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Blood Flow Volume Measurement in Cervical and Intracranial Arteries using Quantitative Magnetic Resonance Angiography and Duplex Sonography (Bocaccia) – A Prospective Observational Study

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Blood Flow Volume Measurement in Cervical and Intracranial Arteries using Quantitative Magnetic Resonance Angiography and Duplex Sonography (Bocaccia) – A Prospective Observational Study

Messung des Blutflussvolumens in zervikalen und intrakraniellen Arterien mittels quantitativer Magnetresonanzangiografie und Duplex-Sonografie (Bocaccia) – eine prospektive Beobachtungsstudie

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Key words
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ABSTRACT

Purpose Cerebral blood flow volume is an important factor for the accurate diagnosis of neurovascular diseases and treatment indication. This study aims to assess correlations of blood flow volume measurements in cervical and intracranial arteries between duplex sonography and quantitative magnetic resonance angiography (qMRA).

Materials and Methods Consecutive patients with suspicion of cerebral vascular pathology underwent qMRA and duplex sonography of cervical and intracranial arteries with measurement of blood flow volume in bilateral common (CCA), internal (ICA) and external carotid arteries, vertebral and basilar arteries, middle, anterior, posterior cerebral and posterior communicating arteries using 2 different ultrasound machines. Ten patients underwent all examinations twice. Correlations between blood flow volume measurements were evaluated using Spearman's correlation coefficient and inter-class correlation coefficient (ICC).

Results In total, 21 subjects (15 males, mean age: 56.3 ± 6.2 years) were included in the study. Duplex sonography inter-investigator correlation was excellent (ICC = 0.972, $p < 0.0001$) as well as intra-investigator correlations of both qMRA and duplex sonography (ICC > 0.990, $p < 0.0001$). Mostly high correlations were recorded between qMRA and duplex sonography in particular cervical arteries but only low to moderate correlations were obtained for intracranial arteries. The mean differences between blood flow volume measurements were 10.9 ± 8.1 % in the CCA and its branches when using qMRA and 15.0 ± 11.9 % when using duplex sonography, 13.5 ± 11.8 %/35.4 ± 34.2 % in the ICA siphon and its branches when using qMRA/duplex sonography, and 24.1 ± 19.7 %/ 44.9 ± 44.0 % in both vertebral arteries and the basilar artery when using qMRA/duplex sonography.

Conclusion Duplex sonography as well as qMRA allow for highly reproducible measurement of blood flow volume in cervical and intracranial arteries in routine clinical practice.

ZUSAMMENFASSUNG

Ziel Das zerebrale Blutflussvolumen ist ein wichtiger Parameter für die Diagnosestellung bei neurovaskulären Erkrankungen und die Therapieindikation. Ziel dieser Studie ist es, die Übereinstimmung von Blutflussvolumenmessungen zwischen Duplex-Sonografie und quantitativer Magnetresonanzangiografie (qMRA) in zervikalen und intrakraniellen Arterien zu beurteilen.

Material und Methoden Bei konsekutiven Patienten mit Verdacht auf zerebrale Gefäßpathologie wurden eine qMRA und Duplex-Sonografie der zervikalen und intrakraniellen Arterien mit Blutflussvolumenmessung mit 2 verschiedenen Ultraschallgeräten in der bilateralen A. carotis communis (CCA), A. carotis interna (ICA) und externa, A. vertebralis und A. basilaris und in der A. cerebri media, anterior und posterior und in der A. communicans posterior durchgeführt. Zehn Patienten wurden 2-mal untersucht. Die Übereinstimmungen zwischen den Blutflussvolumenmessungen wurden mittels Spearman-Korrelationskoeffizient und Interklassen-Korrelationskoeffizient (ICC) bewertet.

Ergebnisse Insgesamt wurden 21 Probanden (15 Männer, Durchschnittsalter 56,3 ± 6,2 Jahre) in die Studie eingeschlossen. Die Übereinstimmung zwischen den Untersuchern der Duplex-Sonografie war ausgezeichnet (ICC = 0,972; $p < 0{,}0001$), ebenso die Übereinstimmung zwischen Untersuchern in der qMRA und der Duplex-Sonografie (ICC > 0,990; $p < 0{,}0001$). Meistens wurden hohe Korrelationen zwischen qMRA und Duplex-Sonografie insbesondere für zervikale Arterien festgestellt, jedoch nur geringe bis mäßige Korrelationen für intrakranielle Arterien. Die mittleren Differenzen zwischen den Blutflussvolumenmessungen in der CCA und ihren Ästen betrugen 10,9 ± 8,1 % in der qMRA und 15,0 ± 11,9 % in der Duplex-Sonografie, im ICA-Siphon und seinen Ästen 13,5 ± 11,8 % (qMRA) und 35,4 ± 34,2 % (Duplex) und in beiden A. vertebralis und A. basilaris 24,1 ± 19,7 % (qMRA) und 44,9 ± 44,0 % (Duplex).

Schlussfolgerung Sowohl die Duplex-Sonografie als auch die qMRA erlauben eine gut reproduzierbare Messung des Blutflussvolumens in zervikalen und intrakraniellen Arterien in der klinischen Routinepraxis.

Purpose

Quantification of blood flow to the brain is useful for distinguishing patients at risk for cerebral ischemia caused by hemodynamic compromise [1]. Measurement of blood flow volume in cervical and cerebral arteries might be important not only for the accurate diagnosis of neurovascular diseases, but also for the refinement of indication criteria for invasive treatment [1–3].

