INTRODUCTION

According to the World Health Organization, about 15 million people suffer a stroke each year with roughly one-third resulting in death and another one-third sustaining severe permanent disability. Even in developed nations, stroke is the third leading cause of death. It also costs billions of dollars through lost productivity, premature mortality and care for stroke survivors ***(Offner et al., 2017).***

Due to the high incidence and recurrence rate of Acute ischemic stroke it mandates aggressive and rapid evaluation and management from the moment of symptom onset ***(Lazzaro et al., 2010)***.

Extra cranial severe carotid stenosis or occlusion is a known risk factor for ischemic stroke. The risk of stroke increases in patients with concurrent severe stenosis of extra- and intracranial vessels ***(De Silva et al., 2007).***

Cerebral ischemia is a result of acute arterial occlusion or severe narrowing resulting in impaired blood flow to the brain tissue. Collateral circulation is a dynamic system that helps in preserving cerebral perfusion along with pathophysiologic changes. Recruitment of these anastomosis has a huge role in cerebral homeostatic response to ischemia when the primary pathways fail to provide perfusion to critical parts of the brain ***(Liebeskind et al., 2003)***.

These anastomotic conduits include ‘primary collaterals’ which are a part of the circle of willis and secondary collaterals which are the distal counterpart include leptomeningeal or pial vessels ***(Liebeskind et al., 2005)***.

During acute ischemia, primary collaterals supply blood flow to large portions of cerebral hemispheres in both anterior and posterior circulations, while secondary collaterals, including the leptomeningeal vessels and ophthalmic artery, have a less direct connection that evolves gradually providing additional support at times of cerebral ischemia forming anastomotic connections between internal and external carotid.

Acute cerebral ischemia usually triggers the recruitment of both primary as well as secondary collaterals that supply cortical blood flow in a retrograde fashion **(*Dissing-Olesen et al., 2015).***

The cerebral collaterals are recruited to compensate the decreased intracranial blood flow to maintain cerebral homeostasis. The phenomenon of reversed ophthalmic artery flow (ROAF) is well known, but its clinical implication in patients with severe cervical carotid stenosis remains poorly understood ***(van Everdingen et al., 1998).***

The evaluation of hemodynamics, autoregulation and collaterals is cardinal for clinical outcomes, **(*Xiong et al., 2017).*** Advanced neuroimaging techniques provide detailed

information and allows interpretation of collateral circulation, especially in the setting of acute proximal vessel occlusions to determine the pathophysiology and predict the clinical outcome ***(Malhotra et al., 2015).***

Doppler ultrasonography is used for the diagnosis of internal carotid artery (ICA) stenosis. It has shown to have >90% sensitivity when compared with angiography if performed by experienced sonographers ***(Jogestrand et al., 2002).***

The Use of Transcranial Doppler (TCD) in detecting reversal of blood flow direction especially in anterior communicating and ophthalmic arteries, and flow diversion between anterior and posterior circulation provide critical information on ipsilateral collateral status ***(Kim et al., 2009).***

The impact of collateral status has been correlated with clinical symptoms, reperfusion success and functional outcome at discharge. A rationale now exists for imaging assessment to guide physicians in the precision medicine of stroke care ***(Liebeskind et al., 2017)***.

AIM OF THE WORK

The aim of study was:

1. Evaluation of hemodynamics in ophthalmic artery as a collateral.

2. Its value as a prognostic factor.

In patients with extra cranial carotid artery stenosis in acute cerebrovascular stroke.

