J Chin Med Assoc

ORIGINAL ARTICLE

Single-phase computed tomography angiography sufficiently predicts outcomes after mechanical thrombectomy

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Abstract

Background: Arterial collateral (AC) assessed by single-phase computed tomography angiography (CTA) or multiphase CTA has been used to predict clinical outcomes in patients undergoing mechanical thrombectomy (MT). Recently, venous opacification (VO) was proposed as another accurate image marker. This study aimed to compare the efficacy using AC and VO as predictors of MT outcome.

Methods: Patients with occlusion of the proximal anterior circulation undergoing MT were included retrospectively. We assessed the AC status respectively according to different methods: modified Tan score, Miteff score in single-phase CTA, and pial arterial filling score in multiphase CTA. VO was assessed according to cortical vein opacification score. Favorable clinical outcome was defined as modified Rankin Scale 0-2 90 days after MT. Logistic regression models were established and receiver operating characteristics curve were used to determine the predictability of favorable outcome in patients with adequate AC and VO.

Results: A total of 75 patients were enrolled. Adequate AC identified by modified Tan score (odds ratio, 7.3; $p < 0.001$), Miteff score (odds ratio, 4.5; $p = 0.009$), significantly predicted favorable outcome, but not adequate VO. The area under the curve was largest for adequate AC in model of modified Tan score 0.730 (95% CI, 0.60-0.86), while adequate VO showed the least area under the curve: 0.577 (95% CI, 0.43-0.73).

Conclusion: We considered adequate AC in single-phase CTA could be reliable enough as an imaging marker rather than adequate VO to predict favorable outcome after MT.

Keywords: Arterial collateral; Computed tomography angiography; Intra-arterial mechanical thrombectomy; Venous opacification

1. INTRODUCTION

Mechanical thrombectomy (MT) has been a standard treatment in acute ischemic stroke (AIS) caused by large vessel occlusion of less than six after several large randomized trials published.[1–5] Still, there are some patients unable to be benefited from MT.

Many studies have demonstrated different methods evaluating arterial collateral (AC) by single-phase computed tomography angiography (CTA) is a good predictor of clinical outcome after MT,[6–8] along with multiphase CTA.[9,10] Both approaches are fast and easy to interpret by clinicians across all specialties involved in the multidisciplinary management of MT.

The value of venous opacification (VO) as a surrogate imaging marker of viable tissue in the ischemic penumbra has been discussed in several studies. They proposed different interpretation methods to evaluate cerebral venous flow and used it as a predictor of clinical outcome after MT.[11–14] Jansen et al[11] based their cortical vein opacification score (COVES) on the hypothesis that the degree of cortical venous drainage reflects the degree of cerebral microcirculation and perfusion generally. At their suggestion, patients with superficial VO should benefited from MT.

Thus, we aimed to compare the efficacy of imaging markers as predictors of MT benefit between AC and VO.

2. METHODS

2.1. Study population

All patients who underwent MT from November 2015 to August 2018 were retrospectively recruited. This study was approved by the local institutional review board, which waived the need for individual patient consent. The inclusion criterion was (1) large vessel occlusion at anterior circulation, that is, terminal internal carotid artery and middle cerebral artery (M1, M2) confirmed by CTA; (2) patients who presented with National Institutes of Health Stroke Scale (NIHSS) ≥ 6; and (3) unenhanced computed tomography (CT) to rule out intracranial hemorrhage and Alberta Stroke Program Early CT Score (ASPECTS) ≥ 6; patients

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Author Contributions: Dr. Chao-Bao Luo and Dr. Yung-Yang Lin contributed equally to this work.

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2020) 83: 478-483.

Received November 19, 2019; accepted January 21, 2020.

doi: 10.1097/JCMA.0000000000000300.

with thrombus located in the posterior circulation, suboptimal images due to motion artifacts, or inability to be evaluated by all collateral scoring methods were excluded. The decision-making of initial patient enrollment into MT was shared by neurologists and neuroradiologists on duty. After confirmation of large vessel occlusion, patients were sent to undergo MT.

