

# Relationship between the time required for transfer and outcomes in patients with appendicitis

## Experience at a tertiary military hospital in South Korea

Young Eun Ko, MD<sup>a</sup>, Se Jin Park, MD<sup>b</sup>, Ho Seung Kim, MD<sup>c,\*</sup>

### Abstract

A few studies have compared patients who were directly admitted with patients who were transferred to a tertiary facility for an appendectomy. However, there have been no reports of an association between the time to transfer and outcome in patients who underwent an appendectomy. As the only tertiary military hospital in South Korea, we occasionally encountered patients who were delayed for transfer due to the military environment. We hypothesize that patients with a longer time to transfer have a worse outcome. This study aimed to evaluate the relationship between the time to transfer and the outcome of patients who underwent an appendectomy.

Patients who underwent appendectomy in the tertiary military hospital in South Korea from May 2015 to April 2017 were analyzed retrospectively. The groups were divided by the time for the transfer. Four hours was used as the cut-off point to divide the early and delayed transfer groups. Time from symptom onset to hospitalization, time from diagnosis to surgery, and time from hospitalization to surgery were also analyzed to assess the effect of time for the transfer.

A total of 449 patients were analyzed: 293 with direct admission, 110 with early transfer, and 46 with delayed transfer. The time required for transfer was more critical for delaying appendectomy than the time from hospital admission to surgery. There was no difference in outcomes among the groups. When patients were compared according to the perforation, no differences were found in time from hospitalization to surgery, time from diagnosis to surgery, and presence of transfer. Multivariate analysis showed that a greater than 72 hours delay from symptom onset to hospitalization was associated with perforation (odds ratio=12.61; 95% confidence interval: 3.84–41.40;  $P < .001$ ).

Even if a long transfer time is necessary, an appendectomy can be performed safely if patients were administered antibiotics immediately after diagnosis.

**Abbreviations:** AFCH = Armed Forces Capital Hospital, BMI = body mass index, CRP = C-reactive protein, CT = computed tomography, ESR = erythrocyte sedimentation rate, WBC = white blood cell.

**Keywords:** appendectomy, delay, outcome, transfer

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REK and SJP contributed equally to the work.

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<sup>a</sup> Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sunkyunkwan University School of Medicine, Seoul,

<sup>b</sup> Department of Surgery, The Armed Forces Capital hospital, Gyeonggi-do,

<sup>c</sup> Department of Surgery, Yonsei University College of Medicine, Seoul, Korea.

\* Correspondence: Ho Seung Kim, Department of Surgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-Gu, Seoul 03722, Korea (e-mail: thankjkk@naver.com).

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### 1. Introduction

Since healthcare facilities use diagnostic tools, such as computed tomography (CT) and ultrasonogram, many patients can be diagnosed with appendicitis and then transferred for surgery. The time required to transfer to a hospital means these patients have a longer time from diagnosis until surgery compared with patients who are admitted directly. Previous studies have found that patients in rural areas have a higher rate of complicated appendicitis.<sup>[1,2]</sup> Although there has been debate as to whether appendicitis is a condition requiring emergency surgery,<sup>[3–6]</sup> early appendectomy is beneficial for the patients.

A few studies have compared patients who were directly admitted with patients who were transferred to a tertiary facility for appendectomy.<sup>[7–9]</sup> These studies found that there was no difference in the incidence of complications between the 2 groups. One study found that patients who were transferred were associated with higher rates of perforation and open conversion, as well as a longer hospitalization.<sup>[7]</sup> These studies did not include data for the amount of time to transfer, but only categorized patients based on whether they were transferred to the hospital or directly admitted. Further research on the association between the time to transfer and the outcome is necessary.

As the only tertiary military hospital in South Korea, many patients with appendicitis have been transferred to Armed Forces Capital Hospital (AFCH) for an appendectomy. Most patients come to our hospital immediately after the diagnosis is made. Occasionally, the time to transfer has been delayed due to the military environment. We hypothesize that patients with a longer time to transfer have a worse outcome. The aim of this study was to evaluate the relationship between the time to transfer and the outcome of patients who underwent appendectomy and to determine the factors that affect the clinical outcome.

