Volumetric and Spatial Accuracy of Computed Tomography Perfusion Estimated Ischemic Core Volume in Patients With Acute Ischemic Stroke

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Background and Purpose—The volume of estimated ischemic core using computed tomography perfusion (CTP) imaging can identify ischemic stroke patients who are likely to benefit from reperfusion, particularly beyond standard time windows. We assessed the accuracy of pretreatment CTP estimated ischemic core in patients with successful endovascular reperfusion.

Methods—Patients from the HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) and EXTEND-IA TNK (Tenecteplase Versus Alteplase Before Endovascular Therapy for Ischemic Stroke) databases who had pretreatment CTP, >50% angiographic reperfusion, and follow-up magnetic resonance imaging at 24 hours were included. Ischemic core volume on baseline CTP data was estimated using relative cerebral blood flow <30% (RAPID, iSchemaView). Follow-up diffusion magnetic resonance imaging was registered to CTP, and the diffusion lesion was outlined using a semiautomated algorithm. Volumetric and spatial agreement (using Dice similarity coefficient, average Hausdorff distance, and precision) was assessed, and expert visual assessment of quality was performed.

Results—In 120 patients, median CTP estimated ischemic core volume was 7.8 mL (IQR, 1.8–19.9 mL), and median diffusion lesion volume at 24 hours was 30.8 mL (IQR, 14.9–67.6 mL). Median volumetric difference was 4.4 mL (IQR, 1.2–12.0 mL). Dice similarity coefficient was low (median, 0.24; IQR, 0.15–0.37). The median precision (positive predictive value) of 0.68 (IQR, 0.40–0.88) and average Hausdorff distance (median, 3.1; IQR, 1.8–5.7 mm) indicated reasonable spatial agreement for regions estimated as ischemic core at baseline. Overestimation of total ischemic core volume by CTP was uncommon. Expert visual review revealed overestimation predominantly in white matter regions.

Conclusions—CTP estimated ischemic core volumes were substantially smaller than follow-up diffusion-weighted imaging lesions at 24 hours despite endovascular reperfusion within 2 hours of imaging. This may be partly because of infarct growth. Volumetric CTP core overestimation was uncommon and not related to imaging-to-reperfusion time. Core overestimation in white matter should be a focus of future efforts to improve CTP accuracy. **(*Stroke*. 2018;49:2368-2375. DOI: 10.1161/STROKEAHA.118.020846.)**

Key Words: cerebral infarction ■ magnetic resonance imaging ■ reperfusion ■ tenecteplase ■ thrombectomy ■ tomography, X-ray computed

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Early reperfusion in acute ischemic stroke is the key to reducing disability.[1] Multiple randomized trials[2–8] have shown that endovascular thrombectomy reduces disability versus standard care within 6 hours of stroke onset. The DAWN (Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo)[9] and DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke)[10] trials have successfully used imaging selection based on computed tomography perfusion (CTP) or magnetic resonance imaging (MRI) processed with RAPID software (iSchemaView, Mountain View, CA) to identify patients >6 hours after last known well time who benefit from reperfusion. Although analyses of 0 to 6 hours data have not shown an interaction between CTP core volume and the treatment effect of endovascular thrombectomy, CTP may have diagnostic and prognostic value for patients within 6 hours.[11–13] Several studies assessing contemporaneous CTP and diffusion-weighted MRI (MR-DWI) have shown reasonable agreement in estimates of the extent of permanently injured tissue.[14,15] However, CTP results have varied between postprocessing techniques and thresholds applied by different software.[11,16,17]

Although CTP is fast and easily accessible in the acute setting of ischemic stroke, it is recognized that cerebral blood flow (CBF) map segmentations tend to include false-positive regions in areas of hypodense white matter (leukoaraiosis).[18] CBF is physiologically lower in white versus gray matter and further reduced in regions of leukoaraiosis.[18] Given DAWN and DEFUSE 3 results, standardized CTP postprocessing software with validated thresholds is likely to be increasingly used clinically to select patients for reperfusion therapies beyond standard therapeutic time windows. A crucial question, therefore, is how reliable CTP estimates of irreversible injury are in the current endovascular paradigm of fast reperfusion.[19]

We aimed to assess the volumetric and spatial agreement of estimated ischemic core on CTP with follow-up infarct on DWI. We hypothesized that CTP data, when appropriately thresholded, could provide a reliable volumetric and spatial estimation of the follow-up infarct.

