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Transcatheter arterial embolization for advanced gastric cancer bleeding

A single-center experience with 58 patients

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Abstract

To investigate computed tomography and angiography findings and clinical outcomes after transcatheter arterial embolization for acute upper gastrointestinal bleeding from advanced gastric cancers.

From January 2005 to December 2014, 58 patients with pathologically proven gastric cancer were treated at our institution with transcatheter arterial embolization due to acute upper gastrointestinal bleeding recalcitrant to endoscopic treatment. The electronic medical records for each patient were reviewed for clinical presentation, endoscopy history, computed tomography and angiographic findings, blood transfusion requirements, and follow-up results.

Angiography findings were positive in 13 patients (22.4%): contrast extravasation was found in 9 patients and pseudoaneurysm in 4 patients. All patients with positive angiograms underwent selective embolization treatment. Those with negative angiography findings underwent empirical embolization. Gelfoam, n-butyl cyanoacrylate, coils, or a combination of these were used as embolic agents. The overall clinical success rate was 72.4% (42/58), and the success rate for patients with positive angiography was 53.8% (7/13). The median survival was 97.5 days (range, 7–1415 days), and the 1-month survival rate was 89.6% (52/58). The 1-month survival rate of the clinical success group was 95.2% (40/42), which was significantly higher than that of the clinical failure group ($P = .04$). The clinical success group also required significantly fewer transfusions (2.43 units, range 0–24 units) ($P = .02$).

Transcatheter arterial embolization is a highly effective treatment for advanced gastric cancer with active bleeding. It should be considered as an additional treatment, especially when endoscopic or surgical treatment fails or when these approaches are difficult.

Abbreviations: CT = computed tomography, EGDS = esophagogastroduodenoscopy, GDA = gastroduodenal artery, LGA = left gastric artery, LGEA = left gastroepiploic artery, NBCA = n-butyl cyanoacrylate, RBC = red blood cell, RGA = right gastric artery, RGEA = right gastroepiploic artery, TAE = transcatheter arterial embolization, UGIB = upper gastrointestinal bleeding.

Keywords: advanced gastric cancer, bleeding, CT, transcatheter embolization

1. Introduction

Bleeding from advanced gastric cancer accounts for 1% to 8% of the total prevalence of acute upper gastrointestinal bleeding (UGIB).[1–3] Such bleeding may cause delays in scheduled chemotherapy, increased transfusion requirements, and even death.[4,5]

Esophagogastroduodenoscopy (EGDS) is the treatment of choice for UGIB because it enables a specific diagnosis of the cause of the bleeding, and hemostasis can be achieved using various techniques. However, it may fail to stop the bleeding because the exact focus of bleeding may be masked by profuse blood in the stomach or blood oozing diffusely from the tumor mass.[6–8] Surgical treatment can be performed in cases of

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endoscopic failure, but this leads to high morbidity and mortality.[9–12] Due to advances in angiographic devices and embolic materials, embolization is becoming accepted as the first-line treatment modality for this condition.[2] However, only a few studies have been conducted on this subject, and these were based on a relatively small number of patients. The present study aimed to investigate clinical outcomes after transcatheter arterial embolization (TAE) for UGIB in advanced gastric cancer.

2. Materials and methods

2.1. Study population

The institutional review board approved this study, and informed consent was waived due to the retrospective nature of the research. We retrospectively reviewed the electronic medical records of 58 patients with pathologically proven advanced gastric cancer (46 males, 12 females; mean age ± standard deviation [SD], 62.5 ± 12.79 years; range, 22–87 years), who were treated at our institution with TAE for UGIB due to gastric cancer from January 2005 to December 2014.

2.2. Endoscopy and computed tomography

Endoscopy is the first-line diagnostic and therapeutic modality for patients with suspected acute arterial UGIB, including those with advanced gastric cancer, at our institution. However, if active bleeding or pseudoaneurysm is found on computed tomography (CT), angiography can be performed prior to endoscopy at the discretion of the primary physician.

Contrast-enhanced CT is performed before angiography when recurrent bleeding occurs after endoscopic treatment, when UGIB is still suspected even after negative endoscopic findings, or when endoscopy is not applicable.

