

## Transcranial Doppler in a Hispanic–Mestizo population with neurological diseases: a study of sonographic window and its determinants

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### Abstract

Between 5% and 37% of patients are not suitable for transtemporal insonation with transcranial Doppler (TCD). This unsuitability is particularly frequent in elderly females and non-Caucasians. We aim to evaluate TCD efficiency in a mixed Hispanic population in Santiago, Chile and to determine whether factors associated with the presence of optimal windows depend exclusively on patient-related elements. Seven hundred forty-nine patients were evaluated with power mode TCD. Optimal temporal windows (TWs) included detection of the middle, anterior, posterior cerebral arteries and terminal carotid. The patient's age and sex, the location of the examination, the time of day, whether the test was conducted on weekends and whether mechanical ventilation was used were recorded. Percentages of optimal windows were calculated. Examinations were deemed ideal if both TWs were optimal. TWs were obtained in 82% of cases. In univariate analyses, male sex ( $P < 0.001$ ), an age below 60 years ( $P < 0.0001$ ) and mechanical ventilation ( $P = 0.04$ ) correlated with ideal TWs. Using logistic regression where dependent variable was a non-ideal window only male sex odds ratio (OR) 2.3 (1.51–3.45) and age below 60 OR 13.8 (7.8–24.6) were statistically significant. Our findings indicate that Hispanic populations have detection rates for TWs similar to Europeans and are affected by patient-related elements.

### Introduction

Transcranial Doppler (TCD) is a noninvasive, low-cost exploratory method that can be used at the bedside to evaluate flow velocity in the basal cerebral arteries. It is useful in stroke treatment for identifying occlusions and stenoses of intracranial vessels, monitoring thrombolytic therapy, and demonstrating arterial reocclusions. Among other applications, it has been used in neurointensive care for diagnosing vasospasms in patients with subarachnoid hemorrhages and for following up cases of intracranial hypertension (Aaslid et al. 1982; Hassler et al. 1998; Demchuk et al. 2000, 2001; Alexandrov and Grotta 2002; Suárez et al. 2002; Sloan et al. 2004).

A major limitation of TCD is that between 5% and 37% of patients have unsuccessful insonation of the transtemporal

window because the ultrasound cannot penetrate the temporal bone. The elements originating this situation depend on factors related to the patient and on the equipment. The patient-related circumstances are mainly female sex, advance age, and non-Caucasian origin; furthermore, a proportion of those explored has increased thickness of the temporal squama and inhomogeneity of temporal bone (Halsey 1990; Itoh et al. 1993; Marinoni et al. 1997; Jarquin-Valdivia et al. 2004; Kwon et al. 2006). As for the equipment probe frequencies of less than 2 MHz or higher emitted power, improve the window detection (Yagita et al. 1996; Klötzsch et al. 1998; Georgiadis et al. 1999; Cullinane and Markus 2001).

The failure rate of TCD for the Latin population in the Western Hemisphere and the influence of elements external to the patient are currently unknown. The aim of this study was to demonstrate the efficiency of TCD by evaluating a

mixed-Hispanic population in Santiago, Chile, to determine whether the factors associated with the presence of optimal windows depend exclusively on patient-related elements.

## Methods

The subjects were a prospective cohort of patients referred for TCD examination at the Clínica Alemana de Santiago between January 2004 and December 2009. We excluded examinations performed on patients under 15 years of age, foreigners, those who had a suspected diagnosis of brain death or who had undergone a hemicraniectomy and evaluations in which one temporal window (TW) was missing. Patients with incomplete studies in which both TWs were examined were included. An experienced sonographer (AB) used an FDA-approved power-mode TCD unit (100 M, Spencer Technologies, Seattle, WA) with a 2-MHz probe at 100% power and a 6-mm sample volume for the examination. A standard insonation protocol was used. An insonation depth of 45–65 mm was used to identify the M1 middle cerebral artery (MCA), and a depth of 30–45 mm was used for the M2 MCA through the transtemporal window. The proximal anterior cerebral artery (ACA) was identified at a depth of 58–70 mm, aiming the probe inferiorly and anteriorly. The terminal internal carotid artery (TICA) was identified at a depth of 60–70 mm. The posterior cerebral artery (PCA) was identified at a depth of 58–67 mm, with the probe aimed 30 degrees posteriorly.

Vertebral artery (VA) was identified by insonating through the transforaminal window at a depth of 40–79 mm, with the probe aimed at the bridge of the nose. The basilar artery (BA) was identified at a depth of 80–100 mm. For the transorbital window, the TCD power was decreased to 10% and the ophthalmic artery was identified at a depth of 50–52 mm. The carotid siphon was identified at a depth of 60–64 mm.

