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Use of the Kono-S anastomosis in pediatric Crohn's disease: a single-institution experience

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Abstract

Objectives About 24% of children with Crohn's Disease (CD) require surgery. In 2003, Kono et al. described a novel anastomosis reported to decrease the rate of anastomotic CD recurrence. Subsequent studies have reproduced these outcomes, but none has demonstrated its effect in pediatric patients. This study evaluates short-term outcomes of pediatric patients following ileocolic resection and Kono-S anastomosis.

Methods A retrospective review of patients < 18 years old who underwent ileocolic resection followed by Kono-S anastomosis compared with those who underwent a stapled anastomosis.

Results Nine Kono-S patients were matched with nine patients preceding them who received traditional side-to-side and end-to-side anastomoses. All patients underwent minimally invasive surgery. Demographics, pre-operative medication usage, and symptom profiles were not significantly different. Traditional anastomosis (TA) patients had longer lengths of stay (4.6 vs 2.9 days; p=0.03) but had no statistically significant differences in blood loss, procedure length, and pathologic findings. One Kono-S patient had a superficial surgical site infection, and one TA patient had an anastomotic leak requiring reoperation within 30 days. More TA patients experienced post-operative symptoms at both 30-day and 6-month follow-up (66.7% vs 33.3%; p=0.16 and 77.8% vs 25%; p=0.03).

Conclusion The Kono-S anastomosis appears to be safe in pediatric CD when compared to traditional stapled anastomoses.

Keywords Kono-S anastomosis · Pediatric Crohn's disease · Ileocolic resection · Stapled anastomosis

Abbreviations

- CD Crohn's disease
- EEN Exclusive enteral nutrition
- POR Post-operative recurrence
- RCTs Randomized-controlled trials
- TA Traditional anastomosis

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Introduction

Crohn's disease (CD) is a chronic inflammatory disease that predominantly affects the gastrointestinal tract. Along with ulcerative colitis, it is thought to affect 1.3% of the US population and has an annual incidence of 3-20 cases per 100,000 [1, 2]. There is currently no known cause or cure for CD. Unfortunately, despite medical therapy, refractory disease can cause irreversible bowel wall damage and clinically can result in delayed growth and development, decreased quality of life, school absence, and pubertal delay [3-5]. In the pediatric population, the incidence of disease continues to increase, and concern for disease recurrence remains high [6]. Up to 8% of pediatric CD patients will require surgical intervention within the first year of diagnosis, and that rate increases to 47% by 5 years [7]. Recurrence in the pediatric population has been reported in up to 50% at just 1 year. While much is known about methods to prevent postoperative recurrence (POR) in the adult population, few if any studies have looked specifically at medical and surgical methods for POR prevention in children [8].

Over 50% of operations for pediatric Crohn's are ileocecal resections making this the most common surgical procedure in this population [5, 9]. Biologic therapy has impacted the need for surgical therapy but has not eliminated it. Differences in surgical technique can also impact recurrence [5]. In 2003, Kono et al. described a new surgical anastomotic technique, the Kono-S anastomosis, to decrease anastomotic recurrences. Initial outcomes demonstrated that surgical recurrence was significantly lower when compared to the traditional stapled or hand-sewn anastomoses [10]. Multiple subsequent studies of the Kono-S anastomosis have demonstrated its effectiveness and reproducibility in adults, but no studies have demonstrated its effect in the pediatric population [11-13]. Given that pediatric CD is known to be a more aggressive phenotype than adult-onset CD, it begs the question whether the same techniques will have the same effect on post-operative outcomes [14, 15]. This study sought to identify the 30-day and 6-month clinical and surgical outcomes for pediatric patients who underwent a Kono-S anastomosis and how those outcomes compare to a similar cohort who underwent traditional anastomoses. Our goal was to describe the early experience with the utilization of the Kono-S anastomosis in the pediatric population with the assumption that it would result in the same positive effects upon post-operative recurrence in the long term.

