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Evaluation of cerebral autoregulation using transcranial doppler ultrasound in patients with moderate and severe traumatic brain injuries

Taysser Zaytoun[1], Amr Abdalla[2], Bassem Beshay[3], Ahmed Elbeheiry[4], Moustafa Shebl[5]

[1-3,5]Department of Critical Care Medicine, Faculty of Medicine, University of Alexandria.
[2]Department of Radiodiagnosis, Faculty of Medicine, University of Alexandria
Email: : doctor.islam.ahmed@gmail.com

ABSTRACT

Introduction: Traumatic brain injury (TBI) has been increasing with greater incidence. It remains a leading cause of death. Cerebral pressure autoregulation impairment is a well-known pathology after TBI that worsens the prognosis and outcome. Transcranial Doppler (TCD) can be used to assess Transient Hyperaemic response ratio (THRR) after carotid compression which is a well demonstrated valid index for cerebral autoregulation. A relative increase in mean flow velocity (MFV) of middle cerebral artery (MCA) above the baseline following the release of carotid compression denotes preserved autoregulation and sequentially predicts good outcome, whereas absence of such response indicates altered autoregulation with poor outcome.
Design: Observational prospective cohort study
Setting: Alexandria Main University Hospital, Department of Critical Care Medicine
Patients & Methods: 120 patients with moderate or severe TBI according to Glasgow Coma Score (GCS) underwent daily TCD for 5 days post trauma. The primary end point is the Glasgow outcome score (GOS) as a measure of outcome to assess THRR after carotid compression as an indicator of cerebral pressure autoregulation as a predictor of GOS as well as a being prognostic tool. Other measures of TCD as MFV of MCA and Pulstility Index (PI) were also used as predictors of GOS and correlated with THRR. The length of stay as well as mortality were recorded and correlated to THRR.
Results: There was a significant correlation between THRR and GOS (patients with THRR ≥ 1 had favorable outcome). There was also significant correlation between THRR and length of stay and mortality. Also significant correlation between THRR and MFV as well as PI was found.
Conclusion: THRR provides a clinically useful index of cerebral autoregulation. THRR after carotid compression is a good predictor of GOS as well as being a prognostic tool in patients with moderate and severe TBI.

Keywords: Critical; Trauma; Injury; Transcranial; Ultrasound

INTRODUCTION

Traumatic brain injury (TBI) is a major public health and socio-economic problem worldwide. It one of the leading causes of death and disability among young adults. Prolonged disability is common in those who survive.[(1)] Every year, approximately 1.5 million people die from TBI. The major burden (90%) is in developing countries.[(2,3)]

It is well demonstrated that neurological outcome after TBI depends on the severity of initial injuries and the extent of secondary brain damage such as ischemia and hypoxia [(4)]. Prevention and treatment of such secondary injuries are mandatory and are considered a major concern of ICU management. In this situation, the maintenance of adequate cerebral blood flow (CBF) is critical [(5,6)].

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Transcranial Doppler (TCD), first described in 1982 [7]. Transcranial Doppler (TCD) is a noninvasive ultrasound (US) study used to measure cerebral blood flow velocity (CBF-V) in the major intracranial arteries. It involves use of low-frequency (≤2 MHz) US waves to insonate the basal cerebral arteries through relatively thin bone windows. TCD allows dynamic monitoring of CBF-V and vessel pulsatility, with a high temporal resolution. It is relatively inexpensive, repeatable, and its portability offers increased convenience over other imaging methods, allowing continuous bedside monitoring of CBF-V, which is particularly useful in the intensive care setting [8].

Cerebral pressure autoregulation can be defined as the maintenance of CBF despite changes in CPP between 50 and 150 mmHg [9]. Cerebral pressure autoregulation impairment is a well-known pathology after TBI that worsens the prognosis as well as outcome [10].

Transient Hyperaemic response ratio (THRR) after carotid compression (ratio of hyperaemic blood flow velocity (MFV) of MCA after release of compression to baseline blood flow velocity) is a well demonstrated valid index for cerebral autoregulation [11]. It can be assessed using TCD. A relative increase in mean flow velocity (MFV) of middle cerebral artery (MCA) above the baseline following the release of carotid compression denotes preserved autoregulation which predicts good outcome, whereas absence of such response indicates altered autoregulation which in turn predicts poor outcome [12].

