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Comparison of transcranial color Doppler imaging (TCDI) and transcranial Doppler (TCD) in children with sickle-cell anemia

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Abstract *Background.* Transcranial Doppler (TCD) has been demonstrated to identify those at highest risk of stroke among children with sickle-cell disease. Based on a randomized clinical trial [Stroke Prevention in Sickle-Cell Anemia Trial (STOP)], which ended in 1997, the National Heart Lung and Blood Division of NIH has recommended TCD screening and chronic blood transfusion based on Nicolet TC 2000 dedicated Doppler (TCD). Studies performed using TCD imaging modalities need to be correlated to that used in the clinical trial to provide information for treatment decisions when screening with TCDI.
Objective. To correlate transcranial arterial time-averaged mean velocities obtained from an Acuson Transcranial Doppler Imaging to those obtained using the TCD as the gold standard for treatment decisions based on STOP.
Materials and methods. A total of 29 children with sickle-cell disease, age 3–16 years, were studied at one of two scanning sessions using both techniques and a scanning protocol based on that used in STOP performed and read independently. The average difference in the measured velocities for each arterial segment was tested to determine difference from zero. Differences were compared before and after modifications to the TCDI technique were made to mimic the STOP protocol more closely.
Results. TCDI velocities were generally lower than TCD velocities for the same segment, but the difference was reduced (from 15 % to 10 % for the middle cerebral artery) by modifications to the TCDI protocol.
Conclusions. Measurements using the Acuson system are modestly lower than those obtained with dedicated Doppler using the Nicolet TCD.

Background and purpose

Ischemic stroke is a frequent and potentially devastating complication of homozygous sickle-cell anemia (HbSS). It occurs in 11 % of patients with HbSS before the age of 20 [1, 2]. These strokes are primarily the result of stenosis or occlusion of the distal intracranial internal carotid arteries (ICA) and/or proximal middle cerebral arteries (MCA). These sites of stenosis are readily assessable by transcranial Doppler (TCD). A series of papers on TCD demonstrated that HbSS patients who have high velocity flow in the distal ICA and proximal MCA have a significantly increased risk of stroke [3–5]. The ability to select high-risk patients using TCD led to the first randomized, controlled clinical trial of stroke prevention in HbSS [6]. The Stroke Prevention in Sickle Cell Anemia Trial (STOP) confirmed that children with time-averaged mean of the maximum (TAMM) flow velocities of ≥ 200 cm/s in the distal ICA or proximal MCA have a stroke risk of about 10 %/year that is

Fig. 1 Head measurement technique for TCD and TCDI

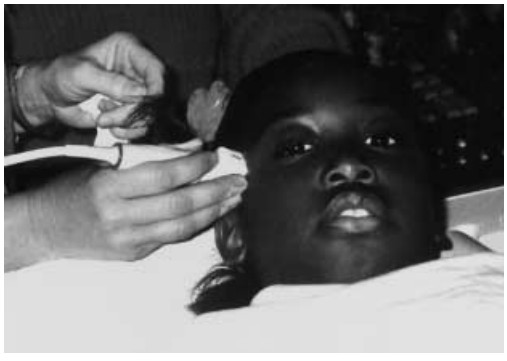

Fig. 2 Transducer placement for transtemporal approach for TCD and TCDI

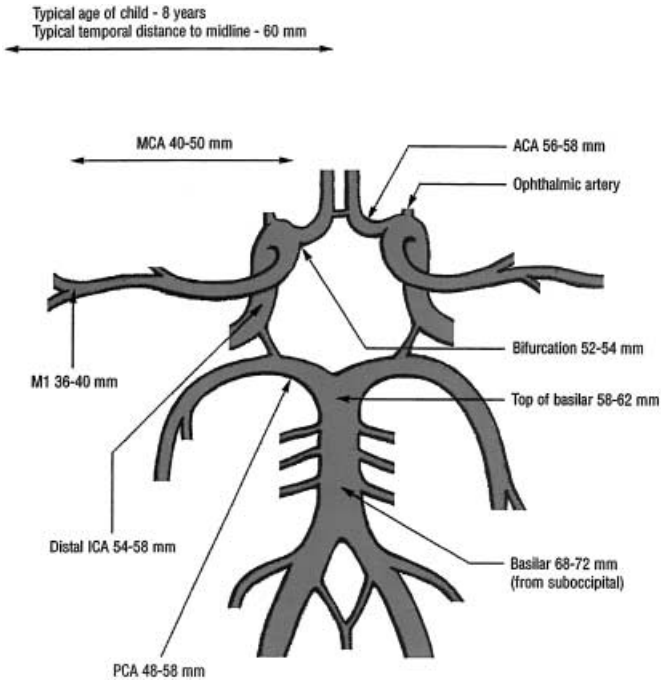

Fig. 3 Arterial segments recorded using the STOP TCD protocol and typical distance from the skin using the transtemporal approach

10–20 times that of children with HbSS of the same age [2]. The study demonstrated that this risk is reduced to < 1 %/year by regular blood transfusions sufficient to reduce the HbS from about 90 % (untreated) to < 30 % of total hemoglobin [6].

