ON-LINE APPENDIX

Methods: Visual Collateral Scoring

MRA images were coregistered (red-green shift overlay of vessel) and presented as maximum intensity projections (20-mm slab thickness, 1-mm increment). Illustrations of visual scores of TOF- and CE-MRA are shown in On-line Fig 1.

Methods: Automated Atlas-Based Collateral Quantification

A continuous automated imaging parameter was established to measure CVA. The relative signal intensity of MCA vasculature in the ischemic hemisphere was compared with that in the normal contralateral hemisphere. The signal intensity of all MCA vascular voxels in each hemisphere distal to the M1-MCA segment was measured by using a statistical cerebroarterial atlas derived from 700 normal MRA datasets (On-line Fig 2).[1] In brief, TOF- and CE-MRA images of each subject were registered to the arterial atlas (0.5-mm, isotropic, Montreal Neurological Institute-152 space) by affine 3D-transformation with 12 *df* by using a N3-intensity-normalized mean TOF reference image in atlas space (Analyze 11.0; AnalyzeDirect). The inverse transformation matrix was applied to the arterial atlas for transformation into the native space of each TOF- and CE-MRA dataset.

For calculation of CVA per hemisphere in MRA images, the total mean vascular intensity was sampled by using the intensities of each voxel *xyz* weighted by the empiric atlas-based probability of belonging to MCA vasculature P_{xyz} (MCA) (voxels with <5% vessel probability were excluded).

$$1)\quad CVA = \Sigma_{xyz}\, MRA\text{-}Intensity_{xyz} \times P_{xyz}\,(\mathrm{MCA}); \qquad 0.05 \le P_{xyz}\,(\mathrm{MCA}) \le 1.$$

The collateral index for each MRA technique was defined as the ratio of the MCA branch vessel intensities in the ischemic hemisphere compared with the normal hemisphere:

$$2)\quad CI = \frac{CVA_{\text{ischemic hemisphere}}}{CVA_{\text{normal hemisphere}}};\ 0 \le CI \le 1.$$

Methods: Definition and Measurement of Tissue-Outcome End Points

Final infarct volume was segmented section by section in follow-up imaging (targeted at 48-hour onset to imaging). For PPS, the total ischemic tissue in Tmax MR-perfusion maps and infarct core in DWI was segmented (On-line Fig 3). Tissue-at-risk to infarct was classified by Tmax bolus delay (VOL_{Tmax}). Lesion masks of tissue-at-risk (VOL_{Tmax}), initial infarct core (VOL_{DWI}), and final infarct volume were registered to calculate the percentage of penumbra saved.

Assessment of reperfused penumbra (PPS) was based on previously established viability thresholds. The definition of penumbra, tissue-at-risk to infarction, is linked to 2 outcome scenarios: salvage in case of reperfusion and infarction in case of lack of reperfusion. The brain tissue "at risk" defined by the optimal threshold Tmax > 6 seconds is thus the best representation of the real penumbra that is technically achievable on the basis of prior established viability thresholds.[2-6]

By definition, all segmented voxels with Tmax > 6 seconds and normal DWI (ADC) amount to the volume of "infarction if not reperfused" (= penumbra). By comparing each voxel-at-risk (Tmax > 6 seconds) with its final state (infarct yes or no), we identified voxels that reperfused (= penumbra saved).

Methods: Atlas-Based Collateral Index of Contrasted MCA Vessels in CE-MRA in Comparison with Visual DSA Collateral Rating

A subanalysis of patients who underwent DSA for intra-arterial treatment is provided to correlate the atlas-based CE-MRA collateral index (ratio between the signal of MCA vasculature of the ischemic side to the normal side as a representation of collateral supply; range, 0–1) with the DSA collateral rating (score = 0–3).

DSA collateral supply was rated according to leptomeningeal filling of MCA vasculature distal to the occlusion in anteroposterior and lateral projections. A 4-point score was used (0 = absent collaterals in >50% of the MCA territory; 1 = diminished collaterals in >50% of the MCA territory; 2 = diminished collaterals in <50% of the MCA territory; 3 = complete filling of the MCA territory).

