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Original Article

Associations of Polyp Characteristics in Children and Adolescents Presenting with Less Than Five Colorectal Polyps: A Full Colonoscopy Is Still Required

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Background/Aims: A full colonoscopy is currently required in children and adolescents with colorectal polyps, because of their potential of neoplastic transformation and complications such as intussusception. We aimed to analyze the associations of polyp characteristics in children and adolescents with colorectal polyps. Based on these findings, we also aimed to reevaluate the necessity of conducting a full colonoscopy.

Methods: Pediatric patients <18 years of age who had undergone a colonoscopic polypectomy and those with <5 colorectal polyps were included in this multicenter, retrospective study. Baseline clinicodemographics, colonoscopic and histologic findings were investigated.

Results: A total of 91 patients were included. Multivariate logistic regression analysis showed that polyp size was the only factor associated with the presence of any polyps located proximal to the splenic flexure (odds ratio [OR], 2.25; 95% confidence interval [CI], 1.28 to 4.28; p=0.007). Furthermore, polyp location proximal to the splenic flexure and sessile morphology were associated with the presence of any adenomatous polyp (OR, 8.51; 95% CI, 1.43 to 68.65; p=0.023; OR, 18.41; 95% CI, 3.45 to 173.81; p=0.002, respectively).

Conclusions: In children and adolescents presenting with <5 colorectal polyps, polyp size and the presence of any adenomatous polyp were positively associated with polyp location proximal to the splenic flexure. This finding supports the necessity of a full colonoscopic exam in pediatric patients with colorectal polyps for the detection of polyps before the occurrence of complications such as intussusception or neoplastic transformation. **(Gut Liver 2023;17:441-448)**

Key Words: Colonic polyps; Adenoma; Splenic flexure; Sessile; Size

INTRODUCTION

Colorectal polyps are commonly diagnosed between 2 to 5 years of age, usually presenting with painless rectal bleeding.[1] They are the most common cause of isolated lower gastrointestinal (GI) bleeding in children.[2] Colorectal polyps can be divided into two types according to histologic findings.[3] The majority are hamartomas, which

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are observed in juvenile polyps (JPs) and Peutz-Jeghers syndrome (PJS). They generally possess minimal potential for neoplastic change and are benign, although polyps in PJS have an increased risk of GI malignancy with the increase of age.[4] The other minority are adenomatous polyps, which are neoplastic and possess the potential for malignant change. Adenomatous polyps are usually associated with polyposis syndromes such as familial adenomatous polyposis (FAP).

JPs comprise 70% to 80% of pediatric colorectal polyps, and are mostly observed as a solitary polyp.[3,5] Meanwhile, juvenile polyposis syndrome (JPS) is a rare autosomal-dominantly inherited disease characterized by the development of multiple hamartomatous polyps of the GI tract.[6] JPS can be diagnosed by excluding the extraintestinal features consistent with *PTEN* hamartoma tumor syndrome, and when five or more JPs are observed in the colon or rectum, or when JPs are observed in other parts of the GI tract, or when there is a positive family history of JPS regardless of the number of JPs.[6,7] They possess an increased risk of GI malignancy of 38% to 68%.[6] Therefore, there is no doubt that a full colonoscopy is required in patients with syndromic polyps, such as JPS, PJS, or FAP.

While it is generally acknowledged that JPs possess minimal risk for neoplastic change, a recent study has reported that JPs are also capable of possessing potential for adenomatous transformation.[8] According to the study, JPs harboring adenomatous foci were reported in 26 patients (12%), and were significantly more likely to be proximally distributed, highlighting the necessity of a full colonoscopy when polyps are suspected.[8] Another study reported that colorectal polyps located in the right colon were significantly larger than left colonic polyps, also emphasizing the necessity of a full colonoscopy.[9] However, to date no study has comprehensively analyzed the associations between polyp characteristics, and have derived the conclusion that a full colonoscopy is necessary based on association analyses of polyp characteristics.

Therefore, we aimed to investigate the associations between polyp characteristics in children and adolescents with colorectal polyps with <5 polyps. Based on these findings, we also aimed to reevaluate the necessity of conducting a full colonoscopy.

