

Original Article

Endovascular treatment for hemorrhagic cerebral venous sinus thrombosis: experience with 9 cases for 3 years

Shizhong Zhang^{1,2}, Yanyan Hu³, Zhen Li², Dezhang Huang¹, Mingran Zhang², Chenglong Wang¹, Zhigang Wang¹

¹Department of Neurosurgery, Qilu Hospital of Shandong University, NO.758, Hefei Road, Shibei District, Qingdao 266035, Shangdong, China; ²Department of Neurosurgery, Taian Central Hospital, NO.29, Longtan Road, Taian 271000, Shangdong, China; ³Color Ultrasonic Room, Taian Central Hospital, NO.29, Longtan Road, Taian 271000, Shangdong, China

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Abstract: Aim: We experienced a series of patients with hemorrhagic CVST, who were successfully treated with endovascular treatment (EVT). The aim was to explore the best scheme for the future through our treatment data of hemorrhagic CVST. Material and Methods: A retrospective analysis was conducted, selecting nine hemorrhagic CVST patients, who were mainly treated with EVT. Characteristics of hemorrhagic CVST were recorded, including risk factors, thrombus location, presenting symptoms, and treatment details included type of EVT. We also recorded clinical outcomes, degree of sinus recanalization, thrombus recurrences, periprocedural complications, degree of neurological deficit at last follow-up. Results: Catheter thrombolysis and mechanical thrombectomy were applied in all of the nine hemorrhagic CVST patients, stent retriever was used in 7 patients, one of them combined with balloon-assisted thrombectomy. Besides EVT, two patients accepted emergency surgical decompression, one in the local hospital, and the other in our hospital. The follow-up duration ranged from 4 to 28 months. All of them have a neurological and symptomatic improvement, 6 patients have a good outcome, the rest 3 patients have a poor outcome, no thrombus recurrences and death in them. Seven patients had complete recanalization and two patients had partial recanalization at last follow-up. Conclusion: EVT is an effective and safe procedure for potentially catastrophic hemorrhagic cerebral venous sinus thrombosis.

Keywords: Cerebral venous sinus thrombosis, hemorrhagic, endovascular treatment

Introduction

Cerebral venous sinus thrombosis (CVST) is a rare condition which accounts for 0.5-1% of all strokes. This disease usually affects young to middle-aged adults with fatality rate of 6%-10% [1-3]. The initial treatment for CVST is systemic anticoagulation, which has been associated with improved neurological outcomes in small randomized studies [4]. Most CVST prognosis is good, but 30-40% of CVST patients presents with intracranial hemorrhage, brain edema and cerebral hemorrhage [5].

Although the use of dose-adjusted unfractionated or low-molecular weight heparin anticoagulant treatment has been shown to be safe. In addition, it is associated with potentially important reduction in the risk of death or dependen-

cy without promoting ICH [3]. However, there is still a controversy because intracranial hemorrhage (ICH) might occur or aggravate in CVST patients [6, 7]. Additionally, with anticoagulation alone, large and extensive thrombi are unlikely to dissolve, and thus approximately one-third patients with severe presentation have a high risk of incomplete recovery [8].

The obstruction of the blood flow from a clot in veins of head leads to a blood backflow and increasing blood pressure in the blood vessels before the obstruction [9]. The goals of CVST therapy are to re-establish circulation distal to the occlusion, prevent further development of thrombus, treat the underlying cause, and prevent recurrence [10, 11]. Current endovascular techniques include direct catheter thrombolysis, balloon-assisted thrombectomy, mechani-

