

# Color Duplex Measurement of Cerebral Blood Flow Volume in Healthy Adults

Peter Scheel, MD; Christian Ruge; Uwe R. Petrich, MD; Martin Schöning, MD

**Background and Purpose**—Global cerebral blood flow (CBF) is an important yet largely unknown quantity in the treatment of neurological intensive care patients. Color duplex sonography of the extracranial cerebral arteries can be used to measure global CBF volume directly at the bedside. To establish reference data on global CBF volume and to test the influence of sex and age on this parameter, a prospective study was performed in a group of 78 healthy adults aged 20 to 85 years (39 women, 39 men; mean age,  $52 \pm 19$  years in either sex).

**Methods**—The common, external, and internal carotid arteries and the vertebral arteries were examined with the use of a 7.0-MHz transducer of a computed sonography system. Angle-corrected time-averaged flow velocity and the diameter of the vessel were measured. Intravascular flow volumes were calculated as the product of angle-corrected time-averaged flow velocity and the cross-sectional area of the circular vessel. CBF volume was determined as the sum of flow volumes in the internal carotid and vertebral arteries of both sides.

**Results**—From 20 to 85 years of age, CBF volume decreased significantly ( $P \leq 0.0001$ ), on average by  $\approx 3$  mL/min per year. There were no sex-linked differences in CBF volume. The mean relative contributions of the internal carotid artery and the vertebral arteries to global CBF volume remained constant with age (76% versus 24%). The reference data on CBF volume established for the groups aged 20 to 39 years, 40 to 59 years, and 60 to 85 years were  $727 \pm 102$ ,  $656 \pm 121$ , and  $603 \pm 106$  mL/min, respectively.

**Conclusions**—The data presented here provide additional information on the natural development of global cerebral perfusion in “benign aging.” CBF volume reference data for different age groups were also established. These data provide a basis for the clinical application of CBF volume measurements at the bedside, especially in the monitoring of CBF volume in neurological intensive care patients. (*Stroke*. 2000;31:147-150.)

**Key Words:** aging ■ cerebral blood flow ■ ultrasonography, Doppler, duplex

Global cerebral blood flow (CBF) is an important yet largely unknown quantity in the treatment of neurological intensive care patients suffering, for example, from cerebrovascular disorders and/or intracranial hypertension. Until now, the quantitative measurement of global CBF has only been possible by exposing patients to invasive or to radionuclide techniques.<sup>1-3</sup> These methods are not suitable for either bedside evaluations or follow-up measurements of CBF.

Reports on flow volume measurements in extracranial cerebral arteries using Doppler and duplex methods<sup>4-7</sup> were followed by the first systematic description of global CBF volume estimation in a group of young and middle-aged healthy adults by Schöning et al.<sup>8</sup> The same authors found the intradiane and interdiene and intraobserver and interobserver reproducibility of global CBF volume measurement to be high,<sup>9</sup> comparable in fact to the intradiane reproducibility of CBF with the use of  $H_2^{15}O$  positron emission tomography.<sup>10</sup>

Most intensive care and stroke patients are older than 60 years. Reference data on CBF volume for this age group are

not yet available. In the present study we measured CBF volume in a group of healthy adults aged 20 to 85 years to provide reference data for different age groups and to test the natural influence of age and sex on this parameter.

## Subjects and Methods

Seventy-eight healthy adults (39 women; mean age,  $51.9 \pm 19.1$  years; 39 men; mean age,  $51.8 \pm 19.4$  years) participated in this prospective CBF volumetric study. To achieve a homogeneous distribution of age and sex in the study group, we planned to examine cohorts of 3 women and 3 men in each 5-year period between 20 and 85 years of age. There was only 1 exception to this rule: in the group aged 80 to 85 years, 1 healthy 87-year-old woman was enrolled. All subjects lived an independent life and were free of (and had no history of) cardiac, neurological, or cerebrovascular disease. Only subjects without sonographic evidence of plaque formation in the carotid bulb were included in this study. One 82-year-old man was on mild antihypertensive therapy, but none of the other participants received any medication. Informed consent was obtained before the examination. The study was approved by the local ethical committee of the university.

