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Miscellaneous

On-Table Catheter-Based Neurosalvage Performed by Cardiologists for Embolic Complication during an Endovascular Procedure

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Objectives: To report our experience and clinical results of neurosalvage techniques, performed by interventional cardiologists without moving the patient, to manage cerebral thromboembolic complications.
Background: Iatrogenic emboli may be released during an endovascular procedure, causing permanent neurological complications and catastrophic outcomes.
Methods: Between July 2013 and December 2017, a total of eight patients suffered from embolic complications during endovascular procedures (two radiofrequency catheter ablation, five coronary angiogram/angioplasty, and one subclavian artery angioplasty). Catheter-based neurosalvage was attempted by experienced interventional cardiologists promptly in the same catheterization room.
Results: The embolized locations were the M1 segment of the middle cerebral artery in four patients, the M2/M3 segments in three, and the basilar artery in one. Access to the supra-aortic vessels was achieved. Local intra-arterial thrombolysis was given in five patients (63%) and balloon angioplasty in three (38%). Intra-arterial thrombectomy with a stent retriever was attempted in three patients but failed in one. A combination of different techniques was used in three patients (38%). Final thrombolysis in cerebral infarction grade 3 flow was achieved in seven patients (88%). Favorable clinical outcomes at 1-month follow-up (modified Rankin scale of 0-2) were observed in seven patients (88%), and none of the patients had died at 12 months.
Conclusion: Our experience demonstrated that acute embolic complications during an endovascular procedure can be salvaged by interventional cardiologists with acceptable angiographic and clinical results.

Key Words: Acute stroke intervention • Cardiologist • Embolic complication • Neurosalvage

INTRODUCTION

Neurological complications after/during left heart catheterization or percutaneous coronary intervention (PCI) are infrequent. The overall rate ranges from 0.2% to 0.4%,[1-3] but they are associated with a high risk of morbidity and mortality.[1-5] Embolic stroke accounts for

Abbreviations

CT	Computed tomography
MRS	Modified Rankin scale
NIHSS	National Institutes of Health Stroke Scale
PAO	Proximal artery occlusion
PCI	Percutaneous coronary intervention
RFCA	Radiofrequency catheter ablation
rt-PA	Recombinant tissue plasminogen activator
TICI	Thrombolysis in cerebral infarction

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the majority of these complications, with several potential mechanisms for arterial occlusion including thrombus, air embolization, and atheroma debris embolization from the aortic wall.[6] Although several neurosalvage options have been proposed, the principle aim of treatment is to restore cerebral blood flow in the occluded intracranial artery without time delay.[7] However, the major problem with acute stroke interventions in most countries is the limited availability of modern treatments and limited number of trained neuroradiologists to offer around-the-clock service. Transporting patients to specialized neuroradiology teams inevitably delays treatment, and interfacility transport has been associated with worse neurological outcomes.[8] Interventional cardiologists/vascular surgeons have established networks of catheterization laboratories and the necessary infrastructure to provide rapid access to prompt stroke interventions. Although a few studies have been reported in the literature,[9,10] it has always been questioned whether safe and effective stroke interventions can be performed by interventional cardiologists/vascular surgeons. Here, we report our experience and clinical results of catheter-based neurosalvage procedures, combining intra-arterial pharmacotherapy, balloon angioplasty, and mechanical thrombectomy, which were all performed by cardiologists promptly in the management of embolic complications during an endovascular procedure.

MATERIALS AND METHODS

Between July 2013 and December 2017, a total of eight patients (five men, 73.6 $\pm$ 7.7 years old) had embolic complications during endovascular procedures. Routine preprocedural heparin bolus was given to maintain an activated clotting time longer than 300 s before radiofrequency catheter ablation (RFCA) in the left heart and 250 s before the coronary/endovascular intervention. When a neurologic deficit occurred unexpectedly during the procedure, experienced interventional cardiologists with carotid intervention skills were called and performed a diagnostic intracranial angiogram in the same catheterization room. Once intracranial artery occlusion compatible with neurologic symptoms had been confirmed, catheter-based techniques for neurosalvage were attempted. Our interventional cardiologist team previously developed a structured approach for embolic complications during carotid interventions.[10] It combines stepwise utilization of intra-arterial pharmacotherapy with heparin, nitroglycerin, and recombinant tissue plasminogen activator (rt-PA), balloon angioplasty, and intracranial stenting. This stepwise technique was utilized for neurosalvage before 2017 (Patients 1-5).

