Stroke: Vascular and Interventional Neurology

ORIGINAL RESEARCH

Late Window Imaging Selection for Endovascular Therapy of Large Vessel Occlusion Stroke: An International Survey

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BACKGROUND: Current stroke guidelines recommend advanced imaging (computed tomography [CT] perfusion or magnetic resonance imaging) prior to endovascular therapy (EVT) in patients with late presentation of large vessel occlusion. Adherence to guidelines may be constrained by resources or timely access to imaging. We sought to understand the factors which influence late window imaging selection for EVT candidates with large vessel occlusion.

METHODS: We conducted an international survey from January to May 2022. The questions aimed to identify advanced imaging and treatment decisions based on access to imaging, time delays, and simulated patient scenarios.

RESULTS: There were 3000 invited participants and 1506 respondents, the majority (89.6%) from comprehensive stroke centers in high-income countries. Neurointerventionalists comprised 31.8% and noninterventionalists 68.2% of respondents. Overall, 70.7% reported routine use of advanced imaging for late EVT selection, and 63.6% reported its usage in every case. There was greater availability of advanced imaging in comprehensive stroke centers versus primary stroke centers (67.0% versus 33.7%; $P<0.0001$), and high- versus low-middle income countries (70.5% versus 44.5%; $P<0.0001$). When presented with a

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late window patient, 41.6% would complete CT perfusion or magnetic resonance imaging prior to EVT, 25.4% would perform CT perfusion or magnetic resonance imaging prior to IVT and EVT, and 25.8% would refer to EVT without advanced imaging. If advanced imaging was not readily available, 70.1% would refer a patient to EVT based on CT in the late window. Additional time delay within 20 minutes to obtain advanced imaging was considered acceptable in 77.7% of respondents.

CONCLUSION: Current guidelines for imaging late window EVT candidates are inconsistent with imaging decisions by physicians. Most respondents consider an imaging delay of greater than 20 minutes unacceptable. Access to advanced imaging was greater in comprehensive stroke centers and high-income countries. In the case of limited access most respondents would consider EVT based on CT only.

Key Words: endovascular therapy ■ large vessel occlusion ■ late window ■ mechanical thrombectomy

In 2018, the DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention) and DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3) trials opened the paradigm of care for patients with large vessel occlusion (LVO) stroke presenting in the late window, demonstrating a benefit of endovascular therapy (EVT) for selected patients with LVO 6 to 24 hours from last known well.[1,2] Advanced imaging modalities computed tomography perfusion (CTP) and magnetic resonance imaging (MRI) were utilized in these studies to select patients with salvageable tissue who were deemed likely to benefit from late window reperfusion therapy. Although the trial selection criteria and conclusions have been the object of criticism,[3,4] subsequent guidelines recommended the use of advanced imaging in the selection of patients presenting in the late window, sometimes limiting access to questionable perfusion thresholds. For example, the 2019 American Heart Association (AHA)/American Stroke Association (ASA) Guidelines for the Early Management of Patients With Acute Ischemic Stroke stated "DAWN or DEFUSE 3 eligibility should be strictly adhered to in clinical practice," and the 2019 European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischemic Stroke stated that advanced imaging is "necessary" prior to treatment of these patients.[5,6] The EVT guidelines in Japan stated that "Mechanical thrombectomy within 16 hours of time last known well (TLKW) is strongly recommended…. with Alberta Stroke Program Early CT Score (ASPECTS) ≥7 on MRI DWI," and "within 24 hours, recommended for patients with mismatch between ischemic core volume (CTP or MRI DWI) and neurological deficits or a hypoperfusion lesion on perfusion imaging."[7] Other guidelines, including that of the Chinese Stroke Association[8] and the Society of Vascular and Interventional Neurology,[9] have been less specific.

Adherence to these guidelines may not be practical or necessary in many practice paradigms, especially in lower resource settings[4,10,11] or more generally when additional imaging may incur unnecessary delays to treatment.[12,13] Access to acute MRI or CTP is not readily available 24/7, within acceptable delays, or performed across many stroke centers.[11,14–16] In a survey of imaging resources across 17 countries in Africa, CT scan was available in all countries, whereas CTP was available in only 2 countries, and MRI available in 16 countries. Whether or not these imaging modalities were available in an acute emergency was not reported.[15–18] Moreover, several centers in Central America and the United Kingdom have not offered thrombectomy in the late window during evening or weekend hours for lack of available staff to run the advanced imaging protocols (personal communication, TNN 2021).

