

Appendix e-1: Ultrasound Screening Protocol for CCSVI

Adapted from Appendix A, Zivadinov et al, Neurol 2011, through discussions of the Canadian Institute for Health Research (CIHR) CCSVI Imaging Meeting, September 6, 2011.

General Comments

- Each image should be documented regarding the vein examined, the side, and body posture (supine vs. upright).
- Studies can begin with the participant either in the upright or supine posture – studies can be performed in either order, with order of positions documented. There should be a minimum of two minutes after changing positions. In addition, patients should be encouraged to take several deep breaths after changing position.
- When upright, note should be made of whether legs are straight out or hanging below level of bed. The importance of this is unknown, but recording it seems appropriate.
- Assessment should be performed with the participant in the neutral posture, looking straight forward.
- If the participant has travelled by air, the assessment should be performed a minimum of 24 hours after the participant has flown; document duration of travel.
- Minimal probe pressure should be used, to avoid artifactual changes in vessel.
- All assessments should be captured in such a fashion as to permit later confirmation through over-reading.
- Attempts should be made to blind ultrasound technicians regarding the participant's diagnosis.
 - If possible, different staff should be positioning the patient prior to the arrival of the ultrasound technician; consider patients listening to iPod or other device to reduce conversation between participant and technician; consider blinding assessment for both technician and patient (i.e. "Did you think the technician was unblinded?").

Criterion 1: Reflux in IJV's and/or VV's

Definition: Reflux (backwards flow) present in the internal jugular vein and/or vertebral vein for greater than 0.88 seconds with the head at both 90⁰ and 0⁰.

Technical notes:

- With colour Doppler, scan entire IJV for reflux. Once reflux is found by colour, it should be measured with spectral analysis. Only spectral analysis should be used to define duration of reflux.
- A sample measurement should be made in the middle of the vessel, plus elsewhere if reversal is seen on the colour Doppler.
- Assessment is performed in the sagittal plane only.

- Retrograde flow at any point along the IJV may be used to qualify for reflux. Reflux anywhere across the IJV may be used for measurement, including only adjacent to the vessel wall. The entire cross-section of the vein does not need to demonstrate reflux to qualify. The ultrasound "sampling-window" should then be placed across the region showing reflux to measure duration of backwards flow.
- The location of reflux should be noted (i.e. middle of vessel, adjacent to a wall, etc).
- Assessment should be done at end-expiration of a normal breath
- The same technique is used on the vertebral veins, but should include the vertebral artery to show the same direction of flow.
- Reflux should be documented with spectral analysis.

Pathology Definition:

- Reflux is flow directed toward the brain for a duration of >0.88 sec, in the IJVs and/or VV`s. To be denoted as positive, reflux must be noted in both supine and upright position in the same vein and same side.

Criterion 2: Reflux propagated upward in the deep cerebral veins (DCVs) or from the white matter (WM) to the SCGM

Definition: Reflux (backwards flow) present in the DCVs and/or from the WM to the subcortical gray matter (SCGM) greater than 0.50 seconds. Internal cerebral veins, vein of Rosenthal and Galen vein are the DCVs considered for colour doppler assessment.

Technical notes:

- TCD technology should be used and should be consistent for all participants assessed at a site.
- Assessment is in both upright (90°) and supine (0°) positions.
- For QDP technology, probe is placed onto the left cheek, at the level of the condylar process of the mandible, anterior to the tragus with approximately 40° posterior angle and 20° upward angle. Repeating the assessment on the right side is not necessary, but can be done if veins are not visualized on the left.
- For TCD, assessment of both left and right temporal windows should be performed. Absence of temporal windows should be noted.
- With colour Doppler, scan DCVs for directional information.
- Only spectral analysis should be used to define duration of reflux (not colour video clip).
- The minimum assessment is two veins, including vein of Rosenthal, vein of Galen, and internal cerebral vein.
- The vein assessed should be noted, if possible (although this is often not possible with QDP).

Pathology Definition:

- Reflux is noted as reverse flow for a duration of >0.5 seconds, in any one of the DCVs - internal cerebral vein, basal vein of Rosenthal or great vein of Galen. To be denoted as positive, reflux is noted in supine or upright position in any one of the DCVs veins.

