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Assessment of computed tomography perfusion RAPID estimated core volume accuracy in patients following thrombectomy

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Riwaj Bhagat, Allison Muha, Kerri Remmel, Wei Liu

Department of Neurology, University of Louisville, Kentucky, USA

Keywords
Cone-Beam Computed Tomography; Diffusion Magnetic Resonance Imaging; Perfusion Imaging; Stroke; Endovascular Procedures

Abstract

Background: Computed Tomography Perfusion (CTP) maps ischemic core volume (CV) and penumbra following a stroke; however, its accuracy in early symptom onset is not well studied. We compared the accuracy of CTP RAPID estimated CV with diffusion weighted imaging (DWI) infarct volume (IV) in patients following thrombectomy.

Methods: Charts of anterior circulation large vessel occlusion post-thrombectomy cases with thrombolysis in cerebral infarction (TICI) 2b/3 reperfusion from 2017 to 2019 were reviewed. CTP time was dichotomized as 0-3 hours and ≥ 3 hours from the last known normal (LKN) cognition. The volumetric difference (VD), defined as DWI IV minus CTP CV, core volume overestimation (CVO), defined as CTP CV minus DWI IV and Alberta stroke programme early CT score (ASPECTS) were calculated. Large CV was defined as ≥ 50 ml CV. Modified Rankin Score (mRS) at 90 days were reviewed. We performed independent sample t-test and Spearman correlation coefficient test.

Results: Total cases (n) were 61. In < 3 hours window from LKN (n = 27), the mean VD was 58.3 ± 0.1 ml (P = 0.990) and CVO (n = 11; 40.7%) was 39.6 ± 35.7 ml (P = 0.008). Mean large CV (n = 8) was 78.3 ± 25.4 ml with median ASPECTS of 8 [interquartile range (IQR) = 6.5-9.0] and median mRS at 90 days of 2 (IQR = 0.8-3.3). In ≥ 3 hours window from LKN (n = 34), CVO (n = 5) was uncommon and large CV had median mRS at 90 days of 5 (IQR = 4.0-6.0).

Conclusion: CTP more frequently overestimates CV in patients who are < 3 hours from LKN. The treated patients with large CV in < 3 hours and > 3 hours had good and poor functional outcomes, respectively.

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Corresponding Author: Riwaj Bhagat
Email: forriwaj@gmail.com

Introduction

Computed tomography perfusion (CTP) estimates ischemic core and penumbra volume for large vessel anterior circulation strokes based on cerebral blood flow (CBF), cerebral blood volume (CBV), Time-to-Maximum (Tmax), and mean transit time (MTT).[1] Various CTP post-processing programs have been introduced to estimate ischemic core volume (CV) and tissue at risk of death, including CTP RAPID iSchemaView, which was used in major trials for determining the usefulness of mechanical thrombectomy (MT) in patients with anterior circulation large vessel occlusions (ACLVO)[2-4] and extending the alteplase use window.[5] The most accurate estimate of ischemic core lesion was found when CBF was < 30% using the RAPID software and when volumetric accuracy was verified by diffusion-weighted imaging (DWI) on magnetic resonance imaging (MRI).

The median time between CTP and MRI imaging studies in subjects with the most accurate CV estimation was 36 minutes.[1] Studies have shown that CTP overestimates the ischemic CV when compared to DWI, hypothesizing that it falsely recognizes region of leukoaraiosis as ischemic CV.[6] Therefore, this study aimed to investigate the accuracy of CTP estimated CV soon after symptom onset in patients with ACLVO by comparing with DWI infarct volume (IV).