STOP used dedicated Doppler ("blind" or non-imaging TCD) [7] to identify children for treatment. The TCD protocol was specifically adapted for use in children with sickle-cell anemia, emphasizing meticulous TCD scanning technique and signal optimization with documentation of the highest TAMM. As a result of the findings of this study, the NIH released a Clinical Alert (September 18, 1997), which stated "The STOP Trial confirmed that TCD can identify children with sickle-cell anemia at high risk for first-time stroke. Since the greatest risk of stroke occurs in early childhood, it is recommended that children ages 2–16 receive TCD screening. Screening should be conducted at a site where clinicians have been trained to provide TCD of comparable quality and information content to that used in the STOP trial and to read them in a manner consistent with what was done in STOP. .. It is recommended that centers that wish to start screening children with sickle-cell anemia for stroke risk do studies to compare their current equipment with STOP trial TCD equipment" [8]. This Clinical Alert identified a potential problem in the use of the TCD data from STOP: although TCD and TCDI both use the Doppler principle to determine the velocity of blood flow, there are differences in the way that data are acquired and processed that could result in differences in the measured velocity. Significant discrepancy can result in failure to identify children who need to be treated or treatment of children at relatively low risk, which may not be indicated. If the STOP results are to be widely utilized for identification and treatment of children at risk for stroke, the comparability of the two methods should be evaluated.

As a result of the STOP findings, the demand for TCD screening of children with HbSS has increased. While "blind" TCD is an affordable, reproducible technique that has been used since 1982, it is not available in all medical centers. Many centers without access to "blind" TCD do have access to color Doppler imaging systems (TCDI) [9]. The TCD technique has been previously described [10] and uses 2-MHz pulsed Doppler insonation through the temporal bone to identify flow velocities in the anterior and posterior portions of the circle of Willis (Figs. 1–3). In the absence of a B-mode image, the head diameter, sample volume depth, flow direction, vessel traceability, and probe position are used to identify the specific intracranial arteries and

Table 1 Head diameter versus expected depths for arterial segments (*ICA* internal carotid artery, *MCA* middle cerebral artery, *ICA BIF* ICA bifurcation, *PCA* posterior cerebral artery)

Transtemporal head diameter (cm)	MCA (mm)	ICA BIF (mm)	PCA (mm)
11	30–48	46–50	40–56
12	30–54	48–54	40–60
13	30–58	50–58	42–66
14	34–62	56–62	46–70

Table 2 Expected vessel depth and flow direction: transtemporal approach, bitemporal head diameter: 120 mm (*dICA* distal ICA, *ACA* anterior cerebral artery, *TOB* top of basilar)

Artery	Depth (mm)	Flow direction
M-1 (MCA)	36–38	Toward transducer
MCA	40–50	Toward transducer
BIF	50–52	Bidirectional
dICA	54	Toward transducer
ACA	54–56	Away from transducer
PCA (P-1)	50–58	Toward transducer
TOB	60	Bidirectional

document abnormal flow velocities. TCDI superimposes the color Doppler flow information onto a B-mode image of the intracranial landmarks. The color Doppler provides a visual display of flow direction, mean frequency shift (kHz) and the intracranial arterial anatomy. Although TCDI has been used in HbSS [9, 11, 12], it is important to determine the comparability of the velocities obtained by TCD and TCDI, so that users of TCDI can correctly identify those children at highest risk of stroke, who need prophylactic transfusion, avoiding transfusion in those who do not.

The objective of this research was to compare the TCD and TCDI velocities, acquired by experienced operators, in children with HbSS who were stroke free and for whom the recommendations of the Clinical Alert apply. Our initial comparison demonstrated that TCDI velocities were routinely lower than those obtained by TCD. As a result, modifications in the TCDI scanning protocol were made, and a second comparison series was performed using instrument settings, and velocity measurements to more closely resemble those used in STOP. This article presents the results of these two series.

