Analysis of negative DSA findings in patients with acute nonvariceal gastrointestinal bleeding: A retrospective study of 133 patients

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ABSTRACT

Purpose: To analyze causes of acute nonvariceal gastrointestinal bleeding (GIB) with negative digital subtraction angiography (DSA) results.

Materials and methods: The clinical and follow-up data of 133 patients - recruited between February 2008 and November 2016 - with acute nonvariceal GIB and negative DSA results were included in this study. DSA results, diagnoses, and clinical outcomes were recorded.

Results: The DSA results were negative in all 133 patients. Of the total, 55 patients (41.4%) chose to undergo surgery and 78 (58.6%) opted for conservative treatment. Within 30 days, there was no significant difference in the rebleeding or mortality rates between the two groups ($P < .05$). Of all 133 patients, 76 (57.1%) had upper GIB and 57 (42.9%) had lower GIB; within 30 days, the rebleeding rate in the upper GIB group (44.7%, 34/76) was significantly higher than that in the lower GIB group (26.3%, 15/57). There was no significant statistical difference ($P < .05$) within 30 days in the mortality rates between the two groups.

Among patients with upper GIB, 26 (34.2%, 26/76) opted to undergo surgery and 50 (65.8%, 50/76) chose conservative treatment; within 30 days, the rebleeding rate in the group that chose surgery (61.5%, 16/26) was higher than that in the conservative treatment group (36%, 18/50). There was no significant difference ($P < .05$) within 30 days in the mortality rate between the two groups.

Among the patients with lower GIB, 29 (50.9%, 29/57) chose to undergo surgery and 28 (49.1%, 28/57) opted for conservative treatment. Within 30 days, the rebleeding rate in the surgery group (13.8%, 4/29) was lower than that in conservative treatment group (39.3%, 11/28). There was no significant difference ($P < .05$) within 30 days in the mortality rate between the two groups.

Sixteen patients underwent prophylactic arterial embolization; in 6 of these, bleeding was stopped for 30 days. DSA was then repeated in these 16 patients after a median interval of 1 day, and a positive bleeding site was found in 9 of the 16. Causes of bleeding were found in 111 patients by surgery or endoscopy, whereas the causes remained unknown in 22 patients.

Conclusions: Upper GIB with negative DSA results was stopped by conservative treatment, whereas lower GIB required surgery to detect the culprit bleeding site. Rare causes of GIB should be considered and appropriate management selected in a timely manner in order to detect unusual causes.

1. Introduction

Digital subtraction angiography (DSA) plays an important role in the diagnosis and treatment of acute nonvariceal gastrointestinal bleeding (GIB). It can serve to detect the bleeding site and perform arterial embolization or local drug infusion to stop the bleeding.[1–4] However, angiography does not show positive signs of bleeding in a large proportion of patients with acute GIB, and the negative rates of diagnosis by DSA as reported in the literature are between 24% and 78%.[5,6]

Although digestive endoscopy is difficult to perform in the emergency

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setting, transcatheter arterial embolization (TAE) can be used as an alternative because it can provide data regarding both the condition and its treatment simultaneously.[7] Although DSA can locate most bleeding sources, a number of negative cases remain. Few studies have reported or analyzed the negative DSA results for acute nonvariceal GIB patients, but they deserve careful attention. This study was designed to analyze the causes of negative DSA results for patients with acute nonvariceal GIB, to plan and administer appropriate and timely treatment, and to improve the rate of positive clinical diagnoses.

2. Materials and methods

Our study was approved by our institutional review board. Written informed consent was waived due to the retrospective nature of the study.

2.1. General information

A total of 133 patients (96 males and 37 females; median age, 56 years; range, 11–90 years) who had acute nonvariceal GIB and negative DSA results were recruited from our hospital between February 2008 and November 2016. Inclusion criteria were as follows[8]: (1) Unstable acute GIB within 6 h or a previous history of chronic GIB with acute attacks, hematemesis, black stool/hematochezia, and syncope. (2) No bleeding site found on gastrointestinal endoscopy or patient's inability/unsuitability to undergo endoscopy. (3) Hemodynamic instability within 6 h, with active bleeding, heart rate greater than 100 beats per minute, and systolic pressure below 90 mm Hg.