## 2. Methods

A retrospective analysis of 520 patients who underwent appendectomy in AFCH from May 2015 to April 2017 was performed. Patients admitted directly to our hospital were diagnosed with appendicitis using CT in the emergency department. Cephalosporin and metronidazole were started once the diagnosis of appendicitis was made. All patients who were transferred had been diagnosed with appendicitis using CT in other military hospitals. Surgeons in the other military hospitals usually administer antibiotics immediately after diagnosis and call surgeons in our hospital for possible surgery. Surgeons in our hospital performed appendectomies on a rotating basis determined by the call schedule. Patients were discharged when they could perform their duties in the army.

The exclusion criteria are as shown in Figure 1. We excluded patients who had no preoperative laboratory test in our hospital, had incorrect medical records, underwent interval appendectomy, or underwent an incidental appendectomy. Those with appendectomy due to the failure of nonoperative treatment were also excluded. Because two-thirds of the patients arrived for

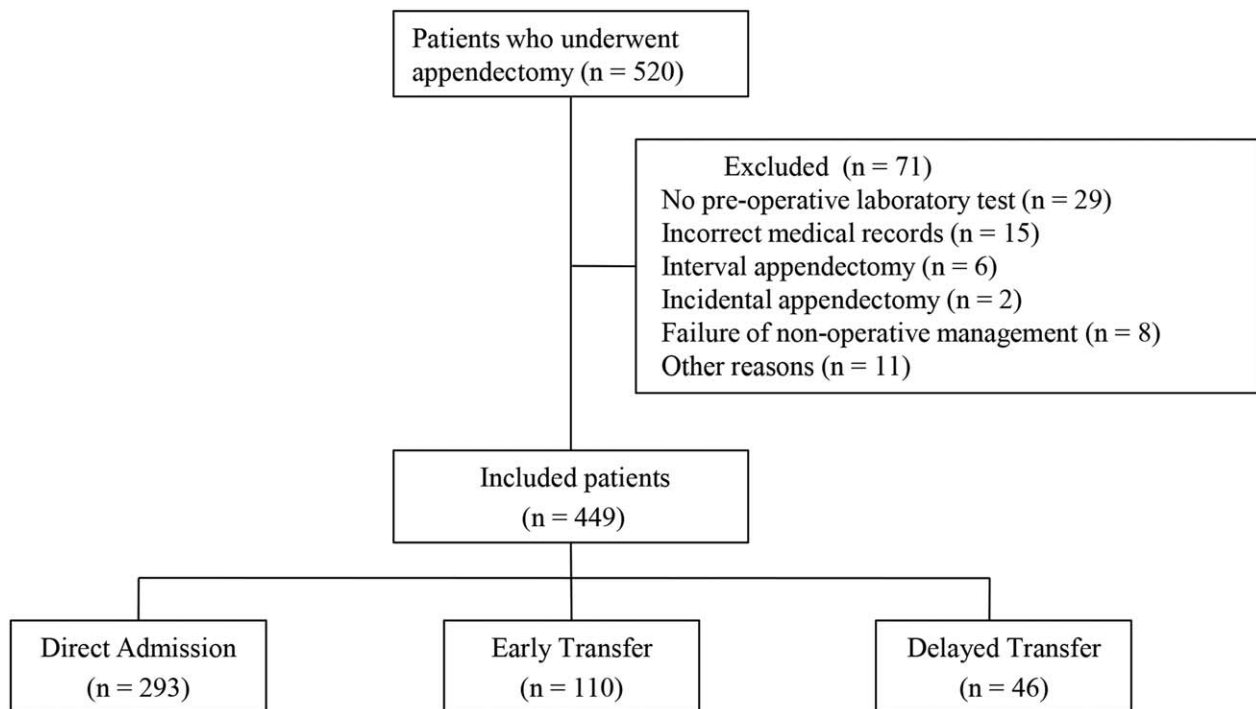
surgery within 4 hours, we used 4 hours as the cut-off point for defining the early and delayed transfer groups. A total of 449 of the 520 identified patients met the inclusion criteria and were analyzed.

