SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY

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CT angiogram as a predictor of outcome in Symptomatic Internal Carotid Artery Occlusion

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DECLARATION

I, **Dr. Soumya Sundaram**, hereby declare that the projects in this book were undertaken by me under the supervision of the faculty, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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INTRODUCTION

Stroke continues to impose an overwhelming burden on global health, imparting devastating disability and is the second most common cause of death, with most of the 16 million cases occurring in developing countries.[1] Ischemia, or restricted blood flow, is the main cause of stroke, typically due to occlusion of a cerebral artery as a result of progressive atherosclerosis or an embolus from the heart or neck vessels.[2] Irrespective of cause or mechanism of ischemia, perfusion via alternative indirect pathways like collaterals might offset potential injury to the brain.[3]

Digital subtraction angiography is the gold standard investigation to identify collateral vessels in patients with acute stroke, but because of its invasive nature it has not gained widespread popularity. Newer imaging techniques, especially multimodal cranial Computed Tomography scans, can assist with identification of collaterals including leptomeningeal circulation.[4]

In patients with ischemic event, depending on the extent of collateral perfusion, infarction might not be complete for hours or even days. In some cases of MCA occlusion, infarction is complete in less than an hour, but other patients might show evidence of viable tissue for days, if not indefinitely.[5] In patients whose tissue survives for a long period despite proximal arterial occlusion, retrograde filling of pial arteries (a surrogate indicator of leptomeningeal collateral vessels) is often evident in imaging studies and might have an important protective role.[4]

In the acute phase of stroke, the main predictors of outcome are stroke severity and age of patient. Additional important predictors include functional status

prior to stroke onset and the presence of co-morbid medical conditions. Although various studies have been published regarding predictors of outcome in ischemic stroke, there is not much information in literature regarding whether status of cerebral circulation and the collateral network favours a good outcome in ICA occlusion patients. Arterial insufficiency due to thromboembolism, hemodynamic compromise, or a combination of these factors may lead to the recruitment of collaterals.[6]

Additionally, patients with good collaterals might respond better to reperfusion therapy and have a lower risk of haemorrhagic complications from such treatments than do other patients.[7]

Pathophysiological recruitment of these potential anastomotic connections is frequently observed in various ischemic conditions, yet knowledge of the collateral circulation remains limited. Hence this study is undertaken to assess whether the presence of good collateral circulation predicts the outcome in patients with symptomatic internal carotid artery occlusion.

REVIEW OF LITERATURE

Acute ischemic stroke is characterized by abrupt neurologic dysfunction due to focal brain ischemia resulting in persistent neurologic deficit or accompanied by characteristic abnormalities on brain imaging. If the symptoms persisted for less than 24 hours, the condition was termed transient ischemic attack (TIA).[8]

Etiology of stroke

Etiology of stroke can be classified into ischemic and hemorrhagic. Ischemic stroke results from a heterogeneous group of disorders whose final common pathway is interruption of blood flow through vascular occlusion leading to clinical manifestations.

Stroke mechanisms

Two major mechanisms are responsible for ischemia in acute stroke:-

i) Thrombo-embolism

ii) Hemodynamic failure.

Less common vascular pathologies leading to vessel stenosis or occlusion include arterial dissection (intracranial or extracranial), fibromuscular dysplasia, vasospasm, radiation induced vasculopathy, extrinsic compression such as tumor or other mass lesion, or Moyamoya disease.

Hemodynamic failure usually occurs with arterial occlusion or stenosis, when collateral blood supply maintains cerebral blood flow (CBF) at levels that are sufficient for preservation of brain function under normal circumstances. In these

situations, cerebral ischemia may be triggered by conditions that decrease perfusion proximally to the arterial lesion (systemic hypotension or low cardiac output) and increased metabolic demands (fever, acidosis) or conditions that lead to ‘‘steal’’ of blood from affected to unaffected areas in the brain (carbon dioxide retention). Strokes occurring through these mechanisms occur predominantly in the border zones or watershed regions such as Middle cerebral artery-Anterior cerebral artery or Middle cerebral artery-Posterior cerebral artery interface.[9]

Cerebral blood flow (CBF)

In persistent large vessel occlusion, local perfusion pressure is the main factor influencing the eventual outcome of tissue which depends on several factors such as the presence and extent of collaterals and systemic arterial pressure. The normal CBF is 40-60mL/100g/min and the critical threshold is 12mL/100g/min below which infarct core develops. The penumbra has a CBF between 12-20mL/100g/min and the surrounding area of oligemia, represents mildly hypoperfused tissue with CBF between 20-40 mL/100 mg/min. If vessel occlusion persists, the penumbra may shrink because of progressive recruitment into the core and with vessel recanalization it may return to a normal state. [10]

Arterial supply of brain

The arterial supply of the brain is derived from two pairs of internal carotid and vertebral arteries, which forms the Circle of Willis. About 80% of the brain’s blood supply comes from the carotid, and the remaining 20% from the vertebral artery.

Internal Carotid Artery (ICA)

The internal carotid arteries and their major branches supply blood to the forebrain, with the exception of the occipital lobe. ICA arises from the bifurcation of the common carotid artery, ascends in the neck and enters the carotid canal of the temporal bone. ICA is divided into seven segments.

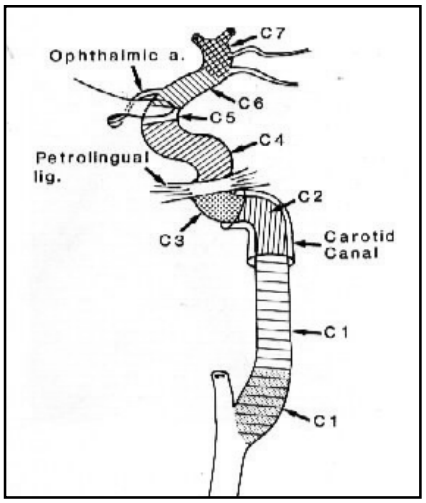


Figure showing segments of ICA: 1- cervical; 2-Petrous; 3-Lacerum; 4-Cavernous; 5-Clinoid; 6-Ophthalmic; 7-Communicating

Anterior cerebral artery (ACA)

The ACA is the smaller of the two terminal branches of the ICA. The surgical nomenclature divides the vessel into three parts:

- A_1 - from the termination of the ICA to the junction with the Anterior Communicating artery (ACoA)
- A_2 - from the junction with the ACoA to the origin of the callosomarginal artery

- A_3 - distal to the origin of the callosomarginal artery. This segment is also known as the pericallosal artery

The two ACAs travel together in the great longitudinal fissure. They pass around the curve of the genu of the corpus callosum and then along its upper surface to its posterior end, where they anastomose with posterior cerebral arteries. They give off cortical and central branches.

Middle Cerebral Artery (MCA)

The MCA is the larger terminal branch of the ICA. The surgical nomenclature identifies four subdivisions: -

- M_1 - from the termination of the ICA to the bi/trifurcation
- M_2 - the segment running in the lateral (Sylvian) fissure
- M_3 –the segment coming out of the lateral fissure
- M_4 - cortical portions.

Cortical branches of the MCA therefore supply the motor and somatosensory cortices representing the whole of the body other than the lower limb, the auditory area and the insula.

Vertebral artery

The vertebral arteries and their major branches (referred to as the 'vertebrobasilar system') essentially supply blood to the upper spinal cord, the brain stem, cerebellum and occipital lobe of the cerebrum. The vertebral arteries are derived from the subclavian arteries. They ascend through the neck in the foramina

transversaria of the upper six cervical vertebrae and enter the cranial cavity through the foramen magnum. They converge medially as they ascend the medulla and unite to form the midline basilar artery at approximately the level of the junction between medulla and pons.

Basilar artery

Basilar artery is formed by the union of the vertebral arteries at the mid medullary level and extends to the upper border of the pons. The basilar artery terminates by dividing into two posterior cerebral arteries at a variable level but most frequently in the interpeduncular cistern, behind the dorsum sellae. The anterior inferior cerebellar artery is given off from the lower part of the basilar artery and the superior cerebellar artery arises near the distal portion of the basilar artery, immediately before the formation of the posterior cerebral arteries.

Posterior cerebral artery (PCA)

The PCA is a terminal branch of the basilar artery. The surgical nomenclature identifies three segments:

- P_1 - from the basilar bifurcation to the junction with the posterior communicating artery (PCoA)
- P_2 - from the junction with the PCoA to the portion in the perimesencephalic cistern
- P_3 - the portion running in the calcarine fissure

Circulus arteriosus (Circle of Willis)

The Circle of Willis (COW) is a large arterial anastomosis which unites the internal carotid and vertebrobasilar systems. It lies in the subarachnoid space within the deep interpeduncular cistern, and surrounds the optic chiasma, the infundibulum and other structures of the interpeduncular fossa. Anteriorly, the anterior cerebral arteries are joined by the small anterior communicating artery. Posteriorly, the two posterior cerebral arteries are joined to the ipsilateral internal carotid artery by a posterior communicating artery. In the majority of instances, the posterior communicating arteries are very small and a limited flow is possible between the anterior and posterior circulations. This is important because the primary purpose of the vascular circle is to provide anastomotic channels if one vessel is occluded.

There is considerable individual variation in the pattern and calibre of vessels which make up the COW. Although a complete circular channel almost always exists, one vessel is usually sufficiently narrowed to reduce its role as a collateral route. Cerebral and communicating arteries individually may all be absent, variably hypoplastic, double or even triple. The circle is rarely functionally complete.

The haemodynamics of the circle is influenced by variations in the calibre of communicating arteries and in the segments of the anterior and posterior cerebral arteries which lie between their origins and their junctions with the corresponding communicating arteries. Commonly, the diameter of the precommunicating part of the posterior cerebral artery is larger than that of the posterior communicating artery; in which case the blood supply to the occipital lobes is mainly from the vertebrobasilar system. Sometimes, the diameter of the precommunicating part of the PCA is smaller

than that of the posterior communicating artery, in which case the blood supply to the occipital lobes is mainly from the internal carotids via the posterior communicating arteries.[11]

Anatomic studies note absence of the ACoA in 1% of subjects, absence or hypoplasia of the proximal ACA in 10%, and absence or hypoplasia of either PCoA in 30%.[12]

Collateral circulation

The cerebral collateral circulation refers to the subsidiary network of vascular channels that stabilize cerebral blood flow when principal conduits fail. Arterial insufficiency due to thromboembolism, hemodynamic compromise, or a combination of these factors may lead to the recruitment of collaterals.

Classification of collaterals

Collateral circulation is divided into primary or secondary collateral pathways. [13]

(i) Primary collaterals include the arterial segments of the circle of Willis

(ii) Secondary collaterals include ophthalmic artery and leptomeningeal vessels.

Collateral circulation can also be classified into the following three:-

(i) Extracranial–intracranial anastomoses

(ii) Collateral circulation through Circle of Willis

(iii) Leptomeningeal collaterals.

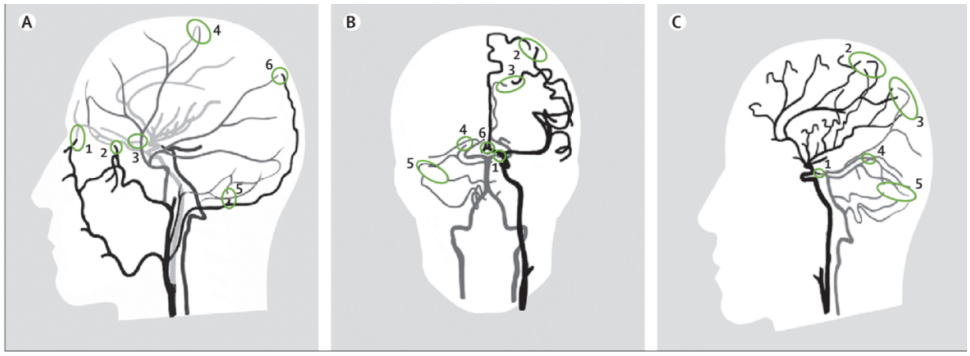
Extracranial- Intracranial anastomoses: - The external carotid artery gives rise to many branches in the neck that is a potential source of collateral flow, especially in the event of chronic stenosis or occlusion of the ICA. Important collateral circuits include flow through the ophthalmic (retrograde) and superficial temporal arteries to the intracranial vessels, normally supplied by the ICA.[14] In the posterior circulation, many anastomoses exist between the vertebral arteries and muscular branches at the cervical level. The anterior and posterior spinal arteries also communicate with branches of the proximal intracranial arteries supplying the medulla and pons.

Collateral circulation through COW: - The blood supply to the brain is unique because four major arteries coalesce to form an equalising distributor, the circle of Willis, which can redistribute blood flow in the event of a sudden occlusion of a parent vessel. Interhemispheric blood flow across the anterior communicating artery and reversal of flow in the proximal anterior cerebral artery provide collateral support in the anterior portion of the circle of Willis. The posterior communicating arteries may supply collateral blood flow in either direction between the anterior and posterior circulations. Anastomoses between distal segments of the major cerebral arteries also contribute ancillary collateral blood flow. The number and size of these anastomotic vessels are greatest between ACA and MCA with smaller and fewer connections between MCA and PCA and even less prominent terminal anastomoses between PCA and ACA.

Leptomeningeal collateral circulation: - Leptomeningeal and dural arteriolar anastomoses with cortical vessels further enhance the collateral circulation. Leptomeningeal anastomoses potentially provide arterial blood to the cortical surface.

In these vessels, blood can flow in both directions as a function of the haemodynamic and metabolic needs of the two territories that they connect. The leptomeningeal anastomoses linking distal sections of the major cerebral arteries are small arteriolar connections (~50–400μm) that allow retrograde perfusion of adjacent territories. They are important routes for collateral flow, especially in times of acute vascular occlusion. These arteriolar anastomoses join the MCA with both the ACA and PCA. Anastomoses from the anterior cerebral artery potentially supply the superior or anterior divisions of the MCA, with most collateral flow of inferior division of the MCA arising from the PCA.[15]

Other collateral routes are less commonly encountered in acute stroke, such as the tectal plexus joining supratentorial branches of the PCA with infratentorial branches of the superior cerebellar artery; the orbital plexus linking the ophthalmic artery with facial, middle meningeal, maxillary, and ethmoidal arteries; and the rete mirabile caroticum connecting internal and external carotid arteries.



