



Retrospective Study

Single-center retrospective study of the diagnostic value of double-balloon enteroscopy in Meckel's diverticulum with bleeding

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Abstract

BACKGROUND

The study aimed to analyze the characteristic clinical manifestations of patients with intestinal disease Meckel's diverticulum (MD) complicated by digestive tract hemorrhage. Moreover, we aimed to evaluate the value of double-balloon enteroscopy (DBE) in MD diagnosis and the prognosis after laparoscopic diverticula resection.

AIM

To evaluate the value of DBE in the diagnosis and the prognosis after laparoscopic diverticula resection for MD with bleeding.

METHODS

The study retrospectively analyzed relevant data from 84 MD patients treated between January 2015 and March 2022 and recorded their clinical manifestations, auxiliary examination, and follow-up after laparoscopic resection of diverticula.

RESULTS

(1) Among 84 MD patients complicated with hemorrhage, 77 were male, and 7 were female with an average age of 31.31 ± 10.75 years. The incidence was higher in men than in women of different ages; (2) Among the 84 MD patients, 65 (78.40%) had defecated dark red stools, and 50 (58.80%) had no accompanying symptoms during bleeding, indicating that most MD bleeding appeared a dark red stool without accompanying symptoms; (3) The shock index of 71 patients (85.20%) was < 1 , suggesting that the blood loss of most MD patients was less than 20%–30%, and only a few patients had a blood loss of $> 30\%$; (4) The DBE-positive rate was 100% (54/54), 99mTc-pertechnetate-positive scanning rate was 78% (35/45) compared with capsule endoscopy (36%) and small intestine computed tomography (19%). These results suggest that DBE and 99mTc-pertechnetate scans had significant advantages in diagnosing MD and bleeding, especially DBE was a highly precise examination method in MD diagnosis; (5) A total of 54 MD patients with hemorrhage underwent DBE examination before surgery. DBE endoscopy revealed many mucosal manifestations including normal appearance, inflammatory changes, ulcerative changes, diverticulum inversion, and nodular hyperplasia, with ulcerative changes being the most common (53.70%). This suggests that diverticular mucosal ulcer was the main cause of MD and bleeding; and (6) Laparoscopic dissection of diverticulae was performed in 76 patients, The patients who underwent postoperative follow-up did not experience any further bleeding. Additionally, follow-up examination of the 8 cases who had declined surgery revealed that 3 of them experienced a recurrence of digestive tract bleeding. These findings indicate that laparoscopic diverticula resection in MD patients complicated by bleeding had a favorable prognosis.

CONCLUSION

Bleeding associated with MD was predominantly observed in male adolescents, particularly at a young age. DBE was a highly precise examination method in MD diagnosis. Laparoscopic diverticula resection effectively prevented MD bleeding and had a good prognosis.

Key Words: Meckel's diverticulum with bleeding; Double-balloon colonoscopy; 99mTc-pertechnetate scanning; Capsule endoscopy; Ectopic gastric mucosa

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Core Tip: Our study aimed to analyze the characteristic clinical manifestations of patients with intestinal disease Meckel's diverticulum (MD) complicated by digestive tract hemorrhage. Our study found that MD tends to occur in young men, and double-balloon enteroscopy has a high diagnostic value for MD. The main endoscopic manifestation of MD accompanied by bleeding was ulcer, and gastric/pancreatic mucosal ectopia was the main pathological factor causing ulcer.

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INTRODUCTION

Meckel's diverticulum (MD), a common congenital true diverticulum, is a distal ileal diverticulum formed by incomplete vitelline duct degeneration during embryonic development[1]. This congenital intestinal malformation was first described in 1809 using the knowledge of human anatomy and histoembryology known at that time and thus named MD after the founder's surname[2]. MD is usually located within 200 cm of the distal ileum and is more common at 10-100 cm. The prevalence rate of asymptomatic MD is 0.3%–2.9% in the general population, with insignificant differences between males and females. Symptomatic MD occurs disproportionately in males and is dominant in males[3]. Moreover, most cases occur before age 40, particularly in younger populations[4]. Varying-degree complications mostly manifest MD symptoms. Specifically, life-threatening and disturbing complications include intestinal bleeding, inflammation, intestinal obstruction, hernia, intussusception, fistula, umbilical sinus, tumor, and other ectopic tissues. Among them, gastrointestinal bleeding is the most common clinical MD manifestation, characterized by rapid onset and development and is even life-threatening in severe cases. Due to the lack of specific symptoms and signs of bleeding caused by MD, preoperative diagnosis is difficult, and it is easy to be clinically misdiagnosed or even missed. Accordingly, we retrospectively analyzed the clinical data of 84 patients admitted to the Department of Gastroenterology of the First People's Hospital of Yunnan Province with gastrointestinal bleeding and were then diagnosed as MD with bleeding. This may help clinicians to respond better to this diagnostic challenge of gastrointestinal abnormalities.

MATERIALS AND METHODS

Patients

We collect the information of patients who, due to gastrointestinal bleeding, underwent gastroscopy and colonoscopy. We did not find bleeding lesions, but the patients were considered to have small intestinal bleeding and were admitted to the Department of Gastroenterology of the First People's Hospital of Yunnan Province between January 2015 and March 2022. Based on the diagnosis and treatment of small intestinal bleeding[5], personally selected examinations, including examination of ^{99m}Tc-pertechnetate, small intestine computed tomography (CT), capsule endoscopy (CE), and double-balloon enteroscopy (DBE), 84 patients were eventually diagnosed with MD. This study was organized by the First People's Hospital, affiliated with the Kunming University of Science and Technology Ethics Committee in Yunnan Province. All patients or their legal representatives provided informed consent, and all personal information before analysis was confidential.