MT was performed by three expert neurointerventionists with 12-30 years of experience. Stent retrievers, including Solitaire FR (Medtronic, Dublin, Ireland), Revive (Codman & Shurtleff, Raynham, MA, USA), and Trevo (Stryker, Kalamazoo, MI, USA), were used in 52 cases in combination with the thrombus suction device, Penumbra (Alameda, CA, USA). Aspiration-only was used in 23 cases. In general, a maximum of three passes or suctions were attempted until control angiography indicated successful recanalization. Successful recanalization was defined as a final thrombolysis in cerebral ischemia score ≥ 2b–3.[15] Primary clinical outcome was evaluated independently 24 hours after the procedure using the NIHSS score and 90 days after the procedure using the modified Rankin Scale by a neurologist (Y.-Y.L.). The modified Ranking score ≤2 were considered favorable outcome. Symptomatic intracranial hemorrhage (ICH) was defined by any intracranial hemorrhage plus an increase of four points or more on the NIHSS score.[16]

2.2. Image protocol

The CT protocol was performed on a 64-section CT scanner (Brilliance 64; Philips, Best, The Netherlands) and included non-contrast CT and CTA with the following parameters: 120 kVp, 250 mA, slice thickness of 0.625 mm. A contrast bolus of 60 mL (mainly Ultravist [370 mg/dL; Bayer AG, Berlin, Germany] and Omnipaque [350 mg/dL; GE, Cork, Ireland], and Xenetix [350 mg/dL; Guerbet, Roissy, France]) was injected at the rate of 4 mL/s and followed by injection of 50 mL of normal saline. The first phase of image acquisition was triggered by bolus tracking of 150 housefield unit as threshold at aorta; the region of interest was from aortic arch to skull vertex in the first phase and skull base to vertex in the remaining two phases. The second phase was acquired at 30 seconds after contrast injection, while the late phase was acquired at 40 seconds after contrast injection. The technicians processed images into multiplanar 8 mm maximum-intensity projection reconstructions with 3 mm intervals in axial and coronal views.

2.3. Image analysis

Image was retrospectively assessed by two radiologists (K.-W.Y. and C.-J.L.) with different levels of experience and who both were not aware of the clinical data. When a discrepancy existed between two readers, it was resolved by consensus. The adequacy of different imaging markers including Miteff score,[17] Maas score,[18] modified Tan score,[19] Pial arterial filling score,[10] and COVES[11] were all conducted as previous studies described.

In short, modified Tan score was a two-category system evaluating more or less AC comparing to the asymptomatic hemisphere. Miteff score was a three-point system focusing retrograde filling at Sylvian fissure. Maas score was a five-point system assessing not only Sylvian fissure but included leptomeningeal collaterals. The above noted three scoring systems were evaluated in single-phase CTA. In multiphase CTA, pial arterial filling score, a six-point system comparing collaterals between different phases, was applied.[10] COVES, is a two-category evaluating method in single-phase CTA,[11] suggested that absence of cortical vein in the affected hemisphere appearing to have no benefit from MT, whereas presence of cortical vein does. There is an example demonstrated how images were assessed with modified Tan score and COVES (Figs. 1 and 2).

2.4. Statistical analysis

All statistical analysis was performed using SPSS for Mac (V.23; IBM-SPSS, Chicago, IL, USA). The statistical difference between favorable and poor outcome groups was assessed using the chi-square test or Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. Univariable logistic regression analysis was performed to estimate the odds ratio (OR) of different factors associating with favorable clinical outcome. We established multivariate logistic regression models based on different imaging markers, respectively. Variables showed p value < 0.05 in univariate logistic regression were included and as previous studies suggested, successful recanalization could possibly impact the prognosis of MT; thus, thrombolysis in cerebral ischemia score was also included. We compare performance of different imaging markers in their model, and last, a receiver operating characteristic curve was used to analyze the ability of imaging markers to predict favorable outcome.

3. RESULTS

A total 107 patients with AIS were sent to MT. Twenty-seven patients with thrombus located in the posterior circulation, one with suboptimal images due to motion artifacts and four patients who were unable to be evaluated by all collateral scoring methods were excluded. Finally, 75 patients were included.

The mean age was 72.3 ± 14.7 years and 60% of patients were male. The baseline median NIHSS score was 18 (interquartile range, 13-21). The median baseline ASPECTS was 9 (7-10). The median symptom onset-to-recanalization time was 259 minutes. In total, 32 patients (42.7%) received intravenous recombinant tissue plasminogen activator treatment along with MT. Among all the population, most patients had occlusion at M1 (58.7%). Stent retriever was used for 49 patients (65.3%). Successful recanalization was achieved in 50 patients (66.7%). Twenty patients (26.7%) achieved functional independence (modified Rankin Scale 0-2) after 3 months. Only two patients (2.6%) presented with symptomatic intracranial hemorrhage.