Experimental factors such as duration of common carotid artery compression and magnitude of the decrease in blood flow velocity during common carotid artery compression can significantly influence THRR. These factors should be controlled if the transient hyperaemic response test is used for a comparison between repeated measurements. A compression time of 10 seconds and a compression ratio of 40% or more, allow maximum expression of the hyperaemic response in healthy volunteers. Also carotid compression is accepted only when FV is stable with no further decrease during the whole period of compression otherwise the compression will be terminated and repeated 60 seconds later [11].

In this study, the THRR test was applied to patients who had received a moderate and severe head injury according to Glasgow Coma Score [13] (GCS) ≤ 8 or 9 – 12 respectively, and the value of the test was assessed by comparing its result with other TCD parameters as MFV and PI as well as correlating it to length of stay and mortality and outcome using Glasgow Outcome Score [14] (GOS).

The aim of the work was to assess cerebral autoregulation and its relation to outcome in patients with moderate and severe traumatic brain injury using Transcranial Doppler Ultrasound. Other measures of TCD as MFV of MCA and PI was also used as predictors of GOS and correlated with THRR. The length of stay as well as mortality were recorded and correlated to THRR.

PATIENT AND METHODS

This is an observational prospective cohort study which was conducted on 120 patients with moderate or severe TBI and who arrived within 8 hours of injury with a Glasgow Coma Score [13] ≤ 8 or 9 - 12 admitted to Alexandria main university hospital after being assessed for eligibility for the study. They were selected randomly. A signed written informed consent was obtained from patient relatives as well as local ethical committee approval.

Both genders were eligible for the study. No acceptance of health volunteers. Only admitted patients with severe traumatic brain injury who arrived within 8 hours of injury with a Glasgow Coma Score ≤ 8 or 9-12 after initial management and stabilization stage were included in this study.

Patients aged less than 6 years or more than 70 years, those with life threatening trauma (e.g. tension pneumothorax, intra-abdominal bleeding) or hemodynamic instability after initial resuscitation, those with severe anoxic intracerebral damage or brain death, surgical patients as well as pregnant patients and lactating female were excluded from our study. Also those with inadequate ultrasound window or temporal bone fracture or transcalvarial brain herniation were excluded.

All patients enrolled in this study – diagnosed as Traumatic Brain Injury (TBI) with Glasgow Coma Scale (GCS)≤ 8 or 9 - 12 without exclusion criteria – were subjected Initial assessment (ABCs), detailed history and complete physical examination. Investigations including plain chest radiography, abdominal ultrasonography, laboratory investigations and Computerized Tomography (CT) brain on admission (day1), follow up after 48 hrs (day3) and day 5 was done. Characteristics of CT brain of the head was described using Marshall CT classification model [15], and Rotterdam CT scan score [16].

Enrolled patients received the standard treatment for management of TBI on the guidelines for the management of head injury of the American Association of Neurologic Surgeons. [17]

Measurements:

- The patient's condition – body temperature, heart rate and respiratory rate, blood pressure, and blood oxygen saturation – were monitored continuously at the bedside with monitoring apparatus.
- Daily evaluations of neurologic status over the initial 14-days period was performed via GCS score. Other morbidities and mortality will be observed.
- TCD ultrasonography was performed within the first 24 hours, immediately after hemodynamic and respiratory stabilization as well as in 2nd, 3rd, 4th and 5th days post trauma :

