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Original Article

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Significance of Follow-Up Ultrasonography 24 Hours Post-Reduction in Detecting Intussusception Recurrence

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Purpose: The objective of this study was to identify the significance of 24-hour post-reduction ultrasonography (US) in pediatric patients with intussusception.
Methods: A total of 229 patients with intussusception who were treated with saline reduction at Severance Children's Hospital between January 2014 and September 2020 were retrospectively reviewed. The 229 patients with successful saline reduction were divided into two groups: a recurrence at 24 hours group (R, n=41) and a non-recurrence group (NR, n=188). The full patient sample was divided into two groups: follow-up US (FU) or no follow-up US (NFU); the recurrence group was divided into follow-up (R-FU) and non-follow-up (R-NFU) subgroups, and stratified analyses were performed.
Results: There were no significant differences in age, sex, laboratory findings, symptoms, and sonographic findings between the NR and R groups. In the R group, 24 patients underwent follow-up US, and 17 patients did not. Specific sonographic findings were statistically significant in the R-FU group compared to the R-NFU group (p=0.002). The R-FU group had fewer admissions (p=0.012) and longer mean hospitalization times (p<0.001) than the R-NFU group. The NFU group had a 12.2% recurrence rate, while the R-FU group recurrence rate was 25.8% (p=0.0099), suggesting that the omission of some recurrent events and follow-up US was a significant variable in the recurrence of intussusception. The median time to recurrence was 21 hours which supports the 24-hour follow-up protocol.
Conclusion: Twenty-four-hour follow-up US was shown to be valuable for detecting early recurrence of intussusception.

Keywords: Intussusception; Pediatrics; Recurrence; Ultrasonography

INTRODUCTION

Intussusception is one of the most common causes of abdominal pain and intestinal obstruction in pediatric patients [1]. The intussusception rate is 35/100,000 infants in the United States and 28.3/100,000 in South Korea, with a male predominance in both countries [2,3].

The major symptoms are irritability, abdominal pain, vomiting, and hematochezia. Ultrasonography (US) is a definitive diagnostic tool, and US-guided enema is the most common treatment [4-6].

The reported recurrence rates are highly variable. A meta-analysis of the Cochrane database that included pediatric patients aged 0-18 years from 1996 to 2011 found a recurrence rate of 12.7% following contrast enema, and 7.5% after US-guided non-contrast enema [7]. The recurrence rate after reduction was 3.9% in the first 24 hours and 6.6% in the first 48 hours [7]. Predictive factors for recurrence vary across studies, and include age at diagnosis, C-reactive protein (CRP) level, and time interval from symptom onset to initial reduction [8]. Early detection with successful reduction is essential because intussusception can result in bowel infarction, perforation, and even death [9].

After reduction of intussusception, it is common for patients to stay in the hospital for 24 to 48 hours for observation of recurrence with or without follow-up US. There are controversies surrounding the necessity of a follow-up US as its benefit lacks evidence [3,10-12]. During hospitalization, patients undergo a follow-up US 24 hours post-reduction to confirm its success. One study presented short-term emergency department observations and concluded that US is a safe practice in more than 90% of selected cases [13]. Currently, no studies have specifically evaluated the use of follow-up US.

From 2017 onward, patients with intussusception at our institution were admitted after reduction for observation of recurrence with a follow-up US at 24 hours. The purpose of this study was to identify the significance of 24-hour follow-up US after reduction to check for recurrence during hospital admission.

MATERIALS AND METHODS

Study population

A total of 305 patients under the age of 18 years who were diagnosed with intussusception by US and successfully reduced by saline positive pressure at Severance Children's Hospital, Seoul, Korea, from January 2014 to September 2019, were included in this study. A retrospective analysis of the electronic medical records was performed. Patients with failed sonographic reduction who underwent surgery were excluded from the study.

This study was approved by the Institutional Review Board (IRB No. 4-2021-0722) of Severance Children's Hospital, and the study protocol was in accordance with the Declaration of Helsinki. The requirement for informed consent was waived owing to the retrospective nature of the study.

Data collection

Patients with successful saline reduction were divided into two groups: the recurrence group (R) and the non-recurrence group (NR). The full patient sample was divided into two groups according to follow-up US (with follow-up US [FU] vs. no follow-up US [NFU]), and a subgroup analysis was performed according to US follow-up within the R group (R-FU and R-NFU). R-NFU patients were diagnosed with recurrence of intussusception after revisiting an emergency room or an outpatient clinic after discharge without follow-up US.