Patients with favorable functional results were significantly associated with younger age (mean: 68.1 vs 73.8), lower baseline NIHSS scores (median: 12 vs 19), lower NIHSS scores at 24 hours (median: 6 vs 19 h), and reduced symptom onset time to recanalization (median: 211.5 vs 280 min). No statistical significance existed among sex, underlying disease such as hypertension, diabetes mellitus, and atrial fibrillation. There were also no statistically significant difference regarding IV thrombolysis treatment, time from symptom onset to CTA, or time from symptom onset to puncture between patients with favorable and poor functional outcome (Table 1).

In logistic regression analysis, adequate AC in different imaging markers showed significant correlation with favorable functional outcome, including Miteff score (OR, 4.5; p = 0.009), Maas score (OR, 3.2; p = 0.029), and modified Tan score (OR, 7.3; p < 0.001). All of the above scores were assessed by single-phase CTA, and pial arterial filling score in multiphase CTA (OR, 4.1; p = 0.017). However, there was no significant association between presence of cortical vein opacification, that is, COVES > 0 and favorable clinical outcome after MT (Table 2). We intended to build different models including variables that were statistically significant in predicting functional outcomes and factor was known to possibly impact the prognosis of MT. Thus, age, baseline NIHSS and symptom onset time to recanalization and successful recanalization were included in the model with imaging markers, respectively. The Miteff score, Maas score, pial arterial filling score, and COVES were not statistically

