Original article

Clinical and Radiological Predictors For Early Detection Of Cerebral Vasospasm After Subarachnoid Haemorrhage

Abd Elnaser A. Morad[a], Magdy K. Massoud[b], Maged K. F. Botros[a], Shaimaa M. kasem[a], Tariq M.Soliman[c]

[a] Departement of Neurology Faculty of Medicine, Benha University, MD., Egypt,[b] Department of Neurology and head of neuropsychiatric department at El Mataria teaching hospital, c Neuropsychiatry at El Mataria teaching hospital

Corresponding author: Tariq Mahmoud Soliman. Address: 110 Reyad street with Gamal Abdelnaser street,Tanta,E.Mail: dr.tariqsamy.14@gmail.com
Mobile: 00201006711476

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Background

Cerebral vasospasm after subarachnoid haemorrhage is a potentially preventable and reversible condition where an early identification can prevent or limit cerebral infarction. Vasospasm may be assessed on a clinical, radiographic, or angiographic basis.

Aim: Early detection of cerebral vasospasm in a sample of Egyptian patients presented with spontaneous subarachnoid haemorrhage.

Methods and subjects: In this study we enrolled 40 aSAH patients diagnosed by non-contrast brain CT and CT angiography and managed by interventional aneurysmal embolization . Early detection of vasospasm and DCI was assessed on clinical and radiological basis using transcranial duplex studies (TCD) on the 1st, 3rd, 5th, 7th and 10th days of the onset of the symptoms . Results: Fourty patients with aSAH , of them 67.5% developed vasospasm but only 33.3% progressed to DCI. The most significant day of vasospasm development as detected by TCD was on the 7th day.The most common arteries undergoing vasospasm were the MCA followed by the ACA and lastly the PCA. Clinical scalas on admission as (GCS,HHS,WFNS and Ogilvy and Carter scale) are highly significant predictors of cerebral vasospasm

Conclusion: Clinical risk factors and the use of TCD are tools for early detection of vasospasm following SAH. This allows for early therapeutic intervention before irreversible ischemic neurological deficits take place.

Keywords: Aneurysmal subarachnoid hemorrhage, Transcranial duplex, CT angiography, Interventional embolization.

Key Messages: Clinical predictors and early detection of cerebral vasospasm by TCD after spontaneous aneurysmal subarachnoid haemorrhage are highly valuable for preventing patients from delayed cerebral ischemia occurrence and lessen its impact irreversible neurological deficits by early therapeutic and endovascular interventions.

Abbreviations:

A.com: Anterior communicating artery; ACA: Anterior cerebral artery; aSAH: Aneurysmal subarachnoid hemorrhage; AUC: area under curve; CV: Cerebral vasospasm; DBP: Diastolic blood pressure; DCI: Delayed cerebral ischemia; GCS: Glasgow Coma Scale; HHS: Hunt and Hess Scale; ICA: Internal carotid artery; MAP: Mean arterial pressure; MCA: Middle cerebral artery; MFV: Mean flow velocity; NIHSS: National Institute of Health Stroke Scale; P.com: Posterior communicating artery; PCA: Posterior cerebral artery; RBS: Random blood sugar; ROC curve: Receiver operating characteristic curve; SAH: Subarachnoid haemorrhage.

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Introduction

Cerebral vasospasm is the delayed narrowing of large capacitance intracranial arteries following SAH, often associated with radiographic or clinical evidence of diminished perfusion in the distal territory of the affected arteries[1][2] and is a leading contributor to the morbidity and mortality associated with aSAH [3]It is prolonged sometimes severe but ultimately reversible .Symptomatic vasospasm occurs in 20%–30% of patients with SAH [4]. It usually does not begin before day 3. Its occurrence peaks during days 7–8 and resolves spontaneously after 21 days [5]. Cerebral vasospasm constitutes a unique clinicopathological entity characterized by reversible vasculopathy, impaired auto regulatory function,[6] Clinical features of cerebral ischemia after SAH mostly consist of focal neurological signs, such as aphasia or hemi paresis, or a decrease in the level of consciousness, typically with gradual and often fluctuating onset. Signs of cerebral ischemia are sometimes reversible but may also progress to cerebral infarction, which can cause severe disability.[7] Although these clinical deficits often occur in conjunction with angiographic evidence of vessel narrowing, each may occur independently of the other.[8] Transcranial Doppler (TCD) is a non-invasive ultrasound (US) study which can detect the blood flow velocities in the cerebral blood vessels that can be a useful tool in early prediction of vasospasm after aSAH [9]. Rational thinking suggests that the complications secondary to vasospasm can be mitigated by identifying this subgroup of patients early and instituting appropriate treatment

