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Original Article

Transcranial Doppler assessment of patients with cerebral small vessel disease

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Abstract

Background

Cerebral small vessel disease (SVD) refers to any pathology in all vascular structures (small arteries, arterioles, capillaries, venules, and small veins). Transcranial Doppler is a bedside, inexpensive, noninvasive technique that can assess intracerebral circulation in real time and can be used for continuous monitoring.

Aim of the work

Our study tried to detect the pathogenesis of cerebral SVD, especially the implication of the cerebral large artery disease. Moreover, it assessed the ability of transcranial Doppler in evaluating the severity of cerebral SVD and people who are at risk. Patients with cardioembolic risk were excluded.

Patients and methods

A cross-sectional study was conducted including 50 patients recruited from El-Sahel Teaching Hospitals, either inpatient or outpatient clinic departments.

Results

We proved a relation between cerebral large artery disease and severity of cerebral SVD but not embolic in nature.

Conclusion

There is a relationship between cerebral large artery disease and severity of cerebral SVD, but we cannot hold microemboli as a pathogenesis of cerebral SVD. In addition, cerebral SVD affects cerebral vasomotor reactivity especially in hypertensive patients, so we can use Breath-Holding Index (BHI) for prediction of occurrence of cerebral SVD in high-risk people, especially hypertensive.

Keywords: Cerebral small vessel disease, intracerebral circulation, transcranial doppler

Introduction

Ischemic stroke is defined as an episode of neurologic dysfunction caused by vascular stenosis or occlusion leading to focal cerebral, spinal cord, or retinal infarction within a specific vascular territory [1].

Stroke, including both ischemic and hemorrhagic types, is a major health burden globally, affecting 15 million people each year. It is the second leading cause of death for people above the age of 60 years and the fifth leading cause for those aged 15–59 years. Stroke is the most common cause of adult disability and the second most important cause of dementia worldwide. According to WHO figures, global stroke deaths were 5.8 million in 2005 and are projected to increase to 6.5 million in 2015 and 7.8 million in 2030 [2].

There is currently no active national registry for stroke in Egypt, and only limited community-based data exist on stroke incidence and prevalence. Crude prevalence in Assiut, one of the southern governorates of Egypt, is 9.63/1000.

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A prevalence of 5.6/1000 was seen in the New Valley (data collected in 2007). Earlier studies in 1996 reported the incidence in another southern governorate (Sohag) to be 1.8/1000, and the prevalence was 5.08/1000. Nonetheless, if the incidence rates reported in these small local studies can be generalized, then the number of new strokes in Egypt per year may be around 150 000–210 000. Moreover, stroke accounts for 6.4% of all deaths and thus ranks third after heart disease and gastrointestinal (especially liver) diseases [3].

According to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification system, which is a classification of subtypes of ischemic stroke using clinical features and the results of ancillary diagnostic studies, there are five categories: large artery atherosclerosis (embolus/thrombosis) 25%, cardioembolism 20%, cerebral small vessel disease (SVD) 25%, stroke of other determined etiology 5%, and stroke of undetermined etiology 25% [4].

Cerebral SVD has become a popular and very widely used term today. Current definition of small vessels refers to all the vascular structures (small arteries, arterioles, capillaries, venules, and small veins) that are located in the brain parenchyma or in the subarachnoid space [5].

Brain lesions owing to SVD are white matter lesions, lacunar infarcts, and microbleeds. However, there are six subtypes of neuroimaging lesions: recent small subcortical infarcts, lacunes of presumed vascular origin, enlarged perivascular spaces, cerebral microbleeds, central brain atrophy, and white matter hyperintensity of presumed vascular origin or leukoaraiosis (term describes changes in the hemispheric cerebral white matter seen on neuroimaging; initially as areas of low attenuation on computed tomogrpahy (CT) and subsequently as hyperintensities on T2-weighted or Fluid Attenuated Inversion Recovery MRI) [5].