cal thrombectomy, rheolytic catheter thrombectomy, aspiration thrombectomy, and stent retriever thrombectomy [12-15]. Hemorrhagic CVST is sometimes a diagnostic and therapeutic challenge. Randomized controlled trials are lacking for defining the failure of conservative therapy [4, 7]. Furthermore, paucity of information could demonstrate endovascular therapy is efficacious. Case series suggest that thrombolysis infusion is safer than thrombectomy, while methods of administration, dose, and duration of therapy are different in various cases [16, 17]. Considering the possibility of aggravating the intracranial hemorrhage, systematic anticoagulation will be contradiction until the clot was removed. The advantage of EVT seems to be without increasing the incidence of ICH [12, 13, 16, 18, 19]. Endovascular intervention is an alternative option for patients with neurological deterioration despite the use of anticoagulation [20]. Existing literature provides only a selection of case studies describing individual techniques, which might be unhelpful in guiding therapy or in standardizing treatment. By this retrospective analysis of a series of hemorrhagic CVST patients, we find EVT may be another treatment option in patients which was undered more severe or medical refractory clinical conditions.

Materials and methods

The retrospective analysis was conducted in the Department of Neurosurgery of our hospital from October 2013 to October 2016. In this period, a total of 23 patients with CVST were enrolled, including 12 females and 7 males. About 39% (9/23) cases suffered with hemorrhagic CVST. All patients gave written informed consent. The study was approved by our local Ethics Committee.

Hemorrhagic CVST patients contain 5 males and 4 females with the mean age of 39.2 years old. The average time for coming to our hospital is 20.1 days after the first clinical symptoms appeared. Only one patient has family history of deep vein thrombosis. Dates of signs/symptoms and Glasgow Coma Scale (GCS, record the patient's best eye, verbal and motor responses) scores symptom onset on admission were noted.

Diagnosis of CVST was based on the relevant clinical and neurologic findings and confirmed

by imaging studies, including brain computed tomography (CT) and/or magnetic resonance imaging (MRI) scans and magnetic resonance venography (MRV), with or without digital subtraction angiography (DSA). During hospitalization, all hemorrhagic CVST patients underwent DSA for further confirmation of involved sinuses. After that, the type of EVT would be applied on the patients was chosen. Details on these patients and treatment were recorded including risk factors, presenting symptoms, the GCS scale, thrombus location, the type and size of stent retriever or balloon and the duration of the continuous thrombolysis. Outcome and complication data contained degree of sinus recanalization at last follow-up, thrombus recurrences, periprocedural complications, degree of neurological deficit at last follow-up. Neurological deficit was categorized into mild, moderate, or severe, which corresponded to a modified Rankin Scale (mRS) score of 1-2, 3-4, and 5, respectively.

The use of the systemic anticoagulant is according to the guidelines of American Heart Association/American Stroke Association. Warfarin was maintained for 6 months at least. Recurrence of CVST would use warfarin lifelong. We monitored international normalized ratio (INR) and adjusted the dose of warfarin, a target INR of 2-3 limits the risks of hemorrhage. The monitoring of coagulation function would be conducted in the local hospital. In addition to administering antithrombotic therapy, the efforts were made on identification of predisposing factors or precipitating conditions, intracranial pressure management, seizure control, and headache treatment.

After 24 h treatment of intracranial pressure management, seizure control, or headache treatment, the neurological worsening evolving was with coma and cerebral hernia and the GCS scale was 7. Another CT scan showed an aggravated intracranial hemorrhage and brain edema (**Figure 1**). Before transferred to this hospital, decompressive craniectomy was performed on the patient. Post-operation the GCS scale was still 7, which was the same to pre-operation, and there was no consciousness improvement in the patient. The third CT scan was performed, which showed that the volume of right temporal intracranial hemorrhage had no reduce and even increased. MRV in our hospital revealed the right transverse-sigmoid