2.2. Intervention

After conventional disinfection, 1% lidocaine was injected layer by layer at the fluctuation point in 1–2 cm of the femoral artery below the right inguinal ligament. The Seldinger technique was used to puncture the femoral artery on the right side. Arteriography was then performed successively in the peritoneal artery, the superior mesenteric artery, and the inferior mesenteric artery. Super-selective angiography was performed on the branch arteries at the suspected bleeding site.

Positive DSA findings of GIB required contrast extravasation, pseudoaneurysms, and artery cut-off. Negative angiography produced none of these signs.

2.3. Statistical analysis

Patients were divided into two groups according to the bleeding site, whether it was at the proximal or distal end of the ligament of Treitz: the upper GIB group and the lower GIB group. In addition, in terms of treatment, patients were divided into two groups: the surgery group and the conservative treatment group. All of the statistical analyses were performed using SPSS 20.0 software: the skewed distribution data were represented by median, *M*; the chi-square test was used to compare the skewed distribution data. The error probability of class I was 0.05, and $P < .05$ indicated statistical difference.

3. Results

At the end of the study there were no signs of pathologic bleeding on DSA in 133 patients. Among them, 55 patients (41.4%) had chosen to have surgery and 78 (58.6%) opted for conservative treatment. The rebleeding rates within 30 days were 36.4% and 37.2% in the surgery and conservative treatment groups, respectively; the mortality rates in the two groups were 20% and 17.9%, respectively, with no statistical difference ($P < .05$) between the two groups (Table 1).

The 133 patients were divided into two groups depending on whether the bleeding site was at the proximal or distal end of the ligament of Treitz. Of the total number of patients, 76 (57.1%) had upper GIB and 57

Table 1
Outcomes and rebleeding rates after surgery or conservative treatment in patients with acute nonvariceal gastrointestinal bleeding.

		Surgery		Conservative treatment		P value
		N	N%	N	N%	
Outcome	Deceased	11	20.0%	14	17.9%	.766
	Improved	44	80.0%	64	82.1%	
Rebleeding	None	35	63.6%	49	62.8%	.923
	Occurred	20	36.4%	29	37.2%	

(42.9%) had lower GIB. The rebleeding rate within 30 days in the upper GIB patients (44.7%, 34/76) was significantly higher than that in the lower GIB patients (26.3%, 15/57). There was no significant statistical difference ($P < .05$) within 30 days in the mortality rates between the two groups (Table 2).

Of the patients with upper GIB, 50 (65.8%, 50/76) chose conservative treatment whereas 26 (34.2%, 26/76) opted for surgery. The rebleeding rate within 30 days in surgery group (61.5%, 16/26) was higher than that in conservative treatment group (36%, 18/50). There was no significant statistical difference ($P < .05$) within 30 days in the mortality rates between the two groups (Table 3).

Among the patients with lower GIB, 29 (50.9%, 29/57) chose to undergo surgery and 28 (49.1%, 28/57) opted for conservative treatment; the rebleeding rate within 30 days in surgery group (13.8%, 4/29) was lower than that in conservative treatment group (39.3%, 11/28). There was no significant statistical difference ($P < .05$) within 30 days in the mortality rates between the two groups (Table 3).

Prophylactic embolization was performed in 16 patients with negative DSA results, including 13 cases of upper GIB and 3 cases of lower GIB. Four patients with upper GIB and 2 with lower GIB stopped bleeding within 30 days after having undergone embolization; the success rate of preventive embolization was 37.5%.

Repeated DSA was performed in 16 patients; the median interval for reimaging was 1 day. Twelve patients had upper GIB and 4 had lower GIB. Positive bleeding sites were found in 6 patients with upper GIB and 3 patients with lower GIB for a positive rate of 56.2%.