Cerebral SVD is more frequently considered to be vascular in origin. Increased prevalence of vascular risk factors such as diabetes mellitus (DM), hypertension (HTN), obesity, dyslipidemia, metabolic syndrome, and tobacco smoking may be attributed to the accompanied urbanization and change of dietary habits [6].

From histopathological point of view, cerebral SVD is mostly associated with lipohyalinosis and atherosclerosis. Lipohyalinosis is a destructive vessel lesion characterized by loss of normal arterial architecture, mural foam cells migration, fibrinoid necrosis, hyaline thickening, and ectasia of vessel wall. Such vascular lesions involve small arteries and cause correspondingly small often asymptomatic, cerebral infarcts. However, intracranial atherosclerosis is pathologically similar to the more familiar disease affecting the larger cervicocranial arteries. Intracranial atherosclerosis affects somewhat larger perforating arteries than lipohyalinosis causing correspondingly larger infarcts, which are more often symptomatic [7].

From the clinical point of view, cerebral SVD is associated with acute events like lacunar and hemorrhagic strokes or chronic events like cognitive deficit in the form of subcortical dementia, mood deficit in the form of late-onset depression, sphincteric affection, and gait apraxia [8]. Irrespective of the severity of leukoaraiosis and burden of lacunes and microbleeds, the topographic distribution of lacunes or hemorrhage at strategic locations such as the thalamus, basal ganglia, and internal capsule is associated with increased cognitive and motor manifestations [6].

From the hemodynamic point of view, in patients with cerebral SVD, occasional decreases in their systemic blood pressure could lead to significant decrease in blood flow to the white matter; this effect is attributable to the inability of sclerotic vessels to dilate, thus suggesting a presumptive impairment of the cerebral autoregulation, so the periventricular white matter might be considered an area prone to become seriously ischemic under conditions of moderate blood flow deficit [9].

Furthermore, in experimental animals, cerebral hypoperfesion leads to white matter changes after permanent bilateral carotid occlusion and less severe changes after transient occlusion of the middle cerebral artery (MCA). Although it remains unclear whether the decreased blood flow is the cause of white matter damage or the consequence of the reduced metabolism in areas of the white matter that became atrophic by other causes, transient brain edema might be another cause of white matter changes. The increased interstitial fluid concentration in the white matter may be a consequence of arterial HTN or impaired venous return in the deep white matter compartment; thus, the perfusion pressure is increased on the arterial side of the capillary bed [10].

Preventing or delaying disability in patients with cerebral SVD depends not only on the understanding of its pathological processes but also on the identification of its early stages. Definitions of criteria and tools sensitive enough to describe these conditions are seriously needed. However, using MRI to screen for ‘subclinical’ lesions is not cost effective, whereas the CT scan is associated with the risks of radiation and the images do not have high quality. In addition, these imaging methods are capable of presenting the anatomical but not the physiological disorder. Hence, it is important to find a cost-benefit method that, in addition to anatomical data, can be used to simply obtain physiological and hemodynamical data of the disease [11].

Transcranial Doppler (TCD), which became available in 1982, is a noninvasive ultrasonic technique that uses a handheld low-frequency sector transducer that sends fixed or pulsed sound waves to measure the blood flow velocities in the basal intracranial arteries of the brain. Hence, normal flow velocity

can be easily distinguished from the accelerated velocities associated with vasospasm, arterial stenosis, and arteriovenous malformation. An advantage of TCD is that it can be performed at the bedside and repeated as needed or applied for continuous monitoring [12].

The pulsatility index (PI) measured by TCD characterizes the shape of a spectral waveform. This index, first described by Gosling and King is postulated to reflect the degree of downstream vascular resistance. Low resistance vascular beds have high diastolic flow with rounded waveforms and lower PIs, whereas higher resistance beds have low diastolic flow, a peaked waveform, and higher PIs. Compared with other organs, the intracranial cerebral vasculature has relatively low downstream vascular resistance, providing a potent blood supply to the brain. One potential cause of increased downstream resistance in the cerebral circulation is narrowing of the small vessels owing to lipohyalinosis and microatherosclerosis [13].

