuring patient knowledge in inflammatory bowel disease. *Am J Gastroenterol* 1999;94:3560-3566.
39. Kim JY, Yoon H, Hwang JS, Yang SK, Park SH, Loftus EV Jr. Comparison of disease-related knowledge of patients with inflammatory bowel disease between the West and the East using an updated questionnaire (IBD-KNOW). *J Clin Gastroenterol* 2020;54:720-724.
40. Graff LA, Walker JR, Bernstein CN. Depression and anxiety in inflammatory bowel disease: a review of comorbidity and management. *Inflamm Bowel Dis* 2009;15:1105-1118.

EMJ THE EWHA MEDICAL JOURNAL

Original Article

Ewha Med J 2022;45(2):46-54
https://doi.org/10.12771/emj.2022.45.2.46
eISSN 2234-2591

텍스트 마이닝을 활용한 COVID-19에 대한 대중의 관심 주제와 정서 분석

권나현*, 오종민*, 하은희
이화여자대학교 의과대학 환경의학교실

Topic and Trends of Public Perception and Sentiments of COVID-19 Pandemic in South Korea: A Text Mining Approach

Nahyun Kwon*, Jongmin Oh*, Eunhee Ha
Department of Environmental Medicine, Ewha Womans University College of Medicine, Seoul, Korea

Objectives: Public health risks and anxiety have been increasing since the outbreak of Coronavirus disease 19 (COVID-19). The public expresses questions related to the COVID-19 issue through the web base. The aim of this study was to analyze public perception and sentiments of COVID-19 Pandemic in South Korea.
Methods: We collected the text data (questions: 252,181) related to COVID-19 from Naver Knowledge-iN during January 1, 2020 to December 31, 2020. The search keywords included related to COVID-19 using Korean words for "SARS-Cov-2", "COVID19", "COVID-19", "Wuhan pneumonia", "Coronavirus", "Corona". A topic modeling analysis was used to investigate and search trends of public perception. The sentiment analysis was conducted to analyze of public emotions in the questions related to COVID-19. We performed the Pearson's correlation analysis between daily number of COVID-19 cases and daily proportion of negative sentiment in documents related to COVID-19 by COVID-19 outbreak period.
Results: A total of 241,776 documents used in this study. The most frequent words in the documents to appear cough, symptoms, tests, confirmed patients, mask and etc. Twenty topics (COVID-test, Economy, School, Hospital/Diagnose, Travel/Overseas, Health, Social issue, Symptom 1 (respiratory), Relationships, Symptom 2 (e.g., fever), Workplace, Mask/Social distancing, infection/Vaccine, Stimulus Package, Family, Delivery Service, Unclassified, Region, Study/Exam, Worry, Anxiety) were extracted using the topic modeling. There was a positive association between the daily counts of COVID-19 patients and proportion of negative sentiment. By COVID-19 period, Stage 4 had the highest correlation.
Conclusion: This study identified the South Korean public's interest and emotions about COVID-19 during the prolonged pandemic crisis. **(Ewha Med J 2022;45(2):46-54)**

Received January 24, 2022
Revised April 15, 2022
Accepted April 22, 2022

Corresponding author
Eunhee Ha
Department of Environmental Medicine,
Ewha Womans University College of Medicine,
260, Gonghang-daero, Gangseo-gu, Seoul
07804, Korea
Tel: 82-2-6986-6234, Fax: 82-2-6986-7022
E-mail: eunheeha@ewha.ac.kr

*These authors contributed equally to this work.

Key Words
COVID-19; Data mining; Sentiment analysis; Korea

서 론

2021년 11월 기준 전세계 코로나바이러스감염증-19 (Coronavirus disease 19, COVID-19, 코로나19) 누적 확진자는 2억 5천만명을 돌파하였다. 해외 유입 국내 COVID-19 감염자 발생은 2020년 1월 20일 처음 발생하였으며, 해외 유입이 아닌 국내 첫 환자 발생은 1월 30일 발생하였다. 이후 기하급수적으로 COVID-19 누적 확진자가 증가하였다.

국민들은 다양한 언론 매체, SNS, 포털 사이트 등을 통해 COVID-19의 발병 상황에 대해 언급하고 있다. 포털 사이트의 지식 응답은 사회 현상에 대해 즉각적인 커뮤니케이션을 요구하며 이러한 자료들은 주로 텍스트 형태의 빅데이터 자료로 존재한다[1].

텍스트 데이터는 구조화된 정형데이터와 달리 많은 양의 데이터를 가지고 있으며, 구조화되지 않은 형태의 자연어로 쓰여진 형태이다. 최근, 이러한 비정형 데이터인 텍스트 자료에 대해 텍스트 마이닝(text mining) 분석하여 여러 사회현상을 설명하려는 시도가 활발하게 이루어지고 있다.

이전의 몇몇 국외 연구들은 레딧(Reddit) 또는 트위터(Twitter)와 같이 소셜 미디어 자료를 기반으로 COVID-19 관련 텍스트 마이닝 분석을 수행한 바 있다[2,3]. 국내 트위터 및 네이버 지식인 자료를 이용하여 COVID-19과 대중의 인식, 불안 확산에 관해 수행한 연구들이 있다[4-6]. 이전 국내 연구들은 최소 1개월-최대 3개월의 비교적 짧은 기간 동안 수행되었다.

본 연구는 2020년 1월부터 2020년 12월까지 네이버 지식인에 등록된 COVID-19 관련 질의에 대하여 텍스트 마이닝 기법을 이용하여 국민들의 COVID-19과 관련된 주요 질문 주제와 핵심어를 도출하고자 하였다.

방 법

1. 자료 수집

본 자료는 2020년 1월 1일부터 2020년 12월 31일 동안 네이버 지식인에 COVID-19 관련 질의에 해당하는 일일 자료를 크롤링하였다. COVID-19 관련 검색 키워드는 다음과 같다: “SARS-Cov-2”, “COVID19”, “COVID-19”, “우한폐렴”, “코로나바이러스”, “코로나”. 네이버에서 제공하는 검색 결과는 최대 1,000건의 검색 결과만 제공하고 있다. 관련 검색 키워드를 네이버 지식인에 검색하면 한 페이지당 최대 10건의 질의를 제공하고 있다. 따라서 1일 최대 100페이지에 해당하는 질문 링크를 얻을 수 있다. 이중 중복되는 URL은 제거하였으며, CSV 파일 형태로 저장하였다.

