Factor analysis of postsurgical gastroparesis syndrome after right hemicolectomy for colon cancer

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Abstract. The present study aimed to investigate factors influencing postsurgical gastroparesis syndrome (PGS) in patients with right-sided colon cancer. In total, 260 patients who underwent complete mesocolic excision for right-sided colon cancer were included in the present analysis. Among the included patients, 69 underwent open radical right-sided colon resection, 175 underwent laparoscopic radical right-sided colon resection and 16 underwent robot-assisted radical right-sided colon resection. The occurrence of PGS was observed, and both the χ^2 test and multivariate regression analysis were conducted to identify influencing factors. Among the 260 patients, 32 experienced PGS, with an incidence rate of 12.3%. Univariate analysis demonstrated that age, perioperative blood glucose levels, self-rated anxiety scale scores and surgical approach were significantly associated with PGS ($P<0.05$), whereas sex, surgical duration, diabetes and perioperative albumin levels were not significant factors ($P>0.05$). Multivariate logistic regression analysis showed that age >70 years, perioperative blood glucose ≥11.1 mmol/l, a self-rating anxiety scale score ≥50 and radical extended right-sided colon resection were risk factors for PGS occurrence. In conclusion, the occurrence of PGS in patients with right-sided colon cancer was revealed to be associated with age, perioperative blood glucose levels, self-rated anxiety scale scores and surgical approach.

Introduction

Colorectal cancer is one of the most common malignant tumors of the digestive tract. According to 2020 statistics, the incidence of colorectal cancer (including colon and rectal cancer) in China ranked second among all malignant tumors, accounting for ~12.2% of all newly diagnosed cancer cases in the country, with >550,000 new cases reported (1). Several factors, including changes in dietary habits, increased meat consumption, environmental pollution and rising rates of constipation (attributed to various factors, including lifestyle changes, dietary habits, medical conditions and shifts in social environments), have contributed to the rapid increase in the incidence of colorectal cancer. With economic development, growing health awareness among the population and the widespread adoption of screening technologies, the early- and mid-stage diagnosis rates of colorectal cancer have improved, which are favorable conditions for curative treatments (2).

Right hemicolectomy is the primary surgical procedure for the treatment of colorectal cancer and is particularly suitable for early-to-mid-stage malignant tumors of the right colon (3). With advancements in medical technology, right hemicolectomy has evolved from an open surgery approach to increasingly precise laparoscopic and robotic-assisted approaches (4). This refinement in surgical technique has led to a reduction in trauma and a corresponding decrease in postoperative complications (5). However, among the various complications associated with right hemicolectomy, postsurgical gastroparesis syndrome (PGS) is quite prevalent (the occurrence rate of PGS is between 5 and 10% in general, but it is more common following gastric surgeries, such as gastric resection or fundoplication), and is closely linked to patient characteristics and surgical techniques. PGS is a significant risk factor for poor prognosis, making the prevention and treatment of postoperative PGS after surgery a matter of growing importance (6).

PGS is defined as a gastric emptying dysfunction caused by gastrointestinal motility disorders that occur postoperatively in the absence of mechanical obstruction. The primary clinical manifestations include nausea, vomiting, early satiety, a lack of appetite, upper abdominal discomfort and weight loss (7,8). Previous studies (9-11) have indicated that 2-3% of patients may experience PGS following abdominal surgery. Once it occurs, PGS can prolong the duration of enteral and parenteral nutrition, worsen patient suffering and economic burden, exacerbate psychological stress, extend hospital stays and hinder postoperative recovery (12). The incidence of PGS after a right hemicolectomy is generally higher compared with that after other lower abdominal surgeries, regardless of whether the procedure is a traditional open surgery, laparoscopic minimally invasive surgery or robotic-assisted surgery (13-15). In

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recent years, with minimally invasive and refined surgery, the incidence of PGS has changed markedly. In the present study, a retrospective analysis was conducted using the clinical data of 260 patients with right colon cancer to investigate the clinical factors that influence the occurrence of PGS after right hemicolectomy (16).