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From the study population, demographic data; medical history of infection, including fever and upper respiratory symptoms prior to diagnosis; major symptoms at the time of diagnosis, such as abdominal pain, irritability, vomiting, and hematochezia; and laboratory parameters indicating inflammation were reviewed. Specific sonographic findings, length of hospital stay, and number of recurrences and re-admissions were analyzed.

Cost-effectiveness was defined as the number of recurrences exceeding the number of admissions: number of recurrences +1>number of admissions.

Statistical analysis

Statistical analysis was performed at the Biostatistics Collaboration Unit, Department of Biostatistics, Yonsei University College of Medicine and were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). Differences between groups were evaluated using an independent two-sample *t*-test, Mann–Whitney U-test, chi-square test, and Fisher's exact test, as appropriate for data type. All tests were 2-sided with a 5% significance level.

RESULTS

Patient characteristics between non-recurrence and recurrence groups

We extracted data for 248 patients from the database records. Among these, 229 were successfully treated via saline reduction, and 19 underwent surgery due to repetitive reduction failure (**Fig. 1**).

The NR group included 188 patients who were initially treated with reduction and did not experience recurrence. The R group included 41 patients who experienced recurrence of invagination after the initial reduction. Within the R group, 24 and 17 patients were in the R-FU and R-NFU subgroups, respectively.

Among the 229 selected patients in our study, there were no significant differences in characteristics between the NR (n=188) and R (n=41) groups, except for the length of hospital stay. The age at diagnosis was 1.67±1.57 years, 1.60±1.48 years, and 2.02±1.93 in the overall sample, NR group, and R group, respectively (p=0.18). Majority of the selected patients were male (64.2%). The overall white blood cell (WBC), erythrocyte sedimentation rate (ESR), and CRP counts were 10,986.44±4,312.87/μL, 20.49±17.78 mm/hr, and 10.96±17.49 mg/L,

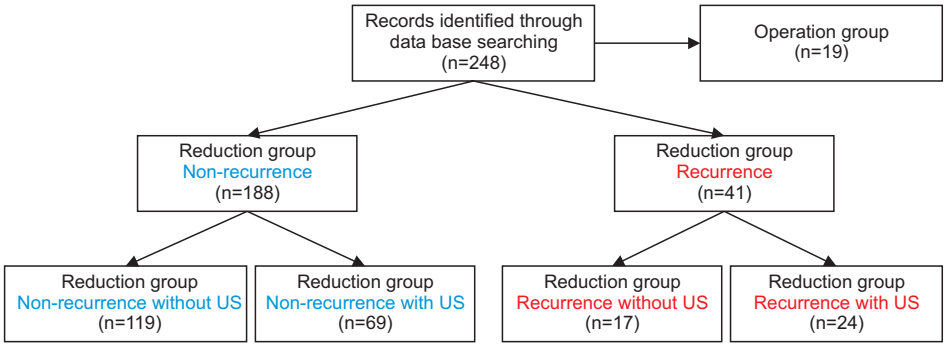

Fig. 1. Patient group selection from the database.
US: ultrasonography.

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Table 1. Patient characteristics of the non-recurrence and recurrence groups

Variable	Overall (n=229)	Non-recurrence group (n=188)	Recurrence group (n=41)	*p*-value
Age (y)	1.67±1.57	1.60±1.48	2.02±1.93	0.18*
Sex				0.90†
Female	82 (35.8)	67 (35.6)	15 (36.6)	
Male	147 (64.2)	121 (64.4)	26 (63.4)	
WBC (/μL)	10,986.44±4,312.87	11,108.37±4,370.57	10,439.27±4,049.52	0.37*
ESR (mm/hr)	20.49±17.78	20.571±17.706	20.12±18.39	0.89*
CRP (mg/L)	10.96±17.49	11,108.37±44.57	11.95±21.41	0.74*
Intussusception type				0.55‡
Ileocolic	225 (98.3)	185 (98.4)	40 (97.6)	
Ileocolic and small bowel	4 (1.7)	3 (1.6)	1 (2.4)	
Infection history	65 (28.4)	53 (28.2)	12 (29.3)	0.89†
Abdominal pain or irritability	221 (96.5)	181 (96.3)	40 (97.6)	>0.99‡
Vomiting	84 (36.7)	74 (39.4)	10 (24.4)	0.07†
Hematochezia	38 (16.6)	32 (17.0)	6 (14.6)	0.70†
US findings				0.47†
Non-remarkable	89 (38.9)	71 (37.8)	18 (43.9)	
Specific findings	140 (61.1)	117 (62.2)	23 (56.1)	
Hospital days (d)	1.21±1.87	1.03±1.81	2.02±1.94	0.0018*