2. 텍스트 자료 전처리

수집된 자료는 비정형 한글 텍스트 자료이기 때문에 분석 가용한 자료 형태로 변경하기 위해 텍스트 전처리를 수행하였다. (1) 결측 제거, (2) 숫자 제거, (3) 영문 제거, (4) 공백/띄어쓰기 제거, (5) 한글 불용어(stop words) 제거, (6) 구두점 제거 등을 수행하였다. (7) 한글 특성을 고려하여 ‘확진자가’, ‘확진자랑’, ‘확진자와’처럼 조사가 붙는 단어의 경우 ‘확진자’와 같이 하나의 명사로 처리하였다. 이후 통계적 기법을 적용할 수 있도록 질의 당 단어들에 대해 문서-단어 행렬(document-term matrix, DTM) 형태로 변환하였다. 단순히 단어의 출현 빈도가 아니라 특정 문헌에서 특정 단어의 출현 빈도의 비중을 고려한 term frequency-inverse document frequency (TF-IDF)를 가중치로 사용하였다. TF-IDF는 전체 문서들에서 빈번하게 출현하는 단어는 특정 문서의 구분에 잘 활용되지 않으므로 중요도를 낮게, 특정 문서에서 빈번하게 출현하는 단어의 중요도를 높게 고려하는 것으로 문서 빈도의 역수인 역문서 빈도와 단어 출현 빈도를 고려하여 계산한다[7].

3. 월별 단어 추이 분석

국민들의 COVID-19 관련 주제에 대한 추이를 살펴보기 위하여 단어별 빈도를 집계하였다. 전체 문서에서 출현 빈도가 높은 상위 20개 단어들을 추출하여, 상위 단어들의 월별 추이를 살펴보았다.

4. 토픽 모델링

본 연구에서는 토픽 모델링(topic modeling)을 수행하기 위해 주로 이용하는 비지도 학습 기법인 latent dirichlet allocation (LDA)를 이용하였다[8]. 토픽 모델링은 문서나 문헌 속의 텍스트에서 확률적으로 주제들을 추출하는 텍스트 마이닝 기법의 하나이다. LDA는 연속 확률 분포이며 다항분포인 디리클레 분포(Dirichlet distribution)를 허용하고 각각의 단어를 특정 주제에 할당하여 문장 내에 잠재된 의미(토픽)을 발견하는 방법이다[8].

LDA는 토픽별 단어의 분포와 문서별 토픽의 분포를 모두 추정하며 생성 과정은 다음과 같다.

$$p(\beta_{1:K},\theta_{1:D}Z_{1:D}W_{1:D}) = \prod_{i=1}^{K} p(\beta_i)\prod_{d=1}^{D} p(\theta_d)\left(\prod_{n=1}^{N} p(Z_{d,n}|\ \theta_d)p(w_{d,n}|\ \beta_{1:K},Z_{d,n})\right)$$

여기서 K는 토픽 수, D는 문서 수, n은 d번째 문서의 총 단어 개수를 의미한다. 토픽 분포 $Z_{d,n}$은 문서당 토픽의 분포 θ_d에 의존한다. $\beta_{1:K}$는 각 토픽을 의미하며 β_K는 주제별 어휘 분포

를 의미한다. d번째 문서의 n번째 단어인 단어 W_d는 유일하게 관찰 가능한 변수이며, 나머지 변수는 추정해서 얻어낼 수 있다.

토픽의 수는 토픽 분류의 정확성과 타당성에 영향을 미치기 때문에 토픽 결정 수에 따라 토픽 주제는 조금씩 달라질 수 있다. 따라서, 적절한 토픽의 수를 정하기 위해 모형의 복잡도(perplexity)와 로그 가능도(log-likelihood)를 계산하였다(Fig. 1)[9]. 전체 자료를 3:1로 훈련 자료(train set)와 검증 자료(validation set)로 분할하여 평가하였다. 복잡도를 평가하기 위해 토픽의 수는 2부터 100까지 그리드 서치(Grid search)하였다. 토픽의 수는 일반적으로 복잡도의 감소 폭이 완만해지는 지점으로 결정한다. 본 연구에서는 너무 많은 토픽의 수를 결정하는 것은 대중의 실제 관심사/이슈가 무엇인지 파악하기 어렵다고 판단하였고, 너무 적은 토픽의 수는 실제 관심사를 적게 반영한다고 고려하였다. 따라서 적정 토픽의 수를 10-30개 사이로 정하기로 고려하였고 최종적으로 토픽의 수를 20으로 결정하였다(Fig. 1).

각 추출된 토픽에 대해 연구진 협의를 거쳐 적정 토픽 레이블을 명명하였다(Table 1). 각 정의한 토픽 주제 20개의 주별 등장 확률을 계산하여 국내 유행 시기별 추이를 살펴보았다.

5. 감성 분석

연구 기간 동안 COVID-19 관련 주제에 대한 국민들의 인식을 살펴보기 위해 감성 분석(sentiment analysis)을 수행하였다. 감성 분석이란 감성 어휘(sentiment terms)와 어휘의 긍정 및 부정의 정도를 나타내는 극성(polarity)으로 구성된 감성 사전(sentiment dictionary or sentiment lexicon)을 활용하여 감성을 정량화 하는 것을 의미한다[10,11]. 대표적인 한국어 감성 사전으로는 서울대학교에서 개발한 한국어 감성분석 코퍼스(KOSAC)과 군산대학교에서 구축한 KNU 감성 사전이 있다. KNU 감성 사전에서 정의되는 감정은 인간의 보편적인 감정 표현을 나타내는 표현을 위주로 사용하고 있어 본 연구에서 활용하였다. KNU 감성 사전은 다양한 분야에서 사용될 수 있는 범용 감성 사전으로 국립국어원 표준국어대사전의 뜻풀이 분석을 통한 긍/부정 어휘를 추출하여 총 14,843개의 어휘(관용구, 문형, 축약어, 이모티콘)에 대한 극성 값이 계산되어 있다[12,13] .