Materials and methods

Clinical data. In total, 260 patients with right colon cancer were selected, who were treated at The First Affiliated Hospital of Soochow University (Suzhou, China) between January 2018 and December 2021. All patients underwent complete mesocolic excision for right hemicolectomy. Among them, 69 underwent open radical right hemicolectomy, 175 underwent laparoscopic radical right hemicolectomy and 16 underwent robot-assisted radical right hemicolectomy. Among the 260 patients, 145 were male and 115 were female, with ages ranging from 23 to 95 years, and a mean age of 69.8 years. The inclusion criteria were as follows: i) Elective surgery for right colon cancer; ii) clear surgical indications without evident distant metastasis; iii) age range, 23-95 years; iv) no contraindications for surgery and no serious comorbidities; and v) no recent use of medications affecting gastrointestinal function and the ability to eat normally preoperatively. The exclusion criteria included: i) Serious complications in other vital organs that would preclude surgery; and ii) use of medications affecting gastrointestinal function prior to surgery. The present study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Soochow University (approval no. SUDA20171205H01) and written informed consent was obtained from all patients.

Diagnostic criteria for PGS. The international criteria (17) for diagnosing PGS include: i) The presence of symptoms such as early satiety, postprandial bloating, nausea, vomiting, abdominal distension and upper abdominal discomfort; ii) the absence of mechanical obstruction at the gastric outlet; and iii) evident gastric emptying delay. Since functional dyspepsia can present with similar symptoms, it is essential to determine whether these symptoms are due to gastroparesis. This can be achieved through trials using prokinetic medications or gastric electrical stimulation. Various methods are available to objectively assess gastric emptying, with solid-phase meal gastric emptying scintigraphy being the most effective. Diagnosis relies on the finding that >10% of a standard meal remains in the stomach after 4 h (7,18). In China, there is no unified standard for diagnosing PGS. A large proportion of domestic literature refers to the diagnostic criteria proposed by Fudan University's Zhongshan Hospital: i) ≥1 examinations indicate no mechanical obstruction at the gastric outlet, with upper gastrointestinal imaging using contrast agents confirming the absence or significant reduction of gastric peristaltic waves, while excluding distal small bowel obstruction as a cause of gastric retention; ii) a gastric drainage volume >800 ml per day for >10 days; iii) no significant disturbances in electrolyte, acid-base balance and an absence of underlying conditions causing gastroparesis, such as diabetes or hypothyroidism; and iv) no recent use of medications affecting smooth muscle function, such as morphine or atropine (19-21).

PGS, paralytic ileus and small bowel stasis all share common gastrointestinal symptoms, such as abdominal bloating, nausea and vomiting. However, their underlying mechanisms, clinical presentations, diagnostic approaches and treatments differ. PGS is characterized by delayed gastric emptying, which causes food to accumulate in the stomach, leading to symptoms such as nausea, vomiting and bloating. PGS is most often seen after abdominal surgeries (22). Paralytic ileus is typically caused by a temporary halt in bowel movement, particularly after major surgery, and presents with widespread abdominal bloating, constipation and an inability to pass gas (23). Small bowel stasis occurs when small bowel motility slows or stops, resulting in the accumulation of intestinal contents, gas and fluids. Small bowel stasis is commonly seen following surgeries involving the small intestine, such as bowel resections or anastomosis. The pathophysiology of small bowel stasis is often linked to factors such as anesthesia, postoperative inflammation and nerve damage to the intestines (24).

Clinical presentation. Symptoms of PGS are primarily localized to the upper abdomen, including fullness, early satiety, nausea and vomiting, usually of gastric contents. Symptoms typically worsen after eating (25). Paralytic ileus is marked by extensive abdominal bloating, constipation and the inability to pass gas. Vomiting may include both gastric contents and undigested food, and severe constipation is common (26). Symptoms of small bowel stasis include persistent bloating, nausea and vomiting, often containing gastric contents or undigested food. Constipation and difficulty passing gas are also typically present (27).

Imaging differences. Gastric emptying studies of PGS show delayed gastric content, while CT or X-ray may indicate gas accumulation in the stomach. X-ray or CT imaging of patients with paralytic ileus will show small bowel dilation and fluid-gas levels, suggesting reduced motility. X-ray or CT imaging of patients with small bowel stasis shows dilation of the small bowel with visible fluid-gas levels and gas accumulation within the bowel lumen (28-30).