Several studies have since emerged describing noncontrast CT (NCCT) as an alternative modality with comparable outcomes as advanced imaging in the triage of patients presenting in the late window.[17–20] In a multicenter study of patients presenting in the late window presenting directly to an endovascular center (n=484 patients), longer door-to-puncture times were noted in patients who were selected with CTP (median [interquartile range] 93 [72–118) minutes) or MRI (98, [78–135] minutes) compared with NCCT alone (76 [50–107] minutes; $P<0.001$).[19]

There is considerable uncertainty regarding the proper care of patients presenting in the late time window. The best course of action (ie, transfer the patient to a stroke center for advanced imaging prior to EVT versus NCCT alone or CTP at the local institution prior to EVT) remains unknown.[24,25] This uncertainty may translate into a wide variability in practice.[26] Knowledge of the remaining clinical uncertainty may help in planning future trials.

In this context, we aimed to understand the current perspectives and approaches to late window imaging selection of patients with LVO for EVT by circulating a questionnaire to physician stroke and neurointerventional providers involved in the care of the acute stroke patient. We hypothesized that access to advanced imaging would not be readily available across most stroke centers, that access would be less available in primary stroke centers (PSCs, compared with comprehensive stroke centers [CSC]) and centers in low- or middle-income (compared with high-income) countries.

Nonstandard Abbreviations and Acronyms

ASPECTS	Alberta Stroke Program Early CT Score
CTA	computed tomography angiography
CTP	computed tomography perfusion
LVO	large vessel occlusion
NCCT	noncontrast computed tomography

CLINICAL PERSPECTIVE

- We sought to understand physician perspectives on the use of advanced imaging (magnetic resonance imaging, computed tomography perfusion) for late window endovascular therapy candidates, in accordance with current stroke treatment guidelines. In the context of limited access to advanced imaging or potential time delays in treatment, physician opinions conflicted with American Heart Association/American Stroke Association or European Stroke Organisation guidelines for late window endovascular therapy candidates. Moreover, access to advanced imaging was significantly lower in low- or middle-income countries and primary stroke centers.
- Results of the MR CLEAN LATE (Endovascular Treatment of Acute Ischemic Stroke in the Netherlands for Late Arrivals) and RESILIENT-Extend (Randomization of Endovascular Treatment in Acute Ischemic Stroke in the Extended Time Window) trials will be important in understanding treatment decisions in the absence of computed tomography perfusion or magnetic resonance imaging for an extended time window.

METHODS

Data are available from the corresponding author upon reasonable request.

Design

Study data were collected and managed using the Research Electronic Database Capture system, a secure, web-based application hosted at Boston University, Clinical and Translational Science Institute 1UL1TR001430.1.[27]

The online survey consisted of 11 questions on 11 distinct web pages, with estimated time completion of 3–5 minutes. The survey was divided into 9 sections: participant background, simulated case study, imaging triage decisions, decision making according to guidelines, availability and use of advanced imaging, time to complete advanced imaging studies, case of large core patient in the late window, and regret questions related to the pursuit or deferral of EVT. The questions were developed by the lead, senior author, and methodologists with subsequent feedback from coauthors. The rationale for the creation of simulated case-scenarios was based on the lack of specific guidelines or where therapeutic decisions were under current debate (eg, case 1: diagnostic and therapeutic decisions for a patient with a wake-up stroke, 9 hour time last known well, ASPECTS 9, M1 occlusion; and case 2: diagnostic and therapeutic decisions for a patient presenting 7 hours from symptom onset, National Institute of Health Stroke Scale 17, a left M1 occlusion and CT ASPECTS of 4 to mimic the results of RESCUE (Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism) -Japan LIMIT trial[27].