Early detection of SVD may be critical in arresting this progressive disease process, allowing aggressive medical treatment including control of vascular risk factors. Thus, a TCD finding of diffusely elevated PIs may suggest previously undiagnosed SVD and prompt a search for and treatment of underlying vascular risk factors. Future studies will be required to determine whether serial TCDs are a useful measure of either disease progression or the effectiveness of therapeutic interventions such as antiplatelet agents [13].

Aim of the work

The following were the aims of this work:

(1) To detect the TCD parameters of patients with cerebral SVD
(2) To detect implication of the cerebral large artery disease on the pathogenesis of the cerebral SVD.

Patients and methods

Patient selection

A cross-sectional study was conducted including 50 patients recruited from El-Sahel Teaching Hospitals, either inpatient or outpatient clinic departments. Ethical Committee approval was taken.

Inclusion criteria

The following were the inclusion criteria:

(1) Both sexes.
(2) Age above 40 years
(3) Patients presenting with cerebrovascular stroke (lacunar infarcts) verified by brain MRI
(4) Patients having a past history of intracerebral hemorrhage in deep supratentorial regions or brain stem.

Exclusion criteria

The following were the exclusion criteria:

(1) Bilaterally absent transtemporal window
(2) Any contraindications for MRI
(3) Patients with any other cause of nonischemic leukoencephalopathy
(4) Patients diagnosed clinically and radiologically as having normal pressure hydrocephalus
(5) Watershed infarction or border zone infarcts occur at the border between cerebral vascular territories where the tissue is most vulnerable to reductions in perfusion
(6) Large artery atherosclerosis which is defined as cortical or cerebellar lesions and brain stem or subcortical hemispheric infarcts greater than 2 cm in diameter on CT or MRI
(7) Cardiac source of emboli, for example, atrial fibrillation, paroxysmal atrial fibrillation, prosthetic valve, and valvular heart disease
(8) Lobar intracerebral hemorrhage, subarachnoid, subdural, and extradural hemorrhages
(9) Traumatic intracerebral hemorrhage
(10) Cerebral venous thrombosis
(11) Hematological diseases and coagulopathies.

Study methods

Patients in this study were subjected to the following:

(1) Detailed medical history
(2) Thorough general and neurological examination
(3) Full metabolic profile to exclude coagulopathy: complete blood picture, fasting and postprandial glucose serum level, glycated hemoglobin, coagulation profile, lipid profile, renal and liver functions, and blood electrolytes
(4) ECG and transthoracic echocardiogram, to exclude cardiac source of emboli
(5) Carotid and vertebral duplex
(6) CT brain to exclude various types of hemorrhage
(7) MRI brain:
    Basal ganglia and centrum semiovale regions are rated from 0 to 4, in which 0 means no enlarged perivascular spaces (EPVS), 1 means 1–10 EPVS (mild), 2 means 11–20 EPVS (moderate), 3 means 21–40 EPVS (frequent), and 4 means more than 40 EPVS (severe), whereas midbrain region is rated 0 if no EVPS visible or 1 if EPVS visible Staals *et al*. [14] operated a SVD scale from 0 to 4 in which one point was awarded when deep white matter hyperintensity (DWMH) (fazekas score 2 or 3) and/or preventricular hyperintensity (PVH) (fazekas score 2 or 3) are present, one point was awarded when 1 or more lacunes are present, one point was awarded when 1 or more microbleeds are present, one point was awarded when moderate to severe (Potter scale grade 2–4) enlarged perivascular spaces are present
(8) TCD:
    (a) Intracranial vessels
    (b) Breath holding test
    (c) Monitoring MCA.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± SD.

Qualitative data were expressed as frequency and percentage. *P* value less than or equal to 0.05 was considered significant, *P* value less than or equal to 0.001 was considered as highly significant, and *P* value more than 0.05 was considered insignificant.