Mechanical thrombectomy

Since 2017, mechanical thrombectomy has been utilized as the first-line neurosalvage technique once intracranial large vessel occlusion has been detected. NeuroMax 088 (90 cm, straight tip, 6 Fr, Penumbra, CA, USA) was used as the guiding sheath. A 0.014-inch coronary angioplasty wire (Runthrough NC Floppy, Terumo, Tokyo, Japan) was advanced to the intracranial artery under the assistance of a support catheter (Navien, 6 Fr, straight tip, 125 cm, Covidien/Medtronic, Paris, France) and microcatheter (Marksman, 2.8 Fr, 150 cm, Covidien/Medtronic). The wire was navigated across the emboli into the distal vessel, and then the microcatheter was advanced. The distal true lumen was confirmed by contrast media injection via the microcatheter. Solitaire FR (Covidien/Medtronic) was used to retrieve the emboli. Three heparinized solution bags (normal saline 1000 mL with 5000 units of heparin) were connected to the catheters to provide continuous flushing during the procedure.

Structured neurosalvage

In Figure 1, we propose a new structured neurosalvage approach when neurologic deterioration occurs unexpectedly during an endovascular procedure. The treatment strategy was initiated depending on whether proximal artery occlusion (PAO) was identified, defined as occlusion of the middle-cerebral-artery trunk and its immediate branches, with or without intracranial occlusion of the internal carotid artery. Mechanical thrombectomy was attempted first in the patients with PAO. Otherwise, combination treatment with the stepwise utilization of intra-arterial pharmacotherapy with heparin, nitroglycerin, and rt-PA, balloon angioplasty, and intracranial stenting was performed in the patients with non-PAO.

Brain computed tomography (CT) without contrast was performed immediately and 1 week after the procedure. A complete neurologic examination, including assessment of National Institutes of Health Stroke Scale

(NIHSS) and modified Rankin scale (MRS) was done by an independent neurologist < 24 hours and 1 month later. Neurologic sequelae, intracranial hemorrhage, and death were recorded. An angiogram was reviewed by two independent technicians, blinded to the patients' clinical outcome at the time of interpretation, using the thrombolysis in cerebral infarction (TICI) grading system.[11] The retrospective review of the clinical information and radiologic records of the patients was approved by the Institutional Review Board at National Taiwan University Hospital.

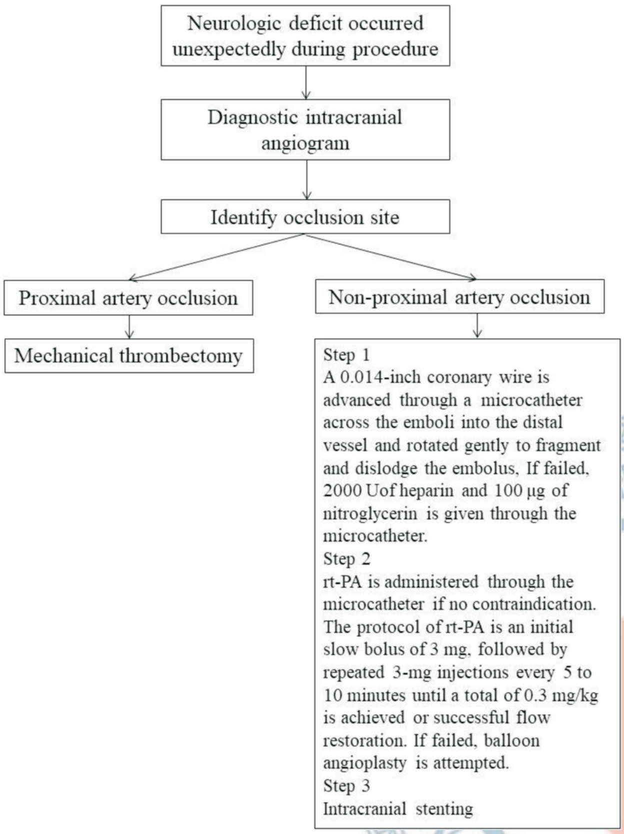

Figure 1. *Structured neurosalvage approach. rt-PA, recombinant tissue plasminogen activator*