Quantitative magnetic resonance angiography (qMRA) and duplex sonography (DS), including duplex sonography of cervical arteries (DSCA) and transcranial color-coded sonography (TCCS), are noninvasive diagnostic methods which may be used for the measurement of blood flow in cervical and intracranial arteries [4–8].

qMRA is a relatively new technique that uses traditional time-of-flight and phase-contrast magnetic resonance imaging to visualize extracranial and intracranial vascular anatomy and to measure volumetric blood flow [6, 8]. A recent study established a range of normal blood flow rates for individual blood vessels and for regional cerebral blood flow in healthy adult volunteers [8]. They also used qMRA blood flow volume assessment in various clinical conditions in order to stratify stroke risk in symptomatic vertebrobasilar disease [1–3], to evaluate vertebrobasilar flow in patients with subclavian steal syndrome [9], to screen for intracranial in-stent stenosis [10], to assess blood flow after extracranial artery Wingspan stent placement [11], to evaluate leptomeningeal collateral blood flow in large vessel cerebrovascular disease [12], and to quantify shunt reduction in transarterial embolization of vein of Galen malformations [13].

Duplex ultrasound investigations of extracranial and intracranial vessels make it possible to obtain both hemodynamic data using Doppler mode, including blood flow velocities and calculated pulsatility indices, and morphological data using B-mode imaging [4, 5, 7]. The blood flow volume may then be quantified using various approaches. Duplex ultrasound systems are able to calculate blood flow volume as a product of the mean flow velocity and cross-sectional vessel area. Conventionally, the time-averaged mean velocity is used, which is an intensity-weighted mean velocity integrated over time, obtained with a sample volume that covers the entire vessel diameter. The cross-sectional area of the vessel is usually calculated from a static vessel diameter measured from a B-mode image at the Doppler sample volume location, which assumes a circular vessel configuration [5]. Alternatively, other methods could be used, including a quantitative blood flow meter, which integrates Doppler and A-mode information, and color M-mode approach with simultaneous determination of local flow velocities with a time-domain-based color duplex system and functional vessel diameter [4, 7, 14].

Duplex sonography (DSCA and TCCS) and qMRA may be used not only for the measurement of cerebral blood flow volume but also for the measurement of blood flow volume in particular cervical or intracranial arteries [7, 8, 15]. Thus, we hypothesize that blood flow measurements in particular extracranial and intracranial arteries measured using qMRA and DS will correlate significantly.

The primary aim of this study was to assess the correlation of blood flow volume measurements in cervical and intracranial arteries between qMRA and DSCA/TCCS in routine clinical practice. The secondary aim was to assess the inter-investigator and intra-investigator correlations of both qMRA and DSCA/TCCS in blood flow volume measurements.

Materials and Methods

Patients

Consecutive patients referred for qMRA or DSCA/TCCS due to suspicion of cervical or intracranial vascular pathology were included in the prospective observational study over a period of 2 months (August-September 2018).

The inclusion criteria were: 1) age 25–70 years; 2) indication for qMRA or DS due to suspicion of cervical or intracranial vascular pathology; 3) signed informed consent.

The exclusion criteria were: 1) pacemaker or claustrophobia as contraindication for magnetic resonance imaging; 2) uncontrolled involuntary movements; 3) other condition preventing a patient from quietly maintaining a supine position for prolonged periods of time.

The entire study was conducted in accordance with the Helsinki Declaration of 1975 (as revised in 2004 and 2008). The study was approved by the Ethics Committee of the [České Budějovice] hospital (no. 102/18; on June 22, 2018). All patients provided written informed consent. The study was registered at ClinicalTrials.gov (Identifier: NCT03591523).

Location and timing of blood flow measurement

All patients underwent qMRA, DSCA, and TCCS over the course of 4 h. Both DSCA and TCCS examinations were performed by two experienced sonographers using two ultrasound machines.

The blood flow volume was assessed in the following arterial segments: bilateral common carotid artery (CCA), internal carotid artery in its proximal part distal to the carotid bulb (ICA) and in the distal ICA siphon, external carotid artery (ECA), vertebral artery in the V2 and V4 segments, middle cerebral artery, anterior cerebral artery in pre-communicating and post-communicating segments, posterior cerebral artery, posterior communicating artery, and basilar artery. Total blood flow volume was defined as the sum of the blood flow volumes of the CCA and V2-vertebral arteries on both sides. The cerebral blood flow volume was defined as the sum of the flow volumes of the ICA and vertebral arteries on both sides.

Ten patients underwent qMRA and DSCA/TCCS performed by the same investigators twice in a time interval of 2–10 days. All investigators were blinded to the diagnosis and obtained measurement results using other diagnostic methods.

Quantitative magnetic resonance angiography

The qMRA images were acquired using a 3 T whole-body Philips Ingenia scanner (Philips Medical System, Nederland B.V, Best, The Netherlands). The scanner was equipped with commercially available qMRA software NOVA flow analysis system (Vassol, Chicago, IL, USA). A standard axial three-dimensional time-of-flight MRA of intracranial and cervical arteries was obtained. The acquired images were then transmitted to a workstation in order to reconstruct the 3 D surface-rendered vessel images. After determining the optimal perpendicular scan plane and setting the baseline coordinates, a retrospectively gated, fast 2 D phase-contrast sequence was performed. Velocity encoding was automatically adjusted by the software and validated by a radiologist. Blood flow volumes in each individual arterial segment were calculated and recorded for the database system.

Duplex sonography of cervical arteries and transcranial color-coded duplex sonography

Two ultrasound scanners were used for duplex sonography: Mindray Resona 7 (Mindray, Shenzhen, China) with a 3–9 MHz linear duplex probe (LU9-3U) for DSCA and a 2–5 MHz transcranial duplex probe (SP5-1U) for TCCS, and Toshiba Aplio 500 (Toshiba Medical Systems Corporation, Otawara, Japan) with a 4–12 MHz linear duplex probe (PLT-704SBT) for DSCA and a 2–4 MHz transcranial duplex probe (PST-25BT) for TCCS. In all patients, angle-corrected peak systolic velocity, end-diastolic velocity, mean blood flow velocity, arterial diameter, time-averaged maximum blood flow velocity, intensity-weighted mean frequency, and time-averaged mean velocity were measured in particular arterial segments (► **Fig. 1–4**).