(A) Extra cranial arterial collateral circulation. Shown are anastomoses from the (1) facial, (2) maxillary, and (3) middle meningeal arteries to the ophthalmic artery; dural arteriolar anastomoses from the (4) middle meningeal artery and occipital artery through the (5) mastoid foramen and (6) pariet al foramen. Intracranial arterial collateral circulation in frontal (B) and lateral (C) views. (1) PCoA (2) leptomeningeal anastomoses between ACA and MCA and (3) between PCA and MCA (4) the tectal plexus between PCA and superior cerebellar arteries (5) anastomoses of distal cerebellar arteries and (6) the anterior communicating artery. [6]

Primary collaterals provide immediate diversion of cerebral blood flow to ischemic regions through existing anastomoses. Secondary collaterals such as leptomeningeal anastomoses may be anatomically present, although enhanced capacity of these alternative routes for cerebral blood flow likely requires time to develop.

Factors determining the development of collateral circulation

The efficacy of collateral vessels likely depends on age, duration of ischemia, and associated co-morbidities. The influence of co-morbidities and other clinical variables on the development of intracranial collaterals in humans is unknown, as no prospective studies have been conducted.

Chronic hypoperfusion due to arterial flow restrictions such as extracranial carotid stenosis or intracranial stenotic disease promotes collateral development. Secondary collateral pathways that require time to develop are presumed to be recruited once primary collaterals at the circle of Willis have failed. The presence of secondary collateral pathways is considered a marker of impaired cerebral hemodynamics. Increasing severity of carotid stenosis has been correlated with a greater extent of collateralization.

The effectiveness of collateral flow varies greatly between patients. Several systemic factors might adversely affect recruitment of collateral vessels, resulting in extensive infarction.

Conditions that might adversely affect collateral status are the following [13]

- Congenital lack of collateral anatomy (i.e., incomplete circle of Willis)
- Dehydration, increased blood viscosity
- Hyperthermia, hyperglycaemia, electrolyte and renal dysfunction
- Systemic infections
- Pulmonary compromise, cardiac failure
- Drugs that inhibit physiological augmentation of blood pressure (i.e., high-dose antihypertensives)
- Widespread cerebral atherosclerosis

The functional compensatory capacity of collaterals might also diminish with age. Atherosclerosis, especially intracranial disease, also results in vessel stiffening and could inhibit blood flow.[15]

Hypertension decelerates the development of collaterals in rats, and the anastomoses are significantly narrower, with diminished collateral capacity. In stroke-prone spontaneously hypertensive rats, the anastomosis are significantly narrower and blood flow through the anastomosis is less than in normotensive rats. Tissue infarction invariably develops in the territory of the occluded MCA in hypertensive rats. So the luminal width of the anastomosis is a major determinant of blood flow into the territory of the occluded artery and of the amount of tissue protected from infarction by collateral circulation.[16]

In thrombotic and embolic stroke, intravascular pressure distal to the occlusion falls immediately. Concurrently, pressure within the pial vessels is relatively well preserved, resulting in a gradient that can promote flow through anastomoses. Animal studies suggest that systemic blood pressure can affect the magnitude of this gradient and the ability to stimulate collateral recruitment. Induced hypotension in these animals results in neurological deficits, which can be reversed if systolic blood pressure is high.[17]

The use of statins could enhance new vessel development mediated by an increase in endothelial progenitor cell growth.[18]

Incomplete circle of Willis

Roughly 50% of individuals have a normal or complete configuration of the circle of Willis. The presence of any of the anatomical variants like atretic vessels or fet al PCA, particularly atretic communicating vessels, can seriously compromise ability to compensate for sudden occlusions of parent vessel.[19]

Degree of occlusion and collateral formation

Severe intracranial arterial stenosis was also shown to be an important determinant of pial collateral circulation in the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) trial. Patients with mild to moderate intracranial stenosis did not have the same degree of pial collaterals as compared to patients with severe stenosis.[19]

Etiology of occlusion of parent vessel and collateral formation

Another factor that could have an important effect on the robustness of collaterals is the pace of occlusion. Gradual chronic occlusion as in progressive atherosclerotic ICA stenosis at the bulb, or neovascularisation that occurs in Moyamoya syndrome allows compensatory collateral flow changes more often than does abrupt arterial occlusion.[20]

Assessment of collateral circulation

Although no ideal or specific imaging modality is available for demonstration and accurate measurement of the collateral circulation, several techniques can provide insight into collateral flow in patients with ischemic stroke. However, these methods measure the general status of collaterals and not actual anatomical connections. Furthermore, no techniques used to study cerebral collaterals have been systematically studied or validated.[13] Diagnostic assessment of collateral circulations is best done by direct visualization which is limited to angiographic methods including transcranial doppler (TCD), CT angiography (CTA), MR angiography (MRA) and digital substraction angiography (DSA).

(i) DSA: - Incomplete information regarding collaterals is obtained unless multivessel injections are performed otherwise conventional angiography is considered the gold standard. But because of its invasive nature it has not gained widespread popularity.

(ii) MRA: - Collateral assessment with MRA is generally limited to proximal arterial segments at the circle of Willis.

(iii) CTA: - CTA source images may contain valuable information regarding collaterals.[6]

(iv) TCD: - TCD provides little information about collateral flow and only at the circle of Willis. TCD helps to assess the retrograde flow through ophthalmic, anterior, and posterior communicating arteries.

Grading of collateral circulation

No validated scoring system for cerebral collateral circulation is available. Following are the 2 grading system on CTA based on 2 studies.

Grading system by Miteff et al[4]

Grade 1 (good): entire MCA distal to occlusion reconstituted with contrast

Grade 2 (moderate): some branches of MCA reconstituted in Sylvian fissure

Grade 3 (poor): distal superficial branches reconstituted

Maas et al 2009 grading of leptomeningeal collateral circulation[21]

Grade 1: absent

Grade 2: less than contralateral side

Grade 3: equal to contralateral side

Grade 4: greater than contralateral side

Grade 5: exuberant

Factors determining outcome of stroke patients

The retrospective study from Canadian stroke registry which included 12,262 community-based patients presenting with an acute ischemic stroke showed that older age, male sex, severe stroke, non lacunar stroke subtype, glucose ≥7.5mmol/L (135mg/dL), history of atrial fibrillation, coronary artery disease, congestive heart failure, cancer, dementia, kidney disease on dialysis, and dependency before the stroke were predictors of 30-day and 1-year mortality.[22]

Role of collateral circulation in stroke outcome

Studies of permanent MCA occlusion in mice have shown that infarction size is significantly smaller in inbred mice with extensive collateral vessels than in those with fewer collaterals. Number, length, and diameter of collateral vessels were inversely related to the volume of cerebral infarction.[23]

Miteff et al studied whether collateral vessel status, as seen on CTA, can predict the fate of penumbral tissue identified on perfusion CT and thereby influence clinical outcome. Of 92 patients with proximal intracranial vessel occlusion, good collateral status (51/92) was significantly associated with reduced infarct expansion and more favourable functional outcomes (mRS 0–2). Notably, none of the 37 patients with a perfusion computed tomography mismatch ratio had a favourable outcome. In patients with perfusion CT mismatch, significant independent predictors of favourable outcome were good collateral status, major reperfusion and baseline NIHSS. In patients with proximal vessel occlusion, perfusion CT mismatch is a prerequisite for a favourable clinical response, but good collateral status appears a critical determinant

of ultimate outcome, particularly if major reperfusion occurs. The response to thrombolytic therapy was strongly related to the presence or absence of collateral vessels.[4]

Poor collaterals were evident in 38% of patients within 1 h of symptom onset and this value decreased to 12% of patients imaged 12–24 h after onset. There were no fluctuations in prehospital symptoms in patients with poor collaterals. However, in hospital worsening of symptoms was four times more likely in patients with poor collaterals than in those with normal or exuberant collaterals.[21]

Lima et al studied 196 patients with complete occlusion of the intracranial ICA and/or the MCA (M1 or M2 segments). In the multivariate analysis, robust leptomeningeal collaterals remained an independent predictor of good long-term outcomes along with younger age, lower pre stroke mRS and baseline NIHSS scores, administration of intravenous recombinant tissue plasminogen activator, and absence of diabetes.[24]

In a study of 111 patients (84 men) with occlusions of the intracranial vessels of the distal carotid, and M1 and M2 segments of the MCA, cerebral angiography was used to assess collateral status. Most patients were treated with intra-arterial thrombolysis, and the Barthel index was used at 90 days to establish outcome. In patients with distal carotid occlusions, the presence of good collaterals was associated with a significantly improved outcome compared with no collateral supply (40% versus 8%, $p<0{\cdot}01$). Similarly, in M1 and M2 MCA occlusions, the presence of collaterals was linked to better outcomes.[25]

Lee et al 2009 assessed collateral flow using MRA in 52 patients within 3 h of the onset of stroke with proximal intracerebral arterial occlusion (including M1: 22 patients; M2: 16 patients; and M3: 11 patients). Distal hyperintense vessels have a serpentine appearance, and might be an indicator of slow retrograde collateral flow. Prominent distal hyperintense vessels were evident in 46% of patients, and subtle distal hyperintense vessels in a further 27% of patients. Patients with distal hyperintense vessels had smaller initial lesions, smaller 24-h and subacute lesions, larger diffusion–perfusion mismatch, and smaller final lesions viewed with diffusion-weighted imaging than did patients with no distal hyperintense vessels.[26]

Symptomatic ICA occlusion

Internal carotid artery (ICA) occlusion is an important cause of transient ischemic attack (TIA) and stroke.

Epidemiology

A retrospective analysis done by Flaherty et al in US revealed annual symptomatic ICA occlusion incidence as 6 per 100 000 persons (age and gender adjusted to the 2000 US white population). Risk of cerebral infarction during follow-up was 8% at 30 days, 10% at 1 year, and 14% at 5 years. Five of 11 cerebral infarctions occurred within the first week after diagnosis of occlusion. Risk of myocardial infarction was 0% at 30 days, 8% at 1 year, and 24% at 5 years. Risk of death was 7%, 13%, and 29%, respectively.[27] Based on 20 follow up studies on symptomatic ICA occlusion the annual risk of stroke was 5.5%, and that of ipsilateral stroke was 2.1%. [28]

Mechanism of stroke in ICA occlusion

Patients with TIAs or minor ischemic stroke who are found to have an ipsilateral occlusion of the ICA are at risk for further stroke and other vascular events. The causes of ischemic stroke associated with a previously occluded ICA are still a matter of debate. It has been hypothesized that the deficits are caused by emboli, either from the distal or proximal stump or from atherosclerotic plaques in the common carotid artery or external carotid artery, which find their way to the ipsilateral hemisphere or retina via collateral pathways involving the ECA.[29] In addition, trans-hemispheric passage of microemboli may cause ischemic events ipsilateral to the occluded ICA. Arguments in favor of this hypothesis are the cessation of symptoms after excision or clipping of the proximal stump, after endarterectomy in contralateral ICA stenosis, or after treatment with antithrombotic agents.[30] In addition, some pathological evidence is consistent with embolism from the distal tail of the occluded ICA.

Over the last several years, evidence has been accumulating that in addition to embolism a compromised CBF may play a role in causing TIAs and stroke in patients with occlusion of the ICA. In such cases ischemia would occur by failure of the collateral blood flow via the circle of Willis, the ophthalmic artery, or the leptomeningeal collaterals.[28]

Clinical features of symptomatic ICA occlusion

Ischemic stroke caused by ICA occlusion can present with clinical features that are indistinguishable from those associated with other causes of stroke. In some

patients, however, careful history taking may uncover a hemodynamic cause. Occurrence of TIA or stroke subsequent to extensive blood loss, cardiac failure, or, more commonly, to rising from a sitting or lying position may indicate a hemodynamic origin of cerebral or retinal ischemia, suggesting ICA occlusion.[31] Another symptom attributed to hemodynamic compromise is "limb shaking TIA" first described by Fisher in 1962. Patients complain of repetitive involuntary movements of one or both limbs on one side, resembling partial seizures. Electroencephalograms during attacks do not show any epileptiform activity, diminished CBF has been documented and symptoms may disappear after endarterectomy or STA-MCA bypass surgery.[32] Less well known are symptoms of (transient) retinal ischemia that occur on looking into bright light (retinal claudication), caused by an increase in metabolic demand in the retina that cannot be met by an already marginal perfusion.[33]

Syndrome of Chronic ocular ischemia (SCOI)

Patients complain of progressive loss of visual acuity, often but not necessarily accompanied by pain around the eye. Early retinal signs of SCOI are mid-peripheral microaneurysms and small dot and blot intraretinal hemorrhages or nerve fiber layer splinter hemorrhages, narrowing of arteries, and dilatation and tortuosity of veins, a pattern often referred to as venous stasis retinopathy. Cotton-wool spots and edema of the optic disc may develop, as well as (in a later stage) neovascularization of the optic disc, retina, and iris (rubeosis iridis), in turn leading to uveitis and neovascular glaucoma. Rubeosis iridis is considered a bad prognostic sign.[34] Manifestations of SCOI have been reported in 4% to 18% of patients with severe stenosis or occlusion of the ICA.[35]

Specific Pattern of infarcts

Infarction in the border zone area between the vascular territories of major cerebral arteries has been assumed to indicate a hemodynamic origin of ischemic stroke. Huppert's et al in a study showed ICA occlusion to be significantly more frequent in a group of patients with border zone infarcts than in patients with other infarcts.[36] Border zone areas are located in the most distal part of the perfusion territory of the main cerebral arteries or between the deep and superficial supply area of the MCA.