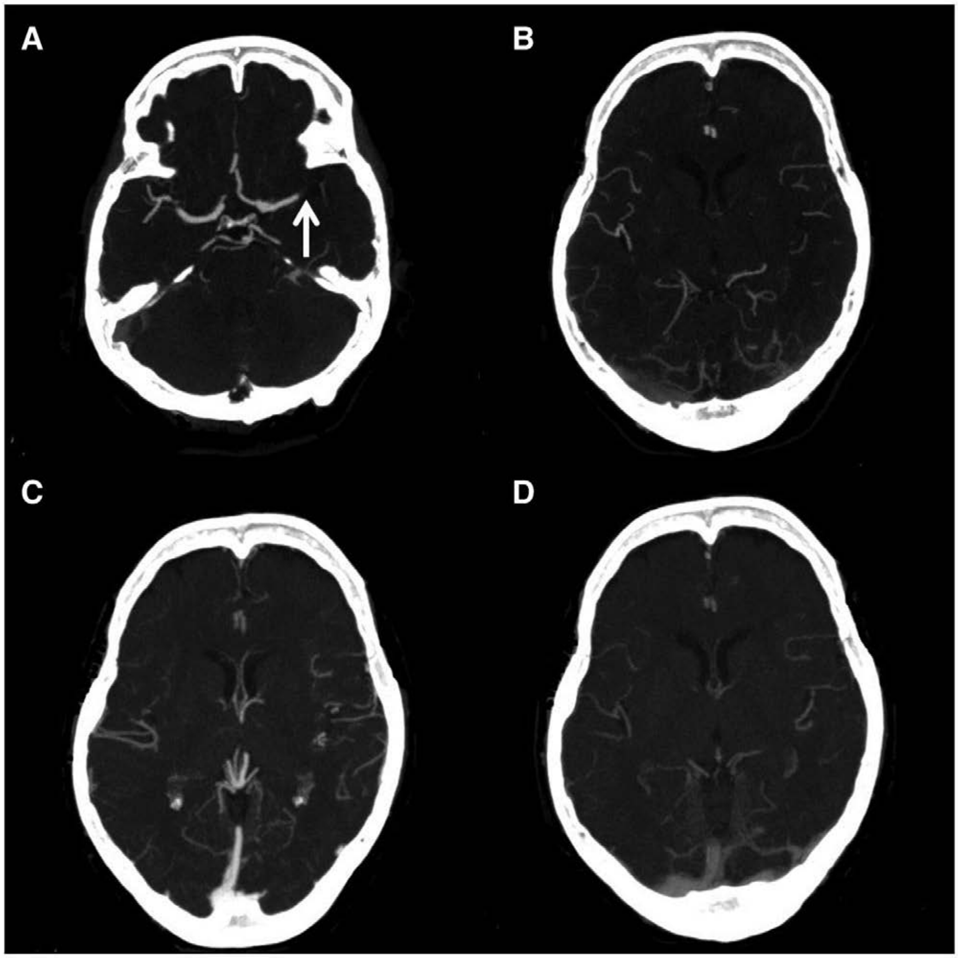

Fig. 1 An example of adequate arterial collateral (AC) in single- and multiphase computed tomography angiography (CTA). A–D, Case of an elderly patient in the sixth decade of life with left side M1 occlusion (white arrow) (A). CTA illustrates more than 50% of the MCA territory collaterals compared with the contralateral hemisphere at different levels (B). This is considered adequate AC in single-phase CTA. Images illustrate intermediate to good collaterals with prominent extent in symptomatic side (C and D). This is considered adequate AC in multiphase CTA MCA = middle cerebral artery.

Fig. 2 An example of adequate venous opacification (VO). A–C, Case of an elderly patient in the seventh decade of life with left side M1 occlusion (white arrow) (A). Computed tomography angiography (CTA) illustrates visible full opacification at the sphenoparietal sinus on the symptomatic side (white arrow) (B), and moderate opacification in the superficial cerebral vein (white arrow) (C). This is considered adequate VO.

significant predictors in their models, respectively. Modified Tan score was the only image marker that significantly predicted favorable functional outcomes after MT (Table 3).

The receiver operating characteristic analysis was also performed. The highest area under the curve among all the imaging marker models was modified Tan score: 0.730 (95% CI,

Table 1

Comparison of demographics and imaging variables between patients with favorable and poor functional outcome

Characteristic	Favorable (n = 20)	Unfavorable (n = 55)	p
Age, mean (SD)	68.1 (9.7)	73.8 (15.9)	0.019
Male, n (%)	12 (60)	23 (41.8)	0.163
Hypertension, n (%)	14 (70)	29 (52.7)	0.181
Diabetes, n (%)	6 (30)	10 (18.2)	0.341
Dyslipidemia, n (%)	6 (30)	9 (16.4)	0.207
Cardiovascular disease, n (%)	2 (10)	8 (14.5)	0.609
Cerebral vascular disease, n (%)	2 (10)	9 (16.4)	0.717
Atrial fibrillation, n (%)	7 (35)	9 (16.4)	0.112
Baseline NIHSS, median (IQR[a])	12 (10-18.5)	19 (15-21)	<0.001
NIHSS at 24 h, median (IQR[a])	6 (3-13)	19 (15-24)	<0.001
Baseline ASPECTS, median (IQR[a])	9 (7.25-10)	9 (7-10)	0.519
IV r-tPA treatment, n (%)	11 (55)	21 (38)	0.193
Occlusion site, n (%)			
M1	13 (65)	31 (56.4)	0.502
M2	4 (20)	9 (16.4)	0.737
Terminal ICA	3 (15)	15 (27.3)	0.493
Time to CTA, median (IQR[a])	109.5 (58-202.3)	116 (65-166)	0.573
Time to groin puncture, median (IQR[a])	164 (134.75-231.25)	222.5 (160-288.75)	0.087
Time to recanalization, median (IQR[a])	211.5 (191.75-297.5)	280 (229-360)	0.018
Symptomatic ICH, n (%)	0 (0)	3 (3.6)	1.000
Successful recanalization (TICI score 2b/3), n (%)	16 (80)	34 (61.8)	0.140

ASPECTS = Alberta Stroke Program Early CT Score; CTA = computed tomography angiography; ICA, internal carotid artery; ICH = intracranial hemorrhage; IQR = interquartile range; IV r-tPA = intravenous recombinant tissue plasminogen activator; NIHSS = National Institute of Health Stroke Scale; TICI = thrombolysis in cerebral ischemia.

[a]IQR denotes 25% to 75% quartiles.

Table 2

Univariate and multivariate logistic regression analysis of different imaging markers associated with favorable outcome

Variables	OR (95% CI)	p
ASPECTS	0.8 (0.19-3.56)	0.798
Miteff score	4.5 (1.43-14.17)	0.009
Maas score	3.2 (1.10-9.46)	0.029
Modified Tan score	7.3 (2.28-23.50)	<0.001
Pial arterial filling score	4.1 (1.23-14.00)	0.017
COVES	1.9 (0.67-5.35)	0.224

ASPECTS = Alberta Stroke Program Early CT Score; COVES = cortical vein opacification score; OR = odds ratio.