Materials and Methods

Patient Selection

This study pooled individual patient data from 7 randomized trials of endovascular thrombectomy (HERMES collaboration [Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials])[2–8,20,21] and from the EXTEND-IA TNK trial (Tenecteplase Versus Alteplase Before Endovascular Therapy for Ischemic Stroke).[22] The EXTEND-IA TNK trial tested the safety and efficacy of intravenous tenecteplase versus alteplase before thrombectomy in ischemic stroke patients. The data that support the findings of this study are available from the corresponding author on reasonable request. The degree of reperfusion postthrombectomy was assessed on the final angiogram using the modified Treatment in Cerebral Infarction (mTICI) score. To best estimate the accuracy of baseline CTP after endovascular reperfusion, only patients who had substantial reperfusion (defined as mTICI 2b/3, ie, reperfusion of >50% of the affected territory) were included in this analysis. Sensitivity analysis was performed in patients achieving mTICI 2c/3, that is, reperfusion of all but a few distal cortical branches.[23] Patients were required to have technically adequate baseline CTP and 24 hour DWI follow-up. The following patient characteristics were noted: age, sex, baseline National Institutes of Health Stroke Scale, baseline estimated ischemic core volume, hypertension, atrial fibrillation, diabetes mellitus, blood glucose, and smoking. Ethics approval was obtained from the local institutional review boards, and written informed consent was obtained from patients or legal representatives.

CTP Postprocessing

CTP data were postprocessed using RAPID (v4.5, Research Mode) and visually checked for artifacts. Ischemic core was defined as relative cerebral blood flow (rCBF) <30% of normal brain (online-only Data Supplement).

Data Coregistration and Segmentation

The 24-hour follow-up DWI was coregistered to the baseline CTP. Hemorrhagic transformation (HT) was graded using the European Co-operative Stroke Study (ECASS) classification.[24] Sensitivity analysis was performed excluding patients with hemorrhagic infarction type 2 and parenchymal hematoma.

Assessment of Volumetric and Spatial Agreement

The volumetric difference between CTP and DWI ischemic core was defined as DWI volume minus CTP core volume. Magnitude of volumetric difference is also reported. CTP and DWI lesion overlap was calculated using FSLMaths (online-only Data Supplement) and spatial agreement assessed using FSLStats and the EvaluateSegmentation tool.[25] The Dice similarity coefficient was calculated to assess spatial agreement between CTP and DWI lesions. The positive predictive value (PPV) was used to assess the proportion of the initial CTP lesion that fell within the 24 hour diffusion lesion. Unlike Dice, PPV is not diminished by regions of infarction at 24 hours that fall outside the baseline CTP lesion, potentially reflecting infarct growth. We also used the average Hausdorff distance (the average of all minimum distances between the 2 segmentations) to quantify spatial agreement.[25] Patients with 0 mL ischemic core within the CTP coverage were included in volumetric analyses but excluded from spatial analyses as the outcome measures were not calculable.

Regions of apparent CTP misclassification were visually assessed for topography (white versus gray matter) and coregistration accuracy. The quantity of CTP lesion outside the follow-up infarct (defined as core volume overestimation) was quantitatively trichotomized as 0 to 5, 5 to 10, and >10 mL. To quantitatively assess the impact of coregistration inaccuracies on the outcome metrics, we segmented the ventricles of 13 HERMES patients and 56 EXTEND-IA TNK patients (online-only Data Supplement).

Statistical Analysis

Statistical analysis was performed using SPSS (v24 IBM, Armonk, NY). Spearman correlation coefficient (ρ) was calculated for correlations between variables.

Results

One hundred twenty patients with baseline CTP and 24 hour MRI met inclusion criteria for this study. Follow-up imaging was performed at median 24.4 hours (interquartile range [IQR], 22.0–27.8 hours). In HERMES, 523 of 738 (71%) patients assigned to thrombectomy had substantial reperfusion,[7,8,21] and 61 had requisite imaging. On March 20, 2017, 130 stroke patients were included in the EXTEND-IA TNK trial, 76 of 130 (58%) achieved substantial angiographic reperfusion, and 59 had requisite imaging. Overall, 118 of 120 (98%) patients were treated <6 hours after symptom onset. Only 2 HERMES patients had stroke onset-to-treatment time >6 hours (8.2 and 8.8 hours). Patient characteristics are detailed in Table 1.