Values are presented as mean±standard deviation or number (%).
WBC: white blood cell, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, US: ultrasonography, Infection history: fever, upper respiratory symptoms, Specific findings: terminal ileitis, lymph node enlargement.
*Independent two-sample *t*-test. †Chi-square test. ‡Fisher's exact test.

respectively, with no significant differences found between the R and NR groups. Majority of patients (96.5%, n=221) presented with abdominal pain or irritability, and some patients showed symptoms of vomiting (36.7%, n=84) and hematochezia (16.6%, n=38). Additionally, 28.4% (n=65) of the patients with intussusception had a history of previous infection. Most intussusceptions were ileocolic (98.3%, n=225), whereas 1.7% (n=4) were both ileocolic and small bowel intussusceptions. Specific sonographic findings other than intussusception, including terminal ileitis and lymph node (LN) enlargement, were detected in 140 patients (61.1%). The mean hospital stay was 1.21±1.87 days, and this was significantly different between the NR and R groups (1.03±1.81 days and 2.02±1.94 days, p=0.0018, **Table 1**).

Patient characteristics according to follow-up US in the recurrence group

The mean age at diagnosis was 2 (1-3.5) years in the R-FU group and 2 (1-2) years in the R-NFU group, with no significant differences. Of the patients, 29.2% (n=7) in the R-FU group were female, while 47.1% (n=8) in the R-NFU group were female. WBC, ESR, and CRP counts were higher than normal, without significant differences between the two groups. Most patients had abdominal pain or irritability (R-FU=100%, R-NFU=94.1%), whereas some presented with vomiting (R-FU=20.8%, R-NFU=29.4%) and hematochezia (R-FU=16.7%, R-NFU=11.8%). Finally, 33.3% (n=8) of patients in the R-FU group and 23.5% (n=4) in the R-NFU group had a history of infection. Most baseline characteristics between the R-FU and R-NFU groups were not significantly different (**Table 2**).

In the R-FU group, there were more specific US findings, such as terminal ileitis and LN enlargement (p=0.0024, **Table 2**). The number of admissions was significantly lower and the hospital stays were longer (3 [2-4.5] days) in the R-FU group than in the R-NFU group (0 [0-1] days, p<0.0001, **Table 3**). Most patients in both groups experienced recurrence at least once, with no significant difference between groups (p=0.17). With respect to cost-effectiveness, R-FU was significantly more cost-effective than NR-FU (p=0.0083, **Table 3**).

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Table 2. Patient characteristics according to follow-up US in the recurrence group

Variable	Overall (n=41)	Recurrence without US group (n=17)	Recurrence with US group (n=24)	*p*-value
Age (y)	2 (1–3)	2 (1–2)	2 (1–3.5)	0.42*
Sex				0.24†
Female	15 (36.6)	8 (47.1)	7 (29.2)	
Male	26 (63.4)	9 (52.9)	17 (70.8)	
WBC (/μL)	9,600 (8,030–12,100)	9,600 (8,430–11,360)	9,275 (7,600–13,465)	0.95*
ESR (mm/hr)	15 (4–29)	16.5 (4.5–36)	15 (4–26)	0.63*
CRP (mg/L)	4.5 (1.9–14.95)	6 (1.1–10.15)	3.65 (2.05–15.95)	0.78*
Intussusception type				>0.99‡
Ileocolic	40 (97.6)	17 (100)	23 (95.8)	
Ileocolic and small bowel	1 (2.4)	0	1 (4.2)	
Infection history	12 (29.3)	4 (23.5)	8 (33.3)	0.73‡
Abdominal pain or irritability	40 (97.6)	16 (94.1)	24 (100)	0.41‡
Vomiting	10 (24.4)	5 (29.4)	5 (20.8)	0.71‡
Hematochezia	6 (14.6)	2 (11.8)	4 (16.7)	>0.99‡
US findings				0.0024‡
Non-remarkable	18 (43.9)	13 (76.5)	5 (20.8)	
Terminal ileitis	18 (43.9)	4 (23.5)	14 (58.3)	
Lymph-node enlargement	2 (4.9)	0	2 (8.3)	
Both	3 (7.3)	0	3 (12.5)	

Values are presented as median (Q1–Q3) or number (%).
US: ultrasonography, WBC: white blood cell, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, Infection history: fever, upper respiratory symptoms.
*Mann–Whitney U-test. †Chi-square test. ‡Fisher's exact test.

