OPEN

Computed Tomography Perfusion Data for Acute Ischemic Stroke Evaluation Using Rapid Software: Pitfalls of Automated Postprocessing

Frans Kauw, MD,† Jeremy J. Heit, MD, PhD,* Blake W. Martin, BS,* Fasco van Ommen, MSc,*† L. Jaap Kappelle, MD, PhD,‡ Birgitta K. Velthuis, MD, PhD,† Hugo W.A.M. de Jong, PhD,† Jan W. Dankbaar, MD, PhD,† and Max Wintermark, MD**

Abstract: Computed tomography perfusion (CTP) is increasingly used to determine treatment eligibility for acute ischemic stroke patients. Automated postprocessing of raw CTP data is routinely used, but it can fail. In reviewing 176 consecutive acute ischemic stroke patients, failures occurred in 20 patients (11%) during automated postprocessing by the RAPID software. Failures were caused by motion (n = 11, 73%), streak artifacts (n = 2, 13%), and poor contrast bolus arrival (n = 2, 13%). Stroke physicians should review CTP results with care before they are being integrated in their decision-making process.

Key Words: CT perfusion, acute ischemic stroke, postprocessing failures, endovascular treatment

(*J Comput Assist Tomogr* 2020;44: 75–77)

Acute ischemic stroke (AIS) patients can be treated with intravenous thrombolysis and endovascular treatment (EVT) in late time windows.[1,2] Treatment eligibility depends on brain perfusion parameter cutoffs, which can be evaluated either by computed tomography (CT) or magnetic resonance imaging (MRI).[2–6]

After the raw CT perfusion (CTP) data have been collected, the data need processing before perfusion parameters can be calculated. Key elements of postprocessing include the determination of the symmetry axis and selection of the arterial input function (AIF) and venous output function (VOF). Automated processing is routinely used in stroke imaging protocols, but this method is not perfect and failures can occur.

A few studies previously discussed failures of automated perfusion postprocessing. For instance, in one large EVT trial, automated postprocessing was successful in only 58% of the cases initially and in 98% of the cases in a second round of postprocessing.[7] Previously described failures were mostly caused either by severe motion or by poor arrival of the contrast bolus.[3] Postprocessing failures may lead to incorrect volumes of infarct core and penumbra. As treatment eligibility criteria are partly based on these volumes, treatment strategies and patient outcomes may be affected by failures in postprocessing CTP data.[3,4]

The goal of this study was to investigate (1) how often failures occur during automated processing of CTP data, (2) which patient factors are associated with such failures, and (3) whether such failures affected patient management.

MATERIALS AND METHODS

Selection of Patients

We included consecutive AIS patients undergoing CTP for EVT triage between 2012 and 2018, which were identified from our prospective database. We excluded patients where no CTP was performed as part of the acute stroke work-up or if the results of automated postprocessing were missing from our electronic imaging archive.

Patient Characteristics

We collected baseline data including age, sex, admission National Institutes of Health Stroke Scale (NIHSS), time from symptom onset to CTP imaging, administration of intravenous tissue plasminogen activator (tPA), and EVT. Imaging data included side of occlusion and occlusion site as determined on CT angiography (CTA).

Image Acquisition

The CTP and CTA were performed as part of our routine acute stroke work-up, respectively. The CTP was performed with cine mode on 80 kV and 100 mAs with 37 phases at 1-second time interval followed by 33 phases at 3-second time interval on 128-slice scanners. Either 1 run or 2 runs with 5 mm slices were performed covering at least Alberta stroke program early CT score levels 1 and 2 of the brain. The CTA was performed on 120 kV and 225 mAs and covered the aortic arch up to the apex of the brain. Slice thickness for CTA was set to 0.625 mm. The iodinated contrast dose was 40 mL for the CTP runs and 70 mL for the CTA, injected at 4 to 5 mL per second.

Image Analysis

Automated postprocessing of the CTP images was done by using a commercially available software package (RAPID; iSchemaView, Menlo Park, CA) that uses a proprietary delay-insensitive algorithm.[8,9] Midline axis determination and selection of the AIF and VOF were automatically performed. Processed maps

From the *Department of Neuroradiology, Stanford University, Palo Alto, CA; †Department of Radiology, and ‡Brain Center Rudolf Magnus, Department of Neurology and Neurosurgery, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.

Received for publication April 25, 2019; accepted September 11, 2019.

Correspondence to: Frans Kauw, MD, Department of Radiology, room Q.01.4.46, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands (e-mail: f.kauw-3@umcutrecht.nl).