Methods

A single-institution retrospective review was performed following Cleveland Clinic institutional review board and pediatric research review committee approvals. In May 2022, our team transitioned to Kono-S reconstruction following ileocolic resection for pediatric CD. All consecutive patients < 18 years old who underwent ileocolic resections with Kono-S anastomotic reconstruction since our surgical program's transition to the technique were included in this study. Nine patients were noted to comprise this group. After the point in which our program transitioned to the Kono-S anastomosis, no patients underwent an alternative anastomosis. The nine consecutive patients who were < 18 years of age and underwent traditional stapled reconstruction prior to our transition to the Kono-S anastomosis were chosen as a comparison group. All Kono-S surgeries were performed by a pediatric surgeon (A.D.) and a colorectal surgeon (J.L.). Five of the TA cases were also performed by both a pediatric and colorectal surgeon, while the remaining four cases were performed by a pediatric surgeon. Regular follow-up for all patients occurred within the same institution by the surgical team as well as the treating gastroenterologists.

Data collected from the electronic medical record included patient demographics, family history, CD history, medication history, intra-operative details, pathology, 30-day, and 6-month follow-up complications, symptoms, and medication usage. Pre-operative medication usage was defined as documented active usage of any medication of interest within 3 months of the day of surgery. The primary endpoint was the presence of 30-day complications and reoperation rate. The secondary endpoint was the presence of 6-month complications and reoperation rate.

Surgical technique

A laparoscopic ileocolic resection was performed in all cases. A stapled ileocolic resection was performed for all patients via the umbilical incision or the trephine when a prior stoma site was present. A Kono-S anastomosis was performed as described by Kono, et al. [10] as a double-layer hand-sewn anastomosis following 7 cm enterotomies (Fig. 1). Non-Kono-S anastomoses consisted of either side-to-side (1) or end-to-side (8) stapled anastomosis. These were all performed laparoscopically either with three ports or via a single site (4).

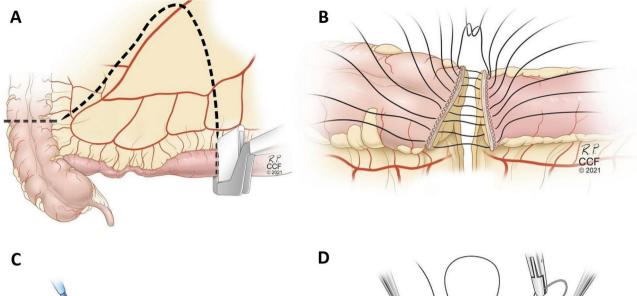
Statistical analysis

Categorical and continuous variables are presented as both frequency and proportions. Continuous variables were tested with Welch two-sample t test to determine difference between those who underwent a Kono-S anastomosis and those who did not. Categorical variables were assessed via the Pearson's chi-squared test. Missing values were not inferred. An overall significance level of 0.05 was used for this study. Data were analyzed using R, version 4.2.2 (RStudio, Boston MA).

Results

Demographics and pre-operative characteristics

Between January 2019 and December 2022, 18 pediatric patients underwent ileocolic resection. Kono-S was performed in all 9 patients after March 2022, and traditional stapled anastomosis performed in the 9 preceding patients (TA). Patients in the Kono-S and TA groups were on average 15.4 and 16.2 years of age, respectively (range 12–18, p = 0.32) 55% of Kono-S patients were female whereas 66.7% of the TA group were female (p=0.63). The majority of patients identified as white (100% and 77.8%; p=0.32), and the average BMI was 21.6 kg/m² and 20.1 kg/m² in the Kono-S and TA groups, respectively (p=0.27). Family history of CD was not significantly different between the Kono-S and TA groups (44.4% vs 33.3%; p=0.63). The average time from diagnosis to ileocolic resection was also



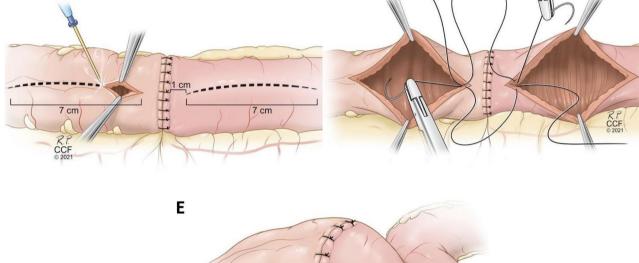


Fig. 1 Kono-S anastomosis surgical technique. **A** Transverse bowel ligation with optional extended mesenteric resection via high ligation of the ileocolic pedicle. **B** Creation of supporting column by suturing staple lines together. **C** Creation of anti-mesenteric enterotomies 1 cm

CCF

not significantly different between both groups (469.4 vs 464.6; p = 0.98).

