Transcranial Color-Coded Duplex Ultrasound for Assessing Cerebrovascular Reserve in Intracranial Dissection with Aneurysm

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Abstract
Intracranial artery dissection (IAD) is an uncommon cause of cerebral ischemia. It may lead to symptoms due to rupture of subadventitial aneurysms or thromboembolism from subintimal disruption. Severe stenosis may lead to reduced cerebrovascular reserve (CVR). While there are many methods of assessing CVR, we report a case of IAD with hemodynamic complications diagnosed by transcranial color-coded duplex (TCCD) ultrasonography. Our patient is a 38-year-old female who presented with a 2-month history of nausea, then feeling faint whenever she got up suddenly. On the day of admission, she had gotten up to walk, felt nauseous, and the left upper limb felt “funny,” after which she lost consciousness. Clinical and neurological
examination was normal. Brain magnetic resonance (MR) imaging was normal. MR angiogram and subsequent computed tomography (CT) angiogram showed flow attenuation in the M1 segment of the right middle cerebral artery (RMCA), with a possible flap. Catheter angiography was suggestive of a dissection with 2.7 mm pseudoaneurysm. TCCD showed very high velocities in the RMCA. The Breath-Holding Index (BHI) was 0.56, suggestive of reduced CVR in the RMCA territory. Acetazolamide-enhanced single-photon emission CT showed reduced right frontal CVR. She was given clopidogrel for secondary prevention, and has remained well. BHI as measured by TCCD is a new method for assessing CVR in patients with cerebral ischemia.

Introduction

Intracranial artery dissection (IAD) is an uncommon and often overlooked cause of stroke, especially in young adults [1]. Subintimal dissection leads to luminal stenosis (and hemodynamic compromise), or thromboembolism and subsequent cerebral ischemia; subadventitial dissection could lead to the formation of a pseudo-aneurysm and compression of surrounding structures [2]. Hemodynamic failure due to stenosis and inadequate compensatory collateral flow can lead to limb-shaking attacks [3]. Impaired cerebrovascular reserve (CVR) carries an almost 4-fold odds of stroke among those with significant carotid occlusive disease [4]. There are many modalities for the assessment of CVR – positron emission tomography, single-photon emission computed tomography (SPECT), perfusion and nuclear CT, perfusion magnetic resonance imaging (MRI), and transcranial Doppler (TCD); vasodilator challenges include carbon dioxide and acetazolamide [4]. TCD is an established technique for assessing cerebral vasomotor reactivity and autoregulation [5]. Increasing the carbon dioxide levels in the body by breath-holding provides a convenient and well-tolerated way of assessing carbon dioxide reactivity without requiring the administration of carbon dioxide [6]. A Breath-Holding Index (BHI) of <0.69 as measured by TCD raises the stroke risk by more than 3 fold [7]. Transcranial color-coded duplex (TCCD) ultrasound, also known as transcranial color-coded sonography, transcranial sonography, and transcranial imaging, which combines TCD with B-mode imaging and color-coding of Doppler flow, resembles TCD in probe frequency, acoustic windows employed, and velocity indices and criteria for normal and disease [8]. However, it differs from TCD in that B-mode imaging is first used to image the butterfly-shaped midbrain, then color-coded Doppler is employed to accurately visualize, locate, and identify the arteries of the Circle of Willis, before interrogating them with Doppler to determine flow characteristics – this removes vessel identification errors inherent in "blind" TCD. While TCCD has been used in the assessment of CVR capacity in healthy controls [9] and cognitive impairment [10], it has not yet been reported for cerebrovascular disease. We report a case of assessing CVR with BHI as measured by TCCD in a patient with IAD, with corroboration from acetazolamide-enhanced SPECT.
Case Presentation

Our patient is a 38-year-old female, right-handed, who presented with a 2-month history of nausea, then feeling faint whenever she got up suddenly, occasionally with palpitations. On the day of admission, she had gotten up to walk, felt nauseous, the left upper limb felt “funny,” then she lost consciousness for a few seconds, during which she was seen to have upward rolling of the eyes, stiff limbs, and was cold and sweaty. No incontinence or tongue bites occurred, and she was well postictally. She had a history of asthma, but no hypertension, diabetes mellitus, hyperlipidemia, or smoking. She was not on medication, but her father had had seizures.