An experienced radiologist reviewed the CT images retrospectively, and the findings were divided into 4 categories: presence of contrast extravasation (category 1), presence of arterial pseudoaneurysm (category 2), prominent tumor feeding vessel (category 3), and no visible abnormal findings (category 4). Categories 1 to 3 were defined as positive CT findings, while category 4 was defined as negative.

2.3. Angiography and embolization

Emergency angiography was performed before TAE on all patients in this study. Celiac and superior mesenteric arteriography were performed using a 5-F Rösch-Hepatic or Cobra catheter (Cook, Bloomington, IN, USA). If there were no definite signs of bleeding, further coaxial selective angiography was performed using a 2.4-F or 2.0-F microcatheter (Renegade HI-FLO [Boston Scientific, Natick, MA, USA] or Progreat ® [Terumo, Somerset, NJ, USA]) in the left gastric, right gastric, short gastric, posterior gastric, gastroduodenal, or pancreaticoduodenal arteries to rule out false-negative results.

The angiographic findings were classified into 3 categories: presence of contrast extravasation (category 1), presence of arterial pseudoaneurysm (category 2), and other tumor staining and/or no visible abnormal findings (category 3). Categories 1 and 2 were defined as positive, while category 3 was defined as negative.

Transcatheter arterial embolization was performed in all cases. Although the choice of embolic material was at the operators discretion. All procedures were conducted in accordance with the following strategy. In patients with positive angiographic findings for active bleeding or pseudoaneurysm, superselective embolization was performed with n-butyl cyanoacrylate (NBCA) or microcoils. The tip of the microcatheter was inserted into the target artery as close as possible to the focus of bleeding. Under continuous fluoroscopic monitoring, 5% dextrose solution was used to flush the microcatheter. Then a mixture of NBCA and lipiodol (ratio of 1:2 to 1:3) was infused using a 1-ml syringe. When the degree of selection was insufficient for safe NBCA, this procedure was not performed and TAE using microcoils was performed instead. For patients with angiographic findings of hypervascular tumor staining, we used microcatheters to select the feeding vessels, which were embolized using Gelfoam particles. However, when angiography showed no abnormal findings, empirical embolization was performed on the left gastric artery (LGA) as the main target vessel and on additional gastric arteries that, based on CT findings, were suspected of being tumor feeders.[13]

2.4. Endpoints

The primary endpoint of this study was the clinical success rate, which was defined as the patients survival without recurrent bleeding on the 14th day after embolization.[13] Recurrent bleeding was diagnosed based on comprehensive consideration of

Table 1

Comparison of clinicoradiologic characteristics based on procedural success.

Patient characteristics	Success group	Fail group	*P* value
Continuous variables			
Age (years)	64 ± 12.2	60 ± 14.2	.298
No. of packed RBCs			
Admission to procedure	3.17 ± 2.12	3.88 ± 2.58	.289
Procedure to 24 h after procedure	1.50 ± 2.21	2.69 ± 2.68	.090
24 h after procedure to discharge	1.14 ± 1.75	5.81 ± 7.28	.022
No. of procedures	1.2 ± 0.61	1.6 ± 0.96	.193
Survival (days)	229.4 ± 365	143.6 ± 176.6	.023
Categorical variables			
Angiographic findings			.468
Extravasation	5 (8.6)	4 (6.9)	
Pseudoaneurysm	3 (5.2)	1 (1.7)	
Tumor staining or negative	34 (58.6)	11 (19)	
CT findings			.642
Extravasation	8 (13.8)	5 (8.6)	
Pseudoaneurysm	1 (1.7)	1 (1.7)	
Exposed vessel within tumor	12 (20.7)	2 (3.4)	
Negative	8 (13.8)	3 (5.2)	
No CT	13 (22.4)	5 (8.6)	
Embolized vessels			.674
Gastric artery (LGA, RGA)	23 (58.6)	8 (22.4)	
Non-gastric artery (LGEA, RGEA, hepatic artery)	1 (1.7)	1 (1.7)	
Combined	18 (31.0)	7 (12.1)	
Embolization material			.323
Gelfoam	34 (58.6)	10 (17.2)	
Glue	3 (5.2)	3 (5.2)	
Gelfoam + glue	4 (6.9)	2 (3.4)	
Glue + coil	1 (1.7)	1 (1.7)	
One-month survival	40 (72.4)	12 (27.6)	.043

Data in parentheses are percentages of each item. LGA = left gastric artery, LGEA = left gastroepiploic artery, RBCs = red blood cells, RGA = right gastric artery, RGEA = right gastroepiploic artery.

