ORIGINAL ARTICLE

Non-Contrast CT and CT-Angiogram for Late Window Ischemic Stroke Treatment Selection

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ABSTRACT: ***Introduction:*** The benefit of late window endovascular treatment (EVT) for anterior circulation ischemic stroke has been demonstrated using perfusion-based neuroimaging. We evaluated whether non-contrast CT (NCCT) and CT-angiogram (CTA) alone can select late-presenting patients for EVT. ***Methods:*** We performed a retrospective comparison of all patients undergoing EVT at a single comprehensive stroke center from January 2016 to April 2017. Patients planned for EVT were divided into early (<6 hours from onset) and late (≥6 hours from onset or last time seen normal) window groups. Incidence of symptomatic hemorrhagic transformations (sHTs) at 24 hours and 3-month modified Rankin scores (mRSs) were compared. ***Results:*** During the study period, 204 (82%) patients underwent EVT in the early and 44 (18%) in the late window. Median (interquartile range) NIH Stroke Scale Score was similar between groups (early: 18 [15–23] vs. late: 17 [13–21]), as were median ASPECT scores (early: 9 [8–10] vs. late: 9 [7–9]). In the late window, 42 (95%) strokes were of unknown onset. Similar proportions of sHT occurred at 24 hours (early: 12 [6%] vs. late: 4 [9%], $p = 0.43$). At 3 months, the proportion of patients achieving functional independence (mRS 0–2) were comparable in the early (80/192 [42%]) and late (16/41 [39%]) windows ($p = 0.76$). ***Conclusion:*** NCCT- and CTA-based patient selection led to similar functional independence outcomes and low proportions of sHT in the early and late windows. In centers without access to perfusion-based neuroimaging, this pragmatic approach could be safe, particularly for strokes of unknown onset.

RÉSUMÉ : Tomographie par ordinateur sans contraste et angiographie par tomodensitométrie dans le cas d'un traitement tardif destiné à un accidents ischémique cérébral. ***Introduction :*** Dans la fenêtre tardive, le bénéfice du traitement endovasculaire de l'accident vasculaire cérébral (AVC) ischémique a été démontré en utilisant la neuro-imagerie avec séquences de perfusion. Nous avons évalué dans quelle mesure la tomographie par ordinateur sans contraste et l'angiographie par tomodensitométrie peuvent à elles deux seules permettre de sélectionner les patients pour le traitement endovasculaire dans la fenêtre tardive. ***Méthodes :*** Nous avons effectué une comparaison rétrospective entre tous les patients à qui l'on a administré un tel traitement au sein d'un seul établissement de soins complets de l'AVC (comprehensive stroke center) entre janvier 2016 et avril 2017. Les patients pour qui un traitement endovasculaire avait été planifié ont été divisés en deux groupes : ceux ayant bénéficié d'un traitement précoce (< 6 heures à partir des premiers signes) et les autres pour qui le traitement a été prodigué de façon tardive (≥ 6 heures à partir des premiers signes ou de la dernière fois que le patient était vu normal). L'incidence de transformations hémorragiques symptomatiques (THS) au bout de 24 heures et l'état fonctionnel à 3 mois (échelle modifiée de Rankin (EmR)) ont été comparés entre les deux groupes. ***Résultats :*** Au cours de la période d'étude, 204 patients (82 %) ont bénéficié d'un traitement endovasculaire précoce tandis que 44 (18 %) ont reçu un traitement tardif. Les scores médians (EI) au National Institutes of Health Stroke Scale (NIHSS) se sont révélés semblables d'un groupe à l'autre (traitement précoce : 18 [15–23] contre tardif : 17 [13–21]). Il en est allé de même avec les scores médians au Alberta Stroke Programme Early CT score (ASPECT) (traitement précoce : 9 [8–10] contre tardif : 9 [7–9]). Dans le groupe de traitement tardif, on ignorait pour 42 cas (95 %) le moment du début des symptômes. Les pourcentages de THS étaient similaires au bout de 24 heures (traitement précoce : 12 [6 %] contre tardif : 4 [9 %] ; p = 0,43). La proportion de patients autonomes sur le plan fonctionnel au bout de 3 mois (EmR : 0–2) s'est avérée comparable d'un groupe à l'autre (traitement précoce : 80/192 [42 %]) contre tardif : 16/41 [39 %] ; p = 0,76). ***Conclusion :*** Dans les fenêtres précoces et tardives du traitement endovasculaire de l'AVC ischémique, en sélectionnant les patients avec la tomographie par ordinateur sans contraste et l'angiographie par tomodensitométrie, on a obtenu des résultats similaires en matière d'autonomie fonctionnelle et d'incidence de THS. Dans les centres de prise en charge des AVC n'ayant pas accès à la neuro-imagerie avec séquences de perfusion,

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une telle approche pragmatique pourrait être sécuritaire, particulièrement dans les cas d'AVC ischémiques à heure du début des symptômes inconnue.