MATERIALS AND METHODS

1. Patients and study design

This study was a multicenter, retrospective, cross-sectional study conducted in 14 medical centers in South Korea; Kyungpook National University Children's Hospital affiliated with Kyungpook National University Chilgok Hospital, Eulji University Hospital, Ajou University Medical Center, Soonchunhyang University Bucheon Hospital, Chungnam National University Hospital, Jeonbuk National University Medical School, Keimyung University Dongsan Hospital, Kosin University Gospel Hospital, Chung-Ang University Hospital, Korea University Anam Hospital, Kyungpook National University Hospital, Inje University Ilsan Paik Hospital, Wonju Severance Christian Hospital, and Hallym University Sacred Heart Hospital. Pediatric patients of the age of <18 years who had undergone a colonoscopic polypectomy from January 2015 to December 2020 were included. Medical charts were reviewed and those whose colonoscopy failed to intubate up to the cecum were excluded.

Baseline clinicodemographics including sex, age at diagnosis, family history of multiple colorectal polyps, and growth indicators were investigated. Characteristics of colorectal polyps including the number, location, size, morphology, and histology of polyps were also retrieved from medical charts. Diagnosis of the colorectal polyps, including JP, adenomatous polyp, JPS, PJS, and FAP were also analyzed based on medical charts. Those with <5 colorectal polyps were ultimately included, while those with ≥5 polyps were excluded. Data for polyp size was derived from histology reports, and the maximum length of the polyp was designated as the polyp size.

Comparative analysis was performed separately between patients divided according to polyp characteristics of polyp location, presence of adenomas, and presence of sessile morphology. Thereafter, further analyses of associations between factors were conducted by logistic regression analyses.

2. Statistical analysis

For statistical comparison between the two groups, the chi-square test or the Fisher exact test was used for categorical variables, and the Student t-test or the Wilcoxon rank-sum test was used for continuous variables. Comparative data for continuous variables are reported as median (interquartile range) or mean (standard deviation). Univariate and multivariate logistic regression analyses were conducted to examine the association between the presence of adenomas on histology with other variables. Univariate logistic regression analysis was performed to investigate the crude odds ratio (OR) for each factor. Factors showing a significance of $p<0.1$ were included in the multivariate logistic analysis. The results were expressed as adjusted ORs with 95% confidence intervals (CIs). Additionally, receiver operating characteristic curve analysis was conducted to determine the optimal cutoff value of

statistically significant continuous variables that could best stratify patients according to categorical variables. The results were expressed as area under the curve with 95% CIs, sensitivity, specificity, positive predictive value, and negative predictive value. Data were considered to be statistically significantly different if p<0.05. Statistical analyses were conducted using R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

3. Ethics statement

This study was conducted with approval from 16 participating institutions including the Institutional Review Board of Kyungpook National University Chilgok Hospital (IRB number: 2021-07-016), and informed consent was waived due to the retrospective nature of the study.

RESULTS

1. Baseline characteristics

Among 108 patients who had conducted a colonoscopic polypectomy, four patients whose colonoscopy failed to intubate up to the cecum were excluded. Among the remaining 104 patients, those with JPs comprised 78.8% (82/104), followed by adenomatous polyps 8.7% (9/104), JPS 4.8% (5/104), PJS 3.8% (4/104), and FAP 3.8% (4/104). Ninety-one patients had <5 colorectal polyps, and were ultimately included (Fig. 1).

Male sex comprised 61.5% (56/91) of the patients, and the median age of the patients was 6.0 years (interquartile range, 3.7 to 10.4 years). Solitary polyps comprised 92.3% (84/91) of the patients and 82.4% (75/91) of the patients had polyps located only in the left colon. The median size of the polyps was 15 mm (interquartile range, 10 to 20 mm), and 27.5% (25/91) of the patients had a polyp of sessile morphology. Regarding diagnosis based on histology, 90.1% (82/91) patients had all JPs, while 9.9% (9/91) had any adenomatous polyp (Table 1).

2. Factors associated with the presence of any polyps located proximal to the splenic flexure

When patients were divided according to polyp location, 16 patients (17.6%) had at least one polyp located proximal to the splenic flexure, while 75 patients (82.4%) had all polyps located in the left colon. Patients with any polyps located proximal to the splenic flexure showed a significantly older age at diagnosis (median, 13.2 years vs 5.7 years, p=0.038), lower proportion of patients with solitary polyps (75.0% vs 96.0%, p=0.017), larger polyp size (median, 21 mm vs 14 mm, p=0.034), and higher proportion of patients with any adenomatous polyp (25.0% vs 6.7%, p=0.048) (Table 2).