Methods

The clinical data of 84 patients diagnosed with MD and hemorrhage by DBE and other auxiliary examinations (small intestine CT, nuclide scan, and CE) in the past 7 years were retrospectively analyzed. Clinical data included sex, age, bleeding characteristics, blood routine, biochemical indicators, coagulation function test, imaging or endoscopy, post-operative pathological examination, and follow-up results.

Instrument and equipment

A DBE system was used, either an EN-450P5 diagnostic endoscope or a 450T5 therapeutic endoscope (Fujinonsee Inc. Japan Saitama).

DBE preoperative preparation

The day before the DBE examination, the patient began eating a low-fat, ash-free diet and avoided colored food. After oral examination, the patient fasted from solid food for 12 h and liquid food for 6 h. After anal examination, 2000 mL of diluted polyethylene glycol electrolyte powder (69.56 mg × 2) was taken 5–6 h before the examination and operation, with an administration duration not exceeding 2 h. Patients who could not tolerate large liquid volumes were told to do it in stages, with 1000 mL given the night before the exam, and the other 1000 mL given 4–6 h before the exam. Deep sedation was performed under endotracheal intubation in patients undergoing oral examination, while patients undergoing anal examination were sedated with intravenous propofol combined with fentanyl. Oxygen was administered throughout the examination, and an electrocardiogram (ECG) monitor monitored vital signs. Before DBE, ECG, routine blood, blood biochemical, and coagulation examinations were completed.

Operation method

All DBEs were performed by two experienced endoscopists in the Digestive Endoscopy Center of our hospital. The oral or anal examination route was selected by combining the bleeding characteristics and preoperative examination results. The examination was done in close coordination with a doctor and a nurse. Before the operation, water was poured into the space between the endoscope and the external cannula to reduce friction. During the examination, the technique of Yamamoto *et al*[6] was performed which involves the systematic manipulation of the small intestine onto the endoscopic body using the "push and pull" action. Additionally, we employed the fixed effect of an airbag inflating and deflating to stabilize the small intestine, facilitating the insertion of the colonoscope into the small intestine cavity to achieve maximum depth. The examination was completed when the target lesion was detected or when the endoscope physician decided that no further endoscopy was necessary according to the situation. If no lesion was detected, either through submucosal injection of methylene blue or using a release clamp device marker, the endoscopy proceeded in the other direction on the same day or was rescheduled for a later date. In cases with MD detection, the distance between the diverticulum and the ileocecal valve was recorded by the distance accumulation method.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. The count data were expressed as frequency and component ratio (%), and the ratio was compared by chi-square test or *F*-exact test. Measurement data were tested for normality, and the variance of measured data was tested for normality and homogeneity. Normally distributed data were reported as means ± standard deviation and between-group differences were compared by Student's *t*-tests. *P* values < 0.05 were considered statistically significant.

RESULTS

Analysis of clinical characteristics

The results revealed 84 MD patients complicated with hemorrhage; 19 cases (21.60%) defecated black stool, and 65 (78.40%) defecated dark red stool. In the course of bleeding, 50 cases (58.80%) had no concomitant symptoms, 21 cases (27.10%) had abdominal pain, 11 cases (11.80%) had shock manifestations such as coldness and syncope, and 2 cases (2.40%) had abdominal pain and shock manifestations. This suggests that MD bleeding was significantly (*P* < 0.01) manifested in dark red blood stool and that most patients had no other concomitant symptoms. The shock index was

evaluated by the ratio of heart rate to systolic blood pressure after bleeding[7,8]; the shock index of 71 patients (85.20%) was less than 1.5, and only 1 patient (1.10%) had a shock index greater than 1.5. This indicates that the blood loss of most MD patients was less than 20%–30%, and that only a few patients had a blood loss of greater than 30% ($P < 0.01$). The blood biochemistry results revealed that patients with MD bleeding had secondary hemoglobin decline (75 cases, 89.80%), hypoalbuminemia (42 cases, 47.80%), and coagulation dysfunction (23 cases, 25.00%), but most patients had secondary hypohemoglobinemia and no secondary coagulation dysfunction, with a significant difference between the two groups ($P < 0.01$; Table 1).

Differences of age- and sex-onset

The study included 84 MD patients complicated by bleeding, 77 men and 7 women. The minimum age was 12 years, and the maximum age was 57 years. Among them, 17 patients were younger than 18 years of age, with an average age of 14.35 ± 2.18 years. The average age of 67 adults was 31.31 ± 10.75 years. In different age periods, the incidence of MD hemorrhage was more significant in male patients. In addition, the incidence of MD hemorrhage in the group under 30 years of age was significantly higher than that in other age groups, suggesting that the onset age of adult MD hemorrhage patients was more significant in younger patients (Figure 1 and Table 2).

Characteristics of MD in DBE examination

Of the 54 patients who completed the DBE examination, a diverticulum was found in 51 by anal examination. No diverticulum was found in 3 patients by anal examination, and a diverticulum was found by oral examination, which was an inverted diverticulum. The MD location was recorded by the distance accumulation method[9]. The shortest distance to the ileocecal valve was 12 cm, the longest was 140 cm, and the average distance was $63.64 \text{ cm} \pm 30.05 \text{ cm}$. By endoscopy, MDs were characterized by a “double cavity sign” having a mucosal ridge in the ileocece and a cavity on each side of the ridge, one of which had a blind end. However, the mucosal layer of the intestinal segment of the blind end had various endoscopic manifestations, including normal mucosal expression in 7 cases (12.96%), inflammatory changes such as congestion and erosion in 9 cases (16.67%), ulcerative changes in the blind end, internal diverticula, and diverticular ridge in 29 cases (53.70%), diverticular inversion in 2 cases (3.70%), and nodular hyperplasia in 7 cases (12.96%), indicating that most MD patients with bleeding had ulcerative lesions in the mucosa under the endoscope. This suggests that concomitant ulceration was the main cause of MD bleeding (Figure 2 and Table 3).