CHAPTER ONE

VASCULAR ANATOMY

The brain is one of the most perfused organs in the body, it is supplied by two vascular systems; the anterior circulation that originates in the internal carotid arteries and the posterior (vertebrobasilar) circulation that originates in the vertebral arteries ***(Drake et al., 2015).***

The Internal Carotid Artery (ICA) supplies the anterior part of the brain, the eye and its appendages, and sends branches to the forehead and nose. It has a number of curvatures along its course. It occasionally has one or two flexures near the base of the skull, while in its passage through the carotid canal and along the side of the body of the sphenoid bone, it describes a double curvature and resembles the italic letter S ***(Felten et al., 2015).***

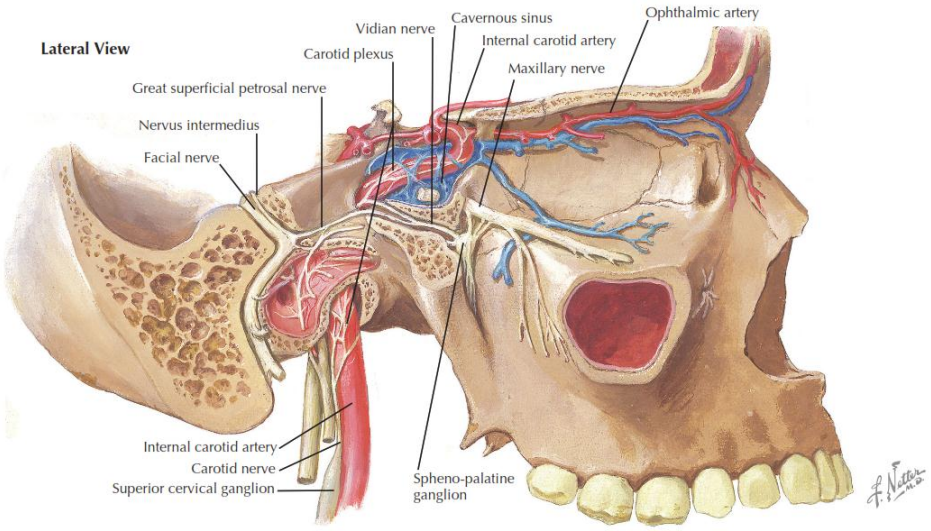

Figure (1): Shows the course of ICA after bifurcation of CCA. Netter's Atlas of Neuroscience - 3rd edition, 2015.

The left common carotid is a direct branch of the arch of aorta while the Right common carotid arises from the arch's second branch the Brachiocephalic trunk ***(Drake et al., 2015).***

The common carotid artery then ends by splitting into the ICA and the External Carotid Artery(ECA) at the upper border of the thyroid cartilage.

The ICA is divided into four portions: cervical, petrous, cavernous, and cerebral.

The Cervical Portion begins at the bifurcation of the common carotid, and runs perpendicularly upward, to the carotid canal in the petrous portion of the temporal bone. It lies behind and lateral to the external carotid in the carotid triangle. It is in relation, behind, with the Longus capitis, the superior cervical ganglion of the sympathetic trunk, and the superior laryngeal nerve; laterally, with the internal jugular vein and vagus nerve. At the base of the skull the glossopharyngeal, vagus, accessory, and hypoglossal nerves lie between the artery and the internal jugular vein ***(Henry Gray, 2016).***

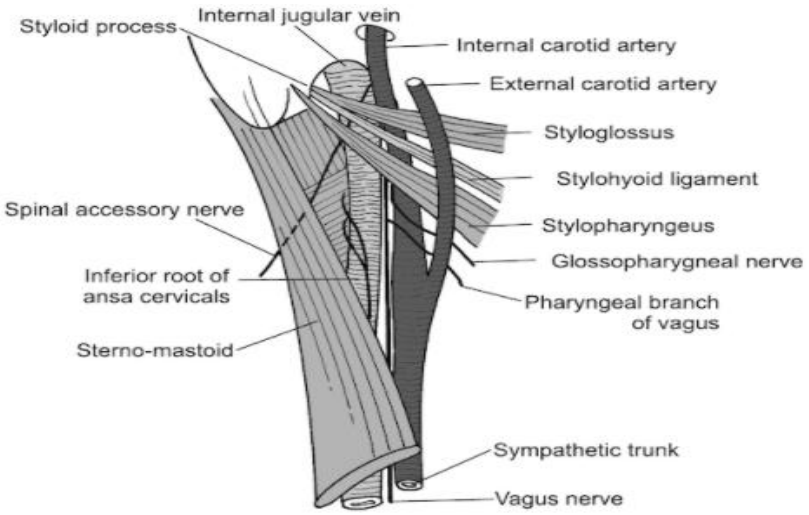

Figure (2): Structures intervene between ECA and ICA ***(Mahdi and Partap, 2009).***