A pilot phase was conducted where coauthors conducted a test-run of the survey and provided additional feedback for final release of the survey. The survey was distributed from January 20, 2022 to May 11, 2022. RESCUE-Japan LIMIT study presented at the International Stroke Conference on February 5, 2022, a question was added regarding management of large core infarction,[27] at which time point 174 responses had been received.

The survey was translated into Chinese by a native Chinese speaker (Y.C.). This translation was verified by another Chinese physician (X.H.) to ensure consensus in the translated version. The survey was tested by Y.C. to ensure the identical branching logic would occur in the translated Chinese version.

Approval by the local research ethics board was obtained via the Boston Medical Center Institutional Review Board (IRB H-37519). The study was classified as exempt.

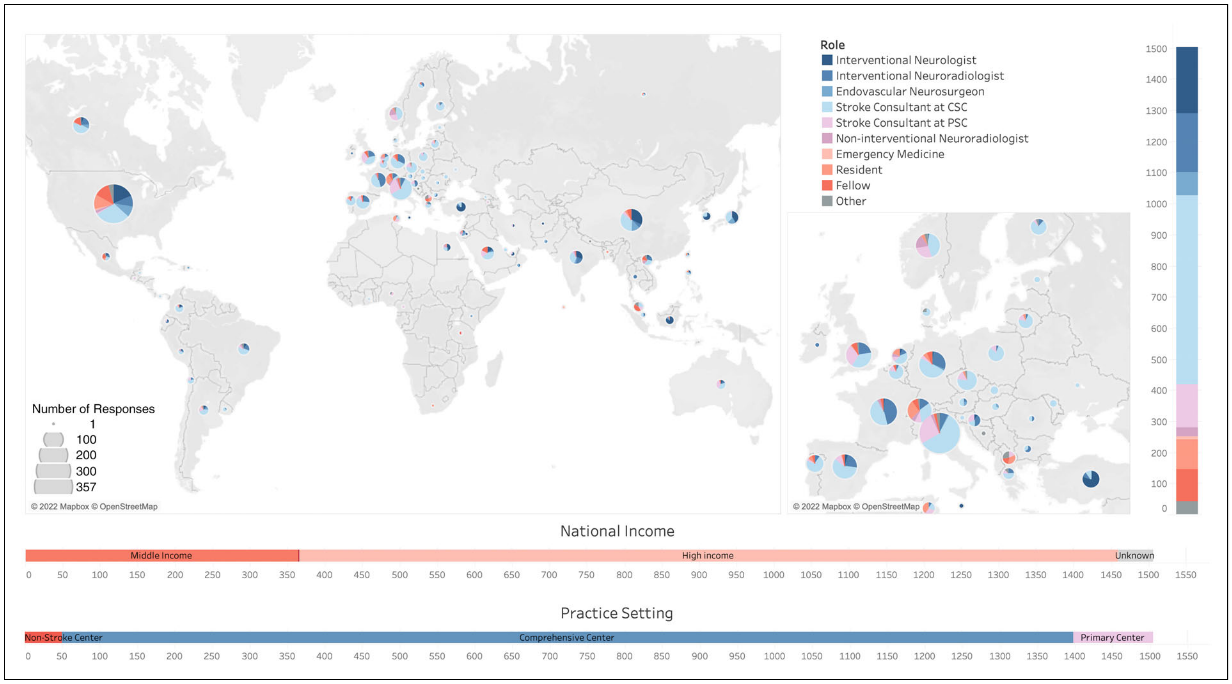

FIGURE 1. World map demonstrating responses from each country by physician specialty, distribution by comprehensive versus primary stroke center, and middle- versus high-income country.

Distribution

Organizations that distributed the link included the Argentina Neurology Society, Brazil Stroke Society, German Stroke Trial Network, the Italian Stroke Society, the Colombia Association of Neurology, the Norwegian Stroke Organization, the Japanese Society for Neuroendovascular Therapy (JSNET), Dutch Neurovascular Society, the British and Irish Association of Stroke Physicians, Welsh Association of Stroke Physicians, Stroke Clinical Trials Network in Ireland, International stroke trial network of a coauthor (U.F.), the Brazil Stroke Society, the Italian Stroke Association, the Madrid Association of Neurology, Indonesian Neurointerventionalists, the Lithuanian Stroke Association, the Society of Vascular and Interventional Neurology (SVIN), the Global SVIN COVID-19 stroke registry, the Whatsapp or Telegram group for 3 Neurointerventional groups, the WeChat Stroke Network in China, MT2020, and Women in Neurointervention.