Diagnostic value of DBE in MD hemorrhage

Of the 84 MD patients complicated by hemorrhage, 52 completed CT examination of the small intestine, of whom 10 (19%) were positive. Twenty-five patients completed CE, and 9 (36%) were positive. Forty-five patients underwent ^{99m}Tc -pertechnetate scanning, and 35 (78%) were positive. Fifty-four completed DBE, and 54 (100%) were positive (Figure 3).

The positive rate of MD bleeding diagnosed by DBE was significantly higher than that by ^{99m}Tc -pertechnetate scan, small intestine CT, and CE. The positivity rate of the ^{99m}Tc -pertechnetate scans was higher than that of small intestine CT and CE, suggesting that DBE and ^{99m}Tc -sertechnetate scans had significant advantages in diagnosing MD and bleeding, among which DBE had the highest accuracy in MD diagnosis (Table 4).

MD laparoscopic treatment

Herein, 76 patients underwent laparoscopic diverticula resection, and 8 refused surgery and were followed up. Of 55 patients with first gastrointestinal hemorrhage, 50 were treated with laparoscopic diverticula resection. Of 29 cases of recurrent gastrointestinal bleeding, 26 underwent laparoscopic diverticula resection.

MD laparoscopic findings

Laparoscopic observation of 76 cases of diverticulum shape presented a clear base and basal organization resembling the normal bowel; MD is the simple type[10]. The shortest length of the diverticulum was 2 cm, the longest was 10 cm, the average was $4.91 \text{ cm} \pm 1.53 \text{ cm}$, the minimum width was 1 cm, the maximum width was 4 cm, and the average was $2.41 \text{ cm} \pm 0.87 \text{ cm}$. Analysis of length and width[11] indicated that when the long diameter was significantly greater than the wide diameter, the aspect ratio was equal to or larger than 3:1. In such circumstances, 11 cases were identified as tubular. Conversely, when the aspect ratio was less than 3:1, 65 cases were classified as saccate. This suggests that MDs with a wide base were more likely to be complicated by bleeding (Figure 4).

Pathological features after laparoscopic surgery

Simultaneously, three types of pathological tissues were found in 76 cases of MD, inflammatory cell infiltration in the small intestine in 39 cases (51.3%), ectopic tissue in gastric mucosa in 35 cases (46.1%), and ectopic tissue in the pancreas in 2 cases (2.6%). Preoperative DBE diagnosis was completed in 50 patients undergoing surgery; the pathogenesis of the diverticulum with bleeding was analyzed by combining the mucosal manifestations and histopathology under the endoscope. Of the 17 patients with normal mucosa, inflammatory changes, and varus diverticulum by endoscopy, 3 cases of gastric mucosa/pancreas ectopic location were found, while among the 33 patients with ulcer/hyperplasia under endoscopy, 17 cases of gastric mucosa/pancreas ectopic location were found. There was significant significance between these two groups, suggesting that the formation of endoscopic ulcers and mucosal layer hyperplasia were correlated with the ectopic location of gastric mucosa/pancreas tissue (Table 5).

Table 1 General clinical manifestations

Clinical analysis		Cases, <i>n</i>	Percentage	χ^2	<i>P</i> value
Sex	Male	77	92.0%	124.45	< 0.01
	Female	7	8.0%		
Features of gastrointestinal bleeding	Black stool	19	21.6%	56.82	< 0.01
	Dark red bloody stool	65	78.4%		
Characteristics of disease course	First bleeding	55	65.9%	17.82	< 0.01
	Recurrent bleeding	29	34.1%		
Concomitant symptoms	Nothing	50	58.8%	82.31	< 0.01
	Abdominal pain	21	27.1%		
	Shock	11	11.8%		
	Abdominal pain and shock	2	2.4%		
Shock index	< 1.0	71	85.2%	163.06	< 0.01
	1.0 < index < 1.5	12	13.6%		
	> 1.5	1	1.1%		
Anemia	Nothing	9	10.2%	111.36	< 0.01
	Exist	75	89.8%		
Albumin	Normal	46	52.2%	0.36	> 0.05
	Reduce	42	47.8%		
Abnormal coagulation function	Nothing	66	75.0%	42.03	< 0.01
	Exist	23	25.0%		

Case number (*n*) and percentage (%) of Meckel's diverticulum patients with different clinical manifestations were analyzed by frequency, and the difference ratio was compared by chi-square test after *F*-exact test.

Table 2 Meckel's diverticulum hemorrhage incidence and age group analysis

Age in yr	Cases, <i>n</i>	Percentage	χ^2	<i>P</i> value
≤ 30	51	61%	30.41 ^a	< 0.01
30 < age ≤ 40	17	20%	28.56 ^b	< 0.01
> 40	16	19%	0.04	> 0.05
Total	84	100%	N/A	N/A

^a*P* < 0.01: Comparison of bleeding incidence in MD group ≤ 30 years of age with > 40 years of age (Mann-Whitney *U* test).

^b*P* < 0.01: Comparison of bleeding incidence in MD group age ≤ 30 with 30 < age < 40 years (Mann-Whitney *U* test). *P* > 0.05: MD groups of 30 < age < 40 years and < 30 years of age were of no difference in bleeding incidence (Mann-Whitney *U* test).