During an initial 20 minutes of rest with the subjects in a supine position, the intracranial arteries were examined by transcranial

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Bilateral Flow Volumes in Extracranial Arteries and Global CBF Volume in Different Age and Sex Groups

Age group, y	n	CBF Volume	CBF Volume		VA	ICA	ECA	CCA
			Men	Women				
20–85	78	657±120	670±117	644±123	158±48 (24±7)	499±108 (76±7)	328±111	816±198
20–39	24	727±102	725±87	730±87	173±41 (24±6)	554±99 (76±6)	290±63	853±197
40–59	24	656±121	663±126	648±120	147±36 (23±6)	508±114 (77±6)	350±146	868±223
60–85	30	603±106	633±108	572±99	155±58 (25±8)	448±85 (75±8)	340±103	745±160

Values are mean±SD, expressed in milliliters per minute. The percentage of the relative contributions of ICA and VA flow volumes to global CBF volume is shown in parentheses.

color-coded duplex sonography (the results of which are not part of this study). Then the extracranial arteries, ie, the common carotid arteries (CCA), the external (ECA) and internal carotid arteries (ICA), and the vertebral arteries (VA) of both sides were explored with a 7.0-MHz linear array transducer of a computed sonography system (Acuson 128/XPI10).

The test persons continued to lie supine with the head slightly elevated and turned to the contralateral side by  $\approx 10^\circ$  for CCA and VA measurements and by  $25^\circ$  to  $40^\circ$  for ICA and ECA measurements. Flow volume measurements were generally taken in the C4–C5 intertransverse segment of the VA, 1.5 to 2 cm below the carotid bulb in the CCA, and 1 to 2 cm above the carotid bulb in the ECA and ICA.

The luminal diameter (d) was determined on the enlarged B-mode image of the vessel as the distance between the internal layers of the parallel walls. The mean of 2 measurements was evaluated. The calipers could be adjusted in 0.1-mm increments. At the same site, a sample volume was positioned to cover the entire luminal width. Exact angle correction was performed. We aimed to keep the angle of insonation as low as possible, in most cases  $\approx 60^\circ$ . The angle-corrected time-averaged flow velocity (TAV) was determined as the integral of the mean flow velocities of all moving particles passing the sample volume over 3 to 5 complete cardiac cycles (in this way, the pulsatile parabolic flow is mathematically transformed into a continuous plug flow). The intravascular flow volume (FV) was calculated as the product of TAV and the cross-sectional area (A) of the circular vessel according to the formula  $FV = TAV \times A = TAV \times [(d/2)^2 \times \pi]$ . CBF volume was determined as the sum of the flow volumes of the ICA and the VA of both sides. Each measurement was recorded with a video printer. The complete examination took  $\approx 20$  minutes. To maintain the noninvasive character of the examination and to avoid any stress for the subjects, blood parameters (such as hematocrit or arterial blood gas analysis) were not determined.

The program SAS (version 6.12, SAS Institute) was used for the statistical analysis. All parameters are shown as mean±SD. Student's *t* test was used to reveal any differences between the sexes. Age correlation of flow volume parameters was evaluated with Spearman's rank correlation coefficient. The level of statistical significance was set at  $P \leq 0.01$  for all tests.

## Results

All extracranial vessels could be examined with the exception of 1 ECA in a 25-year-old man. Mean±SD values for CBF volume and the bilateral flow volumes of ICA, VA, CCA, and ECA for the whole study group are shown in the Table.

There was an inverse correlation of CBF volume with age (Spearman's rank correlation coefficient  $r = -0.45$ ;  $P < 0.0001$ ). On average, CBF volume decreased at a rate of  $\approx 3$  mL/min per year from 20 to 85 years of age (Figure 1).

The bilateral sum of ICA flow volumes (feeding the anterior cerebral circulation) declined significantly with age ( $r = -0.45$ ;

$P \leq 0.0001$ ; Table and Figure 2). A mild reduction in the sum of VA flow volumes (which feed the posterior cerebral circulation) with increasing age was not significant ( $r = -0.16$ ;  $P = 0.17$ ). The mean relative contribution of the anterior and posterior cerebral circulation (75% to 77% versus 23% to 25% in different age groups) to global CBF volume did not change significantly with age ( $r = 0.11$ ;  $P = 0.35$ ). The bilateral sum of CCA flow volumes decreased with age ( $r = -0.28$ ;  $P = 0.01$ ), while the ECA flow volumes remained constant ( $r = 0.18$ ;  $P = 0.12$ ).

In the whole study group, there were no significant differences between men and women in CBF volume ( $670 \pm 117$  versus  $644 \pm 123$  mL/min;  $P = 0.34$ ) or the bilateral sum of flow volumes in the ICA ( $518 \pm 105$  versus  $480 \pm 108$  mL/min;  $P = 0.11$ ), VA ( $152 \pm 43$  versus  $164 \pm 51$  mL/min;  $P = 0.26$ ), and CCA ( $858 \pm 212$  versus  $774 \pm 176$  mL/min;  $P = 0.06$ ), respectively. The bilateral sum of flow volumes in the ECA was higher in male than in female subjects ( $361 \pm 84$  versus  $298 \pm 118$  mL/min;  $P \leq 0.001$ ).

