

The Utility of Transcranial Doppler in the Acute Ischemic Stroke

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The first clinical trials on the utility of Transcranial Doppler (TCD) in acute ischemic stroke (AIS) were conducted still in the pre-thrombolysis stage. Middle cerebral artery (MCA) mean flow velocity (MV) below 20 cm/sec or 50% below contralateral MCA within 24 hours translates worse prognostics factors¹. Intravenous thrombolysis in the management of AIS brought forth an even higher utility of TCD in the acute phase – to add to emergency evaluation – thus allowing the identification of intracranial occlusion and acting as a unique tool for continuous monitoring of vessel recanalization². More recent study designs suggest that changes found in TCD should be added to inclusion criteria for the use of intravenous thrombolytic, since that therapeutic regimen is potentially indicated and beneficial in cases of encephalic ischemia with intracranial artery branch occlusion³⁻⁵.

TCD has been absorbed by major university services in our country, as well as by hospitals that assist patients with cerebrovascular diseases⁶. In addition to being non-invasive, TDC has other major advantages: it is low-cost, dynamic, fast for specific cases, and portability. It may be carried out and repeated many times, by the bed side, and may also stand for therapeutic potential⁷⁻⁹. Major difficulties posed by the method are: it belongs to the group of operator-dependent complementary exams, and the lack of studies on interpretation criteria that can be uniformly accepted⁷. In regard to acute AIS – concurrently to imaging exams such as computed axial tomography (CAT Scan) and nuclear magnetic resonance (NMR) – TCD has been innovating concepts and treatments, contributing for better assistance to patients who are thrombolysis candidates and non-candidates. Research on micro emboli – a unique tool – and high sensitivity for the detection and follow-up of intracranial stenoses have turned TCD into a routine exam for cerebrovascular disease patients^{3,10}. The present review will focus on the assistance for acute cerebrovascular diseases (CVD). It is important to point out that major studies are related to the analysis of MCA, whose topography corresponds to most ischemic cerebral events. Whenever possible, non-invasive extracranial investigation should be carried out with ultrasound of cervical vessels – carotid, vertebral and subclavian arteries – to help interpret and therefore increase accuracy of TCD¹¹.

Thrombolysis

Although patients with acute AIS can still count on few services for treatment in our country, the tendency for therapy improvement is imperative and promising. 'Post-hoc' studies have made it clear that although most patients submitted to thrombolysis have shown better prognostics for improvement when compared to placebo, a significant group still does not report benefits, thus showing selective therapeutic effect based on certain characteristics of acute AIS^{12,13}. When reviewing pioneer coronary studies, one notices that the core factor related to thrombolysis is circulation close to thrombosed vessel, which is graded through flow on arteriography - TIMI – 'thrombolysis in myocardial ischemia'¹⁴. Using that classification as a model, in 2001 Demchuk and collaborators described a systematic analysis of MCA in AIS through TCD – called 'thrombolysis in brain ischemia' - Table 1³. The purpose is to determine residual flow velocity as well as its correlation with AIS severity, functional independence after index ischemic event included. Major limitation is the lack of flow in the vessel - 'grade 0', to be distinguished from the difficulty in ultrasound transmission through squamous portions of the temporal bone, found in approximately 11% of patients, as well as from the inexistence of a golden pattern for method comparison^{4,6}. Counting on a well-trained team and making use of a standard protocol, TCD may be carried out in less than 15 minutes, therefore not interfering in the therapeutic window for thrombolysis¹⁵.

A number of experimental studies have already demonstrated that ultrasound makes fibrinolytic agents activities easier due to improvement in medication transportation, change in fibrin structure, and higher tPA-fibrin binding⁸. The 'CLOTBUST' study has demonstrated a possible potentialization of thrombolysis when concurrent to TCD in cases where MCA occlusion evolution is recorded as under 3 hours. The group under constant monitoring of IV thrombolytic infusion reported higher recanalization and improvement of functional independence when compared to patients not constantly monitored through TCD⁵. On the other hand, a recent study - 'TRUMBI' – where authors reviewed the correlation between ultrasound low intensity (300Khz) and potential thrombolysis had early discontinuation due to higher incidence of symptomatic intraparenchymatose

Key words

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Grade	FV* Pattern	Characteristics
0	Absent	1) No FV signal despite different grades of background noise.
1	Minimal	1) Velocity systolic peak and duration variable; 2) No diastolic FV during cardiac cycle based on visual interpretation of periods with no flow at the end of diastole; (reverberating flow is a minimal pattern)
2	Blunted	1) Delayed or blunted systolic acceleration, with variable duration as compared to control; 2) Positive end-diastolic velocity; 3) PI < 1.2 **
3	Dampened	1) Normal systolic acceleration; 2) Positive end-diastolic velocity; 3) Reduction of mean flow velocity \geq 30% when compared to contralateral vessel (control).
4	Stenosis	1) Mean flow velocity > 80cm/sec and difference > 30% compared to control 2) If difference between velocities is < 30%, observe turbulence signs; 3) If velocity in both sides is < 80cm/sec, observe 30% difference and turbulence signs;
5	Normal	1) Difference from control side < 30%; 2) Similar wave spectrum in both sides.