Materials and Methods

This study was exempted by the University of Louisville Institutional Review Board (20.0416). This is a retrospective analysis of consecutive patients who underwent MT for ACLVO from 2017 to 2019. Patients with adequate baseline CTP and follow-up 36-hour brain MRI were included. To best estimate the accuracy of DWI IV after reperfusion, only patients who had adequate reperfusion, were included in the analysis. Adequate reperfusion was defined in this study as a thrombolysis in cerebral infarction (TICI) score 2b/3 (reperfusion > 50% of the affected territory) or higher. Patients with parenchymal hematoma, as graded per the European Cooperative Acute Stroke Study (ECASS II) classification were excluded. The following patient baseline characteristics were noted: age, sex, National Institutes of Health Stroke Scale (NIHSS) score at admission, last known normal (LKN) cognition to CTP time, LKN cognition to MRI time, LKN cognition to reperfusion time, and CTP to reperfusion time. The CTP RAPID estimated CV was defined as relative CBF < 30% of normal brain. LKN cognition to CTP time was dichotomized as 0-3 hours and ≥ 3 hours. DWI IV was manually calculated with ABC/2 formula [i.e maximum length (A), width (B) and height (C) all in centimeters of the ellipsoid DWI lesion] and verified by two expert physicians to minimize error. For patchy strokes, the largest IV was considered. The difference between DWI IV and CTP CV was defined as volumetric difference (VD) and difference between CTP CV and DWI IV as core volume overestimation (CVO).

Large CTP CV was defined by CV > 50 ml. Finally, Alberta stroke programme early CT score (ASPECTS) and Modified Rankin Scale (mRS) at 90 days were reviewed to analyze patient functional outcomes. Statistical analysis was performed using SPSS software (version 26, IBM Corporation, Armonk, NY, USA). Standard descriptive statistics, independent sample t-test, and Spearman correlation coefficient (rho) were used as statistical tools.

Results

There were 61 MT cases that met the criteria of adequate baseline CTP, 36-hour follow up brain MRI, and adequate reperfusion of TICI 2b/3. The mean ± stranded deviation (SD) of age of the subjects was 66 ± 13.9 years, among who 57.4% were male. The patients were dichotomized into two groups based on CTP time from LKN cognition. Group A included subjects with CTP time from LKN < 3 hours while group B included subjects with CTP time from LKN cognition ≥ 3 hours. The baseline characteristics and volumetric analysis for both groups are included in table 1.

Volumetric analysis

Less than 3 hours window from LKN cognition (Group A): 27 cases had CTP within 3 hours from LKN cognition with the median time of 74 minutes [interquartile range (IQR) = 56.0-122.0)]. The mean CTP CV and DWI IV were 36.9 ± 33.4 and 52.1 ± 37.1 ml, respectively. In addition, the mean VD was 58.3 ± 0.1 ml, which was not statistically significant (P = 0.990). 11 (40.7%) cases had significant CVO as 39.6 ± 35.7 ml (P = 0.008). An example of CVO is illustrated in figure 1.

Greater than 3 hours window from LKN cognition (Group B): 34 cases had CTP > 3 hours from LKN cognition with median time 378 minutes (IQR = 245.0-521.3). The mean CTP CV and DWI IV were 47.4 ± 28.81 and 75.3 ± 69.5 ml, respectively, moreover, the mean VD and CVO (n = 5) were respectively 61.8 ± 46.5 ml (P = 0.002) and 41.27 ± 25.20 ml (P = 0.600).

Table 1. Patient characteristics, imaging timing, and volumetric assessment of patients with baseline computed tomography perfusion (CTP) at different time frames from symptom onset

Characteristics	LKN cognition to CTP (< 3 hours), Group A	LKN cognition to CTP (≥ 3 hours), Group B	P
Patients (n)	27	34	
Age (year) (mean ± SD)	62.9 ± 13.2)	68.4 ± 14.1	
Sex (male) [n (%)]	14 (42.4)	21 (61.7)	
Imaging timing			
Median Baseline NIHSS (IQR)	17 (11.0-21.0)	17 (12.3-20.8)	0.401
Median LKN cognition to CTP time, mins (IQR)	74 (56.0-122.0)	378 (245.0-521.3)	< 0.001*
Median CTP to MRI B time, mins (IQR)	453 (322.0-646.0)	419.5 (337.3- 558.8)	0.728
Median LKN cognition to groin time, mins (IQR)	130 (110.0-186.0)	430 (291.8-588.8)	< 0.001*
Median CTP to groin puncture time, mins (IQR)	46 (36.5-70.0)	55 (33.5-74.3)	0.431
Volumetric assessment			
CTP core volume (ml) (mean ± SD)	36.9 ± 33.4	47.4 ± 28.8	
DWI core volume (ml) (mean ± SD)	52.1 ± 37.1	75.3 ± 69.5	
VD (ml) (mean ± SD)	58.3 ± 0.1	61.8 ± 46.5	