The Spearman rank correlation coefficient was calculated. Furthermore, the discriminative power for good tissue outcome (FIV < 90 mL) was compared by ROC AUC analysis.

Results: Atlas-Based Collateral Index of Contrasted MCA Vessels in CE-MRA in Comparison with Visual DSA Collateral Rating

Twenty-nine intra-arterially treated patients underwent DSA. The mean DSA collateral score was 2.10 ± 0.61. The mean $CI_{CE\text{-}MRA}$ in patients with DSA was 0.66 ± 0.20. Both collateral measures were significantly correlated (Spearman $\rho = 0.83$, $P < .003$). After ROC analysis, the discriminative power of $CI_{CE\text{-}MRA}$ and DSA for good outcome of FIV < 90 mL was significant (DSA: AUC = 0.93; $CI_{CE\text{-}MRA}$: AUC = 0.89, $P < .01$). After pair-wise comparison of ROC AUC, there was no significant difference between DSA and $CI_{CE\text{-}MRA}$ (difference between areas, 0.04 ± 0.02, $P = .6$).

Methods: Odds Ratio for Good Outcome between Good and Poor Collateral Status

Successful recanalization was classified by DSA (TICI grade 2b, 3) in intra-arterially treated patients. In IV-treated patients, recanalization status was assessed by either follow-up imaging (MRA if available) or transcranial Doppler. Complete recanalization in transcranial Doppler was diagnosed if low-resistance stenotic or normal signal was found throughout the MCA stem (carotid bifurcation to M2 branches) with no other signs of persisting distal occlusion.[7] Patients were dichotomized into good and poor collateral status on the basis of the determined optimal cutoff value of $CI_{CE\text{-}MRA}$ for good outcome (FIV < 90 mL) in Table 3. The odds ratio for good outcome between patients with recanalization with good-versus-poor $CI_{CE\text{-}MRA}$ collateral status was calculated.

Results: Odds Ratio for Good Outcome between Good and Poor Collateral Status

Successful recanalization was diagnosed in 32 of 44 patients (25 in 29 intra-arterially treated patients versus 7 in 15 IV-treated patients). The recanalization rate in intra-arterially versus IV-treated patients was significantly higher (86% versus 47%, $P <$

.001). Good collateral status was diagnosed in 28 of 44 patients on the basis of the determined optimal collateral cutoff value of $CI_{CE\text{-}MRA}$ for good outcome defined by FIV $<$ 90 mL (Table 3).

Of 32 successful recanalizers, 21 had good collateral status, and 11, poor collateral status. Of 21 recanalizers with good collateral status, 19 had good outcome and 2 had poor outcome. Of 11 recanalizers with poor collateral status, 6 had good outcome and 5 had poor outcome. The positive odds ratio for good outcome between recanalizers with good collateral status and those with poor collateral status was 7.9 ($P < .05$).

Of 12 nonrecanalizers, 7 had good collateral status and 5 had poor collateral status. Of 7 nonrecanalizers with good collateral status, 4 had good outcome and 3 had poor outcome. Of 5 nonrecanalizers with poor collateral status, zero had good outcome and 5 had poor outcome. The odds ratio for good outcome between nonrecanalizers with good collateral status versus nonrecanalizers with poor collateral status was not significant (14.1, $P = .11$).

Results: Visual Collateral Scores

The visual collateral score is shown in On-line Fig 4.