Pre-operatively, all patients were on medical therapy, including biologics, immunomodulators, steroids, and antibiotics. There was no statistically significant difference in the use of any medication between the Kono-S and TA groups. While not reaching statistical significance, steroids, from supporting columns. **D** Formation of double-layer hand-sewn anastomosis which will result in a transverse luminal diameter of 7 cm. **E** Final appearance of the bowel anastomosis now overlying the supporting column

including prednisone and budesonide, were more commonly used in the TA group (55.6% and 11.1% vs 33.3% and 0%; p=0.16). No patient was still utilizing steroids at the time of operation. There were no statistically significant differences between pre-operative use of immunomodulators, biologics, or other medications (p=0.60, p=0.30, and p=1). Pre-operative exclusive enteral nutrition (EEN) was more commonly utilized in the TA population than the Kono-S population (55.6% vs 0%; p=0.01). The most common preoperative symptom was abdominal pain, followed by nausea and emesis (Table 1).

Intra-operative details

TA cases took on average more time to complete (170.9 min vs 139.7 min; p = 0.10) and involved more reported blood loss (68.3 ml vs 16.7 ml; p = 0.10), but these differences were not statistically significant. Three of the Kono-S and none of the TA patients had previous stomas (1 double barrel end ileostomy and 2 end ileostomies) prior to surgical repair (p = 0.06). Each group had a patient who underwent an additional surgery during their ileocolic resection. A Kono-S patient underwent multiple stricturoplasties, and a TA patient underwent a formal right hemicolectomy. The average ileal resection was similar between groups (15.81 cm vs 13.78 cm; p = 0.67), and the most common pathologic findings were inflammation, ulceration, and structuring, and were the same in both groups (p=0.13). Overall, TA patients spent more days in the hospital than Kono-S patients (4.6 vs 2.9 days; p = 0.03) (Table 2).

30-Day follow-up

At the time of follow-up, two patients, one from each treatment group, had a post-op complication. The Kono-S patient developed a superficial surgical site infection, while the TA patient had an anastomotic leak resulting in reoperation. No patients required post-operative steroids. No additional medications, such as antibiotics, anti-inflammatories, or antidiarrheals, were needed by either group. Overall, TA patients reported experiencing post-operative symptoms more frequently than Kono-S patients (66.7% vs 33.3%; p = 0.16). Abdominal pain was again the most noted symptom. The average number of bowel movements was similar between groups (2.25 BMs/day vs 1.71 BMs/day; p = 0.44) (Table 3).

6-Month follow-up

Average follow-up was 196.5 days (182–268 days) in the Kono-S group and 227.2 days (189 to 301 days, p = 0.18) in the TA group. One Kono-S patient relocated and did not have a 6-month follow-up within our institution. By 6 months, one TA patient developed a post-operative small bowel obstruction managed non-operatively with a short inpatient admission, whereas no further complications were observed in the Kono-S group (p = 0.33). No patient required any further use of steroids. Immunomodulators were more commonly utilized by the TA group (55.6% v 12.5%; p = 0.06) of which methotrexate was the immunomodulator prescribed most frequently. All patients were on post-operative biologics,

most commonly infliximab. Biologics were restarted 9-129 days (mean 44) post-operatively in the Kono-S group and 14-392 days (mean 154) post-operatively in the TA group. Post-operatively, two TA patients subsequently required use of antidiarrheals where none were required in the Kono-S group (22.2% vs 0%, p = 0.16). Clinically, at the time of 6-month follow-up, more TA patients endorsed post-operative symptoms (77.8% vs 25%; p = 0.03). The most commonly observed symptoms were intermittent abdominal pain, bloating, and nausea. These symptoms were experienced by two (22.2%) TA patients noting decreased energy levels, whereas all Kono-S patients returned to their baseline energy levels (p=0.16) by 6 months. The average number of bowel movements was decreased in both the Kono-S and TA group from their 30-day follow-up average (1.92 BMs/ day v 1.69 BMs/day; p = 0.61). Only 1 (11.1%) patient in TA group required endoscopic evaluation at 6 months due to concern for abdominal pain, bloating, and loose stools. Colonoscopy demonstrated a non-obstructive anastomotic stricture. No patient required reoperation at time of 6-month follow-up (Table 4).