각 일별 수집 문서 중 명사 단어와 KNU감성사전에서 정의된 부정어/긍정어를 강한 긍정(+2), 약한 긍정(+1), 중간(+0), 약한 부정(-1), 강한 부정(-2)의 점수를 연계하여 총 점수를 합산하였다. 문서에 대하여 합산된 점수가 양수이면 긍정(positive) 문서, 음수이면 부정(negative) 문서로 간주하여 일일 긍정 질의와 부정 질의를 분류 하였다. 수집된 일별 전체 문서를 분모로 하고, 부정 문서를 분자로 하여 일일 부정 정서 비율(proportion of negative sentiment)을 계산하였다.

본 연구에서는 산출한 일일 부정 정서 비율과 일일 확진자 수 간의 상관성을 파악하고자 하였다. 한국의 코로나19 확진자

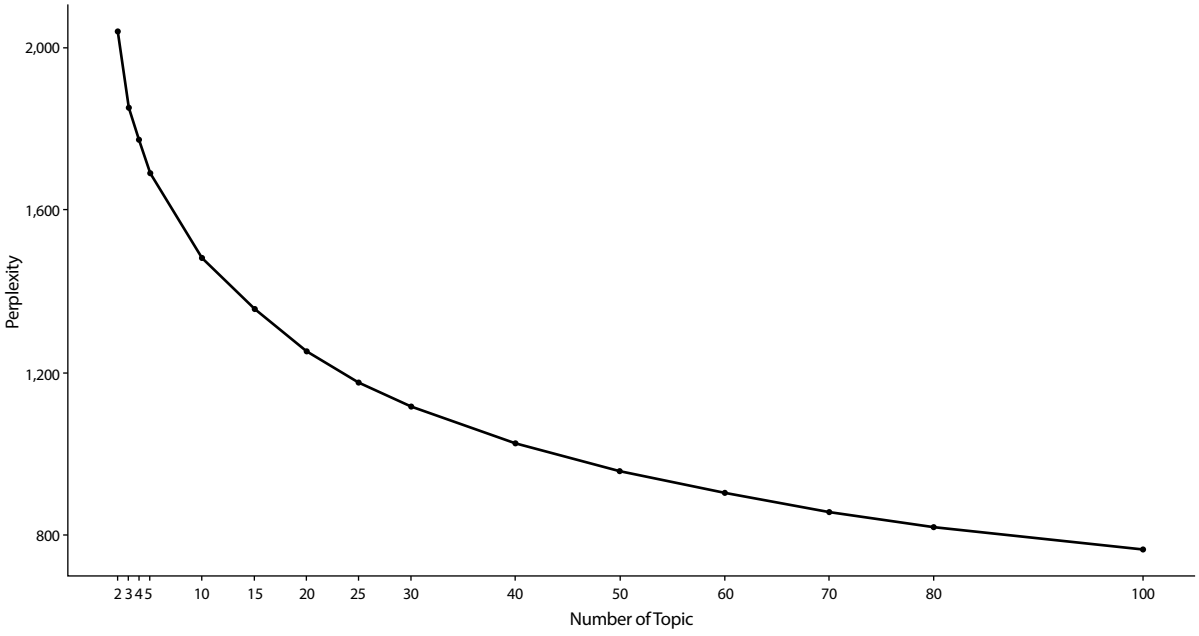

Fig. 1. The Perplexity of topic modeling related to COVID-19. The x-axis indicates the number of topic. The y-axis indicates perplexity of latent Dirichlet allocation (LDA) models.

Table 1. Topics related to COVID-19

OBS	Topic	Top keyword
1	COVID-test	'test', 'confirmed cases', 'sequester', 'self', 'contact', 'public health center', 'visit', 'result', 'negative', 'call'
2	Economy	'loans', 'contract', 'personal', 'progress', 'bank', 'situation', 'operation', 'monthly rent', 'card'
3	School	'school', 'academy', 'student', 'class', 'start of school', 'online', 'postponement', 'teacher', 'attending school', 'lecture'
4	Hospital/Diagnose	'hospital', 'pain', 'treatment', 'left', 'right', 'prescription', 'leg', 'doctor', 'clinic', 'surgery'
5	Travel/Oversea	'travel', 'situation', 'cancel', 'entry', 'oversea', 'refund', 'schedule', 'reservation', 'visa', 'period'
6	Life/Health	'exercise', 'method', 'start', 'day', 'life', 'support', 'health', 'diet', 'dog', 'health'
7	Social issue	'reason', 'thinking', 'government', 'Korea', 'church', 'nation', 'situation', 'country', 'economy', 'a new world'
8	Symptom 1 (respiratory)	'cough', 'symptom', 'runny nose', 'cold', 'sputum', 'fever', 'sneezing', 'rhinitis', 'dry cough', 'tickling'
9	Relationship	'friend', 'contact', 'idea', 'story', 'female', 'male', 'heart', 'worry', 'game', 'present'
10	Symptom 2 (headache, fever)	'head', 'symptom', 'headache', 'muscle pain', 'slight fever', 'body temperature', 'body ache', 'normal', 'suspicion', 'vomiting'
11	Workplace	'company', 'salary', 'work', 'unemployment', 'monthly salary', 'staff', 'resignation', 'job', 'commute', 'period'
12	Mask/social distance	'mask', 'stage', 'distance', 'food', 'cafe', 'bus', 'song', 'wearing', 'disinfection', 'utilization'
13	Infection/Vaccine	'person', 'infection', 'likelihood', 'pneumonia', 'dangerous', 'vaccine', 'Wuhan', 'probability', 'worry', 'Chinese'
14	Stimulus package	'application', 'subsidy' 'support', 'document', 'report', 'income', 'confirm', 'disaster', 'emergency', 'standard'
15	Family	'mother', 'thinking', 'father', 'parents', 'family', 'brother', 'stress', 'heart', 'grandmother', 'person'
16	Delivery service	'use', 'parcel service', 'delivery', 'purchase', 'call', 'internet', 'arrival', 'price', 'number', 'thing'
17	Unclassified	'problem', 'photo', 'partly', 'face', 'skin', 'situation', 'first', 'start', 'washroom', 'total'
18	Region	'region', 'Daegu', 'Busan', 'Gyeonggi', 'week', 'schedule', 'near', 'vacation', 'this year', 'Seoul'
19	Study/Exam	'study', 'examination', 'ready', 'school year', 'English', 'university', 'math', 'term', 'high school', 'middle term'
20	Worry/Anxiety	'worry', 'anxiety', 'stuffy', 'chest', 'symptom', 'usual', 'situation', 'uncomfortable', 'day', 'menstruation'

수 추이는 해외 유입, 신천지 관련, 집단 발병, 확진자 접촉, 개별 사례 등의 이유의 원인으로 시기별로 구분할 수 있다. 다만 코로나19 확진자 수의 증감 시기를 연구자 임의로 구분하기 어렵기 때문에 중앙대책본부 역학조사분석단에서 발표한 사회적 거리두기 지침에 따라 시기를 구분하였다. 정의한 코로나19 발생 양상의 기간(1–5기)에 따라 일일확진자수와 부정 정서 비율에 대해 피어슨 상관분석하였다[14].