LKN: Last known normal, CTP: Computed tomography perfusion, NIHSS: National Institutes of Health Stroke Scale, MRI B: Magnetic resonance imaging of brain, DWI: Diffusion-weighted imaging, SD: Standard deviation; VD: Volumetric difference
*P value <0.05.

Large core volume ASPECTS and functional outcome: In group A, eight cases had a large CV with a mean volume of 78.3 ± 25.4 ml and median ASPECTS of 8 (IQR = 6.5-9.0).

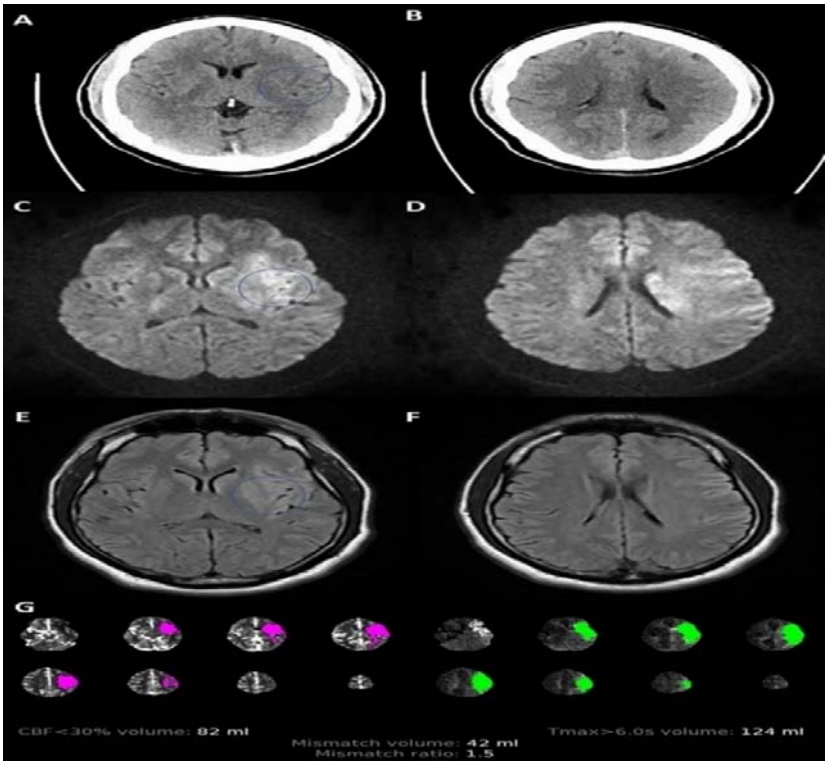

Figure 1. Head imaging of patient with symptom onset less than 3 hours showing core volume overestimation

Computed tomography (CT) scan of head at (A) nuclear level and (B) supranuclear level show hypodensity at left middle cerebral artery (MCA) territory [Alberta stroke programme early CT score (ASPECTS) of 8]. Magnetic resonance imaging (MRI) of head after 16 hours from thrombectomy shows (C,D) restricted diffusion in diffusion weighted imaging sequence and (E,F) hyperintensity in T2- fluid inversion recovery sequence at left MCA territory, and (G) computed tomography perfusion (CTP) RAPID iSchemaView shows volume with cerebral blood flow < 30% (core volume) of 82 ml.