Results

Table 1 shows that 18 (36.0%) were less than 50 years of age, 12 (24.0%) were 50–60 years old, and 20 (40.0%) were more than 60 years of ag. Moreover, 18 (36.0%) were female and 32 (64.0%) were male.

Table 2 shows that the fazekas were seen in 24 (48.0%), lacunes in 46 (92.0%), EPVS in 32 (64.0%), and microbleeds in 30 (60.0%) of MRI scans (SVD score).

Table 3 shows stable plaques in 36%, unstable plaques 8%, significant stenosis more than 50% in 20%, and diffuse atherosclerosis in 68% of patients on carotid Duplex findings.

Table 4 shows the focal area in 48%, diffuse atherosclerosis in 32%, increased PI of MCA in 52%, microemboli detection in 0%, and vasomotor reactivity (BHI) as poor in 72% and good in 28%.

Table 5 shows a statistically significant relation between lacunes and DM.

Table 6 shows a statistically significant relation between EPVS and HTN and total number of risk factors.

Table 7 shows a statistically significant relation between microbleeds and HTN.

Table 8 shows a statistically significant relation between focal area and HTN, DM, and total number of risk factors.

Table 9 shows a statistically significant relation between vasomotor reactivity BHI and HTN and dyslipidemia.

Table 10 shows a statistically significant relation between significant stenosis more than 50% and microbleeds and total MRI SVD score.

Table 1: Demographic data distribution of the study group

Demographic data	*N*=50 [*n* (%)]
Age (years)	
<50	18 (36.0)
50-60	12 (24.0)
>60	20 (40.0)
Range (mean±SD)	40-73 (56.40±10.29)
Sex	
Female	18 (36.0)
Male	32 (64.0)

Table 2: MRI small vessel disease score distribution of the study group

MRI (SVD score)	*N*=50 [*n* (%)]
Fazekas	
No	26 (52.0)
Yes	24 (48.0)
Lacunes	
No	4 (8.0)
Yes	46 (92.0)
EPVS	
No	18 (36.0)
Yes	32 (64.0)
Microbleeds	
No	20 (40.0)
Yes	30 (60.0)
Total MRI (SVD score)	
1	6 (12.0)
2	12 (24.0)
3	26 (52.0)
4	6 (12.0)

SVD, small vessel disease.

Table 3: Carotid duplex finding in the study group

Carotid duplex	*N*=50 [*n* (%)]
Plaque	
Stable	
No	32 (64.0)
Yes	18 (36.0)
Unstable	
No	46 (92.0)
Yes	4 (8.0)
Significant stenosis >50%	
No	40 (80.0)
Yes	10 (20.0)
Diffuse atherosclerosis (increased IMT)	
No	16 (32.0)
Yes	34 (68.0)

IMT, intima-media thickness.

Table 4: Transcranial Doppler distribution of the study group

Transcranial Doppler	*N*=50 [*n* (%)]
Signs of steno-occlusive disease	
Focal area	
No	24 (48.0)
Yes	26 (52.0)
Diffuse atherosclerosis (diminished flow)	
No	34 (68.0)
Yes	16 (32.0)
Increased PI of MCA	
No	24 (48.0)
Yes	26 (52.0)
Microemboli detection	
No	50 (100.0)
Yes	0 (0.0)
Vasomotor reactivity (BHI)	
Poor	36 (72.0)
Good	14 (28.0)

MCA, middle cerebral artery; PI, pulsatility index.