Statistical Analysis

All statistical analyses were conducted using JMP 15 software (SAS Institute, Cary, NC). Duplicate responses, blank responses, responses without an email address provided, and responses to demographic questions only were discarded prior to analysis. Country income was stratified according to World Bank classification. Differences between groups were assessed with the chi-squared or Fisher's exact test. Statistical significance for all tests was set at α=0.05. Figures were created in Tableau.

RESULTS

Of over 3000 invited participants, there were 1696 survey responses across 82 countries (56.5% response). After the removal of 217 duplicate responses, 27 blank responses, 13 responses without email identification, and 42 responses with only answers to the demographic section, there were 1506 responses (50.2% response rate). The completion rate was 63.9% (962/1506) (Figure 1).

Demographics of Respondents

Among respondents, the majority of respondents (89.6%) originated from CSC, compared with 7.1% from PSCs, and 3.3% from nonstroke centers. There were 478 (31.8%) neurointerventionalists and 1027 (68.2%) noninterventional physicians. The distribution by specialty or training level were as follows (n, %): stroke neurologist at PSC (141, 9.4%), stroke neurologist at endovascular center (606, 40.3%), neuroradiologist (27, 1.8%), interventional neurologist (215, 14.3%), interventional neuroradiologist (189, 12.6%), endovascular neurosurgeon (74, 4.9%), emergency medicine (10, 0.7%), fellow (104, 6.9%), and resident (97, 6.5%). The majority of respondents were from high-income

TABLE 1. Descriptive Characteristics of Respondents

Characteristic	n (column %)
Age group	
≤30	94 (6.25)
31–50	1162 (77.21)
51–64	230 (15.28)
65+	19 (1.26)
Specialty	
Stroke neurologist	
At PSC or nonstroke center	141 (9.37)
At CSC	606 (40.27)
Neuroradiologist	27 (1.79)
Neurointerventionist	
Interventional neurologist	215 (14.29)
Interventional neuroradiologist	189 (12.56)
Endovascular neurosurgeon	74 (4.92)
Emergency medicine	10 (0.66)
Trainee	
Fellow	104 (6.91)
Resident	97 (6.45)
Other	42 (2.79)
Specialty category	
Interventionist	478 (31.76)
Noninterventionist	1027 (68.24)
Practice setting	
Comprehensive stroke center	
Academic	924 (61.44)
Public/private	424 (28.19)
Primary stroke center	106 (7.05)
Nonstroke center	50 (3.32)
Continent	
Africa	9 (0.62)
Asia	351 (24.06)
Australia and Oceana	25 (1.71)
Europe	554 (37.97)
North America	436 (29.88)
South America	84 (5.76)
Income	
High income	1093 (74.91)
Middle income	366 (25.09)

CSC indicates comprehensive stroke centers; and PSC, primary stroke centers.

countries (1093, 74.9%) compared with middle-income countries (366, 25.1%) (Table 1).

Late Window Patient Case Triage

A case was presented of a 78-year-old woman from an assisted living facility due to mild cognitive impairment with a wake-up stroke, last known well time 9 hours, with ASPECTS of 9, and M1 occlusion (Q1). There were 1424 respondents of which 41.6% would complete CTP or MRI prior to EVT alone, 25.4% would complete CTP or MRI prior to IVT combined reperfusion therapies (IVT with EVT), whereas 25.8% would go