*FV: Flow Velocity ** PI: Pulsatility Index

Table 1 - TIBI assessed through DTC in patients at AIS acute stage

haemorrhage in the study group¹⁶. Further studies are required for method validation. The IV microbubbles solution has demonstrated to even increase the effect obtained from the association of TCD and the thrombolytic¹⁷.

From all the information provided by the method, TCD also allows recognizing early recanalization of MCA occluded after thrombolytic infusion irrespective of clinical recovery, a condition known as stunned brain^{15,18}. The pattern of recanalization – if spontaneous – must also be distinguished from intracranial stenosis, which may be presented with similar findings at first exam. Sequential exams are crucial for definition, since in recanalization flow velocities return to values close to normal within variable time frame.

Monitoring of microembolism

TCD identifies microembolic signs (MES) in intracranial circulation. Such study is possible, since ultrasound distinguishes signal characteristics through embolic materials – solid or gaseous – from erythrocyte flow velocity. Those differences are present in the wave spectrum – intensity and frequency – and in sonority emission¹⁹.

Embolism may result from cardiac sources, from major arteries – aorta, carotids and vertebral arteries -, intracranial arteries, and paradoxically reach cerebral circulation through a venous-arterial shunt – patent oval foramen or arteriovenous fistula²⁰. The cardioembolic source stands for 20 to 30% of all AISs, with most patients presumptively identified following TOAST criteria, through the combination of clinical symptomatology associated to mid and high risk factors from complementary cardiovascular exams findings - ECG, transthoracic or transoesophageal ECG – and imaging

exams – cranial CAT Scan and NMR²¹. However, none of those methods allows direct identification of the active embolic phenomenon as TCD does. Methodology includes simultaneous monitoring of both MCAs for at least 30 minutes, with fixed transducers in order to reduce movement artifacts. With two possible embolic sources – cardiogenic and carotid plaque – the identification of MES contributes with higher diagnosis accuracy and support for therapy decision making. MES detection, in addition, acts as a predictor for new cerebral ischemic event recurrence^{20,22-24}.

Research lines have been established with monitoring of surgical and endovascular procedures to correlate the presence of MES and post-surgery neurologic changes²⁵⁻²⁹. Such procedure may in the future identify crucial sites for surgical manipulation in carotid stenoses.

TCD technical advance will contribute for deeper knowledge of embolic phenomenon pathophysiology, and will most likely be of great help in showing the most appropriate therapy. At this point in time we could say that studies on micro embolism are useful for patients with non-defined AIS, and which is of probable cardioembolic etiology, as well as for carriers of atheroscleroses of large vessels^{30,31}.

Intracranial stenoses

Intracranial disease corresponds to approximately 8% of AISs, depending on gender and race^{32,33}. Diagnosis is frequently reached through arteriography, the gold standard, whose risks and invasive procedure do not allow large scale use, therefore, with figures probably underestimated. Advances in diagnosis techniques – as angioresonance, angiotomography and TCD – tend to confirm the relevance of that etiology as

an independent risk for CVA, although literature still needs validated criteria^{34,35}.

TCD stands as an ancillary diagnosis tool with increased sensitivity and specificity when strict criteria are complied with³⁶. Sensitivity lies between 70 and 90%, and specificity between 90 and 95% for arteries in the anterior circulation, and a little lower for arteries in posterior circulation, where sensitivity is between 50 and 80%, and specificity is between 80 and 96%³⁷. It is important to point out that in practice, mean velocity analysis to identify intracranial analysis is not enough. It must be combined with other parameters such as asymmetry, segmental elevations, spectral analysis, and knowledge on extracranial circulation. Major confusion factor in interpreting velocities is collateral or vasodilation circulation as compensatory mechanisms in cases associated to extracranial stenoses³⁸. A finding compatible with intracranial stenosis in AIS acute phase must be distinguished from 'vanishing stenosis'. The term defines the process of

recanalization of an occluded vessel that behaves as stenosis hemodynamically speaking. Evolution exams are required for diagnosis differentiation^{10,39}.

When compared to other emergent, non-invasive methods, TCD contributes with the advantage of also monitoring micro emboli at stenosis site, frequently been observed in our practice, and which may influence therapy decision making⁴⁰.

Therefore, the use of TCD in AIS acute phase allows complementary diagnosis – still underestimated in practice – as support to imaging exams in etiology and pathophysiology, therefore guiding neurologists in their therapy conduct, and most likely estimating prognosis for those patients.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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