Table 3. Analysis of number of recurrence and admission with cost-effectiveness according to follow-up US in the recurrence group

Variable	Overall (n=41)	Recurrence without US group (n=17)	Recurrence with US group (n=24)	*p*-value
Number of recurrences				0.17†
1	22 (53.7)	12 (70.6)	10 (41.7)	
2	10 (24.4)	3 (17.6)	7 (29.2)	
3	6 (14.6)	1 (5.9)	5 (20.8)	
4	2 (4.9)	0	2 (8.3)	
5	1 (2.4)	1 (5.9)	0	
Number of admissions				0.012†
1	20 (48.8)	4 (23.5)	16 (66.7)	
2	19 (46.3)	12 (70.6)	7 (29.2)	
3	2 (4.9)	1 (5.9)	1 (4.2)	
Cost-effectiveness	31 (75.6)	9 (52.9)	22 (91.7)	0.0083†
Hospital days (d)	2 (1–3)	0 (0–1)	3 (2–4.5)	<0.0001*

Values are presented as number (%) or median (Q1–Q3).
US: ultrasonography.
*Mann–Whitney U-test. †Fisher's exact test.

Recurrence rate and follow-up US

The recurrence rates were 12.5% (17/136 patients) and 25.8% (24/93 patients) in the NFU group and the FU group, respectively. Sixty-nine patients (36.7%) in the NR group underwent follow-up US compared to 24 patients in the R group (58.5%) (p=0.0099, **Table 4**). A follow-up US 24-hour post-reduction had a significantly higher odds ratio (2.44, p=0.013) in the R group.

Table 4. Chi-square test comparison of follow-up US between non-recurrence and recurrence group

Variable	Overall (n=229)	Non-recurrence group (n=188)	Recurrence group (n=41)	*p*-value
Follow-up US	93 (100)	69 (74.2)	24 (25.8)	0.0099
Non follow-up US	136 (100)	119 (87.5)	17 (12.5)	

Values are presented as number (%).
US: ultrasonography.

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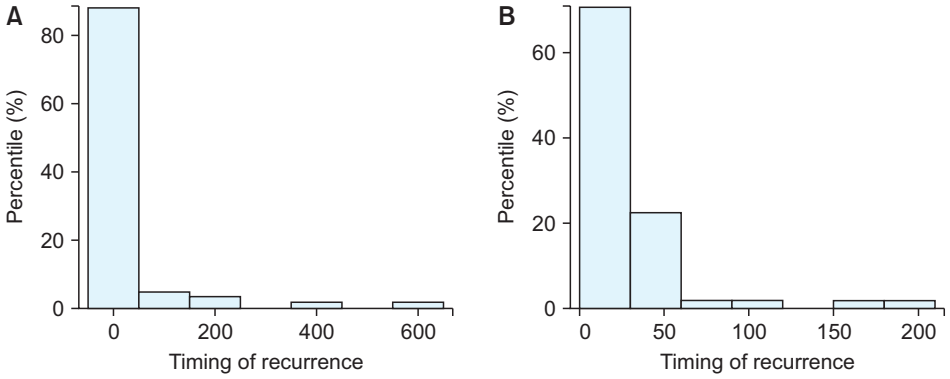

Fig. 2. (A) Histogram of timing of recurrence. (B) Histogram of timing of recurrence after exclusion of three patients with recurrence at 300 hours.

Timing of recurrence

The mean recurrence time was at 45.10±92.15 hours, and the median time was 21.00 hours in the R group. Except for three patients who experienced recurrent intussusception after more than 300 hours, the mean time was 29.69±33.62 hours and the median time was 20.50 hours (**Fig. 2**).

DISCUSSION

Our study aimed to investigate the significance of follow-up US 24 hours after initial reduction in detecting intussusception recurrence.

Many studies have demonstrated that early discharge after successful reduction is reasonable and safe [14-16]. Amuddhu et al. [15] conducted a systematic review and meta-analysis of outcomes from inpatient admission versus the emergency department from nine observational studies and concluded that managing uncomplicated intussusception in patients in an emergency department setting appeared to be safe because there was no significant statistical difference in the recurrence rate and post-discharge recurrence between admitted and emergency room patients.