TABLE 2. Survey Questions and Responses

Question	n (column %)
Q1. 78-year old, wakeup, 9-h LKW, ASPECTS 9, M1	
Complete CTP or MRI prior to EVT	592 (41.57)
Complete CTP or MRI prior to combined IVT and EVT	362 (25.42)
Direct to EVT	368 (25.84)
IVT alone	19 (1.33)
Medical management	51 (3.58)
Refer to EVT center	32 (2.25)
Q2. Agree to CTA/CTA rather than advanced imaging in late window	
Individual decisions	251 (17.12)
CT/CTA/CTP	706 (48.16)
CT/CTA only	373 (25.44)
MRI/MRP	136 (9.28)
Q3. Given uncertainty, which are you most comfortable with?	
Following your standard practice based on your expertise and evidence	444 (30.71)
Following guidelines	584 (40.39)
Following standard of care as established in my region or country	132 (9.13)
No consistent strategy	286 (19.78)
Q4. Is advanced imaging available 24/7 at your institution?	
Yes, and we use it routinely	1020 (70.69)
Yes, but it is not always immediately available	202 (14.00)
No, it is not available	91 (6.31)
No, it is only available on weekdays	63 (4.37)
Only available as a special request	67 (4.64)
Q5. Do you routinely use advanced imaging in late window LVO?	
Advanced imaging is not available	63 (4.38)
No, some cases only	360 (25.00)
No, use CT/CTA only	101 (7.01)
Yes, every case	916 (63.61)
Q6. Late window, immediate advanced imaging unavailable, LVO, n=1376	
Refer to thrombectomy based on CT	964 (70.06)
Refer to center with advanced imaging	167 (12.14)
Medical management only	105 (7.63)
Wait for advanced imaging	103 (7.49)
Enroll in RCT	37 (27.01)
Q7. How long (additional time) to obtain advanced images?	
5 min	307 (24.40)
10 min	428 (34.02)
20 min	254 (20.19)
30 min	155 (12.32)
45 min	53 (4.21)
60 min	42 (3.34)
90 min	11 (0.87)
120 min	8 (0.64)
Q8. How long is acceptable delay for advanced images?	
0 min	35 (2.78)
5 min	220 (17.46)
10 min	442 (35.08)
20 min	282 (22.38)
30 min	204 (16.19)
45 min	22 (1.75)

(*Continued*)

TABLE 2. (Continued)

Question	n (column %)
60 min	39 (3.10)
90 min	6 (0.48)
120 min	10 (0.79)
Q9. 70-year-old, 7 h onset, NIHSS 17, left M1 occlusion, ASPECTS 4	
CTP, then triage	453 (35.61)
Direct to EVT	148 (11.64)
Enroll in RCT	307 (24.14)
Medical management	180 (14.15)
MRI, then triage	184 (14.47)

ASPECTS indicates Alberta Stroke Program Early CT Score; CTA, computed tomography angiography; CTP, computed tomography perfusion; EVT, endovascular therapy; LKW, last known well; LVO, large vessel occlusion; MRI, magnetic resonance imaging; NIHSS, National Institute of Health Stroke Scale; and RCT, randomized controlled trial.

directly to EVT without further imaging (Tables 2 and 3) (Supporting information).

Imaging Triage in Late Window

The results of the CT for Late Endovascular Reperfusion study[19] were reviewed, which showed that patients selected for EVT using CT angiography (CTA) had similar outcomes to those selected with CTP or MRI. Participants were asked if one would agree to base reperfusion therapies for patients in the 6–24-hour window on CT and CTA imaging as compared with CTP/MRI (Q2). The distribution of agreement for imaging modality selection of CT/CTA, CT/CTA/CTP, MRI/MRP, or individual decisions was 25.4%, 48.2%, 9.3%, and 17.1%, respectively (n=1466 responses) (Table 2).

Adherence to Guidelines

The AHA/ASA[9,21] and European Stroke Organisation (ESO)[9,19] guidelines were then reviewed, citing that advanced brain imaging for patient selection was recommended for selection of patients presenting in the late window (Q3). The question was raised given the uncertainty, how one would proceed. There were 30.7% of respondents who would follow standard clinical practice based on their expertise and evidence, 40.4% would follow the current guidelines, 9.1% would follow the standard of care as established in their region or country, whereas 19.8% had no consistent strategy with hybrid of practice-based and guideline-based (n=1446 responses) (Table 2).

Advanced Imaging Availability and Utilization (Q4–6)

We asked participants regarding the availability of advanced imaging (ie, CTP/MRI) at their institution 24/7 (Q4). Respondents stated: (1) yes with routine use, 70.7%, (2) yes but not always immediately available, 14.0%, (3) not available, 6.3%, (4) only available on weekdays, 4.4%, and (5) only available as a special request, 4.6%.