모든 분석은 R 통계 소프트웨어(version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria)를 이용하여 수행하였다. 텍스트 마이닝을 분석을 위해 "*KoNLP*" "*tidyr*", "*tidytext*", "*topicmodels*" 등 R packages을 이용하였다.

결 과

1. COVID-19 관련 검색 키워드 빈도

총 252,181개의 문서 중 241,776개의 문서와 614,682개 단어를 이용하였다. 전체 개별 단어 중에서 가장 빈도가 높은 상위 20개 검색 키워드는 Fig. 2, 월별 추이 결과는 Fig. 3에 제시하였다. 가장 빈도가 높은 단어는 기침이었으며, 증상, 검사, 확진자, 마스크 순이었다(Fig. 2). 20개 키워드 중 12개 키워드('가래', '감기', '감염', '걱정', '기침', '두통', '마스크', '머리', '병원', '사람', '증상', '콧물')는 2월에 급증 이후 감소하는 패턴을 보였다. '신청' 키워드는 3–4월에 증가 추세 이후 감소하는 패턴을 나타냈다(Fig. 3). 5개 키워드('검사', '격리', '친구', '학교', '학원')는 연간 증가 추세를 보였다. '단계' 키워드는 7월 이후 12월까지 급증하였다. '확진자'는 2월 이후 증감을 반복하는 패턴을 보였다.

2. 20개 COVID-19 관련 주제

토픽 모델링으로 결정된 COVID-19 관련 질의에 대한 주제 20개는 Table 1에 제시되어 있다. 토픽 주제는 Topic 1: 검사, Topic 2는 자영업/경제, Topic 3: 학교/등교, Topic 4: 병원/진료, Topic 5: 여행/해외, Topic 6: 일상/운동, Topic 7: 사회현상, Topic 8: 증상 1(호흡기), Topic 9: 대인관계, Topic 10: 증

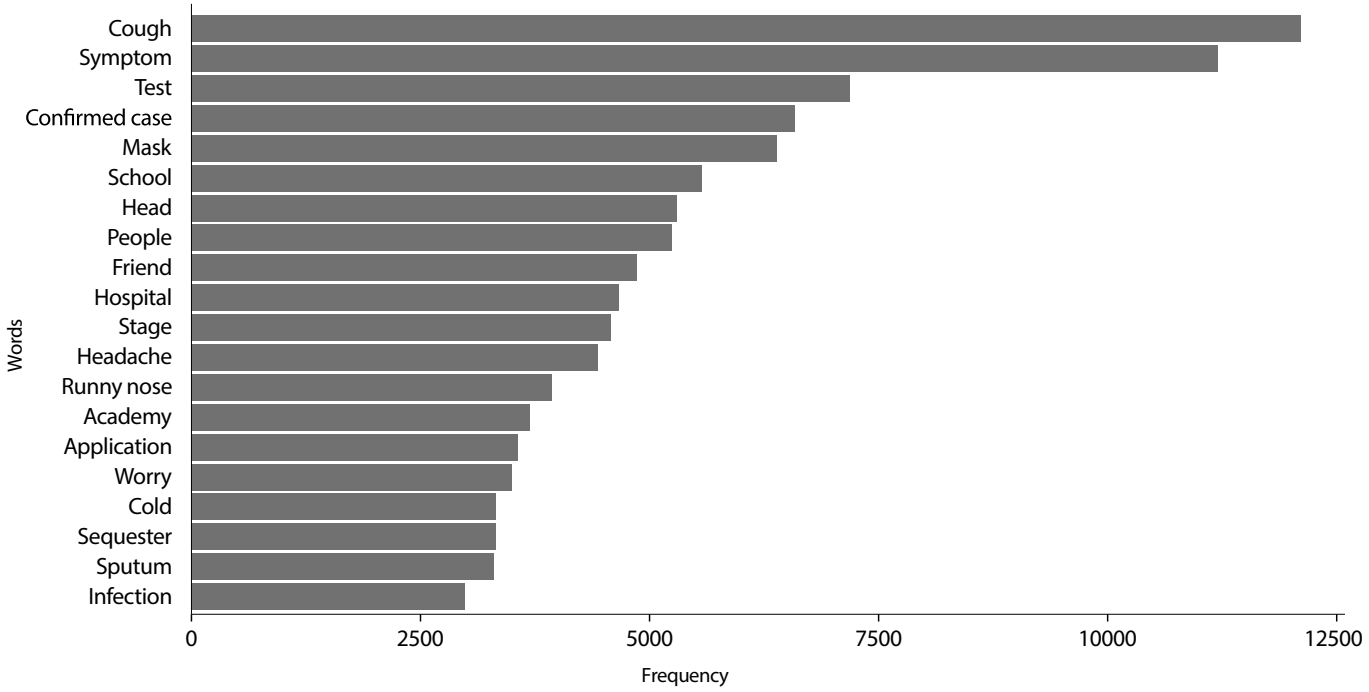

Fig. 2. Top 20 frequent words related to COVID-19 documents.