N/A: Not applicable.

Prognostic analysis of MD

Laparoscopic resection of the diverticulum after follow-up of 76 patients with MD revealed no bleeding. No surgical treatment of the 8 patients in the follow-up revealed 3 cases of gastrointestinal bleeding recurrence. Compared with the follow-up group, laparoscopic surgery effectively avoided recurrent bleeding in MD patients, indicating that surgical resection of MD patients with bleeding had a better prognosis (Table 6).

DISCUSSION

The management of patients with small intestinal bleeding poses a difficulty due to the particularity of small intestine anatomical location, limitations of small intestine examination method and uneven levels of small intestinal endoscopy

Table 3 Mucosal manifestations of Meckel's diverticulum by double-balloon enteroscopy endoscopy

Manifestation	Cases, <i>n</i>	Percentage	χ^2	<i>P</i> value
Normal	7	12.96%	51.02	< 0.01
Inflammation	9	16.67%		
Ulcer	29	53.70%		
Varus	2	3.70%		
Hyperplasia	7	12.96%		
Total	54	100.00%	N/A	N/A

Incidence of ulcers in Meckel's diverticulum with bleeding was compared with absence of ulcers, $P < 0.01$ (one-way ANOVA test). N/A: Not applicable.

Table 4 Value analysis of double-balloon enteroscopy in the diagnosis of Meckel's diverticulum

Diagnosis means	Total cases, <i>n</i>	Positive case, <i>n</i>	Positive rate, %	χ^2	<i>P</i> value
Small intestine CT	52	10	19	2.55 ¹	> 0.05
				73.25 ²	< 0.01
Capsule endoscope	25	9	36	12.01 ¹	< 0.01
				43.34 ²	< 0.01
Nuclide scanning	45	35	78	34.01 ¹	< 0.01
DBE	54	54	100	11.01 ²	< 0.01

¹Comparison of nuclide scanning, small intestine computed tomography (CT), and capsule endoscopy (CE) groups.

²Comparison of double-balloon enteroscopy (DBE), small intestine CT, CE, and nuclide scan groups. Difference ratios were compared by chi-square tests. N/A: Not applicable.

Table 5 Analysis of features and postoperative pathology by Meckel's diverticulum endoscopy

Pathological tissue	Normal	Inflammation	Varus	Ulcer	Hyperplasia	Total	χ^2	<i>P</i> value
Small intestine tissue	5	7	2	13	3	30	5.36 ^a	0.01 < <i>P</i> < 0.05
Gastric mucosa/pancreatic tissue	1	2	0	13	4	20		
Total	6	9	2	26	7	50	N/A	N/A

^a0.01 < P < 0.05: More positive cases displaying the endoscopic ulcer/hyperplasia were found in the gastric mucosa/pancreatic tissue compared with small intestine tissue. Difference ratios were compared by chi-square tests.

N/A: Not applicable.

diagnosis and treatment variables However, in 5–10% of gastrointestinal bleeding cases, upper gastrointestinal endoscopy and colonoscopy cannot diagnose small intestinal bleeding. MD is one of the most common causes of small intestinal bleeding, but the diagnosis rate is lower[12]. Therefore, using CE and balloon-assisted enteroscopy (BAE) has significantly improved the diagnosis and treatment of small intestinal diseases, including MD. With advancements in imaging and endoscopic technologies, clinicians now have access to various tools for comprehensive and multidimensional analysis of MD characteristics and bleeding, leading to improved diagnostic accuracy. Consequently, it is imperative to reassess our understanding of MD and bleeding, considering current medical and technical capabilities. Our study collected data of 84 MD patients with gastrointestinal bleeding between January 2015 and March 2022 in Yunnan province at The First People's Hospital of Medical Diagnosis. The study aimed to analyze the clinical manifestations of characteristic MD with gastrointestinal bleeding in patients with small intestinal diseases, evaluate the DBE value in the diagnosis, and investigate the prognosis of laparoscopic diverticulectomy.

Most included MD patients were male. The minimum age was 12 years, and the maximum age was 57 years. In any age group, the incidence in male patients was predominant (Figure 1). This indicates that the sex ratio of MD patients with hemorrhage did not change with age. This result is consistent with Hansen's systematic review[13]. The male-to-female (M:F 1.5–4.0:1.0) sex distribution was reported to be up to 4 times more frequent in men. Çelebi *et al*[3] reported

Table 6 Postoperative treatment prognosis evaluation of Meckel's diverticulum hemorrhage

Operation	Bleeding frequency		Total	Postoperative bleeding		χ^2	P value
	First bleeding	Recurrent bleeding		No bleeding	Rebleeding		
Non-operative	5	3	8	5	3	19.67	< 0.01 ^a
Surgical treatment	50	26	76	76	0		

^a $P < 0.01$: 76 cases underwent surgical treatment compared with 8 cases without operation, the difference ratio between no-bleeding and rebleeding was analyzed by chi-square tests.