In the present study, all cases of PGS were isolated and did not present in combination with paralytic ileus and small bowel stasis. Only patients who met the criteria for right hemicolectomy were included in the present study.

Perioperative blood glucose monitoring. The postprandial blood glucose levels were measured using peripheral blood samples, with monitoring occurring preoperatively and ≥3 times within 7 days post-surgery. A perioperative blood glucose level of <11.1 mmol/l was established as the threshold for acceptable glucose control.

Perioperative albumin monitoring. Perioperative serum albumin levels were measured using peripheral blood samples, with monitoring occurring preoperatively and at least three times within 7 days post-surgery. A perioperative albumin level of ≥35 g/l was established as the threshold for acceptable albumin status.

Self-rating anxiety scale (SAS). The SAS (31) was used to assess the frequency of symptoms, such as anxiety, fear, palpitations and sleep disturbances. Scoring was assigned to represent the frequency of symptoms as follows: 1, None or rarely; 2, sometimes; 3, most of the time; and 4, nearly all or

Table I. Univariate analysis of factors influencing PGS in 260 patients with right-sided colon cancer.

Factor	No. of patients	PGS	χ^2	P-value
Sex			0.523	0.122
Male	145	18		
Female	115	14		
Age, years			6.342	0.001
>70	121	21		
≤70	139	11		
Duration of operation, min			0.122	0.215
>180	95	12		
≤180	165	20		
Type 2 diabetes mellitus			0.434	0.151
Yes	89	10		
No	171	22		
Perioperative blood glucose, mmol/l			5.332	0.003
≥11.1	107	18		
<11.1	153	14		
Perioperative albumin, g/l			0.622	0.251
<35	71	5		
≥35	189	27		
Anxiety score			6.221	0.018
≥50	52	13		
<50	208	19		
Surgical method			5.311	0.008
Open surgery	69	19		
Laparoscopic surgery	175	10		
Robotic-assisted surgery	16	3		

PGS, postsurgical gastroparesis syndrome.

all the time. The total score from the 20 items was summed and multiplied by 1.25, with the integer part taken as the standardized score. A score of ≥50 was considered to indicate anxiety.

Statistical analysis. Statistical analyses were performed using SPSS software (version 19.0; IBM Corp.). The χ^2 test was used for categorical data comparisons and multivariate regression models were employed for multifactorial analysis. P<0.05 was considered to indicate a statistically significant difference.

Results

All 260 patients underwent successful surgery, with 32 cases of PGS, resulting in an incidence rate of 12.3%. Specifically, there were 19 cases (incidence rate, 27.5%) in the open surgery group, 10 cases (5.7%) in the laparoscopic group and 3 cases (1.9%) in the robotic group. Symptoms, including postprandial discomfort and vomiting, were observed in all cases within 4-7 days of surgery.

All patients with PGS received a comprehensive treatment plan that included continuous gastrointestinal decompression, parenteral nutrition and placement of a jejunal feeding tube for enteral nutrition. Efforts were made to correct electrolyte imbalance. The treatments included metoclopramide and domperidone administered via nasogastric feeding (10 mg metoclopramide every 6-8 h and 10 mg domperidone every 8 h). Additionally, traditional Chinese medicine techniques, such as acupuncture and abdominal massage, were employed to stimulate gastrointestinal motility, improve blood flow and promote the recovery of gastrointestinal function. Psychological support and education were provided to alleviate anxiety and tension.

All 32 patients with PGS successfully regained normal gastrointestinal motility with treatment durations ranging from 15 to 90 days. Normal gastrointestinal motility in patients with PGS was assessed using the following clinical indicators: i) Return of bowel sounds: Auscultation of bowel sounds was performed regularly, with the reappearance of normal bowel sounds (3-5 sounds per min) indicating the recovery of motility; ii) passage of gas or stool: Successful recovery was confirmed by the resumption of flatus or bowel movements, which are key indicators of gastrointestinal function; iii) tolerance to enteral nutrition: Patients were gradually transitioned to oral or enteral feeding, and the ability to tolerate a regular diet without nausea, vomiting or abdominal distension was

Table II. Logistic analysis of factors influencing PGS in 260 patients with right-sided colon cancer.