The arterial diameter of the CCA, ICA, ECA, vertebral artery in the V2-segment, and the middle cerebral artery was measured in B-mode (► **Fig. 1, 2**). The arterial diameter of the MCA was measured as a distance between two echogenic lines in the M1-segment of the MCA similarly as in cervical arteries (► **Fig. 3**). The diameter of other intracranial arteries was measured in color power angio mode using the MCA for gain optimization – color had to fill exactly the area between two echogenic lines (► **Fig. 3, 4**).

DS was performed in all patients by two sonographers using two different machines for assessment of inter-investigator reliability.

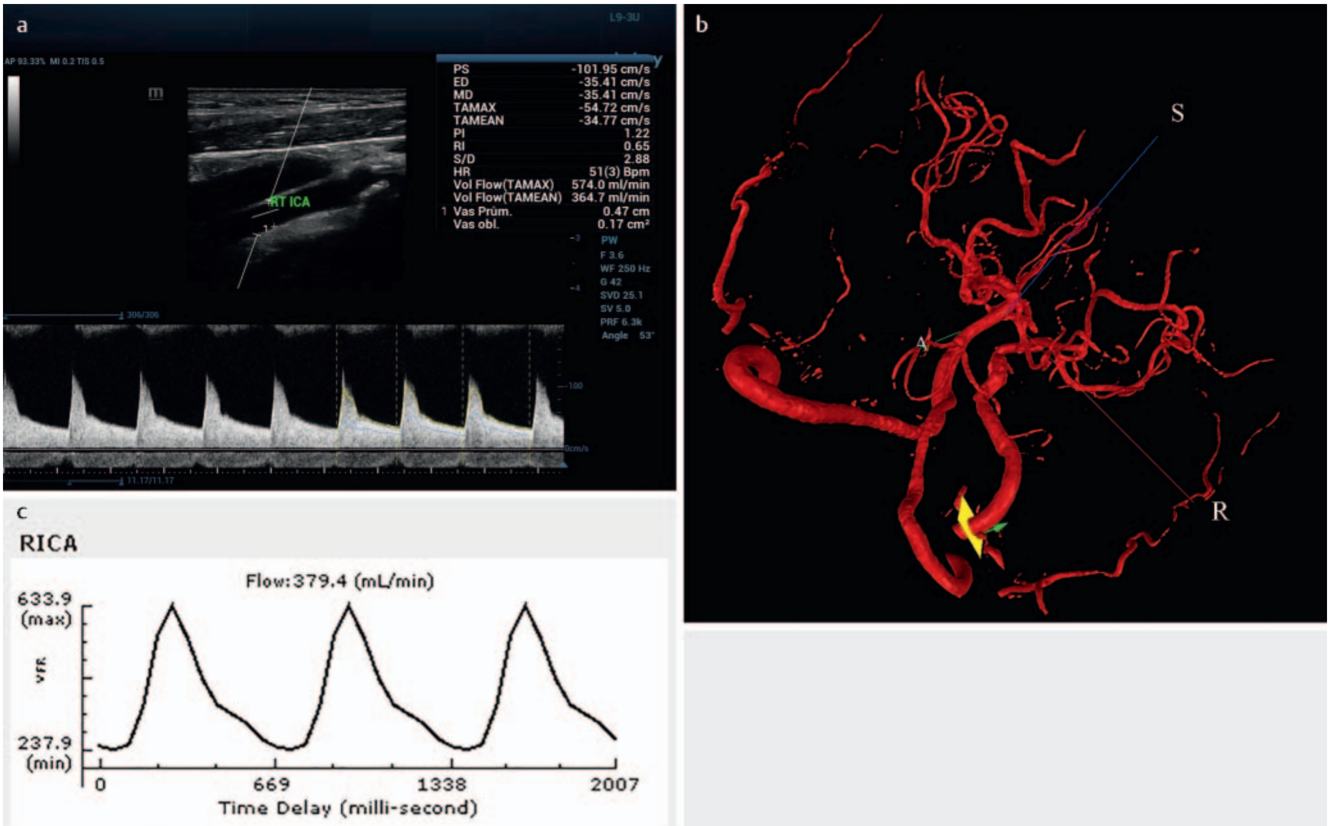
Clinical examination

Neurological and physical examinations were performed in all patients after the informed consent was signed. The following data were collected in all patients: age, gender, weight, height, systolic blood pressure, and diastolic blood pressure. Neurological deficit was assessed using the National Institutes of Health Stroke Scale, while self-sufficiency was determined using the modified Rankin score.

Statistics

An estimate for the minimum sample size needed to reach significant correlation between blood flow measurements in a particular artery measured using qMRA and DS was calculated for correlation $r = 0.30$ and the Spearman correlation coefficient with an alpha level of 5 % and power of 80 %. Pre-study statistical calculations determined that a minimum sample size of 21 patients was required when it was assumed that 5 % of arteries would not be visible due to an insufficient bone window.

The Shapiro-Wilk test was used for normality testing. All data significantly deviated from a normal distribution. Thus, the data are reported as a mean, median, and interquartile range.



► **Fig. 1** Imaging of the proximal part of the internal carotid artery using duplex sonography with measurement of blood flow volume (including measurement of arterial diameter, angle-corrected peak systolic velocity, end-diastolic velocity, mean blood flow velocity, time-averaged maximum blood flow velocity, time-averaged mean velocity maximum and mean and blood flow volume) **a**. Imaging of the same proximal part of the internal carotid artery using quantitative magnetic resonance angiography **b** with measurement of blood flow volume **c**.

The primary goal was to evaluate the correlation of blood flow measurements between qMRA and DS. Secondary goals aimed to evaluate:

1. intra-investigator reliability of blood flow measurement using qMRA performed by the same investigators in two sessions;
2. inter-investigator reliability of blood flow measurement using DS performed by two investigators;
3. intra-investigator reliability of blood flow measurement using DS performed by the same investigator in two sessions;
4. comparison of blood flow measurements in feeding artery and its branches.