### 2.1. Measurement

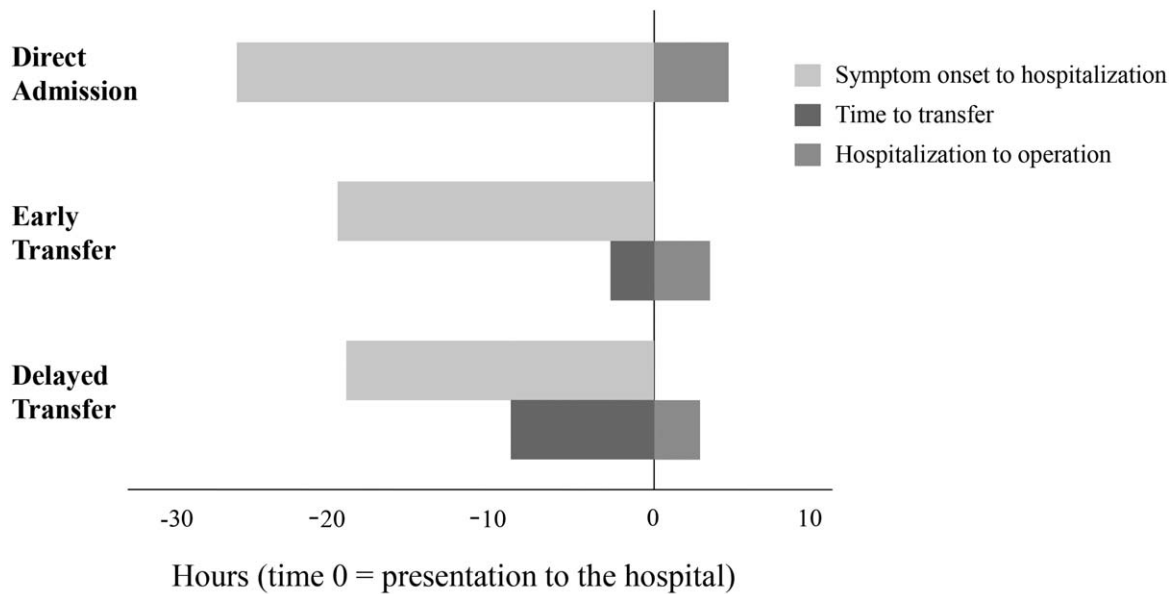
The following patient characteristics were obtained: age, time from symptom to hospitalization, body temperature, body mass index (BMI), white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, time from hospitalization to surgery, and time from diagnosis to surgery for the preoperative status. The outcome was determined based on the following: type of surgery, surgical findings, drain placement, the time required for surgery, the day on which a normal diet was started, duration of treatment with intravenous antibiotics, length of hospital stay, postoperative fever, and complications. To evaluate the time to transfer, we assumed that patients were transferred immediately after diagnosis in other military hospitals and therefore the CT capture time was used as the time of diagnosis. Day-time surgery was defined as being from 08:30 to approximately 17:30. Surgical findings were categorized as inflammation and perforation. To determine the factors that affected perforation, we divided the groups into 2 subgroups based on the presence of perforation.

### 2.2. Statistical analysis

Data analysis was performed using IBM SPSS Statics 21 for Windows. One-way analysis of variance and independent samples *t* test were used for comparison of independent continuous variables. Tukey honest significant difference test



**Figure 1.** Study flowchart. Exclusion and inclusion criteria are outline. We only included patients who visited the hospital through the emergency department and underwent emergency appendectomy.



\* Time to transfer + Hospitalization to operation = Diagnosis to operation

**Figure 2.** Timeline: Events from onset of symptoms to surgery. This figure shows a timeline to illustrate the definition of onset of symptoms to surgery. Time 0 is presentation at the hospital. The time from the onset of symptoms to hospitalization was not significantly different among the groups. Although the time from hospitalization to surgery was shorter in the transferred patient groups, the time from diagnosis to surgery, which includes time to transfer, was increased along 3 groups.

was used for posthoc examination. For categorical data, linear by linear association, the Chi-squared test, and Fisher exact test were used. A multiple logistic regression model was created to estimate the odds ratio. Significance was set at  $P < .05$ .

### 3. Results

#### 3.1. Time before surgery

To understand the patient's progression before surgery, Figure 2 shows each group's timeline of events from symptoms to surgery. The results for time from symptoms to hospitalization and for time from hospitalization to surgery are shown in Table 1. The mean ( $\pm$ standard deviation) time to transfer was  $2.6 \pm 0.7$  and  $8.3 \pm 4.7$  hours for the early and delayed transfer groups, respectively.