Table 5: Relation between lacunes and risk factors among study group

Risk factors	Lacunes [*n* (%)]		χ^2 test	
	No (*n*=4)	Yes (*n*=46)	χ^2	*P*
HTN				
No	0 (0.0)	8 (17.4)	0.828	0.363
Yes	4 (100.0)	38 (82.6)		
DM				
No	0 (0.0)	26 (56.5)	4.710	0.030*
Yes	4 (100.0)	20 (43.5)		
Dyslipidemia				
No	4 (100.0)	34 (73.9)	1.373	0.241
Yes	0 (0.0)	12 (26.1)		
Smoking				
No	4 (100.0)	28 (60.9)	2.446	0.118
Yes	0 (0.0)	18 (39.1)		
Total number of risk factors				
1.00	0 (0.0)	12 (26.1)	2.899	0.235
2.00	4 (100.0)	26 (56.5)		
3.00	0 (0.0)	8 (17.4)		

*Significant. DM, diabetes mellitus.

Table 6: Relation between EPVS and risk factors among study group

Risk factors	EPVS [*n* (%)]		χ^2 test	
	No (*n*=18)	Yes (*n*=32)	χ^2	*P*
HTN				
No	0 (0.0)	8 (25.0)	5.357	0.021
Yes	18 (100.0)	24 (75.0)		
DM				
No	8 (44.4)	18 (56.3)	0.643	0.423
Yes	10 (55.6)	14 (43.8)		
Dyslipidemia				
No	16 (88.9)	22 (68.8)	2.562	0.109
Yes	2 (11.1)	10 (31.3)		
Smoking				
No	14 (77.8)	18 (56.3)	2.317	0.128
Yes	4 (22.2)	14 (43.8)		
Total number of risk factors				
1.00	2 (11.1)	10 (31.3)	10.359	0.006*
2.00	16 (88.9)	14 (43.8)		
3.00	0 (0.0)	8 (25.0)		

*Significant. DM, diabetes mellitus; HTN, hypertension.

Table 7: Relation between microbleeds and risk factors among study group

Risk factors	Microbleeds [*n* (%)]		χ^2 test	
	No (*n*=20)	Yes (*n*=30)	χ^2	*P*
HTN				
No	6 (30.0)	2 (6.7)	4.861	0.027*
Yes	14 (70.0)	28 (93.3)		
DM				
No	10 (50.0)	16 (53.3)	0.053	0.817
Yes	10 (50.0)	14 (46.7)		
Dyslipidemia				
No	14 (70.0)	24 (80.0)	0.658	0.417
Yes	6 (30.0)	6 (20.0)		
Smoking				
No	12 (60.0)	20 (66.7)	0.231	0.630
Yes	8 (40.0)	10 (33.3)		
Total number of risk factors				
1.00	6 (30.0)	6 (20.0)	1.389	0.499
2.00	10 (50.0)	20 (66.7)		
3.00	4 (20.0)	4 (13.3)		

*Significant. DM, diabetes mellitus; HTN, hypertension.

Table 8: Relation between focal area and risk factors among study group

Risk factors	Focal area [*n* (%)]		χ^2 test	
	No (*n*=24)	Yes (*n*=26)	χ^2	*P*
HTN				
No	6 (25.0)	2 (7.7)	4.782	0.035*
Yes	18 (75.0)	24 (92.3)		
DM				
No	16 (66.7)	10 (38.5)	3.978	0.046*
Yes	8 (33.3)	16 (61.5)		
Dyslipidemia				
No	18 (75.0)	20 (76.9)	0.025	0.874
Yes	6 (25.0)	6 (23.1)		
Smoking				
No	16 (66.7)	16 (61.5)	0.142	0.706
Yes	8 (33.3)	10 (38.5)		
Total number of risk factors				
1.00	8 (33.3)	4 (15.4)	9.402	0.009*
2.00	16 (66.7)	14 (53.8)		
3.00	0 (0.0)	8 (30.8)		

*Significant. DM, diabetes mellitus; HTN, hypertension.

Table 11 shows a statistically significant relation between diffuse atherosclerosis 'increased intima-media thickness' and fazekas and total MRI SVD score.

Table 12 shows a statistically significant relation between focal area of stenosis and lacunes, EPVS, and total MRI SVD score.

Table 13 shows a statistically significant relation between diffuse atherosclerosis 'diminished flow' and microbleeds and total MRI SVD score.