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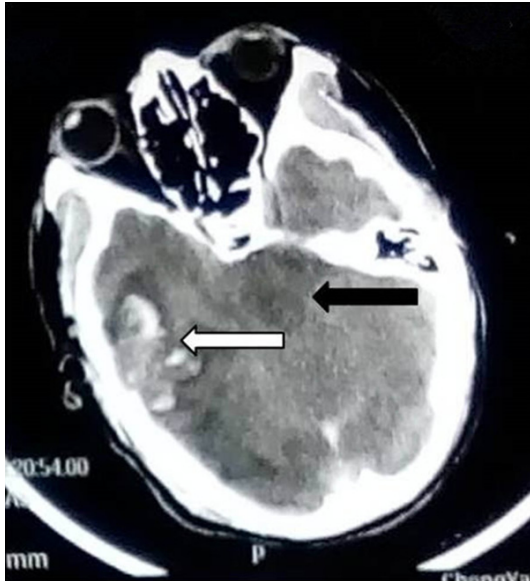


Figure 1. Brain CT scan in the local hospital showed the right temporal lobe hemorrhage (white arrow) and the cisterna ambiens was compressed severe (black arrow), then decompressive craniectomy was performed.

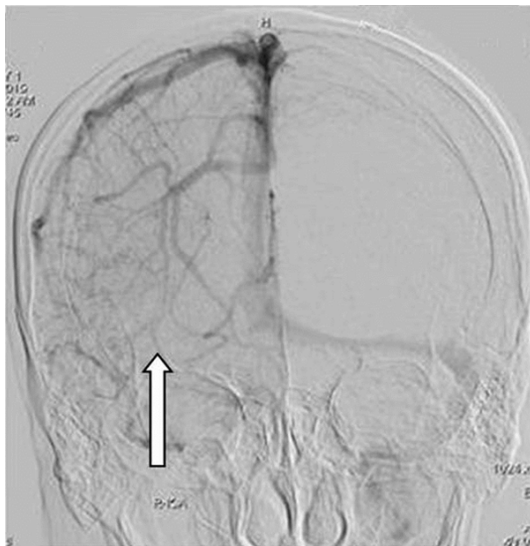


Figure 2. DSA showed extensive venous sinus occlusion of right transverse-sigmoid sinus (white arrow).

sinus thrombosis, which confirmed our suspicions for CVST.

For the volume of brain hematoma was larger than pre-operation and severe brain edema, the man was treated with endovascular techniques. The patient was placed under general anesthesia. At first the left femoral artery was punctured with a 5F introducer (Terumo Cor-

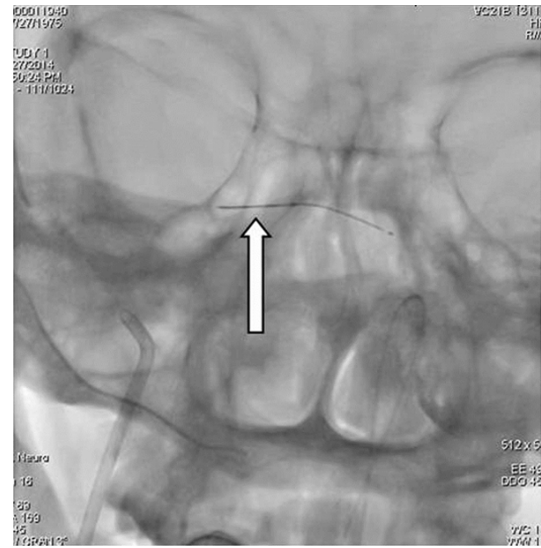


Figure 3. 6 mm×30 mm Solitaire AB stent (white arrow) was positioned into the occluded sinus and was pulled from one extreme in a dynamic way.