RESULTS

Baseline clinical data of the eight patients who underwent neurosalvage are listed in Table 1. Two patients had embolic complications during RFCA for persistent atrial fibrillation and Wolff-Parkinson-White syndrome with left side bundle of Kent, respectively. Five patients had embolic complications during coronary angiography/angioplasty and one during subclavian artery angioplasty. In the same period, a total of 9897 coronary and vascular diagnosis/angioplasty (except carotid diagnosis/intervention) and 2639 RFCA procedures were performed at our catheterization laboratory. Thus, the embolic complication rates were 0.06% in coronary and vascular diagnosis/angioplasty and 0.08% in RFCA. The embolized locations were the M1 segment of the middle cerebral artery in four patients, the M2/M3 segments in three, and the basilar artery in one.

Neurosalvage procedure, angiographic, and clinical outcomes are summarized in Table 2. The sequential

Table 1. Baseline clinical and procedural data

Patient no.	Age (years)	Sex	DM	HTN	Hyperlipidemia	CAD	CKD/ ESRD	Af	Procedure causing the embolic event	M1, left
1	77	M	No	Yes	No	No	No	No	RFCA for PSVT	M1, left
2	81	F	No	Yes	No	No	No	Yes	RFCA for Af	M1, left
3	81	M	Yes	Yes	No	Yes	Yes	No	PCI for NSTEMI	Basilar artery
4	75	M	No	No	No	Yes	No	No	PCI for CAD	Superior division of M2, left
5	57	M	Yes	No	Yes	Yes	No	No	Diagnostic angiogram for CAD	M2, right
6	75	F	Yes	Yes	Yes	No	No	No	PTA for left subclavian artery stenosis	M1, left
7	70	F	Yes	Yes	Yes	Yes	Yes	No	Diagnostic angiogram for CAD	M2, right
8	73	M	Yes	No	Yes	Yes	No	No	PCI for CAD	M1, left

Af, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; ESRD, end-stage renal disease; F, female; HTN, hypertension; M, male; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; PSVT, paroxysmal supraventricular tachycardia; PTA, percutaneous transluminal angioplasty; RFCA, radiofrequency catheter ablation.

Table 2. Neurosalvage procedure, angiographic, and clinical outcomes

Patient no.	Presalvage TICI flow	Neurosalvage procedures	Symptoms to TICI 3 flow (min)	Postsalvage TICI flow	Postsalvage NIHSS	Hemorrhagic complications	1-month NIHSS	1-month MRS	1-month neurologic deficit
1	0	IA rt-PA injection, balloon angioplasty	50	3	14	No	5	2	Right hemiparesis & motor aphasia
2	0	IA rt-PA injection, balloon angioplasty	56	3	3	No	2	1	Right hemiparesis & dysarthria
3	0	Balloon angioplasty	44	3	1	No	0	0	No deficit
4	0	IA rt-PA injection	40	3	5	No	0	0	No deficit
5	0	IA rt-PA injection	48	3	1	No	0	0	No deficit
6	0	IA rt-PA injection IA thrombectomy attempt, but failed wiring across lesion		1	8	No	15	4	Right hemiplegia & motor aphasia
7	0	IA thrombectomy	38	3	4	No	1	1	Mild left arm weakness
8	0	IA thrombectomy	55	3	3	No	0	0	No deficit

IA, intra-arterial; MRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator; TICI, thrombolysis in cerebral infarction.

combination of intra-arterial rt-PA injection and balloon angioplasty was performed in Patients 1 and 2, who were both complicated with acute left M1 occlusion during RFCA. In Patient 3, the neurosalvage procedure was performed using balloon angioplasty only because of a prior history of chronic subdural hematoma. In Patients 4 and 5, TICI 3 flow was achieved using intra-arterial rt-PA injection only. In Patients 6-8, mechanical thrombectomy was attempted, but it failed in Patient 6 because of wire crossing failure. Therefore, an adjunctive intra-arterial rt-PA injection was performed in Patient 6.