According to univariate logistic regression, age at diagnosis, presence of multiple polyps, polyp size, and any adenomatous polyp were significantly associated with the presence of any polyps located proximal to the splenic flex-

Table 1. Baseline Characteristics of the Patients

Characteristics	Value (n=91)
Male sex	56 (61.5)
Age at diagnosis, yr	6.0 (3.7 to 10.4)
Height Z-score	0.02±0.87
Weight Z-score	0.16±1.18
Body mass index Z-score	0.02 (–0.80 to 0.97)
Family history of colorectal polyps	5 (5.5)
No. of polyps	
1	84 (92.3)
2	4 (4.4)
3	1 (1.1)
4	2 (2.2)
Polyp located only in the right colon	4 (4.4)
Polyp located only in the left colon	75 (82.4)
Polyp size, mm	15 (10 to 20)
Polyp morphology	20 (19.4)
All pedunculated	66 (72.5)
Any sessile	25 (27.5)
Diagnosis based on histology	
All juvenile polyps	82 (90.1)
Any adenomatous polyp	9 (9.9)

Data are presented as number (%), median (interquartile range), or mean±SD.

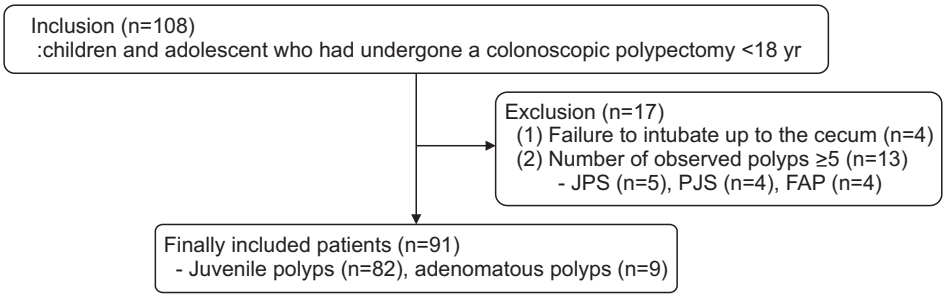

Fig. 1. Flow diagram of patient inclusion and exclusion.
JPS, juvenile polyposis syndrome; PJS, Peutz-Jeghers syndrome; FAP, familial adenomatous polyposis.

Table 2. Comparison between Patients Divided According to Polyp Location

Variable	Any polyp proximal to splenic flexure (n=16)	All polyps distal to splenic flexure (n=75)	p-value
Male sex	8 (50.0)	48 (64.0)	0.446
Age at diagnosis, yr	13.2 (4.3–16.2)	5.7 (3.5–8.8)	0.038
Solitary polyp	12 (75.0)	72 (96.0)	0.017
Polyp size, mm	21 (11–33)	14 (10–20)	0.034
Sessile morphology	4 (25.0)	21 (28.0)	1.000
Any adenomatous polyp	4 (25.0)	5 (6.7)	0.048

Data are presented as number (%) or median (interquartile range).

Table 3. Logistic Regression Analyses of Factors Associated with the Presence of Any Polyps Located Only Proximal to the Splenic Flexure

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Sex (male vs female)	0.56	0.19–1.69	0.300	-	-	-
Age at diagnosis, yr	1.14	1.03–1.27	0.010	1.13	1.00–1.27	0.053
Solitary polyp (yes vs no)	0.12	0.02–0.63	0.012	0.14	0.02–1.06	0.052
Polyp size, mm	1.84	1.14–3.06	0.013	2.25	1.28–4.28	0.007
Sessile morphology (yes vs no)	0.86	0.22–2.78	0.807	-	-	-
Any adenomatous polyp (yes vs no)	4.67	1.03–20.24	0.037	4.41	0.59–29.48	0.127

OR, odds ratio; CI, confidence interval.