Keywords: Stroke, Endovascular treatment, Late window, Imaging

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Introduction

Recent trials have established the benefit of perfusion imaging-based patient selection for endovascular treatment (EVT) in patients with anterior circulation large vessel occlusion (LVO) stroke presenting 6–24 hours after last time seen normal (LTSN). Eligibility was based on varying definitions, relying on imaging criteria (core-penumbral mismatch)[1] or a combination of clinical and imaging findings (core-NIHSS (NIH Stroke Scale Score) mismatch).[2] Accordingly, in late-presenting patients (>6 hours from onset or LTSN), imaging, rather than time alone, has become the basis of selection criteria for EVT. While perfusion-imaging methods allow estimations of core and penumbral volumes, they are not available in all stroke centers.

In contrast, standard neuroimaging (consisting of a non-contrast enhanced CT-scan (NCCT) and CT-angiography (CTA)) is widely accessible as part of existing acute ischemic stroke evaluation protocols. Multiple trials have demonstrated the benefit of EVT for patients presenting in the early window (<6 hours from onset or LTSN) based on NCCT and CTA results. The capacity of NCCT and CTA alone to select patients for EVT in the late window has, however, not yet been determined.

The primary aim of the study was to determine the ability of NCCT and CTA to select patients for EVT in the late window. The primary hypothesis was that NCCT and CTA-based selection would lead to similar efficacy and safety outcomes for patients undergoing EVT in the early and late windows.

Methods

Study Design

We conducted a retrospective analysis of all patients undergoing EVT for acute anterior circulation ischemic stroke at a single comprehensive stroke center (CSC) (Centre Hospitalier de l'Université de Montréal (CHUM), Canada) from January 2016 to April 2017. The CHUM performs > 150 thrombectomies annually, mostly following transfers from primary stroke centers (PSCs).

Patients planned for EVT were identified via a prospectively collected electronic patient record system used for acute stroke evaluations. All patients with an anterior circulation stroke undergoing EVT were included. Patients were then classified into early and late window groups (<6 and ≥6 hours from LTSN to CSC). Those in the late window were additionally classified as strokes of known or of unknown onset (i.e., wake-up strokes or non-wake-up unwitnessed onset).

Baseline demographic criteria (age, sex, vascular risk factors, and premorbid modified Rankin scores (mRSs)) and initial NIHSS scores were collected. Standard imaging protocol included an initial NCCT followed by CTA to confirm arterial occlusion. A triple-phase CTA was obtained for all patients presenting directly at our institution, whereas a single-phase CTA was performed in patients evaluated at PSC and subsequently transferred to CSC for EVT. Perfusion imaging (CT-perfusion/magnetic resonance (MR)-perfusion) was not performed for EVT selection during the study period. Eligibility for EVT was at the treating physician's discretion. Typically, EVT selection at our institution is based on the presence of an intracranial LVO, a significant neurological deficit (NIHSS ≥ 6), and favorable parenchymal imaging (Alberta Stroke Program Early CT Score (ASPECTS) ≥ 6). ASPECT scores were reported as initially documented. Imaging upon CSC arrival was not routinely repeated for patients transferred from PSC. Arterial occlusion as reported on CTA was noted. Standard stroke treatment metrics were calculated. Collaterals were retrospectively evaluated by two raters (CO and FF) and graded from 0 to 4 as defined by Souza et al.[3]

Patients planned for EVT (based on initial vascular imaging results) but with subsequent documented recanalization on direct angiography were included in the analysis. Recanalization of the artery occluded on initial CTA was reported using the modified Treatment in Cerebral Ischemia (mTICI) score. All CT-scans at 24 hours after EVT were reviewed and 24 hours asymptomatic or symptomatic intracranial hemorrhages (sICHs) (based on European Cooperative Acute Stroke Study III definition) were recorded.[4] mRSs were determined at 3-month clinical follow-up or by telephone interview by certified personnel as part of our existing standard of care for all EVT cases.