0.60-0.86), followed by Miteff score: 0.675 (95% CI, 0.54-0.81), pial arterial filling score: 0.655 (95% CI, 0.52-0.79), and Maas score: 0.632 (95% CI, 0.48-0.78). COVES showed the least area under the curve: 0.577 (95% CI, 0.43-0.73) (Fig. 3).

Two raters independently assessed all imaging markers. Interrater agreement was measured by using unweighted k values. The agreement showed substantial reliability for modified Tan score (k = 0.87), Miteff score (k = 0.83), and moderate reliability on Maas score (k = 0.72), pial arterial filling score (k = 0.73), and COVES (k = 0.66).

4. DISCUSSION

Our result support that in the same scenario of single-phase CTA, adequate AC scores (Miteff, Maas, modified Tan) were statistically significant for favorable clinical outcomes, while there was no statistically significant benefit for adequate VO to undergo MT.

The role of CTA is important in AIS patients with large vessel occlusion. It is known that more collateral arteries supplying the penumbra may lead to smaller infarction core, and CTA allows physicians to identify the extent of collateral arteries and has good accessibility worldwide, which enable doctors to make quick and efficient plans for reperfusion therapy.[19] However, some patients initially considered to have good ACs failed to achieve favorable outcome after successful recanalization.[20]

The drawbacks of single-phase CTA are known to be limited temporal resolution, overestimation of thrombotic length, as well as underestimating ACs. Collateral flow in multiphase CTA provided more information about antegrade and retrograde vessel filling, which might partly reflect the brain tissue viability, but not as accurately as CT perfusion. Recent large trials such as Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo and Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke study[21,22] have shown evidence of CT perfusion in identifying true infarction core volume and extended the time interval to 24 hours after symptom onset. Some automatic perfusion analysis software programs can provide timely and reliable estimations of tissue viability, but increased radiation, only fair accessibility and no uniform program or interpretation were still underlying problems for CT perfusion.

Thus, VO was proposed as another tool to evaluate the benefits of MT.[13,14,23] Previous studies on intracranial occlusion balloon tests claimed that venous drainage could be an indicator of cerebral microcirculation.[24] Reduced venous outflow represents poor cerebral microcirculation and could indicate poor functional outcome.[11,12] Studies have used single-phase CTA, dynamic CTA, or susceptibility-weighted images to assess venous collateral status, such as Prognostic Evaluation based on Cortical vein score difference In Stroke score or combined arterial and venous grading scales.[12,14,23] The requirement included judging superficial cortical vein and deep medullary veins. The study by Jansen et al[11] provided a method to evaluate superficial cortical veins in single-phase CTA. Previous study have also suggested better predictability of COVES comparing with Prognostic Evaluation based on Cortical vein score difference In

Table 3

Multivariate logistic regression analysis of different imaging markers associated with favorable outcome

	Single-phase CTA		Multiphase CTA		Cortical vein opacification	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Age	1.0 (0.99-1.09)	0.099	1.0 (0.99-1.09)	0.082	1.0 (0.99-1.09)	0.086
Baseline NIHSS	1.2 (1.04-1.39)	0.009	1.2 (1.05-1.40)	0.008	1.2 (1.09-1.44)	0.001
Time to recanalization	1.0 (0.99-1.01)	0.201	1.0 (0.99-1.01)	0.133	1.0 (0.99-1.01)	0.152
Successful recanalization	3.2 (0.64-16.02)	0.155	2.8 (0.62-13.20)	0.176	2.7 (0.62-12.09)	0.184
Modified Tan score	4.4 (1.17-16.75)	0.028				
Pial arterial filling score			2.3 (0.57-9.76)	0.235		
COVES					0.9 (0.24-3.20)	0.858

COVES = cortical vein opacification score; CTA = computed tomography angiography; NIHSS = National Institute of Health Stroke Scale; OR = odds ratio.

Stroke,[25] which gave us the reason to choose it as a representative imaging marker for VO.

However, some limitations in evaluating cortical venous drainage was also indicated anatomical variability in superficial venous structures. Reliable cortical venous drainage assessment required sufficient time to fill the venous structure; the short scanning time and inappropriate timing of image acquisition in single-phase CTA may have failed to adequately demonstrate all cortical venous structures. The gray zone between faint opacification and nonopacification in venous imaging increased and may be distorted by motion artifacts even in the asymptomatic hemisphere of the brain.