Outcome after symptomatic ICA occlusion

In a study by Burke et al showed that patients with symptomatic ICA occlusion were more likely to have in-hospital death, neurological worsening, and poor functional outcome and were less likely to be discharged home compared to patients with severe, moderate, or mild/no stenosis. In ICA occlusion, recurrent in-hospital stroke occurred in 6.7% of patients, myocardial infarction in 2.5%, and mortality in 12% with an average length of stay of 18 days.[37]

Klinjn et al followed up 97 patients with symptomatic ICA occlusion for 26 months. The annual risk of stroke was 5.3% for all strokes (95% CI 2.9%–9.6%) and 3.8% for ipsilateral stroke (95% CI 1.9%–7.7%). Hyperlipidaemia and severe stenosis of the contralateral ICA were independent risk factors.[38]

Collateral circulation in symptomatic ICA occlusion

In an earlier study using cerebrovascular reactivity (CVR) by TCD determining the outcome in ICA occlusion patients (23 patients were asymptomatic and 42

symptomatic) showed that an impairment of CVR to hypercapnia is significantly associated with an increased risk of ischemic events ipsilateral to carotid occlusion. 11 symptomatic patients and 1 asymptomatic patient had another ischemic event ipsilateral to carotid occlusion. 11 patients who developed an ischemic event during the follow-up period had a breath holding index value <0.69. [39]

Rutgers et al prospectively studied 112 patients with symptomatic ICA occlusion. Compared with patients without recurrent stroke, patients with recurrent events had significantly higher total blood flow to the brain, i.e., ICA+BA flow (mean 536mL/min versus 410mL/min; P<0.05), and significantly higher contralateral ICA flow (355mL/min versus 209mL/min; P <0.001), whereas BA and MCA flow showed no significant differences. Also, they more often had Willisian collateral flow (P<0.05), mainly caused by increased collateral flow via the PCoA; (71% versus 28%; P<0.05), whereas collateral flow via the OA and leptomeningeal anastomoses did not differ significantly. So the authors concluded that recurrent ipsilateral ischemic stroke in patients with symptomatic ICA occlusion is associated with high volume flow to the brain and increased collateral PCoA flow.[40]

Collateral ability of the Circle of Willis in patients with unilateral ICA occlusion was studied using MRA. Fifty-one patients (35 symptomatic, 16 asymptomatic) and 53 control subjects were investigated. Almost 92% of the patients without border zone infarcts (n 26) had Willisian collateral flow compared with 60% of patients with border zone infarcts (n 25; P<0.05). This increase in collateral flow was caused by the high prevalence of collateral flow via the PCoA in patients without border zone infarcts (50% versus 12%; p<0.05). So the conclusion was in patients

with unilateral ICA occlusion, the presence of collateral flow via the PCoA is associated with a low prevalence of border zone infarcts.[41]

Augmentation of cerebral blood flow in acute stroke

Supportive medical care for patients with acute stroke, including adequate hydration and the avoidance of wide fluctuations in blood pressure, can help to maintain collateral flow capabilities. Optimization of systemic factors like blood pressure, blood sugar and serum electrolytes could help to minimise the risk of collateral failure, particularly in patients with proximal arterial occlusions. Several interventions aimed at increasing CBF via collateral vessel recruitment or stabilisation might be therapeutically useful in acute ischaemic stroke.[4]

Experimental techniques aimed at increasing cerebral blood flow are: -

(i) Volume expansion with or without increased blood pressure

(ii) Stimulation of the sphenopalatine ganglion

(iii) Partial aortic occlusion

(iv) External pressure cuffs

On the basis of the available evidence it was concluded that volume expansion or haemodilution is not recommended in patients with acute stroke and the use of vasodilators are also not recommended.[42] A meta-analysis of 18 trials in which hemodilution was initiated within 72 hours of symptom onset was reported. A combination of phlebotomy and plasma volume expanders was used in 8 trials, and volume expansion alone was used in 10 trials. Hemodilution did not significantly reduce deaths within the first 4 weeks (OR, 1.1; 95% CI, 0.9–1.4) or within 3 to 6

months (OR, 1.0; 95% CI, 0.8–1.2). There was no increased risk of serious cardiac events among patients with hemodilution. [43]

Data from animal models and from human research demonstrate that aortic occlusion, which is commonly performed by cross clamping the descending aorta for vascular control during aortic surgery, results in net flow diversion to the cerebral from the lower-extremity circulatory beds, thereby increasing cerebral blood flow. A randomized controlled multicenter trial enrolling patients with ischemic stroke within 14 hours of symptom onset showed that there were no significant differences in clinical outcome between treatment groups compared with controls (11.3% versus 6.3%, respectively). [44]

Revascularisation procedures in ICA occlusion

Direct procedure for revascularization

External carotid–internal carotid bypass surgery: - the superficial temporal artery to middle cerebral artery bypass can improve CBF in patients with symptomatic unilateral carotid occlusion.[45] However, a large, randomised clinical trial failed to show any benefit of this bypass over contemporary medical treatment in preventing stroke in patients with symptomatic ICA occlusion.[46] A newer technique using a venous transplant for a bypass between the proximal superficial temporal artery and the most distal, intracranial part of the ICA or the proximal MCA results in a larger increase in blood flow (‘‘high-flow’’ external carotid–internal carotid bypass) and may be more effective at restoring CBF.[47]

Indirect procedures

Endarterectomy or angioplasty stenting of contralateral ICA: - the contralateral ICA is often the most important source of collateral flow in ICA occlusion. In patients with ICA occlusion and a severe stenosis of the contralateral ICA, carotid endarterectomy of the contralateral ICA resulted in a long-term cerebral haemodynamic improvement not only on the side of surgery but also on the side of the ICA occlusion.[47] Gonzalez et al have recently reported endovascular treatment (angioplasty and stenting) of contralateral ICA to be safe and effective in patients with a symptomatic ICA occlusion and a severe stenosis of the contralateral ICA.[48] However, no large, controlled studies have evaluated the efficacy and safety of these therapeutic approaches in ICA occlusion.

AIMS OF THE STUDY

1. To study whether CT Angiogram is able to predict the stroke severity and outcome of patients with symptomatic internal carotid artery occlusion.

2. To study whether the status of collateral circulation can predict the risk of recurrent events in patients with symptomatic internal carotid artery occlusion

MATERIALS AND METHODS

Study design:

The study is designed as a retrospective study of patients with acute ischemic stroke or transient ischemic attack attending the Stroke Unit, Department of Neurology, SCTIMST. Sixty-five consecutive patients with symptomatic ICA occlusion fulfilling the inclusion and exclusion criteria were selected for the study during the period from January 2011 to December 2013 who underwent CTA as a part of evaluation of stroke.

Study period:

The study was conducted over a period of 3 years from January 2011 to December 2013.

Inclusion criteria:

1. Patients with TIA or ischemic stroke aged above 18 years
2. Extracranial ICA occlusion on the ipsilateral ischemic territory.
3. CT angiogram done within 3 weeks from symptom onset.

Exclusion criteria:

1. Patients aged below 18 years.
2. Patients with hemorrhagic stroke.
3. Patients with asymptomatic ICA occlusion.
4. Patients with intracranial ICA occlusion
5. Patients with tandem middle cerebral artery occlusion.

Selection of subjects:

Cases: Those subjects who satisfy the inclusion and exclusion criteria with symptomatic ICA occlusion during the study period from January 2011 to December 2013 were included in the study.

Assessment of the cases:

Demographic profile like age, gender and comorbid condition was collected from the case records. The type of index event whether acute stroke or TIA was noted. The vascular risk factor profile like history of hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, congestive cardiac failure, dyslipidemia and smoking was also noted.

The premorbid modified Rankin scale (mRS) and stroke severity by National Institute of Health Stroke Scale (NIHSS) was assessed at baseline. The clinical features were recorded and history any previous neurological events and transient monocular blindness were noted.

Coronary artery disease was defined as a history of myocardial infarction (MI), angina, coronary angioplasty, or coronary artery bypass grafting. Dyslipidemia was defined as total cholesterol ≥240mg//dL, low-density lipoprotein ≥160mg/dL, high-density lipoprotein ≤40mg/dL, or patients receiving pharmacological treatment. The above mentioned cut off values has borderline increased risk for vascular events. [50]

In accordance with Joint National Committee 7 guidelines, hypertension was defined as a systolic blood pressure consistently ≥140 mm Hg or a diastolic pressure consistently ≥90 mm Hg before the index event, or those who receive pharmacological treatment.[51]

The CT scan, MRI (if available) and CT angiogram finding of the patients was reviewed by a radiologist and neurologist. The baseline computed tomography scan was used for Alberta Stroke Programme Early CT score (ASPECTS). The degree of contralateral ICA stenosis was assessed according to North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria.[52]

Cerebral circulation was assessed from CT Angiogram based on the presence of flow through the Circle of Willis and the leptomeningeal collaterals. The cerebral collateral circulation was classified into primary collaterals if the collateral flow was through circle of Willis and secondary collaterals if there is adequate flow through ophthalmic artery and leptomeningeal collaterals.

Anterior communicating artery, ipsilateral posterior communicating artery and contralateral posterior communicating artery was graded into two based on presence of poor or good collateral flow. Ophthalmic artery on ipsilateral side was graded as good collateral flow if it is filled from external carotid artery or poor flow if it is not visible.

Leptomeningeal collateral circulation was classified into 5 grades as per Maas et al.[21]

Grade 1: absent

Grade 2: less than contralateral side

Grade 3: equal to contralateral side

Grade 4: greater than contralateral side

Grade 5: exuberant

Since the sample size was small the leptomeningeal collaterals were dichotomized into two- poor collaterals (grade 0 and 1) and good collaterals (grade 3, 4 and 5).

Follow up:

All patients were followed up at 90 days. Any recurrent neurological events were recorded and other vascular events were also noted. The functional outcome was assessed by modified Rankin scale and mRS ≤ 2 was regarded as good outcome.

STATISTICAL ANALYSIS

All statistical analysis was performed using SPSS software. Good clinical outcome was defined as mRS ≤2 and poor outcome as mRS ≥3 at 90 day follow-up.

Continuous variables are reported as mean ± SD or as median ± interquartile range (IQR). Categorical variables were reported as proportions. Baseline characteristics were compared between the good and poor outcome group. Differences in continuous variables were assessed by 1-way analysis of variance and differences between proportions were assessed by the X2 test. This study also compared the various clinical parameters between the good and poor leptomeningeal collateral group.

Univariate analysis was used to test the association between different variables and the outcome (follow-up mRS). Multivariate logistic was used to identify independent predictors for good outcome. Variables significantly associated with a favourable outcome in the univariate analysis (P ≤0.1) were included in the multivariate model.

RESULTS

Seventy three patients with symptomatic ICA occlusion from January 2011 to December 2013 was taken for the study, of which 6 patients with tandem M1 occlusion and 2 patients with intracranial ICA occlusion were excluded. The mean age of subjects was 57 ±11.6 (range 32-80) and 92% were males.

Outcome

All the 65 patients were followed up at 90 days after the index event. The median mRS was 3 (range 0-6) and 31 (47.69%) patients had good outcome (mRS ≤2)

Mortality

Out of 65 patients, 4 (6.2%) had expired. Three patients died in hospital due to malignant MCA infarct. One of these patients developed contralateral MCA infarct also. One patient died in local hospital due to myocardial infarction.

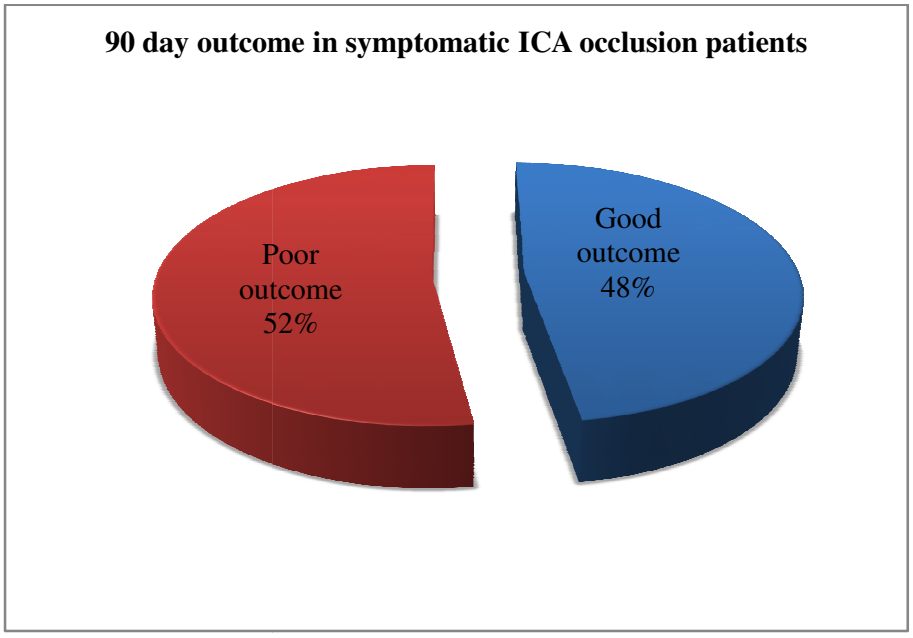
Recurrent vascular events

Only 2 patients (3.1%) had recurrent event; 1 patient had worsening of weakness after 2 weeks on the symptomatic side which improved within 24 hours and other patient developed myocardial infarction and expired.