Materials and methods

TCD

The TCD methods used in STOP, and applied to this comparison, have been previously described [3, 6, 10] and are detailed in Tables 1–3. The TCD examination protocol, developed for STOP, was designed to insure correct arterial segment identification based on depth of sampling, direction of flow, and spatial relationship of the arterial segment to other arterial segments. Prior to the study, the examiner used a caliper to measure the bi-temporal diameter (BTD; Fig. 1) and algorithms for expected depths of arterial segments were developed and applied to aid in correct identification (Table 1). The STOP study data found that the ICA bifurcation was generally about 10 mm from the midline; the midline was determined by dividing the BTD in half. Awareness of the approximate depth of the ICA bifurcation was critical to the examiner and the interpreter, since this intracranial landmark served as a reference point for vessel identification and was the most frequent site of focal lesions. The expected vessel depths and flow direction, using the temporal approach, are described in Table 2.

Table 3 Summary of STOP TCD examination protocol

1. Measure and record BTD; midline is 1/2 BTD.
2. Explain procedure to patient; position comfortably on back with head supported and stable; child must be awake and quiet for entire examination.
3. Document instrument settings and sample volume size (6 mm).
4. Identify MCA signal, optimize, and then trace to shallowest depth.
5. Record first MCA signal (M-1), at depth of 36–38 mm.
6. Trace entire course of MCA by increasing the depth of the sample volume, optimizing signal and saving spectral waveforms at 2 mm increments.
7. Follow MCA to BIF, identified by a bidirectional signal; optimize and record.
8. Increase depth to track ACA (flow away from transducer) to 4 mm beyond BIF.
9. Decrease depth to identify BIF; angle inferiorly to insonate the dICA; increase depth by 4 mm and record distal ICA signal.
10. Decrease depth, swing sample volume superiorly, and identify the BIF signal.
11. Continuing to use the temporal window, angle posteriorly/inferiorly and identify the P-1 segment of PCA, at a depth of 50–58 mm, with flow toward transducer.
12. Track PCA to midline; bidirectional signal at midline is TOB.
13. Turn patient to side, chin to chest, and place transducer at base of skull, mentally aiming the ultrasound beam toward top of nose; set depth to 74 mm; basilar artery flow is away from transducer; trace to 78 mm, recording and optimizing at 2-mm increments.
14. Identify strongest signal at each depth, optimize and record; studies are always bilateral.

Fundamental to a successful TCD examination is identification of an optimal transtemporal "window" and localization of the MCA signal (Fig. 2). The STOP protocol requires the examiner to trace the entire course of the MCA and record spectral waveforms at 2-mm increments, from the shallowest depth (Fig. 3) to the ICA bifurcation. These 2-mm advances assure vessel identification and documentation of focal lesions. The spectral waveform documents flow direction and anatomy; the ICA bifurcation is identified by a bidirectional flow signal, indicating the termination of the ICA and origins of MCA and ACA. To assure accurate vessel identification, the protocol requires the examiner also to record a bifurcation signal, one ACA measurement (4 mm deeper than the bifurcation) and one distal ICA measurement (4 mm deeper and

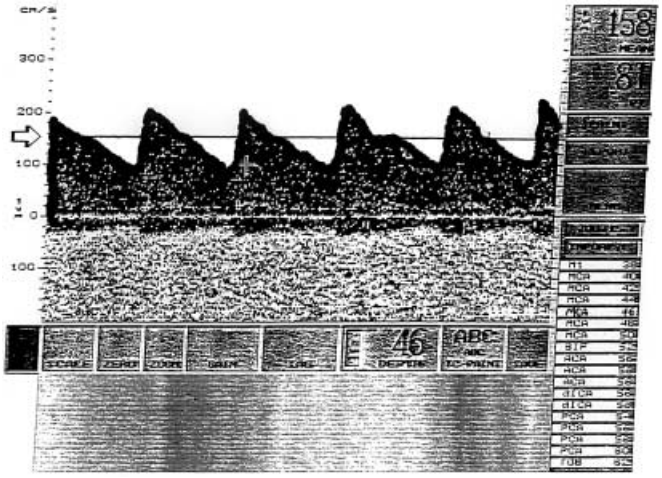

Fig. 4 TCD spectral trace and cursor placement that was used in STOP to estimate the TAMM velocity. This figure shows depth at 46 mm and cursor placement (velocity) at 158 cm/s, which by STOP protocol standards would be interpreted as a normal examination

inferior to the bifurcation). Using the same temporal window and angling posteriorly, the PCA was traced to the midline (top of Basilar). This measurement assures proper separation of anterior and posterior circulation and prevents high-volume collateral flow from the PCA being mistaken for MCA flow in the presence of progressive narrowing of the dICA or MCA. A portion of the basilar artery was recorded from the suboccipital approach at depths of 74–80 mm; ophthalmic TCD was not performed as part of the STOP protocol because it was not well tolerated in young children during the pilot study.