The Petrous Portion begins when the internal carotid artery enters the canal in the petrous portion of the temporal bone, it first ascends a short distance, then curves forward and medial ward, and again ascends as it leaves the canal to enter the cavity of the skull. The artery lies at first in front of the cochlea and tympanic cavity. Farther forward, it is separated from the semilunar ganglion by a thin plate of bone, which forms the floor of the fossa for the ganglion and the roof of the horizontal portion of the canal. Frequently this bony plate is more or less deficient, and then the ganglion is separated from the artery by fibrous membrane. The artery is separated from the bony wall of the carotid canal by a prolongation of dura mater, and is surrounded by a number of small veins and by filaments of the carotid plexus, derived from the ascending

branch of the superior cervical ganglion of the sympathetic trunk ***(Nein et al., 2010).***

In the Cavernous Portion the artery lies between the layers of the dura mater forming the cavernous sinus, but covered by the lining membrane of the sinus. It at first ascends toward the posterior clinoid process, then passes forward by the side of the body of the sphenoid bone, and again curves upward on the medial side of the anterior clinoid process, and perforates the dura mater forming the roof of the sinus. This portion of the artery is surrounded by filaments of the sympathetic nerve, and on its lateral side is the abducent nerve ***(Mahdi and Partap, 2009).***

The Cerebral Portion starts after the ICA perforates the dura mater on the medial side of the anterior clinoid process, it then passes between the optic and oculomotor nerves to the anterior perforated substance at the medial extremity of the lateral cerebral fissure, where it gives off its terminal or cerebral branches ***(Mahdi and Partap, 2009).***

The length of the internal carotid varies according to the length of the neck, and according to the point of bifurcation of the common carotid. The course of the artery, instead of being straight, may be very tortuous ***(Henry Gray, 2016).***

The cervical portion of the internal carotid gives off no branches while the intracranial part gives origin to the ophthalmic

artery, anterior choroidal, posterior communicating artery and eventually terminating at the medial end of the lateral sulcus immediately after giving rise to the posterior communicating artery, by dividing into the Anterior Cerebral Artery (ACA) and the Middle Cerebral Artery (MCA) ***(Wanda, 2017).***

The ophthalmic artery arises from and is the first major branch of the internal carotid, just as it is emerging from the cavernous sinus, on the medial side of the anterior clinoid process, then it enters the orbital cavity through the optic foramen, below and lateral to the optic nerve. It passes over the nerve to reach the medial wall of the orbit, and then horizontally forward.

The branches of the ophthalmic artery divided into an orbital group, which supplies the orbit and its surrounding parts; and an ocular group, which reaches the muscles and bulb of the eye ***(Mahdi and Partap, 2009).***

Orbital group consists of Lacrimal, Anterior Ethmoidal, Posterior Ethmoidal, Medial Palpebral, Supraorbital, Dorsal Nasal and the Frontal artery. While the Ocular group included the Central artery of Retina, Short Posterior Ciliary, Long Posterior Ciliary and the Anterior Ciliary artery.

As a result of its position as the first branch of the ICA, emboli from atherosclerotic plaques found at the bifurcation of the common carotid artery may dislodge and reach

the ophthalmic artery, resulting in a transient ischemic attack with the symptom of transiet blindness (amaurosis fugax) in the affected eye ***(David Felten, 2016).***

The anterior choroidal artery gives deep branches to the posterior two-thirds of the internal capsule, adjacent optic and auditory radiations, medial portion of the globus pallidus, and tail of the caudate nucleus; and superficial branches to piriform cortex and uncus, hippocampal head, amygdala, and most lateral portion of the thalamic lateral geniculate nucleus ***(Palomeras, 2008).***

The Anterior Cerebral Artery (ACA) is one of the terminal branches of the ICA, it courses anteromedially over the superior surface of the optic chiasm, toward the longitudinal fissure.