Reference data on CBF volume and the sum of bilateral flow volumes in the ICA, VA, CCA, and ECA for different age groups were established (Table).

## Discussion

To date, 2 color duplex volumetric studies exist that describe the normal development of CBF volume: from childhood to adulthood, a slight increase was shown from 3 to 6 years of age and

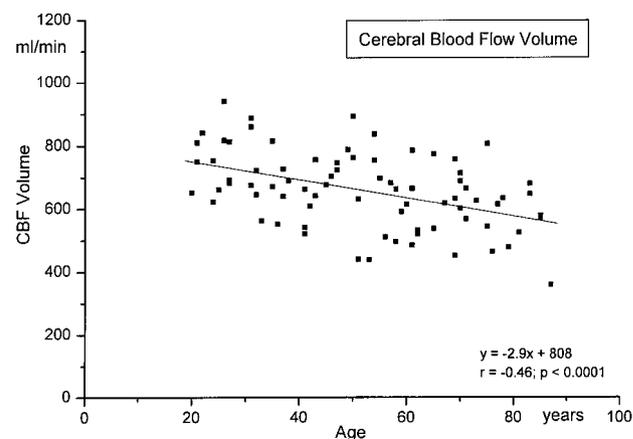
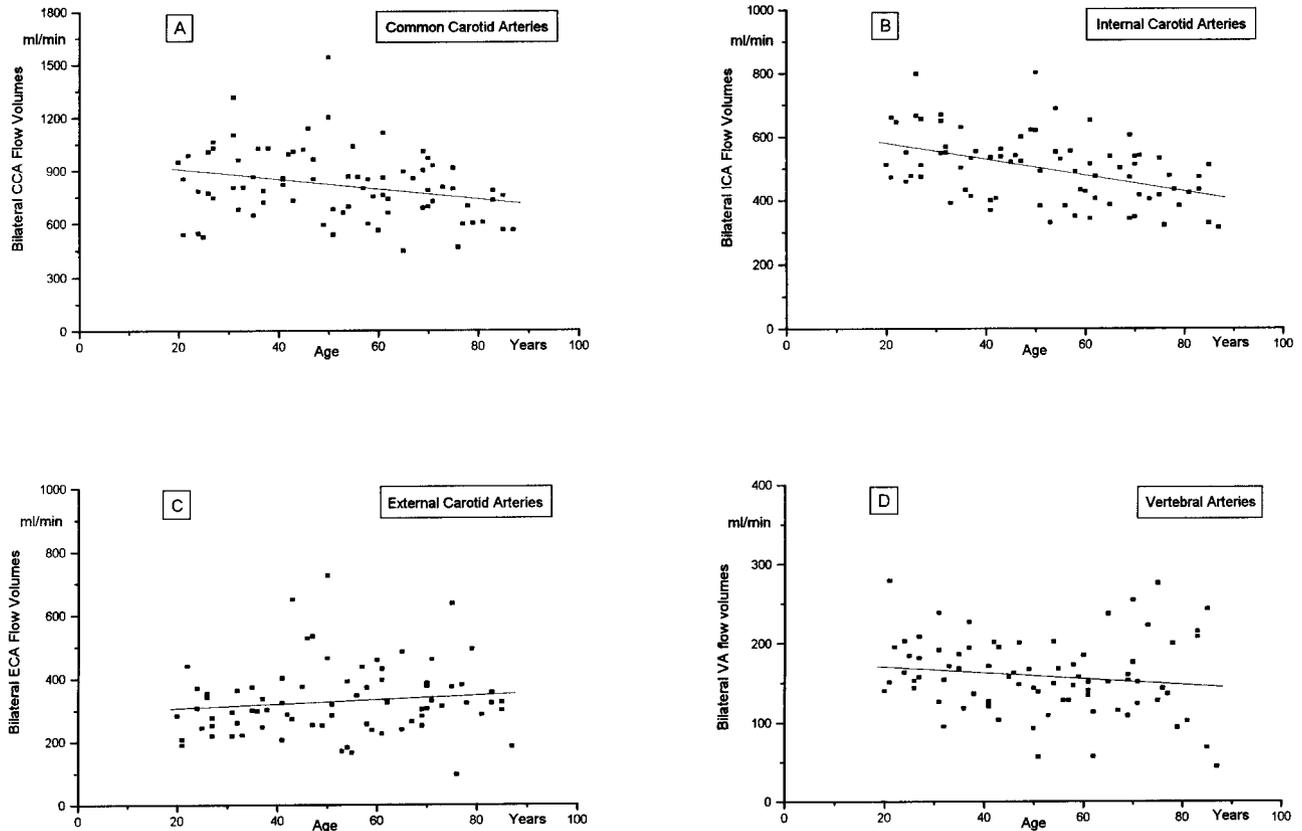


Figure 1. Development of global CBF volume with age (20 to 85 years).