Aim of the work:

This study aims to predict the occurrence of cerebral vasospasm using TCD monitoring as a tool in early diagnosis of cerebral vasospasm following aSAH.

Patients and Methods

A prospective study was done during a period of one year starting from April 2017 data was collected from 40 aSAH patients who were admitted to the neurovascular unit and ICU of the neurology department, Mataria Teaching Hospital, Cairo. The study procedures are approved by ethical committee Mataria teaching hospital.

Out of the 40 patients only 27 patients developed cerebral vasospasm. These 27 patients who developed vasospasm were divided into two groups: 18 patients who were diagnosed as cerebral vasospasm without clinical evidence of DCI and 8 patients who were diagnosed as cerebral vasospasm with clinical evidence of DCI.

Patients excluded from this study were non-aneurysmal SAH, patients with previous history of disabling brain injuries causing focal neurological signs, GCS < 6, patient with decompensate systemic illness eg. Hepatic, renal and cardiac as all these will cause deterioration in consciousness level and any obstacle facing TCD assessment as a closed temporal window.

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Table (1)
The rate of development of vasospasm regarding risk factors, clinical scales and aneurysmal site, and size

		Total (n = 40)	No vasospasm (n = 13)	Vasospasm (n = 27)	P value
			n (% of total)	n (% of total)	
Age	< 60	27	10(37%)	17(63%)	0.484
	≥ 60	13	3(23%)	10(77%)	
Sex	Males	16	5 (31.25%)	11 (68.75%)	1.000
	Females	24	8 (33%)	16 (67%)	
Hypertension	Non-hypertensive	21	12 (57.1%)	9 (42.9%)	0.006*
	Hypertensive	19	1 (5.3%)	18 (94.7%)	
Diabetes	Non diabetics	34	13 (38.2%)	21 (61.8%)	0.152
	Diabetics	6	0 (0%)	6 (100%)	
Smoking	Non-smokers	29	13 (44.8%)	16 (55.2)	0.007*
	Smokers	11	0 (0%)	11 (100%)	
Systolic BP	<160 (mmHg)	18	7 (38.9%)	11 (61.1%)	0.509
	≥160 (mmHg)	22	6 (27.2%)	16 (72.8%)	
Diastolic BP	<100 (mmHg)	19	11 (57.9%)	8 (42.1%)	0.002*
	≥100 (mmHg)	21	2 (9.5%)	19 (90.5%)	
MAP	≤100 (mmHg)	5	5 (100%)	0 (0%)	0.001*
	>100 (mmHg)	35	8 (22.8%)	27 (77.2%)	
RBS	< 200 (mg/dl)	28	13 (46.4%)	15 (53.6%)	0.001*
	≥ 200 (mg/dl)	12	0 (0%)	12 (100%)	
Cholesterol	<200 (mg/dl)	38	13 (34.2%)	25 (65.8%)	1.000
	≥200 (mg/dl)	2	0 (0%)	2 (100%)	
GCS	<15	19	1 (5.3%)	18 (94.7%)	0.006*
	15	21	12 (57.1%)	9 (42.9%)	
HHS	<3	25	13 (52%)	12 (48%)	0.005*
	≥3	15	0 (0%)	15 (100%)	
Fisher scale	<3	19	9 (47.4%)	10 (52.6%)	0.092
	≥3	21	4 (19%)	17 (81%)	
WFNS scale	<3	33	13 (39.4%)	20 (59.6%)	0.074
	≥3	7	0 (0%)	7 (100%)	
Aneurysm site	MCA	13	0 (0%)	13 (100%)	0.004*
	A.com	12	5 (41.7%)	7 (58.3%)	
	P.com	8	3 (37.5%)	5 (62.5%)	
	ICA	5	3 (60%)	2 (40%)	
	PCA	2	2 (100%)	0 (0%)	
Aneurysm size	<11mm	28	12 (42.9%)	16 (57.1%)	0.063
	≥11mm	12	1 (8.3%)	11 (91.7%)	

*significant

All participants or their first-degree relatives received detailed information concerning this research work and its aim and who agreed to participate signed an informed consent before being enrolled into the study.

