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Original Research Article

A Retrospective study of the unique Clinical and Imaging profile of Spontaneous Intra-cranial dissections in the Cerebral vasculature

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ABSTRACT

Aim: This study was designed to look at the unique clinical profile, neuro-imaging features and functional outcomes, of Intra-cranial dissections in the cerebral vasculature, seen at two tertiary stroke care centers in Southern India.

Materials and Methods: In this retrospective study spanning five years (Dec 13 to Dec 18), a total of 496 patients underwent CT Brain with Angiography for evaluation of an Acute stroke syndrome/ Transient ischemic attack (TIA), at our two study centers. 21/496 (4.2%) of these patients had imaging evidence of intra-cranial dissections which was further confirmed by Contrst MR angiograppy. The clinical and imaging data of these cases was recorded on a predesigned stroke proforma. The pattern of vessel involved and morphology of vessel dissection was analyzed as per standard radiology criteria. All cases had follow up data ranging from 1 to 3 years, which was used to classify the functional outcomes based on the modified Rankin Scale (mRS).

Results: There were 15 males and 6 females in the study, and the mean age was 44.1 years (range 23 to 73 years). Focal neurological deficits, with or without raised intra cranial pressure symptoms occurred in all these patients. 10/21 (48%) dissections were in the anterior circulation, whereas 11/21 (52%) were in the posterior circulation. Subarachnoid or parenchymal hemorrhage at presentation was seen in 11/21 (52%). The Internal Carotid artery (C2-C4 segments) was the commonest vessel involved in the anterior circulation in 64% cases (7/11), while in the posterior circulation, Vertebral artery (V4 segment) was most frequently involved in 60% (6/10) cases. In the entire study cohort, a good functional outcome (mRS 1-2) was seen in 13/21 (62%) cases, and death (mRS-5) was seen in 2/21 (9.5%). Digital Subtraction Angiography (DSA) and stenting/coiling procedures were undertaken in 3/21 (14%) cases.

Conclusion: This hospital based study brings out the unique clinical spectrum of intra-cranial dissections, with both ischemic and hemorrhagic forms of presentation. The dissections in the intra-cranial compartment of the cerebral vasculature commonly result in pseudo-aneurysm formation with Subarachnoid hemorrhage or parenchymal bleeds. CT angiography coupled with contrast MR angiography is sufficient in majority of cases to establish the diagnosis and plan management. An interval DSA may be needed in a small minority of cases for planning stenting/coiling procedures.

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1. Introduction

Cerebral arterial dissections are being increasingly recognized as a cause of wide spectrum of stroke syndromes, and may account for up to 10- 20% of

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strokes in adults.¹ Dissections of the cranial arteries can affect all age groups, but spontaneous vessel dissections have a distinct peak in the fifth decade of life.² Dissection of any artery usually arises from an intimal tear, which is commonly due to sudden rise in blood pressures, atherosclerotic plaque rupture or trauma.³ The tear allows blood under arterial pressure to enter the wall of the artery

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and form an intramural hematoma, in the so called "false lumen". 4 A sub-intimal dissection tends to result in stenosis of the arterial lumen and hemodynamic failure or distal embolism in the cerebral circulation. A sub-adventitial dissection usually causes aneurysmal dilatation of the artery, often referred to as "pseudoaneurysms", with subarachnoid hemorrhage (SAH) or intra-parenchymal hematomas. This phenomena of dissecting aneurysms, is much more common in the intra-cranial circulation, as the muscular layer of the tunica media is thinned out and permits the blood in the vessel wall to leak outwards. 5 We thus undertook a retrospective study of angiographically confirmed cases of spontaneous Intra- cranial cerebral dissections, and systematically captured the data, to bring out their rather distinct clinical spectrum and the pattern of vessel involvement, along with functional outcomes in these patients.

2. Materials and Methods

This retrospective study was carried out for the period covering Dec 13 to Dec 18 (5 years), at Departments of Neurology & Radiology, INHS Asvini, Mumbai & Command Hospital Air Force, Bangalore. These are tertiary referral centers of the Armed Forces, with state of the art dedicated stroke set up including, 16 Slice Multi Detector Computerized Tomography (MDCT), 1.5 Tesla Magnetic Resonance Imaging (MRI) and a Digital Subtraction Angiography (DSA) lab.