#### 3.2. Patient characteristics and comparison between different groups

A total of 449 patients were evaluated in this study: 293 with direct admission, 110 with early transfer, and 46 patients with delayed transfer. Patient characteristics are shown in Table 1. Age, time from symptoms to hospitalization, body temperature, BMI, ESR, and CRP levels were similar among the 3 groups. WBC count and neutrophil count were lower in the delayed transfer group compared with the other groups. Surgery was performed after 17:30 more often in both transfer groups. The time from diagnosis to surgery was shorter in the direct admission group. The time from hospitalization to surgery, which indicates an in-hospital delay, was shorter in both transfer groups compared to the direct admission group. Other factors related to outcome were not different among the 3 groups.

#### 3.3. Patient characteristics and comparison between nonperforated and perforated groups

Table 2 summarizes patient characteristics regarding perforation. A total of 51 patients (11.4%) had a surgical finding of perforation. Patients with perforated appendicitis were more likely to have waited longer following symptom onset, higher body temperature, and ESR. There was no difference among the groups for time from hospitalization to surgery, time from diagnosis to surgery, or presence of transfer. Other factors related to outcome, other than complications, were worse in patients with perforation.

#### 3.4. Clinical factors associated with perforation

Table 3 shows the results of a logistic regression analysis to evaluate the risk factors for perforation. Time from symptoms to hospitalization, body temperature (odds ratio=3.69; 95% confidence interval: 2.21–6.17;  $P < .001$ ), and ESR (odds ratio =1.12; 95% confidence interval: 1.06–1.17;  $P < .001$ ) were significantly associated with perforation. The time from onset of symptoms to hospitalization was significant only for patients who had symptoms for more than 72 hours (odds ratio=12.61; 95% confidence interval: 3.84–41.40;  $P < .001$ ).

### 4. Discussion

Our analysis demonstrates that the time to transfer was not associated with the outcome in patients with appendicitis. As we divided the patients according to the time to transfer, we hypothesized that the delayed transfer group would have a worse outcome than the directly admitted group. Due to the particular conditions related to the military, many patients with long transfer times were included; the longest time to transfer was

**Table 1**  
**Baseline characteristics.**

	Direct admission (n=293)	Early transfer (n=110)	Delayed transfer (n=46)	P
Age, yr	23.5±5.5	22.7±3.9	23.4±4.3	.316
Body mass index, m/kg <sup>2</sup>	23.2±2.8	23.5±2.6	23.9±2.4	.309
Body temperature, °C	37.0±0.7	36.9±0.5	36.7±0.6	.056
Laboratory test				
White blood cell count, $\mu$ L	13,274±4195	14,267±3532	12,107±3726	.006
Neutrophil count, %	78.0±9.9	80.1±9.8	73.9±10.1	.002
ESR, mm/h	5.5±5.8	5.6±5.7	6.4±7.1	.606
CRP, mg/dL	3.9±26.6	2.9±4.5	3.3±3.8	.911
Time interval before surgery, h				
Symptom to hospital	26.1±37.2	19.2±23.7	18.5±24.5	.098
Diagnosis to surgery	3.8±2.2	5.8±1.8	10.9±4.8	<.001
Hospital to surgery	4.3±2.3	3.2±1.8	2.7±1.3	<.001
Time of operation				.028
Day time	143 (48.8)	38 (34.5)	18 (39.1)	
Night time	150 (51.2)	72 (65.5)	28 (60.9)	
Type of operation				.525
Laparoscopic appendectomy	289 (98.6)	108 (98.2)	46 (100)	
Open appendectomy	0 (0)	1 (0.9)	0 (0)	
Open convulsion	4 (1.4)	1 (0.9)	0 (0)	
Perforation	36 (12.3)	13 (11.8)	2 (4.3)	.189
Drain placement	104 (35.5)	38 (34.5)	14 (30.4)	.538
Operating time, min	50.2±21.6	50.9±23.6	47.7±16.8	.696
Normal diet (POD)	2.2±0.9	2.1±0.8	2.1±0.6	.296
Antibiotics (POD)	2.2±2.1	2.2±2.3	1.7±1.4	.294
Length of hospital stay (POD)	10.6±5.3	11.7±9.1	10.1±3.4	.247
Postoperation fever	39 (13.3)	7 (6.4)	5 (10.9)	.189
Complications				
Wound infection	12 (4.1)	5 (4.5)	0 (0)	.965
Abscess	1 (0.3)	0 (0)	1 (2.2)	
Ileus	1 (0.3)	1 (0.9)	0 (0)	
Port hematoma	1 (0.3)	1 (0.9)	0 (0)	

Values are reported at the mean  $\pm$  standard deviation or n (%) of patients.