Factor	β	Wald χ^2	OR	95% CI	P-value
Sex	0.563	0.332	1.872	0.312-9.545	0.243
Age	2.933	8.121	9.565	1.545-68.221	0.001
Time of operation	0.772	0.871	2.211	0.544-10.332	0.082
Type 2 diabetes mellitus	0.336	0.553	1.923	0.434-8.614	0.211
Perioperative blood glucose	3.236	4.925	7.973	1.231-53.246	0.009
Perioperative albumin	1.324	3.125	4.763	0.931-25.342	0.289
Anxiety score	2.347	6.269	10.235	1.458-49.273	0.009
Surgical method	2.411	6.324	8.441	1.256-39.326	0.005

PGS, postsurgical gastroparesis syndrome; OR, odds ratio.

considered a sign of restored gastrointestinal motility; iv) resolution of gastric residuals: Monitoring the volume of gastric residuals via nasogastric tube showed a decrease to <200 ml per day, suggesting improved gastric emptying; v) subjective symptom relief: Patients reported relief from symptoms such as bloating, abdominal pain and nausea, further confirming the recovery of gastrointestinal function; and vi) imaging findings: Imaging studies, such as abdominal X-rays, ultrasound or CT scans, were used to evaluate the resolution of gastric distension, absence of fluid-air levels and restoration of normal intestinal peristalsis, providing objective confirmation of gastrointestinal recovery. These clinical markers, used in combination, provided a comprehensive evaluation of normal gastrointestinal motility recovery in all patients. Univariate analysis demonstrated that the age, perioperative blood glucose levels, anxiety scores and surgical method were significantly associated with the occurrence of PGS (P<0.05). By contrast, factors such as sex, duration of surgery, type 2 diabetes mellitus and perioperative albumin levels were not significantly associated with PGS (P>0.05; Table I).

Using the occurrence of PGS as the dependent variable, multivariate logistic regression analysis was performed, incorporating eight potential influencing factors as covariates. The results indicated that age, elevated perioperative blood glucose levels, high anxiety scores and type of surgical approach were significant factors influencing the occurrence of PGS (P<0.05; Table II).

Discussion

In recent years, the widespread adoption of minimally invasive techniques has significantly increased the use of laparoscopic and robotic surgeries, offering advantages such as smaller incisions, reduced gastrointestinal exposure and faster recovery times (32-34). PGS is a common early complication of abdominal surgery characterized by various clinical presentations. The causes of PGS may be linked to neuromuscular dysfunction; however, the precise mechanisms remain unclear. Previous studies (7,35,36) have shown that factors such as blood pressure, surgical duration, blood loss and hemoglobin levels do not significantly affect the incidence of PGS.

Recent findings (37-39) have indicated that the incidence of PGS is notably high after open right hemicolectomy, whereas laparoscopic and robotic approaches tend to have lower rates of PGS. The present retrospective analysis of the incidence of PGS in patients undergoing radical surgery for right colon cancer identified several associated risk factors, including the type of surgical method, age, anxiety scores and perioperative blood glucose levels. Furthermore, related studies (40-42) have shown a statistically significant difference in the incidence of postoperative PGS between laparoscopic and open gastric cancer surgeries, suggesting that the precision of laparoscopic techniques can help reduce the incidence of gastrointestinal dysfunction. The findings of the present study support this conclusion.

As the population continues to age, older patients often experience diminished physiological functions and organ reserves, increased tissue fragility and vascular sclerosis, which can lead to a higher risk of bleeding. Additionally, a decline in gastrointestinal motility and impaired cardiopulmonary function can further reduce postoperative activity levels (43,44). Older adults tend to have a lower capacity to cope with surgical stress, making them more susceptible to postoperative gastrointestinal dysfunction (45).

During stress, perioperative fasting can induce insulin resistance, which impairs the ability of insulin to regulate blood glucose levels (46). Elevated blood glucose levels, particularly those >15 mmol/l, can inhibit motilin secretion, disrupt autonomic nerve function, interfere with normal gastric slow-wave activity, increase gastric fundal compliance and reduce intragastric pressure, ultimately delaying or preventing gastric emptying (47). Controlling perioperative blood glucose levels within the normal range is crucial for reducing the incidence of postoperative PGS, with the present study providing strong evidence to support this recommendation (48).

