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Comparative Analysis of Simultaneous Transcranial Doppler and Perfusion Computed Tomography for Cerebral Perfusion Evaluation in Patients with Traumatic Brain Injury

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Abstract

The aim was to investigate the feasibility of simultaneous comparison of cerebral circulation in major vessels and microvasculature in patients suffering traumatic brain injury (TBI) with or without intracranial hematomas (IH).

Methods.—170 patients were divided into two groups: Group 1 – diffuse TBI (75 patients); and Group 2 – TBI with IH (95 patients: 18 epidural, 65 subdural and 12 multiple). Perfusion computed tomography (PCT) for assessment of volumetric cerebral blood flow (CBF) was done 2–15 days after admission to hospital. Simultaneous assessment of cerebral blood flow velocity (CBFV) in both middle cerebral arteries was done by transcranial Doppler.

Results.—In patients with diffuse TBI, CBF had statistically valid correlations with CBFV ($r = 0.28$, $p = 0.0149$ on the left side; $r = 0.382$, $p = 0.00075$ on the right side). In patients with TBI and IH, the analysis did not reveal any reliable correlations between the CBFV and CBF velocity in the temporal lobes, either on the side of the removed IH or on the opposite side.

Conclusion.—The greatest linear correlation was noted in patients with diffuse TBI without the development of a coarse shift of the midline structures and dislocation syndrome. This correlation decreases with the increase in injury severity and development of secondary complications in the acute period, which probably reflects impairment of the coupling of oxygen consumption by brain tissue and cerebral microcirculation.

Keywords

Traumatic brain injury; Perfusion computer tomography; Cerebral blood flow; Doppler; Cerebral blood flow velocity; Intracranial hematoma

1 Introduction

The common definition of cerebral autoregulation (CA) describes the brain's ability to maintain adequate microcirculation in the context of changes in mean arterial pressure [1, 2]. Cerebral autoregulation assessment techniques, used clinically, typically evaluate responses in cerebral blood flow (CBF) and cerebral blood flow velocity (CBFV) to changes in arterial blood pressure (ABP) alone [3]. Comparative studies have investigated the relationship between CBF and CBFV [2, 4, 5] during steady-state changes in mean arterial pressure (MAP); however, no comparison has been made between CBF and CBFV in traumatic brain injury (TBI). To provide insight into the utility of correlations between CBF and CBFV as a measure of autoregulation in this patient group, and to add to the body of comparative literature on this topic [6], we performed a comparison between CBF and CBFV in TBI patients without intracranial hematomas (IH) and after neurosurgical removal of developed IH.

The aim of our work was to investigate the feasibility of simultaneous comparison of the cerebral circulation in major vessels and microvasculature, using perfusion computer tomography (PCT) and transcranial Doppler in traumatized brain with and without IH.

2 Materials and Methods

This single-center prospective study complies with the Declaration of Helsinki and the protocol was approved by the local Ethics Committee. All the patients gave informed consent to participate in the study. All 170 patients with TBI were treated at the Nizhny Novgorod Regional Trauma Center Level I in 2012–2017. Mean age of the patients was 35.5 ± 14.8 (range 15–73) years; 65 women/105 men. The patients were divided into two groups: Group 1 included 75 patients with diffuse TBI (Marshall II–III and Rotterdam 1–3) without hematomas; and Group 2 included 95 patients with TBI after neurosurgical removal of IH (18 epidural, 65 subdural, 12 multiple). These two groups were comparable in age and severity of TBI (GCS) and concomitant lesions (Injury Severity Score). All patients in Group 2 underwent surgery within the first 3 days. A complex of the neuromonitoring 'Centaurus' was used during the study (Ver. 2.0, Nizhny Novgorod State Medical Academy, Russia). The neuromonitoring system is shown in Fig. 1.

All patients were subjected to dynamic PCT by 64-slice tomograph Philips Ingenuity CT (Philips Medical Systems, Cleveland, USA). The tomography was performed 1–12 days after

TBI (mean 4 ± 3 days) in Group 1 and 2–8 days (mean 4 ± 2 days) after surgical evacuation of the hematoma in Group 2. The perfusion examination report included an initial contrast-free CT of the brain. Extended scanning was further performed in 16 areas of interest, 160 mm in thickness, within 60s, with a contrast agent (Perfusion JOG mode). The scanning parameters were 160 kVp, 160 mA, 70 mAs, 512×512 . The contrast agent Ultravist 370 (Schering AG, Germany) was administered with an automatic syringe injector (Stellant, Medrad, Indianola, USA) into a peripheral vein through a standard catheter (20 G) at a rate of 4–5 ml/sec in a dose of 30–50 ml per examination.

After scanning, data were transferred to a Philips Extended Brilliance Workspace workstation (Philips HealthCare Netherlands B.V., Best, the Netherlands). Artery and vein marks were automatically recorded, followed by the manual control of indices in the time-concentration diagram. Regions of interest (ROI) were established in subcortical areas of the middle cerebral artery. Perfusion maps were derived from the tissue time-attenuation curve on the basis of the change in X-ray attenuation, which is linearly related to iodinated contrast concentration on a per-voxel basis with time. Errors introduced by delay and dispersion of the contrast bolus before arrival in the cerebral circulation were corrected by block-circulant deconvolution algorithm. Quantitative perfusion indices, including CBF, were calculated on a voxel-wise basis and were used to generate color-coded maps. The voxels with volumetric CBF > 100 mL/100 g/min or cerebral blood volume (CBV) > 8 mL/100g were assumed to contain vessels and removed from the ROI, using the Remote vessels' mode.