Shortly afterwards, it forms an anastomosis with the contralateral ACA which is called the anterior communicating artery.

The ACA is divided into five segments A1-5. As it proceeds beyond A1, it begins its posterior course toward the parieto-occipital sulcus, following the contour of the callosal sulcus between the two cerebral hemispheres. Throughout this whole course, the ACA provides deep and cortical branches; these arise from the proximal and distal portions of ACA, respectively.

The ACA primarily supplies blood to the medial aspect of the cerebral cortical surface. This area includes portions of the frontal lobes and the superomedial parietal lobes ***(Kim, 2016).***

The Middle Cerebral Artery (MCA) is the most common site of stroke, also large-territory MCA strokes often carry a very poor prognosis as it supplies many critical cerebral structures along its course. The artery has a relatively consistent route and is divided into multiple segments ***(Sada, 2014).***

It originates from the bifurcation of the ICA, just lateral to the optic chiasm at the medial end of the Sylvian and then passes laterally along the ventral surface of the frontal lobe, entering the Sylvian fissure between the temporal lobe and insular cortex. Within this area, the artery divides, giving rise to two or three principal trunks. These trunks extend superiorly and inferiorly over the insular surface, supplying and extending over most of the lateral surface of the cerebral hemisphere including all of the insular cortex, opercular surface, the superior and middle temporal gyri, the inferior parietal lobule and much of the postcentral gyrus, and a frontal territory that includes the inferior and middle frontal gyri, much of the precentral gyrus, and the lateral part of the orbital surface ***(Walcott, 2014).***

The posterior cerebral circulation supplies many of the nervous system's most critical centers. Also known as the

vertebrobasilar circulation, it consists of the vertebral arteries, the basilar artery and several branches from these main conduits. This circulation supplies blood to the posterior portion of the brain which includes the occipital lobe, the brainstem, and the cerebellum ***(Walcott, 2014).***

The Basilar artery is formed by the union of the vertebral arteries, it then travels along the midline anterior pons, and terminates near the pontomesencephalic junction. After entering the brain through the foramen magnum it gives rise to two important branches. The posterior inferior cerebellar artery (PICA) which supplies the dorsolateral region of the medulla and a region of the ventral surface of the cerebellar hemispheres. and a small branch which joins its contralateral counterpart to form the descending midline anterior spinal artery ***(Chandra, 2017).***

During the basilar artery course, it gives several perforating arteries to the pons, the anterior inferior cerebellar and superior cerebellar arteries which supply a broad cerebellar territory, and much of the posterior cortical surface through its terminal split into the posterior cerebral arteries (PCAs) ***(Chandra,2017).***

Posterior cerebral artery (PCA) usually arises bilaterally from the terminal bifurcation of the basilar arteries, it then encircles the midbrain at the pontomesencephalic junction, it supplies the posterior, medial and basal aspects of the cerebral hemisphere ***(Chandra, 2017).***

CHAPTER TWO

CEREBRAL COLLATERALS

The collateral circulation is a physiologic pathway of specialized endogenous bypass vessels that is present in most tissues and protects against ischemic injury during initial oligemic status ***(Faber, 2014).***

In the brain the anatomy of this arterial circulation includes an extra cranial source which can supply intracranial vessels, along with an intracranial route that can supply other intracranial areas when pathophysiologic mechanisms become activated ***(Faber, 2014).***

The intracranial collateral perfusion of the brain consists of a primary and secondary route.