Clinically, she was well, fully alert and orientated. She was not pale. Blood pressure was equal in both upper limbs and normal, pulse rate and rhythm were normal. There was no postural hypotension, and cardiac examination was normal. No ocular or cervical bruit was present, and neither were aphasia, anopia, and neglect. No neurocutaneous were stigmata found, the pupils were equal in size and reactive, and fundoscopy was normal. She had full eye, face, palate, tongue, neck movements. Limb tone, power, reflexes, and coordination were normal, as were pain sensation and gait.

MRI of the brain was normal. MR angiogram and subsequent CT angiogram showed flow attenuation in the M1 segment of the right middle cerebral artery (RMCA), with a possible flap (Fig 1). Catheter angiography was suggestive of a dissection with 2.7 mm pseudoaneurysm (Fig. 1).

TCCD showed very high velocities in the RMCA. BHI was 0.56, suggestive of reduced CVR in the RMCA territory (Fig. 2, Table 1). SPECT showed reduced right frontal CVR (Fig. 3).

Full blood count, glucose, renal, and liver panels were normal. LDL-cholesterol was 106 mg/dL. Fasting homocysteine was normal. Electroencephalogram was normal. Electrocardiogram and transthoracic echocardiography were normal. Twenty-four-hour Holter monitoring showed occasional ectopic beats. The tilt table test was positive.

The patient was commenced on clopidogrel and advised to get up slowly whenever she needed to. She is still on follow-up 4 months after the onset of symptoms.

Discussion

In this case report, we were able to demonstrate reduced CVR by TCCD in a patient with symptoms suggestive of hemodynamic cerebrovascular ischemia, imaging evidence of significant intracranial stenosis, and supported by another established CVR technique (acetazolamide-enhanced SPECT).

Our patient presented with symptoms of cerebral ischemia after sudden posture change – her global cerebral hemodynamic failure was supported by her positive tilt table test where she quickly lost consciousness very soon after being moved to the upright position. The occurrence of left upper-limb weakness just before she lost consciousness was suggestive of
an additional mechanism of severe stenosis of arteries supplying her right hemisphere. This
was subsequently found to be due to RMCA stenosis owing to dissection.

Further evidence of reduced right hemispheric CVR was found in her reduced BHI on
TCCD. In this modality, the velocity of blood flow in a large intracranial artery, usually the
MCA, is measured before and after a period of breath-holding, usually for 30 s. BHI is calcu-
lated by dividing the percentage increase in the mean flow velocity (MFV) occurring due to
breath-holding, by the length of time (s) that subjects hold their breath after a normal inspira-
tion (\(\frac{\text{MFV at the end of breath-holding minus rest MFV}}{\text{rest MFV}} \times 100}{/ s of breath-
holding\)). A value of <0.69 indicates reduced CVR and increased stroke risk [8]. Our patient
had a BHI of 0.56.

There are some technical challenges with performing CVR using TCCD. The hand-held
probe for TCCD is bigger in size and bulkier than the probe used for TCD. It can be tiring hold-
ing such a probe steadily throughout the procedure. Minute unintentional head movements
could have an impact on the stable position of a hand-held probe. There is no commercially
available head frame for the TCCD probe; such frames are widely available for the TCD probes
and allow continuous monitoring throughout the test and the probes stay in a stable position
despite head movements. Possible solutions include supporting the hand holding the probe
as much as possible, e.g. with pillows or small sand bags; thus, the study can be performed
without a break; the patient is also asked to stay as still as possible. Another approach is to
perform the insonations only at the start and end of breath-holding for just a few seconds or
at least until the waveforms are stable. This, however, requires the presence of a neuro-
sonologist to again locate the intracranial artery, which can take a little time and the effect of
breath-holding may be missed; the probe may be unwittingly placed at a slightly different lo-
cation, which may have an impact on the amplitude of velocities recorded. For the patient de-
scribed herein, the first approach was successfully used after a thorough explanation to the
patient who was very compliant. Another issue is that the left- and right-side TCCD insona-
tions were done consecutively and not simultaneously (as is occurs with TCD using a head
frame). Machine software does not routinely allow 2 probes to be in operation simultane-
ously; TCCD headframes are not available unlike TCD where the 2 probes can be mounted on
a frame and operate simultaneously. It will be difficult to obtain 2 TCCD machines and to op-
erate them simultaneously – 2 neurosonologists will thus be needed, one to insonate each side.
Thus, 2 studies are needed, one on each side; the studies need to be performed consecutively
after a short break to allow return to baseline, and the patient needs to be able to hold the
breath fully during both studies – this is what was done in our patient.