**Figure 2.** Sum of bilateral flow volumes in the CCA (A), ICA (B), ECA (C), and VA (D) in healthy subjects aged 20 to 85 years.

a subsequent decline from 7 to 18 years of age,<sup>11</sup> after which CBF volume appeared to remain constant up to the age of 60 years.<sup>8</sup> However, in a larger and homogeneously distributed group of adults, we now are able to delineate a mean decrease in CBF volume by  $\approx 3$  mL/min per year from 20 to 85 years of age.

There are few reports on CBF volume measurements. Buijs et al<sup>12</sup> recently published a study on CBF volume measurements in the supratentorial part of the brain using 2-dimensional phase-contrast MR angiography of the ICA and the top of the basilar artery. In the whole study group (250 subjects, aged 19 to 88 years), they found a mean CBF volume of  $616 \pm 143$  mL/min and a mean decrease of 4.8 mL/min per year. Applying the same MRI technique to 24 healthy subjects between 12 and 70 years of age, Kashimada et al<sup>13</sup> reported a mean CBF volume of 694 mL/min and a mean reduction of 3.9 mL/min per year.

Most publications dealing with CBF measurements in healthy adults report a decline in CBF with increasing age, mainly due to a reduction of cortical blood flow,<sup>14–25</sup> while only few authors found that global CBF remains constant during healthy normal aging.<sup>2,26,27</sup> Shaw et al<sup>20</sup> calculated the decrease in global CBF to amount to a rate of 0.5 to 1.0 mL/100 g per minute per year. The reduction in CBF and CBF volume can be attributed to a progressive loss of neurons,<sup>28</sup> diminished activity of the neurons, and a diminution of synaptic density<sup>25,29,30</sup> with increasing age.

In the present study there were no significant differences in CBF volume between men and women. These findings are also

in accordance with those of Buijs et al.<sup>12</sup> A color duplex volumetric study of 94 healthy children and adolescents was likewise unable to detect any sex-related difference in CBF volume.<sup>11</sup> On the contrary, global CBF (per 100 g brain weight) was found to be higher in women than in men.<sup>23,31,32</sup> Rodriguez et al<sup>24</sup> reported that global CBF is  $\approx 11\%$  higher in women than in men. It is well known that brain weight from the first years of life is an average of 10% higher in men than in women of the same age group.<sup>33,34</sup> These opposing trends may explain why there is no difference in global CBF volume (expressed in milliliters per minute) between men and women.

The only sex-related difference we found was in the territory of the ECA, where the flow volume rate was significantly higher in men than in women. Similar observations have not yet been reported, and we do not have any physiological explanation for this finding.

Since there is no significant sex-related difference in CBF volume (or in ICA and VA flow volumes), we are now able to establish common reference data for groups of young, middle-aged, and elderly healthy adults (Table).

Regional CBF can be measured with single-photon emission CT and positron emission tomography examinations, while color duplex volumetric examination of the brain-feeding arteries can only yield information about the relative contributions of the anterior and posterior cerebral circulation to global CBF volume. We found a mean contribution of the VA to global CBF volume of  $\approx 24\%$ , which remained almost constant with increasing age. From early childhood to adulthood, the relative contribution of the posterior

cerebral circulation to CBF volume was shown to decline from 31% to 24%.<sup>8,11</sup> Kashimada et al<sup>13</sup> estimated that the VA contribute 24.7% of the global CBF volume. To date, there are no other reports on the relative contributions of the anterior and posterior circulation to global CBF volume in humans.

Until now, CBF has been estimated in critically ill patients by measuring flow velocities in the intracranial arteries with the use of Doppler or duplex sonography or through invasive procedures. Color duplex volumetric examination of the brain-feeding extracranial arteries is a highly reproducible,<sup>9</sup> noninvasive method of measuring CBF volume at the bedside. The reliability of the method must still be confirmed in comparative studies with established radionuclide procedures, which, for ethical reasons, can only be performed in patient groups for clinical purposes. It must be stressed that the reliability of CBF volume measurements depends on the technical skills of the examiner and that a meticulous measurement technique must be observed. The method is easy to perform on healthy cooperative subjects. In intensive care unit patients, CBF volume measurement may be hampered by catheters and dressings at the neck, restlessness of the patient, or artifacts produced by various machines. However, in our experience flow volume measurement is possible in all the extracranial brain-feeding arteries in >90% of all intensive care patients. The reference data provided in this study may make it possible to use this method to monitor CBF volume in intensive care patients with increased or reduced cerebral perfusion caused, for example, by arteriovenous malformations, intracranial hemorrhage, and intracranial hypertension.

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