Statistics

Continuous variables are reported as means and standard deviations (SDs) or median and interquartile ranges, as appropriate. Dichotomous variables are reported as proportions and were compared by Pearson's chi-squared test. Clinical outcomes were dichotomized as favorable (mRS 0–2) or unfavorable (mRS 3–6) and compared using Pearson's chi-squared test. The significance level for two-sided testing of hypotheses was 0.05. SPSS 25 was used for statistical analyses.

Ethics

Retrospective chart review was approved by our medical institutional review board for all EVT cases.

Results

Baseline Population Characteristics

Over the study period, a total of 248 patients underwent EVT, 204 (82%) <6 hours, and 44 (18%) ≥6 hours from LTSN. Baseline characteristics including age, sex, and vascular risk factors did not differ between groups (Table 1).

Most patients treated by EVT were transfers from PSC in the early (152 (75%)) and late (32 (73%)) windows. Median (IQR) LTSN to CSC time was 188 (134–242) minutes in the early and 586 (430–799) minutes in the late window (difference: 398 minutes). Median (IQR) first time seen symptomatic to CSC time was

Table 1: Baseline characteristics of patients undergoing EVT

	Early window ($n = 204$)	Late window ($n = 44$)
Age (mean ± SD)	70 ± 15	70 ± 16
Women, n (%)	99 (49)	21 (48)
NIHSS (median, IQR)	18 (15–23)	17 (13–21)
ASPECTS (median, IQR)	9 (8–10)	9 (7–9)
Hypertension, n (%)	127 (62)	29 (66)
Dyslipidemia, n (%)	103 (50)	19 (43)
Diabetes, n (%)	39 (19)	9 (20)
Smoking, n (%)	44 (22)	10 (23)
Atrial fibrillation, n (%)	62 (30)	11 (25)
Premorbid mRS 0–2, n (%)	173 (85)	39 (89)
Witnessed onset, n (%)	164 (80)	2 (5)
Wake-up stroke, n (%)	6 (3)	29 (66)
Unwitnessed onset (non-wake-up), n (%)	34 (17)	13 (29)
Transfer from PSC, n (%)	152 (75)	32 (73)
Occlusion site		
Cervical carotid, n (%)	3 (1)	2 (5)
Tandem occlusion	20 (10)	8 (18)
Intracranial carotid	40 (20)	8 (18)
M1	114 (56)	20 (45)
M2	23 (11)	6 (14)
M3	2 (1)	0
A2	2 (1)	0
Collaterals		
Collateral grading available, n (%)	149 (73)	30 (68)
0 (n, % of available)	27 (18)	8 (27)
1	59 (39)	6 (20)
2	43 (29)	10 (33)
3	16 (11)	3 (10)
4	4 (3)	3 (10)

170 (122–210) minutes in the early and 197 (152–282) minutes in the late window (difference: 27 minutes) (Table 2). The late window group mainly consisted of patients with strokes of unknown onset (42 (95%)) rather than late-presenting strokes (2 (5%)). Amongst late window strokes of unknown onset, 29/42 (69%) were wake-up strokes.

Initial median (IQR) NIHSS scores were similar (early: 18 (15–23) vs. late: 17 (13–21)), as were median ASPECT scores (early: 9 (8–10) vs. late: 9 (7–9)). Collateral status was available in 149 (73%) patients in the early and 30 (68%) in the late window. The proportion of patients with poor collateral status (grade 0–1) was slightly higher in the early (86/149 (58%)) than in the late (14/30 (47%)) window.

Recanalization Therapy and Functional Outcomes

Thrombolysis was more frequently administered to early-presenting patients (137 (67%) vs. 18 (41%)). Standard stroke

Table 2: Recanalization therapy in patients undergoing EVT

	Early window ($n = 204$)	Late window ($n = 44$)
Intravenous thrombolysis, n (%)	137 (67)	18 (41)
Door to needle (median, IQR)	48 (35–70)	46 (32–62)
LTSN to CSC	188 (134–242)	586 (430–799)
FTSS to CSC	170 (122–210)	197 (152–282)
CSC to groin	17 (12–38)	21 (13–41)
CSC to recanalization	57 (40–82)	58 (39–73)
Recanalization		
TICI 0–1, n (%)	35 (17)	7 (16)
TICI 2 A	28 (14)	8 (18)
TICI 2B-3	141 (69)	29 (66)

FTSS = first time seen symptomatic.