The primary pathways include the permanently active components of the circle of Willis, and the secondary pathways include less direct routes that develop over time. The blood supply to the brain is unique because four major arteries coalesce to form a system of communication, i.e., the circle of Willis, which, despite its variability and asymmetry, can redistribute blood flow in the event of sudden occlusion of a parent vessel ***(Nieuwenhuys, 2007).***

The *circle of Willis* interconnects the anterior cerebral artery and the internal carotid artery of both sides with the vertebro-basilar system. It is located at the base of the brain and

surrounds the infundibulum and the optic chiasm. It includes the *anterior communicating artery*, which interconnects the anterior cerebral arteries, immediately in front of the optic chiasm, and the two *posterior communicating arteries*, which form an anastomosis between the most distal part of the internal carotid and the posterior cerebral artery near their origin from the basilar artery ***(Nieuwenhuys, 2007).***

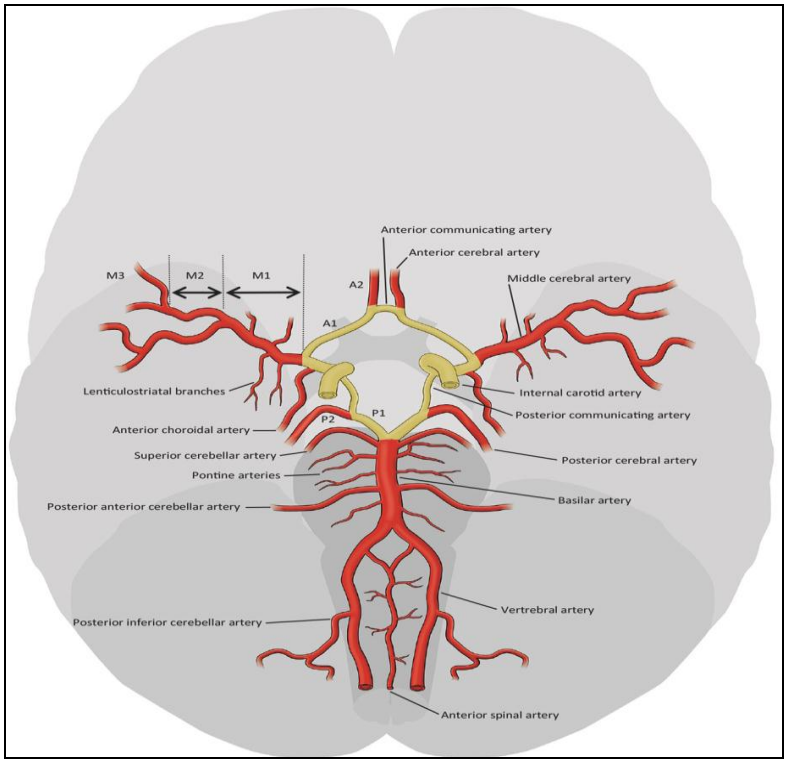

Figure (3): Showing the anatomy of circle of willis ***(Stroke Guidelines of the University Hospital of Bern 2017).***

The external carotid artery gives rise to many branches in the neck that are potential sources of collateral blood flow, particularly when chronic stenosis or occlusion has developed in the internal carotid artery, the facial, maxillary, middle

meningeal, and occipital arteries are the main branches that can shunt flow via anastomoses to the intracranial arteries. Apart from these branches, common anastomotic routes include the ophthalmic artery. *The ophthalmic artery* provides blood supply to the eye via multiple short posterior ciliary arteries and the central retinal artery communicates with the middle meningeal artery and the sphenopalatine branch of the ECA, it which may fill in a retrograde direction to serve as a circulatory collateral ***(Liebeskind, 2014).***

Extra cranial severe carotid stenosis or occlusion is a known pathogenic factor for ischemic stroke. Cerebral collaterals are recruited to compensate for diminished intracranial blood flow to maintain cerebral homeostasis, including the circle of Willis as the primary collateral pathway and ROAF as the secondary collateral, ROAF can occur as a result of intracranial hemodynamic compromise with insufficient collaterals from the circle of Willis ***(Chang et al., 2009)***.