poration, Japan), DSA was done in accordance with Seldinger's piercing technology and showed extensive venous sinus occlusion of right transverse-sigmoid sinus (**Figure 2**). Then the right femoral venous puncture was done with the introducer 6F (Terumo Corporation, Japan), and catheterization of the right sigmoid sinus with a catheter guider 6F (Codman Shurtieff, Inc. USA). Then transfixing the clot with a microguide wire (Traxcess 14, Micro-Vention, Inc. USA), the next step was mechanical thrombectomy, we repeatedly rotated, pushed and pumped back the microguide wire. After that Rebar-27 microcatheter (Micro Therapeutics, Inc. d/b/a ev3 Neurovascular, USA) was guided into the sinus thrombolysis by microguide wire, and 6 mm 30 mm Solitaire AB device (Micro Therapeutics, Inc. d/b/a ev3 Neurovascular, USA) was positioned into the thrombosis (**Figure 3**), pulling it from one extreme to another of the occluded lateral sinus two times in order to reach a further clot fragmentation, in this process, clot fragmentation was pulled out as (**Figure 4**). After partial recanalization by mechanical thrombolysis, the third step was local pharmacological thrombolysis with urokinase (Livzon Pharmaceutical Group Co. Ltd, China) infused through the microcatheter at a total dose of 200000IU. Angiography showed a poor recanalization in the right transverse-sigmoid sinus (**Figure 5**), and the arteriovenous circulation time was prolonged. In the fourth step we positioned the 4

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Figure 4. Clot fragmentation was pulled out by Solitaire AB stent.



Figure 5. Angiography showed a stenosis (white arrow) in the right transverse-sigmoid sinus.

mm×30 mm PTA balloon catheter (ClearStream Technologies Ltd, Ireland) (Figure 6) in a coaxial position and inflated the occluded sinus, another angiography showed a sign of residual thrombi in the right transverse-sigmoid sinus but an improved recanalization compared with the third step. The final step was performed, the Rebar-27 microcatheter was placed inside the distal of right transverse-sigmoid sinus for continuous local urokinase infusion. The bolus dose of urokinase was calculated to be 960000

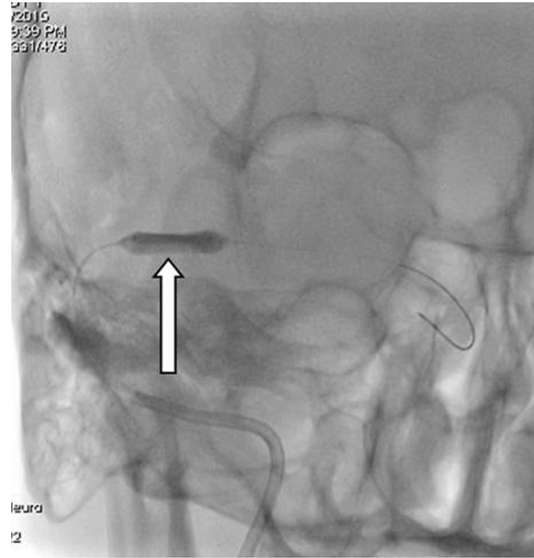


Figure 6. 4 mm×30 mm PTA balloon catheter (white arrow) was positioned and inflated the occluded sinus.

U/day. It was diluted in a 480 ml saline and set up for a 24-h infusion at a dose of 40000 U/hr in 20 ml/hr of fluid, and the Rebar-27 microcatheter was reserved at the third day post-endovascular treatment. And synchronize in time the guider catheter was placed inside proximal of right transverse-sigmoid sinus for continuous local heparin (Fosunpharma, Shanghai, China) infusion at a dose of 6250 IU/day.

Results

The clinical characteristics and outcomes of the CVST patients are shown in **Table 1**. At time of diagnosis, mean age of patients (male, 5; female, 4) was 39.2 years (23-65 years). In terms of predisposing factors, postpartum were identified in three patients (33.3%), deprivation of body fluids such as diarrhea, dehydration caused by sweating in three patients (33.3%), the rest three patients were respectively hashimoto's thyroiditis (11.1%), family history of deep vein thrombosis (DVT) (11.1%), facial herpes zoster (11.1%). The most common symptom was headache (8/9, 88.9%), focal motor deficits (6/9, 66.7%), followed by seizure (3/9, 33.3%), disturbance of consciousness (3/9, 33.3%). Mean duration of illness at presentation was 20.1 days (range, 3-120 days). Imaging results indicated that all the nine (100%) had suffered ICH, the most locations of