Table 3: Adverse event in patients undergoing EVT

	Early window ($n = 204$)	Late window ($n = 44$)	p-Value
Asymptomatic hemorrhagic transformation, n (%)	38 (19)	12 (27)	0.19
Symptomatic hemorrhagic transformation	12 (6)	4 (9)	0.43
Vessel perforation	8 (4)	1 (2)	0.60
Distal embolization	7 (3)	1 (2)	0.69
Arterial dissection	4 (2)	2 (5)	0.31

treatment metrics, including door-to-needle, CSC-to-groin, and CSC-to-recanalization, did not differ (Table 2). Proportions of favorable recanalization (mTICI 2b-3) were similar in the early (141 (69%)) and late (29 (66%)) windows.

Safety Outcomes

The proportions of sHT at 24 hours did not differ in the early (12 (6%)) and late (4 (9%)) windows ($p = 0.43$). When combining 24-hour symptomatic hemorrhagic transformation (sHT) and asymptomatic hemorrhagic transformation, more events occurred in the late window (early vs. late: 50 (25%) vs. 16 (36%)), but this did not reach statistical significance ($p = 0.11$) (Table 3).

Three-Month Outcomes

Among patients with available 3-month mRS scores (early: 192/204 (94%) and late: 41/44 (93%)), the proportions achieving functional independence (mRS 0–2) were similar (early: 80 (42%) vs. late: 16 (39%), $p = 0.72$) (Figure 1).

Discussion

In this study, we found that EVT selection based on standard neuroimaging resulted in similar proportions of functional independence in both early and late windows, with no significant

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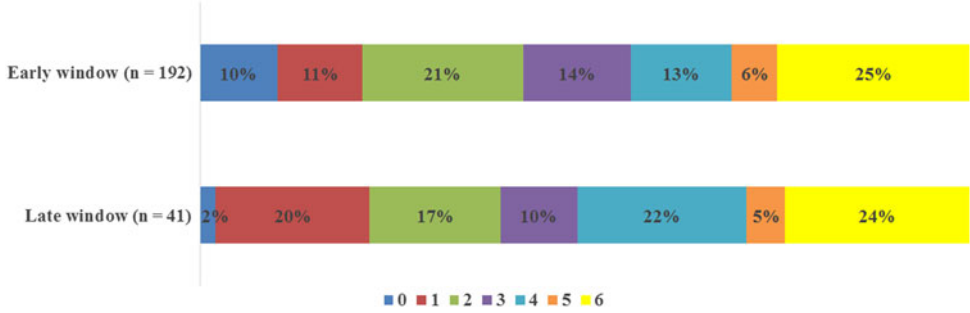

Figure 1: *Three-month modified Rankin scores (mRSs) after endovascular therapy (EVT) in the early and late windows.*
All patients undergoing EVT with a documented mRS score are included. Scores on the mRS range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, and 6 death. Clinical outcomes are dichotomized as favorable (mRS 0–2) or unfavorable (3–6).

increase in hemorrhagic transformation. These results are concordant with previous studies retrospectively evaluating NCCT- and CTA-based late window stroke patient selection for EVT.[5,6] These findings specifically apply to patients with strokes of unknown onset, as they formed almost all the late window group.

American Heart Association guidelines recommend strict application of the DAWN and DEFUSE-3 perfusion-based criteria for patient selection if LTSN is $\geq$ 6 hours, as no other eligibility criteria have been prospectively validated.[7] Canadian guidelines make the same recommendation for EVT admissibility in the late window.[8] However, no recommendations are made for centers without access to perfusion neuroimaging.

Late window LVO stroke selection strategies should seek to identify patients for whom the estimated benefit of recanalizing penumbra offsets the risk associated with hemorrhagic transformation and other complications of EVT. Perfusion-based trial's inclusion criteria allowed for moderate core volumes (up to 21–51 mL in DAWN and 70 mL in DEFUSE-3). However, EVT-treated patients had significantly smaller median estimated core volumes (7.6 mL in DAWN and 9.4 mL in DEFUSE-3, with a median estimated penumbra of 114.7 mL). Haussen et al. established a fair correlation between ASPECTS and CT-perfusion results.[9] NCCTs with an ASPECTS $\geq$ 6 had a CT-perfusion median core volume $\leq$ 20 mL, and most were $\leq$50 mL. Another study found no difference between ASPECTS and CT-perfusion's accuracy for hyperacute MRI diffusion lesion volume prediction.[10] Further data suggest higher inter-rater agreement of ASPECTS with increasing time from stroke onset, making the score more reproducible in the late window.[11] On the other hand, while NCCT might be able to estimate core volume, it cannot measure penumbra. Clinical-radiological mismatch could serve as a surrogate for penumbra, particularly with very proximal occlusions (terminal internal carotid artery or M1) and high ASPECT scores ($\geq$8), suggesting sizeable brain regions at risk and small core volumes.