Table 1. Patient Characteristics (N=120)

Mean age, y (SD)	69.6 (12.9)
Sex, n (%) male	59 (49)
Median baseline NIHSS (IQR)	16 (14–21)
Hypertension, n (%)	82 (69)
Atrial fibrillation, n (%)	43 (36)
Diabetes mellitus, n (%)	16 (13)
Median glucose blood level, mmol/L (IQR)	6.4 (5.6–7.4)
Smoking history, n (%)	39 (35)
Median baseline core volume, mL (IQR)	7.8 (1.8–19.9)
Median 24 h follow-up infarct volume, mL (IQR)	30.8 (14.9–67.6)
Median volumetric difference, mL (IQR)	25.4 (10.0–63.7)

NIHSS indicates National Institutes of Health Stroke Scale.

Volumetric and Spatial Agreement Analysis

For the 19 of 120 (16%) patients without detectable ischemic core within the CTP coverage, the median follow-up infarct volume (and thus median volumetric difference between baseline CTP ischemic core and follow-up infarct volume) was 13.1 mL (IQR, 7.9–21.3 mL). In the remaining 101 (84%) patients, the median estimated baseline ischemic core lesion volume of 7.8 mL increased to 30.8 mL on 24 hour DWI with a median difference of 25.4 mL (Table 1). Overall, the median volumetric difference was 25.4 mL (IQR, 10.0–63.7 mL). In sensitivity analysis excluding patients with HT, the median volume difference was 20.9 mL. Median volume difference in the 20 patients with HT was 69.1 mL (IQR, 24.3–142.2 mL). Increased absolute volumetric difference was associated with increased estimated baseline ischemic core volume (ρ=0.36; P<0.0001; Figure 1).

The median Dice was 0.24 (IQR, 0.15–0.37). The median overlap of baseline and 24 hours lesions was 4.4 mL (IQR, 1.2–12.0 mL). However, the median PPV was 0.68 (IQR,0.40–0.88). The median average Hausdorff distance was 3.1 mm (IQR, 1.8–5.7 mm). Data are summarized in Table 2, and results of sensitivity analysis in patients with almost complete reperfusion were similar (Table I in the online-only Data Supplement). As a measure of the influence of registration accuracy on the maximum achievable spatial agreement, manual segmentation of ventricles had median Dice 0.79 (IQR, 0.71–0.84), median PPV 0.81 (IQR, 0.72–0.87), and median average Hausdorff distance 0.4 mm (IQR, 0.2–0.6 mm).

Ischemic Core Overestimation and Expert Visual Qualitative Assessment

There were 6 of 120 (5%) patients with CTP estimated ischemic core volume larger than the 24 hour DWI lesion volume, median volumetric difference 4.5 mL (range, 0.6–18.9 mL). Visual analysis of lesion spatial overlap indicated that 91 of 120 (76%) patients had some region of baseline core outside the 24 hour infarct. Apparent core overestimation was 0.1 to 5.0 mL in 63 of 120 (53%) patients (median, 1.1 mL; IQR, 0.3–3.1 mL) and located in white matter in 46 of 63 patients. There were 21 of 120 (18%) patients with 5 to 10 mL core overestimation (median, 6.9 mL; IQR, 5.9–8.1 mL), which was located in white matter in 18 of 21 patients. There were 17 of 120 (14%) patients with >10 mL core overestimation (median, 18.3 mL; IQR, 14.3–25.5 mL), which was located predominantly in white matter in 14 of 17 patients. Nine patients (9%) showed regions of baseline ischemic core that were not included in the follow-up infarct most likely because of poor registration, as judged by the same anatomic structures being included in both lesions. Although misregistration may also have contributed to ischemic core overestimation in other patients, the overrepresentation of white matter regions was substantial (Figure 2).