The patient’s reduced BHI was corroborated by acetazolamide-enhanced SPECT, where
the relative blood flow of the hemispheres is assessed using HMPAO and is compared before
and after the intravenous administration of acetazolamide, a carbonic anhydrase inhibitor
that raises the level of carbon dioxide in the blood. There is a strong correlation between CVR
assessment by TCD and acetazolamide-enhanced SPECT [11].

As mentioned above, a reduced CVR is not a benign condition as it carries a high stroke
risk [4, 7]. Among those with symptomatic, significant MCA stenosis, reduced CVR carries an
annual risk of stroke of 14% [12]. Thus, our patient is at significant risk of stroke ipsilateral to
her MCA stenosis.
The most appropriate management of IAD is still unclear [1]; there are no randomised controlled trials to inform on the best approach. Even in the setting of extracranial cervical artery dissection, there is no clear evidence of the superiority of anticoagulation over antiplatelet therapy in reducing the risk of recurrent cerebral ischemia [13]. We thus decided to treat her with antiplatelets – as she had asthma, clopidogrel was given.

It is also unclear what the best treatment for intracranial dissecting aneurysms is. While those with hemorrhage may best be treated surgically, by clipping or wrapping of the aneurysm, the treatment for those with ischemia is unknown [14]. Overall, for intracranial stenosis, stenting has a higher complication rate than best medical therapy for atherosclerotic disease; the role of indirect surgical revascularization is unknown [15].

Conclusion

CVR has important prognostic value for patients with cerebral ischemia. While there are a number of modalities for assessing CVR, the BHI as determined by TCD is a simple, inexpensive, safe, and valuable parameter of CVR. We have shown in this case report that TCCD may also be used to assess CVR.

Statement of Ethics

This research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient gave informed consent to publish the case.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Narayanaswamy Venketasubramanian – conceived the project, was the principle clinician managing the patient, performed the ultrasound study, and wrote the manuscript. Andrew Eik Hock Tan – nuclear radiologist managing the patient, performed and interpreted the SPECT study, and reviewed the manuscript. Wee Thong Neo – diagnostic radiologist managing the
patient, performed and interpreted the MRI and CT scans, and reviewed the manuscript. Manish Taneja—interventional radiologist managing the patient, performed and interpreted the cerebral angiogram, and reviewed the manuscript.

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Fig. 1. Intracranial dissection as seen by MR angiogram (a), CT angiogram (b), and digital subtraction angiogram (c).

Fig. 2. Transcranial color-coded Doppler ultrasonography of the middle cerebral arteries showing high velocities at baseline (a) and only slight increase after breath-holding (b) in the RMCA. This compares with normal velocities at baseline (c) and increase after breath-holding (d) in the left middle cerebral artery (LMCA).
Fig. 3. Single-photon emission tomography before (a) and after (b) acetazolamide, showing a reduced blood flow in the right frontal region.

Table 1. Transcranial color-coded duplex findings before and after breath-holding

| Artery | Right | | | | | Left | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Depth, mm | PSV, cm/s | EDV, cm/s | MV, cm/s | PI | Depth, mm | PSV, cm/s | EDV, cm/s | MV, cm/s | PI |
| MCA | 45 | 144 | 87 | 93 | 0.83 | 50 | 110 | 48 | 68 | 0.91 |
| | 50 | 155 | 72 | 99 | 0.82 | 55 | 154 | 70 | 98 | 0.86 |
| | 55 | 248 | 143 | 178 | 0.59 | 60 | 202 | 117 | 145 | 0.59 |
| Before breath-holding | 60 | 199 | 111 | 141 | 0.63 | 60 | 172 | 72 | 105 | 0.96 |
| After breath-holding | 60 | 223 | 139 | 167 | 0.50 | 58 | 191 | 110 | 137 | 0.59 |

BHI. RMCA = (167–141) × 100 / (141 × 33) = 0.56. LMCA = (137–105) × 100 / (105 × 39) = 0.78. PSV, peak systolic velocity; EDV, end-diastolic velocity; MV, mean velocity; PI, pulsatility index.