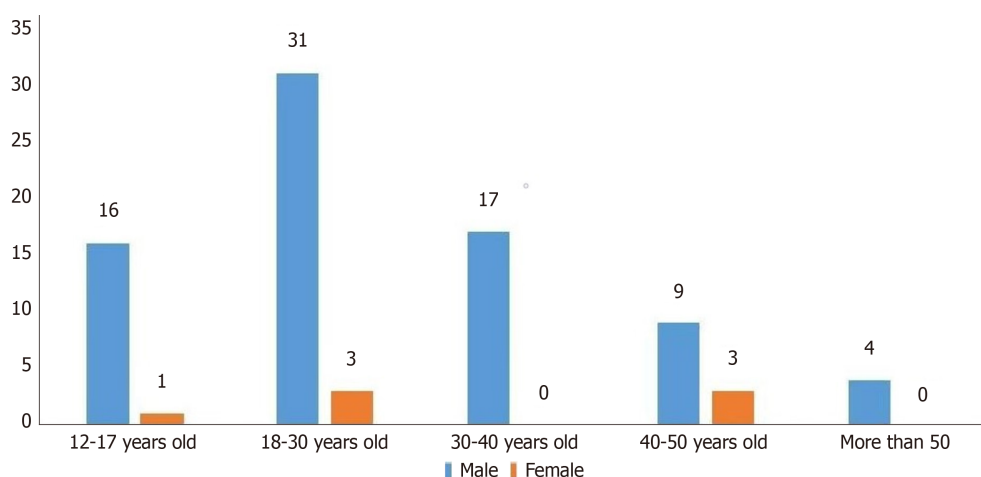


Figure 1 Age and sex proportion of 84 Meckel's diverticulum hemorrhage patients. Incidence was significantly higher in men than in women ($P < 0.01$).

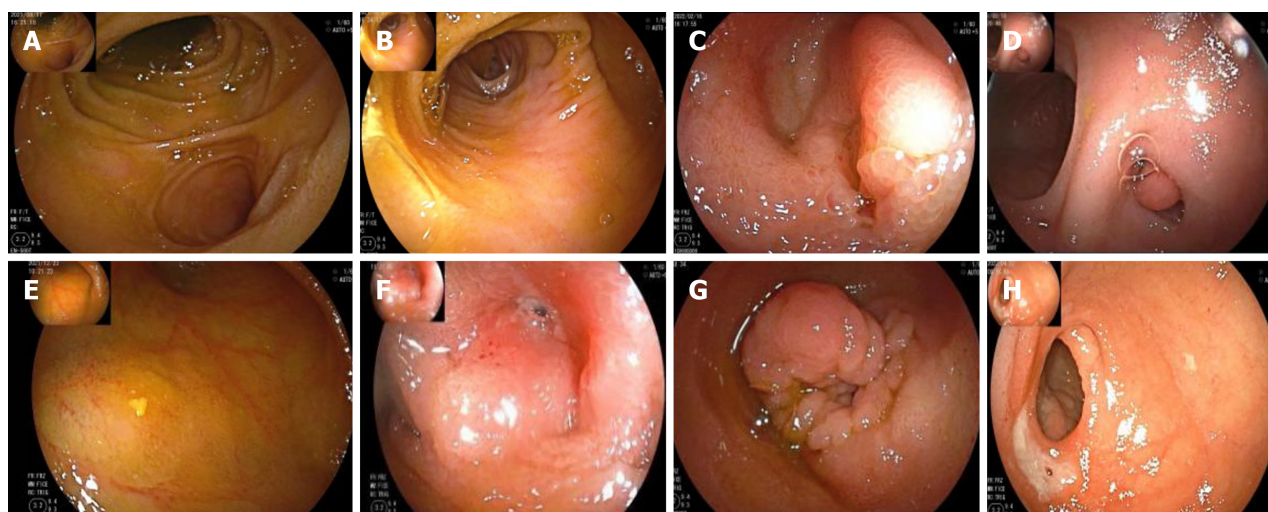


Figure 2 Appearance of Meckel's diverticulum by double-balloon enteroscopy. A: Mucosal ridge; B: Blind end of diverticulum; C: Inflammation in the diverticulum; D: Diverticulum varus; E: Ulceration in diverticulum; F: Blind ulcer stenosis; G: Diverticulum varus hyperplasia; H: Edge ulcer of the diverticulum.

possible reasons for the high incidence in men. Our study also showed that gastric mucosa/pancreatic mucosa was the main pathological factor causing mucous ulcer in Meckel's diverticulum, which further explained the possible cause of the high incidence in male patients. The incidence of MD hemorrhage in the group under 30 years of age was higher than in other age groups (Table 2). The age of onset shifted from before 40 to earlier, consistent with other studies[4]. Advancements in the diagnosis and treatment technology of MD hemorrhage can be attributed to enhanced awareness among doctors and patients regarding minor intestinal bleeding and the standard techniques employed.

While the clinical manifestations of MD are varied, a comprehensive understanding of the distinctive bleeding patterns associated with MD can greatly assist clinicians in developing immediate and accurate diagnosis and treatment strategies.

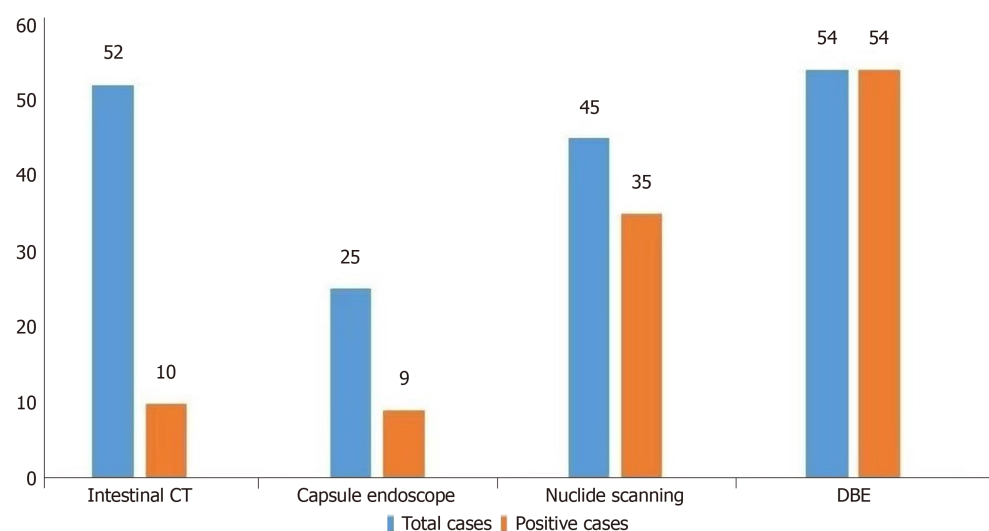


Figure 3 Diagnosis of Meckel's diverticulum complicated by hemorrhage. CT: Computed tomography; DBE: Double-balloon enteroscopy.