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, POD = postoperative day.

20.8 hours. Contrary to our expectations, no differences among the groups were found.

This result is part of the currently changing concept that appendicitis does not require emergency surgery. Some surgeons suggest that semi-elective surgery is sufficient.<sup>[4,10–12]</sup> A number of reports suggest that a short, in-hospital delay of appendectomy does not increase perforation rates or result in a worse outcome.<sup>[3,4,6,12–16]</sup> In our data, the time to transfer caused delaying time to appendectomy compared with the time from hospitalization to surgery. The mean time from diagnosis to surgery in transferred patients was 7.28 hours (range: 3.35 to 23.22 hours). This is similar to the previously reported in-hospital delay of 6 to 24 hours.<sup>[3,4,6,12–16]</sup>

We postulate that the lack of a difference among the groups can be attributed to the administration of antibiotics. The decreased WBC and neutrophil counts in the delayed transfer group is a clue for this hypothesis. Farach et al also suggested that the lack of a difference between the short- and long-delay transfer groups may be attributed to the administration of antibiotics once the diagnosis of appendicitis has been made.<sup>[8]</sup> Recent studies have shown the effectiveness of antibiotics in appendicitis.<sup>[17–19]</sup>

Leberer et al suggested that transferred patients show higher perforation and open conversion rates and require longer hospitalization than patients who are directly admitted.<sup>[7]</sup> This result, however, has a selection bias as the transferred patients had higher American Society of Anesthesiologists physical status

scores. Most enrolled patients in our study were healthy young men. A few patients older than 30 years had a chronic illness. There were no clinical preoperative characteristic differences among the groups. Only 1 open appendectomy was performed due to a patient's pulmonary risk of asthma. Our study did not show differences in perforation rate, type of surgery, or length of hospital stay.

Another important finding was that surgery was performed more frequently in the evening and the night (after 17:30) in transferred patients. This is similar to results from a previous study that showed that directly admitted patients were significantly more likely to arrive between the hours of 09:00 and 17:59 when compared to the transferred patients.<sup>[8]</sup> We thought that this result was due to the amount of time to transfer. Although patients were diagnosed during the day in other hospitals, they would arrive at our hospital in the evening. There was no difference in outcome according to the time of the surgery. Yardeni et al demonstrated that a semi-elective approach to acute appendicitis affords a better work environment for the entire operating room team and has substantial implications for healthcare workers in cases where there are work-hour limitations.<sup>[4]</sup>

Consequently, the major risk factor for perforation and poor outcome was the time from onset of symptoms to hospitalization. This finding is similar to that of previous studies.<sup>[15,20]</sup> Ditillo and colleagues suggested that prehospital delays were more pro-

**Table 2**  
Patient characteristics and comparison between non-perforated and perforated groups.

	Nonperforation (n=398)	Perforation (n=51)	P
Age, yr	23.2±4.7	24.1±7.2	.379
Body mass index, m/kg <sup>2</sup>	23.3±2.7	23.6±3.1	.433
Body temperature, °C	36.9±0.5	37.5±0.9	<.001
Laboratory test			
White blood cell count, µL	13313±4006	14052±4223	.218
Neutrophil count, %	77.9±10.0	79.8±9.9	.191
ESR, mm/h	4.8±4.7	11.8±9.6	<.001
CRP, mg/dL	3.2±22.8	7.2±7.3	.207
Time interval before surgery			
Symptom onset to hospital, h	20.4±29.0	48.4±50.7	<.001
Diagnosis to surgery, h	5.0±3.3	4.9±3.8	.878
Hospital to surgery, h	3.9±2.1	4.1±2.5	.436
Transfer-in patients	141 (35.4)	15 (29.4)	.396
Time of operation			
Day time	175 (44.0)	24 (47.1)	.765
Night time	223 (56.0)	27 (52.9)	
Type of operation			
Laparoscopic appendectomy	395 (99.2)	48 (94.1)	.001
Open appendectomy	1 (0.3)	0 (0)	
Open convulsion	2 (0.5)	3 (5.9)	
Drain placement	113 (28.4)	43 (84.3)	<.001
Operating time, min	47.2±17.8	72.8±33.1	<.001
Normal diet (POD)	2.1±0.6	3.2±1.4	<0.001
Antibiotics (POD)	1.8±1.5	5.1±3.5	<.001
Length of hospital stay (POD)	10.4±5.5	14.0±10.2	.018
Postoperative fever	31 (7.8)	20 (39.2)	<.001
Complications	19 (4.8)	4 (7.8)	.316

Values are reported at the mean±standard deviation or n (%) of patients.