Several limitations to our study should be considered. First, to define a more homogenous cohort, the sample size of our study was relatively small and confined in anterior circulation only. The arterial occlusion site was also various including M1, M2, and terminal internal carotid artery. However, it would influence more on VO and was accepted in previous studies of COVES evaluation.[11] Second, three kinds of contrast with two different iodine concentrations were used in the current study, which

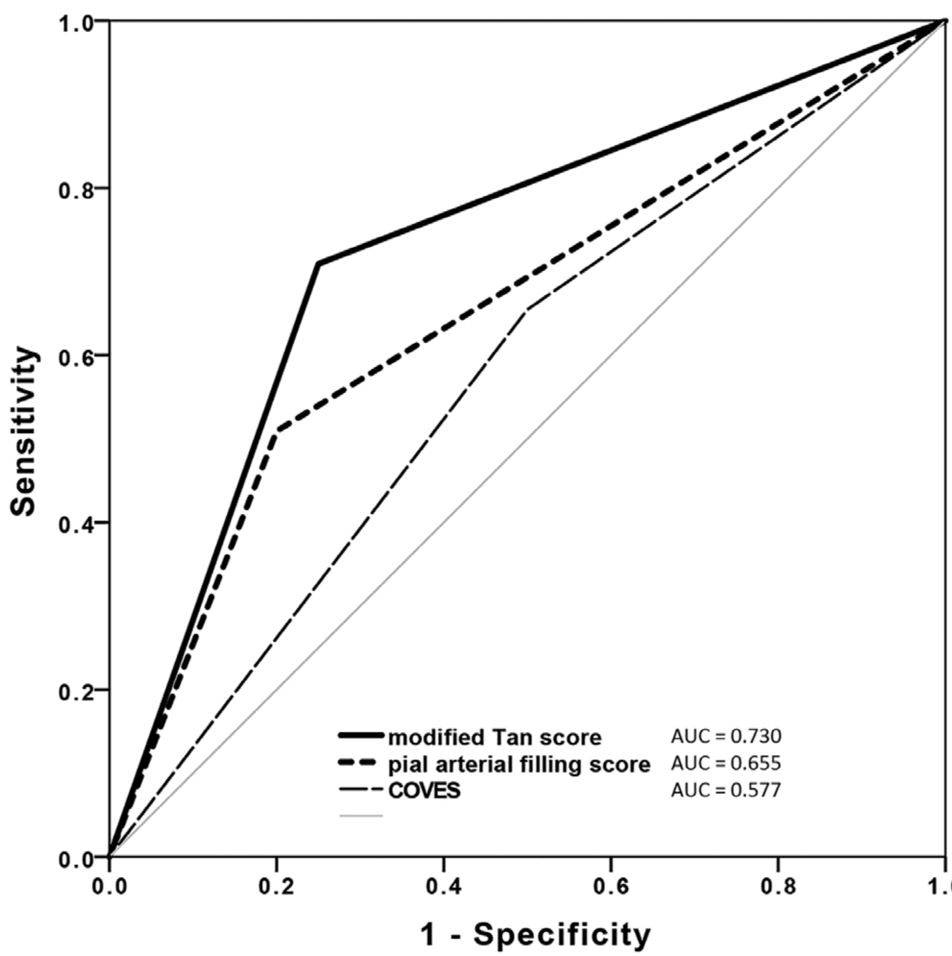

Fig. 3 Receiver operating characteristic (ROC) curve of different imaging markers predicting favorable clinical outcome. ROC curves for different prediction models. The predictive area under the curve (AUC) was largest in modified Tan score. COVES =cortical vein opacification score.

might influence the signal to noise ratio of CTA, especially in later phase or venous structure.

In conclusion, a simple CTA imaging marker assessing AC in single-phase CTA such as modified Tan score could be sufficient to predict functional outcomes and also has better inter-rater reliability rather than assessing VO.

ACKNOWLEDGMENTS

This work was supported by the Ministry of Science and Technology grants (NSC108-2314-B-075-004-MY2 for Dr. Luo; MOST105-2314-B-010-007-MY3 for Dr. Y.-Y. Lin) and Taipei Veterans General Hospital (V109C-084 for Dr. Luo; V107C-044 for Dr. Y.-Y. Lin).

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