The insonation of the transtemporal windows was considered optimal if the flow signals could be measured for the mean, peak, and end-diastolic velocities with the pulsatility indices at a depth of 64, 55, and 45 mm for the MCA, and if the ACA, TICA, and PCA were identified. Windows were considered suboptimal if one or more of the segments were not accessible, and windows were considered absent when no flow signals were detected.

The transforaminal window was classified as optimal if both the VA and basilar segments were identified at depths of 80, 90, and 100 mm, and if flow signals could be measured for the mean, peak, and end-diastolic velocities, and pulsatility index. A window was suboptimal if one artery or artery segment was not identified, and the window was considered absent if no flow signals were detected.

In the case of the transorbital window, the examination was classified as optimal if the ophthalmic artery and the carotid siphon were identified, as suboptimal if one of them

could not be detected, and as absent if both arteries were not identified.

Data on the patient age, sex, place of examination (emergency room [ER], intensive care unit [UCI], hospital ward [HW], and neurosonology laboratory [NSL]), and time of day (day time, 8:00–19:59 vs. night time, 20:00–7:59) were recorded. Additional collected information included whether the evaluation was conducted during a workday or on a weekend or holiday and whether the patient was connected to a mechanical ventilator.

This study protocol was reviewed and approved by the Institutional Ethics and Scientific Committee of the Universidad del Desarrollo–Clínica Alemana de Santiago. All patients or their relatives gave informed consent.

## Statistical analysis

We calculated the percentage of optimal, suboptimal, and absent windows for the transtemporal, transforaminal, and transorbital windows.

An additional analysis was performed to combine both TWs. We considered patients in whom both the TWs were optimal as ideal and those patients who had one or two TWs with one of them suboptimal or absent insonation as nonideal. For these groups, Fisher's exact and  $\chi^2$ -tests with a *P*-value of 0.05 were used to evaluate the association between ideal or nonideal windows and age, sex, the location where the examination was performed, the time of day at which the patient was evaluated, whether the evaluation was conducted during regular working hours versus weekends and holidays, and the presence of mechanical ventilation. For this analysis, the patients were divided into the following three age groups: under 60 years, between 60 and 79 years, and 80 years or more.

Statistically significant variables were tested in a logistic regression model using the incidence of a nonideal window as the dependent variable. The odds ratios for having ideal windows were calculated for the factors in the regression. Finally, the association between the incidence of optimal transforaminal windows and mechanical ventilation was examined.

## Results

A total of 992 first TCD examinations were performed between January 2004 and October 2009; 93 studies were excluded because they were performed for possible diagnosis of brain death, 61 because they were performed on foreign patients of different origins, 51 had one or more unevaluated TWs or had undergone hemicraniectomy, 20 were performed on individuals under 15 years of age, and 18 patients declined to participate. The data from a total of 749 patients were analyzed. The patients with incomplete studies did not differ from those who were included in the study. The baseline characteristics of the study population are

presented in Table 1. A total of 749 left and right TWs were evaluated. In addition, 714 transforaminal windows and 717 right and 711 left orbital windows were included. The TCD studies were performed on patients with the following diagnoses: stroke (ischemic, hemorrhagic, and transient events), 393 cases; subarachnoid hemorrhage, 59 cases; traumatic brain injury, 62 cases; carotid pathologies, 46 cases; and other diagnoses, 189 cases. The duration of the examination varied depending on the location at which the patients were evaluated, and the difference was statistically significant, and the data from this analysis are as follows: ER,  $25.6 \pm 6.4$  min; HW,  $28.6 \pm 7.1$  min; UCI,  $29.9 \pm 7.2$  min; and NSL,  $31.6 \pm 7.6$  min ( $P < 0.0001$ ). Optimal insonation was obtained for all windows in over 80% of the cases (Table 2).

In the univariate analysis, the factors that predicted the presence of an ideal TW were male sex, age below 60 years, and connection to mechanical ventilation (Table 3). In the logistic regression analysis with the presence of a nonideal window as the dependent variable, only male sex and age below 60 were significant factors (Table 4). The patients who were connected to mechanical ventilation were on average 10.5 years younger, which was also a statistically significant

**Table 1.** The baseline characteristics of the patients included in the study.

Number of patients	749
Mean age, years $\pm$ SD (range)	$58.0 \pm 20.7(17-99)$
Female <i>N</i> (%)	393 (52.2%)
Place of examination	
ER <sup>1</sup>	141 (18.8%)
UCI <sup>2</sup>	270 (36%)
HW <sup>3</sup>	235 (31.4%)
NSL <sup>4</sup>	103 (13.8%)
Examination during the day	690 (92.1%)
Examination on weekdays	621 (82.9%)
Connection to mechanical ventilation	98 (13.1%)

<sup>1</sup>Emergency room.