The group A cases with large CV had a median NIHSS at admission of 17 (IQR = 15.0-18.0) and had favorable functional outcomes (defined as mRS ≤ 2 at 90 days) with median mRS at 90 days of 2 (IQR = 0.8-3.3).

In group B, five cases had a large CV with a mean volume of 116.8 ± 75.3 ml and median ASPECTS of 6 (IQR = 5.0-7.0). The group B cases with large CV had a median NIHSS at admission of 16 (IQR = 13.0-19.0) and had poor functional outcomes (defined as mRS > 2 at 90 days) with median mRS at 90 days of 5 (IQR = 4.0- 6.0). Two of these patients died.

Effect of time from imaging to reperfusion: In group A, VD did not increase with the increased time from CTP imaging to the reperfusion (rho = 0.309, P = 0.117). While in group B, VD did increase with longer duration of time from CTP imaging to reperfusion (rho = 0.378, P = 0.028) (Figure 2).

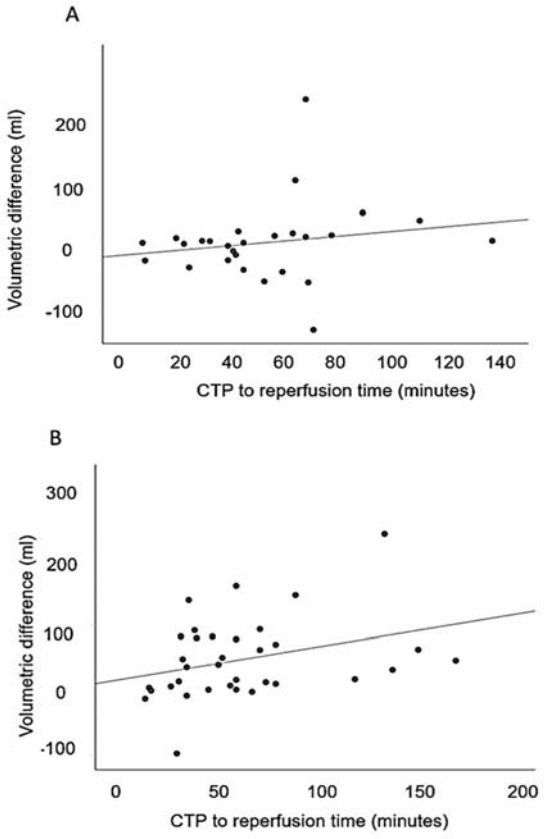

Figure 2. Scatter plots of volumetric difference (VD) and computed tomography perfusion (CTP) to reperfusion time duration (A) within 3 hours window from symptom onset (rho = 0.309, P = 0.117), and (B) ≥ 3 hours window from symptom onset (rho = 0.378, P = 0.028).

Discussion

This study was specifically interested in testing the hypothesis that CTP RAPID estimated CV overestimates core volume. We compared baseline ischemic CV in two groups using a CTP-CBF threshold < 30% of normal brain, which demonstrated a volumetric agreement between CTP CV and follow up DWI lesion greater than three hours from symptom onset. Volumetric overestimation of the ischemic core by CTP scan was seen in more than one third of the patients within three hours from symptom onset. This study suggests there is not volumetric agreement when time of reperfusion from baseline CTP is less than three hours from symptom onset. Further, patients from this group with large CV (> 50 ml) with favorable ASPECTS had good functional outcomes. A previous study showed that treated patients with initial large ischemic core (~70 ml) have poor functional outcomes.[7] Similarly, this study depicted treated patients with large ischemic core (≥ 50 ml) beyond three hours of symptom onset also had poor functional outcome. It is important to recognize these patients early in symptom course because IV grows over time.[8,9] Considering the current study and ones, it has been shown that patients with large CV (> 50 ml) had better functional outcomes when intervening at less than three hours from symptom onset when compared to those with intervention longer than three hours from LKN cognition. In addition to improving patient functional outcome, overestimation of CTP CV could have potential impacts on criteria surrounding interventional action in patients with acute stroke.

