
ORIGINAL ARTICLE

Endovascular Therapy for Cerebral Vasospasm Following Aneurysmal Subarachnoid Haemorrhage

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ABSTRACT

Objectives: To review the treatment and outcome of patients who underwent endovascular therapy for cerebral vasospasm secondary to aneurysmal subarachnoid haemorrhage (SAH).

Methods: Medical records of patients who underwent endovascular therapy at a regional hospital from July 2014 to June 2015 for cerebral vasospasm secondary to aneurysmal SAH were reviewed.

Results: Six women and one man aged 45 to 78 (mean, 56) years had grade-4 aneurysmal SAH and underwent 16 consecutive sessions of endovascular therapy for vasospasm after a mean of 7.5 (range, 4-12) days. They were followed up for at least 10 months. Intra-arterial verapamil was administered at all 16 sessions. In six of the 16 sessions, verapamil injection was followed by percutaneous transluminal balloon angioplasty. All but one session resulted in an immediate angiographic response. There was no treatment-related death or procedural complication. Four patients were free of major motor impairment and had immediate clinical improvement. The remaining three patients had poor outcome or died; all required repeat angioplasty and showed no immediate clinical improvement.

Conclusion: Endovascular therapy is a viable option for cerebral vasospasm secondary to aneurysmal SAH.

Key Words: Angiography, digital subtraction; Endovascular procedures; Intracranial aneurysm; Subarachnoid hemorrhage; Vasospasm, intracranial

中文摘要

血管治療動脈瘤蛛網膜下腔出血引致的腦血管痙攣

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目的：回顧動脈瘤蛛網膜下腔出血（SAH）引致的腦血管痙攣的治療和結果。

方法：回顧2014年7月至2015年6月在一間分區醫院接受血管治療動脈瘤SAH引致的腦血管痙攣的患者病歷。

結果：6名女性和1名男性年約45-78（平均，56）歲的患者均有4級動脈瘤SAH，並在平均7.5（範圍，4-12）天後接受共16次血管痙攣治療。他們被跟進至少10個月。16個療程均有動脈注射維拉帕米，其中6次跟隨進行經皮腔內球囊血管成形術。除一個療程外，所有療程都有即時血管造影反應。

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沒有患者有治療相關的死亡或手術併發症。4名患者有即時臨床改善及無重大運動障礙。其餘3名患者效果不佳或死亡；他們沒有即時臨床改善並需接受重複血管成形術。

結論：血管治療動脈瘤（SAH）引致的腦血管痙攣是一項可行選擇。

INTRODUCTION

Subarachnoid haemorrhage (SAH) accounts for up to 40% of mortality in stroke patients, and is partly related to the development of vasospasm and delayed cerebral ischaemia. Aneurysmal SAH is the most common cause of severe cerebral vasospasm after the initial haemorrhage, resulting in death and disability.¹ Vasospasm occurs in 67% of patients with aneurysmal SAH, and results in infarction in 10% to 45% of them. Only 30% to 45% of survivors return to previous comparable jobs, and 10% to 23% of patients with aneurysmal SAH die.² In patients with aneurysmal SAH, the amount of cisternal and intraventricular haemorrhage is a predictor of delayed cerebral ischaemia and functional outcome.³ Delayed vasospasm usually appears 3 to 14 days following aneurysmal SAH.⁴

According to the American Heart Association / American Stroke Association, management of symptomatic cerebral vasospasm comprises volume expansion, induction of hypertension, and haemodilution (triple-H therapy), whereas management of aneurysmal SAH comprises administration of an oral calcium channel blocker, early management of the ruptured aneurysm, maintenance of blood volume, and avoidance of hypovolaemia.⁵

Early endovascular intervention is beneficial when vasospasm is refractory to medical haemodynamic augmentation therapy. Selective intra-arterial infusion of vasodilators into small arterial branches or when vasospasm is diffuse is beneficial although its effect is short-lasting.⁶ Mechanical angioplasty is effective for larger vessels but is associated with risks of vessel rupture and branch occlusion.⁷ Many studies of balloon angioplasty and intra-arterial vasodilator administration for treatment of vasospasm have been reported.⁸⁻¹⁰ This study reviewed the treatment and outcome of patients who underwent endovascular therapy for cerebral vasospasm secondary to aneurysmal SAH.