Table 1: Functional outcome at 90 days

90 day follow up	N=65 (%)
Good outcome (mRS <3)	31 (47.7%)
Poor outcome (mRS ≥3)	34 (52.3%)

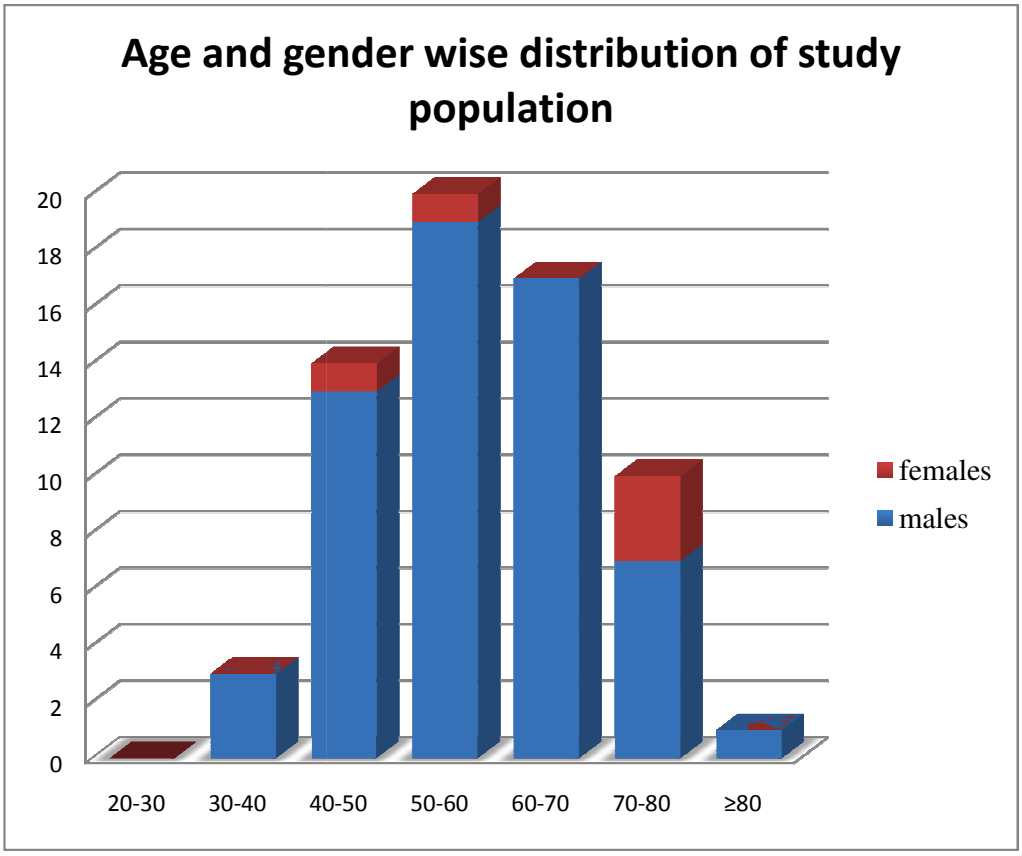
Chart 1: Functional outcome at 90 days



Demographic profile

The mean age of subjects was 57 ±11.6 (range 32-80) and 92% were males.

Chart 2: Age and gender wise distribution of study population



Base line characteristics

The premorbid mRS for all patients was 0 except for two. One patient had right leg fracture underwent surgery and the other patient had mild sensory symptoms in the left leg.

Table 2: Base line characteristics of study population

Base line characteristics	N=65
Mean age	57 ±11.6
Male gender	60 (92%)
Hypertension	29 (44.6%)
Diabetes mellitus	17 (26.2%)
Cardiac disease	14 (21.5%)
Smoking	40 (61.5%)
Previous ischemic events	14 (21.5%)
On preventive therapy	7 (10.8%)

Among the vascular risk factor profile, 29 patients (44.6%) had hypertension, 17 patients (26.2%) had diabetes mellitus and 40 patients (61.5%) were smokers. Fourteen patients (21.5%) had cardiac disease with coronary artery disease in 12, valvular heart disease and atrial fibrillation in 1 patient each. Previous ischemic events were noted in 14 patients (21.5%) and among them 4 patients had transient ischemic attack or stroke within 2 weeks prior to the present clinical event. A total of 7 patients (10.8%) were on preventive therapy for recurrent ischemic events with 6 patients on antiplatelets and 1 patient on oral anticoagulation, but only 4 patients were on statins.

Clinical parameters at admission

Transient ischemic attack (TIA) was the presenting event in 4 patients (6.2%) and the rest presented with stroke. The median NIHSS at presentation was 10 (range 0-22) and 16 patients (24.6%) had NIHSS of less than 5 and 49 patients (75.4%) had NIHSS 5 or more at presentation to our hospital. Among them 8 patients (12.3 %) had NIHSS ≥ 20.

Table 3: Clinical parameters of study population at admission

Clinical parameters at admission	Number of patients =65
Systolic Blood pressure <140mmHg	29 (44.6%)
Systolic Blood pressure ≥140mmHg	36 (55.4%)
Diastolic Blood pressure <90mmHg	38 (58.5%)
Diastolic Blood pressure ≥ 90mmHg	27 (41.5%)
RBS <140mg/dL	42(64.6%)
RBS≥140 mg/dL	23(35.4%)
NIHSS<5	16 (24.6%)
NIHSS≥5	49 (75.4%)
mRS <3 at admission	17 (26.2%)
mRS ≥3 at admission	48 (73.8%)

Lipid profile

The mean serum total cholesterol, LDL cholesterol, HDL cholesterol, Triglyceride was 191.2±52.1 mg/dL, 130.7±47.6 mg/dL, 36.5±10.3 mg/dL and 120.7±40.6 mg/dL respectively. 23 patients (35.38%) had serum total cholesterol of ≥200 mg/dL, 47 patients (72.30%) had serum LDL cholesterol ≥130mg/dL, 45 patients (69.23%) had serum HDL cholesterol <40 mg/dL and 11 patients (16.92%) had serum Triglycerides ≥150mg/dL.

Table 4: Lipid profile of study population

Lipid parameters	N=65
Total cholesterol, mean (mg/dl)	191.2±52.1
LDL cholesterol, mean (mg/dl)	130.7±47.6
HDL cholesterol, mean (mg/dl)	36.5±10.3
Triglyceride, mean (mg/dl)	120.7±40.6

Imaging characteristics

The CT scan done was reviewed for assessing the ASPECTS and type of infarct.

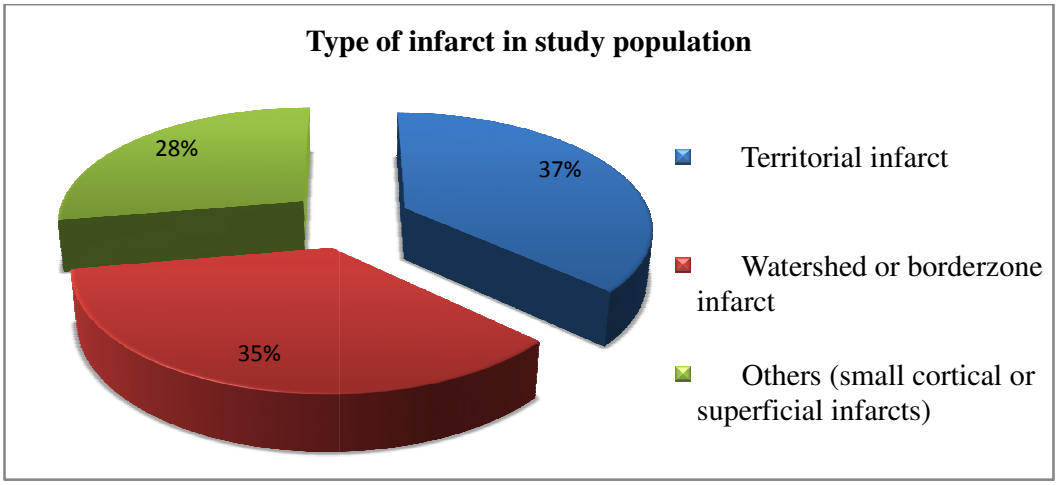
Type of infarct

Out of 65 patients, 24 (36.92%) had MCA territory infarct, 23 (35.38%) had hemodynamic infarct either in MCA- PCA or MCA- ACA watershed region or internal border zone infarcts and 18 (27.7%) had either small cortical or superficial infarcts.

Table 5: Type of infarcts in study population

Type of infarct	N=65
Territorial infarct	24 (36.9%)
Watershed or border zone infarct	23 (35.4%)
Others (small cortical or superficial infarcts)	18 (27.7%)

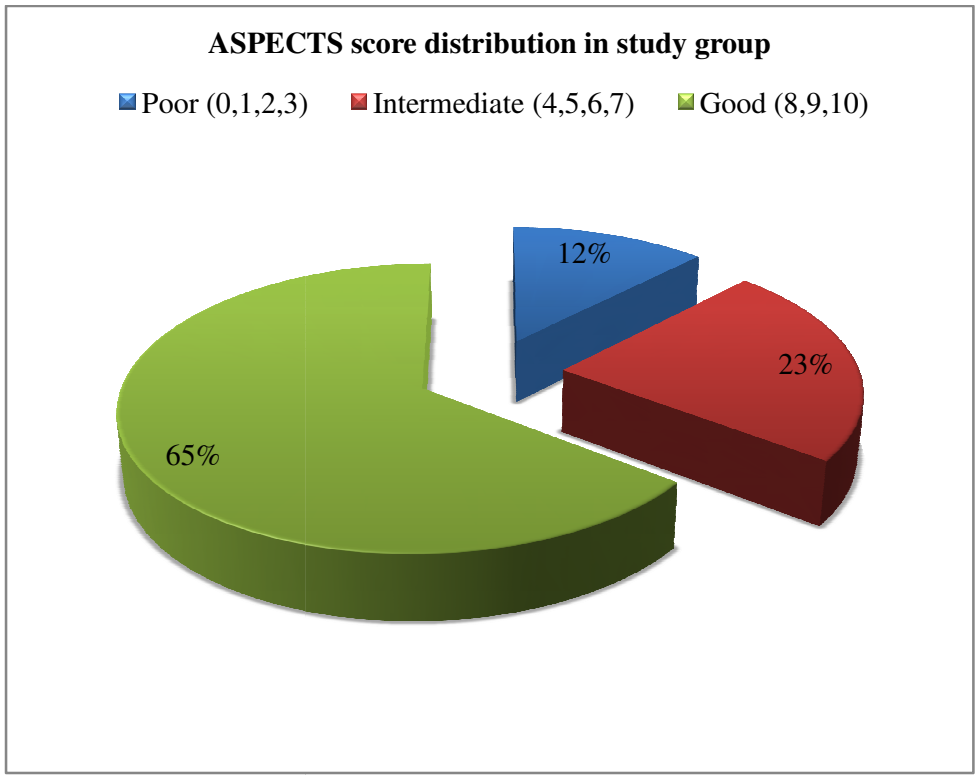
Chart 3: Type of infarcts in study population



ASPECTS score

Out of 65 patients, 8 (12.30%), 15 (23.08%) and 42 (64.62%) patients had poor, intermediate and good ASPECTS respectively.

Chart 4: ASPECTS score distribution in study population



CT angiogram (CTA)

All study patients underwent CTA at presentation to our hospital and all of them had symptomatic ICA occlusion at origin. Flow through primary collaterals (anterior communicating artery and posterior communicating artery) and secondary collaterals (ophthalmic artery and leptomeningeal) were graded as poor flow (absent or inadequate) and good flow (adequate or robust).

Primary Collaterals

Symptomatic side M1 was reformed in 61 patients (93.9%) while in 4 patients (6.2%) M1 segment was not visualized. Fet al PCA was seen in 2 patients and 1 patient had PCoA aneurysm. Hypoplastic A1 was seen in 5 patients on ipsilateral side and 2 patients on contralateral side.

Table 6: Primary collaterals in study population

Primary collaterals	Poor flow	Good flow
ACoA	31 (47.7%)	34 (52.3%)
Ipsilateral PCoA	39 (60%)	26 (40%)
Contralateral PCoA	43 (66.2%)	22 (33.9%)

Of the 65 patients, 31 (47.7%), 39 (60%) and 43 (66.2%) patients had poor flow through ACoA, ipsilateral PCoA and contralateral PCoA respectively.

Secondary Collaterals

The presence of OA with retrograde flow is considered as good flow and if ophthalmic artery is absent or not functioning as collateral is considered as poor flow. Leptomeningeal collaterals if equal to or more than the contralateral side of symptomatic ICA occlusion is considered as good flow.

Table 7: Secondary collaterals in the study population

Secondary collaterals	Poor flow	Good flow
Ipsilateral ophthalmic artery	26 (40%)	39 (60%)
Contralateral ophthalmic artery	7 (10.8%)	58 (89.2%)
Leptomeningeal collaterals	18 (27.8%)	47 (72.2%)

Good flow through ipsilateral ophthalmic artery, contralateral ophthalmic artery and leptomeningeal collaterals was seen in 39 (60%), 58 (89.2%) and 47 (72.2%) patients respectively.

Contralateral ICA

Among 65 patients, 49 (75.4%) had normal or mild stenosis of asymptomatic ICA, while 7 (10.8%) and 5 (7.7%) patients had moderate and severe stenosis respectively. Three patients (4.6%) had complete ICA occlusion of the asymptomatic side.

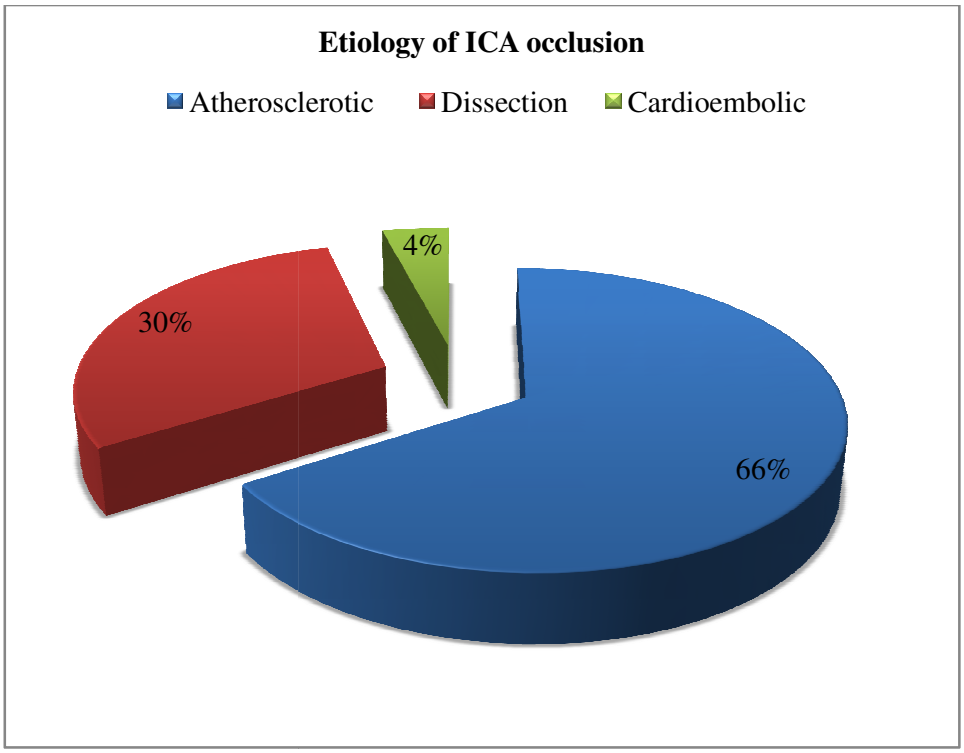
Table 8: Contralateral ICA and study population

Contralateral ICA	N=65 (%)
Normal or <50% stenosis	49 (75.4%)
50-70% stenosis	7 (10.8%)
70-99% stenosis	5 (7.7%)
Occluded	3 (4.6%)

Etiology of ICA occlusion

Out of 65 patients, the etiology of ICA occlusion was atherosclerotic, arterial dissection and cardio embolic in 43 (66.2%), 20 (30.8%) and 2 (3%) patients respectively.

