Transcranial Doppler (TCD) Ultrasound Screening in Sickle Cell Disease

Anne Marsh, MD
Sept 29th, 2017
Objectives

• Review basic TCD concepts
• Review history of how screening TCDs became standard of care for children with SCD
• Review formal STOP study criteria
• Review some of our own TCD reports
What is a TCD?

- An ultrasound technique that evaluates arterial blood flow velocity in the circle of Willis
- Non-invasive
- Painless
- Screening tool for stroke risk stratification in SCD, diagnostic and monitoring tool for other indications
Why TCD for SCD?

• Basic Concept
  • Overt cerebral infarction in SCD is usually associated with vasculopathy in the large intracranial arteries
  • Vasculopathy = narrowed vessel(s)
  • Narrowed vessel ➔ increased blood flow velocity ➔ increased stroke risk
  • Increased blood flow velocity can easily and non-invasively be detected with TCD
Why Screen With TCD?

In the absence of 1° prevention, ~1 in 10 children with SCD will have a stroke.
How Is It Done?

• For SCD screening:
  • Ideally done in a quiet, darkened room
  • Patient should be at “baseline” state (i.e. not in acute pain, not in aplastic episode, not hospitalized, etc.)
  • Patient encouraged to relax, but not fall asleep
  • ~ 3 months since time of last PRBC transfusion
  • Technician insonates vessels in the circle of Willis
  • Typically takes 15-30 minutes to complete
Circle of Willis Anatomy Review

MCA | Middle cerebral artery
BIF | Bifurcation of the internal carotid
ACA | Anterior cerebral artery
dICA | Distal internal carotid
PCA | Posterior cerebral artery
TOB | Top of the basilar artery

M1 segment

BIF

ACA

dICA

TOB

Posterior communicating

Superior cerebellar

Pontine arteries

Anterior inferior cerebellar

Spinal

Vertebral
Temporal Bone Window

Sub-occipital Bone Window
Example of MCA Signal

Peak systole
Mean
End diastole
Audible Example

• Normal sounding L MCA
• Turbulent and abnormal sounding R MCA
• Like cardiac murmurs, the trained, experienced, examiner can audibly recognize abnormalities, but it’s a skill that takes time to acquire
Use of TCD to Predict Stroke in SCD

Adams NEJM 1992

- Prospectively obtained 283 TCDs in 190 patients with SCD
- Abnormal defined (post hoc) as $\geq 170$ cm/sec in the MCA, mean f/u 29 months
- End point: clinically apparent first cerebral infarction

<table>
<thead>
<tr>
<th></th>
<th>Normal TCD</th>
<th>Abnormal TCD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stroke</td>
<td>166</td>
<td>17</td>
<td>183</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Total (%)</td>
<td>167 (88%)</td>
<td>23 (12%)</td>
<td>190</td>
</tr>
</tbody>
</table>
Probability of Remaining Stroke-Free (w/o transfusions)

Adams 1992, NEJM
Adams 1998, Controlled Clinical Trials
Stroke Prevention Trial (STOP)

Adams NEJM 1998

- First stroke prevention trial and first RCT using transfusions in SCA
- 1900+ Pts underwent 3900+ TCDs
- Baseline rate of abnml TCD was ~10%
- Pts (n=130) w/abnml TCD velocities in the MCA or dICA, on 2 separate visits, were randomized to:
  - Standard of care (n = 67) or,
  - Transfusions to reduce Hb S <30% (n = 63)
Stroke Prevention Trial (STOP)

- Study terminated early
- Regular transfusions decreased stroke risk by 92%!!!

<table>
<thead>
<tr>
<th>Variable</th>
<th>Transfusion (n = 63)</th>
<th>Standard (n = 67)</th>
<th>Total (n = 130)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up (mo)</td>
<td>21</td>
<td>18.3</td>
<td>19.6</td>
</tr>
<tr>
<td>No. of strokes</td>
<td>1</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>1</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Intracerebral hematoma</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
NHLBI TCD Recommendations

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In children with SCA, screen annually according to the methods employed in the STOP study, beginning at age 2 and continuing until at least age 16 years.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>2. In children with conditional (170-199 cm/sec) or abnormal (&gt;200 cm/sec) TCD results, refer to a specialist with expertise in chronic transfusion therapy aimed at preventing stroke.</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>3. In children with genotypes other than SCA (e.g. Hb SC, Hb S/beta+ thalassemia) do not perform screening with TCD.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>
Segments Interrogated in STOP