On admission full history taking including clinical risk factors were assessed (as, blood sugar and blood pressure on admission) and neurological examination was done.

All patients were diagnosed by non-contrast brain CT scan on admission, early four –vessel CT angiography to localize the site, size and number of the aneurysms then early interventional embolization of the aneurysms was then done either by simple or balloon assisted coiling.

Using many grading scales on both admission and assessment of vasospasm severity SAH was graded clinically by Glasgow Coma Scale (GCS), Hunt and Hess Scale (HHS) and World Federation of Neurosurgical Societies (WFNS) scale, and radiologically by Fisher and Ogilvy and Carter scales. Daily clinical neurological examination was done using the NIHSS for early detection of new focal neurological signs of DCI. The diagnosis of cerebral vasospasm is based on clinical signs of progressive impairment in mental status and level of consciousness or the appearance of new focal neurologic deficits after the initial SAH that cannot not attributed to any other structural or metabolic cause.

TCD studies were done on the 1^{st}, 3^{rd}, 5^{th}, 7^{th} and 10^{th} days of the onset of the symptoms to detect the vasospasm using phased array transducer of multi-frequency 1–3 MHz, trans-axial mesencephalic view through the temporal window. Mean flow velocities (MFV) of middle, anterior, and posterior cerebral arteries (MCA, ACA, and PCA respectively) were measured. Vasospasm is considered when the MFV of the MCA, ACA, or PCA rises above 120, 90, or 60 cm/s respectively.

The collected data were organized, tabulated and statistically analyzed using Statistical Package for Social Studies (SPSS) version 19 created by IBM, Illinois, Chicago, USA. According to numerical values the range mean and standard deviations were calculated. Also, for categorical variable the number and percentage were calculated and differences between subcategories were tested by Fisher or Monte Carlo exact test. The level of significant was adopted at $p<0.05$.

Results:

The study included 40 aSAH patients who fullfilled the inclusion and exclusion criteria with mean age 51.7 $\pm$ 11.8 years, females represented (60%) while males represented (40%)But there was no significant difference regarding sex between the different patient groups Considering risk factors for SAH from history 19 were hypertensive (47.5%), 6 diabetic (15%), and 12 smokers (28%), while clinical risk variables on admission was as the following 35 patients with MAP above 100 (87.5%) ,SBP$\geq$ 160mmHg were55% ,DBP$\geq$100mmHg were52.5% and those with RBS $\geq$200 were 30.

While grading on admission was 19 with GCS <15 (47.5%), 15 with HHS $\geq$3 (37.5%), 21 with Fisher scale $\geq$3 (52.5%) and 7 with WFNS scale$\geq$3 (17.5%).

Angiography revealed that the ruptured aneurysmal sites were in the MCA (32.5%), anterior communicating artery (A.com) (30%),posterior communicating artery (P.com) (20%), internal carotid artery (12.5%) and posterior cerebral artery

(5%).Regarding the size and number of aneurysms, 12 with aneurysm size ≥11 mm (30%) and all patients had single aneurysms.

Those 27aSAH patients who developed TCD signs of vasospasm; were classified as 11 MCA, 6 ACA, 3PCA and 7 patients with vasospasm in two arteries at the same time.