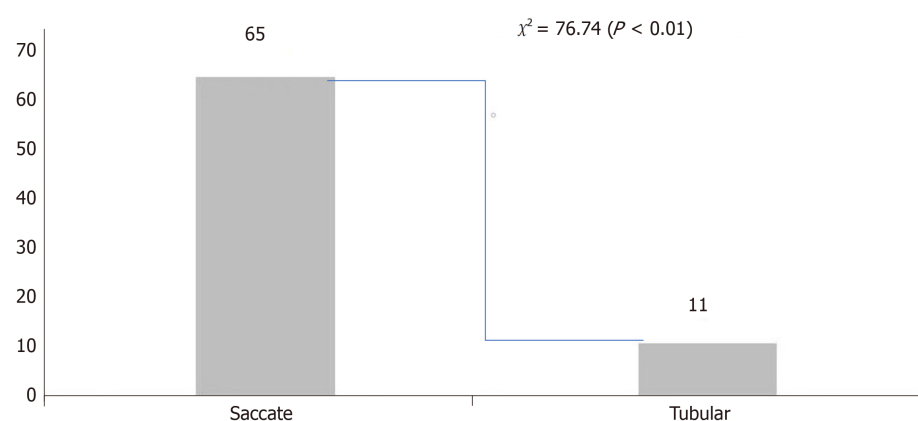


Figure 4 Morphological analysis of Meckel's diverticulum. $P < 0.01$ compared with tubular diverticulum, the incidence of cystic Meckel's diverticulum (MD) is higher in MD with hemorrhage.

Consequently, the clinical characteristic analysis of the 84 cases of MD hemorrhage showed that MD bleeding was significantly manifested by dark red bloody stool (78.40%), with no accompanying symptoms during the bleeding, and a few of cases were secondary to shock (Table 1). After hemorrhage, the shock index (heart rate/systolic blood pressure ratio)[8] evaluation suggested that most MD patients had a bleeding volume of less than 20%–30%, and only a few had a bleeding volume of greater than 30%. Combined with the blood biochemical indicators, most patients with MD bleeding may have had secondary mild hemoglobin decline and no coagulation function disorder. Therefore, most patients with MD bleeding were qualified to complete preoperative DBE examination (Table 1).

Preoperative routine inspection of MD bleeding includes imaging examination (*e.g.*, small bowel CT, small intestine MRI scanning, and high 99mTc-technetium acid salt) and intestinal endoscopy. Small intestinal endoscopies are CE and auxiliary BAE, especially balloon enteroscopy. The auxiliary type is an important test for diagnosing intestinal diseases, but the diagnostic value of MD hemorrhage is rarely reported; therefore, the BAE used in our study was DBE. Herein, of the 54 patients who underwent DBE examination prior to surgery, diverticulum was detected in 51 by anal examination and the remaining 3 were diagnosed with inverted diverticulum through oral examination. The distance between the diverticulum and the ileocecal valve was measured by the distance accumulation method. The results indicate that the shortest recorded distance to the ileocecal valve was 12 cm, the longest was 140 cm, and the average was $63.64 \text{ cm} \pm 30.05 \text{ cm}$. These findings suggest that most MD cases are located in the distal ileum. The transanal examination was more beneficial in detecting MD. However, if no bleeding lesions were found in the transanal route, the possibility of an inverted diverticulum should be examined through an oral approach. The DBE examination of 54 patients was characterized by a “double-chamber sign”. The intestinal mucosa in the diverticulum showed diversification, and the most common diverticulum presented ulcerative changes in the blind end, the inside of the diverticulum, the diverticulum crest (53.70%). Furthermore, 87.04% of cases had significant recent active bleeding following the DBE examination. Notably, the diverticulum mucosa ulceration emerged as the primary cause of MD bleeding (Figure 2, Table 3).

The combined characteristics of patients with pathological histology revealed three types of pathological tissues in 76 cases of MD complicated by bleeding, inflammatory cell infiltration in the small intestine in 52.6%, ectopia of gastric mucosa tissue in 44.9%, and ectopic in pancreas tissue in 2.5%. Preoperative DBE was performed in 51 patients combined

with mucosal signs of the diverticulum observed by endoscopy with postoperative histopathology investigation, which identified the underlying etiology. Meanwhile, in the 50 patients who received DBE before surgery, there were 3 cases of ectopic gastric mucosa/pancreas in 17 patients with normal mucosal manifestations, inflammatory changes, and varus diverticulum under endoscopy and 17 cases of ectopic gastric mucosa/pancreas in 33 patients with endoscopic ulcer/hyperplasia group. Differences of the data in the two groups were statistically significant. It is suggested that ulcer formation and mucosal layer hyperplasia observed by endoscopy were related to the ectopic gastric mucosa/pancreatic tissue. When the balance between the two transcription factors, SOX2 and CDX2, in MD is disturbed, SOX2 participates in gastric epithelial differentiation. Simultaneously, ectopic mucosal acid secretion causes peptic ulcers, erosion, inflammation, and even exposed blood vessels in the adjacent mucosa, eventually leading to diverticular bleeding[14,15]. These results further confirmed that gastric mucosa/pancreatic tissue ectopic is the main cause of MD hemorrhage (Table 5).