2.1. Inclusion criteria

All stroke cases seen at these two centers during the study period, with a confirmed neuro-imaging diagnosis of intra-cranial dissection, were included in the study. The diagnosis of cerebral dissection was based on standard neuro-radiologic criteria on Computerized Tomographic Angiography (CTA) which were characteristic of arterial dissection, such as, stenosis (string sign or tapered narrowing), stenosis with dilation (pearl and string sign), smoothly tapered occlusion (Flame sign) and complex pseudoaneurysm formation. This was further confirmed by a contrast Magnetic Resonance Angiography (CMRA), to establish the diagnosis of dissection, and also to look for additional features like, double lumen sign (presence of a false lumen or an intimal flap) or an intra-mural hematoma in the vessel wall (Crescent sign). A DSA was done only when both modality were inconclusive.

2.2. Exclusion criteria

Patients with history of head trauma or cranial surgery within 6 months before onset were excluded from the study.

The following clinical parameters and radiologic features were captured on a predesigned stroke proforma. The type of onset, vascular risk factors, neuro-imaging features, angiographic findings, management strategy & clinical outcomes by Modified Rankin Scale (mRS). Data was entered and analyzed in Microsoft Excel, using simple descriptive statistics.

A standard CTA was done after bolus injection of non-ionic contrast (1.5 ml / kg body weight) at the rate of 4 ml / second. Acquisition was timed by bolus tracking technique with trigger set in the ascending aorta. Caudo-cranial acquisition from the aortic arch to the cranial vault was obtained after minimum post threshold delay. Further, confirmation by contrast MR angiography (MRA) was performed with dynamic coronal sequences, including the aortic arch to cranial vault, after IV injection of Gadolinium chelate @ 0.2 mmol / kg body weight. Manual scan triggering was done once contrast was noted in the proximal aorta. Diagnostic or therapeutic Digital Subtraction Angiography (DSA) for Stenting or coiling was performed using a Siemens Polystar Top machine at Mumbai, and FD 10 Philips Allura machine at Bangalore.

3. Results

A total of 496 CT Angiograms were done at the two institutes during the study period of five years (Dec 13 to Dec 18). Of these, 382 (77%) cases had an ischemic stroke / Transient Ischemic Attack (TIA) as the clinical and radiologic presentation, and 114 (23%) had a hemorrhagic presentations (SAH or IC bleeds). 22/496 patients (4.4%) had extra-cranial dissections of the cervicovertebral arteries, a subset of which has been published by the authors previously (6), and do not form part of this study. 21/496 patients (4.2%) had features of Intracranial dissections on CTA, which was further confirmed on MRI Brain with contrast MRA in 19/21 cases. A DSA for confirmation of diagnosis was needed in only 2/21 of these cases, with posterior circulation dissections in the Posterior Cerebral artery (PCA) territory. Major differences exist between dissections involving the intracranial and extra cranial cervico-cephalic arteries. The plane of dissection in the cervical internal carotid artery (ICA) or vertebral artery (VA) is "sub-intimal", and usually confined within the media. 6 Intra-cranially, the media is significantly simplified, and dissections of intracranial arteries are usually "subadventitial", and may extend outward through the adventitia resulting in Subarachnoid or parenchymal hemorrhage. We further focused and selectively analyzed the subset of anterior and posterior circulation intra-cranial dissections separately.

3.1. Intra-cranial dissections

In the present study, 10/21 dissections were in the anterior circulation and, 11/21 in posterior circulation. There was significant difference in the clinical profile and imaging features of the dissections, in these two brain compartments.

We therefore analyzed them separately.

3.2. Anterior circulation

3.2.1. Intracranial Internal Carotid artery (ICA)

Dissections in ICA involved the petro-cavernous ICA (C2-C3) in four patients & supra-clinoid portion of the ICA (C4) in three patients. Dissection of the petro-cavernous ICA resulted in ischemic symptoms in all four cases. Two patients manifested with hemiparesis due to distal embolism and middle cerebral artery (MCA) infarcts. The third patient developed ipsilateral vision loss probably due to embolism to ophthalmic artery resulting in central retinal artery occlusion (CRAO) (Figure 1). The fourth case had recurrent MCA territory TIA.