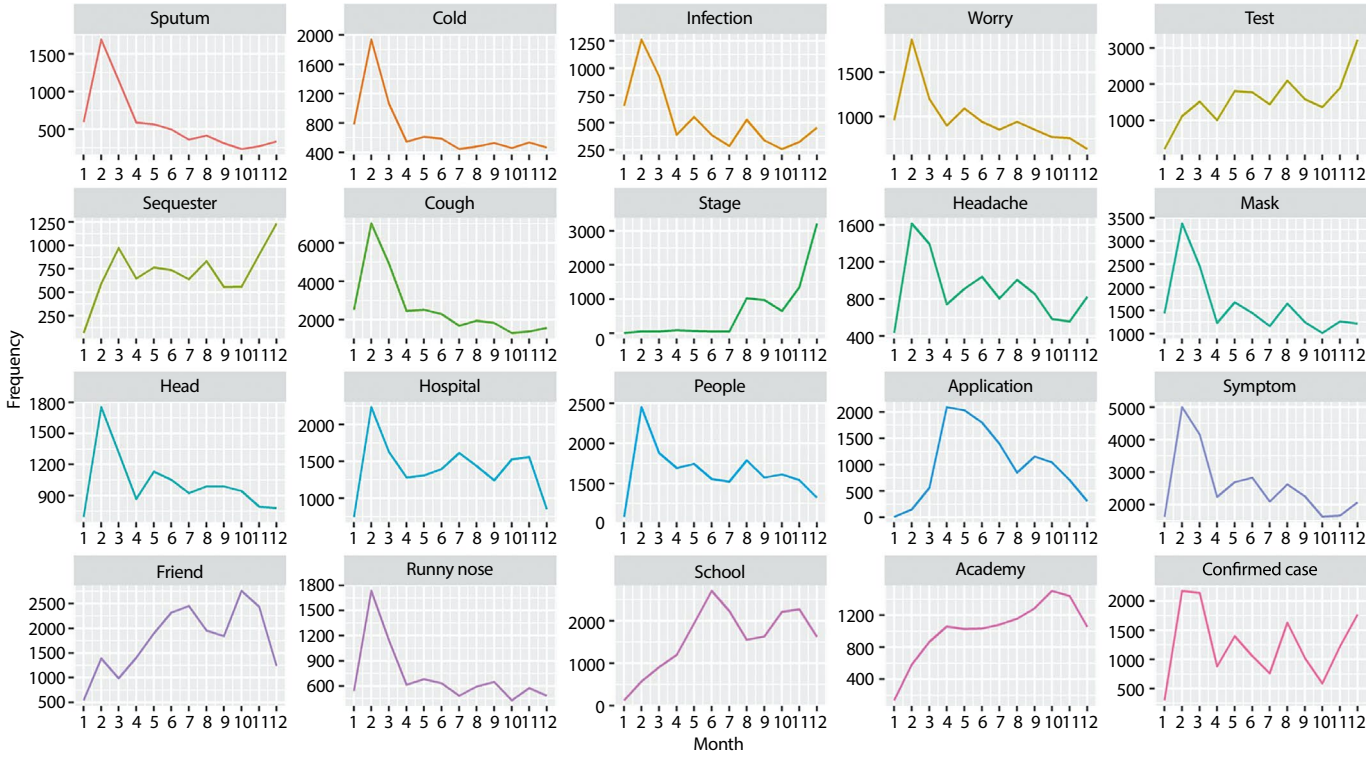

Fig. 3. Top 20 frequent words' monthly trend from January 1, 2020 to December 31, 2020. The x-axis indicates months. The y-axis indicates the frequency of words.

상 2(두통발열), Topic 11: 직장/회사, Topic 12: 마스크/단계, Topic 13: 감염/백신, Topic 14: 재난 지원금, Topic 15: 가족, Topic 16: 택배/구매, Topic 17: 미정, Topic 18: 지역, Topic 19: 공부/시험, Topic 20: 걱정/불안으로 정하였다. Fig. 4는 유행 시기별 토픽 주제의 일별 추이 변화를 보여준다. Topic 1: 검사, Topic 8: 증상 1(호흡기), Topic 12: 마스크/단계, Topic 14: 재난 지원금은 상반기에 증가 추세를 보이다 하반기에 점차 감소하였다. Topic 2: 자영업/경제, Topic 3: 학교/등교, 병원/진료 등은 코로나19 초기에 비해 증가 추세를 나타냈다.

3. 감성 분석 수행 결과

2020년 1월 20일부터 2020년 12월 31일까지 사회적 거리두기 정책변화와 코로나19 일일확진자수 발생 양상에 따른 표는 Table 2 [14]에 제시하였다. 연구 기간 동안 일일 확진자 수와 부정 정서 비율은 Fig. 5에서 볼 수 있다. 부정 정서 비율의 경우 2020년 2월 23일 0.920으로 연구 기간 동안 가장 높은 부정 정서 비율을 보였다. 연구 기간 전체 동안 일일 확진자 수와 부정 정서 비율의 상관계수는 0.170(P=0.001)으로 양의 상관성을 보였다. 제2기(2020.2.8–5.5)의 경우 r=0.659, 제4기(8.12–11.12)의 경우, r=0.739로 가장 높게 나타났으며, 제5기(11.13–12.31)의 경우 r=0.516이었다. 이에 비해 제1기(1.20–2.17)의 경우 r=0.281로 낮은 양의 상관관계를 보였다. 또, 제3기(5.6–8.11)는 가장 낮은 관련성을 보였다(r=–0.164).

고 찰

본 연구는 대규모의 비정형자료에서 토픽모델링을 통해 주요 키워드를 추출하고, 시기별/유행양상별 변화를 파악하며, 감성 분석을 통해 부정 정서 비율과의 연관성을 살펴봄으로써 COVID-19에 대한 대중의 관심 주제와 정서를 도출해낼 수 있음에 그 의의가 있다.