Causes of bleeding were found in 111 patients by surgery or endoscopy, whereas the causes remained unknown in 22 patients (Table 4).

4. Discussion

4.1. The roles of digestive endoscopy, surgery, and conservative treatment

Acute GIB can be classified into two categories, upper and lower. For upper GIB, the preferred approach is digestive endoscopy. However, hemorrhage may sometimes obscure the endoscopic visual field, leading to failure. For lower GIB, colonoscopy remains the first-line approach. However, its positive success rate is significantly reduced in cases of a poorly prepped intestinal tract or when the endoscopic visual field is obscured by blood. In addition, colonoscopy cannot rule out bleeding from the small bowel. Although capsule endoscopy can visualize the entire small bowel, it takes a significant amount of time to do so, and such a delay is not acceptable in the emergency setting. Although endoscopy can locate the source of bleeding in some cases, it can still be difficult to

Table 2
Outcomes and rebleeding rates of patients with acute nonvariceal upper or lower gastrointestinal bleeding.

		Upper GIB		Lower GIB		P value
		N	N%	N	N%	
Outcome	Deceased	17	22.4%	8	14.0%	.223
	Improved	59	77.6%	49	86.0%	
Rebleeding	None	42	55.3%	42	73.7%	.029
	Occurred	34	44.7%	15	26.3%	

GIB, gastrointestinal bleeding.

Table 3
Outcomes and rebleeding rates of patients with upper or lower gastrointestinal bleeding after surgery or conservative treatment.

		Surgery		Conservative treatment		P value
		N	N%	N	N%	
Upper GIB						
Outcome	Deceased	8	30.80%	9	18.00%	.205
	Improved	18	69.20%	41	82.00%	
Rebleeding	None	10	38.50%	32	64.00%	.034
	Occurred	16	61.50%	18	36.00%	
Lower GIB						
Outcome	Deceased	3	10.30%	5	17.90%	.414
	Improved	26	89.7%	23	82.1%	
Rebleeding	None	25	86.2%	17	60.7%	.029
	Occurred	4	13.8%	11	39.3%	

GIB, gastrointestinal bleeding.

Table 4
Causes of acute nonvariceal gastrointestinal bleeding in this study.

Causes of acute nonvariceal GIB	Upper GIB		Lower GIB	
	N	N%	N	N%
Anastomotic bleeding	29	38.2%	7	12.3%
Peptic ulcer	22	28.9%	5	8.8%
Gastrointestinal stromal tumors	2	2.6%	9	15.8%
Peptic malignant tumor	4	5.3%	3	5.3%
Vascular malformation of the intestine	2	2.6%	4	7.0%
Intestinal necrosis	0	0.0%	5	8.8%
Inflammatory diseases of the colon	0	0.0%	4	7.0%
Meckel diverticulum	1	1.3%	3	5.3%
Pancreatitis-associated bleeding	3	3.9%	0	0.0%
Crohn disease	0	0.0%	3	5.3%
Postoperative of ERCP	2	2.6%	0	0.0%
Ectopic pancreas	1	1.3%	0	0.0%
Intestinal duplication	0	0.0%	1	1.8%
Small vessel disease caused by systemic disease	0	0.0%	1	1.8%
Unknown	10	13.2%	12	21.1%

ERCP, endoscopic retrograde cholangiopancreatography; *GIB*, gastrointestinal bleeding.

ensure effective hemostasis in time.

Despite both surgery and conservative treatment, the mortality rate of acute gastrointestinal hemorrhage is still as high as 8–14%; if the patient is hemodynamic unstable, the mortality rate can rise as high as 21–40%.[9,10] Angiography and arterial embolization have been widely employed as the first choice after the failure of endoscopy.[8,11–13] However, DSA positivity varies greatly owing to the characteristics of the disease, the amount of bleeding, the clinical use of drugs, and the time between the onset of bleeding and angiography.[5,6]

In our group, most patients with upper GIB chose conservative treatment, and the bleeding gradually stopped in most of them. Among those who chose surgery, the rebleeding rate within 30 days was higher than the rebleeding rate among those who chose conservative treatment, which may be related to the nature of the primary disease. Most of the upper GIB patients in the group that received surgery had anastomotic bleeding after the previous surgery.