In this study, late window LVO stroke patients selected with NCCT achieved similar 3-month functional independence outcomes as patients in the MR CLEAN trial.[12] These results suggest that in centers where perfusion neuroimaging is not available, NCCT and CTA might accurately select late window EVT candidates, particularly for strokes of unknown onset. This also applies to PSC where automated perfusion software might not be affordable nor justifiable due to low LVO stroke volume, but who nevertheless see patients amenable to EVT. In these cases, repeating perfusion imaging at CSC after transfer might lead to further delays and increase radiation exposure. The ESCAPE trial included patients up to 12 hours from symptom onset using NCCT and CTA results, excluding patients with poor collateral status.[13] A subgroup analysis subsequently showed no heterogeneity in EVT effect in the early and late windows.[13,14] However, the 39% proportion of mRS 0–2 outcomes observed in this study is lower than the 49% in DAWN and 44% in DEFUSE-3. Baseline NCCT ASPECT score modified the effect of EVT in the DAWN trial,[15] but it has not been prospectively demonstrated that late window patients with a favorable ASPECT score alone benefit from EVT.

Two-thirds of the late window patients in this study were wake-up strokes. Epidemiological data suggest that, in Canada, 14% of strokes occur at wake-up.[16] Silva et al. report similar infarct volumes and CT-perfusion cerebral blood flow-cerebral blood volume mismatch rates in strokes of known onset and wake-up strokes.[17] A significant proportion of wake-up strokes likely occur near awakening. In a secondary analysis of the DAWN trial, benefit of EVT was independent of the mode of presentation.[18] Trials should separate wake-up strokes from other unknown onset and late presenting strokes, and the impact of recanalization therapy should be differentially evaluated in these subgroups.

Prior studies support the notion that NCCT and CTA can safely select wake-up stroke patients for reperfusion therapy. Hill et al. thrombolyzed 20 wake-up stroke patients (median ASPECTS = 9) with no incident sICH.[19] Bal et al. documented no sICH amongst a cohort of 29 moderately severe wake-up stroke patients (median ASPECTS = 7) who received recanalization treatment.[20] Efficacy of intravenous thrombolysis for late-window patients has been demonstrated in the WAKE-UP and EXTEND trials, where the benefit of recanalization offset the 1.6–5.3% increase in sICH in the alteplase versus placebo groups.[21,22] These results and our local experience confirm the notion that time is a single variable that must be integrated with imaging results and patient characteristics for recanalization treatment candidate selection.

Limitations of this study include its small size, single-center retrospective design, and use of patients LTSN < 6 hours as the control group, as patients with favorable NCCT profiles in

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the late window might represent a select subset of cases with better penumbral tolerance to ischemia (i.e., the late window paradox).[23] Most patients were strokes of unknown onset, and results are not generalizable to late-presenting strokes of known onset. Collateral grading/triple phase CTA was not available in all cases. Proportions of poor collateral status and occlusion sites varied in the early and late windows, which may have differentially influenced outcomes. This study might have been underpowered to detect a statistically significant difference in adverse events. NCCT and CTA results as well as outcomes were not available for late window patients who were evaluated but not selected for EVT, limiting our finding's generalizability, as other undocumented factors might have influenced the decision to perform EVT. Without documentation of these cases, it was impossible to determine the proportion of late-presenting patients considered eligible for EVT based on NCCT and CTA results.

Conclusion

Late-window LVO anterior circulation stroke patients selected for EVT using NCCT and CTA achieved similar 3-month functional outcomes to early presenting patients, with no increase in sHT. In the late window, NCCT- and CTA-based patient selection for EVT appears safe and could be an alternative to perfusion neuroimaging, especially for strokes of unknown onset with high ASPECT scores. Prospective studies comparing both approaches are warranted.