Regarding the relation between development of cerebral vasospasm and demographic and clinical risk factors 17 with age <60 years (63%), 16 females (59.3%), 18 hypertensive (66.7%), 6 diabetics (22.2%), 11 smokers (40.7%), 16 with SBP ≥160(59.2%), 19 with DBP ≥100 (70.4%), all patients with MAP >100 (100%), 12 with RBS >200 (44.4%), 18 with GCS <15 (66.7%), 15 with HHS ≥3 (55.5%), 7 with WFNS scale≥3 (26%), 13 with MCA aneurysms (48.1%), 7 with A.com aneurysms (26%) and 11 with aneurysm size ≥11 mm (40.7%). significant difference between both patient groups was concluded with hypertension and smoking as co morbidities and with MAP>100 and RBS >200 as risk factors for vasospasm

The most significant TCD changes related to cerebral vasospasm was on the 7th day of the onset of the symptoms 55.6% but only 33.3% developed DCI and on the 5th day was29.2%.

All patients received triple H-therapy and nimodipine. Iinterventional emobilization of the aneurysms was done to all patients either by simple or balloon assisted coiling.

Table (2)
Occurrence of vasospasm and DCI in relation to the day of TCD measurement

Days	Patients with vasospasm= 27				p
	with vasospasm and w/o DCI		with vasospasm andDCI		
	n	%	n	%	
Day 0	0	0.0	0	0.0	1.000
Day 3	1	100.0	0	0.0	
Day 5	4	50,0	4	50.0	
Day7	1	66.7	5	33.3	
Day 10	0	100.0	0	0.0	
	3				

Table (4)
Agreement (sensitivity, specificity) for GCS, WFNS, HHS, Fisher score, and Ogilvy scale with transcranial Doppler for detection of vasospasm.

	Cut off	AUC	P	Sensitivity	Specificity
GCS	< 15	0.808	0.002*	66.7	92.3
WFNS	≥ 3	0.805	0.002*	26.0	100.0
HHS	≥ 3	0.808	0.002*	55.6	100.0
Fisherscore	≥ 3	0.654	0.119	37.0	19.3
Ogilvy scale	≥ 3	0.694	0.050*	22.2	100.0

Table (3)
Occurrence of vasospasm and DCI in relation to MFV of MCA, ACA and PCA measured by TCD

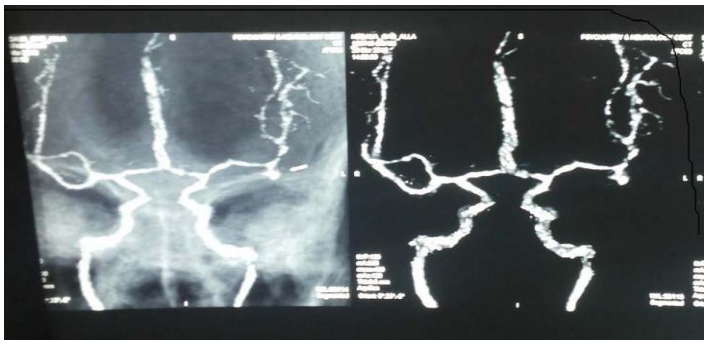
MFV of	Patients Without	Patients with vasospasm

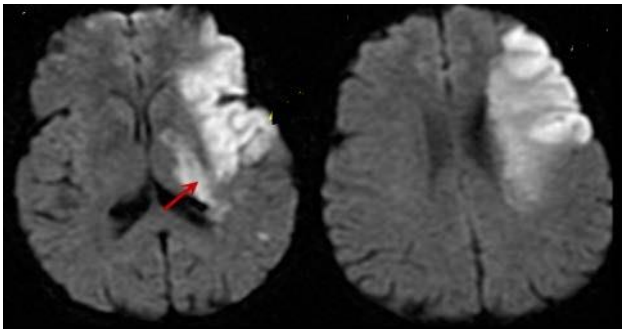
MCA (cm/s)	Patients without vasospasm		Patients with vasospasm w/o DCI		Patients with vasospasm and DCI		p
	n	%	n	%	N	%	
<120=22	22	100.0	0	0.0	0	0.0	0.001*
120-149=13	0	0.0	11	84.6	2	15.4	
≥150=5	0	0.0	0	0.0	5	100.0	