Criterion 3: High resolution B-mode evidence of proximal IJV stenosis and/or other B-mode anomalies

Definition of collected parameters in the worksheet:

- Stenosis - Cross sectional area (CSA) measurement of $\leq 0.3 \text{ cm}^2$ (or $\leq 30 \text{ mm}^2$).
- Block - no colour flow noted in vein, despite deep inspirations
- Paradox - vein wall not reacting to respiratory phase; non-compliant
- Flap - thin linear echogenic structure extending from endothelial lining of vein wall
- Septum - thin linear echogenic structure extending from endothelial lining of vein wall with attachment to vein wall at both ends. Septum may extend across vein to attach on opposing sides or attach on same side
- Web - multiple septae and/or flaps located in a cluster
- Annulus - thickened vein wall, restricting vein from fully expanding with respiratory or positional changes

Technical notes:

- Stenosis is only assessed in the supine position.
- In gray scale, scan from upper most visible portion of left IJV to subclavian vein in transverse plane. Adjust ultrasound controls to obtain best possible image.
- In colour Doppler, scan from superior point of IJV to subclavian vein in transverse plane to gauge the narrowest flow diameter of the IJV.
- Stenosis is assessed at the most narrow point along the vein, regardless of location along the IJV.
- At the narrowest flow diameter, measure CSA in colour.
 - Some sites may choose to measure in B-mode instead of colour. Notation should be made of how CSA is calculated, and consistency maintained within the site.
- If there is no obvious narrowing or stenosis, the level of the isthmus of the thyroid should be chosen for measurement.
- Place mark on skin at point of measurement. When in other position, measure CSA at IJV site marked when in the first position.
- Adjust PRF to avoid oversaturation or under saturation of flow.
- Obtain images to demonstrate stenosis, block, flap, septum, web, paradox or annulus, where these are seen. When anomaly present, document with video clip. The specific b-mode abnormality should be specified.
- Assessment of valves is qualitative and not quantitative. This subjective assessment should be accompanied by ample imaging documentation.
- Both IJV (left and right) should be assessed similarly.

Pathology Definition:

- B-mode anomaly (i.e. flap, web, septum, annulus, paradox, block) noted in the lumen of the IJV or stenosis referenced as $CSA \leq 0.3 \text{ cm}^2$ (measured in colour or B-mode) denotes a positive finding.

Criterion 4: Flow not Doppler detectable in the IJV's and/or VV's despite numerous deep inspirations

Definition: Flow not detected by colour Doppler or spectral analysis in the IJV or VV, despite multiple deep inspirations.

Technical notes:

- In colour Doppler, scan from superior point of left IJV to subclavian vein in transverse plane assessing colour flow in the IJV. Adjust PRF to avoid oversaturation or undersaturation of flow.
- In colour Doppler, turn probe longitudinally, steer colour box to enhance Doppler angles. If minimal or no flow noted, have participant take deep inspirations/expiration, but never valsalva.
- For vertebral vein, identify vertebral artery at C3-4 level using colour flow, then search in region for vein.
- B-mode may be used to look for the vein, but even if no outline of vein is found, use colour and spectral Doppler to hunt for vein in the area of the artery. This can be particularly helpful with the VV.
- Valsalva should never be used to identify either IJV or VV.
- If colour flow not visible in VV, assess with spectral analysis for verification.
- Flow must be absent in both upright and supine positions to meet criteria.
- Surgical sites should be excluded from this analysis. For example, previous cervical spine surgery would exclude VV from fulfilling these criteria.

Pathology Definition:

- Flow not detected by colour Doppler or spectral analysis in the IJV or VV, despite multiple deep inspirations. For criteria to be met, there must be no venous flow by either colour or spectral Doppler in both the upright and supine positions in the same vein (i.e. no flow detectable in right VV in supine and upright position).

Criterion 5: Negative Δ CSA in the IJV

Definition: CSA is calculated by obtaining the width and anterior-posterior (AP) measurement of the vessel flow in the transverse plane. Alternatively, the CSA may be obtained by circumferentially tracing the IJV wall in the transverse plane. The delta (Δ) CSA is calculated by subtracting the upright CSA from the supine CSA.

Technical notes:

- CSA is defined in criteria 3, and the measurement is obtained at the time Criterion 3 is assessed.
- Clear pathology should be avoided as the site for CSA measurement (i.e. stenotic valve)

Pathology Definition:

- A negative Δ CSA represents the loss of the normal postural control denoting a positive finding.

CCSVI STATUS ASSESSMENT:

- Each participant is assigned a total criteria score which is calculated by counting the number of criteria that participant fulfilled.
- CCSVI positive: A participant is considered CCSVI-positive if ≥ 2 criteria are fulfilled.
- CCSVI negative: A participant is considered CCSVI-negative if < 2 criteria are fulfilled.