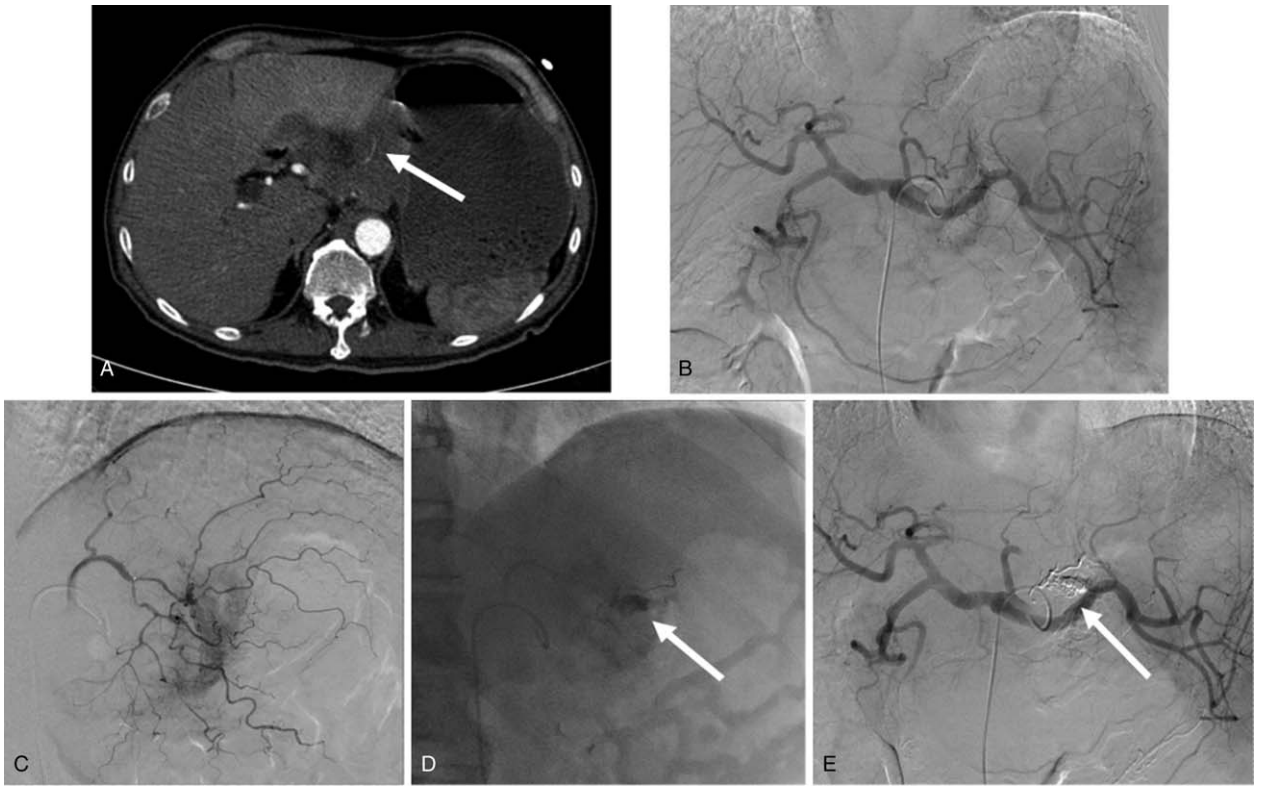

Figure 1. A 63-year-old male presented with hematemesis. (A) Contrast-enhanced CT scan showed wall thickening of the gastric body at the lesser curvature. A fine arterial channel was encased by the tumor (white arrow). (B) Celiac arteriography revealed tumor staining supplied by the left gastric artery (LGA) without active bleeding or pseudoaneurysm. (C) Selective angiogram of the LGA also showed no active bleeding or pseudoaneurysm. However, based on the CT scan, we decided to perform glue embolization of the LGA as the feeding artery. (D) After the tip of microcatheter was positioned more distal to the LGA, we performed embolization using NBCA mixed with lipiodol (white arrow). (E) Completion angiography revealed that the distal branches of the LGA were successfully embolized with a glue cast (white arrow), while the proximal LGA was intact.