Chart 5: Etiology of ICA occlusion



Predictors of outcome

The baseline characteristics and collateral circulation was compared between good outcome group and poor outcome group.

Demographic profile and outcome

The mean age in years is 59.58±10.84 and 56.3±13.2 in good outcome and poor outcome group respectively. Sixteen (59.3%) patients in the age group more than 60 years had good outcome while 11 (40.7%) patients had poor outcome and the results were not statistically significant. Majority of the patients were males and gender had no significant association with outcome.

Table 9: Demographic profile and outcome

Demographic profile	Good outcome group (mRS<3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Mean age in years	59.58±10.84	56.3±13.2		
Age <60 years	16 (40.5%)	22 (59.5%)	38 (100%)	0.2
Age >60 years	16 (59.3%)	11 (40.7%)	27 (100%)	
Male	28 (90.3%)	32 (94.1%)	60	0.6
Female	3 (9.7%)	2 (5.9%)	5	

Vascular risk factors and outcome

The presence of hypertension and smoking was similar in poor outcome and good outcome groups while 58.8% of patients with diabetes mellitus had poor outcome and 41.2% of diabetics had good outcome. The absence of history of dyslipidemia was associated with good outcome (p=0.05).

Table 10: Vascular risk factors and outcome

Vascular risk factors	Good outcome group (mRS<3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Hypertension				
Yes	16 (55.2%)	13 (44.8%)	29 (100.0%)	
No	15 (42.9%)	21 (57.1%)	36 (100.0%)	0.45
Diabetes Mellitus				
Yes	7 (41.2%)	10 (58.8%)	17(100.0%)	
No	24 (51.1%)	24 (48.9%)	47 (100.0%)	0.57
Smoking				
Yes	19 (47.5%)	21(52.5%)	40 (100.0%)	
No	12 (50%)	13 (50 %)	24 (100.0%)	1
Dyslipidemia				
Yes	4 (80 %)	1 (20%)	5 (100.0%)	
No	27 (45 %)	33 (55%)	60 (100.0%)	0.05

Prior neurological events and outcome

Among the 14 patients who had prior ischemic events, 8 patients (57.1%) had good outcome (p=0.5).

NIHSS and outcome

The median NIHSS is 5 and 15 in good outcome and poor outcome group respectively. Out of 16 patients who had minor stroke or TIA at presentation, 15 patients (93.8%) had good outcome while only 1 patient (6.2%) had poor outcome. Similarly of the 49 patients who had NIHSS >5, 33 patients (65.3%) had poor outcome and only 17 (34.7%) patients had good outcome. (p=0.004)

Table 11: NIHSS and outcome

NIHSS	Good outcome group (mRS≤2) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Median NIHSS	5	15		
NIHSS <5	15 (93.8%)	1 (6.2%)	16 (100%)	0.004
NIHSS >5	17 (34.7%)	33 (65.3%)	49 (100%)	

Etiology and outcome

Among the 43 patients who had atherosclerotic ICA occlusion, 23 (52.4%) patients had good outcome and 20 (47.6%) patients had poor outcome. Of the 22 patients who had acute occlusion like dissection or embolism, 59% had poor outcome and only 41 patients had good outcome but the results were not statistically significant.

Table 12: Etiology of ICA occlusion and outcome

Etiology of ICA occlusion	Good outcome group (mRS≤2) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Atherosclerotic	23 (52.4%)	20 (47.6%)	43 (100%)	0.4
Dissection and embolic	9 (40.9%)	13 (59.1%)	22 (100%)	

Blood pressure and outcome

The mean systolic and diastolic BP was similar in good outcome group and poor outcome group (145.5 ±20.4, 84.5±11.3 and 143 ±27.4, 84.8±14.2). Among the 27 patients with high diastolic BP, 59% had poor outcome and 41% had good outcome. The systolic or diastolic blood pressure was not associated with outcome by univariate analysis.

Table 13: Blood pressure and outcome

Blood pressure	Good outcome N=31	Poor outcome N=34	Total	P value
Mean Systolic BP	145.5 ±20.4	143 ±27.4		
SBP <140 mmHg	12 (41.4%)	17 (58.6%)	29 (100%)	0.8
SBP ≥140 mmHg	19 (52.8%)	17 (47.2%)	36 (100%)	
Mean Diastolic BP	84.5±11.3	84.8±14.2		
DBP<90 mmHg	20 (52.6%)	18 (47.4%)	38 (100%)	0.5
DBP ≥90 mmHg	11 (40.7%)	16(59.3%)	27 (100%)	

Random blood sugar at onset and outcome

The mean random blood sugar in the emergency department was higher in poor outcome group when compared to good outcome group. (146.9±66.5 and 129.4 ±66.9; p=0.06)

Table 14: RBS and outcome

Random blood sugar	Good outcome N=31	Poor outcome N=34	Total	P value
Mean RBS (mg/dL)	129.4 ±66.9	146.9±66.5		
RBS< 140 mg/dL	25 (59.5%)	17 (40.5%)	42	0.06
RBS ≥140mg/dL	6 (27.3%)	17 (72.7%)	22	

Lipid profile and outcome

The mean serum total cholesterol (TC), LDL, HDL and Triglyceride levels were 201.8±56.1, 138.4±53.3, 38.1±9.9 and 123.8±50.4 respectively in the good outcome group. By univariate analysis none of the above cholesterol values had any relation with outcome of the study population.

Table 15: Lipid profile and outcome

Lipid profile (mg/dL)	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Mean total cholesterol	201.8±56.1	181.4±46.8		
TC <200 mg/dl	18 (42.9%)	24 (57.1%)	42 (100%)	0.2
TC >200 mg/dl	13 (56.5%)	10 (43.5%)	23 (100%)	
Mean LDL	138.4±53.3	123.7±41.2		
LDL <100 mg/dL	9 (50%)	9 (50%)	18 (100%)	0.5
LDL >100 mg/dL	22 (46.8%)	25 (53.2%)	47 (100%)	
Mean HDL	38.1±9.9	35±10.6		
HDL>40mg/dL	12 (60%)	8 (40%)	20 (100%)	0.1
HDL<40mg/dL	19 (42.2%)	26 (57.8%)	45 (100%)	
Mean triglyceride (TG)	123.8±50.4	118±29.4		
TG<150mg/dL	24 (44.4%)	30 (55.6%)	54 (100%)	0.3
TG>150mg/dL	6 (54.5%)	5 (45.5%)	11 (100%)	

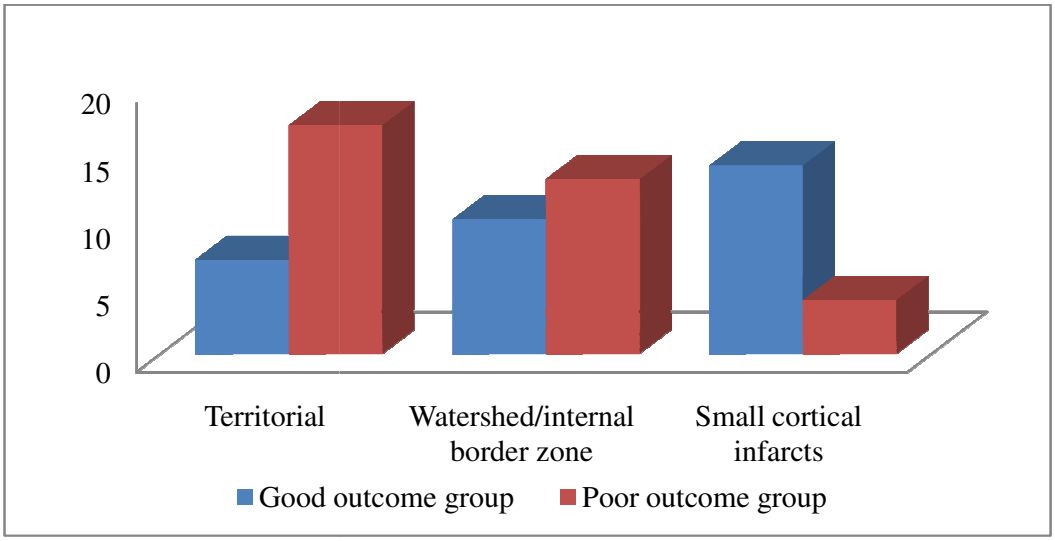
Type of infarct and outcome

Among 24 patients who had territorial infarct, 17 patients (70.8%) had poor outcome and 7 (29.2%) patients had good outcome. Out of the 18 patients with small cortical infarcts, 14 (77.8%) patients had good outcome and only 4 (22.2%) patients had poor outcome.

Table 16: Type of infarct and outcome

Type of infarct	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Territorial	7 (29.2%)	17 (70.8%)	24 (100%)	0.02
Watershed/internal border zone	10 (43.5%)	13 (56.5%)	23 (100%)	
Small cortical infarcts	14 (77.8%)	4 (22.2%)	18 (100%)	

Chart 6: Type of infarct and outcome



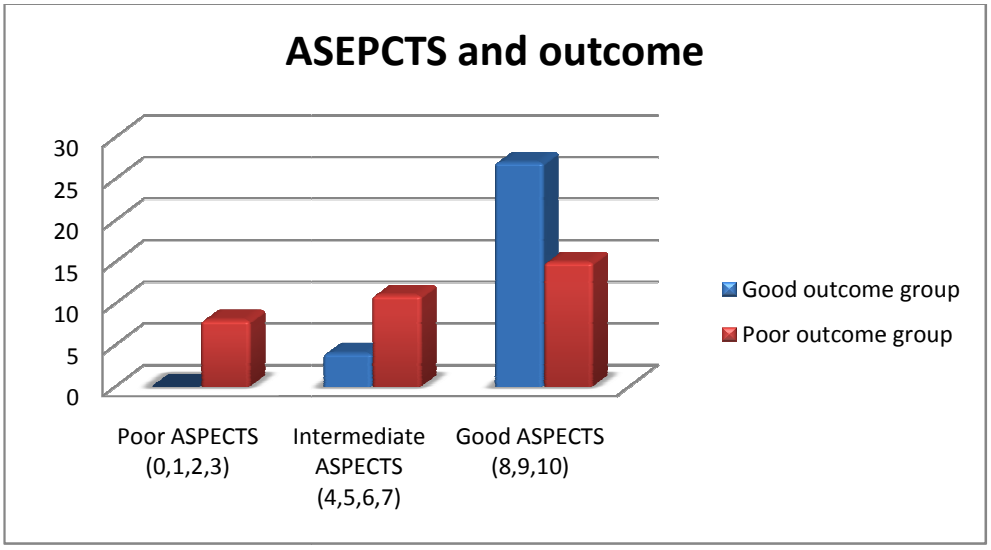
ASPECTS and outcome

All patients (8) who had poor ASPECTS had poor outcome, while 27 (64.3%) patients with good ASPECTS had good outcome and only 15 (35.7%) patients with good ASPECTS had poor outcome.

Table 17: ASPECTS and outcome

ASPECTS	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor (0,1,2,3)	0 (0%)	8 (100%)	8 (100%)	0.01
Intermediate (4,5,6,7)	4 (26.7%)	11 (73.3 %)	15 (100%)	
Good (8,9,10)	27 (64.3%)	15 (35.7%)	42 (100%)	

Chart 7: ASPECTS and outcome



Collateral circulation and outcome

Anterior communicating artery (ACoA)

Among 31 patients with poor flow through ACoA, 17 (54.8%) patients had poor outcome and 14 (45.2%) patients had good outcome. In 34 patients with good ACoA flow, half of them had poor outcome. The presence of good ACoA was not associated with good outcome in symptomatic ICA occlusion patients.

Table 18: ACoA and outcome

ACoA	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	14(45.2%)	17 (54.8%)	31 (100%)	0.8
Good flow	17 (50%)	17 (50%)	34 (100%)	

Ipsilateral posterior communicating artery and outcome

Among 39 patients with poor flow through PCoA, 24 (61.5%) patients had poor outcome and 15 (38.5%) patients had good outcome (p=0.07).

Table 19: Ipsilateral PCoA and outcome

Ipsilateral PCoA	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	15(38.5%)	24 (61.5%)	39 (100%)	0.07
Good flow	16 (61.5%)	10 (38.5%)	26 (100%)	

Contralateral posterior communicating artery and outcome

The presence or absence of good flow through contralateral PCoA was not associated with 3 month outcome in patients with symptomatic ICA occlusion. Among 22 patients with good flow through contralateral PCoA, 50% had good outcome.