- Standing behind the head of the patient, an ultrasound (US) frequency of ≤2 MHz was used to penetrate the skull and reach the intracranial vasculature. Through the transtemporal window, located above the zygomatic ridge between the lateral canthus of the eye and auricular pinna the probe will be placed and oriented slightly upward and anteriorly.
- A red color signal (toward the probe) at a depth between 40-65mm represent the flow in the ipsilateral M1 MCA. The angle and position of insonation adjusted to provide the highest quality Doppler signal.
- By applying pulsed wave on the insonated segment, the systolic (PSV) and diastolic (EDV) velocities were measured and recorded on US machine.
- The mean flow velocity (MFV) then calculated using the formula: (PSV+ (EDVx 2))/3 [18].
- Pulsatility index (PI) provides information on downstream cerebral vascular resistance and was calculated using the formula: (PSV-EDV)/ MFV[19].
- The right and left MCA was explored within 5 minutes and data will be recorded on the ultrasound machine(vivid 3 device (General Electric®, Norway))
- ARI (autoregulation index) was calculated using THRR which is the ratio of MFV 2 minutes after compression of ipsilateral common carotid artery for 10 seconds to baseline MFV. Carotid compression is accepted only when FV is stable with no further decrease during the whole period of compression otherwise the compression will be terminated and repeated 60 seconds later.
- An increase in MFV of MCA after release of carotid compression in relation to intial baseline MFV indicates preserved autoregulation and sequentially good outcome, whereas absence of such increase indicates lost autoregulation and poor outcome [199].
- The following were collected at the time of the TCD study:
  - $PaCO_2$ in Arterial blood gases within 15 minutes of the study.
  - Blood pressure: systolic, diastolic and mean in mmHg.
  - Heart rate (Beats/min)
  - Hemoglobin and hematocrit level. (on the same day of the examination)
  - Temperature (°C)
  - GCS at the time of examination just before the TCD study

The neurological outcome will be evaluated by Glasgow Outcome Scale (GOS) score – after 30 days – which contains five levels of outcomes [206].

For statistical analysis, GOS scores are dichotomized into favorable or unfavorable outcomes. Patients in the upper two GOS outcomes groups (good recovery or moderate disability) are considered favorable outcome, and patients in other groups (severe disability, vegetative state or death) are considered unfavorable outcomes.

Other measures of TCD as MFV of MCA and PI was also used as predictors of GOS and correlated with THRR. Another parameters of outcome as the length of stay as well as mortality were recorded and correlated to THRR.

RESULTS

The current study included 120 adult patients who suffered from severe and moderate traumatic brain injury (TBI). As regard patient characteristics, their age ranged between 12 to 57 years with a median value of 28.50 year. We found that the majority of TBI patients were males who were injured in road traffic accidents (RTA). Their vital signs, oxygen saturation, PaCO2 and HCT were within normal ranges. Also the studied cases CT brain findings according to Marshall CT classification model and Rotterdam CT scan score were described. **(Table-1).**

Regarding GCS in day 1(at admission), 92(76.7%) patients was with severe TBI and 28(23.3) patients was with moderate TBI. Distribution of the patients according to GCS in day1, day 7 and day 14 were described. **(Table-2).**

Regarding relation between MFV and THRR patients with MFV 40 – 70 had THRR 0.91 – 1.39 with mean 1.12 ± 0.11 while those with MFV < 40 had THRR 0.70 – 2.04 with mean 1.08 ± 0.35 in day 1. In day 3 and day 5 patients with MFV < 40 had THRR 0.82 – 1.12 with mean 0.94 ± 0.07 and 0.74 – 1.04 with mean 0.90 ± 0.08 respectively while those with MFV 40 – 70 showed THRR measures of 0.82 – 1.12 with mean 0.94 ± 0.07 and 0.54 – 1.47 with mean 1.07 ± 0.19. There was significant +ve correlation between them in day 3 t(p) **=** 8.690 (<0.001) as well as day 5 t(p) **=** 6.844 (<0.001) **(Table-3).**

Patients with PI >1.2 had THRR in day 1 0.70 – 1.48 with mean 0.98 ± 0.18 while those with PI < 1.2 had THRR 0.77 – 2.04 with mean 1.14 ± 0.24 . Also in correlation to THRR average, those with PI > 1.2 had THRR average ranging from 0.87 – 1.02 with mean 0.94 ± 0.04 and those with PI < 1.2 showed THRR average ranging from 0.87 – 1.42 with mean 1.10 ± 0.12 which was highly significant in both (p <0.001). There was highly significant – ve correlation between THRR in day 1 as well as THRR average and PI (p <0.001, r= -0.438, -0.636 respectively) **(Table-4).**