follow-up diagnostic studies, including endoscopy, angiography, and contrast-enhanced CT, and on the clinical assessment of the physician based on symptoms related to bleeding, such as hematemesis/hematochezia/melena, hemodynamic instability, and decreased hemoglobin levels.

Technical success, a 1-month survival rate, and a reduced requirement for red blood cell (RBC) transfusions were the secondary endpoints. In cases without active arterial bleeding, technical success was defined as either tumor devascularization or stasis of arterial flow in the target vessels. In cases where the angiography revealed active arterial bleeding, technical success was defined as the disappearance of extravasation or complete exclusion of the pseudoaneurysm.[14] One-month survival was defined as being alive on the 30th day after embolization. We reviewed the blood transfusion history of each patient and divided them into 3 groups based on the number of packed RBCs received from the time of admission to the time of the procedure (early transfusion), from the end of the procedure to 24 hours after the procedure (mid-transfusion), and from 24 hours after the procedure to discharge (late transfusion).

2.5. Statistical analysis

The data were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed variables were compared with the independent *t* test and presented as the mean ± SD. Group comparisons of categorical variables were performed using the Chi-Squared test or, for small cell values, Fisher exact test. All statistical analyses were performed using SPSS version 19.0 (SPSS, IBM, Chicago, IL, USA), with $P < .05$ indicating statistical significance.

3. Results

Table 1 summarizes the clinical and radiological data for all patients categorized by clinical success or clinical failure.

3.1. Endoscopy and CT

Fifty three out of 58 patients underwent endoscopy before TAE. Two patients did not undergo preprocedural endoscopy because active bleeding or pseudoaneurysm had already been found on a CT scan, while another 3 had vital signs that were too unstable to undergo endoscopy.

Forty patients (69%, 40/58) underwent contrast-enhanced CT scanning before embolization, and 29 of these showed positive findings (72.5%) (category 1: n = 13, category 2: n = 2, and category 3: n = 14). Among these 29 patients, 11 (37.9%) also showed positive angiographic findings. However, 11 patients with negative CT findings showed no positive angiographic findings.