The following assumptions about blood flow volume (Q) were tested:

a) $Q_{CCA} = Q_{ICA} + Q_{ECA}$

b) $Q_{ICA\text{-}siphon} = Q_{middle\ cerebral\ artery} + Q_{anterior\ cerebral\ artery} + Q_{posterior\ communicating\ artery}$

c) $Q_{basilar\ artery} = Q_{right\ V4\text{-}vertrbal\ artery} + Q_{left\ V4\text{-}vertebral\ artery}$

Correlations between measurements were evaluated using the Spearman's correlation coefficient. A Spearman's coefficient of 0.0–0.3 was considered to show negligible correlation, 0.3–0.5 low correlation, 0.5–0.7 moderate correlation, 0.7–0.9 high correlation, and 0.9–1.0 very high correlation.

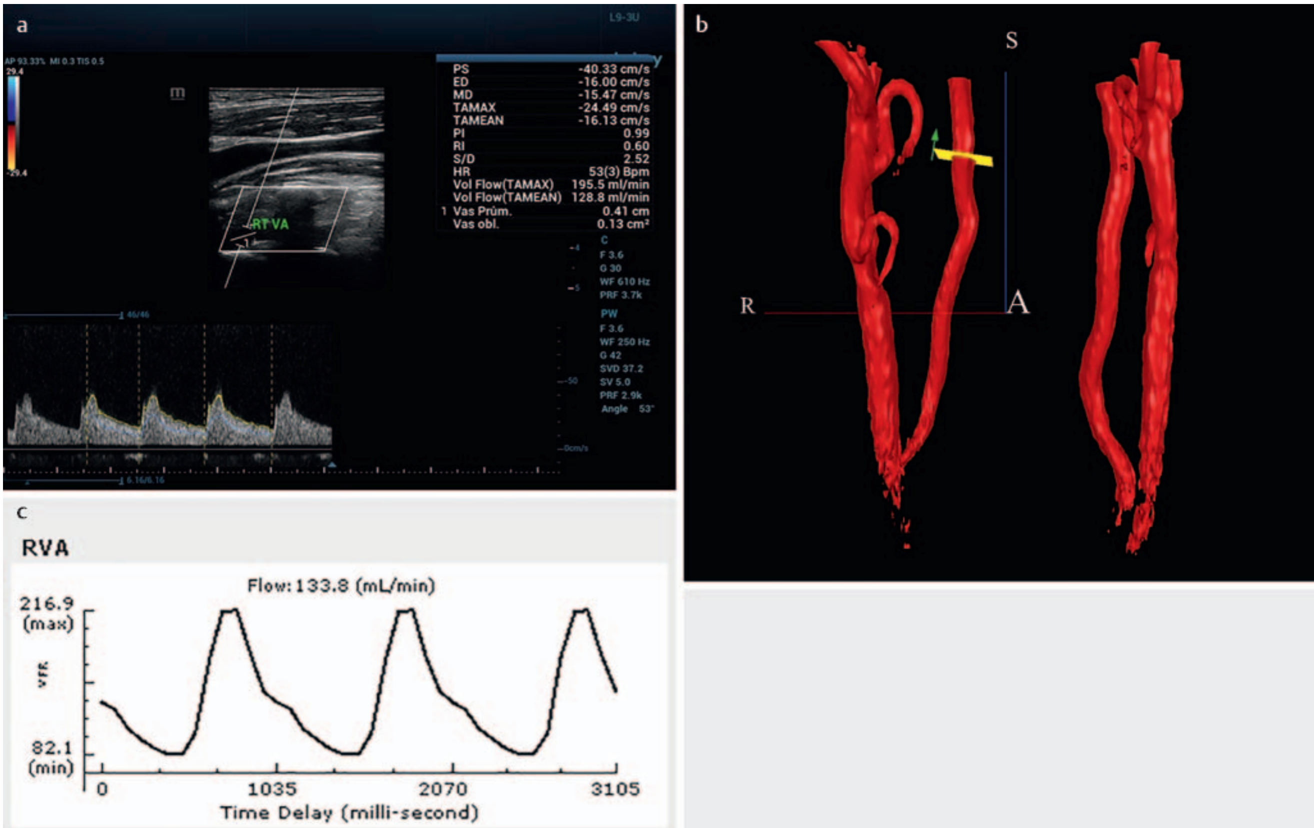
The inter-class correlation coefficient (ICC) was used for the assessment of inter-investigator and intra-investigator reliabilities. ICC 0.00–0.40 was considered to show poor reliability, 0.40–0.59 fair reliability, 0.60–0.74 good reliability, and 0.75–1.00 excellent reliability.

All tests were carried out at a 0.05 α level of significance. Data were analyzed using the SPSS v.22.0 software (IBM, Armonk, NY, USA).

Results

A total of 21 patients (15 males, 6 females, mean age 56.3 ± 6.2 years) were enrolled in the study after the informed consent was signed. The patients' baseline characteristics are shown in ► **Supplementary Table 1** Twelve patients had been diagnosed with arterial pathology of cervical or intracranial artery (three patients with ICA occlusion, two patients with ICA occlusion and intracranial bypass, two patients with ICA stenosis, two patients with arteriovenous malformation, one patient with MCA stenosis, one patient with occlusion of the brachiocephalic trunk with vertebral steal syndrome, and one patient with vertebral artery occlusion) and nine patients had a physiological arterial status.