TICI 3 flow was achieved in all patients except Patient 6. The acute neurologic deterioration recovered completely in Patients 3, 4, 5, and 8 after salvage. No intracranial hemorrhage or subarachnoid hemorrhage was detected immediately by postprocedural brain CT. After 1 month of follow-up, favorable clinical outcomes (defined as a MRS of 0-2) were observed in seven patients (88%). None of the patients had died at 12 months.

An example case of neurosalvage for acute basilar artery occlusion

PCI was performed in Patient 3, an 85-year-old man with non-ST segment elevation myocardial infarction. The patient also had a history of diabetes mellitus, hypertension, and chronic subdural hematoma. Loss of consciousness and brain stem sign were noted after coronary stenting. Emergent oropharyngeal intubation was performed to protect the airways. Without moving the patient, an angiogram showed acute basilar artery occlusion (Figure 2A). A 0.014-inch coronary angioplasty wire was advanced through a microcatheter across the emboli into the left posterior cerebral artery (Figure 2B). Sequential balloon angioplasty under low-pressure inflation (2-4 atm) was then performed in the basilar artery by increasing the balloon size from 1.5 to 2.5 mm (Figure 2C), and TICI 3 flow was then established (Figure 2D). The patient was arousable immediately after the procedure and recovered completely 1 hour later. Follow-up brain magnetic resonance imaging (MRI) showed multiple infarcts in the bilateral cerebellum and left medial temporal lobe. He was extubated the next day and discharged 7 days after the procedure without neurologic sequelae.

An example case of neurosalvage by mechanical thrombectomy

Patient 7 was a 70-year-old woman with underlying diabetes mellitus, hypertension, end-stage renal disease and prior coronary artery disease status post coronary stenting. She received a diagnostic coronary angiogram, which showed no significant in-stent restenosis. Conscious disturbance and left limb weakness were suddenly noted during right coronary artery engagement. An emergent cerebral angiogram showed right M2 occlusion (Figure 3A). After wiring over the occlusion, a Marksman microcatheter was advanced across the embolic segment. A stent retriever (Solitaire FR 4.0 × 20 mm) was deployed (Figure 3B), and blood flow was resumed immediately (Figure 3C). The stent retriever was retrieved into the guiding catheter after 5 min of deployment and the TICI 3 flow was restored immediately. The patient was discharged 7 days after the procedure. The NIHSS score was 1 with residual mild left arm weakness at 1-month follow-up.

DISCUSSION

Embolic complications may occur during any endovascular procedure,[1-7] including electrophysiological studies and RFCA.[12,13] Although its occurrence is rare, stroke is still responsible for a significant proportion of procedural-related in-hospital death, and it has a notable impact on the patient's prognosis and quality of life.[2] Early and timely detection and effective revascularization are crucial in neurosalvage. In our small series, technically successful recanalization (TICI flow 2b or 3) and favorable clinical outcomes (MRS of 0-2) were both achieved in seven patients (88%). Our experience not only illustrates the importance of on-table prompt revascularization without interfacility transport in patients with such complications, but also that interventional cardiologists with experience in carotid interventions can perform time-efficient neurosalvage by combining intra-arterial pharmacotherapy, balloon angioplasty, and mechanical thrombectomy.