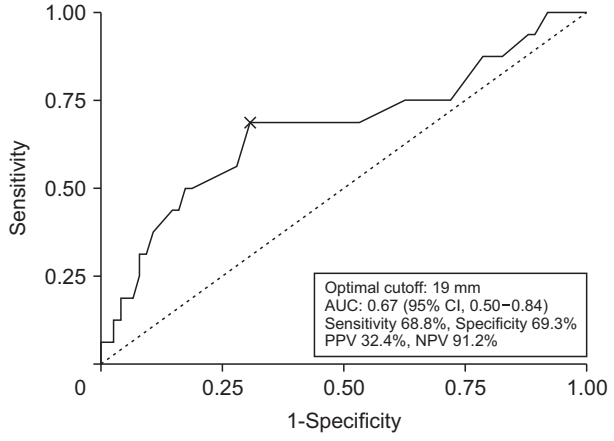

Fig. 2. ROC curve of polyp size stratifying patients with all polyps proximal to and any polyps distal to the splenic flexure.
ROC, receiver operating characteristic; CI, confidence interval; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value.

ure. However, according to multivariate logistic regression analysis, polyp size was the only factor positively associated with the presence of any polyps located proximal to the splenic flexure (OR, 2.25; 95% CI, 1.28 to 4.28; p=0.007) (Table 3).

According to receiver operating characteristic curve analysis, the optimal cutoff polyp size for stratifying between polyps located proximal and distal to the splenic flexure was 19 mm (area under the curve=0.67, 95% CI=0.50 to 0.84; sensitivity 68.8%, specificity 69.3%, positive predictive value 32.4%, negative predictive value 91.2%, p<0.001) (Fig. 2).

3. Factors associated with sessile morphology

When patients were divided according to polyp morphology, 25 patients had at least one polyp with sessile morphology, while 66 patients had all polyps of pedunculated morphology. Patients with sessile polyps revealed significantly smaller polyp size (median, 11 mm vs 17 mm, p=0.005), and higher proportion of patients with any adenomatous polyp (28.0% vs 3.0%, p=0.001) (Table 4).

According to univariate and multivariate logistic regression, any adenomatous polyp was the only factor that was significantly associated with sessile morphology (OR, 9.89; 95% CI, 1.89 to 78.73; p=0.011) (Table 5).

4. Factors associated with the presence of any adenomatous polyp

When patients were divided according to the presence of adenomas on histology, nine patients had adenomas, while 81 patients did not. Patients with any adenomatous polyp showed significantly higher proportion of patients with polyps located only proximal to the splenic flexure (44.4% vs 14.6%, p=0.048), and sessile morphology (77.8% vs 22.0%, p=0.001) (Table 6).

According to univariate logistic regression, polyp location only proximal to the splenic flexure and sessile morphology were significantly associated with the presence of any adenomatous polyps. According to multivariate

Table 4. Comparison between Patients Divided According to Polyp Morphology

Variable	Sessile morphology (n=25)	Pedunculated morphology (n=66)	p-value
Male sex	17 (68.0)	39 (59.1)	0.590
Age at diagnosis, yr	6.2 (3.6–12.0)	5.8 (3.8–9.7)	0.769
Solitary polyp	22 (88.0)	62 (93.9)	0.388
Located only in the left colon	21 (84.0)	54 (81.8)	1.000
Located only in the right colon	3 (12.0)	1 (1.5)	0.062
Polyp size, mm	11 (5–15)	17 (13–21)	0.005
Any adenomatous polyp	7 (28.0)	2 (3.0)	0.001

Data are presented as number (%) or median (interquartile range).

Table 5. Logistic Regression Analyses of Factors Associated with the Presence of Any Polyps with Sessile Morphology

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Sex (male vs female)	1.47	0.57–4.05	0.437			
Age at diagnosis, yr	1.02	0.93–1.12	0.606			
Solitary polyp (yes vs no)	0.47	0.10–2.56	0.351			
Located only in the left colon (yes vs no)	1.17	0.35–4.54	0.807			
Located only in the right colon (yes vs no)	8.86	1.07–184.32	0.065	2.38	0.15–62.36	0.539
Polyp size, mm	0.65	0.36–1.06	0.107			
Any adenomatous polyp (yes vs no)	12.44	2.73–88.62	0.003	9.89	1.89–78.73	0.011

OR, odds ratio; CI, confidence interval.