Table 20: Contralateral PCoA and outcome

Contralateral PCoA	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	20 (46.5%)	23 (53.5%)	43 (100%)	0.8
Good flow	11 (50%)	11 (50%)	22 (100%)	

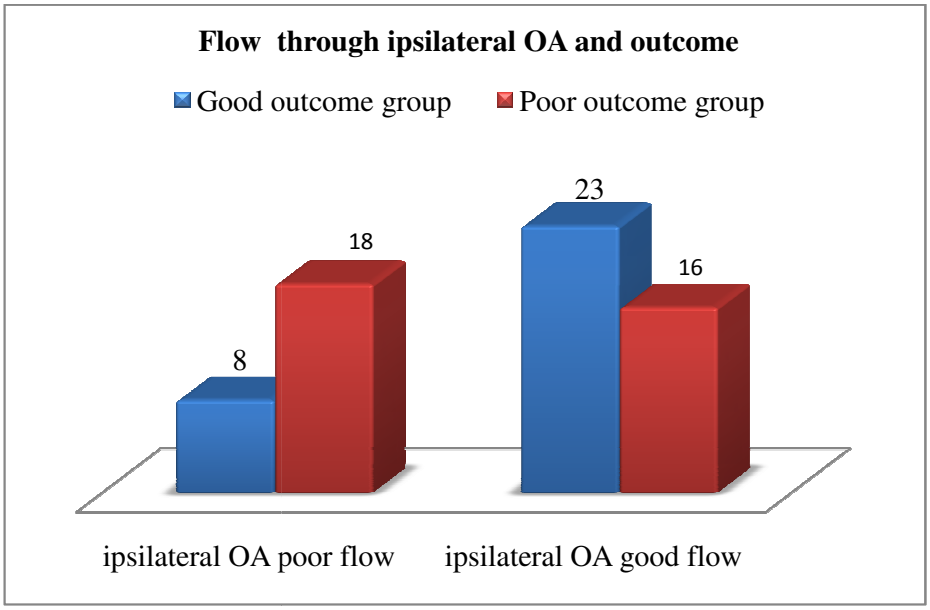
Ipsilateral Ophthalmic artery and outcome

Among 26 patients with poor flow or absent ophthalmic artery on the same side of ICA occlusion, 18 (69.2%) patients had poor outcome and 8 (30.8%) patients had good outcome and the results were statistically significant.

Table 21: Ipsilateral OA and outcome

Ipsilateral OA	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	8 (30.8%)	18 (69.2%)	26 (100%)	0.02
Good flow	23 (59%)	16 (41 %)	39 (100%)	

Chart 8: Ipsilateral OA and outcome



Contralateral Ophthalmic artery and outcome

The presence of good flow or poor flow through ophthalmic artery on the contralateral side was not associated with outcome.

Table 22: Contralateral OA and outcome

Contralateral OA	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	3 (42.9%)	4 (57.1%)	7 (100%)	0.1
Good flow	28 (48.3%)	30 (51.7 %)	58 (100%)	

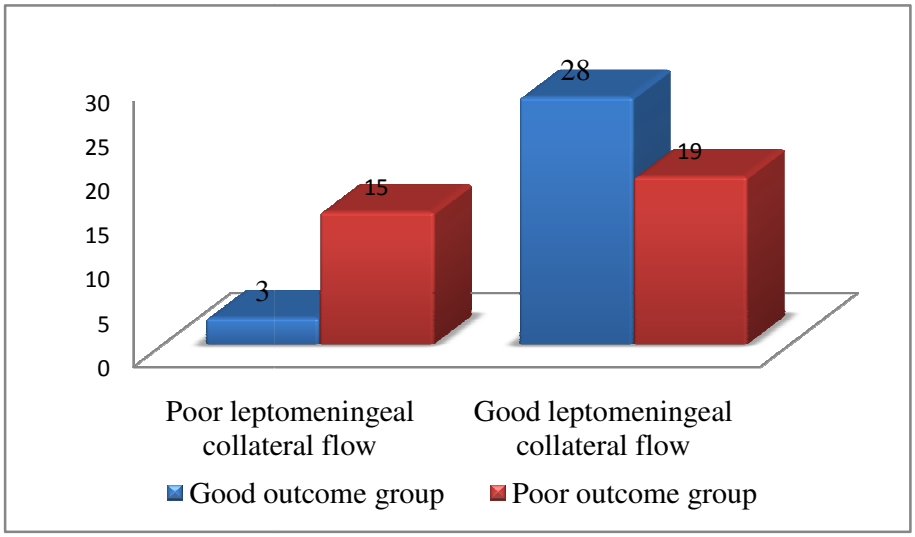
Leptomeningeal collateral circulation and outcome

Among 18 patients with poor leptomeningeal collateral flow, 15 (83.3%) had poor outcome while only 3 (16.7%) patients had good outcome. Hence poor leptomeningeal collateral circulation was associated with poor outcome and the results were statistically significant (p=0.001).

Table 23: Leptomeningeal collateral circulation and outcome

Leptomeningeal collaterals	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor flow	3 (16.7%)	15 (83.3%)	18 (100%)	0.001
Good flow	28 (59.6%)	19 (40.4 %)	47 (100%)	

Chart 9: Leptomeningeal collateral circulation and outcome



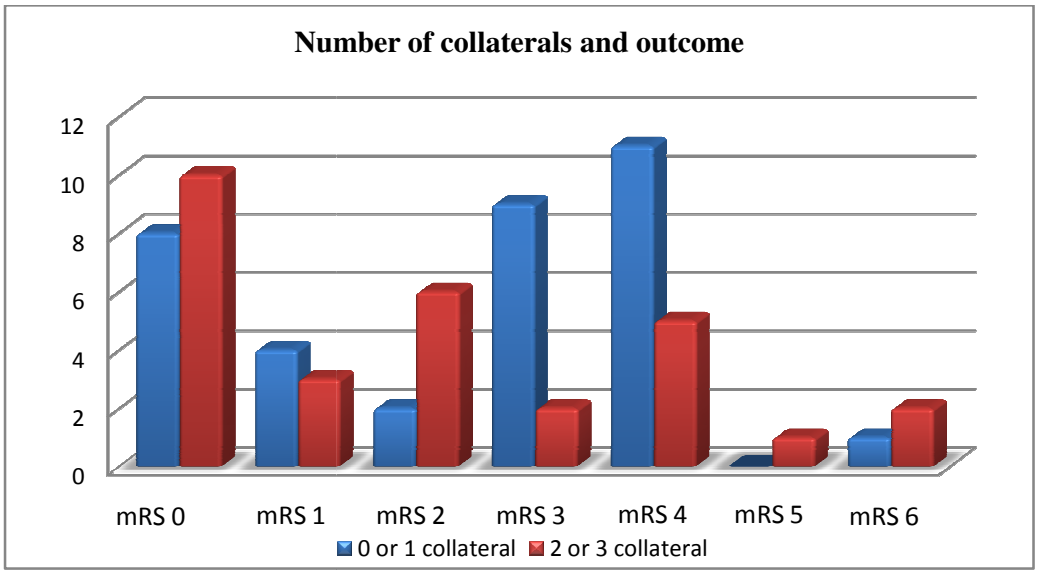
Number of collaterals (ACoA, ipsilateral PCoA and ipsilateral OA) and outcome

Out of 35 patients who had no collaterals or 1 collateral vessel, 22 (62.9%) patients had poor outcome while 18 patients (60%) with 2 or more collaterals had good outcome. (p=0.07)

Table 24: Number of collaterals and outcome

Number of collaterals	Good outcome group (mRS <3) N=31	Poor outcome group (mRS ≥3) N=34	Total	P value
Poor collaterals (0 or 1)	13 (37.1%)	22 (62.9%)	35 (100%)	0.07
Good collaterals (≥2)	18 (60%)	12 (40%)	30 (100%)	

Chart 10: Number of collateral vessels and outcome



Comparison of patients with good and poor leptomeningeal collateral circulation

There was no difference in mean age and gender between good and poor leptomeningeal flow groups. The risk factor profile like diabetes mellitus, hypertension and smoking was slightly higher in the good leptomeningeal circulation group but the results were not statistically significant.

The median NIHSS was 17 in patients with poor leptomeningeal collaterals while mean NIHSS was only 7 in good leptomeningeal group.

In atherosclerotic ICA occlusion, 34 (79.1%) patients had good leptomeningeal collaterals while only 9 (20.9%) patients had poor leptomeningeal collateral flow. However in acute ICA occlusion like in dissection and embolism the 9 (40.9%) patients had poor collateral circulation while 13 (59.1%) patients had good leptomeningeal collateral circulation.

Among 31 patients with good outcome, 28 (90.3%) patients had good leptomeningeal collaterals and 3 (9.7%) patients had poor leptomeningeal collaterals and the results were statistically significant.

Table 25: Comparison of patients with good and poor leptomeningeal collateral circulation

Clinical variable	Poor leptomeningeal collateral N=18	Good leptomeningeal collateral N=47	P value
Mean age	54.5±9.1	57.9±12.3	0.2
Male gender	16 (88.9%)	44 (93.6%)	0.6
Diabetes	4 (23.5%)	13 (76.5%)	0.7
Hypertension	8 (27.6%)	21 (72.4%)	0.6
Smoking	10 (25%)	30 (75%)	0.3
Previous neurological event	4 (28.6%)	10 (71.4%)	0.6
Atherosclerotic ICA occlusion	9 (20.9%)	34 (79.1%)	0.03
Acute ICA occlusion	9 (40.9%)	13 (59.1%)	0.03
Median NIHSS	17	7	0.01
Good 90 day outcome	3 (9.7%)	28 (90.3%)	0.01
Poor 90 day outcome	15 (44.1%)	19 (55.9%)	

Multivariate analysis of predictors of outcome

Multivariate analysis showed good collateral flow through ipsilateral ophthalmic artery (OR 6.4; CI 1.34-30.42) and good leptomeningeal collateral circulation (OR 4.85; CI 0.96-24.55) were independent predictors of good 90 day outcome

Table 26: Multivariate analysis of predictors of outcome

Clinical variable	Significance (p value)	Odds ratio	Confidence interval
Ipsilateral PCoA	0.1	4.06	0.75-21.91
Ipsilateral OA	0.02	6.4	1.35-30.42
Leptomeningeal collaterals	0.05	4.85	0.96-24.55
Number of collateral vessels	0.16	0.26	0.04-1.73

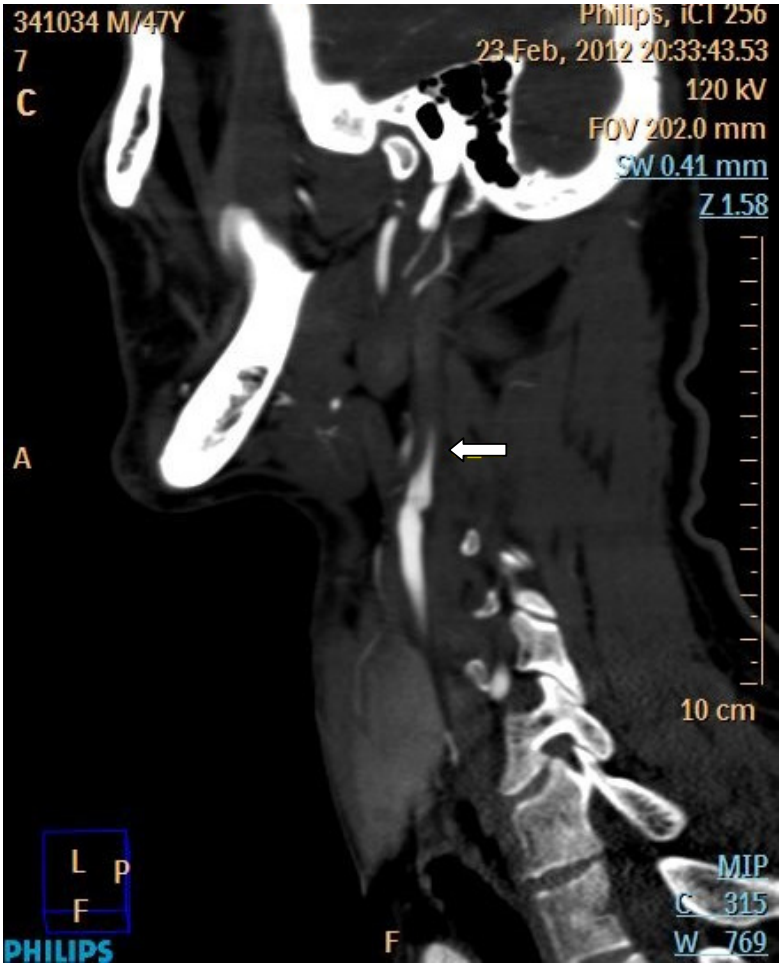


Fig1: left ICA dissection with tapering occlusion (string sign)