Instrument settings were also standardized. The TCD equipment (Nicolet TC 2000, Madison, Wis.) defaulted to a scale setting to accommodate peak systolic velocities of 250 cm/s and a sample volume of 6 mm. This sample volume size is sufficient to localize/identify vessels, but small enough separate individual signals from each intracranial vessel. TCD sonographers employed "signal optimization" so that the sharpest waveform and the highest velocity signal at each depth were obtained. Signal optimization is accomplished by proper transducer positioning and minor manipulation to assure the best angle of insonation. An optimized waveform allows precise tracking of the waveform contour by the electronic waveform follower, resulting in accurate, continuous calculation of mean velocity. TCD sonographers were trained to recognize clues of local high velocity flow: these included turbulence, sudden cut-off of the waveform, or audible clues of high velocity that were not displayed visually on the TCD monitor. Careful attention to the audible components of the Doppler signal was also emphasized. Because the high velocity signals often exceeded the Nyquist limit, producing aliasing, correct instrument and scale settings were emphasized to maximize the displayed waveform for accurate measurements.

Angle correction was not used in this comparison because the TCD is "blind" and produces no visual display of the vessel being insonated; if the sample volume cannot be aligned parallel to the vessel wall, then angle correction cannot be applied. The data acquired during the STOP study were based on non-imaging TCD and these data are the "gold standard" for this comparison. The purpose was not to compare the technique to a true velocity standard, but to compare it to a technique with validation based on long-term clinical observation and rate of stroke. The measurement of Doppler frequency shift depends on the flow velocity and the insonation angle. Although the precise insonation angle is unknown, the anatomy of the skull and intracranial vessels allows the assumption that the insonation angle is less than 30° (close to cosine 1); therefore, the TCD flow velocity closely approximates true velocity if proper examination methods are used. Bulas [13] reported that the use of angle correction precluded reproducibility of STOP findings.

Although the waveform follower was employed throughout the TCD examination to track the highest velocity displayed above the zero baseline, the mean velocity was read offline to assure consistency and optimize examination time. Velocity was read offline using a manual cursor method for measurement and a PC-based reading program. STOP risk data are based on the time averaged mean maximum velocity (TAMM), not peak systolic (PSV) or end-diastolic (EDV) velocity. The examinations were read independently by two readers following a precise protocol. The cursor line was adjusted by the reader in a manner that attempted to equalize the area above (V_1) and below (V_2) the cursor line (Fig. 4) across at least three cardiac cycles. Each waveform acquired during the TCD examination was reviewed, so that the highest velocities were identified. Systolic and diastolic velocities, while not used in risk assessment at present, were recorded for future analysis. TCD was classified as Abnormal (one or both sides = 200 cm/s), Normal (no TAMM > 170 cm/s), Conditional (> 170 cm/s, but < 199 cm/s), or inadequate for unreadable studies.

TCDI

The TCDI examination combines B-mode imaging with color coding of the Doppler information [11, 12]. The Doppler color is determined by the direction of flow relative to the transducer; for this comparison, flow toward the transducer is displayed in red, and flow away is displayed in blue. The Doppler data are superimposed on the B-mode image and provide information about flow direction, mean flow velocity, and spatial relationships between the arterial segments. The TCDI examination protocol [11] was modified to accommodate STOP specifications; angle correction was not used for this comparison because it was not used in the approximately 5,000 non-imaging TCD examinations performed in the STOP study.

The equipment used was the Acuson Aspen (Mountain View, Calif.) with a 2-MHz sector (4V2c) transducer. Using B-mode imaging through the transtemporal window, the cerebral peduncles, the star-shaped echogenic interpeduncular suprasellar cistern (anterior to peduncles) and the lesser wing of the sphenoid bone can be visualized and serve as reference landmarks (Fig. 5a). The top of the basilar is displayed immediately anterior to the cerebral peduncles, with flow in the proximal ipsilateral PCA towards the transducer (displayed red) and flow into the contralateral proximal PCA is away from the transducer (displayed blue). The ICA bifurcation lies anterior and slightly lateral to the top of the basilar. Flow from the ICA into the MCA is displayed as continuous forward flow whose course is displayed in color, passing adjacent to the lesser wing of the sphenoid bone. Flow in the proximal ipsilateral PCA initially is towards the transducer; as the PCA curves around the cerebral peduncle, flow in the more peripheral ipsilateral PCA is away from the transducer (blue). Flow in the ipsilateral ACA is away from the transducer (blue). The distal ICA is detected by locating the MCA/ACA bifurcation, and then angling the transducer slightly inferiorly. A transverse view of the ICA is visualized 4 mm deeper than the bifurcation, with antegrade flow.

