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Optical coherence tomography angiography in patients with cerebral small vessel disease

Thesis

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Sara Mohammad

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List of Abbreviations

Abb.	Full term
Aβ	Amyloid- beta
BBB	Blood brain barrier
CMBs	Cerebral microbleeds
CSF	Cerebro spinal fluid
CSVD	Cerebral small vessel disease
DCP	Deep capillary plexus
DOCT	Doppler OCT
DR	Diabetic retinopathy
DVP	Deep vascular plexus
DWI	Diffusion weighted images
DWMH	Deep white matter hyperintensities
EPVS	Enlarged perivascular spaces
FA	Fluorescein angiography
FAZ AI	Foveal avascular zone acircular index
FAZ FD	Foveal avascular zone foveal density
FAZ	Foveal avascular zone
FLAIR	Fluid attenuated inversion recovery
GCC	Ganglion cell complex
GCL	Ganglion cell layer
INL	Inner nuclear layer
ISF	Interstitial fluid
LACS	Lacunar stroke clinical syndrome
MMSE	Mini-mental state examination
MRA	Magnetic resonance angiography
MRI	Magnetic resonance image
mRS	Modified Rankin scale

List of Abbreviations Cont...

Abb.	Full term
NFL	Nerve fiber layer
NIHSS	National institutes of health stroke scale
NMOSD	Neuromyelitis optica spectrum disorders
OCT	Optical coherence tomography
OCTA	Optical coherence tomography angiography
ONH	Optic nerve head
PVH	Periventricular hyperintensities
RGC	Retinal ganglion cells
RNFL	Retinal nerve fiber layer
RPC	Retinal peripapillary capillary
RPCP	Radial peripapillary capillary plexus
RSSI	Recent single subcortical infarction
SCP	Superficial capillary plexus
SVD	Small vessel disease
SVP	Superficial vascular plexus
VEGF	Vascular endothelial growth factor
WMH	White matter hyperintensities

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INTRODUCTION

Cerebral small vessel disease (CSVD) refers to all pathological changes affecting the small vasculature of the brain including; small perforating arterioles, capillaries and venules ***(Zhang et al., 2020).***

Vascular risk factors that are commonly found in large vessel disease have shown to contribute to CSVD, as well, including hypertension, diabetes mellitus, smoking and dyslipidemia. Also old age is considered to be a risk factor as the prevalence of CSVD increases with age ***(Cannistraro et al., 2019).***

Cerebral amyloid angiopathy is one of the suggested underlying pathologies in some cases of CSVD ***(Zoppo et al., 2014).***

Clinically, CSVD accounts for 25% of ischemic strokes and 50% of dementias ***(Zhang et al., 2020).***

It may present as acute events (focal neurological deficit) known as lacunar syndrome or chronic events as mild cognitive dysfunction, dementia, mood disorders, gait disturbance, sleep disorder and urinary incontinence. Also, it may be a symptomatic ***(Chen et al., 2019).***

Although CSVD is a common reason for strokes and vascular dementia, pathogenesis is still poorly understood. It is suggested that the endothelial dysfunction in cerebral

microvessels may be a key problem. Endothelial failure leads to increased permeability and increased leakage into the vessel wall and the surrounding tissue, damaging of the vessel wall, inflammation, demyelination, glial scar formation, thickening and stiffness of vessels leading to failure of autoregulation, narrowing of the lumen and occlusion, causing featured focal ischemic lesions in the brain parenchyma ***(Wardlaw et al., 2013).***

Neuroimaging markers seen on MRI are classified into: Recent small subcortical infarct (DWI), Lacune of presumed vascular origin (FLAIR), White matter hyperintensity of presumed vascular origin (FLAIR), Perivascular space (T1, T2), cerebral microbleed (T2*-weighted GRE/SWI) ***(Chen et al., 2019).***

The changes in brain microvasculature are difficult to be visualized in vivo. Because of similarities between brain and retina in anatomy, embryology and physiology, investigating the retinal vessels network may reflect the brain condition ***(Lee et al., 2020).***

Optical coherence tomography angiography (OCTA) is a novel, real-time and noninvasive technique to detect retinal and choroidal blood flow in vivo ***(Tsokolas et al., 2020).***

The retinal capillary network is arranged anatomically into several layers as which are: 3 macular plexuses, 4 plexuses in peripapillary region and one capillary layer in midequatorial

and anterior zones where the retina is thinner. OCTA devices are based on (en face) approach to get information of the superficial and deep plexuses. 4 en face zones are detected: superficial plexus in ganglion cell layer, deep plexus, photoreceptors(outer retina) and choriocapillaris. For each en face zone, the indices of perfusion could be reached ***(Sambhav, 2017).***

OCTA has a big advantage over classic methods as retinal microvasculature is segmented into layers and can be visualized and quantified more accurately. It is a safe and rapid technique giving a vascular map of retinal blood flow without using intravenous dye ***(Tsokolas et al., 2020).***

AIM OF THE WORK

The aim of our study is to: - detect changes in retinal structure and microvasculature in patients with cerebral small vessel disease using optical coherence tomography angiography, correlate these changes with brain imaging markers and determine if (OCTA) can be used as a screening tool for cerebral small vessel disease.

Chapter 1

CEREBRAL SMALL VESSEL DISEASE

Anatomy of cerebral micro vessel circulation:

The brain is a highly perfused organ consumes about 20% of cardiac output ***(Xing et al., 2017).***

The arterial system of the brain forms anastomotic ring at the base of the skull called (circle of Willis) which gives rise to 3 main cerebral arteries (anterior, middle and posterior)divide progressively into small arteries and arterioles that penetrate the brain tissue to supply the subcortical parenchyma called (perforating arteries) one of the components of cerebral small vessels. The second component is the leptomeninges vasoganglion derived from covering of the subarachnoid space and the brain convex surface. The cerebral small vessels include small arteries, arterioles, venules and capillaries at size of 50-400 micrometer ***(Qian Li et al., 2018).***

Perivascular spaces (Virchow-Robin spaces) are fluid-filled compartments surrounding the small perforating brain microvessels, act as channels for fluid transport, exchange between cerebro spinal fluid (CSF) and interstitial fluid (ISF) clears waste product from the brain ***(Ballerini et al., 2020).***

Pathophysiology of CSVD:

The pathophysiologic aspects of CSVD are still not clear, but some mechanisms are suggested. The core mechanism of CSVD-related brain injury is ischemia, acting through arteriolar narrowing or occlusion lead to hypoperfusion as (vasospasm, hypotension or impaired autoregulation). The another key problem is diffuse cerebrovascular endothelial failure as endothelial failure leads to increased permeability and increased leakage into the vessel wall and the surrounding tissue, damaging of the vessel wall, inflammation, demyelination, glial scar formation, thickening and stiffness of vessels leading to failure of autoregulation, narrowing of the lumen and occlusion, causing featured focal ischemic lesions in the brain parenchyma ***(Wardlaw et al., 2013).***