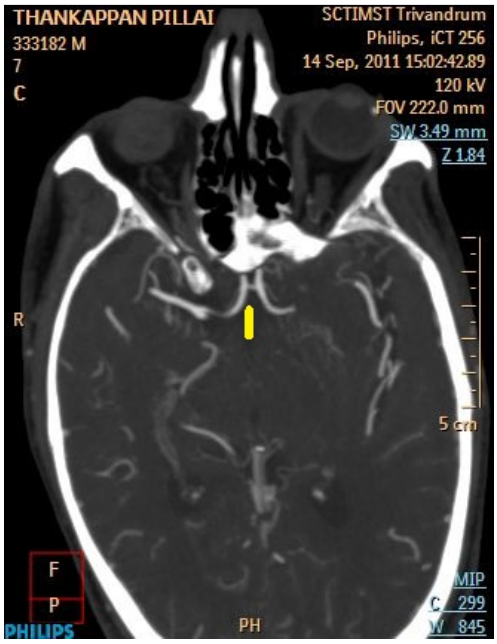


Fig 2: Anterior communicating artery with adequate flow

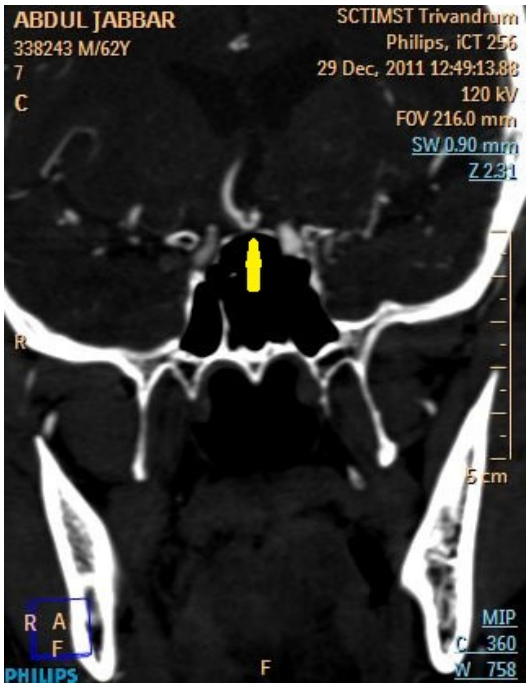


Fig 3: Anterior communicating artery with robust flow

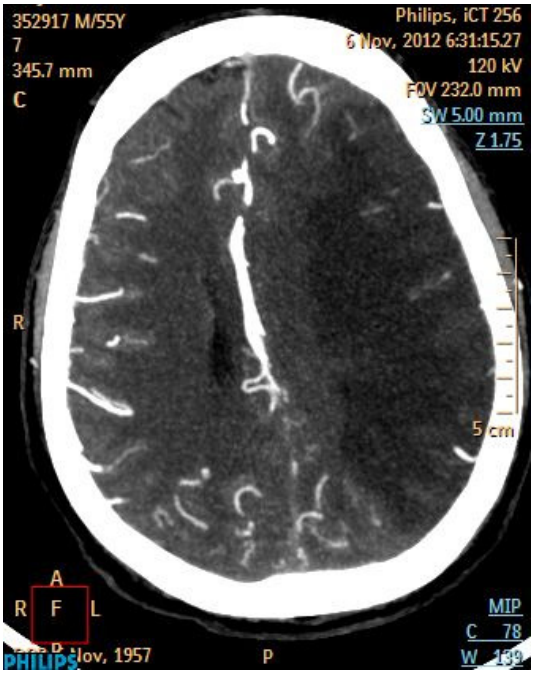


Fig 4: Poor leptomeningeal collateral flow on left compared to right

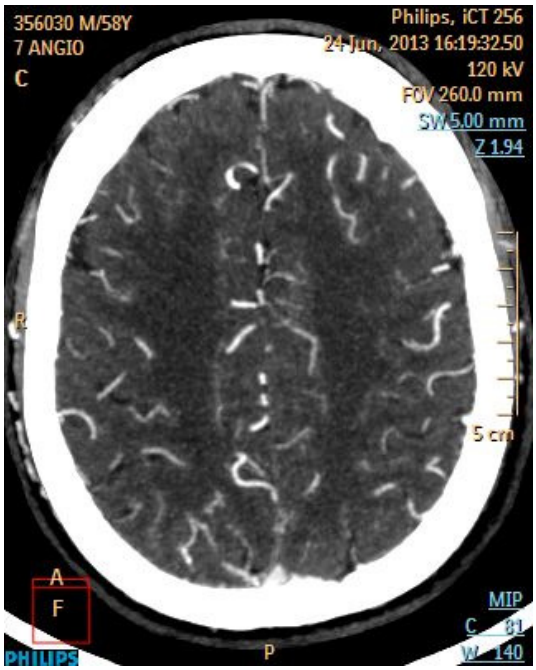


Fig 5: Leptomeningeal collateral flow equal on both sides

DISCUSSION

Among the 65 patients with symptomatic ICA occlusion who met the inclusion criteria the mean age was 57 ±11.6 (range 32-80) and 92% were males.

The median mRS at 90 day follow up was 3 (range 0-6) and 31 (47.7%) patients had good outcome (mRS<3). Three patients died in hospital due to malignant MCA infarct. One of these patients developed contralateral MCA infarct also. One patient died in local hospital due to myocardial infarction. Only 2 patients had recurrent event; 1 patient had worsening of weakness after 2 weeks on the symptomatic side which improved within 24 hours and other patient developed myocardial infarction and expired.

In a study by Burke et al showed that patients with symptomatic ICA occlusion were more likely to have in-hospital death, neurological worsening, and poor functional outcome and were less likely to be discharged home compared to patients with severe, moderate, or mild/no stenosis. In ICA occlusion, recurrent in-hospital stroke occurred in 6.7% of patients, myocardial infarction in 2.5%, and mortality in 12% with an average length of stay of 18 days. The vascular imaging modality used was not uniform and the whether ICA occlusion was acute or chronic was not mentioned in this study, although presumed atherosclerotic occlusion alone was included in the study population. [37]

In a previous study of 75 symptomatic patients with ICA occlusion, the incidence of stroke, myocardial infarction, and mortality at 30 days follow-up was 8%, 0%, and 7%, respectively.[27] Another study of 177 patients with ischemic stroke

and ICA occlusion reported a higher 30 day mortality of 30%, but that study excluded patients with TIA.[53]

The recurrent neurological events are less in our study population, which may be due to the best medical management with dual antiplatelets and high dose statins and the mortality rates were comparable or less to other studies.

Univariate analysis in our study showed that higher baseline NIHSS, low ASPECTS, history of dyslipidemia, higher random blood sugar in emergency department, type of infarct, poor collateral flow through ipsilateral ophthalmic artery, ipsilateral posterior communicating artery and leptomeningeal collaterals were predictors of poor outcome. In multivariate analysis, good collateral flow through ipsilateral ophthalmic artery (OR 6.4; CI 1.34-30.42) and good leptomeningeal collateral circulation (OR 4.85; CI 0.96-24.55) predicted a good 90 day outcome.

In our study, among 26 patients with poor flow or absent ophthalmic artery on the ipsilateral side of ICA occlusion, 18 (69.2%) patients had poor outcome and 8 (30.8%) patients had good outcome and the results were statistically significant.

Most of the literature reports have focused on the effect of primary collateral circulation and cerebrovascular autoregulation in stroke patients, with only a few studies having explored the clinical significance of OA collateral flow. Tsai et al in a retrospective study of patients with severe ICA stenosis or occlusion showed that the patients (n=48) with ICA occlusion had significantly higher incidence (62.5%) of reversed ophthalmic artery flow (ROAF) compared with that of 25.0% in those patients (n=152) with unilateral high-grade carotid stenosis (P<0.001). The patients

(n=159) with history of stroke (P=0.035), ROAF (P=0.023) and intracranial stenosis (P<0.001) exhibited significantly higher incidence of poor functional outcome compared with the corresponding control groups. This study hypothesized that ROAF indicates an impaired cerebral hemodynamics and associates with a poor function outcome in the patients with severe carotid disease. They have used TCD and MRA for ascertaining the collateral circulation which is less specific and sensitive. The time at which the vascular imaging after the index event was not mentioned which could alter the collateral flow as collateral circulation is dynamic. The sample size was small and the poor outcome was defined by mRS >3, while in most studies the poor outcome is defined as mRS >2.[54]

Poor collateral flow through ACoA was observed in 31 patients in our study. Of them 17 (54.8%) patients had poor outcome and 14 (45.2%) patients had good outcome but the results were not statistically significant. Among 39 patients with poor flow through ipsilateral PCoA, 24 (61.5%) patients had poor outcome and 15 (38.5%) patients had good outcome (p=0.07). A good flow through ipsilateral PCoA was associated with good outcome and the results had borderline significance. Eighteen patients had poor leptomeningeal collateral flow and among them, 15 (83.3%) had poor outcome while only 3 (16.7%) patients had good outcome. Hence poor leptomeningeal collateral circulation was associated with poor outcome and the results were statistically significant (p=0.001).

In 66 stroke patients with ICA occlusion due to spontaneous artery dissection, TCD was performed within 24 hours from symptom onset to examine cerebral arteries and the patency of the 3 major intracranial collateral vessels (ophthalmic artery,

anterior and posterior communicating arteries). Forty patients had at least 2 activated intracranial collateral vessels. The remaining 26 patients, with none or only 1 collateral vessel, showed a significant increased risk of poor recovery (modified Rankin Scale score>2; adjusted relative risk 14.9; 95% CI, 3.24 to 68.46).[55]

In another study, 104 patients with symptomatic or asymptomatic ICA occlusion were followed up prospectively for a median period of 24 months. The collaterals assessed were ACoA, PCoA and OA using TCD. The results were statistically significant and the annual risk of recurrent ischemic events was 32.7% in patients with no collateral pathways, 17.5% in patients with 1 collateral pathway, and 2.7% in patients with 2 collateral pathways. However, no patient with 3 compensatory circles had an ischemic event; the estimated risk was 0%. Considering patients with only 1 activated collateral pathway, ipsilateral stroke occurred in 36% of patients with OA, in 38% of patients with PCoA, and in 26% of patients with ACoA. They concluded that the presence of >1 major collateral pathway (ACoA, PCoA, and OA) supplying the hemisphere on the side of the occlusion was positively associated with better outcome in the patients.[39]

In our study, among 35 patients who had none or only 1 collateral vessel, 22 (62.9%) patients had poor outcome while 18 patients (60%) with 2 or more collaterals had good outcome (p=0.07). Hence the presence of more than 1 collaterals (ACoA, PCoA and OA) predicted good outcome which was comparable to the above study by Vernieri et al.

Flow territories of major cerebral arteries were studied in 23 functionally independent ICA occlusion patients and controls using MRA. In functionally

independent patients with symptomatic ICA occlusion, the middle cerebral artery flow territory ipsilateral to the occluded ICA is mainly supplied by the vertebrobasilar arteries, whereas the anterior cerebral artery flow territory on the occluded side is mainly supplied by the contralateral ICA ($P<0.05$). In patients with bilateral ICA occlusion, the vertebrobasilar arteries supplied a significantly ($P<0.05$) larger part of the MCA and ACA flow territories compared with those in the control subjects.[56]

Rutgers et al prospectively studied 112 patients with symptomatic ICA occlusion and quantitative volume flow and COW was assessed with MRA the ophthalmic artery with TCDS, and leptomeningeal anastomoses with conventional angiography. During 49±14 months of follow-up (mean SD), 7 patients had recurrent ipsilateral ischemic stroke. Compared with patients without recurrent stroke, these patients had significantly higher total flow to the brain, i.e., ICA+BA flow (mean 536 mL/min versus 410 mL/min;$P <0.05$), and significantly higher contralateral ICA flow (355 mL/min versus 209 mL/min;$P<0.001$), whereas BA and MCA flow showed no significant differences. Also, they more often had Willisian collateral flow ($P<0.05$), mainly caused by increased collateral flow via the PCoA (71% versus 28%; $P<0.05$), whereas collateral flow via the OA and leptomeningeal anastomoses did not differ significantly. Hence they concluded that recurrent ipsilateral ischemic stroke in patients with symptomatic ICA occlusion is associated with high volume flow to the brain and increased collateral PCoA flow.[40]

The above study showed that, the increased collateral flow was a risk for recurrent neurological events and the authors hypothesised that compensatory increase of flow in the ICAs and BA and recruitment of collateral pathways indicate more

severe cerebral hemodynamic failure. They may be an early indicator of increased risk of future ischemic events. This study had many limitations as only patients with TIA or minor stroke were included and the collateral circulation was assessed within 6 months. It has been suggested that cerebral hemodynamics can change over time after qualifying symptoms occurred. Multiple modalities were used for the assessment of collaterals and treatment aspects were not mentioned in the study. Leptomeningeal collateral flow was not assessed at the same time point as collateral flow in the circle of Willis. To fully appreciate the role of collateral pathways in ICA occlusion it would be preferable to investigate these collaterals at the same time.

Given the absence of recurrent symptoms, patients without recurrent stroke apparently functioned well with the relatively low total cerebral blood flow in the contralateral ICA and BA. Authors speculated that the brain in these patients adapted well to the carotid occlusion and could stand relatively low blood flow to the brain.

No other study has assessed flow across large arteries and outcome in ICA occlusion patients which showed high flow was associated with poor outcome. In most other studies the presence of good collateral circulation is associated with good outcome

Symptomatic side M1 was reformed in 61 patients (93.9%) while in 4 patients (6.1%) M1 segment was not visualized in our study subjects. Various studies have shown than in ICA occlusion reformed M1 segment reduces the infarct size and improves the outcome. Kim et al in a retrospective study showed favourable outcomes at 3 months was significantly higher in patients with collateral MCA flow than those without (41.7% vs. 12.5%, respectively). This study showed that in acute ischemic

stroke with ICA occlusion, patients with collateral MCA flow had less severe initial stroke symptoms and a better outcome at 3 months than those without. However this study had a small sample size, was retrospective in nature, utilised MRA for vascular imaging and has not studied leptomeningeal collaterals.[57]

There was no difference in mean age and gender between good and poor leptomeningeal flow groups in our study. The risk factor profile like diabetes mellitus, hypertension and smoking was slightly higher in the good leptomeningeal circulation group but the results were not statistically significant.

The median NIHSS was 17 in patients with poor leptomeningeal collaterals while median NIHSS was only 7 in good leptomeningeal collateral group. In a retrospective study of sixty-five patients (42 men, 23 women) the initial NIHSS scores were significantly lower, and favourable outcomes at 3 months were better in patients with collateral MCA flow than in those without ($P< 0.001$). Collateral MCA flow was defined as the presence of MCA signals from proximal M1 to distal MCA branches ipsilateral to the ICA occlusion by magnetic resonance angiography. Baseline clinical variables including risk factors did not differ between the two groups (No collateral MCA versus MCA collateral present). Initial NIHSS scores were significantly lower in patients with collateral MCA flow than in those without (median; 6 vs. 13, respectively; $P< 0.001$). [57]

The NIHSS score was significantly lower in patients with good collaterals than in patients in the other two groups (NIHSS 16 vs18, $p=0{\cdot}012$). Robust collaterals as evident on CT angiography were associated with smaller stroke size and better prognosis in patients with MCA occlusions with smaller stroke size and better

prognosis in patients with MCA occlusions.[4] Our study also showed that good leptomeningeal collaterals was associated with lower baseline NIHSS (p=0.01) and higher ASPECTS (p=0.02) which predicted a good outcome.

In atherosclerotic ICA occlusion, 34 (79.1%) patients had good leptomeningeal collaterals while only 9 (20.9%) patients had poor leptomeningeal collateral flow. However in acute ICA occlusion like in dissection and embolism the 9 (40.9%) patients had poor collateral circulation while 13 (59.1%) patients had good leptomeningeal collateral flow (p=0.03). Although the aetiology of ICA occlusion was not predictor of outcome it was a predictor of leptomeningeal collateral formation. Among 31 patients with good outcome, 28 (90.3%) patients had good leptomeningeal collaterals and 3 (9.7%) patients had poor leptomeningeal collaterals and the results were statistically significant.

In our study only 4 patients died and all had territorial infarct and had higher baseline NIHSS and ASPECTS with 3 of them had poor leptomeningeal collateral formation. Only 1 patient underwent thrombolysis and had good outcome with mRS 1. The rest of the patients were not thrombolysed since they were out of the time window or had contraindications.