METHODS

The research protocol was conducted in compliance with Declaration of Helsinki. Medical records of patients who underwent endovascular therapy at a regional hospital in Hong Kong from July 2014 to June 2015 for cerebral

vasospasm secondary to aneurysmal SAH were reviewed (Table).

All patients were admitted under the joint care of the neurosurgical and intensive care units. Clinical presentation was graded using the Hunt and Hess Scale.¹¹ Cerebral computed tomography angiography (CTA), digital subtraction angiography, bedside neurological examinations, and / or transcranial Doppler (TCD) ultrasonography were performed to detect any aneurysm and to establish a baseline. Vasospasm was suspected when patients exhibited neurological deficits not explained by hydrocephalus, seizures, infection, or metabolic disturbances, or in patients with elevated mean velocities on TCD ultrasonography. Standard triple-H therapy was then commenced. When symptoms persisted or elevated TCD velocities deteriorated, neurovascular evaluation and treatment were considered. Images were evaluated independently by two neuroradiology specialists blinded to other clinical details. The severity of aneurysmal SAH was graded using the modified Fisher Scale.¹² The location of a ruptured aneurysm and the presence of vasospasm were recorded. Angiography and endovascular therapy were performed using the Siemens Axiom-Artis system. Treatment included surgical decompression, aneurysm clipping, coil embolisation, and reconstruction by stenting. Clinical outcome was evaluated using the modified Rankin Scale.¹³

RESULTS

Six women and one man aged 45 to 78 (mean, 56) years had grade-4 aneurysmal SAH and underwent 16 consecutive sessions of endovascular therapy for vasospasm after a mean of 7.5 (range, 4-12) days. Three of them had vasospasm evident on the initial CTA. They were followed up for at least 10 months.

In 16 sessions of endovascular therapy, the diagnosis of vasospasm was confirmed by CTA in seven and by clinical features and / or TCD ultrasonography in nine. In five sessions, coiling of the aneurysm was performed at a mean of 6.4 (range, 3-10) days prior to endovascular therapy.

In 16 sessions of endovascular therapy, vessels of

Table. Clinical presentation, endovascular therapy, and outcome of the seven patients.