코로나19 발생 직후인 1–2월에는 코로나19의 일반적 증상에 대한 대중들의 궁금증이 높게 나타났음을 알 수 있다. 또, 이 시기는 공적 마스크 제도가 2020년 3월 9일 시행되기 전으로, 당시의 마스크 품귀 대란에 대한 대중의 관심과 초기 코로나19 감염 확산에 대한 대중들의 우려가 반영되어 '마스크'와 '감염' 키워드가 피크를 나타낸 것으로 해석될 수 있다. '단계'의 경우 질병관리청에 의해 위기 단계 조정이 이루어진 8월

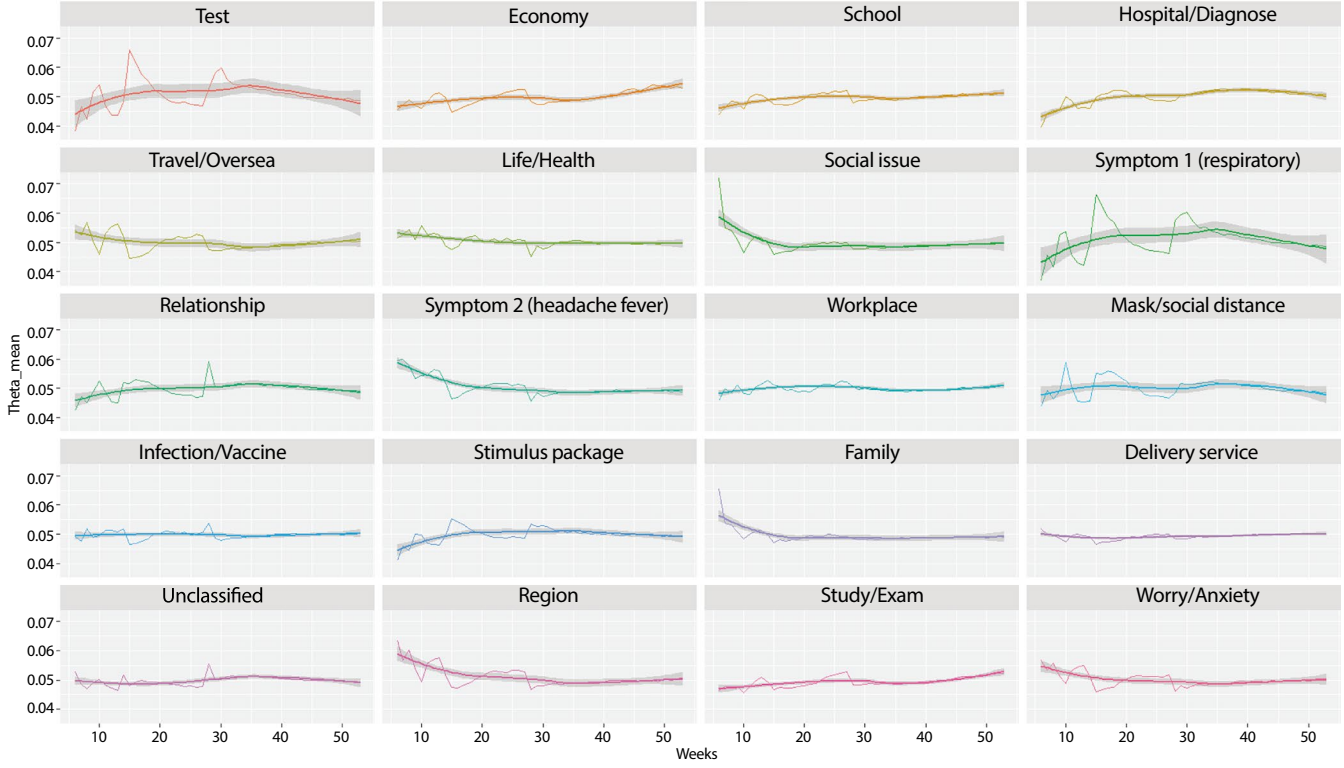

Fig. 4. The time-plot of 20 topics related to COVID-19 documents from January 1, 2020 to December 31, 2020. The x-axis indicates weeks. The y-axis indicates the probability that each topics appear.

Table 2. COVID-19 outbreak period

Categories	Stage 1	Stage 2 (1st Outbreaks)	Stage 3	Stage 4 (2nd Outbreaks)	Stage 5 (3rd Outbreaks)
Date	(2020.1.20–2.17)	(2.18–5.5)	(5.6–8.11)	(8.12–11.12)	(11.13–12.31)
Classification	Imported cases	Large-scale clusters	Local clusters, sporadic cases	Small and medium-scale clusters many outbreaks	A large outbreak nationwide
Confirmed cases	n=30	n=10,774	n=3,856	n=13,282	n=45,173

Adapted from Korea Disease Control and Prevention Agency [14] with CC-BY.