REFERENCES

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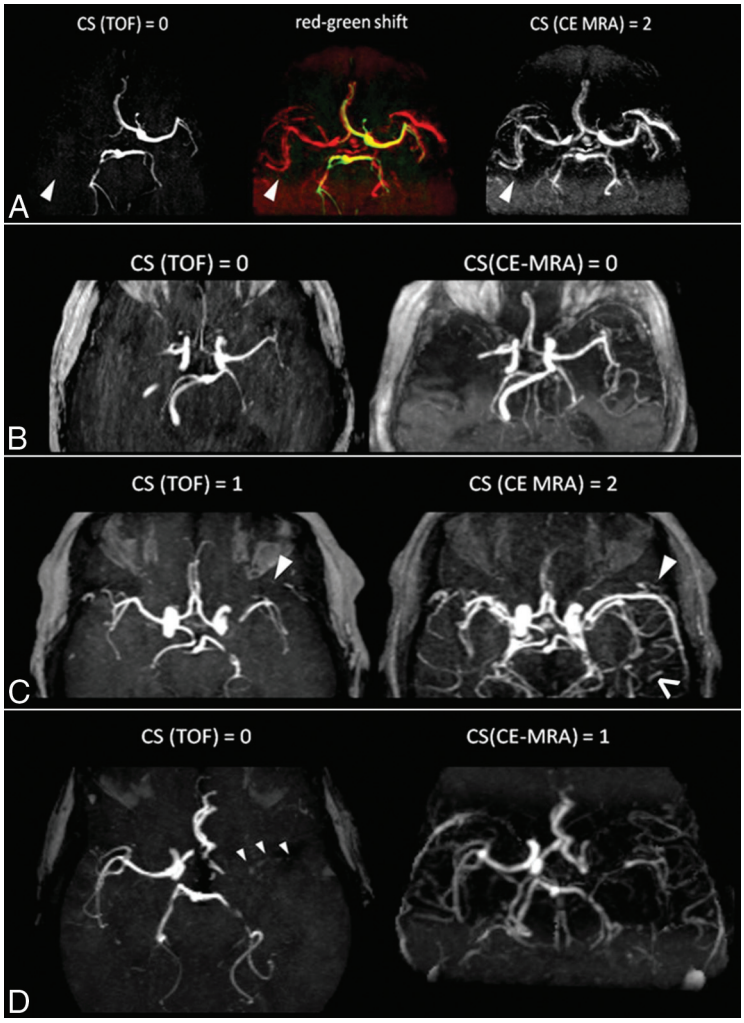
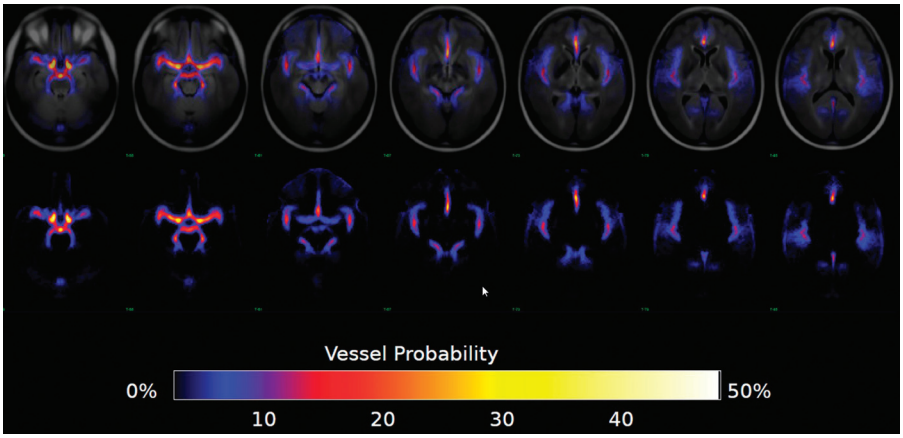
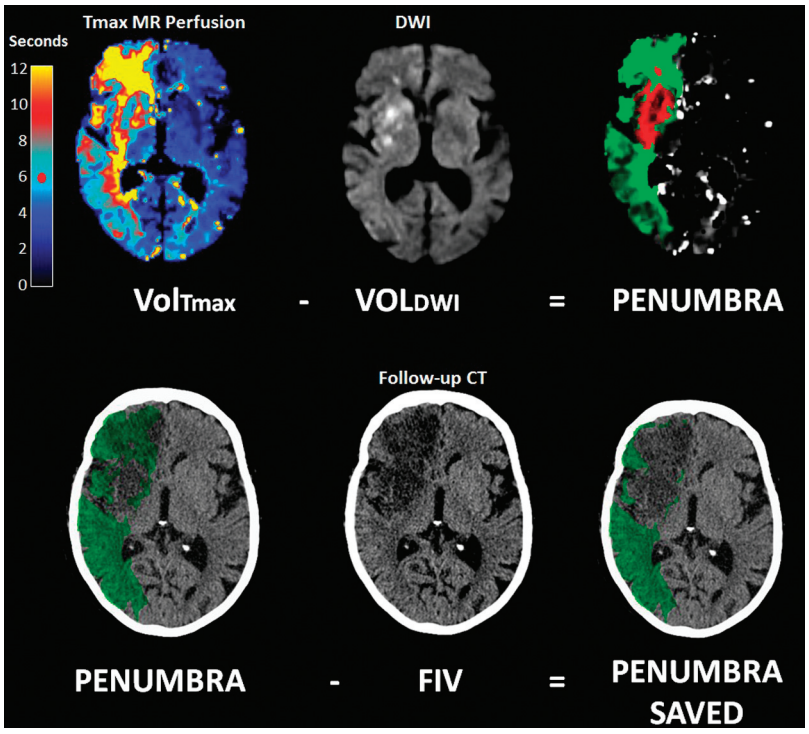
7. Burgin WS, Malkoff M, Felberg RA, et al. **Transcranial Doppler ultrasound criteria for recanalization after thrombolysis for middle cerebral artery stroke.** *Stroke* 2000;31:1128–32