We asked participants regarding utilization of advanced imaging (Q5). Respondents indicated: (1) yes in every case, 63.6%, (2) some cases, 25.0%, (3) advanced imaging is not available 4.4%, and (4) treatment decisions are based on CT/CTA, 7.0% (Table 2). The use of advanced imaging with every case was higher among respondents from CSCs versus PSCs (67.0% versus 33.7%; $P<0.0001$), and higher among respondents from high- versus low-middle income countries (70.5% versus 44.5%; $P<0.0001$) (Table 4, Table 5).

Participants were then asked if advanced imaging was not readily available, how they would manage a patient with LVO presenting in the 6–24 hour time window (Q6). The triage was as follows: 70.1% would refer to EVT based on CT scan imaging, 12.1% would refer to a center with advanced imaging, 7.6% would treat the patient with medical management only, 7.5% would wait for advanced imaging (ie, technologist arrives on call to hospital), and 2.7% would enter the patient in a randomized controlled trial (RCT) (Table 5).

Time to Perform Advanced Imaging

In respondents where advanced imaging was available (n=1376), participants were asked how long it takes to perform the study (Q7). The time duration was as follows: 5 minutes, 24.4%; 10 minutes, 34.0%; 20 minutes, 20.2%; 30 minutes, 12.3%; 45 minutes, 4.2%; 60 minutes; 3.3%; 90 minutes, 0.9%; and 120 minutes 0.6% (Table 2).

Respondents were then asked how long they considered additional time delay would be acceptable to obtain advanced imaging for patient selection, as compared with NCCT (Q8). The time distribution was as follows: 0 minutes, 2.8%; 5 minutes, 17.5%; 10 minutes, 35.1%; 20 minutes, 22.4%; 30 minutes, 16.2%; 45 minutes, 1.8%; 60 minutes, 3.1%; 90 minutes 0.5%; 120 minutes, 0.8% (Tables 2 and 6).

Of these respondents, the median time by which it was greater than acceptable time was 10 minutes, and the mean time by which it was greater was 17.2 minutes.

Large Core Infarct Patient Triage

After the Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism (RESCUE)-Japan LIMIT results, we included in the survey a 70-year-old patient presenting 7 hours from symptom onset, National Institute of Health Stroke Scale 17, left M1 occlusion, and CT ASPECTS of 4 (Q9). Respondents stated for

TABLE 3. Survey Question on Favorable ASPECTS in Late Window

Question	N (row %)						
78-year-old, wakeup, 9-h LKW, ASPECTS 9, M1							
	Complete CTP or MRI prior to EVT	**Complete CTP or MRI prior to combined IVT and EVT**	**Direct to EVT**	**IVT alone**	**Medical management**	**Refer to EVT center**	***P* value**
Overall	592 (41.57)	362 (25.42)	368 (25.84)	19 (1.33)	51 (3.58)	32 (2.25)	–
Specialty category							
Interventionist	206 (45.47)	50 (11.04)	179 (39.51)	2 (0.44)	11 (2.43)	5 (1.10)	<0.0001
Noninterventionist	385 (39.69)	312 (32.16)	189 (19.48)	17 (1.75)	40 (4.12)	27 (2.78)	
Practice setting							
Comprehensive stroke center	549 (42.89)	313 (24.45)	348 (27.19)	16 (1.25)	38 (2.97)	16 (1.25)	<0.0001*
Primary stroke center	26 (26.80)	38 (39.18)	11 (11.34)	2 (2.06)	9 (9.28)	11 (11.34)	
Nonstroke center	15 (33.33)	11 (24.44)	9 (20.00)	1 (2.22)	4 (8.89)	5 (11.11)	
Age							
≤50	508 (42.72)	278 (23.38)	328 (27.59)	9 (0.76)	41 (3.45)	25 (2.10)	<0.0001
>50	84 (35.90)	84 (35.90)	40 (17.09)	10 (4.27)	10 (4.27)	6 (2.56)	
Income							
High income	429 (42.18)	265 (26.06)	257 (25.27)	13 (1.28)	33 (3.24)	20 (1.97)	0.8104
Low or middle income	149 (41.05)	87 (23.97)	98 (27.00)	4 (1.10)	16 (4.41)	9 (2.48)	

ASPECTS indicates Alberta Stroke Program Early CT Score; CTP, computed tomography perfusion; EVT, endovascular therapy; LKW, last known well; and MRI, magnetic resonance imaging.

management as follows: medical management, 14.2%; CTP triage, 35.6%; MRI triage 14.5%; direct to angio for EVT, 11.6%; and randomization into an ongoing large core infarct trial study, 24.1% (Table 2).