Discussion

Management of CD remains challenging in both the adult and pediatric populations. Due to the complex and often severe nature of early onset CD, surgical management has remained relevant despite improved medical therapy. Since a post-surgical disease-free interval has been associated with improved growth and development, further understanding into how to decrease POR is crucial for long-term management of this disease process. While novel medical strategies have been introduced in the pediatric population based on effectiveness in the adult population, the same has not been the case with surgical strategies. The Kono-S anastomosis is a surgical technique which has demonstrated benefits in adults. In this study, we evaluated the Kono-S anastomosis in the pediatric population and found improved clinical outcomes for patients with Kono-S anastomoses compared with those undergoing the traditional stapled anastomoses.

Early advances in surgical management for pediatric CD patients were focused on the utilization of minimally invasive techniques to ameliorate the need for major open surgery. Initial studies found that both single-incision and standard laparoscopy were safe and effective in the pediatric population for treatment of medically refractory ileocolic CD [16, 17]. Subsequent expansion of that work in the pediatric population has been limited, and many of the current surgical practices for management of ileocolic disease have been guided by success seen in the adult population. One such example is the implementation of stapled rather than hand-sewn ileocolic anastomosis in which prior adult

	Pre-operative demographics		
	Kono-S, N=9	Traditional anastomosis, $N=9$	P value
Age (mean)	15.4	16.2	0.32
Sex			0.63
Female	5 (55.6%)	6 (66.7%)	
Male	4 (44.4%)	3 (33.3%)	
BMI (mean)	21.6	20.1	0.27
Race			0.32
White	9 (100%)	7 (77.8%)	
Black/African American	0	0	
Asian	0	1 (11.1%)	
American Indian/Alaska Native	0	0	
Native Hawaiian/Other Pacific Islander	0	0	
Multiple	0	1 (11.1%)	
Other	0	0	
Time from diagnosis to surgery (mean; d)	469.4 (1.3 years)	464.6 (1.3 years)	0.98
Family History			0.63
Yes	4 (44.4%)	3 (33.3%)	
No	5 (55.6%)	6 (66.7%)	
Pre-Op EEN			0.01*
Yes	0	5 (55.6%)	
No	9 (100%)	4 (44.4%)	
Steroids			0.16
Prednisone	3 (33.3%)	5 (55.6%)	
Budesonide	0	1 (11.1%)	
Methylprednisolone	0	0	
Immunomodulators			0.60
Azathioprine	0	1 (11.1%)	
Methotrexate	2 (22.2%)	2 (22.2%)	
6-Mercaptopurine	0	0	
Biologics			0.30
Adalimumab	1 (11.1%)	2 (22.2%)	
Infliximab	7 (77.8%)	5 (55.6%)	
Ustekinumab	1 (11.1%)	0	
Infliximab-abda	0	1 (10%)	
Other medications	2 (22.2%)	2 (22.2%)	1
Ciprofloxacin	0	2	
Metronidazole	0	2	
5-ASA	0	0	
Other	2 (22.2%)	0	
Pre-op symptoms	6 (66.7%)	9 (100%)	0.06
Diarrhea	1	1	
Nausea	2	4	
Vomiting	2	3	
Abdominal pain	6	9	
Hematochezia	0	1	
Frequency	1	0	
Anorexia	0	0	
Weight Loss	1	1	
Fatigue	0	0	
Extra-intestinal manifestations	1	0	
Other	2	2	

EEN exclusive enteral nutrition

*Indicates statistical significance

Table 2 Intra-operative, post-operative, and histopathologic outcomes

	Surgical details		
	Kono-S, $N=9$	Traditional anastomosis, $N=9$	P value
Surgery type	3/9 = trephine 6/9 = lap	9/9 = lap 4/9 = single site 1/9 = side-to-side 8/9 = end-to side	
LOS (mean; d)	2.9	4.6	0.03*
EBL (mean; mL)	16.7	68.3	0.10
Procedure Length (mean; min)	139.7	170.9	0.10
Prior Stoma	3 (33.3%) 1 = double barrel 2 = EI	0	0.06
Extra surgery	1 (11.1%) 1 = stricturoplasty	1 (11.1%) 1 = R hemicolectomy	1
Pathologic Findings	7 (77.8%)	9 (100%)	0.13
Strictures/stenosis	4	3	
Inflammation	6	9	
Ulceration	3	8	
Fibrosis	5	2	
Granulomas	1	2	
Pyloric gland metaplasia	0	4	
Fistula	2	1	
Ileal resection length (mean; cm)	15.81	13.78	0.67