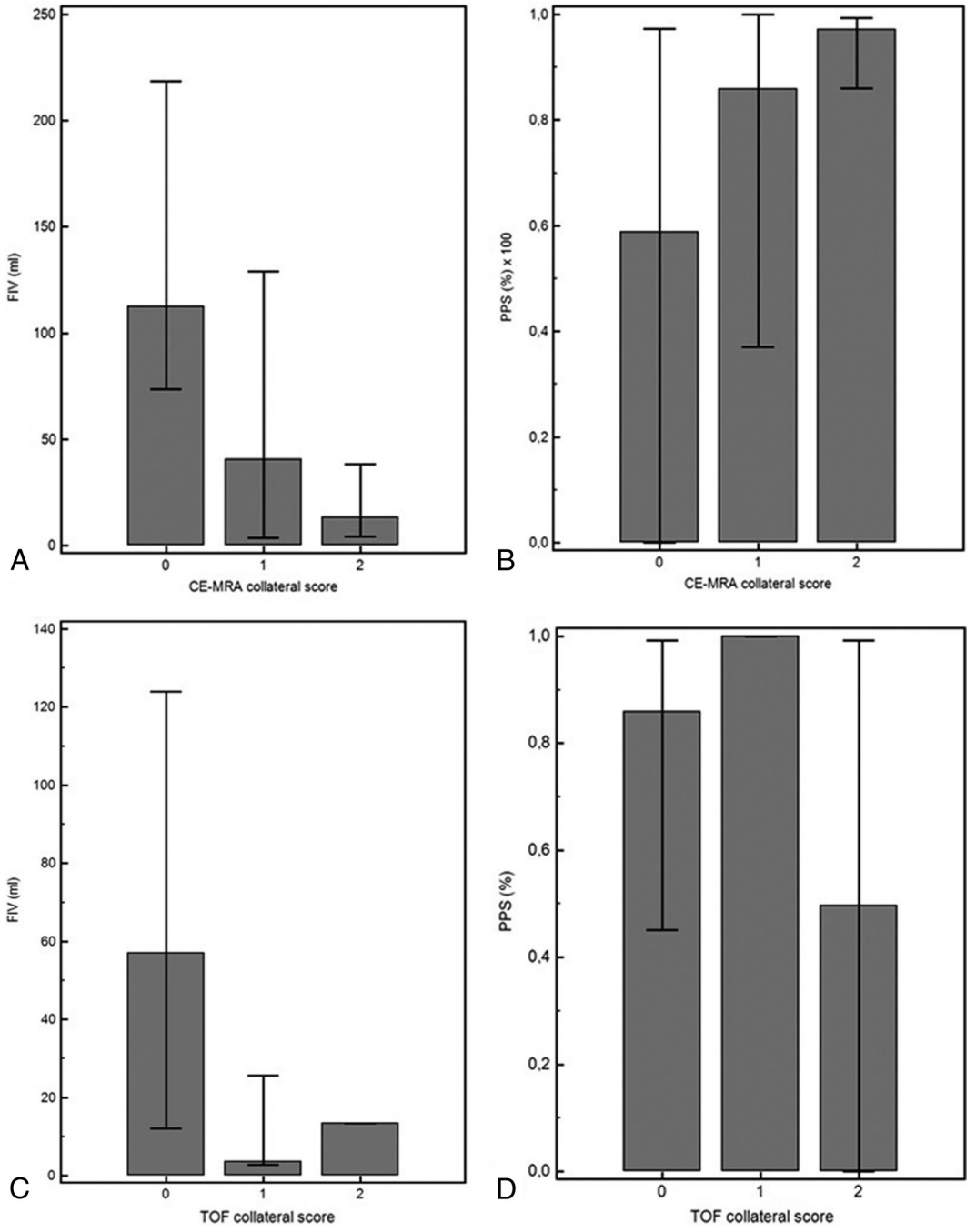
ON-LINE FIG 1. Visual collateral assessment in TOF- and CE-MRA. *A*, No collateralized vessel is seen distal to the right ICA occlusion in TOF-MRA, rated as $CS_{TOF} = 0$. Abundant collateralized MCA branches are seen in CE-MRA (*arrows*), rated as $CS_{CE\text{-}MRA} = 2$. The combined score is $CS_{combined} = 0 + 2 = 2$. The red-green shift shows voxelwise registration of TOF- and CE-MRA vessels. *B*, No collateralized MCA branches are seen in TOF- and CE-MRA distal to the right MCA. Visual scores: $CS_{TOF} = 0$; $CS_{CE\text{-}MRA} = 0$; $CS_{combined} = 0 + 0 = 0$. *C*, Abundant collateralized MCA branches are seen in TOF- and CE-MRA distal to the left MCA occlusion relative to the normal side (*open arrow*). Large veins and sinus were excluded in visual scoring to avoid venous contamination (eg, sphenoparietal sinus shown by *closed arrow*). Visual scores: $CS_{TOF} = 1$; $CS_{CE\text{-}MRA} = 2$; $CS_{combined} = 1 + 2 = 3$. *D*, MCA branches in TOF-MRA were rated nonexistent relative to the normal right side ($CS_{TOF} = 0$), even