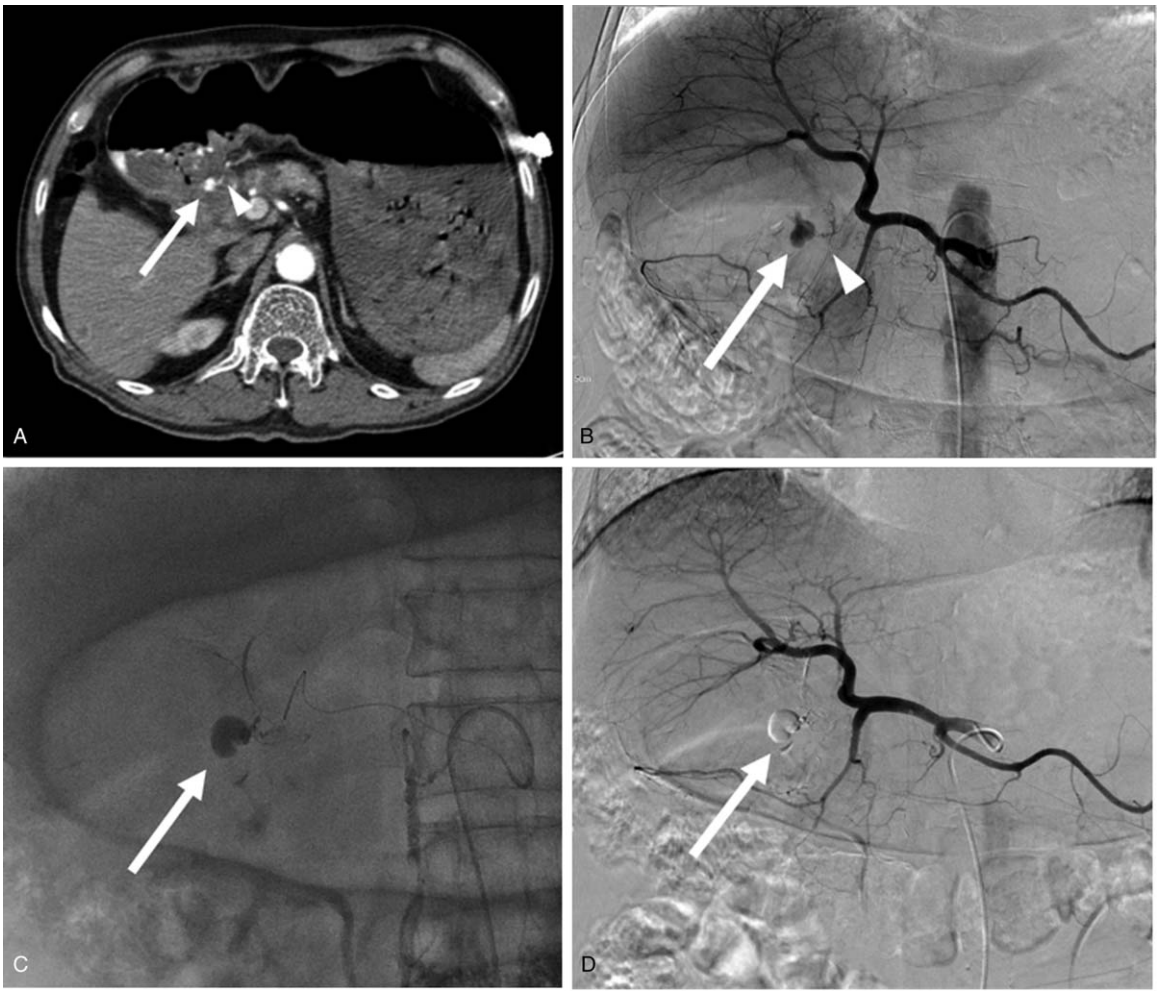

Figure 2. A 76-year-old male presented with hematemesis. (A) Contrast-enhanced CT showed focal wall thickening of the gastric pylorus and a pseudoaneurysm (white arrow) at the medial wall. A fine arterial channel (white arrowhead) was suspected to be connected to the pseudoaneurysm. (B) Celiac arteriography revealed contrast filling the pseudoaneurysm (white arrow) from a fine feeding artery (white arrowhead) arising from the proper hepatic artery. (C) After the microcatheter tip was advanced closer to the bleeding point, NBCA mixed with lipiodol could fill the pseudoaneurysm (white arrow) without overflowing into the proper hepatic artery. (D) Completion angiography revealed that the pseudoaneurysm and the feeding artery were successfully embolized with a glue cast (white arrow), while the proper hepatic artery was intact.

3.2. Embolization

Among the 45 patients with negative angiograms, 41 were treated with empirical embolization using Gelfoam only (91.1%), as described above. The remaining 4 patients were treated with either Gelfoam and NBCA (n=3) or NBCA and coil (n=1) (Fig. 1).

Thirteen patients with initially positive angiograms, showing contrast extravasation (n=9, 69.2%) or pseudoaneurysm (n=4, 30.8%), underwent embolization with Gelfoam and NBCA (n=3, 23.1%), coil and NBCA (n=1, 7.7%), Gelfoam only (n=3, 23.1%), or NBCA only (n=6, 46.1%) (Fig. 2).

The embolized vessels were the LGA (n=24, 41.4%); right gastric artery (RGA) (n=4, 6.9%); LGA and RGA (n=4, 6.9%); LGA and right gastroepiploic artery (RGEA) (n=9, 15.5%); LGA and left gastroepiploic artery (LGEA) (n=1, 1.7%); LGA and gastroduodenal artery (GDA) (n=2, 3.4%); RGA and RGEA (n=1, 1.7%); RGEA and GDA (n=1, 1.7%); LGA, RGA, and RGEA (n=8, 13.8%); and LGA, RGA, and LGEA (n=1, 1.7%). Atypical vessels were embolized in 6 patients, including the accessory LGA from the left inferior phrenic artery (n=1, 1.7%), the accessory LGA from the left hepatic artery (n=1, 1.7%), the feeder from the right hepatic artery (n=1, 1.7%), the omental branch from the splenic artery (n=1, 1.7%), the posterior gastric artery (n=1, 1.7%), and the right inferior phrenic artery (n=1, 1.7%).

