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Efficacy of transcatheter arterial embolization for spontaneous extraperitoneal hemorrhage

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Objective: Spontaneous extraperitoneal hemorrhage (SEH) is the general term for a spontaneous retroperitoneal hematoma (SRH) and a rectus sheath hematoma, which occurs with no obvious cause. There is no established treatment strategy for SEH. Here we assessed the safety and efficacy of transcatheter arterial embolization (TAE) for SEH.
Methods: This was a retrospective observational analysis of SEH patients who were treated with TAE at the Kitasato University Hospital Emergency and Disaster Medical Center from April 1995 through March 2016. The clinical data from the patients' medical records and the procedural success rate of TAE and rebleeding and complication rates after TAE were assessed.
Results: Twelve of 16 patients with SEH were treated with TAE. Of those, 11 had an SRH, and 1 had a rectus sheath hematoma. Ten patients (83.3%) were treated with antithrombotic therapy. All patients treated with TAE had extravascular leakage of the contrast agent revealed on contrast-enhanced computed tomography. The technical success rate of TAE was 100% with no rebleeding. No patients had complications attributable to TAE. The 30-day mortality was 25%, but there were no bleeding deaths.
Conclusion: TAE is an effective and safe treatment for SEH.

Key words: spontaneous extraperitoneal hemorrhage, spontaneous retroperitoneal hemorrhage, interventional radiology, transcatheter arterial embolization

Introduction

Spontaneous extraperitoneal hemorrhage (SEH) is a generic term for an extraperitoneal hemorrhage within the retroperitoneum, iliopsoas, or rectus sheath, regardless of the cause. Potential causes include an external injury, iatrogenic episode, or the existence of anatomical abnormalities such as vascular malformation and aneurysm.[1] A hemorrhage that is limited to the retroperitoneum is a spontaneous retroperitoneal hemorrhage (SRH).[2] Factors that contribute to the development of an SEH include arteriosclerosis, weakness of an arterial wall (in elderly individuals), and congenital anomalies including defects of the tunica media (in younger individuals).[3] However, detailed mechanisms underlying the occurrence of SEH have not yet been established.

SEH is frequently found in patients who are being treated with an antiplatelet or anticoagulant agent[4-7] and in those with chronic renal failure undergoing maintenance dialysis.[8,9] SEH is a clinical condition with relatively high mortality (7.4%－43%).[10,11] However, there is not yet an established treatment strategy for SEH. At the Kitasato University Hospital Emergency and Disaster Medical Center, SEH and culprit vessels are found with contrast-enhanced computed tomography (CECT) and diagnosed as such. Patients with SEH are treated with transcatheter arterial embolization (TAE). We conducted this retrospective study to assess the safety and efficacy of TAE as a treatment modality for SEH.

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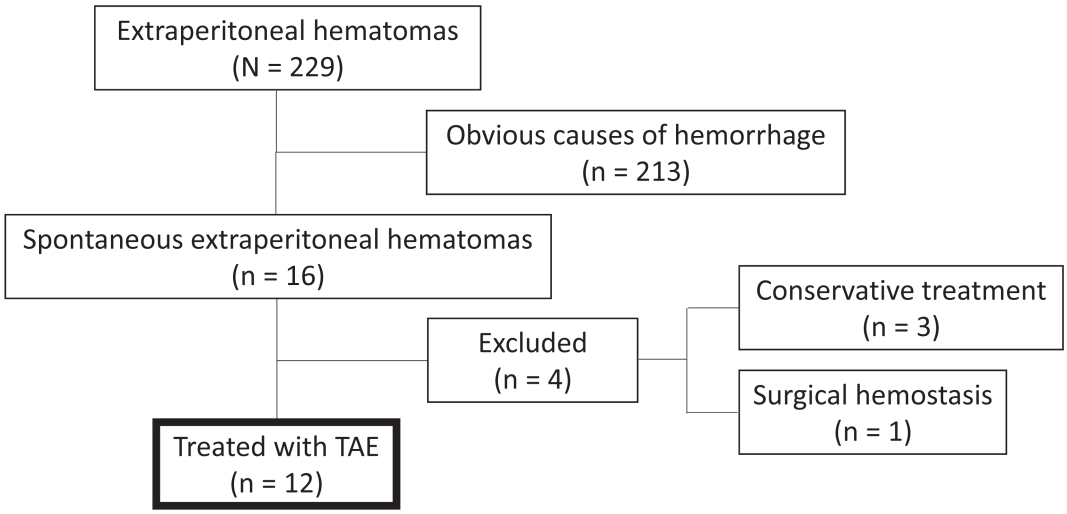