Measurement results for total cerebral blood flow volume and blood flow volume in particular cervical and intracranial arteries



▶ **Fig. 2** Imaging of the intervertebral (V2) segment of the vertebral artery using duplex sonography with measurement of blood flow volume (including measurement of arterial diameter, angle-corrected peak systolic velocity, end-diastolic velocity, mean blood flow velocity, time-averaged maximum blood flow velocity, time-averaged mean velocity maximum and mean and blood flow volume **a**. Imaging of the same intervertebral (V2) segment of the vertebral artery using quantitative magnetic resonance angiography **b** with measurement of blood flow volume **c**.

using two different duplex machines are presented in ▶ **Table 1**. The inter-investigator reliability between the DS blood flow volume measurements in all examined arteries using two different machines was excellent with ICC = 0.972 (95 % confidential interval, CI = 0.959–0.979, P < 0.0001). The intra-investigator reliabilities of qMRA and DS were similar with ICC = 0.995 (95 % CI = 0.987–0.999, P < 0.0001) for qMRA and ICC = 0.992 (95 % CI = 0.985–0.996, P < 0.0001) for DS.

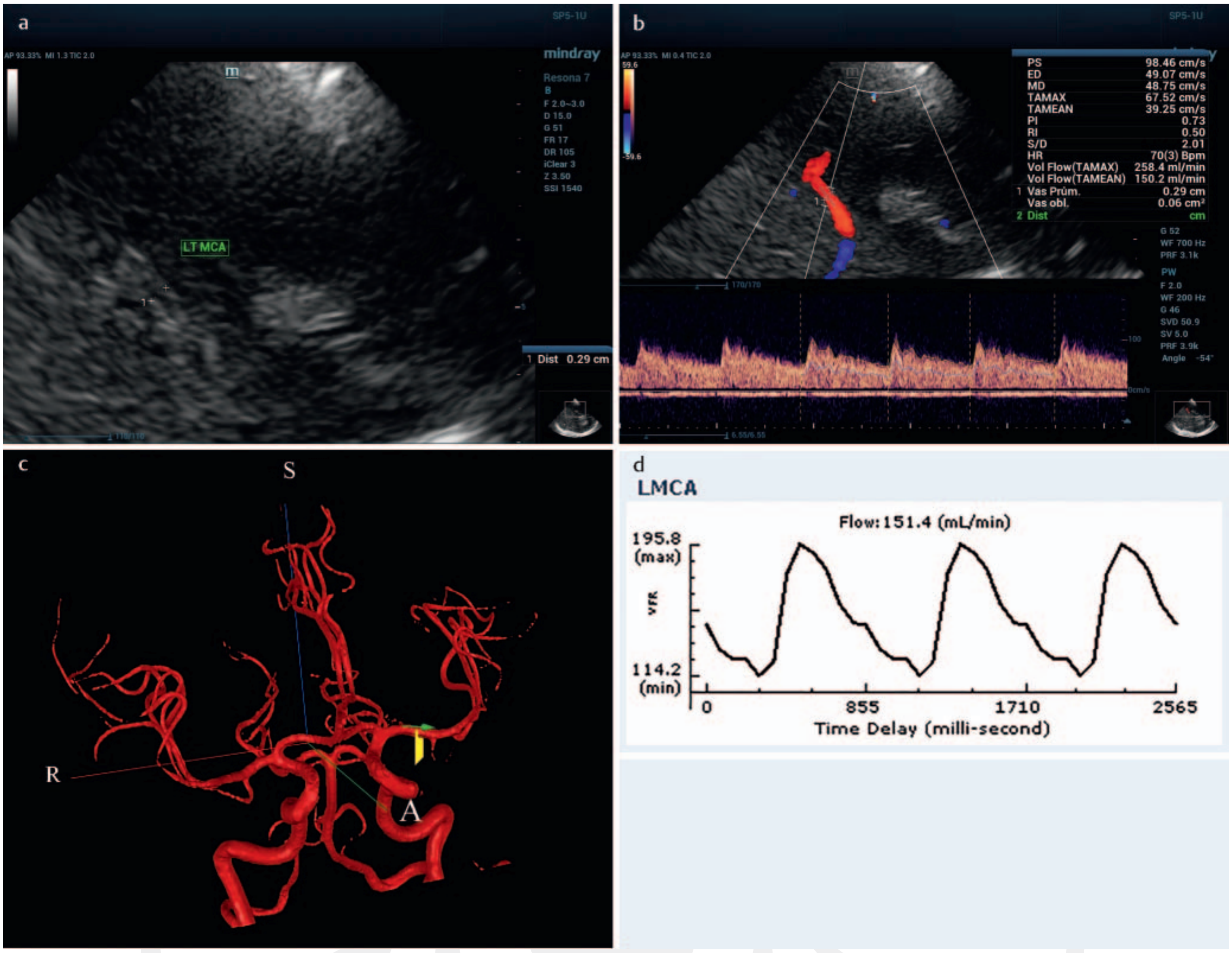
Mostly high correlations were recorded between qMRA and DS measurements of cerebral blood flow volume in particular cervical arteries. The correlations between cerebral blood flow volumes measured using two different ultrasound machines were high or very high. However, the correlations between cerebral blood flow volumes in intracranial arteries measured using qMRA and TCCS or two different ultrasound machines were mostly low to moderate (▶ **Table 2**).

The mean differences between blood flow volume measurements in the CCA and its branches, the ICA and ECA, were only 10.9 ± 8.1 % when using qMRA and 15.0 ± 11.9 % when using DSCA (▶ **Table 3**). More significant differences were achieved when comparing blood flow volume measurements in the ICA siphon and its branches, the middle cerebral artery, the anterior cerebral artery, and the posterior communicating artery (13.5 ± 11.8 % for qMRA and 35.4 ± 34.2 % for TCCS), and in both V4-segments of the vertebral arteries and basilar artery (24.1 ± 19.7 % for qMRA and 44.9 ± 44.0 % for TCCS).