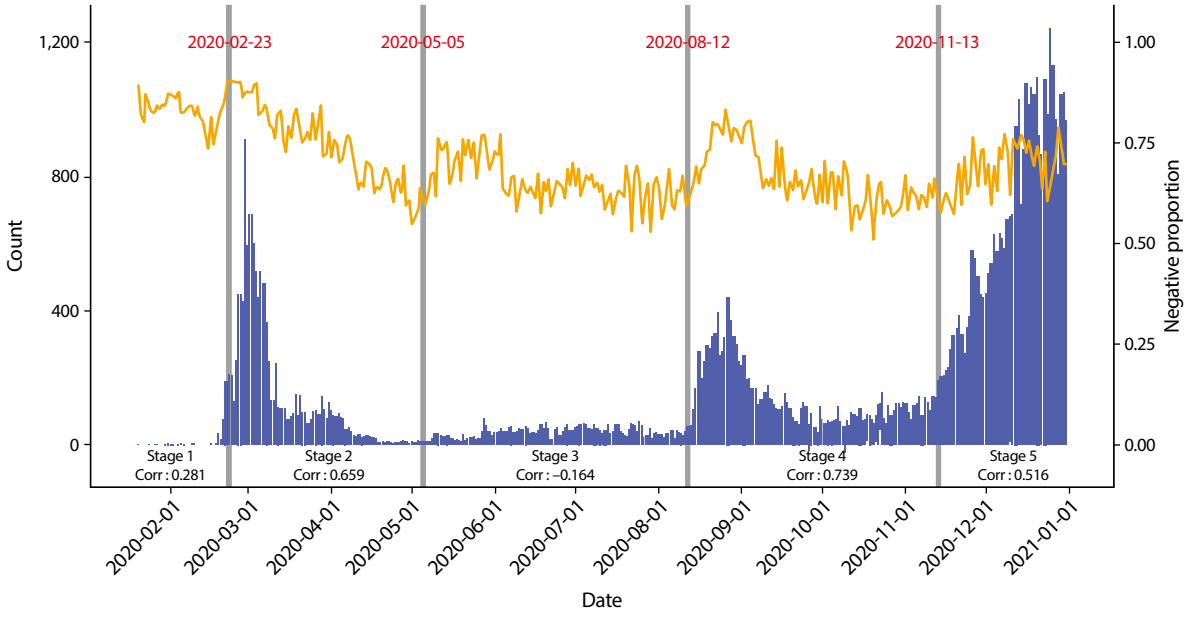

Fig. 5. The correlation of between daily COVID-19 cases and proportion of negative sentiment of documents from January 1 2020 to December 31 2020. The x-axis indicates date. The y-axis indicates the daily number of confirmed COVID-19 case (counts) in Korea. The auxiliary axis indicates the proportion of negative sentiment of documents. The blue bar indicates the daily number of confirmed COVID-19 cases. The orange line indicates the proportion of negative sentiment. Five stages are defined by Table 2. COVID-19 outbreak period (Stage 1: 2020.1.20–2.17, Stage 2: 2.18–5.5, Stage 3: 5.6–8.11, Stage 4: 8.12–11.12, Stage 5: 11.13–12.31).

과 12월에 특히 관심이 고조되었으며, 점점 정책의 변화에 대해 관심도가 높아진 것에 비해, '확진자'의 경우 2월의 대구, 경북 지역 중심의 1차 대유행, 5월의 소규모 집단발생, 8월의 2차 대유행시작 등 실제 확진자 수의 규모에 따라 영향을 받았음을 알 수 있다. '신청'의 경우 5월 긴급 재난 지원금 신청 및 지급 절차에 대한 정부 논의가 구체화되기 시작하여 5–6월에 대중의 관심이 높았음을 유추할 수 있다.

본 연구에서 토픽모델링을 통해 도출된 20개의 대중들의 코로나-19 관련 주제와 발견된 토픽의 1년간 추이를 파악할 수 있었다. 토픽들의 추이 변화는 코로나19 유행 양상, 정부의 지침, 개인의 사회적·경제적 지위, 국내외 코로나19 확진자 수 등에 따라 달라질 수 있으며, 향후 연구에서는 이러한 요인들을 고려할 필요가 있다.

코로나19 기간 동안 대중들의 정서와 일별 확진자 수간 관련성을 파악하기 위해 수행한 감성 분석을 토대로, 부정 정서 비율이 유행 양상과 상관성이 있음을 보인다. 2월 23일(0.920)은 지역사회가 감염되면서 정부에서 감염병 위기 단계를 '경계'에서 '심각' 단계로 격상한 시기와 일치하며 사회적거리두기 실시가 언급되기 직전으로 볼 수 있다. 5월 11일(0.761)은 5월 6일 생활 속 거리두기로 전환된 시점이지만, 5월초 수도권 유흥시설에서 시작된 집단감염 사례가 인근지역으로 확산된 시기와 밀접한 연관이 있다고 볼 수 있다. 8월 21일(0.800)과 8월 26일(0.830)의 경우, 수도권 일부교회 등 종교시설과 대규모 도심 집회 등 집단발생이 다수 일어난 시기와 일치한다. 12월 23일

(0.726)과 12월 28일(0.788)의 경우 코로나19 대유행 이후 최초 1,000명대 진입(12월 13일 이후)으로 2020년 최대 규모의 4차 대유행을 기록하며 고강도 사회적 거리두기가 이루어지던 시기와 연관성이 높다고 볼 수 있다.

부정 정서 비율을 코로나19 유행 양상에 따라 분류한 제5기와 상관분석을 진행한 결과, 제2, 4, 5기에서 부정 정서 비율과 일일 확진자수와의 상관관계가 높게 나타났다. 제2기(2020.2.8–5.5)의 경우 신천지 대규모 유행을 시작으로 의료기관, 종교기관, 다중시설의 집단발생이 전국적으로 발생, 확산되었으며 이로 인해 r=0.659의 높은 상관관계를 나타냄을 유추할 수 있다. 가장 높은 값(r=0.739)을 기록한 제4기(8.12–11.12)의 경우 수도권 종교시설, 대규모 집회 등 집단 발생과 더불어 위중증 환자도 다수 발생한 시기로 이와 관련성이 높다고 생각된다. 제5기(11.13–12.31)의 경우 수도권에서 전국적으로 확산되는 4차대유행과 고강도 거리두기로 인해 r=0.516)로 나타남을 알 수 있다. 이에 비해 제1기(1.20–2.17)의 경우, 중국 등 해외유입위주의 개별적 산발사례 발생 시기로, 감염병 위기단계가 '주의', '경계' 등의 초기 단계로 r=0.281(p=0.140)로 낮은 양의 상관관계를 보였음을 알 수 있다. 또, 제3기(5.6–8.11)는 5월 6일 '생활 속 거리두기' 전환 이후 소규모 집단에서 산발적으로 발생하였으며, 주로 200명 미만의 낮은 확진자 수를 기록하였기 때문에 이 시기의 상관계수가 r=–0.164로 가장 낮게 나타남을 유추할 수 있다.

본 연구의 강점은 다음과 같다. 첫째, 본 연구는 네이버 지식인에 등록된 COVID-19 관련 질의에 대하여 텍스트 마이닝 기법을 이용하여 국민들의 COVID-19과 관련된 주요 질문 주제와 핵심어를 도출하였다. 둘째, 본 연구는 토픽 모델링과 감성 분석을 수행함으로써 중심키워드와 관심의 경향, 유행 시기별 대중의 감정 변화를 유추하였다. 국내의 경우 감성 분석을 진행한 연구가 드물기 때문에 본 연구는 1년 동안 확진자 수, 유행 양상에 따라 국민들의 감성 수준을 확인하였다는 점에서 의의를 가진다.

셋째, 본 연구는 이전 코로나19 관련 초기 국내 연구들과 달리 상대적으로 연구 기간이 길다. 이전의 SNS, 뉴스 기사 등을 활용한 연구들은 연구 기간이 1–3달 내외로 수행되었다. 본 연구는 2020년 한 해 동안 COVID-19 유행양상시기와 코로나19 확진자 수 증감에 따른 질의 변화 추이를 파악할 수 있었다.