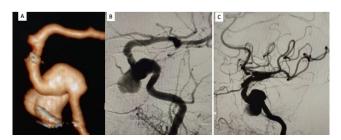


Fig. 1: CT angiogram volume rendered image (A) and left ICA angiogram (lateral projection) (B & C) showing fusi-saccular leftcavernous ICA aneurysm with dysplastic parent artery consistent with a dissecting aneurysm.

The three cases with dissection of supra-clinoid ICA had both ischemic and hemorrhagic presentations. Two had embolism to distal MCA resulting in critical M1 occlusion in one patient, and multiple distal MCA infarcts in the other. The third case developed diffuse SAH due to rupture of a dissecting pseudoaneurysm in the supra-clinoid ICA.

3.3. Middle Cerebral artery

All the three patients with dissections involving the MCA had features of sudden raised intracranial pressure in the form of headache, & vomiting before onset of focal neuro deficits. Two patients had MCA (M1) segment dissections resulting in ipsilateral sylvian fisssrue SAH along with distal MCA infarct. Vascular imaging revealed a dissecting pseudoaneurysm of the M1 region with rupture, followed by partial thrombosis of the pseudoaneurysm. In the third patient, M2 segment dissection resulted in a temporal bleed with sylvian fissure SAH. CT Angiogram revealed a stenosis with dilation of the proximal M2 and cut off beyond distal M2 (Figure 2). There were no cases with Anterior cerebral artery (ACA) dissections in this study. Treatment consisted of mainly antiplatelets and statins, for 6 cases with ischemic lesions, who had ICA dissections. The remaining 4 patients had hemorrhagic presentations with SAH or ICH and were managed with anti-edema measures

and supportive care. Only one patient with a dissecting aneurysm in the supra-clinoid ICA, needed a DSA and stent assisted coiling after 8 weeks, due to persistent symptoms despite medical therapy. He had a good radiologic and clinical outcome. Vascular risk factors were noted in a small proportion of cases (3/10) in this subgroup. Both Diabetes Mellitus and Hypertension were noted in one case and Hypertension with coronary artery disease in another two cases. There was no history of smoking or oral contraceptive use in this group.

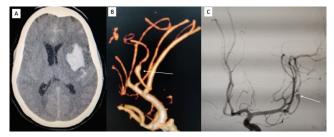


Fig. 2: (A) Non contrast CT Head showing intra parenchymal and subarachnoid hemorrhage and (B) CT angiogram volume rendered image and left ICA angiogram (frontal projection) (C) DSA showing fusisaccular left M2 segment aneurysm (arrows) in the inferior division of the left MCA.

The follow-up period in all these patients ranged from 1-3 yrs. Recovery was complete in one patient. Three patients had mild neurologic deficits (mRS-2), and four others had persistent moderate hemiparesis and dysphasia that interfered with their daily work. Two deaths occurred in this cohort. One patient with critical MCA stenosis, who remained symptomatic despite optimum medical therapy, died of a fatal hypertensive bleed in the ganglio-capsular region. The second case was a dissection in the petrocavernous ICA, who developed a fatal SAH.

The summary of the clinical and radiological profile of dissections in the anterior circulation, is depicted in Table 1

3.4. Posterior circulation

In the study there were 11 cases with dissections in the posterior circulation. Of these 11 cases, 6 involved the intracranial (V4) segment of vertebral arteries, 3 involved the basilar artery and 2 patients had dissections of the proximal (P1-P2) segment of the PCA. The clinical and radiologic features of these 11 cases are summarized in Table 2.

3.5. Vertebral Artery

The dissections in the posterior circulation had a higher proportion of hemorrhagic presentations 64% (7/11) as compared to the anterior circulation 40% (4/10). The intracranial (V4) segment of the vertebral artery was the commonest to be involved in six cases (Figures 3 and 4). These V4 dissections caused distal embolism to the basilar