Sex / age (years)	Hunt and Hess Scale	Fisher Scale	Vessels involved	Clinical presentation	Endovascular therapy	Modified Rankin Scale
F / 50	2	4	Vasospasm of ICA, ACA, MCA, BA	Glasgow Coma Scale remained E1VTM3 after decompressive craniectomy; rising TCD velocities despite triple-H therapy for 6 days; severe vasospasm on CTA	1st session: 10 mg verapamil to each ICA, 5 mg verapamil to left VA; 2nd session: 15 mg verapamil to right ICA, 10 mg verapamil to left ICA	5
F / 78	2	4	Minimal narrowing of distal MCA branches without filling defect	Acute aphasia after coil embolisation of ruptured left posterior communicating artery aneurysm, suspected vasospasm, or embolic event	3 mg verapamil to left ICA, 10 mg abciximab to left ICA, 5 mg verapamil to right ICA	1
F / 48	5	4	ICA	Remained comatose after decompressive craniectomy; deteriorating vasospasm on TCD despite triple-H therapy for 6 days	1st session: 10 mg verapamil to right ICA, balloon 2 x 9 mm to right ICA, 5 mg verapamil to left ICA; 2nd session: 15 mg verapamil to right ICA, 5 mg verapamil to left ICA	5
F / 60	3	4	ACA, MCA	Glasgow Coma Scale deteriorated 3 days after stenting of right paracphthalmic ICA dissecting aneurysm; CTA revealed anterior circulation vasospasm	1st session: 15 mg verapamil to right ICA, balloon 2 x 9 mm to right ICA, 5 mg verapamil to left ICA; 2nd session: 5 mg verapamil to right ICA, 10 mg verapamil to left ICA, 5 mg verapamil to left VA	0
F / 48	3	4	1st session: ACA, MCA; 2nd session: MCA, VA, BA	Clipping of anterior communicating artery aneurysm; severe vasospasm on post-SAH day 5 on TCD; mean velocity of bilateral MCA remained high on post-SAH day 7 despite triple-H therapy, with onset of expressive dysphasia	1st session: 5 mg verapamil to right ICA, 15 mg verapamil to left ICA, 5 mg verapamil to left VA; 2nd session: 5 mg verapamil to right ICA, 10 mg verapamil to left ICA, balloon 2 x 9 mm to left ICA	0
F / 45	3	4	ACA, MCA	Left ACA dissecting aneurysm with parent artery occlusion performed; general condition deteriorated on post-SAH day 9, and triple-H therapy started; vasospasm persisted for 2 days	1st session: 15 mg verapamil to right ICA, 10 mg verapamil to left ICA; 2nd session: 20 mg verapamil to right ICA, 15 mg verapamil to left ICA	0
M / 60	4	4	1st session: MCA, BA; 2nd session: ACA, MCA, BA, VA; 3rd to 5th sessions: ACA, MCA, BA	Grade-4 SAH due to ruptured anterior communicating artery aneurysm, with ventricular drainage and aneurysmal coiling performed; triple-H therapy commenced on post-SAH day 3 for moderate vasospasm on TCD, with initial improvement and extubation; deterioration in general condition on day 5, with high mean velocities of bilateral MCA; fair response after repeated episodes of mechanical and chemical angioplasties	1st session: 5 mg verapamil to each ICA, 10 mg verapamil to left VA, balloon 3 x 9 mm to terminal right ICA, balloon 2 x 9 mm to bilateral M1 and left ICA; 2nd session: 5 mg verapamil to each ICA and right ACA, balloon 2 x 9 mm to left A1, left M1, and right terminal ICA; 3rd session: 10 mg verapamil to each ICA, 5 mg verapamil to left VA, balloon 1.5 x 9 mm to right A1 segment; 4th and 5th sessions: 15 mg verapamil to each ICA, 10 mg verapamil to left VA	6

Abbreviations: ACA = anterior cerebral artery; BA = basilar artery; CTA = computed tomographic angiogram; ICA = internal carotid artery; MCA = middle cerebral artery; SAH = subarachnoid haemorrhage; TCD = transcranial Doppler; VA = vertebral artery.

anterior circulation involved were the internal carotid artery (ICA) [n = 2], anterior cerebral artery (ACA) [n = 10], and middle cerebral artery (MCA) [n = 15], whereas vessels of posterior circulation involved were posterior cerebral artery (PCA) [n = 4], vertebral artery (n = 2), and basilar artery (n = 7).

Intra-arterial verapamil was administered in all 16 sessions to the ICA (n = 16), ACA (n = 1), and vertebral artery (n = 8); dose ranged from 8 to 40 mg based on the position of the vasospastic vessel, the site of vascular injection, and the severity of vasospasm. A lower dose was administered when superselective canalisation and injection were feasible, and when vasospasm was mild. Every 5 mg/2 ml of verapamil was diluted to 5 ml with normal saline. Delivery was via a 5.0 French size Headhunter 1 or Valavanis cerebral angiographic catheter (Cook, Bloomington [IN], USA). Verapamil injection alone sufficed in 63% of the sessions.

In six of the 16 sessions, verapamil injection was followed by percutaneous transluminal balloon angioplasty (Figure). The balloon was applied to the

ICA (n = 3), ACA (n = 2), and MCA (n = 4). In the two patients with balloon applied to the ACA, an Excelsior SL-10 Microcatheter catheter (Stryker, Kalamazoo [MI], USA) or 0.021" Direxion Bern shape Torqueable Microcatheter (Boston Scientific) was used for superselective catheterisation. Gateway over-the-wire co-axial balloon catheters (Boston Scientific, Quincy [MA], USA) with a balloon near the distal tip were used with the support of micro-guidewires. The balloon catheters were advanced through the stenotic arterial portion and nominal pressure was applied. Balloon diameter ranged from 1.5 to 3 mm, but did not exceed the calibre of the vessel in its non-vasospastic state (based on baseline angiography or CTA). Balloon length was 9 mm. When the length of the stenotic segment exceeded balloon length, sequential intermittent balloon inflations and deflations were performed from distal to proximal portions of the vessel. Intra-arterial verapamil was injected again after balloon dilatation to enhance the effect on distal vessels.