Research also indicates that psychological factors serve a key role in the onset and treatment of PGS. Anxiety is particularly prevalent in patients with cancer. Factors, such as a poor understanding of surgery, discomfort from various medical devices, uncertainties regarding treatment outcomes and financial pressures can significantly heighten patients' anxiety and tension. The enteric nervous system, often dubbed the ‘second brain’, is vital in emotional regulation and has been increasingly recognized for its importance in recent studies (49-52).

The present study demonstrated a strong association between anxiety levels and the occurrence and severity of PGS. Specifically, greater anxiety is associated with more severe PGS symptoms, and anxiety can influence the recovery of patients from PGS. During the perioperative period, anxiety, insomnia and neuroticism can provoke a stress response in the body, leading to the activation of the autonomic nervous system (53). This may activate the sympathetic nervous system, inhibit the activation of neurons in the gastrointestinal plexus and result in catecholamine release from sympathetic nerve endings. These catecholamines can bind to a and b receptors on the membranes of gastrointestinal smooth muscle cells, suppress contractions and lead to delayed gastric emptying, thus contributing to PGS (54). Comprehensive psychological interventions can alleviate negative emotions and enhance the patients' sense of agency. Supportive counseling, targeted psychological interventions and complementary therapies, such as music and massage, can aid in restoring endocrine function, reducing the incidence of PGS and promoting recovery. Additionally, psychotropic medications, such as β-adrenergic blockers and benzodiazepines, can be effective in managing PGS and accelerating patient recovery when necessary (55).

For certain types of cancer that are located in the hepatic flexure or proximal transverse colon, lymphatic drainage may flow through Henle's surrounding lymphatic network to the lymph nodes around the right gastroepiploic vessels. The rate of metastasis to the right gastroepiploic vessels has been reported to be ~4% (56-58). According to the American Joint Committee on Cancer staging criteria, lymph nodes below the pylorus are classified as non-regional (59). However, multiple retrospective studies (60-62) have indicated that when metastasis to these nodes is highly suspected, active dissection can enhance the long-term survival rates of patients.

During right hemicolectomy, it is essential to excise the right half of the greater omentum within the arch of the left gastroepiploic vessels, clear the lymph nodes below the pylorus and ligate the right gastroepiploic vessels. This procedure damages the perivascular nerve tissues and disrupts normal gastrointestinal electrical activity. In addition, ligation of the right gastroepiploic vessels can hinder venous return from the greater curvature of the stomach. Traction applied to the gastric body during surgery, especially in open techniques, can lead to impaired signaling and structural atrophy of the interstitial cells of Cajal, resulting in arrhythmias and delayed gastric emptying (63-65). The present study also indicated that the incidence of PGS was significantly higher following open surgery compared with after laparoscopic or robotic approaches. Moreover, the fixed surgical maneuvers required in right hemicolectomy can lead to vascular and nerve damage, thereby increasing the likelihood of PGS. Experts have proposed preserving the right gastroepiploic vessels during lymphadenectomy below the pylorus; however, more research is needed to determine whether this approach complicates the clearance of lymph node 206 and minimizes interference with gastric function (60,66,67). Additionally, right hemicolectomy alters the anatomical structure of the gastrointestinal tract and the surrounding tissues, which may disrupt the balance of gastrointestinal hormones. Further studies are required to investigate the potential feedback mechanisms between the colon and the stomach (14).

Theoretically, initiating enteral nutrition support earlier can positively impact malnutrition correction and prevent complications, such as PGS. However, it is crucial to acknowledge that comprehensive treatment strategies also have certain drawbacks. Approaches such as Sandostatin (a somatostatin analog), placement of jejunal feeding tubes under intervention, psychological therapy, acupressure and acupuncture carry their own inherent risks. For example, although Sandostatin has clear indications and can significantly improve PGS, it has numerous contraindications that may lead to metabolic disturbances. Given that patients with ascending colon cancer often suffer from malnutrition and metabolic issues, careful dosage is essential (68).