Presentation CT/MRI **Angiographic Findings** mRS Case Age Site of lesion 1 47/M Lt hemi MCA infarct RICA (C4) S + D. MCA stenosis 5 Vision loss (L) 2 40/M Fl + LICA occlusion 2 Normal LICA (C3) 3 3 39/M H, Lt hemi MCA infarct RICA (C4) S + D, LICA occlusion 4 Rt Hemi MCA infarct 3 49/M LICA (C3) Fl, LICA occlusion 5 46/M Recurrent TIA MCA infarct RICA (C2) Fl + RICA occlusion 1 3 6 38/F Rt Hemi MCA infarct S + D, LICA occlusion LICA (C2) 7 5 Diffuse SAH 53/M H, V, Seizure LICA (C4) D + P, Aneurysm 3 8 31/M H, V, Lt Hemi Sylvian SAH RMCA (M1) P, Thrombosed 9 2 23/M H, V, Lt Hemi Sylvian SAH RMCA (M1) P, Thrombosed 10 27/M H, V, LOC Temporal ICH LMCA (M2) S +D, M2 occlusion 2

Table 1: Clinical & &radiologic findings in 10 cases of intra-cranial dissection (anterior circulation)

Note - M-male, F-female, Lt Hemi- left hemparesis, Rt Hemi- right hemiparesis, H-headache, V-vomiting, NP-nuchal pain, LOC-loss of consciousness, SAH- subarachnoid hemorrhage, ICH-intra-cerebral hemorrhage, Fl - flame shaped tapering, S - stenosis without dilation, S+D- stenosis with dilation, D-dilated, DL- double lumen sign, P - pseudoaneurysm

Table 2: Clinical & Radiologic findings in 11 cases of intra-cranial dissection (posterior circulation)

Case No	Age/Sex	Presentation	CT/MRI	Site of lesion	Angiographic findings	mRS
1	38/M	H, V, NP	Perimes SAH	PCA (P1)	S + D, P1 stenosis	1
2	67/F	H, V,Diplopia	SAH, Infarct	LVA (V4)	D + P, Aneurysm	2
3	54/M	Episodic LOC	LVA occlusion	LVA (V4)	P, Thrombosed	1
4	29/M	Rt Hemi	Pontine infarct	LVA (V4)	D + P, Aneurysm	3
5	31/F	H,V,giddiness	Perimes SAH	Mid basilar	D + P, Fusiform	1
6	27/M	Quadri, Sz	Pons infarct+ SAH	Mid basilar	D + P, Aneurysm	2
7	64/F	H, V,	Diffuse SAH	LVA (V4)	D + P, Aneurysm	4
8	22/F	H, V, NP	SAH, PCA infarct	PCA (P2)	P, Thrombosed	3
9	35/F	H, V, ataxia	PCA+ Pons infarct	LVA (V4)	S +D, P1 cut off	3
10	73/M	LOC, Ataxia	Mid brain infarct	RVA (V4)	P + Basilar stenosis	3
11	43/M	H, V, NP	Perimes SAH	Mid Basilar	D + P, Fusiform	2

Note – M-male, F-female, Rt Hemi- right hemiparesis, H-headache, V-vomiting, NP-nuchal pain, LOC-loss of consciousness, SAH- subarachnoid hemorrhage, ICH-intra-cerebral hemorrhage, Perimes SAH – perimesencephalic SAH, S - stenosis without dilation, S+ D- stenosis with dilation, D-dilated, P – pseudoaneurysm

in three cases and PCA (P1) in one case, resulting in infarcts in the brain stem and occipital region. In the remaining two cases, one had recurrent TIA due to a thrombosed V4 aneurysm and the other had features of diffuse SAH due to a ruptured aneurysm. Initial CT angiography showed a paeudo-aneurysm formation in the V4 segment with irregular lumen or stenosis in all these patients, which was confirmed on MRA.

3.6. Basilar & Posterior cerebral arteries

The Basilar artery was involved in three cases with perimesencephalic and pre-pontine SAH in two cases and brainstem infarct in one. CT Angiograms showed fusiform pseudoaneurysm formation of the Basilar artery, in all these cases. The least common vessel to be involved in the posterior circulation was the PCA in two cases. Both these cases presented with raised intracranial pressure due to SAH in the basal cisterns. Both patients had PCA infarct due

to a thrombosed P2 aneurysm. CT Angiogram revealed dissecting pseudoaneurysms of the P1-P2 region causing varying degree of stenosis and spasm of the distal PCA. Treatment in all these cases was conservative in the acute phase with anti-edema measures and supportive care.