- M1 segment of MCA
- Basilar
- MCA
- BIF
- ACA
- dICA
- PCA
- TOB

15 segments measured in the STOP protocol

M1 segment of MCA
- MCA
- BIF
- ACA
- dICA
- PCA
- TOB
- Basilar
Interpreting a TCD by STOP Criteria

- Value used for interpretation is the **Time-Averaged Mean Velocity (TAMV)**, not peak systolic velocity (PSV)

- Four potential mutually exclusive outcomes:
  1. **Inadequate** (unreadable)
     - To be considered “readable”, the bilateral MCA and BIF velocities had to have been captured
  2. **Normal**
     - TAMV in all segments <170 cm/sec
  3. **Conditional**
     - TAMV ≥170 but < 200 cm/sec
  4. **Abnormal**
     - TAMV ≥200 cm/sec
How About For Our Patients?

- Definitions are generally the same
- **Inadequate** (unreadable or incomplete)
- **Normal**—TAMMV <170 cm/sec
- **Conditional**—TAMMV ≥170 but < 200 cm/sec
  - Low conditional—170-184 cm/sec
  - High conditional—185-199 cm/sec
- **Abnormal**—TAMMV ≥200 cm/sec
What If TCD is Normal?

• Repeat annually until at least age 16
What If TCD is Conditional?

• We repeat anywhere from 2 weeks to 2-3 months, depending on initial velocities
What If TCD is Abnormal?

- Repeat within 2 weeks or initiate transfusions
- Consider brain MRI/MRA
What If TCD is Inadequate?

- Consider attempting repeat study
- If still inadequate, our practice in Oakland is to obtain MRI/MRA
Sample Report—OHSU

VASC LAB TRANSCRANIAL DOPPLER COMP
Performed: 5/4/2017 1:55 PM Status: Final result Visible to patient: Yes (MyChart)

Details
<table>
<thead>
<tr>
<th>Reading Physician</th>
<th>Reading Date</th>
<th>Result Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5/4/2017</td>
<td></td>
</tr>
</tbody>
</table>

Narrative
Bilateral: Sickle cell disease.
The bilateral intracranial internal carotid, middle, anterior and posterior cerebral arteries were examined with the duplex scanner. The intracranial vertebral arteries and basilar artery were also examined.

The arteries are patent with flow in the normal directions.
In the right hemisphere, the maximum middle cerebral flow velocity measures 138 cm/sec with a mean velocity of 91 cm/sec, and a calculated right hemispheric ratio of 1.92.
In the left hemisphere, the maximum middle cerebral flow velocity measures 137 cm/sec with a mean velocity of 86 cm/sec, and a calculated left hemispheric ratio of 2.57.

Conclusions: Transcranial Doppler evaluation without evidence for vasospasm. The middle cerebral artery velocities are below the potential threshold values indicating increased risk of stroke in patients with sickle cell disease.
The study does not indicate increased stroke risk in a patient with sickle cell disease.

- Correctly examines ICA, MCA, ACA, PCA and basilar (and vertebral)
- Reports mean velocities. Assume this is the TAMMV?
- Reports and interprets only the MCA, no mention of ICA velocities
Sample Report—UW

EXAMINATION: US Intracranial Doppler Complete

DATE: 08/03/2016

COMPARISON: Ultrasound May 5, 2015

TECHNIQUE: Color and spectral Doppler interrogation was performed of the intracranial arteries. Time average mean of the maximum velocities of the intracranial arteries were obtained and are reported below.

FINDINGS:

RIGHT:
Right middle cerebral artery velocities of 158,160,159 cm/sec at a depth of 3.4,3.9,4.4 cm. Previous maximum velocity measured 133 cm/s at a depth of 4.7 cm.

Right anterior cerebral artery: 63 cm/sec
Right terminal internal carotid artery: 104 cm/sec
Right posterior cerebral artery: 35 cm/sec
Right vertebral artery: 51 cm/sec

LEFT:
Left middle cerebral artery velocities of 173,154,148 cm/sec at a depth of 3.5,4.0,4.5. Previous maximum velocity measured 140 cm/s at a depth of 3.3 cm.