<sup>2</sup>Intensive care unit.

<sup>3</sup>Hospital ward.

<sup>4</sup>Neurosonology laboratory.

difference ( $P < 0.001$ ). Finally, a stratified analysis by age, sex, and ideal window is shown in Table 5.

The group with the highest failure rate for detecting ideal TWs was women over 80; this group had only 46.1% ideal TW insonation ( $P < 0.001$ ). By contrast, the highest rate of effective TCDs was observed among male patients under age 60, with an ideal TW rate of 95.5% ( $P < 0.001$  compared to the total population).

**Table 3.** A univariate analysis of the predictors of an ideal transcranial Doppler (TCD) window.

Variables	Ideal window	Nonideal window	<i>P</i>
Age			
Less than 60 years	356 (94.9%)	19 (5.1%)	<0.0001
Between 60 and 79 years	162 (70.4%)	68 (29.6%)	
More than 80 years	81 (56.3%)	63 (43.8%)	
Sex			
Male	306 (86%)	50 (14%)	<0.001
Female	293 (74.6%)	100 (25.4%)	
Place of examination			
ER <sup>1</sup>	114 (80.9%)	27 (19.1%)	0.34
ICU <sup>2</sup>	215 (79.1%)	49 (20.9%)	
HW <sup>3</sup>	186 (79.1%)	49 (20.9%)	
NSL <sup>4</sup>	84 (81.6%)	19 (18.4%)	
Days			
Weekday	497 (80%)	124 (20%)	0.5
Weekends and holidays	102 (79.7%)	26 (20.3%)	
Mechanical ventilation			
Yes	85 (86.7%)	13 (13.3%)	0.04
No	514 (79%)	137 (21%)	
Hour of the day			
Day time (8:00 AM to 19:59 PM)	555 (80.4%)	135 (19.6%)	0.3
Night time (20:00 PM to 7:59 AM)	44 (74.6%)	15 (25.4%)	

<sup>1</sup>Emergency room.

<sup>2</sup>Intensive care unit.

<sup>3</sup>Hospital ward.

<sup>4</sup>Neurosonology laboratory.

**Table 2.** Rate of successful insonation in Chilean patients by window anatomy.

Window	Optimal		Suboptima		Absent	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
Right temporal	635	84.8	78	10.4	36	4.8
Left temporal	620	82.8	78	11.1	46	6.1
Transforaminal	624	87.4	90	12.6	0	0
Right TO	713	99.4	4	0.6	0	0
Left TO	708	99.6	3	0.4	0	0

TO, transorbital window.

**Table 4.** A regression analysis for having a nonideal temporal window.<sup>1</sup>

Variable	OR <sup>2</sup> IC 95.0%
Mechanical ventilation	1.4 (0.73–2.822)
Sex	2.3 (1.51–3.45)
Age ≥80	NA <sup>3</sup>
Age 60–79	1.62 (1.04–2.54)
Age <60	13.87 (7.80–24.64)

<sup>1</sup>The dependent variable was a nonideal window.

<sup>2</sup>Odds ratio.

<sup>3</sup>Not applicable.

**Table 5.** The rate of finding an ideal temporal window stratified by age and sex.

Age (years)	Females				Males			
	Nonideal TW		Ideal TW		Nonideal TW		Ideal TW	
	N	%	N	%	N	%	N	%
<60	11	5.6	186	94.4	8	4.5	170	95.5
60–79	41	38.3	66	61.7	27	22	96	78
≥80	48	53.9	41	46.1	15	27.3	40	72.7
Total	100	25.4	293	74.6	50	14	306	86

TW, temporal window.

The TCD achieved a successful vertebro-basilar assessment, including detecting distal basilar flow, in 87.4% of the patients and was not affected by the use of mechanical ventilation ( $P = 0.5$ ). In the case of the transorbital window, successful insonation was obtained in over 99% of the cases.

## Discussion

Our study demonstrates that in the Chilean Hispanic–Mestizo population, blood-flow signals through TWs were not detected in approximately 5% of those evaluated (4.8% for the right TW and 6.1% for the left). These numbers are similar to those reported for the European population by Marinoni (Marinoni et al. 1997) and Aaslid (Aaslid et al. 1982), who found the rate of inadequate TWs in their patients to range from 5% to 8.2% and that these rates were better than the rates of insonation in Japanese and African-American patients. In these two latter groups, Itoh (Itoh et al. 1993) reported a 22.9% failure rate for MCA insonation, while Halsey (Halsey 1990) reported a failure rate of 23% for males and 50% for females. Our results may be explained by the Chilean population being highly heterogeneous. It is the result of an initial mixture of the indigenous ethnic groups with Hispanic immigrants that was combined with immigrants from all European countries during the 19th and 20th centuries; there were minimal contributions from African or Asian groups. This makes the Chilean population ethnically closer to those evaluated

in the European studies than to Asian or African-American patients (Llop et al. 2006).

