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The Cerebral Circulation Time in the evaluation of neurological diseases

abstract: Background Recent newly developed ultrasound techniques extend our ability to study the cerebral hemodynamics in patients with neurological disease beyond the conventional blood flow velocity analysis. Different ultrasound methods are currently under investigation that either qualitatively or quantitatively describe brain perfusion. The most widely used technique is bolus kinetics. After applying a ultrasound contrast agent bolus, time intensity curves of the wash-in and wash-out phase of the bolus passage through the brain are registered by imaging at a set frame rate and analyzing the ultrasound intensity in a given region of interest. Based on the time intensity curves, different parameters can be extracted such as peak intensity, time to peak, mean transit time, and incremental time (Fig1). These parameters can be displayed in a tissue region of interest defined by the examiner.
studies based on histopathological techniques and on MR imaging demonstrate hypoxia-like brain tissue injury or thrombosis of small veins in patients with Multiple Sclerosis (MS). Applying dynamic susceptibility contrast Magnetic Resonance Imaging, cerebral mean transit time values were found to be significantly prolonged in MS patients.
We present the application of contrast enhanced ultrasound (CEUS) to assess global cerebral circulation time (CCT) in patients with multiple sclerosis (MS). The method is based on the assumption that the time required by an ultrasound contrast agent to pass from the cerebral arteries to the veins should be prolonged in patients with vessel disorders.
Methods We performed CEUS in 82 patients with MS, and 37 controls. The clinical diagnosis was established by neurological evaluation and neuroimaging findings. Impairment was assessed by the EDSS Scale. Cerebral Circulation Time was defined as the time difference of ultrasound contrast bolus arrival between the carotid artery and internal jugular vein.
Results The MS patients were comparable to control subjects for age, sex, systolic and diastolic blood pressure and heart rate. The artery arrival time was similar in MS group and controls. The longest and average Cerebral Circulation Times (CCTL,CCTM) were substantially prolonged in patients with MS compared with controls [CCTL MS patients: median (range) 6.5 sec. (3.3-29.2); controls 5.2 (2.57-7.63; p<0,0001. CCTM MS patients: median (range) 5.8 sec. (2.6-17.5); controls 4.7 (2.5-7.1); p<0,0001] No correlation was found between Cerebral Circulation Times and duration of disease or age in both group of patients and controls. Moreover, the degree of circulatory delay was not correlated with the level of disability (EDSS score).
Conclusions Compared with the healthy control group, MS patients showed a significant prolongation of CCT. Our results suggest that a microvascular or venous outflow impairment could be associated with MS. The CEUS measurement of CCT may be useful tool to disclose cerebral microcirculatory dysfunction in MS patients.

Fig. 1 The time-intensity curve analysis displays the acoustic intensity (in dB) during acquisition time in three different region of interest: the carotid artery, thyroid parenchyma without artery/vein, Internal Jugular Vein. The wash-in curves were analysed and three parameters were measured for the ROI: Arrival Time, Time To Peak and Absolute Intensity Peak.

Fig.2 The CCTL in a MS patient (bottom) and in a control subject (top). The difference was evident (CCTL in control subject was 3.3 s, in MS patient was 6.9s.. The red lined curve depicts the arterial signal, the green lined curve represents tissue signal and yellow lined curve represents the venous signal.

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