본 연구에서는 존재하는 한계점과 향후 연구 방향은 다음과 같다. 첫째, 우리는 질의를 올린 사용자의 인구통계학적 특징(성별, 연령 등)과 사회·경제학적 특징(지역, 소득수준, 직업 등)을 고려하지 못하였다. 또한 한 사람이 여러 질문을 할 수 있기 때문에 고유 대상자는 문서 수보다 적을 수 있다. 하지만 우리는 고유 대상자가 몇 명인지는 수집된 자료에서 알 수 없었다. 향후 사용자에 대해 이러한 특징을 파악할 수 있다면, 연령이나 성별, 지역에 따른 더 구체적인 분석 결과를 제시할 수 있을 것이다.

둘째, 우리는 연구 기간 동안 네이버 지식인에 COVID-19 관련 질의를 모두 모은 것이 아니라, 전체 자료 중 일부만 크롤링하였다. 네이버는 한국에서 가장 자주 사용하는 포털 사이트 중 하나임에도 불구하고 모든 사람들이 온라인 공간에 개인의 정보와 의견을 공유하지 않아 전체 인구 집단을 대표하기에 적절하지 않으며 연구 결과를 일반화하기 어렵다[4]. 연구 기간 동안 질의 전체를 추출한 것이 아니기 때문에 우리 연구에 샘플로서 포함되지 않은 질의들이 많다면, 우리 연구에서 산출한 토픽의 주제와 비율이 다를 수 있다. 또한 백신이나 재난 지원금 등 세부적인 검색 키워드로 주제들을 다루지 않아 도출된 단어나 토픽들로 대중의 관심과 이슈를 구체화하지 못하였다. 셋째, 한글은 영어와 달리 자연어에 영향을 많이 받으며 전처리 과정이 까다롭다. 향후 연구는 한글에 대한 정제된 자연어 처리 과정이 보완될 필요가 있다. 또한 문서 내의 단어의 출현 순서를 고려하지 않고 출현 빈도를 고려한 방법론을 고려했다[8,15]. 향후 연구에는 문서 내 단어 순서의 의미를 고려한 분석 방법론을 적용할 필요가 있다.

본 연구는 2020년 한 해 동안 네이버 지식인에 COVID-19 관련 검색어 관한 질의에 대한 토픽 모델을 수행하여 대중들의 관심사를 파악하고자 하였다. 이 연구는 대규모 한글 텍스트 자료를 처리하여 코로나19 기간 동안 대중들의 코로나19 관련 질의 주제, 주제 동향, 정서를 파악한 점에서 의의가 있다. 추후 연구에서는 코로나19 변이 시기에 따른 변화 양상과 다양한 매체와 자료원(뉴스, 역학조사, 설문자료, 인터뷰 자료 등)을 이용하여 분석 및 결과를 비교할 필요가 있다.

References

1. Lee SM, Ryu SE, Ahn S. Mass media and social media agenda analysis using text mining: focused on '5-day rotation mask distribution system.' *J Korea Content Assoc* 2020;20:460-469.
2. Boon-Itt S, Skunkan Y. Public perception of the COVID-19 pandemic on twitter: sentiment analysis and topic modeling study. *JMIR Public Health Surveil* 2020;6:e21978 .
3. Naseem SS, Kumar D, Parsa MS, Golab L. Text mining of COVID-19 discussions on reddit. In: He J, Purohit H, Huang G, Gao X, Deng K, editors. Proceedings of the 2020 IEEE/WIC/ACM International Joint Conference on Web Intelligence and Intelligent Agent Technology (WI-IAT); 2020 Dec 14-17; Melbourne. Piscataway (NJ): IEEE; 2020. p. 687-691.
4. Jo W, Lee J, Park J, Kim Y. Online information exchange and anxiety spread in the early stage of the novel coronavirus (COVID-19) out-

break in South Korea: structural topic model and network analysis. *J Med Internet Res* 2020;22:e19455.
5. Shim JG, Ryu KH, Lee SH, Cho EA, Lee YJ, Ahn JH. Text mining approaches to analyze public sentiment changes regarding COVID-19 vaccines on social media in Korea. *Int J Environ Res Public Health* 2021;18:6549 .
6. Jo W, Chang D. Political consequences of COVID-19 and media framing in South Korea. *Front Public Health* 2020;8:425.
7. Ramos J. Using TF-IDF to determine word relevance in document queries [Internet]. State College (PA): Citeseer; 2013 [cited 2022 Jan 10]. Available from: https://www.semanticscholar.org/paper/Using-TF-IDF-to-Determine-Word-Relevance-in-Queries-Ramos/b3bf6373ff41a115197cb5b30e57830c16130c2c.
8. Blei DM, Ng AY, Jordan MI. Latent dirichlet allocation. *J Mach Learn Res* 2003;3:993-1022.
9. Maier D, Waldherr A, Miltner P, Wiedemann G, Niekler A, Keinert A, et al. Applying LDA topic modeling in communication research: toward a valid and reliable methodology. *Commun Methods Meas* 2018;12:93-118.
10. Dubey AD. Twitter sentiment analysis during COVID-19 Outbreak [Internet]. Amsterdam: Social Science Research Network; 2020 [cited 2022 Jan 5]. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3572023.
11. Li N, Wu DD. Using text mining and sentiment analysis for online forums hotspot detection and forecast. *Decis Support Syst* 2010;48:354-368.
12. Suh H, So J. A study on the topic and sentiment of national petition data using text analysis. *Korean Data Anal Soc* 2020;22:999-1011.
13. Park SM, Na CW, Choi MS, Lee DH, On BW. KNU Korean sentiment lexicon: Bi-LSTM-based method for building a Korean sentiment lexicon. *J Intell Inf Syst* 2018;24:219-240.
14. Kim Y, Kim YY, Yeom H, Jang J, Hwang I, Park K, et al. COVID-19 1-year outbreak report as of January 19, 2021 in the Republic of Korea. *Public Health Wkly Rep* 2021;14:478-481.
15. Tang J, Meng Z, Nguyen X, Mei Q, Zhang M. Understanding the limiting factors of topic modeling via posterior contraction analysis. In: Xing EP, Jebara T, editors. Proceedings of the 31st International Conference on Machine Learning; 2014 Jun 21-26; Stroudsburg (PA) : International Machine Learning Society; 2014. p. 190-198.

Ewha Womans University College of Medicine