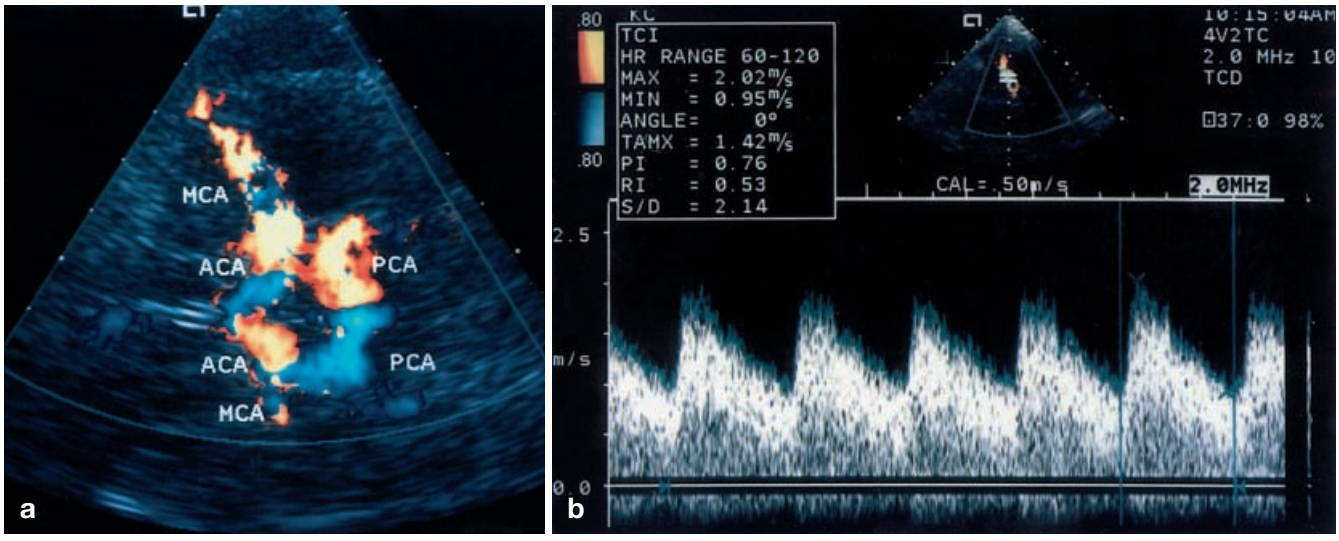

Fig. 5 a Identification of arterial segments using TCDI. Note that both ipsilateral and contralateral MCA, ACA, and PCA arterial segments can be identified. **b** Doppler spectral waveform with sample volume placement in the MCA indicated by color Doppler inserted at *top* of figure

When possible, the color Doppler display was used to display the entire circle of Willis fully.

Once the arterial segment of interest was well depicted on the color display, a 4-mm Doppler sample volume was placed in the arterial segment and a Doppler signal was acquired (Fig. 5 b). The gray scale and color displays were used to guide the velocity acquisition. In order to standardize the TCDI examination results, the color gain was increased until there was minor speckling in the soft tissue, and then decreased by one setting. The color velocity range was set at or near maximum because the flow velocities in these children frequently exceeded the Nyquist limits (the Doppler shift above which aliasing occurs, one-half the pulse repetition frequency), resulting in aliasing of the color display. Aliasing would change the color and intensity of the color Doppler image, but quantification always relied on the spectral display.

Instrument settings were carefully chosen to optimize results and mimic STOP protocol. The "threshold" for electronic measurement was maintained at 35% and the dynamic range at 30–35. The color display usually presents an image of the arterial segment that is larger than the artery ("oversizes" the artery). As a result of this, the Doppler sample volume placement may appear to be well placed in the artery (based on the color display), but in fact may not be optimally positioned. In order to obtain the highest velocities, the TCD sonographer was instructed to use the color image as a guide for sample volume placement, and then adjust the transducer to obtain the highest velocity. Careful attention to the audible components of the Doppler signal improved signal optimization. The TCDI "autoDoppler" method (the Acuson version of the waveform follower providing electronic measurements of the mean of the maximum velocity) was used continuously to assist in signal optimization and assure verification of the highest velocity in each intracranial artery. Velocity calculations were made using this automatic method or by freezing the spectral waveform and manually tracing the envelope curve representing the highest velocities, using a hand-guided point-to-point cursor.

TCDI reading method comparison

The Acuson "autoDoppler" software measures peak systolic velocity (PSV), end diastolic velocity (EDF), and time-averaged mean of the maximum velocity (TAMX). The Acuson TAMX is equivalent to the TAMM measurement used in STOP and is affected by the gain and threshold settings, which were standardized. TCDI measurements were made on-line, during the examination, because post-processing of the Doppler signal could not be done. Interpretation of results was based on the spectral waveforms captured by the TCDI sonographer during the examination.