*Indicates statistical significance

randomized-controlled trials (RCTs) demonstrated the lack of difference between the two techniques regarding risk of POR [18]. Subsequent studies added that specifically wide stapled side-to-side, rather than hand-sewn end-to-end anastomosis, reduced POR [19].

Anastomotic recurrence after ileocolic resection for CD is one of the most frequent long-term complications seen in both the adult and pediatric populations. Pediatric endoscopic, clinical, and surgical recurrence has been reported as up to 29%, 19%, and 2%, respectively, at 1-year followup [3, 20]. As a result, a significant volume of research has been conducted investigating whether a change in surgical technique of the anastomosis might mitigate POR, but all of this research has thus far only been conducted in the adult population. The most cited new surgical technique with promising results is the Kono-S anastomosis which has been shown in recent multicenter international RCTs to reduce significantly the rate of POR at both 5- and 10-year followup [21]. The Kono-S is an anti-mesenteric wide side-to-side anastomosis that also involves creation of a protective supporting column to relocate the anastomosis away from the mesentery. Given that recurrence commonly occurs at the mesenteric border of the anastomosis, newer studies have considered the role of the mesentery in driving the inflammatory process characteristic of CD. In this manner, the Kono-S anastomosis is believed to reduce the rate of POR [22–24]. We hypothesized that the success of the Kono-S anastomosis in the adult population might also be realized in the pediatric population. This study demonstrates that compared to current surgical practices, the Kono-S anastomosis provides similar if not better short-term outcomes and safety compared to traditional techniques. Longer term follow-up is needed to determine if a favorable reduction in recurrence occurs as seen in the adult population.

Risk factors other than the anastomosis have been investigated to minimize POR. In the setting of prior ileocolic resection in children, a consensus of risk factors affecting clinical or endoscopic recurrence is lacking. Some studies have cited diffuse ileocolonic disease, age < 14 at time of diagnosis, presence of upper gastrointestinal disease, and disease presence for more than 4 years as possible factors affecting POR [7]. Subsequent studies also found that younger age at diagnosis and longer disease duration [5] were related to endoscopic recurrence, but these factors were not consistently associated with clinical recurrence. Only female sex was found to be a risk factor for clinical recurrence in one study [3], and none of the previously cited risk factors were found to be significant in a subsequent study [25].

This study found that these same risk factors evaluated in both the TA group and the Kono-S anastomosis group did not result in any significant differences other than the

 Table 3
 30-Day post-operative outcomes

30-Day post-operati	ve outcomes
50 Day post operati	ve outcomes

	Kono-S, $N=9$	Traditional anastomosis, $N=9$	P value
Post-op complications	1 (11.1%)	1 (11.1%)	1
Leak	0	1	
Abscess	0	0	
Ileus	0	0	
SBO	0	0	
SSI	1	0	
Steroids			1
Prednisone	0	0	
Budesonide	0	0	
Methylprednisolone	0	0	
Other meds			1
Ciprofloxacin	0	0	
Metronidazole	0	0	
5-ASA	0	0	
Other	0	0	
Antidiarrheals			1
Loperamide	0	0	
Lomotil	0	0	
Symptoms	3 (33.3%)	6 (66.7%)	0.16
Diarrhea	0	0	
Nausea	0	0	
Vomiting	1	1	
Abdominal pain	0	5	
Hematochezia	0	0	
Frequency	1	0	
Anorexia	0	0	
Weight loss	0	0	
Fatigue	0	1	
Extra-intestinal manifestations	0	0	
Other	1 (bloating)	1 (urgency and discharge)	
Average number bowel movements	2.25	1.71	0.44
Need for reoperation			0.30
Yes	0	1 (11.1%)	
No	9 (100%)	8 (88.9%)	