We must also consider the possibility that our high percentage of optimal windows may be based on the use of power-mode TCD, a technology that uses 33 overlapping Doppler samples to simultaneously display flow signal intensities and direction over 6 cm of the intracranial space. This property leads to more complete spectral analyses and increases the speed at which acoustic windows are found (Moehring and Spencer 2002; Tsivgoulis et al. 2008). This is based on the fact that the average age of our patients was slightly higher than of those evaluated by Marinoni ( $58.0 \pm 20.7$  vs.  $55.2 \pm 16.1$ ) and there was a higher percentage of females in our study. The times used in our evaluations were also shorter than those of other studies (Marinoni et al. 1997). Our TCD studies were more thorough compared to other experiments (Halsey 1990; Itoh et al. 1993), although the suboptimal TWs could have been caused by the absence of the ACA, PCA, and/or the TICA. All of these elements may have biased our results toward a higher proportion of inadequate TWs; in fact, there was a 10–12% proportion of suboptimal TWs in our study.

For the transforaminal window, our proportion of suboptimal windows was similar to that reported by Marinoni et al. (1997), whose rate of 9.0% compares with our rate of 12.6%; these results were not affected by mechanical ventilation. We found a high success rate for TCD in the transorbital window that is probably explained by the absence of bone between the probe and the artery, which is a situation that results in the ultrasound being neither absorbed nor scattered (Ackerman et al. 1982).

The rate of successful TW insonation decreases in females and with advancing age in all population groups (Halsey 1990; Itoh et al. 1993; Marinoni et al. 1997), and the latter factor was the most relevant for our population. This result is in contrast to that reported by Wijnhoud for a European (mostly Caucasian) population, in which gender was the most important variable (Wijnhoud et al. 2008). Age clearly affects the detection of ideal TWs in a more dramatic way in females. Women 80 years or older had optimal windows in only 46.1% of the cases, compared with a rate of 72.7% in males from the same age group. This difference is explained by females having thicker temporal bones and more temporal bone inhomogeneity. The latter factor is related to osteoporosis and poorer arterial detection on TCD (Kwon et al. 2006); some of these anatomical characteristics are shared with African Americans (Halsey 1990).

An important finding of our study was that having ideal TWs is dependent only on the patient characteristics and not on environmental elements, the location of the examination, the time of the day, the use of mechanical ventilation, among other factors. This finding is evident because the difference in the time required for our TCD examinations in different settings did not influence the likelihood of having ideal TWs.

The main strengths of our study are that it used a large group of unselected patients who were representative of those usually studied in this type of clinical setting and that all of the examinations were performed by a single TCD operator, which makes the results obtained in different settings and at different times comparable.

Important limitations of this study are that TCD examinations were performed only depending on the clinical condition of the patient, and without previous measurements of the thickness of the temporal bone to distinguish between patients with ideal or nonideal TWs, a factor related to the absorption and/or scattering of the ultrasound energy (Aaslid et al. 1982). Also, some conditions such as renal failure or diabetes, that are associated with suboptimal windows were not analyzed, as the effect of transducers with frequencies of less than 2 MHz, which could increase the detection of arterial signals in inadequate temporal bone windows, was not explored. Additionally, simply because a single operator performed all of the examinations does not necessarily imply that the results of this study are not reproducible. Finally, we do not know to what extent echo-contrasting agents would have improved the results in our population and whether our results could be applied to transcranial color-coded duplex sonography, a neurosonographic examination that is becoming progressively more popular, based on the fact that reliably identifies blood flow in the intracranial arteries by allowing direct visualization of the vessels insonated; and it offers the opportunity for angle corrections resulting in more accurate measurement of flow velocities. Furthermore, it enables the detection of midline shifts in ischemic strokes and detection of intracerebral hemorrhages (Nedelmann et al. 2009).

## Conclusion

The Hispanic–Mestizo population has a TW detection rate similar to those of European populations, and the rate of optimal insonation is mainly affected by patient characteristics, such as age and sex.

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## Conflicts of Interest

Alejandro M. Brunser reports no conflicts of interest.

Claudio Silva reports no conflicts of interest.

Daniel Cárcamo reports no conflicts of interest.

Paula Muñoz reports no conflicts of interest.

Arnold Hoppe has been paid honoraria and received travel grants as part of research projects by Astra Zeneca and Servier.

Veronica V. Olavarria reports no conflicts of interest.

Violeta Díaz reports no conflicts of interest.

Juan Abarca reports no conflicts of interest.

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