Patients with ICA occlusion were younger (mean age 57 ±11.6) and majority of them were males in our study. In a retrospective, population-based study from Minnesota residents with symptomatic ICA occlusion the mean age was 66.2 (range 40.4 to 87.6) and the males were 73%. [27] Rutgers et al in a study of 112 patients, the mean age was 61±0.9 years and 82% were males.[40] Kim et al in a retrospective study of 65 patients (42 men; 23 women), mean age was 68.43 ± 1.19 years.[57] It is assumed

that the average age of patients with stroke in developing countries is usually 15 years younger than those in developed countries. [58]

Among the vascular risk factor profile 29 patients (44.6%) had hypertension, 17 patients (26.2%) had diabetes mellitus and 40 patients (61.5%) were smokers. Fourteen patients (21.5%) had cardiac disease with coronary artery disease in 12, valvular heart disease and atrial fibrillation in 1 patient each. Previous ischemic events were noted in 14 patients (21.5%) and among them 4 patients had transient ischemic attack or stroke within 2 weeks prior to the present clinical event.

In population based retrospective study in symptomatic ICA occlusion patient's diabetes, coronary artery disease, dyslipidemia, prior cerebral infarction, smoking, and hypertension was seen in 21%, 43%, 54%, 16%, 76% and 65% respectively.[27] In our study also the vascular risk profile was almost similar with slightly lower prevalence of CAD in our study.

TIA was the presenting event in 4 patients (6.2%) and the 61 patients (73.8%) presented with stroke in our study population. The median NIHSS at presentation was 10 (range 0-22) and 16 patients (24.6%) had NIHSS of less than 5 and 49 patients (75.4%) had NIHSS 5 or more at presentation to our hospital. Among the 65 patients, 24 (36.9%) had MCA territory infarct, 23 (35.4%) had hemodynamic infarct either in MCA- PCA or MCA- ACA watershed region or internal border zone infarcts and 18 (27.7%) had either small cortical or superficial infarcts. Eight (12.3%), 15 (23.1%) and 42 (64.6%) patients had poor, intermediate and good ASPECTS respectively.

A prospective study of 177 consecutive patients with first-ever ischemic stroke associated with ICA occlusion from the Perugia Stroke Registry had mean age of 71.4 +/- 14.3 years and 53% were males. The most probable cause of occlusion was atherosclerosis in 65%, cardioembolism in 22%, dissection in 9% and other causes in 4%.[53] In our study 66% had atherosclerotic ICA occlusion, 30.8% had dissection and 3.1% had embolic ICA occlusion

The mean age in years is 59.58±10.84 and 56.3±13.2 in good outcome and poor outcome group respectively. In our study age was not related to outcome in contrast to many previous studies where older age was related to poor outcome. Sixteen (59.3%) patients in the age group more than 60 years had good outcome while 11 (40.7%) patients had poor outcome and the results were not statistically significant. Majority of the patients were males and gender had no significant association with outcome. In our study only 8% were women and hence the results were not comparable due to small sample size.

The absence of history of dyslipidemia was associated with good outcome (p=0.05) while the other vascular risk factors like hypertension, diabetes, CAD, smoking and prior ischemic events was not related to outcome.

The median baseline NIHSS was 5 and 15 in good outcome and poor outcome group respectively. Among 49 patients who had NIHSS >5, 33 patients (65.3%) had poor outcome and only 17 (34.7%) patients had good outcome. (p=0.004). The aetiology of ICA occlusion had no influence in outcome and the results were not statistically significant. As in many previous studies our study also showed that poor ASPECTS correlated with poor outcome (p=0.01).

In our study, patients with territorial infarct had poor outcome when compared to watershed infarcts or small infarcts (70.8%, 56.5% and 22.2% respectively; p=0.02). The development of territorial infarcts in ICA occlusion may result due to lack of collateral formation or due to tandem M1 occlusion. Since M1 occlusion patients were excluded the more likely reason for territorial infarct and hence poor outcome may be due to inadequate collateral circulation.

LIMITATIONS

1. Only 65 patients with symptomatic ICA occlusion was included which was a small sample size.
2. There were no validated methods for the assessment for the collateral circulation. In this study the grading of collaterals was done using the CT angiogram grading done in other larger studies.
3. Noninvasive approaches as in CTA can only assess the simple presence or absence of Willisian or ophthalmic collaterals, and cannot assess the extent of collateral filling of each pathway or the contribution of leptomeningeal anastomosis as better delineated in DSA. But DSA is an invasive approach and not fesible in acute setting.
4. The timing of presentation of patients after index event was variable and we included patients who has presented within 3 weeks. So baseline NIHSS and CTA on the day one is not available due to the delay in presenting to our hospital.
5. Whether patients already on antiplatelets and statins prior to the initial presentation would modify the outcome and collateral formation was not studied.
6. Most of the patients who had symptomatic ICA occlusion had intracranial stenosis of large vessels in the same or opposite side which may influence the outcome and was not considered in this study.

CONCLUSIONS

- The median mRS at 90 day follow up of 65 symptomatic ICA occlusion patients was 3 (range 0-6) and 31 (47.7%) patients had good outcome (mRS≤2). The mortality rate was 6% (4 patients) and recurrent vascular events were 3% (2 patients).

- In univariate analysis, good collateral flow through ipsilateral ophthalmic artery, ipsilateral posterior communicating artery and presence of good leptomeningeal collateral circulation were predictors of good outcome.

- Higher baseline NIHSS, history of dyslipidemia, higher random blood sugar levels in emergency department, low ASPECTS and territorial infarct were predictors of poor outcome.

- In multivariate analysis, good collateral flow through ipsilateral ophthalmic artery (OR 6.4; CI 1.34-30.42) and good leptomeningeal collateral circulation (OR 4.85; CI 0.96-24.55) were independent predictors of good outcome.

- The presence of vascular risk factors in symptomatic ICA occlusion had no association with outcome or collateral formation.

- Patients with at least 2 collateral pathways had better outcome when compared to subjects with none or only 1 collateral ($p<0.05$).

- Our study shows that assessment of collateral circulation using CT angiogram has a role in predicting the stroke severity and outcome in patients with symptomatic ICA occlusion.

- Further larger prospective short term and long term outcome studies are required in symptomatic ICA occlusion patients with special reference to the collateral circulation and recurrence of neurological events.

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SYMPTOMATIC ICA OCCLUSION- CTA AS A PREDICTOR OF OUTCOME

1. DEMOGRAPHIC DATA

1.1. Name of the patient: .....

1.2. Hospital number: ..... 1.3. MRD number: .....

1.4. Gender.....1. Male 2. Female 1.5. Age: .....

1.6. Address: .....

1.7. Date and time of symptom onset: ....

1.8. .Date and time of admission: .....

1.9. . MRS prior to present event:……

2. RISK FACTORS (1=YES, 2=NO)

2.1. Hypertension: ..... Duration: .....

2.2. Diabetes mellitus: ..... Duration: .....

2.3. Current smoking: ..... Duration.....

2.4. Coronary artery disease: ..... Duration.....

2.5. Valvular heart disease: ..... Duration.....

2.6. Congestive heart failure: ..... Duration.....

2.7. Peripheral vascular disease: ..... Duration.....

2.8. Hyperlipidaemia: ..... Duration.....

2.9. Atrial fibrillation: ..... Duration.....

2.1.1. History of prior stroke: .....

2.1.2. History of prior TIA: .....

2.1.3. Known carotid artery disease: .....

2.1.4. Patients currently on treatment ---------- 1.Yes 2.No

2.1.5. If yes,Type of treatment ---------- 1.ASA 2.clopidogrel 3.Aggrenox 4.oral anticoagulants

2.1.6 History of ocular symptoms:…… 1. Transient blindness 2. Progressive loss of vision 3. Retinal claudication 4. none

3. SYMPTOMS

3.1. Visual disturbances: .....1. Absent 2.Amaurosis fugax 3. Blindness 4. hemianopia

3.2. Weakness: ..... 1. Absent 2. Face alone3.arm 4.leg 5.arm and leg6. Arm and face

3.3. Numbness./paresthesia:..... 1. Absent 2. Present

3.4. Speech disturbances: .....1. Absent 2.Aphasia 3.Dysarthria

3.5. Vertigo: ..... 1. Absent 2. Present

3.6. Headache: ..... 1. Absent 2. Present

3.7. Confusion: ..... 1. Absent 2. Present

3.8 loss of consciousness: ..... 1. Absent 2. Present

3.9. Neck pain: ..... 1. Absent 2. Present

4. CLINICAL EXAMINATION (1=ABSENT, 2=PRESENT)

4.1. Pulse: ..... (If Regular =1, Atrial fibrillation =2) rate:...../min

4.2. Blood pressure: Systolic.....mmHg diastolic .....mmHg (first documented BP)

4.3. Blood pressure: Systolic.....mmHg diastolic .....mmHg at time of presentation

4.4. Weakness ..... 1. None 2. Upper limb alone 2. Lower limb alone 3.both upper and lower limb

4.5: .Dysarthria..... 4.6. .Aphasia: .....

4.7. Facial weakness: ..... 4. 8.Cerebellar signs.....

4.9. Sensory: ..... 4.1.1: Hemi spatial neglect .....

4.1.2. Final impression: .....1.Right hemispheric 2.Left hemispheric

4.1.3NIHSS at the time of presentation to local hospital.(if available) ----------

4.1.4. NIHSS score at time of presentation to our department: .....

4.1.5. mRS at time of presentation to our department: .....

4.1.6. NIHSS score at 24 hours if patient was admitted within 24 hours of ictus: .....

5. INVESTIGATIONS

5.1. Blood glucose in ED: .....

5.2. Serum cholesterol: .....

5.3. Serum LDL: .....

5.4. Serum HDL cholesterol: .....

5.5.Serum triglycerides: .....

5.6. ECG: 1.Normal 2.LVH 3.AF

5.7. Echo-trans thoracic ..... 1.Normal 2.LV dysfunction 3.Mural thrombus 4.Valve disease 5.PFO

5.8. Transesophageal.....1.Normal 2.LV dysfunction 3.Mural thrombus 4.Valve disease 5.PFO 6.Aortic plaques 7. Not done

5.9. Holter monitoring .....1.Normal 2.Atrial fibrillation 3.Atrial flutter 4. Not done

6. NEUROIMAGING

6.1. Date of CT scan brain imaging: ……

6.1.1 CT scan brain..... 1. Normal 2.Territorial infarct 3. Other cortical infarcts 4. Small superficial infarcts 5. Internal border zone infarct 6. Small deep infarcts 7. Other deep infarcts 8. Not done

6.1.2 CT brain ASPECTS: ……..

6.1.3. Specify findings, if abnormal: ……..

6.1.4. Repeat CT scan done on: ……..

6.1.5. Hemorrhagic transformation in repeat CT scan: ……. 1. Absent 2. Present

6.2. CT angiogram neck

Ipsilateral ICA: ……. 1. Atherosclerotic 2. Dissection 3. Embolic 4. Undetermined

6.2.1. Contralateral ICA stenosis 1. <50% 2. 50-70 % 3. 70-90% 4. >90% 5. Absent

6.3 CT angiogram intracranial vessels:

Ipsilateral Intracranial ICA: ……1. Normal 2. Occlusion 3. Stenosis

6.3.1. Contralateral intracranial ICA: ……1. Normal 2. Occlusion 3. Stenosis

6.4. CT angiogram of ipsilateral MCA flow

6.4.1. M1 segment: ……. 1. Normal 2. < 50% stenosis 3. > 50% stenosis 4. Occluded

6.4.2. M2 segment: ……. 1. Normal 2. Occluded

6.4.3. M3 segment: …….. 1. Normal 2. Occluded 3. Cannot comment

6.5. Collaterals in CTA:

6.5.1. Anterior communicating artery: …….. 1. Absent 2. Probably present 3. Hairline 4.definitely presents 5. Robust

6.5.2. Posterior communicating artery: ……. 1. Absent 2. Probably present 3. Hairline 4.definitely presents 5. Robust.

6.5.3. Ophthalmic artery: …… 1. Absent 2. Present

6.5.4. Leptomeningeal collaterals: …… 1. Absent 2. Less than the contralateral unaffected side 3.Equal to the contralateral unaffected side 4. More than the contralateral unaffected side

6.5.5 Final impression on collateral circulation: …….. 1. absent 2. Present

6.6. MRI brain scans..... 1. DWI negative 2.DWI positive 3. Not done

6.6.1. DWI positive lesions, whether: ..... 1. Single 2. Multiple

6.6.2. DWI lesions whether: …….. 1.Territorial infarct 2. Other cortical infarcts 3. Small superficial infarcts 4. Internal border zone infarct 5. Small deep infarcts 6. Other deep infarcts 7. Normal

6.6.3 MRI findings specify: .....

6.7. Side of involvement ----------1. Right 2. Left

6.8. Final diagnosis: …….. 1. TIA 2. Minor Stroke 3. Major stroke

6.8.1. Etiology of TIA/ stroke: ..... 1.Large vessel atherosclerosis 2 dissection.3. Cardioembolic 4.Undetermined

7. TREATMENT GIVEN (1. YES 2. NO)

7.1. Aspirin: ..... 7.2. Clopidogrel: .....

7.3. Aggrenox.: ..... 7.4. Warfarin: .....

7.5. Statins: ..... 7.6.Antihypertensives: .....

7.7. CEA on opposite side done …… 1. Yes 2. No

7.8. Date of CEA……

8. FOLLOW UP AT 90 DAYS

8.1. Outcome at 3 months: .....1.normal 2. new vascular events

8.2. If new vascular event then cause:…….. 1.TIA 2. Minor stroke 3. Major stroke 4. Cardiovascular

8.2.1. Date of event: .....

8.3. Blood Pressure:…… 1. Controlled 2. Uncontrolled

8.4. Blood Sugar :…… 1. Controlled 2. Uncontrolled

8.5. Modified Rankin scale at 3 months: .....

8.6. NIHSS score at 3 months: .....

8.7. If died, cause of death: .....1.Vascular 2.Non vascular.

8.7.1. If vascular,specify : ……..