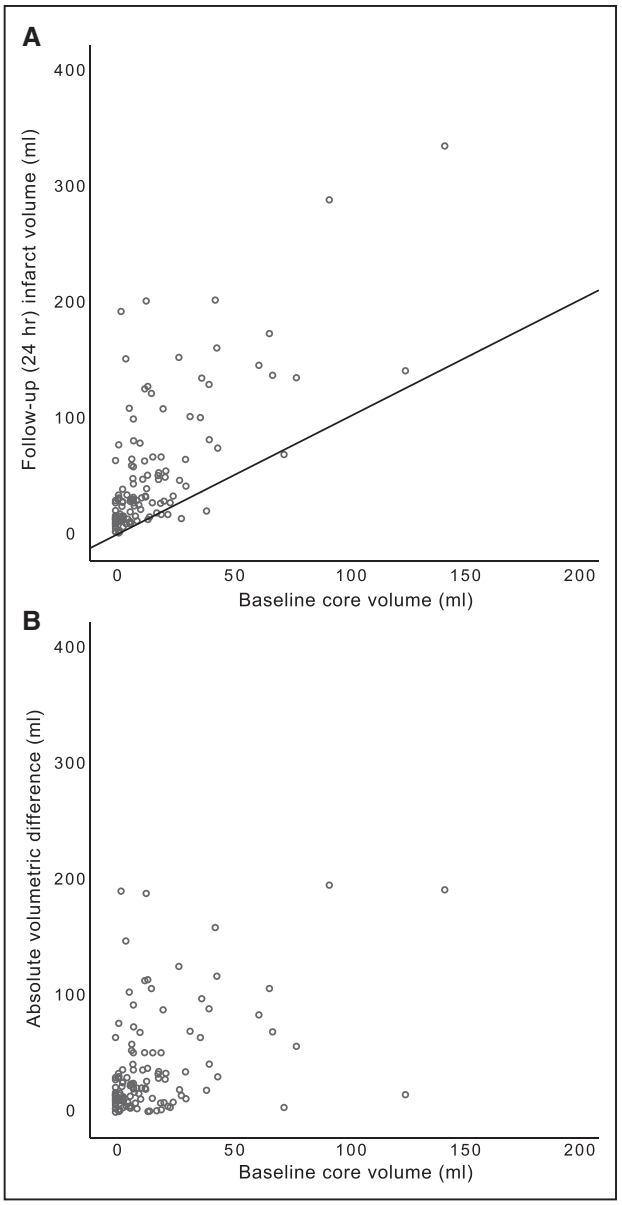

Figure 1. CT perfusion volumetric accuracy. Scatter plots of (**A**) baseline core volume and 24 h follow-up infarct volume (ρ=0.65) (**B**) baseline core volume and absolute volumetric difference (ρ=0.07).

Effect of Time From Imaging to Reperfusion

Median time between baseline imaging and reperfusion was 114 minutes (IQR, 82–159 minutes). CTP spatial accuracy was not associated with imaging-to-reperfusion time using Dice (ρ=–0.08; P=0.41), average Hausdorff distance (ρ=0.08; P=0.43), or PPV (ρ=–0.02; P=0.84). Longer

Table 2. Procedural and Outcome Data

Median onset-to-imaging time, min (IQR) [N=117]	109 (71–152)
Median imaging-to-reperfusion time, min (IQR) [N=117]	114 (82–159)
Median onset-to-reperfusion time, min (IQR) [N=117]	233 (187–288)
Median Dice similarity coefficient (IQR) [N=101]	0.24 (0.15–0.37)
Median precision (IQR) [N=101]	0.68 (0.40–0.88)
Median average Hausdorff distance, mm (IQR) [N=101]	3.1 (1.8–5.7)

imaging-to-reperfusion time, however, was associated with an increased volumetric difference between baseline ischemic core and 24-hour follow-up infarct (ρ=0.2; *P*=0.05; Figure 3). In spatial analysis, there was no significant difference in core overestimation among the 0 to 90, 90 to 180, and >180 minute imaging-to-reperfusion time subgroups (Figure 4). The median core overestimation in spatial analysis was 2.2 mL (IQR, 0.6–7.4 mL) for 0 to 90 minutes, 2.9 mL (IQR, 0.6–6.8 mL) for 90 to 180 minutes, and 7.4 mL (IQR, 3.5–17.8 mL) for >180 minutes subgroups (*P*=0.03 for 0–90 versus >180 minutes and *P*=0.03 for 90–180 versus >180 minutes). The median volume difference was 25.4 mL (IQR, 6.0–35.7 mL) for 0 to 90 minutes, 22.8 mL (IQR, 11.2–51.3 mL) for 90 to 180 minutes, and 60.0 mL (IQR, 21.1–91.7 mL) for >180 minutes subgroups.