In order to explore the possible influence of TCDI velocity calculations on this comparison, both the "autoDoppler" and manual trace methods were used to measure identical MCA waveforms in 16 patients. The mean and standard deviations of the series were compared to the TCD reading for that vessel/depth. Using the manual method, the mean and standard deviation of the series was 87 ± 26 cm/s compared to 71.3 ± 19 cm/s with the autoDoppler method. The TCD velocity from the corresponding series was 83 ± 16 cm/s. It was concluded that the autoDoppler method was preferable because the automated readings were less time consuming to complete, tracked the waveforms more precisely and consistently, and would more readily transfer to the clinical setting. Accordingly, the TCDI velocities used in this comparison are from the autoDoppler method.

Data acquisition

TCD and TCDI examinations were performed twice on two groups of children with sickle-cell anemia without prior history of stroke and free of acute illness at the time of the examination. The TCD and TCDI studies were done sequentially within 1 h of each other, with the order of the examinations randomly assigned and no communication regarding results between the two teams, who were in different rooms. All examinations were performed in quiet, dimly lit rooms. At least two measurements were performed at each depth, and the highest measurements were always used for comparison. The patients were not permitted to sleep during the examination, as carbon dioxide (CO_2) increases with sleep and may cause an increase in velocity (about 2–4% increase for each 1 mm CO_2 increase). The average examination time was 30 min.

Table 4 Descriptive statistics for TCD phase 1

Segment	*N*	Min	Mean	Median	Max
RMCAM	14	89	135	32	195
LMCAM	13	98	137	131	176
RACAM	14	37	110	106	184
LACAM	13	84	114	117	156
RICAM	13	68	91	83	128
LICAM	13	62	93	82	140
RPCAM	13	47	89	92	127
LPCAM	13	65	95	93	139

Table 5 Descriptive statistics for TCDI phase 1

Segment	*N*	Min	Mean	Median	Max	TCD-TCDI[a]	*P*
RMCAM	14	35	109	112	150	26	< 0.001
LMCAM	14	72	105	105	139	29	< 0.001
RACAM	13	50	93	85	153	17	0.04
LACAM	12	44	80	78	128	38	< 0.001
RICAM	5	70	81	81	100	15	0.1
LICAM	9	44	78	79	114	20	0.00 5
RPCAM	13	28	78	77	119	11	0.12
LPCAM	13	54	69	66	106	26	0.003

[a] Mean difference

Table 6 Median values TCD and TCDI: phase I (*R* right, *L* left)

	RMCA	LMCA
TCD	132.5	131.0
TCDI	112.5	105.5

Table 7 Mean difference between TCD and TCDI: phase I

	TCD-TCDI (cm/s)	Difference[a] (%)
RMCA	26	15
LMCA	29	19

[a] Compared to TCD

The first acquisition took place in January 1998 (phase I) and the second in December 1998 (phase II).

Data analysis

The systolic, diastolic, TAMM and TAMX readings from each patient segment were read independently and compared graphically by plotting the TCDI velocity against the TCD velocity. The bifurcation and top of the basilar segments, which are recorded in the STOP protocol for documentation of sample volume location, were not compared. A one-sample *t*-test was used to evaluate whether the average difference between the velocity measures for each segment (TCD-TCDI) differed from zero, and in what direction, if a difference was found. The differences (TCD-TCDI) for each arterial segment from phase I and phase II were compared by *t*-tests. A *P*-value for testing the null hypothesis, that the difference was the same in the two rounds, was computed.

Results

Phase I

Fourteen children with mean age 10 years, range 5–14 years, were studied in phase I (see Tables 4–7). There were 3 girls and 11 boys. Compared to the TCD results, TCDI velocities were significantly lower in all segments except for the right PCA and the right ICA, where data were limited by only five TCDI measurements. This limited success was likely due to inexperience; the TCDI sonographers had not previously tried to acquire the dICA signal and did not have the same level of experience in this specific vessel as the TCD sonographers. Based on the results of phase I, modifications were made to the protocol, so that the TCDI examination technique more closely followed the STOP protocol. In particular, emphasis was placed on optimizing the Doppler signal and making measurements in each arterial segment at 2- to 4-mm increments. The TCDI waveform gain setting was increased to the maximum level before artifactual contamination occurred and maintained at that level for each examination. The sample volume was increased to 6-mm length, and the Doppler spectral waveform display size was maximized. All velocity measurements were made using the auto-Doppler electronic measurements. TCDI sonographers focused more on Doppler signal optimization, including attention to the audible components of the Doppler signal, meticulous tracking of the arterial segments, and careful documentation of the highest velocities.