MFV of ACA (cm/s)	Patients Without vasospasm		Patients with vasospasm with vasospasm w/o DCI		Patients with vasospasm with vasospasm and DCI		p
	n	%	n	%	N	%	
<90=30	30	100.0	0	0.0	0	0.0	0.001*
90-110=6	0	0.0	5	83.3	1	16.7	
≥110=4	0	0.0	0	0.0	4	100.0	

MFV of PCA (cm/s)	Patients Without vasospasm		Patients with vasospasm with vasospasm w/o DCI		Patients with vasospasm with vasospasm and DCI		p
	n	%	n	%	n	%	
<60=35	35	100.0	0	0.0	0	0.0	0.001*
≥60=5	0	0.0	0	0.0	5	100.0	

*significant

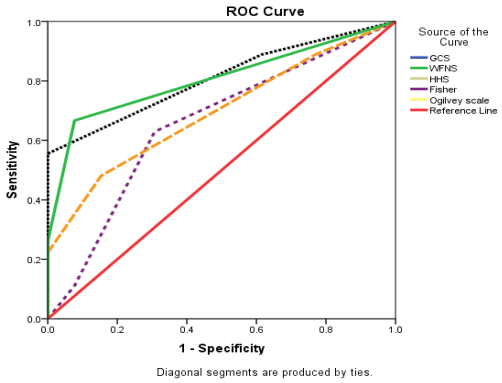




Discussion:

Symptomatic vasospasm is the clinical syndrome of delayed cerebral ischemia which remains the single most important cause of morbidity and mortality in those patients who survive the initial bleed. Cerebral vasospasm is associated with a deterioration in clinical status in 30% of patients after SAH[10].

Regarding risk factors this study revealed that there was a negative relation between age of patients and development of CV and DCI. This observation is in agreement with the work of Kale and colleagues 11].while Elderly patients may be at less risk for developing vasospasm, but they do not tolerate ischemia as well as younger ones do and therefore develop cerebral infarction more frequently.[10]



It was found that hypertension and smoking were most prominent risk factors of vasospasm.This result was in accordance with de Rooij and colleagues [12] who considered hypertension and smoking as a potential predictor of vasospasm. As other studies reported that the effect of hypertension on regional cerebral blood flow intracranial pressure and brain tissue oxygenation after SAH causing cerebral vasospasm [13].The study declared that vasospasm following aSAH is more common among patients with lower GCS, higher HHS scale and Fisher scale. These observations are in accordance with Chhor and colleagues [14], Inagawa and colleagues [15] and Frontera and colleagues [16] respectively. The study showed that cerebral vasospasm is common in patients with high SBP, DBP and MAP on admission. This observation is in agreement with Nakae and colleagues [17] who revealed a positive association between vasospasm and high blood pressure.

It was found that MCA and A.com aneurysms are the most common aneurysmal sites that develop cerebral vasospasm which is was in accordance with Ablaand colleagues [18]. Large size aneurysms were found to be a risk factor for cerebral vasospasm. This observation was in agreement with Macdonald and colleagues [19].The study showed that mild cases of vasospasm regressed spontaneously without progression to DCI while patients with severe vasospasm were more likely to develop DCI. These data was evidenced by TCD abnormalities. These results are in accordance with the work of Aldakkan and colleagues [20] and with that of Mortimer and colleagues [21] who specified that severe angiographic vasospasm is associated with increased risk of DCI and poorer functional out-come following aSAH. The 7th day after aSAH is the most significant day to develop cerebral

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vasospasm. This result is in accordance with Sen and colleagues [22] who stated that vasospasm is seen in 30% to 70% of angiograms at day 7 after SAH with and without clinical deficit.This study showed that TCD is an early detector of vasospasm and predictor of DCI progression TCD is useful not only in the early vasospasm diagnosis but also in the identification of progression and severity of vasospasm. Therefore, TCD could allow both early planning of therapeutic interventions as well as monitoring the effect of these interventions. Which can save golden hours and allow for early interventional spasmolytic injection to relieve the vasospasm. Mortimer and colleagues [21] as well as Jabbarli and colleagues [23] agreed with and declared these results.

Conclusion

clinical risk factors ,clinical grading scales with CD are strong and valuable predictors for early detection of vasospasm following SAH that save precious time and allow for early therapeutic and endovascular interventions.

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