Based on the diagnosis and treatment of small intestinal bleeding specification combined with the clinical characteristics, individual choice small bowel CT scanning, high 99mTc-technetium acid salt, CE, and BAE examination. Each of these examinations has its advantages in evaluating the condition, with BAE being particularly beneficial in diagnosing patients with MD and bleeding. The accurate results obtained from BAE can provide a solid foundation for establishing an appropriate diagnosis and treatment plan for patients with MD-related hemorrhage.

A total of 52 cases were examined by small bowel CT. The diagnosis of MD bleeding was found to have a rate of 19%. Additionally, 25 cases underwent a complete CE examination, revealing a rate of 36%. Furthermore, 45 patients underwent 99mTc-high technetium acid salt scanning, resulting in a rate of 78% (Figure 3). Ultimately, 54 cases underwent complete DBE inspection, with a rate of 100% being observed. Compared with the small bowel CT inspection group, the group receiving CE had more MD in the small intestine. However, an insignificant difference was observed between the two groups in MD. Both small bowel CT and CE had limited sensitivity in diagnosing MD, consistent with foreign[16] literature. Despite active bleeding in the small intestine, small bowel CT examination revealed the extravasation of the contrast agent into the lumen of the ileum and the surrounding region, which occasionally corresponds to the contour of the mucosal fold. However, the blood loss should be more than 0.5 mL/min is easier to find[17]; When considering the evaluation of bleeding in cases where most patients experience a hemorrhage amounting to less than 20%-30% of their total blood volume, the resulting decrease in hemoglobin levels often presents as mild anemia. Consequently, the limited sensitivity of small intestine CT scans in diagnosing MD hemorrhage may be associated with the relatively small amount of blood loss. The acquisition of small bowel CT and CE necessitates high levels of intestinal cleanliness and lumen filling. In patients experiencing gastrointestinal bleeding, there are specific limitations on the quantity of water intake and the utilization of laxatives. Compared with CT examination of the small intestine, CE had a higher requirement for cleanliness of the intestinal cavity. If blood is retained in the intestinal cavity, it restricts the endoscopic field of vision, impeding the comprehensive visualization of the lesion and hindering the ability to establish a definitive diagnosis. MD presents limited mucosal lesions within a single diverticulum under the endoscope, which increases the difficulty of CE diagnosis of MD. Nevertheless, despite CE could not get a definitive diagnosis, identifying blood within the small intestine canal using CE can aid in determining the bleeding origin. This diagnostic approach is highly predictive of MD diagnosis and is a viable and encouraging method for diagnosing MD individuals with an unexplained GIB[18]. In addition, the positive rate of MD detected by 99mTc-perchnetate scan was 78%, which was significantly higher than that in the small intestine CT and CE groups, suggesting that 99mTc-Perchnetate scan has a high sensitivity in MD bleeding diagnosis.

Moreover, 99mTc-perchnetate scan pre-examination preparation is relatively simple and does not need intestinal cleaning preparation. Therefore, it has certain advantages in diagnosing MD bleeding, consistent with literature reports [7]. 99mTc has a special affinity for particular cells of gastric mucosa, which can be ingested, utilized, and secreted by gastric mucosa; 99mTc-Perchnetate salt scanning can detect abnormal isotope concentration of gastric mucosa outside the stomach by high-resolution gamma ray, which has high accuracy in diagnosing symptomatic MD. In patients with active intestinal bleeding, scintillation of suspected Meckel's radionuclides can detect diverticulum as its source[17]. Additionally, our positive rate of DBE diagnosis was 100%, which is significantly better than 99mTc-perchnetate scan, CE, and small intestine CT examination. DBE is more conducive to MD diagnosis due to its intuitive, omnidirectional, and controllable advantages, with the highest accuracy for diagnosing adult MD bleeding. Therefore, DBE should be the preferred method of preoperative diagnosis, consistent with multi-center studies[16,18].

Herein, 76 patients chose to undergo laparoscopic diverticulectomy; length/width analysis[10] revealed 11 cases of tubular and 65 cases of saccular MD, which suggested that saccular and basal width MD was more likely to be complicated with hemorrhage (Figure 4). Of the 76 patients who underwent surgical diverticulectomy, 50 were first MD complicated with hemorrhage, 26 were recurrent MD complicated with hemorrhage, and no further hemorrhage was detected during the follow-up. However, 8 patients who refused surgical treatment were selected for follow-up observation, 3 of whom had recurrent gastrointestinal bleeding. Compared with the follow-up group, laparoscopic diverticulectomy can effectively avoid repeated bleeding in MD patients, indicating that MD patients complicated with hemorrhage can get a better prognosis after diverticulectomy (Table 6).