In all but one session, an immediate angiographic response was evident. There was no treatment-related

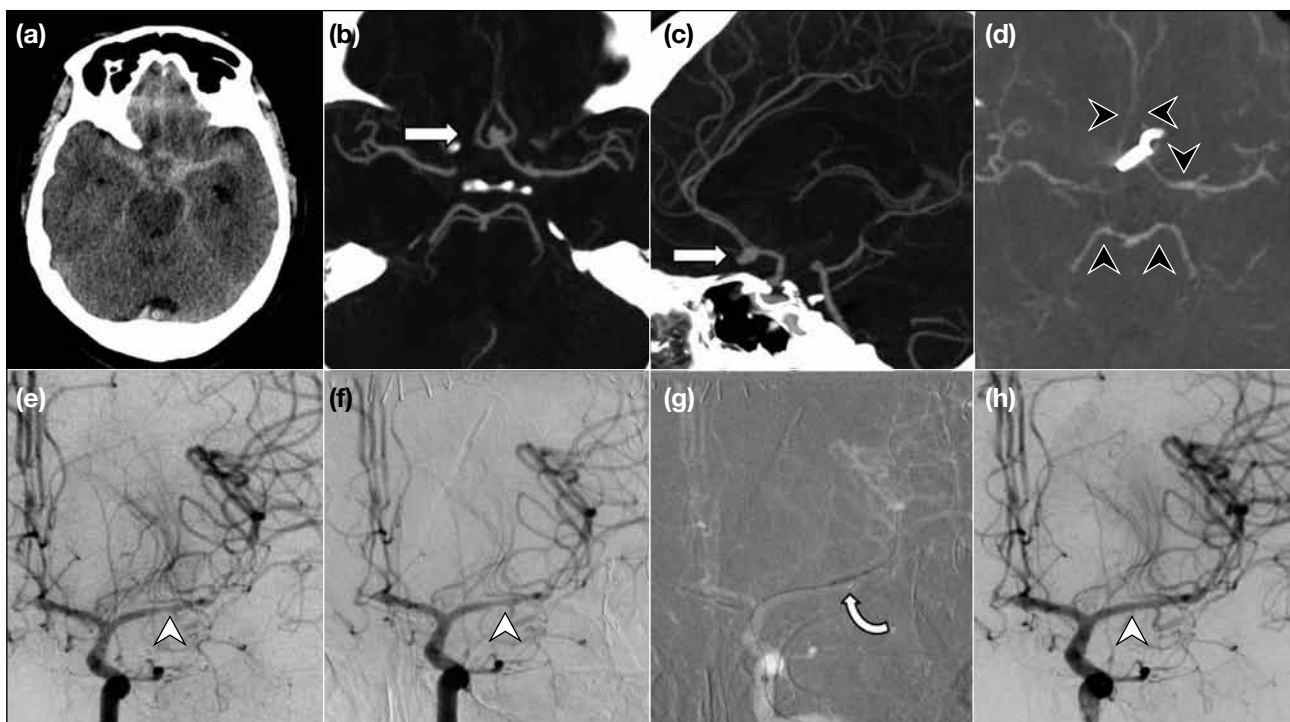


Figure. Computed tomography of the brain showing (a) aneurysmal subarachnoid haemorrhage, (b, c) a 5-mm aneurysm at the anterior circulation (arrows) that was clipped the next day, and (d) diffuse vasospasm and mild narrowing at the bilateral anterior, middle, and posterior cerebral arteries (arrowheads). Digital subtraction angiography showing (e) moderate vasospasm at bilateral middle cerebral arteries, more severe over the left segment (arrowhead), (f) fair response after intra-arterial injection of verapamil (arrowhead), (g) balloon angioplasty (curved arrow) with the aid of a micro-guidewire from distal to proximal end for bilateral middle cerebral arteries, and (h) good response after balloon angioplasty (arrowhead).