Discussion

The study results showed that both qMRA and duplex sonography, including DSCA and TCCS, were able to measure real blood flow volume in particular cervical and intracranial arteries with overall excellent inter-investigator and intra-investigator reliabilities. The correlations between qMRA and DS cerebral blood flow volume measurements in particular cervical arteries were mostly high. Also, the correlations between cerebral blood flow volumes measured using two different ultrasound machines were high or very high. Nevertheless, the correlations between cerebral blood flow volumes in intracranial arteries measured using qMRA and TCCS or two different ultrasound machines were mostly low to moderate.

Similarly to our results, previously published studies confirmed the high reproducibility of both qMRA and DSCA in cerebral blood flow volume measurements with low intra-observer variability [15–19]. Both methods are able to measure blood flow volume also in the CCA, ICA, and vertebral artery with high reliability, although they still remain dependent on examiner skill and experience, especially for DS [17, 20].



► **Fig. 3** Imaging of the middle cerebral artery in B-mode with measurement of the arterial diameter **a** and subsequent measurement of cerebral blood flow (including measurement of arterial diameter in color power angio mode and measurements of angle-corrected peak systolic velocity, end-diastolic velocity, mean blood flow velocity, time-averaged maximum blood flow velocity, time-averaged mean velocity maximum and mean and blood flow volume) in this arterial segment **b**. Imaging of the same middle cerebral artery using quantitative magnetic resonance angiography **c** with measurement of blood flow volume **d**.

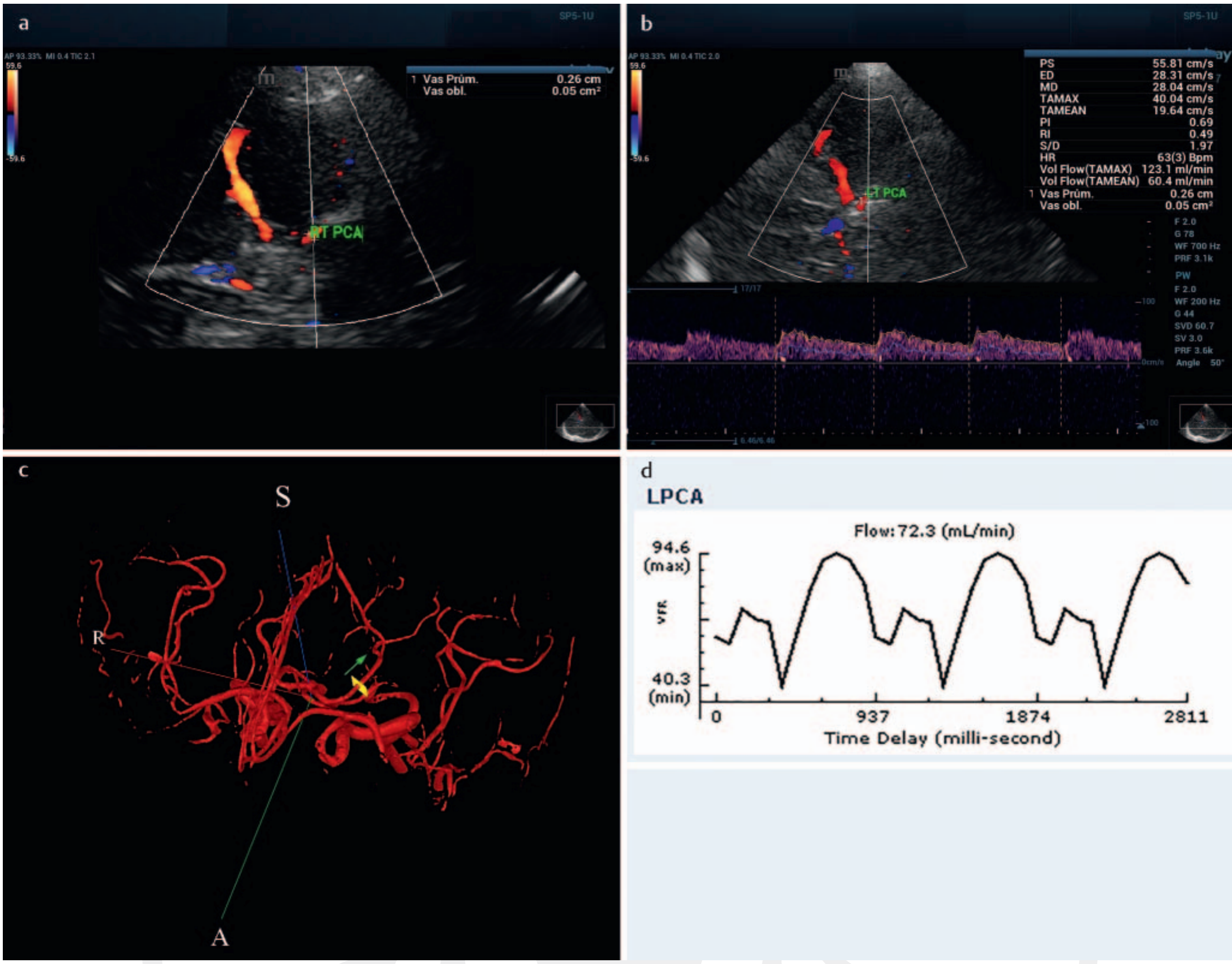
Various methods, including the electromagnetic flowmeter, nitrous oxide[133], xenon (Xe)-single-photon emission CT, Xe-CT, perfusion CT, positron-emission tomography, magnetic resonance, and duplex sonography, have been used to measure regional cerebral blood flow [4–8, 15, 21]. Compared to other methods, the main advantage of magnetic resonance imaging and DS is their noninvasiveness [4–8]. This is a precondition for their common clinical use.

Correlations between the measurement of blood flow volume in particular cervical arteries for qMRA and DSCA were mostly high in our study. Previously published studies with qMRA and DSCA mainly compared cerebral blood flow volume measurements. The level of cerebral blood flow volume (474 to 748 mL/min) found in adults is comparable to our measurements (745.5 and 588.8 mL/min for DS and 695.5 mL/min for qMRA) [8, 15–18, 20, 22, 23]. The broader range of measured values in our study might be due to the inclusion of patients with various vascular pathologies.