In day 1 59 (81.9%) patients with favorable outcome had THRR ≥1 while 13(18.1%) patients had THRR <1. On the other side 15 (31.3%) patients with unfavorable outcome had THRR ≥1 and 33(68.8%) patients had THRR <1. This was highly significant (p <0.001). In day 5 54(75%) patients with favorable outcome had THRR ≥1 while 18(25%) patients had THRR <1, meanwhile 9 (18.7%) patients with unfavorable outcome had THRR ≥1 and 39(81.3%) patients had THRR <1. Similarly, this was highly significant (p <0.001). As regard THRR average in 5 days 60(83.3%) patients with favorable outcome had THRR ≥1 while 12(16.7%) patients had THRR <1. On the other side 13(27.1%) patients with unfavorable outcome had THRR ≥1 and 35(72.9%) patients had THRR <1. This also was highly significant (p <0.001). **(Table-5).**

Table-1. All patients' characteristics

	No.	%	Vital sings	Min. – Max.	Mean ± SD.
Sex			**MAP**	65.0 – 100.0	83.58 ± 9.77
Male	84	70.0	**HR**	69.0 – 108.0	95.99 ± 8.49
Female	36	30.0	**Temperature**	37.0 – 38.50	37.56 ± 0.37
Age (years)			**RR**	18.0 – 30.0	23.65 ± 3.37
≤30	68	56.7	**SaO_2**	94.0 – 99.0	97.03 ± 1.38
>30	52	43.3	**$PaCO_2$**	32.0 – 47.0	39.17 ± 4.28
Min. – Max.	12.0 – 57.0		**HCT**	33.0 – 43.0	38.77 ± 2.65
Median	28.50				

Mode of Trauma	**No.**	**%**
RTA	87	72.5
FFH	28	23.3
Alleged assault	5	4.2

	Day 1		**Day 3**		**Day 5**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Marshall						
I	0	0.0	9	7.5	53	44.2
II	60	50.0	83	69.2	67	55.8
III	60	50.0	28	23.3	0	0.0
Rotterdam						
Min. – Max.	2.0 – 4.0		2.0 – 3.0		2.0 – 3.0	
Mean ± SD.	2.69 ± 0.59		2.53 ± 0.50		2.29 ± 0.46	

Table-2. Distribution of the patients according to GCS

GCS	No.	%
Day 1 (n = 120)		
≤8	92	76.7
9 – 12	28	23.3
Day 7 (n = 120)		
≤8	45	37.5
9 – 12	59	49.2
>12	16	13.3
Day 14 (n = 100)		
≤8	29	29.0
9 – 12	28	28.0
>12	43	43.0

There was highly significant – ve correlation between THRR in day 1 as well as day 5 and THRR average and ICU/hospital stay (p <0.001, r= -0.433), (p <0.001, r= -0.476), (p <0.001, r= -0.485) respectively. The survived patients with THRR < 1 in day 1 were 38(33.9%) and in day 5 were 49(43.8%), while survivors with THRR ≥ 1 were 74(66.1%) and 63(56.3%) in day 1 and day 5 respectively. Also in relation to THRR average ≥ 1 survivors were 73(65.2%) and those with THRR average <1 were 39(34.8%). On the other hand all non survivors 8(100%) had THRR < 1 which was highly significant (p <0.001) **(Table-6).**

In day 1 a THRR ≥ 1 showed sensitivity of 81.9%, specificity of 68.8%, PPV of 79.7% and NPV of 71.7% in predicting patients with favorable outcome. . In day 5 a THRR ≥ 1 showed sensitivity of 75%, specificity of 81.3%, PPV of 85.7% and NPV of 68.4% in predicting patients with favorable outcome. As regard THRR average in 5 days a THRR ≥ 1 showed sensitivity of 83.3%, specificity of 72.9%, PPV of 82.2% and NPV of 74.5% in predicting patients with favorable outcome **(Table-7), (Fig-1).**

DISCUSSION

In our study we used TCD in patients with moderate and severe TBI as a bedside tool to assess cerebral autoregulation simply through THRR after carotid compression without any other complicated maneuvers.

The demographic data of this study showed higher percentage of males (84 patients -70%). This male predominance is a quiet common finding in most of the studies dealing with trauma as males are more vulnerable to injuries due to social and environmental considerations. Similarly, Bahloul et al [20] found 90% of his patients were males and only 10% were females in a study conducted over a 3-year period involved 437 adult patients with traumatic brain injury. Also like the study done by Allard et al [21] who had 55 patients (76%) of them were males, and (24%) were females. These studies were very close to our study as regard sex distribution.