CTP RAPID estimated ischemic core and penumbra volume provide immediate information in decision making for acute revascularization treatment. In patient selection for MT in ACLVO, ASPECTS is dependable for symptom onset less than 6 hours. The use of CTP mismatch ratio and CV criteria has shown to be beneficial in an extended window from 6-24 hours.[2,4] However, ASPECTS is accompanied by constraints, as it is affected by the quality of CT scan, motion artifact, intracranial metals, interrater reliability, cerebral small vessel disease, and structural dissimilarity.[7,10] In such situation, automated perfusion reading of CTP stands to be valuable even for the ACLVO with early symptom onset. There were a higher number of good outcomes in trials that used CTP in the window of 6 hours from symptom onset (EXTEND-1A and SWIFT PRIME)

when compared with trials that primarily used non-contrast ASPECTS (REVASCAT, ESCAPE and MR CLEAN). This supports selective use of CTP RAPID imaging results in better outcome among treated patients.[11-15] These studies showed the importance of and dependence on CTP RAPID imaging results.

In addition to being used in studies determining effective MT candidates, RAPID CTP estimation of CV is also utilized in determination of Alteplase time windows. It is currently recommended that the administration of Alteplase in patients with acute stroke be limited to within 4.5 hours from LKN cognition. Ma et al. found beneficial effects of Alteplase in an extended widow of up to 9 hours after onset of stroke, compared to placebo, in terms of good functional outcome (mRS = 0-1 at 90 days). The study above used CTP RAPID estimated core (< 70 ml) and mismatch ratio (> 1.2) for patient selection.[16] When considering the results of the present study as CTP RAPID estimated CV overestimates CV, patient selection of the study above could have been affected. Because this study limited selection of patients to estimated core of < 70 ml and the present study indicates overestimation of CV in patients at < 3 hours from symptom onset, patients who would benefit from Alteplase intervention may have been missed if they had a CV of greater than 70 ml.

A previous study has suggested hemodynamic fluctuations related to heart failure, cardiac arrythmia, motion, and carotid stenosis, which could affect the CTP outcome.[17] Likewise, "truncation artifact", or error in estimation of the core volume can be seen with shorter CTP duration (less than 40 seconds).[18] This study further supplements limitation of CTP accuracy in estimating CV in the early time window (< 3 hours) from symptom onset. Based on the results of this study, it would be highly beneficial to further investigate the effects on patient outcomes when changing inclusion and/or exclusion criteria for the use of RAPID CTP estimated CV. Another point worth discussion revolves around the question of why there is overestimation of CV by RAPID CTP estimated CV in patients < 3 from symptom onset. As stated above, one hypothesis is that CTP falsely recognizes region of leukoaraiosis as ischemic CV, which would increase total volume on a final read.[6] While this is a hypothesis, there is no consensus on what causes this phenomenon. Additional study specifically on this topic would be beneficial as it may lead to an increased accuracy when using CTP to determine ischemic CV in patients with acute stroke.

The limitation of this study was the small sample size and its associated bias. Interrater variability while estimating DWI IV and CT ASPECTs was reduced by verifying imaging with two expert physicians. Emerging imaging markers, including assessment of collateral scores, have appeared to foresee the IV more readily in short time and is progressively used for patient selection for MT.[19,20] Studies comparing accuracy between these two imaging modalities may have an impact in future patient care as it could change common practice surrounding management in patients with acute stroke.

Conclusion

CTP-CBF < 30% of normal brain volume overestimated the core volume in more than one third of the cases with symptom onset less than three hours after ACLVO. Within this time window, treated patients with overestimated large core volume ≥ 50 ml and favorable ASPECTS had good recovery. Volumetric agreement was noted on CTP CV after three hours of symptom onset with reliable prognostic data.

Conflict of Interests

The authors declare no conflict of interest in this study.

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