This research has been made possible by the Dutch Heart Foundation and the Netherlands Organization for Scientific Research, domain Applied and Engineering Sciences, as part of their joint strategic research program: Earlier Recognition of Cardiovascular Disease (grant number 14732).

The authors declare no conflict of interest.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jcat.org).

DOI: 10.1097/RCT.0000000000000946

were generated for cerebral blood flow, cerebral blood volume, and time-to-maximum (T_{max}), as well as for ischemic core (cerebral blood flow threshold <30% compared with the contralateral normal hemisphere) and penumbra (T_{max} threshold >6 seconds). Potential causes of failures were evaluated by 2 observers (F.K. and M.W.) and included incorrect selection of midline axis, incorrect selection of the AIF and VOF, motion, streak artifact, and issues of time-attenuation curves related to contrast bolus, either as a result of motion or contrast bolus failure. The observers were blinded to all clinical data, but they had access to all imaging data available at the time of patient evaluation. In case of disagreement between the observers, consensus was reached by discussion. We reprocessed failures manually by using IntelliSpace software (Philips, Best, The Netherlands).

Outcome Assessment

Primary outcome was automated postprocessing failure, which was defined as the presence of perfusion abnormalities that were caused by artifacts as verified on follow-up imaging (either CT or MRI), accounting for interval reperfusion. Secondary outcome was inaccurate ischemic core or penumbra volumes as determined with follow-up imaging (either CT or MRI) that might have affected EVT eligibility, defined using the inclusion criteria of the endovascular therapy following imaging evaluation for ischemic stroke 3 trial.[6] Tertiary outcome was poor functional outcome (modified Rankin Scale of 3 or higher) measured approximately 3 months after the stroke.

Statistical Analysis

Associations between potential predictors and postprocessing failures were tested using binary logistic regression. We reported odds ratios (ORs) with 95% confidence intervals (CIs). Statistical analyses were performed in R (version 3.4.2).

RESULTS

A total of 176 AIS patients were included for analysis (Table 1). Automated postprocessing failures occurred in 20 cases (11%). Causes for failures were severe motion (n = 14, 70%), streak artifact (n = 3, 15%), and poor arrival of contrast (n = 3, 15%). No failures were induced by erroneous determination of the midline axis and selection of the AIF or the VOF. One failure caused by motion could be salvaged manually by excluding frames containing motion artifacts at the end of the acquisition. Patients in the failure group were more often male (n = 14, 70% vs n = 72, 46%, $P = 0.045$, respectively) and had higher admission NIHSS (mean ± SD, 18 ± 6 vs 15 ± 7, $P = 0.047$, respectively) compared with the patients in the nonfailure group. In a multivariable model, only higher admission NIHSS was significantly associated with failures (OR, 2.2; 95% CI, 1.1–5.0; $P = 0.046$) (Table 2).

Of 176 patients, 88 patients (50%) received intravenous tPA and 126 (72%) received EVT based on clinical information and on the interpretation of CTP imaging, which included correction for failures. If CTP results had been used for decision-making without correction for processing failures, 130 patients (73%) would have been eligible for EVT. In 5 patients, the automated postprocessing failure resulted in artifacts, which made the ischemic core volume

TABLE 1. Patient Characteristics Stratified by Automated Postprocessing Failures

Characteristic	Total N = 176	Failures N = 20 (11%)	No Failures N = 156 (89%)
Age, mean ± SD, y	72 ± 15	72 ± 14	72 ± 15
Male sex, n (%)	86 (49)	14 (70)	72 (46)
Admission NIHSS, mean ± SD	15 ± 7	18 ± 6	15 ± 7
Time from symptom onset to CTP, median (Q1–Q3)	171 (65–377)	293 (113–566)	159 (65–354)
Intravenous tPA, n (%)	88 (50)	9 (45)	79 (51)
EVT, n (%)	126 (72)	12 (60)	114 (73)
– Reperfusion (TICI IIB-III), n (%)	101 (58)	11 (58)	90 (58)
Findings on CTA			
Occlusion side			
– Right	70 (41)	6 (33)	64 (42)
– Left	92 (54)	10 (56)	82 (54)
– Basilar	5 (3)	2 (11)	3 (2)
– Both	3 (2)	0 (0)	3 (2)
Occlusion site			
– ICA or M1 occlusion	57 (32)	7 (35)	50 (32)
– Other occlusion	111 (63)	11 (55)	100 (64)
Causes of failures			
Motion			
– Significant	14 (8)	14 (70)	0 (0)
Streak artifacts	7 (4)	3 (15)	4 (3)
Contrast bolus			
– Poor arrival	3 (2)	3 (15)	0 (0)
Follow-up			
Poor clinical outcome at 90 d,* n (%)	71 (40)	8 (40)	63 (40)

*Defined as modified Rankin Scale ≥ 3.