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Table 1. The clinical characteristics and outcomes of the CVST patients (n = 9)

No	Sex/ Age	Risk factors	Presenting symptoms	Duration (days)	GCS (admission/discharge)	Location of Hemorrhage	Location of CVST	The type of EVT	The size and type of stent retriever or balloon	Duration of CNT	DC	Recanalization degree	mRS at discharge
1	F/47	Hashimoto's thyroiditis	Headache, focal motor deficits	30	15/15	(L) parietal lobe	SSS/TS	CTT/MCT/STR	6×30 mm Solitare stent	7	No	Partial	1
2	M/40	Dehydration	Headache, focal motor deficits coma	3	7/15	(R) temporal lobe	TS	CTT/MCT/STR	6×30 mm Solitare stent and 4×30 mm PTA balloon catheter	3	Yes	Complete	3
3	M/41	Facial Herpeszoster	Headache	120	15/15	Bilateral parietal-occipital SDH and (L) frontal epidural hematoma	SSS/SS	CTT/MCT/STR	6×30 mm Solitare stent	5	No	Complete	0
4	M/65	Diarrhea	Seizure and coma, focal motor deficits	7	3/15	Bilateral frontal lobe	SSS/TS	CTT/MCT/STR	4×20 mm Solitare stent	4	Yes	Complete	4
5	M/46	Family history of DVT	Headache, focal motor deficits	3	12/15	(L) frontal and parietal lobe	SSS	CTT/MCT/STR	4×20 mm Solitare stent	7	No	Partial	4
6	F/27	Postpartum	Headache, focal motor deficits and vomiting	4	15/15	(L) frontal lobe	SSS/TS	CTT/MCT/STR	6×30 mm Solitare stent	7	No	Complete	0
7	M/23	Diarrhea	Headache, coma	3	6/15	SAH	SS/Vein of Galen	CTT/MCT/STR	No	7	No	Complete	0
8	F/33	Postpartum	Headache, seizure, and focal motor deficits	6	10/15	(L) parietal lobe	SSS	CTT/MCT/STR	4×20 mm Solitare stent	5	No	Complete	0
9	F/31	Miscarriage	Headache and seizure	5	15/15	Bila-terparietal lobe	SSS/TS/SS	CTT/MCT	No	5	No	Partial	0

N = number; SDH = subdural hematoma; SSS = superior sagittal sinus; TS = transverse-sigmoid sinus; SS = straight sinus; DVT = deep vein thrombosis; CTT = catheter thrombolysis; MCT = mechanical thrombectomy; STR = stent retriever; CNT = continuous thrombolysis; DC = decompressive craniectomy.

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Figure 7. The CT after EVT showed no new hemorrhages, the brain edema reduced, and the lateral fissure (white arrow) can be seen clearly than before.

hemorrhage were intracerebral hemorrhage (7/9) include parietal lobe (4/9), frontal lobe (3/9), temporal lobe (1/9), the other two are subarachnoid hemorrhage (SAH) (1/9) and bilateral parietal-occipital subdural hematoma and left frontal epidural hematoma (1/9), respectively (**Table 1**). By location, thrombosis of superior sagittal sinus (SSS) was involved in seven patients, transverse-sigmoid sinus (TS) in five patients, straight sinus (SS) in three patients, and vein of Galen in one patient. Arteriovenous circulation times were more than eleven seconds in all the nine patients.