In the lower GIB group, the rebleeding rate within 30 days among those who received surgery was lower than that in the conservative treatment group, which may be related to the type of bleeding lesion. The diagnoses of lower GIB patients who received surgery included small intestinal stroma and intestinal malformation, which will often stop bleeding after removal of the lesions. The diagnoses of lower GIB patients who received conservative treatment included inflammatory bowel disease with hemorrhage, hemorrhage due to a diffuse bowel lesion, and bleeding of unknown etiology. This may explain why the rebleeding rate within 30 days was higher in the conservative treatment group than in the surgery group.

4.2. Prophylactic embolization

Likely bleeding sites or highly suspected postoperative anastomotic bleeding by endoscopy were found in 16 patients who then received prophylactic arterial embolization. Among these, 6 patients had no bleeding signs within 30 days after embolization and 10 patients failed prophylactic embolization. The possible reason of the failure of prophylactic embolization may have been: (1) failure of complete embolization; (2) rapid establishment of the peripheral collateral circulation immediately after embolization; and (3) venous hemorrhage or diffuse mucosal hemorrhage.

4.3. Possible reasons for negative DSA results

Negative DSA results can occur under the following conditions: (1) the angiography is performed during an interval of nonbleeding; (2) thrombosis has formed in the culprit vessels; (3) there is a low blood volume, decreased vascular perfusion, and insufficient pressure in the lumen, so that the contrast agent cannot exit the lumen; (4) the use of vasoconstrictors, which can cause temporary vasoconstriction; (5) the adhesion of intraperitoneal tissue after surgery, which can retard the diffusion of contrast agent; (6) bleeding from the venous plexus or diffuse bleeding caused by gastrointestinal mucosal lesions; and (7) technical factors (for example, inability to perform super-selective angiography or the presence of obscured imaging conditions).

In looking for the cause of acute nonvariceal GIB, the incidence of gastrointestinal ulcers, postoperative anastomotic bleeding, small intestinal stromal tumors, malignant tumors, and bleeding are relatively common findings. The rare causes of bleeding found in this study were colonic inflammatory disease with bleeding, Crohn disease, ectopic pancreas, Meckel diverticulum, pancreatitis, mesenteric vascular malformation, intestinal duplication, systemic disease caused by diffuse lesions of the intestinal canal or small blood vessels, mesenteric artery embolism leading to bleeding from intestinal necrosis, bleeding, and others.

4.4. Other methods to detect bleeding

Contrast-enhanced barium enema examination can detect digestive tract diverticula or suggest the possibility of ectopic pancreas. As a useful auxiliary examination, multi-slice computed tomography (CT) and CT angiography (CTA) can locate sources of active bleeding such as an abnormal vascular malformation or tumors with bleeding rates as low as 0.5 mL/min.[14] Although nuclear medicine imaging cannot accurately pinpoint the bleeding site, it is more sensitive than CT. Nuclear imaging has been reported to detect a bleeding rate as low as 0.1 mL/min.[15] The nuclear imaging examination also allows for subsequent serial imaging and can reduce the time needed in searching for the bleeding source during surgery.

It is also important to consider two or more causes of bleeding occurring simultaneously in the same patient, such as peptic ulcer disease with hemophilia, postoperative anastomotic bleeding with hemophilia, intestinal vascular malformation with Crohn disease, Meckel diverticulum with intestinal vascular malformation, and small intestinal duplication combined with Meckel diverticulum and peptic ulcer.

5. Conclusions

Upper GIB with negative DSA results was generally stopped with conservative treatment, whereas lower GIB with negative DSA results required surgery to detect the culprit bleeding site. Rare causes of GIB should be considered and appropriate management selected in a timely manner in order to detect these unusual causes.

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