Table 14 shows a statistically significant relation between increased PI of MCA and fazekas and total MRI SVD score.

Table 15 shows a statistically significant relation between vasomotor reactivity BHI and EPVS and microbleeds in MRI SVD score.

Discussion

In our study, we tried to detect the pathogenesis of cerebral SVD, especially the implication of the cerebral large artery disease, using TCD and extracranial duplex. Moreover, we assessed the ability of TCD, as simple inexpensive bedside method, to evaluate the severity of cerebral SVD and people who are at risk.

Table 9: Relation between vasomotor reactivity BHI and risk factors among study group

Risk factors	Vasomotor reactivity (BHI) [*n* (%)]		χ^2 test	
	Poor (*n*=36)	Good (*n*=14)	χ^2	*P*
HTN				
No	8 (22.2)	0 (0.0)	3.791	0.049*
Yes	28 (77.8)	14 (100.0)		
DM				
No	16 (44.4)	10 (71.4)	2.941	0.086
Yes	20 (55.6)	4 (28.6)		
Dyslipidemia				
No	30 (83.3)	8 (57.1)	3.791	0.049*
Yes	6 (16.7)	6 (42.9)		
Smoking				
No	22 (61.1)	10 (71.4)	0.466	0.495
Yes	14 (38.9)	4 (28.6)		
Total number of risk factors				
1.00	8 (22.2)	4 (28.6)	3.042	0.218
2.00	24 (66.7)	6 (42.9)		
3.00	4 (11.1)	4 (28.6)		

*Significant. DM, diabetes mellitus; HTN, hypertension.

Table 10: Relation between significant stenosis more than 50% and MRI (small vessel disease) score

MRI (SVD score)	Significant stenosis >50% [*n* (%)]		χ^2 test	
	No (*n*=40)	Yes (*n*=10)	χ^2	*P*
Fazekas				
No	22 (55.0)	4 (40.0)	0.721	0.396
Yes	18 (45.0)	6 (60.0)		
Lacunes				
No	4 (10.0)	0 (0.0)	1.087	0.297
Yes	36 (90.0)	10 (100.0)		
EPVS				
No	14 (35.0)	4 (40.0)	0.087	0.768
Yes	26 (65.0)	6 (60.0)		
Microbleeds				
No	20 (50.0)	0 (0.0)	8.333	0.004*
Yes	20 (50.0)	10 (100.0)		
Total MRI (SVD score)				
1.00	6 (15.0)	0 (0.0)	10.096	0.018*
2.00	10 (25.0)	2 (20.0)		
3.00	22 (55.0)	4 (40.0)		
4.00	2 (5.0)	4 (40.0)		

*Significant. SVD, small vessel disease.

The most common vascular risk factor among our study group was HTN (84%), DM (48%), dyslipidemia (24%), and smoking (36%). Overall, 67% of them have more than one risk factor. HTN is significantly related to presence of microbleeds, EPVS, intracranial stenosis, and poor vasomotor reactivity. However, DM is significantly related to presence of laccunes and intracranial stenosis, and dyslipidemia is significantly related to the severity of cerebral SVD evaluated by MRI.

Table 11: Relation between diffuse atherosclerosis increased intima-media thickness and MRI (small vessel disease) score

MRI (SVD score)	Diffuse atherosclerosis (increased IMT) [*n* (%)]		χ^2 test	
	No (*n*=16)	Yes (*n*=34)	χ^2	*P*
Fazekas				
No	12 (75.0)	14 (41.2)	4.987	0.026*
Yes	4 (25.0)	20 (58.8)		
Lacunes				
No	2 (12.5)	2 (5.9)	0.647	0.421
Yes	14 (87.5)	32 (94.1)		
EPVS				
No	6 (37.5)	12 (35.3)	0.023	0.880
Yes	10 (62.5)	22 (64.7)		
Microbleeds				
No	6 (37.5)	14 (41.2)	0.061	0.804
Yes	10 (62.5)	20 (58.8)		
Total MRI (SVD score)				
1.00	2 (12.5)	4 (11.8)	9.936	0.019*
2.00	8 (50.0)	4 (11.8)		
3.00	4 (25.0)	22 (64.7)		
4.00	2 (12.5)	4 (11.8)		

*Significant. IMT, intima-media thickness; SVD, small vessel disease.