Table-3. Relation between MFV (F1) with THRR at each day

	MFV (F1) at day 1		MFV (F1) at day 3		MFV (F1) at day 5	
	<40 (n = 47)	40 – 70 (n = 73)	<40 (n = 43)	40 – 70 (n = 77)	<40 (n = 37)	40 – 70 (n = 83)
THRR						
Min. – Max.	0.70 – 2.04	0.91 – 1.39	0.82 – 1.12	0.77 – 1.43	0.74 – 1.04	0.54 – 1.47
Mean ± SD.	1.08 ± 0.35	1.12 ± 0.11	0.94 ± 0.07	1.11 ± 0.14	0.90 ± 0.08	1.07 ± 0.19
t(p)	0.706(0.483)		8.690*(<0.001*)		6.844*(<0.001*)	

t, p: t and p values for Student t-test for comparing between the two groups
*: Statistically significant at p ≤ 0.05

Table-4. Relation between PI (day1) and THRR

	PI (day1)		t	p
	<1.2 (n=89)	>1.2 (n=31)		
THRR average				
Min. – Max.	0.87 – 1.42	0.87 – 1.02	10.349*	<0.001*
Mean ± SD.	1.10 ± 0.12	0.94 ± 0.04		
r(p)	-0.636*(<0.001*)			
THRR Day 1				
Min. – Max.	0.77 – 2.04	0.70 – 1.48	3.507*	0.001*
Mean ± SD.	1.14 ± 0.24	0.98 ± 0.18		
r(p)	-0.438*(<0.001*)			

t, p: t and p values for Student t-test
r: Pearson coefficient
*: Statistically significant at p ≤ 0.05

Table-.5. Relation between GOS and THRR

	GOS				□□	p
	Un favorable (n = 48)		Favorable (n =72)			
	No.	%	No.	%		
THRR Day 1						
<1	33	68.8	13	18.1	31.310*	<0.001*
≥1	15	31.3	59	81.9		
THRR Day 2						
<1	31	64.6	19	26.4	17.286*	<0.001*
≥1	17	35.4	53	73.6		
THRR Day 3						
<1	33	68.8	15	20.8	27.552*	<0.001*
≥1	15	31.3	57	79.2		
THRR Day 4						
<1	25	52.1	22	30.6	5.602*	0.018*
≥1	23	47.9	50	69.4		
THRR Day 5						
<1	39	81.3	18	25.0	36.541*	<0.001*
≥1	9	18.7	54	75.0		
THRR (average)						
<1	35	72.9	12	16.7	38.245*	<0.001*
≥1	13	27.1	60	83.3		

χ^2, p: χ^2 and p values for Chi square test for comparing between the two groups
*: Statistically significant at p ≤ 0.05

In the current study age ranged between 12 to 57 years with a median value of 28.50 year. This was in agreement with the 10008 patients with TBI who were recruited into the Medical Research Council CRASH trial where the mean age was 37±17.1 years, decreasing significantly to 35.8±16 years in low-middle income countries. [3] Similarly, in the IMPACT database which included 8509 patients with median age 30 years. [22]

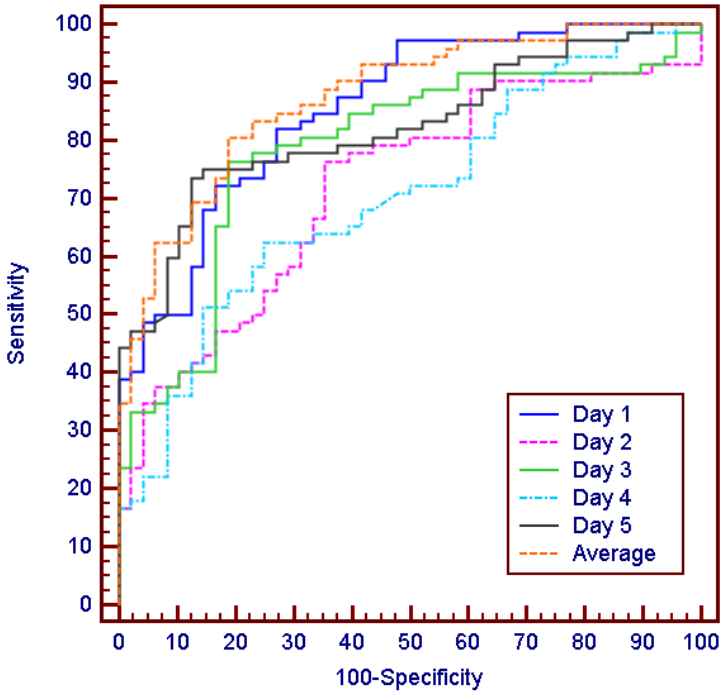
Table-6. Correlation between THRR and ICU stay and Mortality