SSI surgical site infection

more frequent utilization of pre-operative exclusive enteral nutrition (EEN) in the TA group. Use of EEN in children has been found to be an effective means of achieving early remission and is comparable in efficacy to steroids [26, 27]. Cost, formula palatability, availability, and experience to formulate EEN have affected its universal utilization [26, 27]. Given that most of the TA group cases were performed 1–2 years prior to the Kono-S anastomosis group, this difference could be explained predominantly by a change in practice by our institution's gastroenterology group rather than a difference in severity of disease between the two treatment groups. The short-term complication rates in this study illustrate the potential safety of the Kono-S anastomosis compared to TA, with no significant differences discovered at 30-day follow-up and significantly fewer number of complications noted after 6 months of follow-up. Prior studies have demonstrated that short-term complication rates (morbidity within 30 days of surgery) and delayed complication rates (any morbidity after 30 days of surgery) are about 29.5% and 4.9%, respectively [3]. The most common short-term complications have been found to be anastomotic leak, SBO, ileus, wound complications, gastrointestinal bleeding, and venous thromboembolism [28]. Despite the small sample

Table 46-Month post-operativeoutcomes

	Kono-S, $N=8$	Traditional anastomosis, $N=9$	P valu
Time to follow-up (mean; d)	196.5	227.2	0.18
Post- op complications	0	1 (11.1%)	0.33
Leak	0	0	
Abscess	0	0	
Ileus	0	0	
SBO	0	1	
SSI	0	0	
Steroids	0	0	0.81
Prednisone	0	0	
Budesonide	0	0	
Methylprednisolone	0	0	
Immunomodulators	1 (12.5%)	5 (55.6%)	0.06
Azathioprine	0	1	
Methotrexate	1	3	
6-Mercaptopurine	0	1	
Biologics	8 (100%)	9 (100%)	0.81
Adalimumab	1	3	
Infliximab	6	5	
Ustekinumab	0	0	
Infliximab-abda	1	1	
Other meds	0	1 (11.1%)	0.33
Ciprofloxacin	0	0	0100
Metronidazole	0	1	
5-ASA	0	0	
Other	0	0	
Antidiarrheals	0	2 (22.2%)	0.16
Loperamide	0	1	0.10
Lomotil	0	0	
Other	0	2 (colestipol, levsin)	
Symptoms	2 (25%)	7 (77.8%)	0.03*
Diarrhea	0	2	0.05
Nausea	0	3	
Vomiting	0	0	
Abdominal pain	2	5	
Hematochezia	0	1	
	0	0	
Frequency Anorexia	0	0	
Weight loss	0	1	
Fatigue Extra-intestinal manifestations	0 0	0 0	
	0	3	
Bloating	U	3	0.16
Energy	0	7 (77 80)	0.16
Normal	8	7 (77.8%)	
Increased	0	0	
Decreased	0	2 (22.2%)	A 77
Average number bowel movements	1.92	1.69	0.61
Need for reoperation			
Yes	0	0	0.81
No	8	9	

SSI surgical site infection

*Indicates statistical significance

size of this study, the overall lack of significant short-term complications is a promising outcome. Future larger cohort studies will be required to determine the reproducibility of these outcomes.

While this study is the first to evaluate the Kono-S anastomosis in the pediatric population, there are several limitations. The retrospective nature of this study allows for incomplete data and variations in post-operative follow-up. Because endoscopic follow-up is not part of routine early surveillance, we were unable to assess for endoscopic recurrence, which more commonly precedes clinical recurrence and has been found to be a better predictor for risk of surgical re-intervention [7]. Our follow-up period was limited to 6 months, and longer term data are pending analysis. Further studies will better define the efficacy of Kono-S in reducing long-term complications and recurrence. This study is a single- institution review performed at a tertiary center and may not be generalizable. Finally, while most of these patients underwent primary resections, three were re-resections, and the data on future efficacy may be impacted.

Conclusion

The Kono-S anastomosis is a viable and safe technique for anastomosis after ileocecal resection in pediatric CD patients. Longer term follow-up is needed to elucidate its effectiveness in reducing POR both endoscopically and clinically.

Author contributions M.O. collected data, performed the statistical analysis, prepared tables, and wrote the main manuscript text. J.L and A.D. conceived the analysis, contributed data and reviewed the manuscript.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest None.

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