CRP=C-reactive protein, ESR=erythrocyte sedimentation rate, POD=postoperative day.

foundly related to worsening pathology when compared to in-hospital delays.<sup>[20]</sup> Pittman-Waller and colleagues suggested that a patient's delay in the presentation was the only significant factor determining the incidence of complicated appendicitis.<sup>[15]</sup> In our study, only patients who had symptoms for more than 72 hours had a meaningful odds ratio of 12.61 compared with patients who had symptoms for <24 hours (95% confidence interval: 3.84–41.40). There was no statistically significant difference for patients who had symptoms for <72 hours. This result is also consistent with other studies. In these studies, the odds for progressive pathology were 13-times higher for patients with symptoms >71 hours compared with patients with symptoms <12 hours, and the time to surgery had a strong inverse correlation with the risk of histopathologic perforation.<sup>[15,20]</sup>

Most previous studies have shown results of in-hospital delay because prehospital delay is inevitable. In previous studies with a

**Table 3**  
Factors associated with perforation after logistic regression.

	Relative risk (95% CI)	P
Symptom onset to hospital 24≤48 h	1.61 (0.66–3.95)	.291
Symptom onset to hospital 48≤72 h	2.30 (0.63–8.36)	.205
Symptom onset to hospital >72 h	12.61 (3.84–41.40)	<.001
Body temperature, °C	3.69 (2.21–6.17)	<.001
ESR, mm/h	1.12 (1.06–1.17)	<.001

CI=confidence interval, ESR=erythrocyte sedimentation rate.

large number of patients, 12 hours of in-hospital delay was used as the cut-off value.<sup>[3,12,13]</sup> They showed in-hospital delay did not increase the risk of complex appendicitis. However, they did not commented on effects of antibiotics administration. In our data, we are able to see that delays <7 hours appear to have no influence on patient outcomes. We believe that this result may be possible due to immediate antibiotic administration after diagnosis. Further research is necessary on the administration of antibiotics in patients with a surgical plan.

The major limitation of this study is that it is a retrospective analysis and includes a relatively small sample size. Second, the time from the onset of symptoms to hospitalization is difficult to measure. The investigators had to rely on statements from the patients. Third, an observational study at 1 institution limits generalizability to other populations. Nevertheless, as the 1st study including the time to transfer, our results are meaningful for surgeons who have to determine the timing of an appendectomy and to the physicians who need to determine the transfer.

Patients who are diagnosed with appendicitis and transferred from other hospitals for definitive care were not found to have poorer outcomes. Moreover, there was no difference in outcome between the early and delayed transfer groups. Even if a long time is necessary for transfer, an appendectomy can be performed safely if patients were administered antibiotics immediately after diagnosis. As a progressive disease, the outcome of appendicitis is primarily influenced by the time from the onset of symptoms to hospitalization. If this interval is longer than 72 hours, it is associated with a poor outcome.

## Author contributions

**Conceptualization:** Ryoung Eun Ko, Ho Seung Kim.

**Data curation:** Ho Seung Kim.

**Formal analysis:** Se Jin Park, Ho Seung Kim.

**Investigation:** Se Jin Park, Ho Seung Kim.

**Methodology:** Ho Seung Kim.

**Project administration:** Ho Seung Kim.

**Resources:** Ho Seung Kim.

**Software:** Ryoung Eun Ko.

**Supervision:** Ryoung Eun Ko, Se Jin Park.

**Validation:** Ho Seung Kim.

**Visualization:** Ryoung Eun Ko.

**Writing – original draft:** Ho Seung Kim.

**Writing – review & editing:** Ryoung Eun Ko, Se Jin Park.

Ryoung Eun Ko orcid: 0000-0003-4935-5623

Ho Seung Kim orcid: 0000-0002-7378-0584

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