Figure 1. Flowchart of patient selection

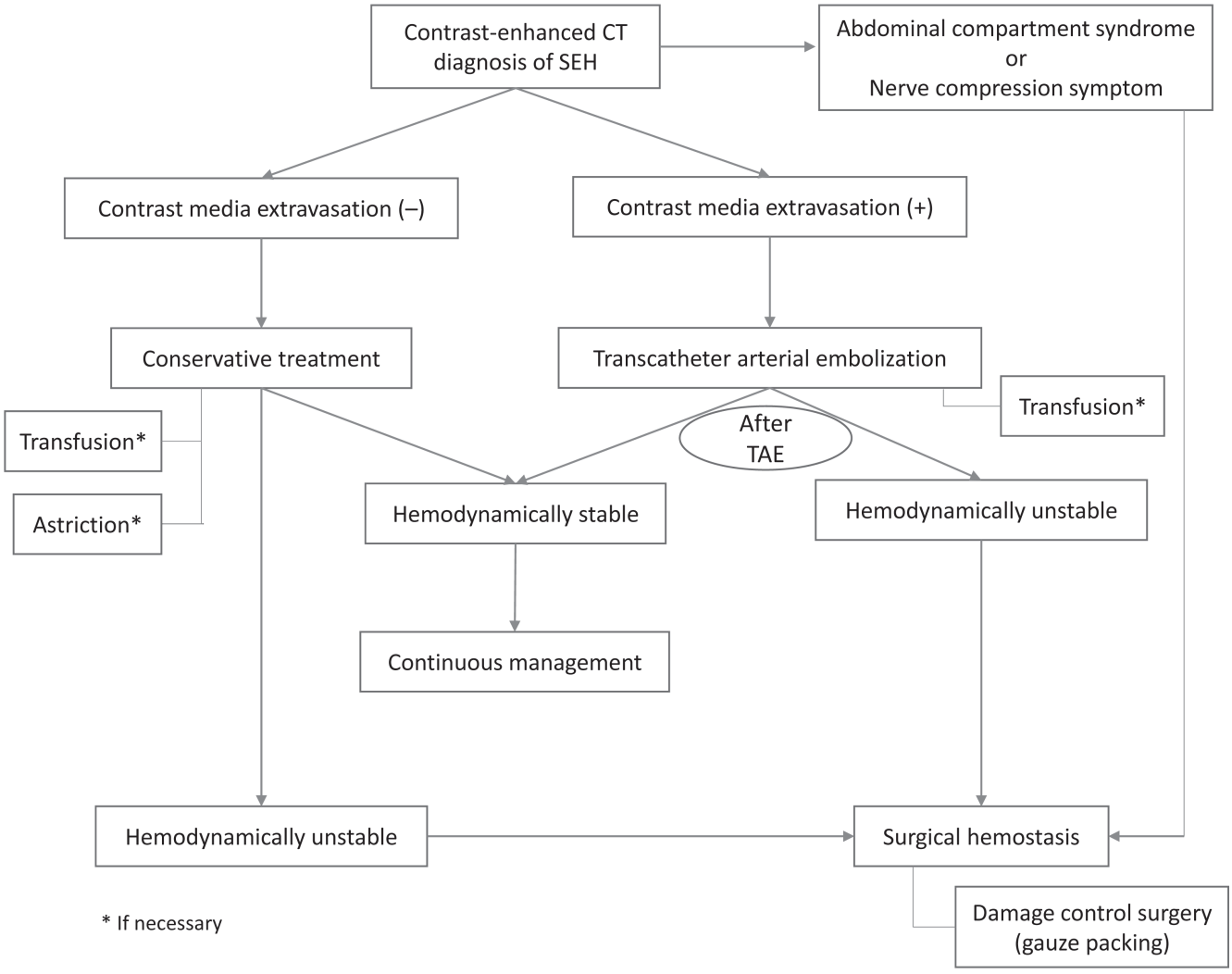

Figure 2. SEH treatment strategy in the Kitasato University Hospital Emergency and Disaster Medical Center

SEH diagnoses were based on CECT findings. For patients in whom extravascular leakage of contrast agent was not revealed by CECT, we preferentially selected conservative treatment. For patients with unstable hemodynamics despite the conservative treatment, or with suspected abdominal compartment syndrome or nerve compression, surgical hemostasis was conducted by damage control such as gauze packing. For patients in whom extravascular leakage of contrast agent was seen on CECT, TAE was performed. Gauze packing was used for patients with unstable hemodynamics even after TAE.