Discussion

This study comparing baseline estimated ischemic core using a CTP-CBF threshold <30% of normal brain has demonstrated moderate spatial and volumetric agreement with follow-up DWI lesion. Volumetric overestimation of the ischemic core was rare. A degree of false-positive core segmentation was detected in 76% of patients using spatial analysis but was >10 mL in only 14%, and coregistration inaccuracy may have also contributed. Most patients who showed quantitative core overestimation by CTP had false-positive areas in white matter adjacent to the lesion. Interestingly, there was no evidence that spatial and volumetric accuracy was reduced in patients with shorter imaging-to-reperfusion time.

Some previous studies of CTP ischemic core segmentation accuracy have used contemporaneous diffusion MRI as the reference standard. CBF-based thresholds consistently outperformed cerebral blood volume–based thresholds.[26–28] However, obtaining both CT and MRI before intervention is impractical in the current era of fast endovascular workflow. There is also potential for partial reversal of diffusion lesions with rapid reperfusion,[29] although reversal is uncommon when a sufficiently low apparent diffusion contrast threshold is used to define ischemic core.[30]

We have taken an alternative approach to CTP accuracy assessment and studied follow-up diffusion lesions in patients with early reperfusion. This has practical advantages, but its accuracy depends on the modality of imaging, the time between CTP and reperfusion (in which infarct growth can continue), and the completeness of reperfusion. Voxel-based subanalysis in the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) database using Philips CTP analysis software (Philips Medical Systems BV, Best, the Netherlands) suggested that CTP misclassified a considerable amount of the ischemic core volume compared with follow-up infarct (median, 34 ml).[17] The different processing software and thresholds for infarction (based on cerebral blood volume) substantially differed from the processing pathway and relative CBF <30% threshold applied in RAPID. Large differences in CTP analysis

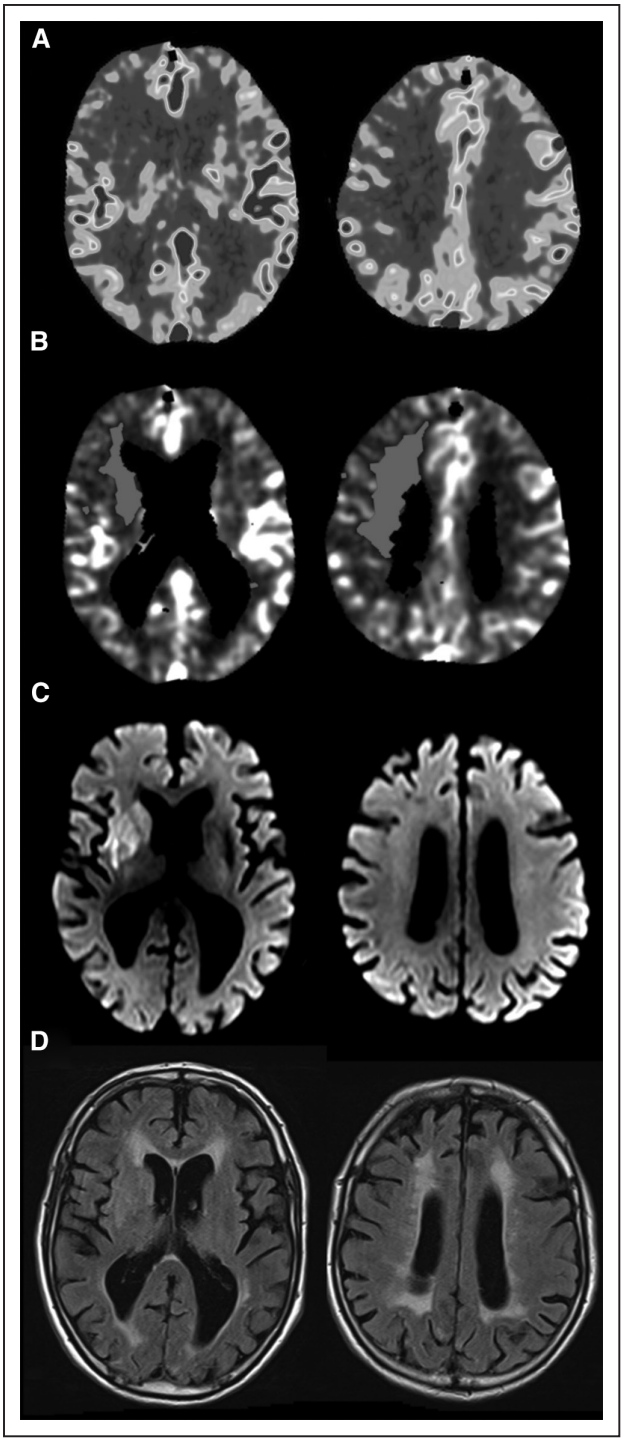

Figure 2. An 89-year-old man with right M1 segment middle cerebral artery occlusion. **A**, Cerebral blood flow map with (**B**) RAPID estimation of ischemic core. **C**, Twenty-four hour diffusion magnetic resonance imaging (MRI) after successful endovascular reperfusion indicating that the basal ganglia core was correctly identified on computed tomography perfusion (CTP), but there was core overestimation in adjacent white matter. **D**, Fluid attenuated inversion recovery imaging indicating leukoaraiosis.