Table 8 Descriptive statistics for TCD phase 2

Segment	*N*	Min	Mean	Median	Max
RMCAM	15	92	147	146	188
LMCAM	15	86	146	153	200
RACAM	14	72	108	98	165
LACAM	15	66	121	125	222
RICAM	10	65	100	106	121
LICAM	13	38	105	112	153
RPCAM	15	45	72	67	107
LPCAM	15	50	84	78	155
BASM	13	68	97	101	128

Table 10 Median values TCD and TCDI: phase 2

	RMCA	LMCA
TCD	147	147
TCDI	132	133

Table 11 Mean difference between TCD and TCDI: phase 2

	TCD-TCDI (cm/s)	Difference[a] (%)
RMCA	16	11
LMCA	13	10

[a] Compared to TCD

Phase II

Fifteen patients, mean age 9 years, range 3–16 years, were studied. There were eight girls and seven boys and none of these children participated in phase I. The patient order of examination was again randomly assigned, and all other aspects of the comparison, except as noted, were the same as in phase I. The results of phase II are shown in Tables 8–11.

In this phase the ICA again proved difficult for TCDI examiners with data recorded from only about half the patients. Velocity differences were again observed, significant for the MCA and ACA, not significant for the ICA, but data were limited for this artery. The PCA velocity differences were in the opposite direction from phase 1 and were significant only for the right side (Table 12).

Discussion

This study demonstrated modest differences in velocity between STOP TCD and TCDI, with TCDI velocities generally lower than TCD. If attention is focused on the MCA and ICA, the most important segments in the STOP protocol, differences between the two modalities were initially in the range of 15% for the MCA. Comparison of the ICA was compromised by limited TCDI data. While TCDI offers the advantage of providing visual orientation, the fact that the ICA is not oriented in the plane of the scan, resulting in a limited transverse view, makes identification of this segment more difficult. The ICA is also a problem for TCD and has an unfavorable angle of insonation. Despite these problems, attempting to insonate the ICA is still recommended. In STOP, the ICA was the highest velocity in about 5% of the screening TCDs and arteriographic data indicate that the distal ICA is a segment often affected by the vasculopathy of HbSS. For practical reasons, transorbital examination was not used in STOP, but could add additional data about the status of the ICA [12]. Phase II modifications in TCDI in both equipment settings and techniques intended to mimic the STOP protocol reduced the differences in velocity obtained. A strong trend was seen in the right MCA and a significant reduction in the left MCA was observed.

This study found that TCDI velocities are lower than those obtained with TCD. Possible reasons include: the smaller TCD transducer size allows greater manipulation; beam shape and differences in signal acquisition, processing and velocity reading could account for differences, but the study was not designed to distinguish relative contributions of these factors. Rather, the goal was to determine how TCDI compared to TCD, which is the standard used in STOP. In this context, the "true velocity" is not pertinent. What is important for clinical use of TCDI in this application is the ability to relate velocity measurements to the large body of reported TCD and clinical outcome (MCG and STOP) data, which is prospective and validated by long-term observation of children for stroke outcome.

Table 9 Descriptive statistics for TCDI phase 2

Segment	*N*	Min	Mean	Median	Max	TCD-TCDI[a]	*P*
RMCAM	15	92	132	131	171	16	< 0.001
LMCAM	15	82	133	144	181	13	0.02
RACAM	14	56	90	92	122	18	0.003
LACAM	13	43	97	85	171	31	0.0 09
RICAM	6	76	104	110	127	7	0.2
LICAM	8	71	100	102	141	–8	0.5
RPCAM	14	47	89	93	132	–18	0.03
LPCAM	14	42	89	81	144	–4	0.7

[a] Mean difference

Table 12 The average difference between TCD and TCDI (TCD-TCDI) for each segment from phases 1 and 2

Segment	Round	Mean difference (TCD-TCDI)	N^a	SD of the difference	P^b
Right MCA	1	26.4	14	22.5	0.15
	2	15.7	15	15.6	
Left MCA	1	29.4	13	14.9	0.02
	2	13.4	15	19.8	
Right ACA	1	16.8	13	26.4	0.86
	2	18.4	14	19.3	
Left ACA	1	37.8	12	23.4	0.53
	2	30.0	13	35.4	
Right ICA	1	14.8	5	16.3	0.016
	2	–16.6	5	16.5	
Left ICA	1	20.4	9	16.0	0.08
	2	–8.0	7	35.4	
Right PCA	1	11.3	13	24.8	0.01
	2	–18.0	14	29.5	
Left PCA	1	26.1	13	26.3	0.02
	2	–3.6	14	35.7	

[a] *N* Number of patients with measurements in each segment in each round

[b] *P P* value for a *t*-test to compare differences between rounds

Because TCDI is widely available and provides a color Doppler display that aids in arterial segment identification and sample volume placement, the technique may have advantages for screening children with HbSS, but attention to certain technical aspects is recommended. For instance, the Doppler sample volume is placed in the area of color display of the artery, but this is usually not done with the equipment in simultaneous B-mode and Doppler mode. This means that the artery may not be precisely located where the color image indicates, and careful transducer adjustment is required to obtain the highest velocity following the STOP protocol.