The type of EVT were also listed in **Table 1**. Direct catheter thrombolysis and mechanical thrombectomy was applied in all of the 9 patients, urokinase infused through the microcatheter at a total dose of 100000 IU to 600000 IU, it varies from person to person. Stent retriever thrombectomy was used in 7 patients, one of them combined with balloon-assisted thrombectomy. After EVT, they were all accepted continuous thrombolysis by the use of urokinase 960000 IU/day through microcatheter for 3-7 days. Additionally, a patient (**Table 1** NO. 4) had severe intracranial hematoma with a consciousness level of 3 on the GCS pre-endovascular treatment, accepted emergency surgical decompression after the EVT proceeding. All of them have a neurological and symptomatic improvement. A good out-

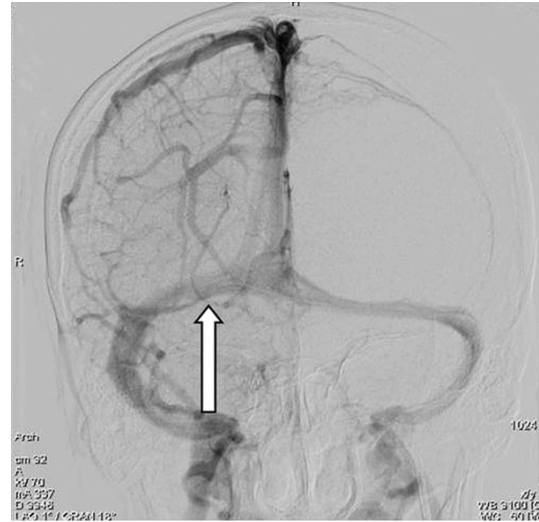


Figure 8. DSA was done four months later after EVT, the right transverse-sigmoid sinus (white arrow) was complete recanalization.

come was defined with an mRS score of 0-2 at discharge, whereas a poor outcome was defined as an mRS score of 3-5. Six patients have a good outcome, the rest three patients have a poor outcome, but no death in them. Recurrence was defined as the presence of both clinical (new or relapse of previous symptoms) and radiologic evidence of re-thrombosis during follow-up after complete or partial recanalization. Complete recanalization are in seven patients, and two patients have partial recanalization (**Table 1** NO. 1 and NO. 5). There was no new intracranial or systemic bleeding complication which was resulted by EVT in all nine cases.

There was improving neurology of the consciousness level, and with GCS of 15 at the second day after endovascular treatment. At the third day a CT scan (**Figure 7**) showed no new hemorrhages and high-density on the right transverse-sigmoid sinus, the brain edema reduced compared with the CT before endovascular treatment. Then the microcatheter and guider catheter were removed, warfarin (Orion Corporation Orion Pharma, finland) anticoagulation was initiated at the time. We evaluated the coagulation function at about every 3-5 days, with a target INR of 2-3. The total hospital days were 21 days, at the discharge time the patient recovered well, with a mild weakness in the left limb. 4 months after discharge, the patient accepted cranioplasty, and another DSA (**Figure 8**), the result showed recanaliza-

tion of the right transverse-sigmoid sinus, and no additional periprocedural complications.

Discussion

Several potential risk factors have been identified including surgery, trauma, pregnancy, puerperium, antiphospholid syndrome, cancer, exogenous hormones, and thrombophilia. In our study, the most common risk factors may be postpartum in women, and deprivation of body fluids in men. The most common clinical presentations reported in large case registries are intracranial hypertension and hemorrhagic cerebral venous infarctions [21, 22]. Diagnosis and management can be difficult because of diversity of underlying risk factors, variation in clinical presentation, and absence of uniform treatment approach [23]. With proper treatment, outcome is often favorable [24].

When the thrombosis happens, the venous pressure raises due to delaying in the venous emptying, altering the CSF absorption, and thereby raising the intracranial pressure [25]. There will be hemorrhagic CVST or/and CVST-related sub-arachnoid and subdural hemorrhages. Due to the presence of a hemorrhagic element in CVST, the administration of anticoagulant treatment stills controversial [25]. Among CVST patients, incidence of cerebral hemorrhage is 35-39% and is usually associated with poorer outcome [26]. However, controversy has been ensured as ICH can be present at the time of diagnosis CVST, and it may also complicate treatment [3]. CVST associated with intracranial hemorrhage and timing of anticoagulation after hemispherectomy is the challenge of determining when to resume anticoagulation for CVST [27]. In addition to the case report, there is no significant experience of EVT on hemorrhagic CVST patient, our study is the first literature focus on this issue.