The placement of jejunal feeding tubes is appropriate for patients with severe conditions who do not receive early enteral nutrition support. However, this procedure can increase patient discomfort and the psychological burden associated with additional tubes, potentially worsening the severity of PGS. Techniques such as acupuncture, abdominal acupressure and manual therapy can effectively alleviate symptoms such as bloating, reduce the impact of surgical trauma and anesthesia on gastrointestinal electrical activity and help restore normal gastrointestinal function (69). Overall, acupuncture and abdominal acupressure can promote recovery from PGS; however, they require skilled healthcare providers. Moreover, abdominal acupressure can alter intra-abdominal pressure, posing a risk of significant bloating (70-72). Additionally, acupuncture can induce stress responses, and considering the heightened stress associated with surgery, the application of acupuncture in elderly patients should be approached with caution and careful consideration (73). In summary, comprehensive treatment may be more suitable for patients with severe conditions and higher risk of complications, and the associated risks must be thoroughly assessed.

The present study had several limitations. First, this was a single-center study with a relatively small sample size. Future research could use a multicenter approach to increase the number of participants. The implementation of robotic surgery is still in its early stages, resulting in a limited number of cases. As the volume of robotic procedures increases in the future, the related data will be further improved. Furthermore, this was a retrospective rather than a prospective study, and retrospective studies are inherently prone to biases, such as selection and recall bias, limiting the ability to establish causal relationships. Corresponding prospective studies can be performed in the future.

The present study investigated the factors influencing PGS in patients with right-sided colon cancer, with a specific focus on mood and anxiety-related factors. Factors such as low mood and anxiety were found to serve key roles in the occurrence of PGS following right hemicolectomy, aspects that have been rarely explored in previous research. The present findings may contribute to the treatment of PGS after right hemicolectomy for colon cancer.

In summary, for patients scheduled to undergo right hemicolectomy, comprehensive preoperative evaluation of the overall health and comorbidities of patients is necessary. It is essential to promptly address and mitigate the clinical risk factors that may trigger PGS and formulate a detailed surgical plan. Routine radical right hemicolectomy is recommended in

patients with ascending colon cancer. For smaller T1 and T2 tumors located in the liver or proximal transverse colon, open right hemicolectomy should be avoided; instead, laparoscopic or robotic surgeries can minimize vascular and nerve injuries, thereby reducing the risk of postoperative PGS (55,74,75). The precision offered by the laparoscopic and robotic techniques results in less impact on the surrounding organs, significantly lowering the incidence of PGS and other complications, as demonstrated in the present study.

The necessity for the routine excision of the subpyloric lymph nodes for larger T3 and T4 tumors warrants further investigation. Currently, the value of routine preoperative CT and other examinations for assessing lymph nodes is limited because their sensitivity and specificity are lower compared with those of pathological N staging, leading to potential false negatives and misdiagnoses (76,77). Utilizing techniques such as nanocarbon and indocyanine green tracing may improve the guidance for excising the subpyloric lymph nodes, allowing for more precise treatment.

Enhancing teamwork and surgical proficiency can help minimize gastric traction and stimulation, particularly by reducing manual pulling of the gastric wall during open surgery, which may help prevent and reduce the incidence of postoperative PGS. Additionally, PGS can result in difficulties with eating and nutrition postoperatively, potentially affecting patient prognosis. For patients requiring adjuvant chemotherapy, PGS can delay treatment; in the present study, the longest recovery time for a patient with PGS was 90 days, notably postponing chemotherapy initiation, which may subsequently impact prognosis. The definitive effects of PGS on disease-free survival and overall survival need to be confirmed through long-term follow-up studies, which will be a focus of future research.

In conclusion, the incidence of PGS following right hemicolectomy for colon cancer is linked to several factors, including age, perioperative blood glucose levels, anxiety self-assessment scores and surgical approach. Older patients are at greater risk of developing PGS and those with inadequate control of perioperative blood glucose levels also have an increased likelihood. Furthermore, higher anxiety scores were associated with a greater probability of PGS, whereas a less invasive surgical approach was associated with a lower risk of PGS occurrence.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

GW wrote the original draft and performed data analysis.GW and SP undertook study conceptualization, supervision, review and editing of the manuscript. Both authors read and approved the final version of the manuscript. GW and SP confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The experimental protocol was established according to the ethical guidelines of The Declaration of Helsinki and was approved by the Human Ethics Committee of the Medical Ethics Committee of The First Affiliated Hospital of Soochow University (approval no. SUDA20171205H01; Suzhou, China). Written informed consent was obtained from individual or guardian's of participants.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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