3.3. Technical and clinical success

Technical success was achieved in 100% of the procedures, while the overall clinical success rate was 72.4% (42/58). The clinical success rate of selective embolization for angiographically positive patients was 53.8% (7/13), and that of empirical embolization for angiographically negative patients was 77.8% (35/45). However, there was no significant difference in clinical success rates between the 2 groups ($P=.22$).

The median overall survival period was 97.5 days (range, 7–1415 days), and the overall 1-month survival rate was 89.6% (52/58). In the clinical success group, the 1-month survival rate was 95.2% (40/42), which was significantly higher than in the clinical failure group (75%, 12/16) ($P=.04$).

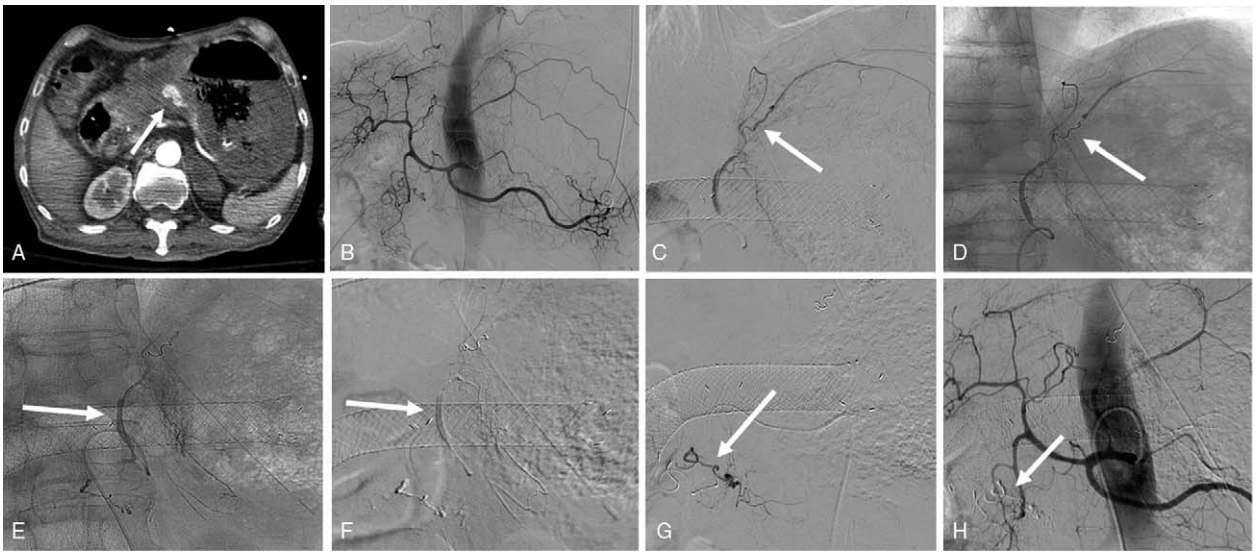

Figure 3. A 67-year-old male presented with hematemesis and melena. (A) Contrast-enhanced CT showed diffuse wall thickening of the gastric body, antrum, and pylorus, with contrast media extravasation from the LGA (white arrow). (B) Celiac arteriography showed no active bleeding or pseudoaneurysm. (C) Selective angiogram of the LGA showed equivocal findings with aneurysmal changes (white arrows). (D) The microcatheter was advanced to the branch of the LGA, and microcoil embolization was performed (white arrow). (E) Follow-up angiogram revealed residual aneurysmal changes in the LGA (white arrow). (F) After the microcatheter tip was located at the aneurysmal portion, additional embolization was performed using NBCA mixed with lipiodol (white arrow). (G) Selective angiogram of the gastroduodenal artery (GDA) showed equivocal findings with aneurysmal changes (white arrows), and we conducted embolization using NBCA mixed with lipiodol. (H) Completion angiography revealed that the abnormal vessels with aneurysmal changes at the LGA and GDA were successfully embolized with a glue cast (white arrow). However, the patient underwent total gastrectomy due to stomach wall perforation.