	THRR					
	Average		Day 1		Day 5	
	r	p	r	P	R	p
ICU stay	-0.485*	<0.001*	-0.433*	<0.001*	-0.476*	<0.001*

THRR	Mortality				Test of sig.	p
	No (n=112)		Yes (n=8)			
	No.	%	No.	%		
Average						
<1	39	34.8	8	100.0	χ^2= 13.313*	FEp <0.001*
≥ 1	73	65.2	0	0.0		
Min. – Max.	0.88 – 1.42		0.87 – 0.92		t= 12.757*	<0.001*
Mean ± SD.	1.07 ± 0.13		0.90 ± 0.02			
Day 1						
<1	38	33.9	8	100.0	13.789*	FEp <0.001*
≥ 1	74	66.1	0	0.0		
Min. – Max.	0.70 – 2.04		0.79 – 0.96		t=2.883*	0.005*
Mean ± SD.	1.12 ± 0.23		0.88 ± 0.07			
Day 5						
<1	49	43.8	8	100.0	9.474*	FEp= 0.002*
≥ 1	63	56.3	0	0.0		
Min. – Max.	0.54 – 1.47		0.71 – 0.91		t=8.310*	<0.001*
Mean ± SD.	1.03 ± 0.18		0.80 ± 0.06			

r: Pearson coefficient
χ^2, p: χ^2 and p values for Chi square test
FE: Fisher Exact for Chi square test
t, p: t and p values for Student t-test
*: Statistically significant at p ≤ 0.05

Figure-1. Agreement (sensitivity, specificity and accuracy) for THRR to predict favorable cases



In our study regarding the mode of trauma Road traffic accident was responsible for TBI in 87(72.5%) of the patients, alleged assault in 5(4.2%) and falling from height in 28(23.3%) patients. Commonly the majority of

Table-7. Agreement (sensitivity, specificity and accuracy) for THRR to predict favorable cases

THRR	AUC	P	C.I (95%)	Youden	Cut off	Sensitivity	Specificity	PPV	NPV
Day 1	0.855*	<0.001*	0.779 - 0.913	0.556	>1.058	72.22	83.33	86.7	66.7
					≥1	81.9	68.8	79.7	71.7
Day 2	0.718*	<0.001*	0.629 - 0.796	0.4097	>0.9884	76.39	64.58	76.4	64.6
					≥1	73.6	64.6	75.7	62.0
Day 3	0.786*	<0.001*	0.701 - 0.855	0.5764	>1.0187	76.39	81.25	85.9	69.6
					≥1	79.2	68.8	79.2	68.8
Day 4	0.704*	<0.001*	0.614 - 0.783	0.3750	>1.0468	62.50	75.0	78.9	57.1
					≥1	70.8	52.1	68.9	54.3
Day 5	0.822*	<0.001*	0.746 - 0.886	0.6111	>1.0105	73.61	87.50	89.8	68.9
					≥1	75.0	81.3	85.7	68.4
Average	0.874*	<0.001*	0.801 - 0.928	0.6181	>1.0079	80.56	81.25	86.6	73.6
					≥1	83.3	72.9	82.2	74.5

TBI patients are young adult males who are injured in motor vehicle accidents. [1, 23]

The primary end point of this study was the GOS as a measure of outcome to assess THRR after carotid compression as an indicator of cerebral pressure autoregulation as a predictor of GOS as well as a being prognostic tool in patients with moderate and severe TBI. Other measures of TCD as MFV of MCA and PI was also used as predictors of GOS and correlated with THRR. The length of stay as well as mortality were recorded and correlated to THRR.