Due to high incidence of re-bleeds in ruptured dissections and pseudo-aneurysm formation, all cases with vertebral dissection and SAH or persisting symptoms, were offered endo-vascular stent assisted remodeling of the diseased vessels at follow up. However, only two patients consented for the high risk procedure and, came back for interval intervention after 12 weeks. Self expanding balloon mounted stents were deployed in the two vertebral arteries. Both cases tolerated the procedure well and had a favorable outcome with good angiographic remodeling of the diseased vessels, and no fresh ischemic events or bleeds at follow up (6-12 months).

In the remaining 9 cases follow up ranged from 1-4 years, and 7 patients had good recovery with mRS 1-2, and other

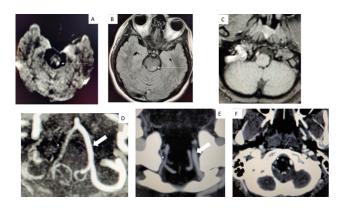


Fig. 3: MRI Brain and CT Angiogram showing (A & B): Axial diffusion and FLAIR – acute left mesencephalic infarct (arrows) (C): High resolution axial T1 showing intramural hematoma (T1 hyperintensity) within the V4 segment of the right vertebral artery (arrow) (D & E): MR and CT angiogram (coronal) showing irregular beaded appearance of the V4 segment of the right vertebral artery (thin arrows). Normal appearance of the left vertebral artery is shown with thick arrow.(F): Axial CT angiogram image showing eccentric thrombus within the V4 segment of the rightvertebral artery (arrow)

2 had significant residual deficits causing impairment of activities of daily living (ADL). None of the patients had evidence of occlusive disease in any other cervico-cephalic artery. Repeat CT angiography were available in only two cases and showed moderate improvement in the stenosis in one PCA, and patent stent in the vertebral (V4) in the other.

Vascular risk factors were noted in a high proportion of cases (7/11) in this subgroup. Both Diabetes Mellitus and Hypertension were noted in four cases and Hypertension alone in another two cases. One patient with P2 dissection was a smoker with ischemic heart disease. All other patients were normotensive, and had no history of use of oral contraceptive or tobacco abuse.

4. Discussion

Spontaneous dissections of the carotid or vertebral artery account for only about 2 percent of all ischemic strokes ⁷ but they are an important cause of stroke in young and middle-aged patients, and account for 10 to 20 percent of such cases. ⁸ Intracranial arterial dissections in adults occur more commonly in the posterior circulation, and in children they occur more commonly in the anterior circulation. ⁹ Across all age groups, the most common sites of Intra-cranial dissections in the anterior circulation are the supra-clinoid portions of the ICA and MCA, and the least common is the anterior cerebral artery territory. ^{10,11} A similar pattern was observed in this study with 7/10 (70%) anterior circulation dissections involving the ICA followed by 3/10 (30%) in the MCA. A majority of dissections in the anterior circulation 60% (6/10), presented with focal cerebral or retinal ischemic



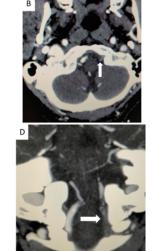


Fig. 4: CT Angiogram showing (A): acute left para-median pontine infarct (thin arrow) (B, C and D): Axial, sagittal and coronal CT angiogram images showing irregular beaded appearance of the V4 segment of the left vertebral artery with patchy luminal opacification (thick arrows)

symptoms. However, a reverse trend was observed in the posterior circulation with 7/11 (64%) having a hemorrhagic presentation (SAH/ICH). This is explained by the media being attenuated in the intracranial arteries, more so in the posterior circulation, allowing extension of dissection outwards into the sub-adventitia, and its leaking or rupture into the subarachnoid space of cerebral parenchyma.