Table 12: Relation between focal area of stenosis and MRI (small vessel disease) score

MRI (SVD score)	Focal area [*n* (%)]		χ^2 test	
	No (*n*=24)	Yes (*n*=26)	χ^2	*P*
Fazekas				
No	12 (50.0)	14 (53.8)	0.074	0.786
Yes	12 (50.0)	12 (46.2)		
Lacunes				
No	4 (16.7)	0 (0.0)	4.710	0.030*
Yes	20 (83.3)	26 (100.0)		
EPVS				
No	12 (50.0)	6 (23.1)	3.926	0.048*
Yes	12 (50.0)	20 (76.9)		
Microbleeds				
No	10 (41.7)	10 (38.5)	0.053	0.817
Yes	14 (58.3)	16 (61.5)		
Total MRI (SVD score)				
1.00	6 (25.0)	0 (0.0)	8.087	0.044*
2.00	4 (16.7)	8 (30.8)		
3.00	12 (50.0)	14 (53.8)		
4.00	2 (8.3)	4 (15.4)		

*Significant. SVD, small vessel disease.

To evaluate arterial stenosis, we used extracranial duplex and TCD. Overall, 22% of patients included in our study have significant (>50%) extracranial carotid stenosis, whereas 52% have signs of intracranial stenosis evaluated by TCD. Both of them have significant relation to the severity of the cerebral SVD, evaluated by MRI SVD score. In addition, there are significant relations

Table 13: Relation between diffuse atherosclerosis (diminished flow) and MRI (small vessel disease) score

MRI (SVD score)	Diffuse atherosclerosis (diminished flow) [*n* (%)]		χ^2 test	
	No (*n*=34)	Yes (*n*=16)	χ^2	*P*
Fazekas				
No	20 (58.8)	6 (37.5)	1.982	0.159
Yes	14 (41.2)	10 (62.5)		
Lacunes				
No	2 (5.9)	2 (12.5)	0.647	0.421
Yes	32 (94.1)	14 (87.5)		
EPVS				
No	14 (41.2)	4 (25.0)	1.236	0.266
Yes	20 (58.8)	12 (75.0)		
Microbleeds				
No	18 (52.9)	2 (12.5)	7.414	0.006*
Yes	16 (47.1)	14 (87.5)		
Total MRI (SVD score)				
1.00	6 (17.6)	0 (0.0)	7.933	0.047*
2.00	10 (29.4)	2 (12.5)		
3.00	16 (47.1)	10 (62.5)		
4.00	2 (5.9)	4 (25.0)		

*Significant. SVD, small vessel disease.

Table 14: Relation between increased pulsatility index of middle cerebral artery and MRI (small vessel disease) score

MRI (SVD score)	Increased PI of MCA [*n* (%)]		χ^2 test	
	No (*n*=24)	Yes (*n*=26)	χ^2	*P*
Fazekas				
No	18 (75.0)	8 (30.8)	9.782	0.002*
Yes	6 (25.0)	18 (69.2)		
Lacunes				
No	2 (8.3)	2 (7.7)	0.007	0.933
Yes	22 (91.7)	24 (92.3)		
EPVS				
No	10 (41.7)	8 (30.8)	0.643	0.423
Yes	14 (58.3)	18 (69.2)		
Microbleeds				
No	10 (41.7)	10 (38.5)	0.053	0.817
Yes	14 (58.3)	16 (61.5)		
Total MRI (SVD score)				
1.00	4 (16.7)	2 (7.7)	8.087	0.044*
2.00	8 (33.3)	4 (15.4)		
3.00	12 (50.0)	14 (53.8)		
4.00	0 (0.0)	6 (23.1)		

MCA, middle cerebral *Significant. artery; PI, pulsatility index; SVD, small vessel disease.

between intracranial stenosis and presence of laccunes and EPVS.