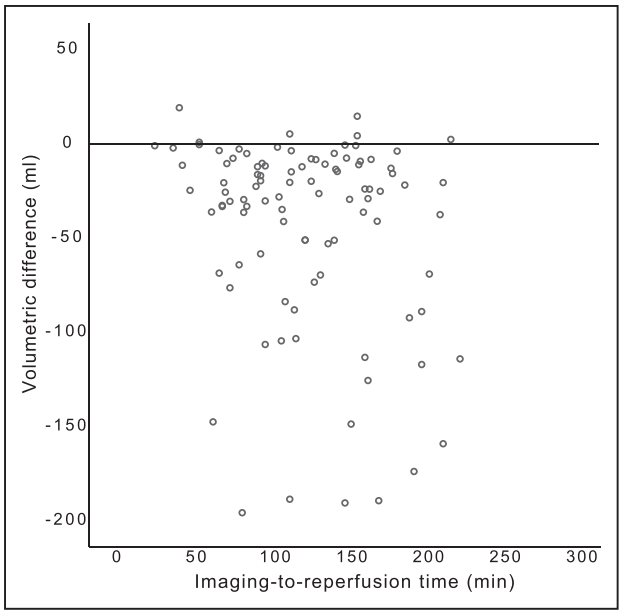

Figure 3. Scatter plot of the association between imaging-to-reperfusion time and volumetric difference (calculated as 24 h follow-up infarct volume–baseline infarct volume).

results between software packages have been demonstrated previously.[31,32] In addition, ischemic core volumes were considerably larger in MR CLEAN than in our study (median, 49.7 versus 7.8 mL), and the difference in results supports our finding that increased baseline ischemic core volume is associated with increased volumetric difference compared with follow-up infarct volume. RAPID has been shown to more accurately estimate the follow-up infarct volume than other imaging packages[33,34] and was used in SWIFT PRIME (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment),[5] EXTEND-IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial),[3] DAWN[9] and DEFUSE 3.[10] A recent subanalysis of the SWIFT PRIME trial[35] using RAPID showed good volumetric accuracy in predicting the follow-up infarct in acute stroke patients. The median baseline ischemic core volume in that study was smaller than in our population (4 mL [IQR, 0–13 mL] versus 7.8 mL [IQR, 2–19 mL]), as was the median follow-up infarct volume (18.7 mL [IQR, 8.9–48.9 mL] versus 30.8 mL [IQR, 14.9–75.2 mL]). Predictably, these smaller infarcts led to smaller volumetric inaccuracies in SWIFT PRIME (14.8 mL [IQR, 4.9–33.7 mL]) than in our study (25.4 mL [IQR, 10.0–63.7 mL]).

Superficially, the spatial agreement of baseline CTP ischemic core and follow-up infarct with a Dice coefficient of 24% appears poor. This might be partially explained by the limitations of coregistering different imaging modalities. Also, sensitivity analysis demonstrated greater inaccuracy in patients who developed HT and associated edema which also impacted the spatial agreement. However, the trend to increased volumetric difference with increasing imaging-to-reperfusion time supports a contribution of interval infarct growth. Infarct growth (which can occur despite endovascular reperfusion because of delay between imaging and reperfusion or incomplete reperfusion) lowers Dice but is unrelated to