though a subtle flow signal is seen in the distal M1 segment (*small arrows*). The atlas-based automated collateral index (range, 0–1) is a continuous imaging parameter that resolves these subtle signal intensities along MCA branches ($CI_{TOF} = 0.025$) compared with the visual 3-point grading score. Visual scores: $CS_{TOF} = 0$; $CS_{CE\text{-}MRA} = 1$; $CS_{combined} = 0 + 1 = 1$.



ON-LINE FIG 2. Probabilistic cerebroarterial atlas in Montreal Neurological Space-152 showing voxelwise arterial vessel probability.



ON-LINE FIG 3. Definition and measurement of lesion masks for tissue outcome end points.



ON-LINE FIG 4. Bar graphs (median and interquartile range) showing tissue outcome parameters (FIV and PPS) in 3 groups of patients based on visual collateral scores ($CS_{CE\text{-}MRA}$ and CS_{TOF}). *A*, Only $CS_{CE\text{-}MRA}$ versus FIV is significantly correlated (Spearman $\rho = -0.48$, $P = .001$). *B*, $CS_{CE\text{-}MRA}$ versus PPS ($\rho = 0.26$, $P = .08$). *C*, CS_{TOF} versus FIV ($\rho = -0.25$, $P = .1$). *D*, CS_{TOF} versus PPS ($\rho = 0.16$, $P = .3$).