Table 6. Comparison between Patients with All Juvenile Polyps and Those with Any Adenomatous Polyp

Variable	All juvenile polyps (n=82)	Any adenomatous polyp (n=9)	p-value
Male sex	51 (62.2)	5 (55.6)	0.729
Age at diagnosis, yr	5.8 (3.8–9.7)	8.7 (3.6–17.1)	0.309
Solitary polyp	77 (93.9)	7 (77.8)	0.141
Located only proximal to the splenic flexure	12 (14.6)	4 (44.4)	0.048
Polyp size, mm	15 (10–20)	11 (10–13)	0.197
Sessile morphology	18 (22.0)	7 (77.8)	0.001

Data are presented as number (%) or median (interquartile range).

Table 7. Logistic Regression Analyses of Factors Associated with the Presence of Any Adenomatous Polyp

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Sex (male vs female)	0.76	0.19–3.27	0.698			
Age at diagnosis, yr	1.09	0.96–1.24	0.168			
Solitary polyp (yes vs no)	0.23	0.04–1.78	0.109			
Located only proximal to the splenic flexure (yes vs no)	4.67	1.03–20.24	0.037	8.51	1.43–68.65	0.023
Polyp size, mm	0.82	0.36–1.59	0.603			
Sessile morphology (yes vs no)	12.44	1.85–105.61	0.015	18.41	3.45–173.81	0.002

OR, odds ratio; CI, confidence interval.

logistic regression analysis, these two factors were the independent factors positively associated with the presence of any adenomatous polyp (OR, 8.51; 95% CI, 1.43 to 68.65; p=0.023; OR, 18.41; 95% CI, 3.45 to 173.81; p=0.002, respectively) (Table 7).

DISCUSSION

In this study, we comprehensively analyzed the associations between polyp characteristics in children and adolescents presenting with <5 colorectal polyps. We found

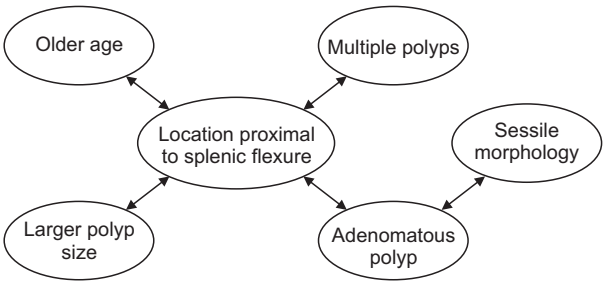

Fig. 3. Diagram showing the associations between polyp characteristics in this study.

that polyp size and the presence of any adenomatous polyp were positively associated with polyp location proximal to the splenic flexure. We also revealed that sessile morphology was associated with the presence of any adenomatous polyps (Fig. 3). These results provide statistical evidence and highlight the necessity of conducting a full colonoscopy in children and adolescents with suspected colorectal polyps.

Historically, it is well known that colorectal polyps that develop in young children are generally solitary, benign JPs, while colorectal polyps that develop in older children of 10 years and older are likely to be adenomatous polyps or polyps occurring as part of a polyposis syndrome.[1] In this study, we have revealed an association between diagnosis age and polyp location for the first time. This finding indicates that colorectal polyps are likely to be encountered in the proximal colon in older children, and emphasizes the necessity of a full colonoscopy especially in this age group.

More than 90% of solitary polyps are known to be located in the left colon.[2] Meanwhile, multiple polyps are capable of being located in the proximal colon.[10,11] In one study, solitary polyps were observed in the left colon in 97% of patients in the non-polyposis group, while no patient in the polyposis syndrome group had only left colonic polyps.[12] In another study, among 45% of children with multiple polyps, 35% of the polyps have been reported to be distributed distal to the sigmoid colon.[13] Moreover, it is also known that polyps located in the right colon are likely to undergo a neoplastic malformation, as well as recur in a higher rate than polyps located in the left colon.[8,14] A recent study by Ibrahimi *et al.*[8] has revealed that JPs harboring adenomatous foci were significantly more likely to be proximally distributed emphasizing the necessity of a pancolonoscopy when suspecting polyps. Meanwhile, the presence of adenomatous transformation within the polyps did not correlate with polyp number or the likelihood of polyp recurrence on repeat colonoscopy in that study.[8] The findings in our study are in the same lines. We have revealed that polyp location proximal to the splenic flexure and sessile morphology were associated with the presence of any adenomatous polyp, while other factors such as polyp number or polyp size were not.