Patients and Methods

This study was a retrospective observational study of patients with SEH who were treated with TAE at the Kitasato University Hospital Emergency and Disaster Medical Center from April 1995 through March 2016. Cases were chosen from the hospital database using the keywords, "retroperitoneal hematoma (hemorrhage)," "iliopsoas hematoma," and "rectus sheath hematoma." Patients with obvious extraperitoneal hematoma causes, including external injuries, vascular malformations, aneurysms, and iatrogenic episodes were excluded to ensure that only cases of SEH were included. Finally, the cases of patients with SEH treated with TAE were selected (Figure 1). To examine the patients' backgrounds, we collected clinical data from their medical records: age, gender, underlying disease, time required for diagnosis, blood examination data on initial arrival, antithrombotic treatments, culprit vessel(s), treatment methodologies, embolic materials, complications, and 28-day mortality.

Diagnosis of and treatment strategy for patients with SEH

CECT was conducted for all patients with SEH except those with impaired renal function or an allergic reaction to a contrast agent. A radiologist and an emergency physician read the CECT images to make the diagnoses. All patients in whom extravascular leakage of the contrast agent was revealed by CECT underwent TAE conducted by interventional radiologists. For patients with SEH who had extravascular leakage of a contrast agent not revealed on CECT, conservative medical treatment including blood transfusion, pharmaceutical treatment, astriction, or surgery was selected (Figure 2).

TAE procedure

TAE was conducted using the following procedure. First, a 5 Fr sheath (Medikit Super Sheath, Medikit, Tokyo) was inserted into the femoral artery. Next, a 5Fr. SHK-Kusano catheter (Hanaco Disposable Torque Catheter; Hanaco Medical, Saitama), a 5 Fr Shepherd Hook Catheter (Hanaco), or a 5 Fr Cobra Catheter (Torcon NB Advantage Catheter, Cook Medical, Tokyo) was inserted into the bleeding culprit vessel, identified on CECT. We introduced a microcatheter (Goldcrest; HI-LEX, Hyogo) into the bleeding point as close as possible, and embolized it using one material or a combination of two materials, including gelatin sponge (1995－2013 Spongel; Astellas Pharma, Tokyo; since 2013, Serescue; Astellas Pharma), metallic coil, and n-butyl-2-cyanoacrylate. Embolic materials and embolizing methods were determined by the operator's discretion.

Study endpoints

The primary endpoints were the TAE procedural success rate and rebleeding rate. Procedural success was determined as the culprit vessel (bleeding source) being embolized with a single procedure. Rebleeding was defined as the bleeding at the same location after successful hemostasis with TAE confirmed by any method such as, repeat CECT, angiography, or surgical sites. The secondary endpoints were 28-day mortality and the incidence of complications associated with TAE. The effectiveness and safety of the TAE for SEH were determined based on these endpoints.

Ethics approval

The study protocol was approved by the Kitasato University Hospital Ethics Committee (approval No. B15-142). Informed consent was not required because of the retrospective nature of this study.

Results

There were 16 patients with SEH and 12 patients with extravasation on CECT who underwent TAE. Of these, 11 patients had an SRH, and 1 patient had a rectus sheath hematoma (Table 1). Ten patients (83.3%) had been treated with antithrombotic therapy due to stroke, myocardial infarction, or having had the underlying disease of atrial fibrillation.

Six patients had hemorrhages at multiple locations. Lumbar arteries were the most common culprit vessels as a bleeding source revealed on angiography. Regarding the embolization materials used for TAE, gelatin sponge was used in most cases. Metallic coils were added for 4 patients because hemostasis was insufficient with only the gelatin sponge material. N-butyl-2-cyanoacrylate was used for 1 patient who had been treated with an oral vitamin K-dependent coagulation factor inhibitor, and that patient's prothrombin time international normalized ratio was elevated to 9.49.

The primary endpoint results were as follows. The procedural success rate was 100% with no cases of rebleeding. No patient had any complications caused by TAE. Three patients died resulting in the 30-day mortality of 25%. Of those 3 patients, there were no hemorrhagic deaths. Their deaths were due to multiple organ failure after hemostasis or exacerbation of their disease.

Discussion

For patients in whom CECT revealed extravascular leakage of the contrast agent, TAE was highly effective,

with a high procedural success rate, no rebleeding, and a low rate of complications. It has been inferred that risk factors in the genesis of SEH are antithrombotic treatment and chronic renal failure,[4-9] and these risks are increasing in elderly populations. Many of the previous reports related to SEH are case serieses[2,10-12] (Table 2). In those reports, patients with SEH were treated with one or a combination of conservative treatments, TAE, and surgical hemostasis. There has been scant discussion on the selection of patient criteria, specific strategies, and treatment methods. In a surgical hemostasis procedure, a diminishing tamponade effect by opening the retroperitoneal space should be considered.[13] Moreover, in many cases of SEH, multiple bleeding sources have been identified, possibly because of a microvessel or microvessels having been broken by pulling or rupture due to an enlargement of a hematoma caused by prolonged hemorrhage.[14] Considering these facts, when a patient