The reported overall incidence of thromboembolic complications during RFCA is 0.6%, with a higher risk (1.6-2.8%) when an ablation procedure is performed in the left heart.[12-14] Embolization from venous sheaths or right-sided radiofrequency lesions causes pulmonary emboli that may be clinically silent. Thus, catheter ablation-induced thromboembolism might occur more frequently than reported. The mechanisms of embolization from left-sided procedures are multifactorial, including dislodged atherosclerotic plaques from major arteries,

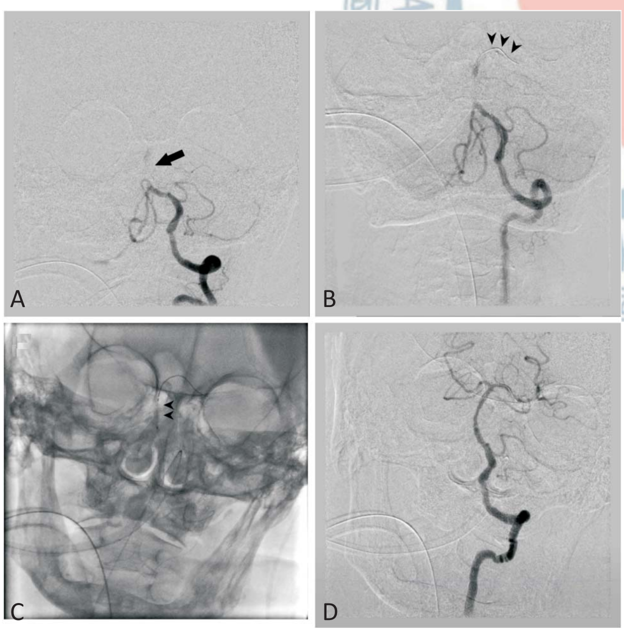

Figure 2. *Neurosalvage for acute basilar artery occlusion in Patient 3. (A) Cerebral angiogram shows occlusion of the basilar artery (arrow). (B) A coronary wire (arrowhead) was advanced across the occlusion into the left posterior cerebral artery. (C) Balloon angioplasty with 2.5 mm coronary balloon (arrowhead). (D) Successful recanalization after balloon angioplasty.*

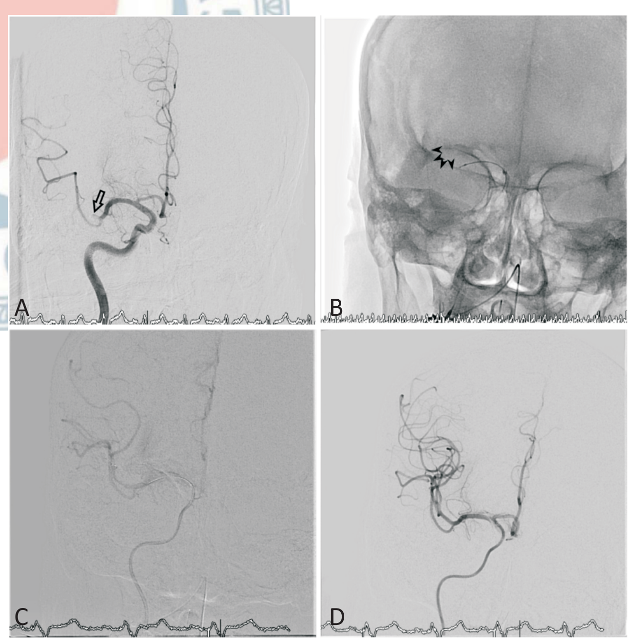

Figure 3. *Neurosalvage by mechanical thrombectomy in Patient 7. (A) Cerebral angiogram shows occlusion of the right middle cerebral artery, M2 segment (arrow). (B) A stent retriever Solitaire FR 4.0 × 20 mm (arrowhead) was deployed. (C) Cerebral blood flow restored after stent retriever deployment. (D) Successful recanalization after retrieving the stent retriever.*

calcification from systemic valves, thrombus formation on left heart catheters and sheaths, air embolus, or endocardial/tissue damage leading to a prothrombotic surface on the endocardium.[15] Measures commonly used to minimize the risk of thromboembolic events include preprocedural transesophageal echocardiography, preprocedural anticoagulation, intraprocedural heparin, continuous trans-septal sheath flushing, and temperature feedback to control the radiofrequency current. However, early embolic stroke can still be occur even in the period of therapeutic anticoagulation, indicating that there is an inherent procedure-related risk of thromboembolism that cannot be completely eliminated even by appropriate anticoagulation, careful catheter and sheath management. Another important factor to consider is the conscious sedation that patients routinely receive during the electrophysiologic intervention. It may delay the detection of thromboembolism events, thus prolonging the initiation of neurosalvage action and the duration of intracranial artery occlusion to be recanalized. This may help to explain how TICI 3 flow was finally achieved, however the first two cases of our series still had significant neurologic sequelae.