The average numbers of packed RBC units received were as follows: early transfusions, 6.61 units (range, 0–9 units); mid transfusions, 1.83 units (range, 0–13 units); and late transfusions, 2.43 units (range, 0–24 units). There was no significant difference in the number of transfused packed RBC units between the success group and the failure group in the early phase. However, there were fewer units transfused in the success group during the mid and late phases; in particular, the number of units received in late transfusions was statistically significantly lower ($P = .02$).

3.4. Complications

One patient with positive CT findings and an equivocal angiographic finding of aneurysmal changes underwent wide embolization using NBCA and microcoils in relatively large vessels. This completely embolized the blood supply to the gastric wall (including the collateral vessels), which had been weakened by the cancer. This eventually led to a procedure-related complication of stomach wall perforation, and the patient underwent total gastrectomy (Fig. 3).

4. Discussion

The incidence of major bleeding from advanced gastric cancer is approximately 5%.[4,15,16] Major bleeding can delay scheduled chemotherapy, increase the need for blood transfusions, or even lead to severe morbidity or mortality. Endoscopic management is less successful at controlling UGIB from malignant tumors than it is at controlling bleeding from other benign causes.[4,5] This is likely because UGIB involves a large area of the arterial bed, which is invaded and eroded by the malignant tumor.[8,17,18] When endoscopic hemostasis fails to stop the bleeding, TAE can be an important and useful second-line treatment.

In this study, we achieved a >70% embolization success rate for patients in whom endoscopic hemostasis had failed, which corresponds well to the success rate of 48% to 79% in the literature.[19,20] Our findings show a statistically significant decrease in the amount of transfused blood after successful TAE, which indicates that the clinical success of TAE appears to be related to favorable 1-month survival outcomes.

As many preprocedural CT scans as possible were performed in our study patients. Since the exact location of a tumor in the stomach can be identified from a CT scan before the procedure, selective embolization can be performed by locating the corresponding feeder. In patients with negative angiography, this approach can be more effective than empirical embolization of the LGA, which is a well-known method.[19,20] In addition, meandering vessels that are encased or invaded by tumor are considered pseudoaneurysmal due to weakened vessel walls, and embolization with permanent embolic materials, such as NBCA or microcoils, can be helpful. This technique can improve the quality of embolization without affecting normal gastric circulation. In this study, 5 patients had active bleeding or exposed vessels within the tumor, which were clearly revealed on a CT scan despite negative angiography. In these cases, we performed additional superselective embolization using NBCA. However, not all enrolled patients underwent CT examinations in this study; therefore, generalization regarding the effect of the treatment on survival rate is limited. Further studies with larger sample sizes are required to validate of our results.

As described above, patients with negative angiograms underwent empirical embolization using Gelfoam. However, we did not consider the natural clinical course or evaluate clinical efficiency for these patients by comparing them with patients who did not receive treatment. Although many reports argue for the usefulness of empirical embolization for UGIB, negative angio-

grams themselves could be relevant to the favorable outcome group (less and temporary bleeding). Therefore, our ability to judge the direct clinical efficacy of empirical embolization in this group was limited. Further research may be required to clarify this issue and validate our findings.

This study has several limitations. First, although the patient pool was larger than in previous studies, it was still not enough for a single statistical analysis. Second, we did not conduct a comparative analysis of the natural clinical course in the negative angiogram group. Third, there may be some bias because this was a retrospective study and it was difficult to set the standard treatment including embolic materials. Lastly, the operator subjectively decided the endpoint via subjective evaluation of certain factors during the procedure, such as flow stasis and tumor devascularization, which may have affected the success rate.

In conclusion, TAE is a very effective treatment for acute bleeding in advanced gastric cancer. It should certainly be considered when an endoscopic or surgical approach is difficult.

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