Table 1. Patients' characteristics

Age, years	63.4	±11.3	Laboratory data		
Males: females	7:5		Hemoglobin at initial arrival, g/dl	10.4	±2.4
Site of hematoma			Minimum hemoglobin, g/dl	7.4	±2.4
Retroperitoneal hematoma	11	91.7%	Platelets, $\times 10^4/mm^3$	25.4	±18.3
Rectus sheath hematoma	1	8.3%	APTT, sec	54.6	±30.2
Underlying disease			PT-INR	2.42	±2.3
Stroke	4	33.3%	Fibrinogen, mg/dl	374.9	±98.6
Myocardial infarction	4	33.3%	Transfusion therapy	11	91.7%
Atrial fibrillation	3	25%	Culprit vessels for TAE		
CKD on HD	3	25%	Lumbar artery	6	50%
Malignant tumor	1	8.3%	Renal capsular artery	4	33.3%
Diabetes	1	8.3%	Inferior epigastric artery	2	16.7%
Antithrombotic therapy	10	83.3%	Profunda femoris artery	1	8.3%
Vital signs at initial arrival			Others	1	8.3%
Systemic blood pressure, mmHg	123	IQR 90－141.5	Embolization material for TAE		
Pulse rate, bpm	108	IQR 82－120.5	Gelatin sponge	6	50%
Shock index >1	5	41.7%	Metallic coil	1	8.3%
			Gelatin sponge + metallic coil	4	33.3%
			N-butyl-2-cyanoacrylate	1	8.3%

IQR, interquartile range; CKD, chronic kidney disease; HD, hemodialysis; APTT, activated partial thromboplastin time; PT-INR, prothrombin time-international normalized ratio; TAE, transcatheter arterial embolization

Table 2. Previous SEH studies with >20 patients

Authors (year)	Materials n	Age (IQR or SD)	Antithrombotic therapy	Treatment	Mortality rate
Sunga et al. (2012)[2]	SRH n = 89	72 (IQR 61－79)	84.7%	TAE, 24.7% Surgical, 6.7%	10.1% (30 days) 19.1% (6 months)
Guzzardi et al. (2014)[12]	SEH n = 30	73.3 (±15.6 SD)	100%	TAE, 100% (Tech. success 100%)	14.8% (6 months) 26% (12 months)
Caleo et al. (2015)[10]	SRH n = 27	68.4 (±12.8 SD)	55.6%	TAE, 48.1% Surgical, 7.4%	7.4%
Farrelly et al. (2011)[11]	SEH n = 25	63.8	71.0%	TAE, 88% Surgical, 12%	29% (30 days) 43% (12 months)

All four studies were retrospective observational studies.
SEH, spontaneous extraperitoneal hemorrhage; SRH, spontaneous retroperitoneal hematoma; IQR, interquartile range; SD, standard deviation; TAE, transcatheter arterial embolization

has been receiving antithrombotic treatment and it is difficult to identify all the bleeding sources under direct vision, the surgeon will naturally encounter difficulties in completing the hemostasis. Isokangas et al.[15] reported that, for 4 of the 5 patients who had undergone surgical hemostasis for SRH, although the bleeding sources could not be identified, hemostases were successful by adding TAE. The use of surgical hemostasis in SEH cases has been extremely limited, and this method may be used for patients in whom it is difficult to achieve hemostasis by TAE, as well as for those in whom a damage control procedure, such as gauze packing, is necessary.

Gelatin sponge is a temporarily obstructing material that is recanalized in a few weeks.[16] Moreover, the obstructing hemostasis effects of gelatin sponge materials and metallic coils are dependent on each individual patient's clotting function. Therefore, the optimal treatment for most patients with SEH undergoing antithrombotic treatment remains to be elucidated, particularly because they are at risk of rebleeding due to recanalization or insufficient hemostasis. In the present patient series, one-third of the patients required using a combination of gelatin sponge material and metallic coils due to insufficient hemostasis by using only one of those modalities. Therefore, for SEH patients with severe coagulopathy, n-butyl-2- cyanoacrylate may be used as a first-choice embolic material, because it is a permanently obstructing material that is not dependent upon the patient's clotting function.[17]

This study has several limitations. There were only 12 patients due to the retrospective observational design of the study conducted at a single medical center. Furthermore, these results may have been affected by the characteristics of this medical center regarding the choice of treatment strategies, materials, and modalities. Moreover, sufficient comparison of surgical hemostasis and conservative therapies with TAE could not be made. Further studies with larger populations of patients with SEH, ideally at multiple medical centers, along with comparisons of surgical hemostasis and TAE, are warranted to validate this treatment strategy for SEH.

This retrospective study indicated the usefulness and low invasiveness of TAE to treat patients with SEH. TAE may be selected as a first-choice treatment for patients in whom extravascular leakage of a contrast agent is observed on CECT.

Conflicts of Interest: None

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