DISCUSSION

Therapeutic decisions in acute stroke care are evolving and become more difficult given new imaging modalities and treatment options.[28] In this late window thrombectomy study comprised predominantly of respondents from CSCs and high-income countries, we found that advanced imaging was available and utilized in the triage of patients presenting in the late window, but its availability was significantly lower in PSCs and low- or middle-income countries. Most respondents indicated they follow the standard of care in their region or the AHA/ASA or ESO guidelines when selecting patients for thrombectomy in the late window.[5,6] However, when presented with a simulated patient scenario, physicians tended to forego advanced imaging. In the event advanced imaging was not immediately available, most respondents would refer the patient directly to EVT, a breach of the guidelines. The responses of the survey reflect the current dilemma with advanced imaging for patient selection in late time window in clinical practice, not only, in terms of limitations of advanced imaging availability 24/7, but also, as it relates to time delay and the question of its necessity in the selection for treatment.

Advanced perfusion imaging has the advantage that infarct volume can be estimated and information about the tissue volume at risk is provided. Interrater variability in CTP interpretation is lower compared with the interrater variability in interpretation of the ASPECTS on NCCT due to software-based calculations of infarct volumes in perfusion imaging.[28] In the early window, perfusion imaging might overestimate infarct core which potentially excludes patients who could benefit from thrombectomy.[29,30] Furthermore, comparative imaging studies demonstrated a better correlation of infarct core estimation between NCCT and CT-perfusion in the extended time window (>6 hours) compared with early time window (<6 hours)[17,18,33] and others stated that NCCT might be more sensitive for indication of irreversible injury in the later time window than perfusion imaging.[34] The CT for Late Endovascular Reperfusion study, a large multinational cohort study, compared the clinical outcomes of patients selected for mechanical thrombectomy by NCCT compared with selection by advanced imaging (CTP or MRI) in the extended time window and found no significant differences in the clinical outcome of these patients.[19] Similar results were found in other studies.[36] These data indicate that NCCT might be a reasonable imaging alternative for patient selection in the extended time window challenging the current guidelines stating that advanced imaging