Regarding MFV in our study in day 1, 73(60.8%) patients were with normal range MFV (40-70) and 47(39.2%) showed decreased MFV (<40). In day 5, 83(69.2) patients were with normal range MFV (40-70) and 37(30.8%) showed decreased MFV (<40).

As for PI 89(74.2%) of our patients were with normal range PI (<1.2) and 31(25.8%) had increased PI (>1.2) which carry poor prognosis.

In correlation to GOS In day 1 59(81.9%) patients with favorable outcome had MFV 40 – 70 while 13(18.1%) patients had MFV < 40 on the other hand 14(29.2%) patients with unfavorable outcome had MFV 40 – 70 and 34(70.8%) patients had MFV < 40. This was highly significant (p <0.001). MFV ≥40 showed sensitivity of 81.94%, specificity of 70.83%, PPV of 80.82% and NPV of 72.34% in predicting patients with favorable outcome. Also In day 5 61(84.7%) patients with favorable outcome had MFV 40 – 70 while 11(15.3%) patients had MFV < 40 on the other hand 22(45.8%) patients with unfavorable outcome had MFV 40 – 70 and 26(54.2%) patients had MFV < 40. Again this was highly significant (p <0.001). MFV ≥40 showed sensitivity of 84.72%, specificity of 54.17%, PPV of 73.49% and NPV of 70.27% in predicting patients with favorable outcome.

Regarding PI 67(93.1%) Patients with favorable outcome had PI < 1.2 while 5(6.9%) patients showed PI > 1.2. 22(45.8) patients with unfavorable outcome had PI < 1.2 and 26(54.2) patients had PI > 1.2. This was highly significant (p <0.001). PI of ≤ 1.2 showed sensitivity of 93.06%, specificity of 54.17%, PPV of 75.3% and NPV of 83.9% in predicting patients with favorable outcome.

Nearly resembling us Tan et al [24] conducted a prospective study to evaluate the contribution of TCD ultrasonography to neurological outcome in a series of 96 severe traumatic brain injury patients. The quantitative variables of TCD ultrasonography included the mean blood flow velocity of the middle cerebral artery (MCA) and pulsatility index within the first 24 hours of admission. Outcome in 6 months post injury was evaluated using the Glasgow Outcome Scale. The mean blood flow velocity of the MCA was larger than 40 cm/s in 30 (51%) patients with good outcome whereas it was less than 40 cm/s in 27 (73%) patients with poor outcome (P<0.025). The mean PI in cases of good outcome (34 patients, 57%) was lower than 1.5 whereas in poor outcome (30 patients, 83%) was higher than 1.5 (P<0.001). The correlations of ICP and CPP to pulsatility index were statistically significant (P<0.01).

Also in line with us, Elsayed et al [25] conducted a study on 40 patients with moderate to severe traumatic brain injury (GCS ≤ 13) admitted to Alexandria university teaching hospital. TCD measurements were performed daily for 7 days. TCD was performed on both middle cerebral arteries(MCA), recording MFV in cm/s and PI. Marshall and Rotterdam head CT neuroimaging scales were recorded on admission, 48 hours and 5 to 7 days later. Glasgow Outcome Scale(GOS)- was assessed six months after discharge for survivors. A significant direct correlation was demonstrated between the ICU LOS and the PI. The MFV were significantly higher on days 2 to 4 in survivors than in non-survivors. On day 2, a MFV of ≤27.31 cm/sec was 94.44 % accurate in detecting non-survivors. On day 3, a MFV of ≤6.62 cm/sec was 100 % accurate in detecting non-survivors. TCD derived parameters predicted survival in TBI patients. TCD derived PI correlated directly with ICU length of stay.