Left anterior cerebral artery: 70 cm/sec
Left terminal internal carotid artery: 126 cm/sec
Left posterior cerebral artery: 121 cm/sec
Left vertebral artery: 77 cm/sec

Basilar artery: 108,80,69 cm/sec

IMPRESSION:
The time average mean of the maximum velocities in the left MCA are conditionally elevated at 173 cm/s.

Reports TAMMV

Correctly examines ICA, MCA, ACA, PCA and basilar.

Overall, an excellent study and format

Vertebral arteries reported, but not part of STOP
Sample Report—Oakland

Transcranial Doppler Report

Location: outpatient

Indication for Procedure: This is a transcranial Doppler study for a 3 y.o. 6 m.o. male who has Hemoglobin S-S disease.

Procedural Notes: Annual screening TCD for a child with SCD on hydroxyurea.

<table>
<thead>
<tr>
<th>Right Arterial System</th>
<th>Left Arterial System</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMCA: 137 cm/sec</td>
<td>LMCA: 127 cm/sec</td>
</tr>
<tr>
<td>RdICA: 92 cm/sec</td>
<td>LdICA: 68.5 cm/sec</td>
</tr>
<tr>
<td>BIF: 121 cm/sec</td>
<td>BIF: 112 cm/sec</td>
</tr>
<tr>
<td>RACA: -95.5 cm/sec</td>
<td>LACA: -84.7 cm/sec</td>
</tr>
<tr>
<td>RPCA: 112 cm/sec</td>
<td>LPCA: 105 cm/sec</td>
</tr>
</tbody>
</table>

Interpretation: Normal study

Return Visit: 1 year

Fails to indicate that velocities are TAMMV

Reports fails to include the basilar velocities, even though they are obtained.
Sample Report—Nevada

TRANSCRANIAL DOPPLER EVALUATION OF THE MIDDLE CEREBRAL ARTERIES

CLINICAL HISTORY:
History of sickle cell disease. Currently off of penicillin and aspirin.

TECHNIQUE:
Time average maximum mean velocities (TAMMV) of the middle cerebral arteries were obtained.

COMPARISON:
None.

FINDINGS:
Right middle cerebral artery:
  Proximal: 102-103 cm/sec.
  Mid: 75-85 cm/sec.
  Distal: 55-81 cm/sec.
Right posterior cerebral artery: 77-82 cm/s.
Right anterior cerebral artery: 55-70 cm/s.
Left middle cerebral artery:
  Proximal: 55-66 cm/sec.
  Mid: 90-102 cm/sec.
  Distal: 97-109 cm/sec.
Left posterior cerebral artery: 64-86 cm/s.
Left anterior cerebral artery: 43-50 cm/s.
There is low resistance waveform without evidence of flow reversal. Preserved systolic upstrokes is seen throughout.
(TAMMV is classified as follows:
Normal: velocities less than 170 cm/s
Conditional: at least one velocity 170-199 cm/s
Abnormal: at least one velocity ≥ 200 cm/s)

IMPRESSION:
Time average maximum velocities of the middle cerebral arteries are within normal published limits. Continued followup in 6-12 months is suggested.

Reports the TAMMV

Correctly examines MCA, ACA, PCA. Fails to examine the ICA and basilar.
Sample Report—Nevada²

EXAMS: 004945400 US DOP TRANSCRANIAL COM SICKLE CELL DISEASE

PROCEDURE: Doppler Transcranial Complete.

DATE: 10/31/2016 10:18 AM
COMPARISON: September 24, 2015
HISTORY: Sickle Cell disease

FINDINGS: Transcranial doppler was performed through transtemporal and suboccipital windows. The results are in mean velocity (cm/sec).

LEFT:
MCA: 144
ACA: 114
VERTEBRAL: 108
BASILAR: 110
PCA: 114

RIGHT:
MCA: 108
ACA: 60
VERTEBRAL: 75
PCA: 74

IMPRESSION: Velocities remain within normal range. Followup study is recommended within one year.

The study is considered normal if all mean velocities are less than 170 cm/s, conditional for velocities between 170 and 200 cm/s, and abnormal if the mean velocity is greater than 200 cm/s.

Reports mean velocities. Assume TAMMV?

Correctly examines MCA, ACA, PCA and basilar. Fails to examine the ICA.

Vertebral arteries reported, but not part of STOP
Discussion

• Other specific TCD cases people want to discuss?
• Questions/comments?
We don't know how strong we really are until being strong is the only choice.

Sickle Cell Strong

UCSF Benioff Children’s Hospital
Oakland