TCDI can measure several different mean velocities but to compare to STOP, the time-averaged mean of the maximum velocities (TAMX) should be used. Systolic and diastolic velocities were recorded in STOP, but at present the stroke predictive capability of these measures in relation to TAMM is still under investigation. It is important to emphasize that the cutoff of 200 cm/s pertains to TAMM. In STOP, a systolic velocity of 200 cm/s was approximately the 50th percentile of all children screened, and most children with abnormal TCD based on TAMM had systolic velocities exceeding 300 cm/s. Such high velocities may pose problems for some TCDI systems and merit attention prior to performing clinical screening.

TCD examinations in STOP used non-angle corrected velocities, and we did not study the effect of attempted angle correction on TCDI in this setting. In other applications some authors have reported lower non-angle corrected TCDI velocities compared to TCD. In 1995, Rosendahl et al. [14] reported that TCDI was 10% lower without angle correction when compared to TCD in a group of primarily adult patients. Fujioka et al. [15] measured the mean velocity by a manual method without angle correction, and found the TCDI to be 5–10% lower than TCD in adults. Neither of these investigators used electronic measurements. Conversely, Schoning et al. [16], using angle correction reported the TCDI to be 10–15% higher than TCD. Application of angle correction might reduce the gap between TCDI and TCD, but it may produce higher velocity calculations based on the cosine of the angle. If compared to the STOP data, velocities classified as "conditional" by TCD may be classified "abnormal" by TCDI due to variations in technique rather than true velocity. The authors agree with Bulas [13] that the use of angle correction in this application is not advised.

The reduction in difference between TCD and TCDI in phase II was probably accounted for by two factors: (1) more time spent in optimizing the Doppler signal; (2) increased gain and gate settings. Both of these would be expected to produce a more robust signal that would be read as a higher velocity by the autoDoppler method. Based on this study, the authors recommend that the intracranial arteries be insonated at 2-mm rather than 4-mm increments. TCDI sonographers should focus on acquiring the highest velocity at each depth, concentrating on sites of expected stenosis. Signals should be carefully optimized to assure documentation of the highest TAMX velocity.

What do the differences found in this study mean in clinical practice? The observation that TCDI is consistently lower for the MCA suggests that, provided other aspects of the STOP protocol are adhered to, a STOP abnormal ($\geq$ 200 cm/s in ICA or MCA) TCDI study would almost surely be abnormal by TCD. High conditional (170–199 cm/s) patients by TCDI pose a greater problem. It should be noted that the 200 cm/s cutoff used in STOP does not represent a biologic threshold

but a practical cutpoint, and patients with conditional TCD are at elevated risk, but the risk-benefit of chronic transfusion has not been determined. Repeat ("confirmation") TCD or TCDI at a second setting is recommended in all abnormal cases. Early re-study, in 6–12 weeks, is a practical approach in those with conditional results to monitor trends. Ideally, each site would perform comparative studies if STOP comparable TCD can be arranged. However, until more comprehensive data are available, the results of this study suggest that children with TCDI TAMX velocities over 180 cm/s should be considered at risk approximately equivalent to 200 cm/s in STOP.

Conclusion

In this comparison using the Acuson Aspen system, TCDI compared to TCD consistently underestimates velocity in the MCA and in most other arterial segments, when velocity is measured using the autoDoppler method, although the differences are relatively small.

The magnitude of the TCDI difference for the MCA, in the range of 15% less than TCD velocity, can be reduced significantly to about 10% by adaptations to the TCDI methods. These adaptations should be used in TDCI screening for stroke risk in SCD. The findings in this study apply only to readings obtained using the autoDoppler method. Manual readings may, in fact, exceed those of STOP TCD and direct comparisons will be needed if manual measurements are used. The ICA remains a problem area, but experience should increase the success rate.

In the absence of additional data to the contrary, patients studied with TCDI according to the methods used in this study who have TAMX velocities of 180 cm/s or higher should be considered at stroke risk at a level approximately equivalent to a 200 cm/s by STOP TCD. Additional studies comparing other TCDI equipment and measurement methods, studying more children who have known abnormal TCD, should be conducted.

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