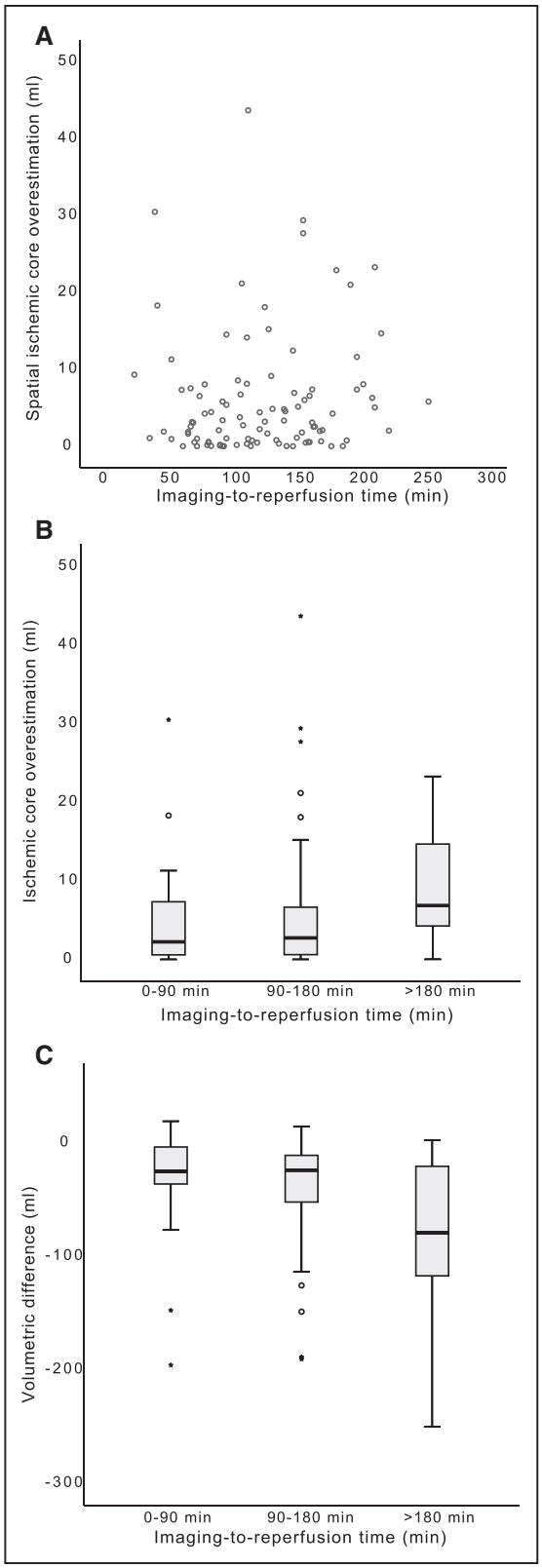

Figure 4. Ischemic core overestimation (spatial analysis) by imaging-to-reperfusion time. **A**, Scatterplot. **B**, Boxplot for the 0 to 90 min, 90 to 180 min, and >180 min imaging-to-reperfusion time subgroups. **C**, Volumetric difference between baseline estimated ischemic core and follow-up infarct volume in 3 subgroups by imaging-to-reperfusion time. Negative volume differences on the *y* axis indicate 24 h volumes higher than baseline estimated core volumes.

CTP core segmentation accuracy. When the potential effect of infarct growth is accounted for using the PPV, a median 68% of the baseline CTP ischemic core fell within the follow-up infarct. This should be viewed in the context of the 81% precision achieved when comparing ventricle segmentations, which provides an estimate of the best possible performance allowing for coregistration inaccuracies. Both contemporaneous DWI and follow-up infarct approaches involve registration of DWI to CT, which has inherent inaccuracies because of echoplanar image distortion and differing slice thicknesses.

In this study, the estimated ischemic core volume on baseline CTP was generally smaller than the infarct volume as shown on the 24-hour follow-up MRI scan. This contrasts with previous studies suggesting that CTP may overestimate the final infarction, leading to concerns about unwarranted exclusion of patients from reperfusion therapies.[19,36] Only 6 patients had smaller infarct volumes on 24 hours DWI than on baseline CTP.

There are several potential reasons for larger infarct volumes at 24 hours than were estimated at baseline. The rCBF threshold of <30% used was specifically selected to increase specificity at the cost of sensitivity.[37] A RAPID rCBF threshold of <38% improves volumetric agreement but substantially overestimates core in some patients. Hence the 30% threshold was chosen to reduce the risk of unwarranted exclusion of patients from treatment. There was potential for interval infarct growth in the median 114 minutes between imaging and reperfusion. Notably, even the subgroup with <90 minutes of imaging-to-reperfusion time generally had smaller CTP volumes compared with DWI follow-up lesion volumes. There was also potential for infarct growth in regions that remained hypoperfused as mTICI 2b only requires restoration of flow to >50% of the affected territory. However, patients with almost complete (mTICI 2c/3) reperfusion had very similar volumetric differences. Vasogenic edema also develops and, while not as pronounced at 24 hours as at 3 to 5 days, may inflate the measured infarct volume. We acknowledge that distinguishing the effect of interval infarct growth and edema from core underestimation by CTP is challenging.