However, 24-48 hours of close observation after reduction in admitted patients is a standard practice in many institutions. One study showed a 43% recurrence rate in the first 48 hours after initial reduction in 35 cited cases [17]. Patients additionally required intravenous hydration and careful observation for gastrointestinal symptoms such as nausea, vomiting, and abdominal pain for several hours until their first feeding [18].

We found no significant differences in demographics between the R and NR groups, except for hospital stay. This result is consistent with those of other prior studies. Eklöf and Reiter [17] reported clinical symptoms in patients with and without recurrence, and found no significant difference between the two groups. Cho et al. [19] also reported no statistically significant differences in age, reduction success rate, or operation rate between patients with and without recurrence.

However, Lee et al. [8] identified factors such as age (>1 year) at diagnosis, elevated CRP level, absence of bloody stools, and no history of infection as predictive of recurrence. Xie et al.

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[20] reported that age >2 years, symptom duration longer than 48 hours, rectal bleeding, and location of the lesion were risk factors for recurrence of intussusception. Guo et al. [21] also found age (>1 year) to be a predictive factor, but they analyzed symptom duration only up to 12 hours. These two studies included patients with failed reduction who underwent surgery; however, such patients were excluded from our study, which might have caused the differing results [20,21]. This suggests that there are some factors that contribute to intussusception recurrence, which are highly flexible and can be affected by other variables.

Most baseline characteristics in the subgroup analysis of the R-FU and R-NFU groups were not significantly different, indicating that the study design dividing patients into these two groups for comparison was valid. In our analyses comparing the R-FU and R-NFU groups, US-specific findings including terminal ileitis and LN enlargement were significantly more common in the R-FU group. This indicates that more detailed results could be obtained by follow-up US after reduction. Fewer admissions and longer hospital stay in the R-FU group indicate that follow-up US can decrease readmission rates.

Cost-effectiveness was defined with respect to reduced admissions. When patients were diagnosed and treated for intussusception, they paid for initial laboratory tests, US, and the reduction fee, including the hospital room cost. The cost of laboratory tests was approximately 330 US dollars (386,518 won). US and reduction fees were approximately 167 USD (195,000 won) and 100 USD (119,000 won), respectively. The room cost for one day of admission is approximately 10 USD for a multiple occupant room and approximately 100 USD (110,000 won) for a double room. If recurrence occurs after discharge, laboratory tests and US will need to be repeated, and additional psychosocial expenses are added upon readmission, such as transportation costs and time consumption. Given all these costs, a minimal number of admissions for patients with recurrence is an important outcome. Cost-effectiveness in the R-FU group was significantly higher than in the R-NFU group, indicating that follow-up US can help reduce medical costs.

Many studies have shown that recurrence rates are not significantly different between inpatient and outpatient groups [22,23]. However, our results showed a higher recurrence rate in the FU group than in the NFU group (12.2% vs. 25.8%), suggesting the omission of some recurrent events. Late detection of recurrence can cause complications, although they are often not severe. Therefore, we suggest that follow-up US after initial reduction is helpful in detecting early recurrence and decreasing the risk of complications of intussusception.

The timing of follow-up US after the initial reduction can be another issue. Gray et al. [7] demonstrated recurrence rates within 24- and 48-hours in a meta-analysis, but there were no data on recurrence time. In our study, the respective mean and median recurrence times were 29.69±33.62 hours and 20.50 hours after exclusion of three R patients. This suggests that follow-up US is helpful approximately 24 hours after the initial reduction.

Our study has several limitations. Our data were based on only one institution and were retrospectively collected. Post-discharge outcomes were determined by medical records, especially for patients who had not undergone follow-up US after reduction (NFU). Therefore, it is possible that we underestimated the NFU recurrence rate. Additionally, the retrospective review design could have led to a bias toward symptomatic patients during admission. Implementing US for evaluation of recurrence was also included in the FU group. Future studies are needed to compare more extensive groups and should be designed as

prospective clinical studies with randomized patients. We defined cost-effectiveness based on the number of admissions and recurrences. We did not analyze actual medical costs; therefore, additional economic analyses are needed for future research.

In conclusion, a significantly higher recurrence rate in the FU versus NFU group suggests that a follow-up US 24-hour post-reduction can reduce recurrent hospitalizations and detect patients with early recurrent intussusception.

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