CBF velocity in the middle cerebral artery (Vav, cm/sec) was measured simultaneously and bilaterally by transcranial Doppler through the temporal window with a 2-MHz probe (Sonomed 300 M, Spectromed, Russia) according to the method developed by R. Aaslid [7]. The probe was positioned over the temporal bone window above the zygomatic arch and fixed. This procedure ensured that the angle and individual depth of insonation remained constant during investigation. The temporal ultrasound window and depth of the insonation provided the highest velocities were used for all measurements. The Doppler probe was fixed over the temple with a special headset.

Statistical Analysis.

The Statistica 7.0 (StatSoft Inc., USA, 2004) was used for all analyses. The obtained data had a normal distribution, so are presented as an average $\pm$ standard deviation (SD). Comparisons between the groups were made using Student's t-test. Spearman's correlation coefficients were used to assess agreement between computed variables. Plots of CBF versus mean CBFV (Vav) were constructed to graphically depict the correlations. The regression line and confidence limits for each are for illustrative purposes only. The level of significance was preset to $p < 0.05$.

3 Results

Basic statistics for recorded parameters (Vav, CBF) and the comparison of the analyzed parameters are shown in Table 1. In patients with diffuse TBI the volumetric CBF had statistically valid, moderately expressed correlations with the cerebral blood flow velocity

(Spearman's $r = 0.28$, $p = 0.0149$ on the left side (Fig. 2a); Spearman's $r = 0.382$, $p = 0.00075$ on the right side (Fig. 2b)).

In patients with TBI after surgical removal of IH, the performed correlation analysis did not reveal any statistically reliable correlations between the linear blood flow velocity in the MCA and the volumetric flow velocity in the temporal lobes, either on the side of the removed hematoma (perifocal zone) or on the opposite side (Fig. 3).

4 Discussion

In this study, we investigated patients with diffuse TBI and focal TBI (after surgery for hematomas) and did not find a statistically significant difference between CBF and CBFV on the left and right side in patients with diffuse TBI which is consistent with previous studies [1].

Previous studies have shown statistically significant correlations between absolute values of flows and velocities were statistically significant in healthy volunteers, and the relationship between CBF and MV was described according to a linear model [4].

The most marked correlation was noted in TBI patients with diffuse lesions without the development of a coarse shift of the midline structures and dislocation syndrome. This correlation decreased with the increase in injury severity and development of secondary complications in the acute period, which probably reflects impairment of the coupling of oxygen consumption by brain tissue and cerebral microcirculation. We assume that the volumetric CBF depends on both the regional blood supply and the linear blood flow velocity.

The nonlinear correlation between the volumetric blood flow and regional blood supply in the damaged brain areas might be similar to Lassen's autoregulation curve [8, 9], which also shows the nonlinear dynamics of changes in volumetric blood flow in the case of brain injuries. We noted a similar pattern when studying patients in the acute phase after the removal of traumatic IH. Although comparison of the perfusion data in patients in Group 2 has not revealed any significant differences between the side of the removed hematoma and the opposite hemisphere, the correlations between these parameters of CBF were seriously disrupted. Thus, we have shown that in patients of this group the volumetric blood flow velocity did not reliably correlate with its linear velocity.

In our opinion, development of the disruption between linear and volumetric cerebral flow reflects a serious disturbance of CBF autoregulation, as an increase in linear blood flow velocity after surgery causes a reverse reaction, i.e. a drop in volumetric blood flow. In contradistinction to our data, in healthy individuals, no such differences have been identified [4]. It is possible that the disparity between the blood flow through the MCA and the capacity of the microvasculature may be one of the reason for the second progression of the parenchymal hemorrhages [1].

We believe that comparative correlation analysis of CBF and CBFV is necessary to specify the development of secondary brain damage and uncoupling between cerebral circulation

and brain tissue oxygen consumption, to determine possible ways to prevent their formation during treatment [2]. The analysis of correlation between CBF and CBFV could help to predict efficiency or limitations of infusion therapy. In the case of the lack of correlation between CBF and CBFV, infusion therapy can provoke detrimental hyperemia or hyperperfusion [1].

5 Conclusion

In this study, the strongest linear correlation between CBF and CBFV was noted in TBI patients with diffuse lesions without the development of a coarse shift of the midline structures and dislocation syndrome. This correlation probably reflects impairment of the cerebral autoregulation and uncoupling of oxygen consumption by brain tissue and cerebral microcirculation. The reported study was funded by RFBR, project number 20-015-00110 and RSF 20-15-00037.

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Fig. 1.
The Neuromonitoring System: white arrow, CT; blue arrow, TCD; red arrow, ECG-ABP monitor; black arrow, syringe injector; and green arrow, cerebral oximeter

Fig. 2. Volumetric CBF plotted against Vav (CBFV) on the left side (**a**) and right side (**b**) in Group 1 with diffuse TBI. Dashed red lines represent 95% confidence intervals for the regression (solid red line)

Fig. 3.

Volumetric CBF plotted against Vav (CBFV) in group 2 after surgical removal of intracranial hematomas (a) on the side of the removed hematoma (b) on contralateral side. Dashed red lines represent 95% confidence intervals for the regression (solid red line)

Table 1

Data on comparison of the analyzed parameters

		Vav (cm/sec)	CBF (ml/100 g × min)
1	Group 1 (left side)	46.1 ± 13.8	31.7 ± 10
2	Group 1 (right side)	45.7 ± 12.9	31.6 ± 10,2
3	Group 2 (ipsilateral side of former hematoma)	36.8 ± 12.8	32.3 ± 17.7
4	Group 2 (contralateral side of former hematoma)	48.7 ± 17.7	28.4 ± 11.1
	P (1–2)	0.983	0.994
	P (1–3)	<0.005 ^{aa}	0.138
	P (1–4)	<0.5 ^a	0.194
	P (3–4)	<0.001 ^{aaaa}	0.247

^aSignificant difference (p < 0.01)