Once the embolic stroke occurs during cardiac catheterization, immediate cerebral angiography is the key factor to achieve successful neurosalvage. De Marco et al.[16] reported six cases of periprocedural ischemic stroke complicating cardiac catheterizations, and those who received immediate cerebral angiography had more favorable neurologic outcomes than those who received an early neuroimaging strategy with brain MRI or CT. In the case of intraprocedural stroke, the major advantage of performing a cerebral angiogram is that the diagnosis of embolism can be confirmed and then treatment can be given immediately using the same fluoroscopy machine.[6] It is definitely more helpful to implement this strategy if the interventional cardiologists are able to perform selective cerebral angiography and if intra-arterial treatment is always available in the catheterization laboratory, rather than consulting an interventional neuroradiologist. We think the favorable results in our cohort are partially attributable to the short time interval from symptom onset to recanalizing the occlusion.

It could be argued that emboli/thrombi leading to stroke during cardiac catheterization may be less likely than other strokes to respond to thrombolysis based on presumptions about their composition. Therefore, combining different neurosalvage techniques is mandatory to provide safe and efficient treatment. Mechanical thrombectomy has been shown to be an effective therapy in cases of large cerebral vessels occluded by fresh large thrombi which are dislodged from the catheter and other interventional devices. In small to medium vessel occlusion, which is not suitable for mechanical thrombectomy, using guidewire or angioplasty balloon manipulation to fragment the thrombus mechanically could be an alternative therapeutic option. Furthermore, combined with intra-arterial thrombolysis, these mechanical thrombus fragmentation methods would not only increase the reactive emboli surface accessible to the lytic agents, but also establish temporary flow through and beyond the emboli. The latter mechanism allows for a further increase in the contact surface between the lytic agents and the embolus.[10] The most difficult situation is when the emboli come from dislodged aortic or large vessel plaques. These emboli are calcified and fibrin-dense and, therefore, not amenable to lysis and guidewire penetration. Therefore, poor clinical and neurological outcomes are unavoidable, such as in case no. 6 in our cohort.

Traditionally, acute stroke interventions have been performed by neuroradiologists, neurosurgeons, or neurologists with a dedicated training background in neurointerventions. Unfortunately, the inadequate number of these specialists has become a major barrier to the widespread use of this modern treatment technique for acute stroke patients in most countries. Interventional cardiologists/vascular surgeons are primarily trained in endovascular interventions, with an increasing number of interventional programs, including training in carotid artery stenting, which is a basic skill for intracranial interventions.[17] However, it has been questioned whether interventional cardiologists/vascular surgeons can perform safe and effective stroke interventions. In collaboration with noninvasive stroke specialists, two reports[9,18] have demonstrated that interventional cardiologists/vascular surgeons with carotid-based skills can perform acute stroke interventions safely and with high technical and clinical success. To our best knowledge, this study is the first to report the results of acute stroke interventions performed by interventional cardiologists for embolic complications during cardiac catheterizations. The major advantage of interventional cardiologists in such a scenario is the timely diagnosis and treatment without the delay caused by consultation and interfacility transfer, thus shortening the time from symptom onset to brain reperfusion, and then optimizing the patients' clinical and neurological outcomes.

CONCLUSIONS

Combining intra-arterial pharmacotherapy, balloon angioplasty, and mechanical thrombectomy, interventional cardiologists with experience of carotid stenting can perform these catheter-based neurosalvage techniques to treat embolic complications during cardiac catheterization with favorable angiographic and clinical outcomes.

DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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