Disclosures

M-CB, AN, FF, FK, ND, GJ, CS, and CO report no conflicts. YD reports personal fees from Servier, outside the submitted work. LCG reports grants and personal fees from Servier, personal fees from Bayer, personal fees from Pfizer, and personal fees from Bristol-Myers Squibb, outside the submitted work. AYP reports research support from Servier and Bayer, outside the submitted work.

Statement of authorship

M-CB and AN designed and conceptualized the study, collected data, performed analysis and interpretation of the data, and drafted the manuscript. FF reviewed imaging and revised the manuscript. FK, ND, YD, LCG, GJ, AYP, and CS provided data and revised the manuscript. CO designed and conceptualized the study, collected data, reviewed imaging, and revised the manuscript.

References

1. 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. 2018;378(1):11–21.
2. 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(8):708–18.
3. Souza LC, Yoo AJ, Chaudhry ZA, et al. Malignant CTA collateral profile is highly specific for large admission DWI infarct core and poor outcome in acute stroke. AJNR Am J Neuroradiol. 2012; 33(7):1331–6.
4. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008; 359(13):1317–29.
5. Santos T, Carvalho A, Cunha AA, et al. NCCT and CTA-based imaging protocol for endovascular treatment selection in late presenting or wake-up strokes. J Neurointerv Surg. 2019;11(2): 200–3.
6. Motyer R, Thornton J, Power S, et al. Endovascular thrombectomy beyond 12 hours of stroke onset: a stroke network's experience of late intervention. J Neurointerv Surg. 2018;10(11):1043–6.
7. 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(3): e46–110.
8. Boulanger JM, Lindsay MP, Gubitz G, et al. Canadian stroke best practice recommendations for acute stroke management: prehospital, emergency department, and acute inpatient stroke care, 6th edition, update 2018. Int J Stroke. 2018;13(9):949–84.
9. Haussen DC, Dehkharghani S, Rangaraju S, et al. Automated CT perfusion ischemic core volume and noncontrast CT ASPECTS (Alberta Stroke Program Early CT Score): correlation and clinical outcome prediction in large vessel stroke. Stroke. 2016;47(9): 2318–22.
10. Demeestere J, Garcia-Esperon C, Garcia-Bermejo P, et al. Evaluation of hyperacute infarct volume using ASPECTS and brain CT perfusion core volume. Neurology. 2017;88(24):2248–53.
11. Naylor J, Churilov L, Chen Z, et al. Reliability, reproducibility and prognostic accuracy of the Alberta stroke program early CT score on CT perfusion and non-contrast CT in hyperacute stroke. Cerebrovasc Dis. 2017;44(3–4):195–202.
12. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015;372(1):11–20.
13. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372(11):1019–30.
14. Evans JW, Graham BR, Pordeli P, et al. Time for a time window extension: insights from late presenters in the ESCAPE trial. AJNR Am J Neuroradiol. 2018;39(1):102–6.
15. Bhuva P, Yoo AJ, Jadhav AP, et al. Noncontrast computed tomography Alberta stroke program early CT score may modify intra-arterial treatment effect in DAWN. Stroke. 2019: Strokeaha1 18024583.
16. Nadeau JO, Fang J, Kapral MK, et al. Outcome after stroke upon awakening. Can J Neurol Sci. 2005;32(2):232–6.
17. Silva GS, Lima FO, Camargo EC, et al. Wake-up stroke: clinical and neuroimaging characteristics. Cerebrovasc Dis. 2010;29(4): 336–42.
18. Jadhav AP, Aghaebrahim A, Jankowitz BT, et al. Benefit of endovascular thrombectomy by mode of onset: secondary analysis of the DAWN trial. Stroke. 2019;50(11):3141–6.
19. Hill MD, Kenney C, Dzialowski I, et al. Tissue Window in Stroke Thrombolysis study (TWIST): a safety study. Can J Neurol Sci. 2013;40(1):17–20.
20. Bal S, Bhatia R, Shobha N, et al. Stroke- on- awakening: safety of CT-CTA based selection for reperfusion therapy. Can J Neurol Sci. 2014;41(2):182–6.
21. Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-guided thrombolysis for stroke with unknown time of onset. N Engl J Med 2018;379(7):611–22.
22. 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(19):1795–803.
23. Albers GW. Late window paradox. Stroke. 2018;49(3):768–71.

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