CONCLUSION

To summarize, the occurrence of MD complicated by bleeding was more prevalent in adolescent men. Additionally, the disease onset tended to manifest at an even younger age. The distal ileum emerged as the most often affected site, whereas basal larger diverticula were more prone to complications involving bleeding. Notably, diverticular mucosal ulcers were identified as the primary etiological factor contributing to bleeding in MD cases. Concurrent hemorrhage in

MD patients presents as the passage of dark red bloody stool without accompanying abdominal discomfort. Following the occurrence of bleeding, the evaluation of the shock index reveals a value significantly lower than 1. Most MD patients experiencing hemorrhage can undergo preoperative diagnosis using DBE. Therefore, MD bleeding should be highly suspected in young men with first-time or recurrent passing dark red blood stool without abdominal pain. DBE can be used as the preferred inspection and should be immediately arranged through anal DBE inspection. Furthermore, a ^{99m}Tc -high technetium acid salt scan can be used as a preoperative assessment for special populations, patients without conditions for small intestinal endoscopy examination. In cases where patients exhibit symptoms of MD and bleeding, it is advisable to conduct an anal examination to rule out the presence of diverticulum. If no diverticulum is identified, additional investigation through an oral route should be pursued to identify the possibility of an inverted diverticulum. This approach offers a reasonable and effective means of diagnosing and developing a timely treatment plan for patients experiencing hemorrhage associated with MD. Nevertheless, there remains a limited incidence of hemorrhagic conditions in individuals with MD across various age groups, resulting in multiple clinical presentations. The diagnostic and treatment procedures for small intestinal bleeding should be tailored to the specific characteristics of the bleeding, anemia, and other relevant parameters. It is important to consider personalized approaches such as the use of small bowel CT, CE, and DBE to achieve a definite diagnosis.

ARTICLE HIGHLIGHTS

Research background

Due to the lack of specific symptoms and signs of bleeding caused by Meckel's diverticulum (MD), preoperative diagnosis is difficult, and it is easy to be clinically misdiagnosed or even missed. As double-balloon enteroscopy (DBE) is a highly precise examination method in MD diagnosis, the study aims to analyze the characteristic clinical manifestations of patients with intestinal disease MD complicated with digestive tract hemorrhage; as well as to evaluate the value of DBE in MD diagnosis and the prognosis after laparoscopic diverticula resection.

Research motivation

The study investigated the prevalent population of MD in a retrospective study to guide early screening and preventive treatment for high-risk individuals; explore the causes of bleeding in MD to facilitate early preventive measures, compare the advantages of DBE with other examination methods to assist in the rational formulation of clinical diagnosis and treatment strategies; and evaluating the therapeutic effectiveness of laparoscopic resection of MD and further exploring more optimal treatment approaches.

Research objectives

The study objectives were to analyze the diagnostic value of DBE in patients with MD and bleeding.

Research methods

The study retrospectively analyzed relevant data from 84 MD patients between January 2015 and March 2022 and recorded their clinical manifestations, auxiliary examination, and follow-up after laparoscopic diverticula resection. The clinical data of 84 patients diagnosed with MD and hemorrhage by DBE and other auxiliary examinations (small intestine CT, nuclide scan, and CE) in the past 7 years were retrospectively analyzed. A dual-balloon colonoscopy system (EN-450P5, a diagnostic endoscope, or 450T5, a therapeutic endoscope) was used. Clinical data were collected and analyzed, which included sex, age, bleeding characteristics, blood routine, biochemical indicators, coagulation function test, imaging or endoscopy, postoperative pathological examination, and follow-up results.

Research results

Firstly, MD with bleeding was more common in young men, and was mostly manifested as dark red bloody stool, with less bleeding. Secondly, we combined the endoscopic manifestations with the pathological results of patients with MD complicated by bleeding. It was found that combined ulcer was the main cause of MD bleeding. The formation of ulcer and mucosal layer hyperplasia were related to gastric mucosa/pancreatic tissue, which guided clinicians to be aware of gastric mucosa/pancreatic tissue heterotopic. Thirdly, this study found that DBE and ^{99m}Tc -pertechnetate scanning had obvious advantages for the diagnosis of MD complicated with bleeding, and laparoscopic surgical resection for MD complicated with bleeding could obtain a better prognosis, guiding clinicians to make the best choice in diagnosis and treatment.

Research conclusions

This study showed that MD with bleeding was more common in young men, and most patients presented with dark red stool defecation. Following the occurrence of bleeding, the evaluation of the shock index revealed a value significantly less than 1, thus most patients with hemorrhage tolerated DBE examination. DBE was used as the first choice for examination, and laparoscopic diverticulectomy had a good prognosis. The diagnostic and treatment procedures for small intestinal bleeding should be further study to the specific characteristics of the bleeding, anemia, and other relevant parameters.

Research perspectives

The small intestine is currently a blind spot for most examination methods. DBE addresses this gap. At our center, it has been observed that a significant portion of unexplained gastrointestinal bleeding is often associated with small intestine diseases. MD is the most common cause of small intestine bleeding. Clearly defining the diagnostic role of DBE in small intestine diseases is beneficial for formulating rational clinical diagnosis and treatment plans.

FOOTNOTES

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Author contributions: Wan P and Guo Q conceived and refined the study; He T and Yang C designed and implemented the study; Wan P, Zhang W, and Zuo Z sponsored the study; Zhong JS and Yin YJ were involved in the data collection; Rao CM and Mao NF were involved in the declaration of institutional review board; Yang C, Li AH, and Luo LL analyzed the data; He T and Wang J drafted the manuscript; Yang C and Zhang W revised the manuscript; all authors were involved in the critical review of the results and contributed to, read, and approved the final manuscript. He T and Yang C contributed equally to this work as co-first authors because both of them were in charge of study execution and manuscript writing; Wan P and Zhang W contributed equally to this work as co-corresponding authors; Zhang W had experience in manuscript writing and publication, made great effort in revising and submitting the manuscript, as well as sponsoring the study; Wan P was the main corresponding author and took primary responsibility for communication with the journal during manuscript submission, peer-review, and the publication processes.

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