Non-invasive vascular imaging (CT / MR angiography) is mandatory in the evaluation of all forms of craniocerberal ischemia and one or a combination of both modalities suffices in clinching the diagnosis. 12 The characteristic angiographic finding is a long segment tapering or occlusion of the cervical ICA with typical sparing of the carotid bulb (distinguishing feature from an atherosclerotic occlusion). ^{13,14} The classic intimal flap is diagnostic, but variably seen. Evaluation of the major collaterals across the Circle of Willis helps to prognosticate the extent of likely hemodynamic cerebral compromise, and also serves to plan an endovascular intervention if needed. Intra-mural hematoma is less often seen in a vertebral artery dissection and the diagnosis must be suspected with observation of an increased vessel diameter and crescentic mural thickening. 15 High resolution vessel wall MR imaging can elegantly demonstrate the intra-mural hematoma and distinguish it from a lipid rich plaque, in cases where a diagnostic dilemma still exists after CT / MR angiography. 16

The management of arterial dissections remains a controversial issue. Our patients did not receive a standardized treatment, and the method of management reflected the judgment of the attending physicians and the amount of information available on neuro-imaging. Most, but not all, focal cerebral ischemic symptoms associated with cervical arterial dissections are presumed to be thrombo-embolic in origin. ¹⁷ Therefore, a course of antiplatelet therapy is usually recommended in patients with ischemic symptoms in the acute phase, in the absence of intracranial hemorrhage. In intracranial arterial dissections, a hemodynamic mechanism due to luminal narrowing may be as important as embolic phenomena and optimum control of blood pressures has an important role. ¹⁸ Furthermore, some patients with intracranial arterial dissections develop a subarachnoid hemorrhage, therefore, anticoagulation and antiplatelet therapy for this group of patients may not be a viable option.

Surgical intervention and repair or endovascular remodeling of the aneurysm are almost always done as an interval procedure after 10-12 weeks. They are generally reserved for patients with a subarachnoid hemorrhage due to an intracranial dissecting aneurysm with a high risk of re-bleed or recurring symptoms despite best medical care. In this study, endovascular intervention in the anterior circulation was done for coiling in one supra-clinoid ICA aneurysm. In the posterior circulation, stent assisted vessel remodelling in two vertebral arteries was carried out. The intervention achieved adequate aneurysm closure and vessel remodeling, with good clinical outcomes at follow up in all three cases. In recent studies the prognosis of intracranial arterial dissections has significantly improved, as compared to what was previously thought. This is probably due to a higher index of suspicion and improved diagnostic methods allowing early diagnosis and treatment. In adults with spontaneous intracranial dissections, the rate of recurrent dissection during the first month is 2-3%, but from that time on, it is approximately 1% per year and inversely related to

The reported rate of death from dissections of the carotid and vertebral arteries is less than 5 percent, and about three fourths of patients who have had a stroke make a good functional recovery. ¹⁷ Headache associated with dissection resolves within a week in about 90 percent of patients, but in a few patients it can persist for many years. ¹⁸ The follow-up in this study group ranged from 1-3 years. A mortality of 2/21 (9.5%) was noted in this study, mainly associated with dissections in the anterior circulation. Of the 21 patients with completed stroke, 13/21 (62%) had a good functional recovery, with a mRS 1-2 at follow up. These findings are consistent with the findings from previous studies on this subject. ^{17,18}

The pathogenesis of arterial dissections is not clear in most cases. Mechanical factors and an underlying arteriopathy have been blamed. History of a trivial and often doubtful trauma is frequent, understandably more so in children than in adults. ¹⁹ A predisposing disorder of the arterial wall, although suspected, cannot be documented in

most patients. Factors such as hypertension, use of tobacco, and oral contraceptives and migraine are often mentioned as risk factors for adults with cervical arterial dissection, which were observed in 70% of our patients (14/21). There are reported associations of spontaneous cervico-cephalic arterial dissections with Fibromuscular Dysplasia (FMD), Cystic Medial necrosis, Marfans Syndrome and Ehlers Danlos. ^{20,21} In the present study, no such collagenosis or dysplasias could be identified.

5. Conclusion

Intra-cranial dissections accounted for 4% of all strokes seen in this retrospective study spanning five years. Dissections of the Intra-cranial arteries have a distinctive clinical profile, with a high incidence of SAH/ICH (60%). CT angiography in conjunction with MR angiography, was able to establish the diagnosis of arterial dissection in majority of the cases (90%). A DSA and intervention was needed only in a minority of cases (14%). Conservative management in the acute phase, and highly selective use of endovascular devices (stents or coils), in a planned interval manner, seems to be a reasonable approach in Intra-cranial dissections. Contrary to conventional wisdom, with the help of modern neuro-imaging and intensive care, almost 60% patients in this study had a good functional outcome at follow up.

6. Source of Funding

None.

7. Conflict of Interest

None.

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