Cerebral blood flow is age-related from childhood to adulthood. A slight increase was shown from 3 to 6 years of age and a subsequent decline from 7 to 18 years of age, after which cerebral blood flow volume appeared to remain relatively constant up to the age of 60 years, with a mean decrease of 3.0–4.8 mL/min per year from 60 to 85 years of age [21, 23–25]. The majority of published studies identified no sex differences in global cerebral blood flow [16, 17, 25].

In contrast to Doppler sonography, the flow velocity determined using qMRA is not subject to nonuniformity problems. Thus, blood flow volume measurements might be more precise with qMRA [14]. An older phantom simulation study performed by Ho et al. showed a poor correlation between blood flow volume measured with spectral Doppler imaging and phase-contrast magnetic resonance imaging [24].

There are also other conflicting results in the literature concerning the accuracy of cerebral blood flow measurements with duplex sonography [14, 18, 20, 26, 27]. The errors in volume



▶ **Fig. 4** Imaging of the posterior cerebral artery in color power angio mode with arterial diameter measurement after optimizing the color power angio gain **a** and subsequent measurement of cerebral blood flow (measurements of angle-corrected peak systolic velocity, end-diastolic velocity, mean blood flow velocity, time-averaged maximum blood flow velocity, time-averaged mean velocity maximum and mean and blood flow volume) in the post-communicating P1-segment of the posterior cerebral artery **b**. Imaging of the same post-communicating P1-segment of the posterior cerebral artery using quantitative magnetic resonance angiography **c** with measurement of blood flow volume **d**.

flow measurement when using sonographic techniques arise from inaccurate estimation of blood velocity and diameter measurement by off-axis sampling, tortuous vessels, turbulent or nonaxial flow, artifactual color signals, poor color setting, variations of vessel diameter during cardiac cycle, and respiratory vessel movement [7, 18]. On the basis of duplex sonography blood flow volume measurement equation, any minor error in vessel diameter measurements may dramatically alter the estimated flow volume. Improvement of B-mode imaging quality or the use of a radiofrequency echo-tracking system for arterial diameter measurements can reduce this potential error [28, 29].

Only negligible differences between measurements of blood flow volume in the CCA and its branches, the ICA and the ECA, using both qMRA and DS confirmed that both methods were able to measure real blood flow volumes in cervical arteries in routine clinical practice.

We measured blood flow volume in two different segments of the ICAs and of the vertebral arteries, one extracranial and one intracranial. The differences between the measured values shown in ▶ **Table 2** are not only due to branching between measured segments (ophthalmic artery and posterior inferior cerebellar artery) but also due to vascular pathologies present in some patients and measuring errors, especially for intracranial arteries. Contrary to the cervical arteries, correlations between blood flow volume measurements in intracranial arteries were low or moderate. The differences between blood flow volume measurements in the ICA siphon and its branches, the middle cerebral artery, the anterior cerebral artery, and the posterior communicating artery, both distal vertebral arteries and the basilar artery were greater than the differences between blood flow volume measurements in the CCA and its ICA and ECA branches.

Smaller examined artery diameter, short arterial segments without branches, and more frequent arterial flexions in intracranial arteries are all causes of greater error in DS and qMRA blood flow volume measurements in intracranial arteries compared to cervical arteries. Other reasons for measurement errors when

▶ **Table 1** Results of blood flow measurement.

blood flow in:	qMRA	DS1	DS2
TBF volume; mean, median (IQR), mL/min	1219.5, 1080.0 (952.0–1165.0)	1270.0, 1121.3 (1048.9–1245.0)	1205.8, 1097.5 (886.2–1192.6)
CBF volume; mean, median (IQR), mL/min	718.4, 695.5 (554.5–810.5)	772.3, 745.5 (629.3–947.8)	657.9, 588.8 (501.7–688.6)
common carotid artery; mean, median (IQR), mL/min	476.4, 445.0 (365.3–514.3)	515.6, 479.2 (337.9–579.4)	505.9, 471.9 (349.4–545.4)
internal carotid artery; mean, median (IQR), mL/min	218.3, 233.0 (191.8–278.8)	268.7, 277.4 (173.9–357.3)	239.5, 211.8 (149.7–341.2)
external carotid artery; mean, median (IQR), mL/min	309.0, 217.0 (181.0–258.8)	235.0, 185.6 (150.5–266.5)	224.9, 204.2 (156.2–252.7)
V2-segment of the vertebral artery; mean, median (IQR), mL/min	138.8, 109.0 (84.3–172.5)	118.2, 110.7 (69.0–161.1)	104.1, 100.3 (48.9–135.5)
siphon of the internal carotid artery; mean, median (IQR), mL/min	242.6, 256.0 (214.5–302)	216.1, 194.0 (163.6–247.5)	222.5, 197.6 (169.6–285.8)
middle cerebral artery; mean, median (IQR), mL/min	143.8, 144.0 (123.0–158.5)	236.6, 222.4 (197.8–271.1)	235.6, 222.4 (191.1–257.7)
A1-segment of the anterior cerebral artery; mean, median (IQR), mL/min	90.9, 92.0 (76.5–118.2)	82.9, 82.8 (66.9–97.3)	65.8, 73.2 (54.9–84.0)
A2-segment of the anterior cerebral artery; mean, median (IQR), mL/min	69.5, 69.0 (56.5–82.5)	66.7, 72.7 (46.6–77.8)	MNP
posterior cerebral artery; mean, median (IQR), mL/min	90.8, 72.0 (64.0–86.3)	59.3, 53.7 (46.2–67.1)	49.9, 44.0 (36.8–54.7)
posterior communicating artery; mean, median (IQR), mL/min	56.5, 56.0 (37.5–84.0)	38.9, 31.2 (25.2–49.2)	MNP
V4-segment of the vertebral artery; mean, median (IQR), mL/min	122.3, 109.0 (73.0–162.0)	69.3, 70.7 (51.1–83.3)	68.3, 68.9 (50.2–87.4)
basilar artery; mean, median (IQR), mL/min	202.8, 163.5 (139.3–197.8)	147.1, 105.9 (88.2–116.7)	150.6, 102.5 (83.0–129.7)