TICI indicates thrombolysis in cerebral infarction; ICA, internal carotid artery.

TABLE 2. Results of Binary Logistic Regression With Respect to Automated Postprocessing Failures

Characteristic	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Age, per 10 y increase	1.0 (0.8–1.4)	—
Male sex	2.7 (1.0–8.0)	—
Admission NIHSS, per 10 points increase	2.0 (1.0–4.2)	2.2 (1.1–5.0)
Time from symptom onset to CTP, per 60 min	1.0 (1.0–1.1)	1.0 (1.0–1.1)
Findings on CTA		
Occlusion side		
– Right	Reference	
– Left	1.3 (0.5–4.0)	1.2 (0.4–3.8)
– Basilar	7.1 (0.8–52.2)	6.0 (0.7–4.7)
Occlusion site		
– ICA or M1 occlusion	0.8 (0.3–2.2)	1.0 (0.4–3.0)
– Other occlusion site	Reference	Reference

*Adjusted for age and sex.
ICA indicates internal carotid artery.

larger than what it actually was, and these patients might have been excluded from treatment if the CTP results had been interpreted without correction (Supplementary Figure 1, Supplemental Digital Content, http://links.lww.com/RCT/A92). In 1 patient, according to follow-up imaging, the automated postprocessing failure made the ischemic penumbra volume smaller than what it actually was, and this patient might have been excluded from treatment if the CTP results had been interpreted literally (Supplementary Figure 2, Supplemental Digital Content, http://links.lww.com/RCT/A92). Thus, in 6 patients (3%), the automated postprocessing failures might have resulted in different treatment decisions if the CTP results had been interpreted literally.

Prevalence of poor functional outcome at 90 days after the stroke was similar for the failure group and the nonfailure group (40% vs 40%, respectively), but many values were missing for this outcome (n = 57, 37% and n = 11, 55%, respectively).

DISCUSSION

In this study, we evaluated prevalence of automated CTP postprocessing failures and associated patient factors. Failures occurred in 11% of the patients and were mostly caused by motion and, to a lesser extent, by streak artifact and poor arrival of contrast bolus. The patient factor significantly associated with failures was higher stroke severity (NIHSS), because such patients are more likely to be agitated and to move during the CTP scanning. Half of the failures led to erroneous ischemic core volumes such that EVT eligibility might have been affected if the CTP results had been interpreted literally.

Our results indicate that the results from automated postprocessing perfusion software should be interpreted with caution. Even though the software was successful in 89% of the cases, 11% showed artifacts leading to erroneous ischemic core volume estimations that might have affected patient management in 3% of the cases. Fortunately, CTP failures were recognized, and subsequent imaging was done to determine correct infarct volumes, which led to appropriate management for all patients.

Strength of this study was the large sample size of consecutive AIS patients, which minimizes the risk of selection bias.

A limitation of this study was its retrospective nature, which we tried to counterbalance by using consecutive patients in our practice. In addition, the loss to follow-up rate was quite high, and therefore, these findings need validation in studies with a prospective design. We only tested 1 specific software package, and the generalization of our conclusions to other software packages will need to be verified. Still, the software program evaluated in our study is widely used, and therefore, our results are pertinent to current clinical practice.

In conclusion, stroke experts should be aware of the pitfalls of postprocessing CTP data especially in patients with more severe strokes.

REFERENCES

1. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2018;49:e46–e110.
2. Ma H, Campbell BCV, Parsons MW, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. *N Engl J Med*. 2019;380: 1795–1803.
3. Campbell BC, Yassi N, Ma H, et al. Imaging selection in ischemic stroke: Feasibility of automated CT-perfusion analysis. *Int J Stroke*. 2015;10:51–54.
4. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288.
5. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2017;378:11–21.
6. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378: 708–718.
7. Kidwell CS, Jahan R, Gornbein J, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. *N Engl J Med*. 2013;368: 914–923.
8. Austein F, Riedel C, Kerby T, et al. Comparison of perfusion CT software to predict the final infarct volume after thrombectomy. *Stroke*. 2016;47: 2311–2317.
9. Koopman MS, Berkhemer OA, Geuskens RREG, et al. Comparison of three commonly used CT perfusion software packages in patients with acute ischemic stroke. *J Neurointerv Surg*. doi:10.1136/neurintsurg-2019-014822.