death or procedural complication (balloon rupture, vascular injury, intra- or extra-cranial dissection, arterial occlusion, or severe haemodynamic compromise requiring resuscitation). Four patients were free of major motor impairment and had immediate clinical improvement, although two who were <60 years of age showed infarcts on brain CT. All four patients were independent in their activities of daily living and had returned to their previous job. The remaining three patients had poor outcome or died; all required repeat angioplasty and showed no immediate clinical improvement.

DISCUSSION

There is concern about possible neurotoxicity with intra-arterial papaverine.¹⁴ The efficacy of intra-arterial administration of calcium channel blockers (nicardipine, nimodipine, and verapamil) has been reported.¹⁵ Verapamil is an injectable calcium channel blocker and has been widely used to treat coronary vasospasm. Patients undergoing ICA balloon occlusion test have been reported to have increased cerebral blood flow following administration of verapamil.¹⁶ Intra-arterial verapamil for post-SAH vasospasm has demonstrated encouraging neurological and angiographic results and may prevent catheter-induced vasospasm following placement of guiding catheters and before insertion of microcatheters for balloon angioplasty.⁶ High-dose verapamil is considered safe with regard to haemodynamic stability.¹⁷ Delivery of verapamil via the transfemoral approach can be achieved with diagnostic catheters used in cerebral angiography.

Balloon angioplasty effectively reverses vasospasm in larger, more proximal cerebral vessels, but has difficulty reaching small, distal vessels or sharply angled vessels, particularly when there is compression of the connective tissue, stretching of the internal elastic lamina, or a combination of compression and stretching of the smooth muscle of the dilated arteries.¹⁸ Balloon angioplasty has more long-lasting results than pharmacological treatment, but is associated with potential complications such as embolism, thrombosis, reperfusion injury, displacement of surgical clips, and vessel rupture.¹⁹ A co-axial over-the-wire balloon catheter may be used. A micro-guidewire can be used to establish a path through the stenosis; a catheter can then be advanced over the micro-guidewire until the balloon on the catheter is positioned across the stenosis. Through an inflated lumen in the catheter, the balloon is then slowly deployed with a handheld inflation device

up to the nominal pressure. The balloon is kept inflated, usually for less than a minute, and then deflated until the next inflation. Intermittent inflation allows blood flow through the artery during balloon deflation. A nitroglycerin solution may be injected to prevent or reverse transient arterial spasm. Inflation of the balloon enables re-establishment of acceptable blood flow through the artery. The number of balloon inflations is titrated according to the length of the targeted segment for angioplasty, and real-time treatment response. In general, balloon angioplasty is performed from the distal part to the proximal part of the vessel as it is technically easier. Balloons should be undersized to prevent vessel rupture. The non-vasospastic calibre of the artery is used to determine the upper limit of balloon diameter. Balloon angioplasty is avoided in hypoplastic vessels and vessels with acute turns and bifurcations due to the increased risk of arterial rupture. The safety and efficacy of both balloon angioplasty and intra-arterial vasodilator infusion have been established.²⁰ In a series of 189 patients with 349 treatment sessions, no procedural-related death was reported, and the procedural complication rate was 1.7% per session and 3.2% per patient.²¹

Poor outcome may be related to complex pathological and physiological changes involved in the natural history of refractory vasospasm, including vessel wall thickening, sub-endothelial fibrosis, and impaired vasodilatation.²² Patients with poor prognostic factors benefit the most from early invasive therapy; nonetheless, they may be poor candidates for endovascular treatment, as they may already have sustained permanent brain damage.²³

CONCLUSION

Endovascular therapy is a viable option for cerebral vasospasm secondary to aneurysmal SAH.

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