Also in this context, Moreno et al.[26] studied 125 severe TBI patients (mean GCS score 6.02 ± 1.81) with invasive ICP monitoring via intraparenchymal catheters

(mean ICP 22.07 ± 17.29), where they calculated a mean PI of 1.26 ± 0.73 mmHg in the first 24 hours of admission. A strong correlation was demonstrated between ICP and TCD derived PI that for each increase of 1 unit in ICP, the PI increased 0.03 units. This increase was statistically significant ($p < 0.0001$). Mean blood velocity, as measured in patients with good outcome (GOS 4-5), was 44 cm/sec, whereas it was 36 cm/sec in those with poor outcome (GOS 4-5) ($p = 0.003$). The mean PI predicting good outcome was 1 and the mean PI predicting poor outcome was 1.56, with 83% of those with a PI of greater than or equal to 1.56 suffering poor outcome. In cases in which the PI was equal to or greater than 2.3, the mortality rate was 100%.

Ract et al. [27] correlated TCD parameters measured on admission of 24 patients with severe TBI with the GOS at 3 months, they found that when TCD was considered abnormal i.e. when two of the three measured values were abnormal using the following thresholds: MFV < 30 cm/sec, dFV < 20 cm/sec, PI > 1.4., the GOS was significantly poorer ($p < 0.006$).

As regard correlation between THRR and GOS in day 1 59(81.9%) patients with favorable outcome had THRR ≥1 while 13(18.1%) patients had THRR <1. On the other side 15(31.3%) patients with unfavorable outcome had THRR ≥1 and 33(68.8%) patients had THRR <1. This was highly significant ($p <0.001$). THRR ≥ 1 showed sensitivity of 81.9%, specificity of 68.8%, PPV of 79.7% and NPV of 71.7% in predicting patients with favorable outcome. The same found in day 5 where 54(75%) patients with favorable outcome had THRR ≥1 while 18(25%) patients had THRR <1, meanwhile 9(18.7%) patients with unfavorable outcome had THRR ≥1 and 39(81.3%) patients had THRR <1. Similarly this was highly significant ($p <0.001$). THRR ≥ 1 showed sensitivity of 75%, specificity of 81.3%, PPV of 85.7% and NPV of 68.4% in predicting patients with favorable outcome.

Regarding THRR average 60(83.3%) patients with favorable outcome had THRR ≥1 while 12(16.7%) patients had THRR <1. On the other side 13(27.1%) patients with unfavorable outcome had THRR ≥1 and 35(72.9%) patients had THRR <1. This also was highly significant ($p <0.001$). THRR ≥ 1 showed sensitivity of 83.3%, specificity of 72.9%, PPV of 82.2% and NPV of 74.5% in predicting patients with favorable outcome.

Greatly supporting our results Smielewski et al [12] conducted a study upon Forty-seven patients, aged 16 to 63 years with head injuries. Signals of intracranial pressure, arterial blood pressure, flow velocity, and cortical microcirculatory flux were digitized and recorded for a period of 30 minutes using special computer software. Two carotid compressions were performed at the beginning of each recording. The transient hyperemic response ratio (THRR: the ratio of the hyperemic flow velocity recorded after carotid release and the precompression baseline flow velocity) was calculated, as was the correlation coefficient Sx (Pearson correlation coefficients between systolic flow velocity and CPP which were calculated and averaged from 10-minute periods of recording that did not include compressions) used to describe the relationship between slow fluctuations in the systolic flow velocity and CPP throughout the period of recording. No significant changes in CPP were found during compression. There was a significant correlation between the THRR and the Sx, the cortical microcirculation responded to the brief carotid compression in a similar way to flow velocity ($r = 0.49$, p , 0.0001). The hyperemic response proved to be lower (<1) in patients who exhibited a poor clinical grade at presentation (GCS scores, 6, $p = 0.01$) and lower in patients achieving a poor outcome (GOS scores of 3, 4, and 5, $p = 0.003$) and higher (>1) in patients with good outcome. Loss of post compression hyperemia occurred when the CPP fell below 50 mm Hg.

CONCLUSIONS

Prediction of outcome in TBI patients is possible with TCD through measuring MFV and PI which may serve as good predictors of outcome in patients with TBI. THRR after carotid compression provides a clinically useful index of cerebral autoregulation. The test is simple, can be applied repetitively as well as potentially being a good predictor of GOS and also it can be a prognostic tool in patients with moderate and severe TBI.

Ethics

After ethical approval for this clinical trial from the local committee of ethics in the faculty of medicine of Alexandria University and the department of critical care, Informed consents for participating and publishing were taken from the next of kin of patients after approval by critical care department committee.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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