Overall, 68% of our studied patients had increased intima-media thickness in their extracranial part of the carotid artery, which indicates diffuse atherosclerosis visualized by duplex and significantly related to the severity of the cerebral SVD, evaluated by MRI score, especially fazekas score. However, 32.0% were suggested to have intracranial diffuse atherosclerosis or multiple distal stenosis depending on decreased mean Flow velocities (MFV) and increased PI of all intracranial vessels without significant stenosis in their extracranial part. Moreover, it is also significantly related to MRI SVD score.

A study published in 2018 by Ao and colleagues included 928 participants and found a relation between large artery atherosclerosis and cerebral SVD. Another study found that cerebral SVD is associated with stroke recurrence in patients with large artery atherosclerosis evaluated by MRI and MRA [15]. Moreover, there is a relation between large artery atherosclerosis and presence of microbleeds [16]. Beside, hypoperfusion was significantly related to summed cerebral SVD score [17] especially leukoaraiosis [18].

Because cerebral SVD is diffuse and affects the small arteries, arterioles, capillaries, and venules, the impairment of cerebral and extracerebral [19] autoregulation is global [20]. Our study emphasizes the same result that patients with poor BHI represent 72% of studied patients and mostly are hypertensive and have EPVS.

In an autopsy study done by Zheng *et al*. [21], it was found that laccunes were strongly correlated with cerebral atherosclerosis, and also an evidence of thrombi was noticed in neighboring meningeal arteries, suggesting the possibility of artery-to-artery thromboemboli. However, no microemboli signals were detected by TCD in our study, although 44% of them have carotid plaques and 18% of those are unstable plaques.

Geurt *et al*. [22] detected a lower number of perforating arteries and a higher PI in patients with cerebral SVD using two-dimensional phase contrast MRI at 7 T for the first time. In line with previous studies, there was a relation between elevated PI of MCA, measured by TCD, and MRI manifestations of the SVD, especially PVH and DWMH [11,13]. In context, 52% of our patients have increased PI of MCA with significant relation to fazekas and total SVD scores. Our study shows that, there is no significant relation between increased PI of MCA and HTN.

Conclusion

There is a relation between cerebral large artery disease and severity of cerebral SVD, but we cannot hold microemboli as a pathogenesis of cerebral SVD. Moreover, cerebral SVD affects cerebral vasomotor reactivity especially in hypertensive patients, so we can use BHI for prediction of occurrence of cerebral SVD in high-risk people, especially hypertensive.

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Conflicts of interest

There are no conflicts of interest.

Table 15: Relation between vasomotor reactivity BHI area and MRI (small vessel disease) score

MRI (SVD score)	Vasomotor reactivity (BHI) [*n* (%)]		χ^2 test	
	Poor (*n*=36)	Good (*n*=14)	χ^2	*P*
Fazekas				
No	20 (55.6)	6 (42.9)	0.651	0.420
Yes	16 (44.4)	8 (57.1)		
Lacunes				
No	4 (11.1)	0 (0.0)	1.691	0.193
Yes	32 (88.9)	14 (100.0)		
EPVS				
No	10 (27.8)	8 (57.1)	3.773	0.049*
Yes	26 (72.2)	6 (42.9)		
Microbleeds				
No	18 (50.0)	2 (14.3)	5.357	0.021*
Yes	18 (50.0)	12 (85.7)		
Total MRI (SVD score)				
1.00	6 (16.7)	0 (0.0)	2.686	0.443
2.00	8 (22.2)	4 (28.6)		
3.00	18 (50.0)	8 (57.1)		
4.00	4 (11.1)	2 (14.3)		

SVD, small vessel disease.

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