Thereby any therapy which can re-establish circulation distal to the occlusion will be considered as the treatment of CVST. Anticoagulant treatment has been shown to be safe and associated with potentially important reduction in the risk of death or dependency without promoting ICH [28]. But conventional anticoagulant therapy is still a controversy when the hemorrhagic CVST has been occurred. Additionally, part of the patients who suffered with large, extensive thrombi and long-segment CVST have

a high risk of incomplete recovery [3, 10]. And the optimal therapy for CVST is controversial, since there are limited studies that fulfill the criteria necessary for establishment of therapeutic guidelines [29]. The advantages of EVT include that clot can be rapidly removed in angiography, reduce the dosage of systemic anticoagulants and increase local drug concentration by catheter thrombolysis. Continuous thrombolysis can also reduce the risk of systemic bleeding. In our therapeutic process, all of the nine patients have a neurological and symptomatic improvement, include a patients with a consciousness level of 3 on the GCS pre-EVT. We confirm that EVT such as catheter thrombolysis, mechanical thrombectomy, stent retriever, continuous thrombolysis, balloon-assisted thrombectomy is a good choice for the hemorrhagic CVST patients.

Horowitz et al published their protocol for the treatment of refractory sinus thrombosis using mechanical thrombolysis along with intrasinus administration of thrombolytic medication [30]. Local intra-sinus thrombolysis can be an effective and relatively safe treatment for acutely deteriorating patients who have not responded to conventional anticoagulant therapy [31]. The first report about the use of stents in the intracranial venous sinus system was a procedure performed following mechanical thrombolysis treatment and the use of angioplasty balloon, after clinical worsening in a dural arteriovenous fistula associated with occipital sinus thrombosis [32]. The use of stents can be considered as a viable treatment option in the case of failure of endovascular treatment for the severe form of CVST [33, 34].

There is accumulating evidence that local thrombolytic treatment of CVST, often combined with mechanical techniques, yields positive results. In combined pharmacological and mechanical thrombectomy, the dose of the thrombolytic drug and duration of infusion can be decreased because of the increased surface area of the thrombus exposed to the drug [35]. A recent systematic review assessed 185 patients who underwent mechanical thrombectomy, noting that in severe cases venous anticoagulation may not be the treatment of choice, with indication for intrathrombolysis and/or mechanical thrombolysis [36]. Endovascular techniques have significantly evolved over the past decade, but data regarding the efficacy

and safety of endovascular treatment for CVST are poorly defined [20]. Endovascular therapy may be considered if patients deteriorate despite medical therapy. The systematic review summarize 235 patients concluded that endovascular mechanical thrombectomy is an effective salvage therapy for refractory CVST, with a reasonable safety profile. Chemical thrombolysis, in conjunction with endovascular mechanical thrombectomy, did not appear to result in additional harm or benefit. Further analysis is warranted to determine predictors of success after EMT for CVST. For the lack of randomized controlled trials, there is no recommendation as to the specific endovascular therapy to be employed in the treatment of CVST and hemorrhagic CVST. In view of the study on hemorrhagic CVST patient by EVT is lack, we hope our EVT experience in hemorrhagic CVST patients can be helpful for the future clinical work, although there is limitation of insufficient number of cases.

In conclusion, EVT is an effective and safe procedure for potentially catastrophic hemorrhagic CVST which is controversy treated with systematic anticoagulation alone at present, and EVT is a good treatment option in patients with hemorrhagic CVST.

Disclosure of conflict of interest

None.

Address correspondence to: Zhigang Wang, Department of Neurosurgery, Qilu Hospital of Qingdao Branch, Shandong University, NO. 758, Hefei Road, Shibei District, Qingdao 266035, Shandong, China. Tel: +86-15153876703; E-mail: wangzhigang367@163.com

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