In visual assessment of reasons for spatial inaccuracies, almost all the patients had estimated CTP core in white matter regions that fell outside the follow-up infarct at 24 hours. Although these only amounted to >10 mL in 14% of patients, the accurate classification of tissue viability in white matter should be a focus of future attempts to improve the accuracy of CTP ischemic core segmentation. The challenges of quantitatively different CBF and tolerance of ischemic insult in gray and white matter are well known, and the presence of old established ischemic damage as well as leukoaraiosis exacerbates this with further reductions in CBF.[38] Robust automated gray/white segmentation on CT would be required to implement differential CBF thresholds based on tissue type into current processing pipelines, and this remains challenging.

A limitation of this analysis is the potential for infarct growth beyond 24 hours. It is known that ischemic core continues to evolve in the days after stroke onset, although true expansion into previously unaffected territory is less likely after substantial reperfusion, as was required in this study.[39] However, all time points for assessment have limitations. Later assessment at 5 days, for example, in DEFUSE 2,[40] is at the peak of edema and overestimates the true infarct volume. At 90 days, there is atrophy which underestimates the true infarct volume. Our results apply to 1 specific CTP rCBF threshold processed with RAPID software and would differ with other thresholds and likely with other software.[31,32] Patients included in the HERMES and EXTEND-IA TNK database had relatively small ischemic core volumes at baseline, despite broad inclusion criteria in most of the contributing trials. MR CLEAN, ESCAPE (Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke), REVASCAT (Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours), and EXTEND-IA TNK had no upper limit on core volume, EXTEND-IA allowed up to 70 mL, and SWIFT PRIME up to 50 mL. The distribution of core volumes in this analysis was similar to that in DAWN and DEFUSE 3 which supports the generalizability of our data. However, this analysis provides limited information on the accuracy of ischemic core volume prediction in patients with larger baseline ischemic core which may differ, based on the observed association between baseline infarct volume and volumetric discrepancy.

Conclusions

CTP estimated ischemic core volumes were substantially smaller than follow-up DWI infarct lesions at 24 hours, particularly in patients with longer imaging to reperfusion times. Despite effective endovascular reperfusion, this may have resulted, at least in part, from infarct growth between CTP and reperfusion or subsequent infarct growth because of incomplete reperfusion or HT. This presents a methodological challenge for ischemic core validation studies. Detailed analysis revealed core overestimation predominantly in white matter regions that should be the target of future efforts to improve CTP ischemic core accuracy. Importantly, volumetric overestimation of ischemic core by CTP was rare. Contrary to previous literature, we did not find that shorter imaging-to-reperfusion time was associated with volumetric or spatial overestimation of core volume using CTP.

Disclosures

Dr Majoie has consulted for Stryker and the Dutch Heart Foundation (paid to institution). Dr Marquering is a founder and shareholder of Nico-lab. Dr van der Lugt has consulted for Stryker and reports grants to his institution from Penumbra. Dr van Zwam has consulted for Stryker and Cerenovus (paid to institution). Dr Saver is an employee of the University of California (UC) that has patent rights on retrieval devices for stroke; has served as an unpaid site investigator in multicenter trials sponsored by Medtronic, Stryker, and Neuravi for which the UC Regents received payments on the basis of clinical trial contracts for the number of subjects enrolled; has consulted for Medtronic, Stryker, and Neuravi; and has received stock options from Rapid Medical for services as a consultant. Dr Jovin has consulted for Stryker Neurovascular as Principal Investigator for the DAWN trial; has consulted for Fundacio Ictus as member of the Executive Committee RACECAT trial (Direct Transfer to an Endovascular Center Compared to Transfer to the Closest Stroke Center in Acute Stroke Patients With Suspected Large Vessel Occlusion); has served as advisor for Silk Road, Anaconda, Route92, FreeOX Biotech, and Blockade Medical; and has served in the Data Safety Monitoring Board of Cerenovus. Dr White has consulted for Microvention and Stryker and his institution received a grant from Microvention. Dr Muir reports grants to his institution for the PISTE trial (Pragmatic Ischaemic Stroke

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