There is little evidence regarding the association between polyp location and size. However, a recent study by Dipasquale *et al.*[9] reported that right colonic polyps were significantly larger than left colonic polyps.[15] We also identified this finding. The underlying cause of this difference in polyp size according to location should be elucidated. However, one hypothesis could be that right-sided colon polyps tend to be diagnosed much later than left-sided colon polyps.[16] Because the feces tend to form harder approaching the distal gut, hematochezia is more likely to occur in patients with distal polyps than proximal polyps. Therefore, symptoms may be delayed until right-sided polyps grow which may explain why they are found larger than left-sided polyps. Moreover, according to our analysis, a cutoff of 19 mm was capable of stratifying between polyps located proximal and distal to the splenic flexure with an negative predictive value of 91.2%. This is a novel finding which could be applied in the prediction of polyp location when combining other modalities such as abdominal ultrasonography. For example, because of the high likelihood of polyps located distal to the splenic flexure to be smaller than 19 mm, the radiologist could be more careful when searching for polyps in the distal colon. Abdominal ultrasonography in the detection of colorectal polyps is becoming more popular, and according to a recent study by Di Nardo *et al.*,[17] the combination of abdominal ultrasonography, fecal calprotectin, and digital rectal examination obtained a specificity and positive predictive value of 100%. Another study showed that colonic JPs were associated with elevated levels of fecal calprotectin which normalized after polypectomy.[18] It would be fascinating to know the location of a polyp before conducting a colonoscopy. Moreover, this could possibly affect the currently recommended practice of conducting a full colonoscopy when polyps are suspected. Furthermore, the development of colon capsule endoscopies combined with artificial intelligence may be a promising tool that may substitute diagnostic pancolonoscopy in the near future.

However, to date there is lack of evidence to recommend a partial colonoscopy or sigmoidoscopy in children with suspected colorectal polyps. The findings of our study based on association analyses between factors emphasize the necessity of a full colonoscopy. As large polyps are likely to cause intussusception, the finding of our study that large polyps are associated with location proximal to the splenic flexure reinsures that a pancolonoscopy is warranted. Furthermore, as adenomas are capable of ma-

lignant transformation, the finding of our study that any adenomatous polyp are associated with location proximal to the splenic flexure again emphasizes the need for a full colonoscopy.

This study has some limitations. First, the retrospective nature of the study may have introduced selection bias into this study. Furthermore, selection bias may have been introduced by excluding patients who failed to intubate up to the cecum, although the number of these patients were small (n=4). Second, the number of patients included in this study were relatively small compared to several previous studies. Hence, the number of patients with any adenomatous polyp were only nine, which was relatively small for sufficient statistical analysis. Therefore, caution is required when interpretating these results. Despite these limitations, this study is the first to comprehensively analyze the associations between polyp characteristics, and derive the conclusion that a full colonoscopy is necessary based on association analyses of polyp characteristics.

In conclusion, larger polyps are likely to present proximally to the splenic flexure in children and adolescents presenting with <5 colorectal polyps. Moreover, adenomatous polyps are also likely to present proximally to the splenic flexure. This finding supports the necessity of a full colonoscopic exam for the detection of polyps before the occurrence of complications such as intussusception or malignancy transformation.

CONFLICTS OF INTEREST

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

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AUTHOR CONTRIBUTIONS

Study concept and design: J.Y.K., Y.B.K. Data acquisition: S.C., H.J.K., Y.M.L., H.J.J., Y.J.C., Y.K., K.J.L Data analysis and interpretation: S.C.K., S.Y.C., D.Y.Y., Y.L., S.J.H., J.H.H., S.K., B.H.C. Drafting of the manuscript: J.Y.K., Y.B.K. Critical revision of the manuscript for important intellectual content: B.K. Statistical analysis: J.Y.K., Y.B.K., B.K. Obtained funding: B.K. Administrative, technical, or material support; study supervision: B.K. Approval of final manuscript: all authors.

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