CBF – cerebral blood flow; DS1 – duplex sonography – examiner 1; DS2 – duplex sonography – examiner 2; IQR – interquartile range; MNP – measurement not performed; qMRA – quantitative magnetic resonance angiography; TBF – total blood flow.

using TCCS include lower quality B-mode images due to the use of a probe with lower ultrasound frequencies (2–4 MHz) and use of the color mode or power color angio mode instead of B-mode for the measurement of arterial diameter in the majority of intracranial arteries.

This study has several limitations. First, a limited number of patients were enrolled in the study. Second, the second qMRA and DS examinations for the evaluation of intra-investigator correlations were performed in only ten patients. Third, patients with both abnormal and normal vascular findings in cervical and intracranial brain arteries were enrolled to demonstrate the usefulness of both methods in real clinical practice. Fourth, limitations and strengths of qMRA and DS may differ between particular vessels and vascular pathologies. The low number of included patients and limited number and types of vascular pathologies did not allow testing of the limitations of both methods in particular arteries. This has to be studied in future studies. Fifth, the measurement of the diameter of intracranial arteries in our study is unique and this method has to be validated by other researchers. Sixth, there is no reference standard for the comparison of our results. Seventh, the influence of sample volume settings on blood flow volume measurement was not tested. One may hypothesize that a larger or smaller or slightly incorrectly set sample volume could influence the value of measured average intensity. Finally, the low number of patients with particular pathologies did not allow evaluation and comparison of changes and the clinical relevance of blood flow volume measurement in particular arteries. Further studies are needed to assess the clinical relevance of these measurements.

Conclusion

The results of the presented study demonstrated that both qMRA and DS were able to measure real blood flow volume predominantly in cervical arteries with excellent inter-investigator and intra-investigator reliabilities, and mostly high correlations between qMRA and DS in particular cervical arteries. However, in

▶ **Table 2** Correlation between blood flow measured using quantitative magnetic resonance angiography and duplex sonography.

	qMRA vs. DS1	qMRA vs. DS2	DS1 vs. DS2
total	0.568*	0.639*	0.786*
common carotid artery	0.758*	0.743*	0.803*
internal carotid artery	0.754*	0.747*	0.862*
external carotid artery	0.756*	0.597*	0.818*
V2-segment of the vertebral artery	0.786*	0.780*	0.940*
siphon of the internal carotid artery	0.428§	0.426§	0.651*
middle cerebral artery	0.540*	0.318§	0.588*
A1-segment of the anterior cerebral artery	0.636*	0.504*	0.417§
A2-segment of the anterior cerebral artery	0.517	NA	NA
posterior cerebral artery	0.403§	0.276§	0.357§
posterior communicating artery	0.685*	NA	NA
V4-segment of the vertebral artery	0.591*	0.777*	0.559*
basilar artery	0.464§	0.547§	0.649*
all arteries	0.815*	0.803*	0.930*

* – $p < 0.01$; § – $p < 0.05$; DS1 – duplex sonography – examiner 1; DS2 – duplex sonography – examiner 2; IQR – interquartile range; NA – not available due to less than 10 measurements; qMRA – quantitative magnetic resonance angiography; total = sum of blood flow in both common carotid arteries and both vertebral arteries (V2-segment).

▶ **Table 3** Blood flow measurement in different arterial segments using quantitative magnetic resonance angiography and duplex sonography.

	qMRA	DS
blood flow in the common carotid artery; mean, median (IQR), mL/min	512.4, 395.0 (343.8–505.3)	534.7, 504.4 (373.6–610.9)
sum of blood flow in ICA+ECA; mean, median (IQR), mL/min	503.3, 437.0 (283.0–510.3)	520.7, 502.2 (366.5–611.8)
difference in mL/min; mean±SD	53.2 ± 46.8	79.3 ± 76.2
difference in %; mean±SD	10.9 ± 8.1	15.0 ± 11.9
blood flow of the ICA siphon; mean, median (IQR), mL/min	257.1, 264.0 (193.5–318.5)	251.2, 224.3 (187.2–272.6)
sum of blood flow in MCA+ACA+PComA; mean, median (IQR), mL/min	280.9, 267.5 (228.5–340.5)	354.9, 348.1 (309.6–389.0)
difference in mL/min; mean±SD	38.0 ± 41.6	125.7 ± 65.4
difference in %; mean±SD	13.5 ± 11.8	35.4 ± 34.2
sum of blood blow in both V4-segments of the vertebral arteries; mean, median (IQR), mL/min	238.7, 200.0 (173.5–237.5)	148.2, 150.2 (117.8–171.5)
blood flow in the basilar artery; mean, median (IQR), mL/min	202.8, 163.5 (139.3–197.8)	107.1, 102.4 (86.0–109.5)
difference in mL/min; mean±SD	36.7 ± 23.6	43.1 ± 31.3
difference in %; mean±SD	24.1 ± 19.7	44.9 ± 44.0

DS – duplex sonography; IQR – interquartile range; qMRA – quantitative magnetic resonance angiography; SD – standard deviation; ICA – internal carotid artery; ECA – external carotid artery; MCA – middle cerebral artery; ACA – anterior cerebral artery; PComA – posterior communicating artery.

intracranial arteries, mostly low to moderate correlations were detected between qMRA and TCCS or two different ultrasound machines. A potential bias in measured blood flow volume in particular intracranial arteries is much higher than in cervical arteries, especially for TCCS.

Conflict of Interest

The authors declare that they have no conflict of interest.

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