TABLE 4. Imaging Preferences in Late Window

Question	n (column %)				
Agree to CTA/CTA rather than advanced imaging in late window					
	Individual decisions	**CT/CTA/CTP**	**CT/CTA only**	**MRI/MRP**	***P* value**
Overall	251 (17.12)	706 (48.16)	373 (25.44)	136 (9.28)	–
Specialty category					
Interventionist	64 (13.59)	184 (39.07)	164 (34.82)	59 (12.53)	<0.0001
Noninterventionist	187 (18.81)	521 (52.41)	209 (21.03)	77 (7.75)	
Practice setting					
Comprehensive stroke center	223 (16.93)	629 (47.76)	344 (26.12)	121 (9.19)	0.3961
Primary stroke center	22 (21.57)	54 (52.94)	17 (16.67)	9 (8.82)	
Nonstroke center	6 (13.04)	22 (47.83)	12 (26.09)	6 (13.04)	
Age					
≤50	209 (17.08)	589 (48.12)	321 (26.23)	105 (8.58)	0.1098
>50	42 (17.43)	117 (48.55)	51 (21.16)	31 (12.86)	
Income					
High income	183 (17.13)	539 (50.47)	274 (25.66)	72 (6.74)	<0.0001
Low or middle income	61 (17.38)	148 (42.17)	87 (24.79)	55 (15.67)	
Given uncertainty, which are you most comfortable with?					
	Following established standard of care	Following guidelines	Following own standard practice based on evidence and expertise	No consistent strategy	*P* value
Overall	132 (9.13)	584 (40.39)	444 (30.71)	286 (19.78)	–
Specialty category					
Interventionist	29 (6.26)	140 (30.24)	179 (38.66)	115 (24.84)	<0.0001
Noninterventionist	103 (10.49)	443 (45.11)	265 (26.99)	171 (17.41)	
Practice setting					
Comprehensive stroke center	103 (7.92)	516 (39.69)	419 (32.23)	262 (20.15)	<0.0001
Primary stroke center	19 (19.19)	47 (47.47)	15 (15.15)	18 (18.18)	
Nonstroke center	10 (21.74)	20 (43.48)	10 (21.74)	6 (13.04)	
Age					
≤50	103 (8.54)	477 (39.55)	374 (31.01)	252 (20.90)	0.0414
>50	28 (11.72)	107 (44.77)	70 (29.29)	34 (14.23)	
Income					
High income	97 (9.19)	406 (38.45)	356 (33.71)	197 (18.66)	0.0019
Low or middle income	28 (8.09)	159 (45.95)	81 (23.41)	78 (22.54)	
Do you routinely use advanced imaging in late window LVO?					
	Advanced imaging is not available	No, some cases only	No, use CT/CTA only	Yes, every case	*P* value
Overall	63 (4.38)	360 (25.00)	101 (7.01)	916 (63.61)	–
Specialty category					
Interventionist	58 (4.63)	310 (24.76)	85 (6.79)	799 (63.82)	0.4779
Noninterventionist	49 (5.02)	239 (24.49)	67 (6.86)	621 (63.63)	
Practice setting					
Comprehensive stroke Center	33 (2.55)	313 (24.15)	82 (6.33)	868 (66.98)	<0.0001
Primary stroke center	20 (20.41)	34 (34.69)	11 (11.22)	33 (33.67)	
Nonstroke center	10 (22.22)	13 (28.89)	8 (17.78)	14 (31.11)	
Age					
≤50	50 (4.16)	306 (25.48)	78 (6.49)	767 (63.86)	0.2763
>50	12 (5.04)	54 (22.69)	23 (9.66)	149 (62.61)	
Income					
High income	31 (2.95)	229 (21.79)	50 (4.76)	741 (70.50)	<0.0001
Low or middle income	29 (8.43)	119 (34.59)	43 (12.50)	153 (44.48)	

CTA, computed tomography angiography; CTP, computed tomography perfusion; LVO, large vessel occlusion; and MRI, magnetic resonance imaging.

TABLE 5. Availability of Advanced Imaging and Low ASPECTS Case Scenario

Question	n (column %)					
Late window, immediate advanced imaging unavailable, LVO						
	Refer to thrombectomy based on CT	**Refer to center with advanced imaging**	**Medical management only**	**Wait for advanced imaging**	**Enroll in RCT**	***P* value**
Overall	964 (70.06)	167 (12.14)	105 (7.63)	103 (7.49)	37 (2.69)	–
Specialty category						
Interventionist	373 (83.63)	19 (4.26)	12 (2.69)	28 6.28)	14 (3.14)	<0.0001
Noninterventionist	591 63.63)	147 (15.82)	93 (10.01)	75 (8.07)	23 (2.48)	
Practice setting						
Comprehensive stroke center	886 (72.15)	135 (10.99)	76 (6.19)	94 (7.65)	37 (3.01)	<0.0001*
Primary stroke center	54 (53.47)	24 (23.76)	18 (17.82)	5 (4.95)	0 (0.00)	
Nonstroke center	23 (50.00)	8 (17.39)	11 (23.91)	4 (8.70)	0 (0.00)	
Age						
≤50	826 (71.64)	130 (11.27)	80 (6.94)	88 (7.63)	29 (2.52)	0.0132
>50	137 (61.71)	37 (16.67)	25 (11.26)	15 (6.76)	8 (3.60)	
Income						
High income	715 (73.18)	121 (12.38)	46 (4.71)	66 (6.76)	29 (2.97)	<0.0001
Low or middle income	222 (62.71)	44 (12.43)	47 (13.28)	34 (9.60)	7 (1.98)	
70-year-old, 7-h onset, NIHSS 17, M1, ASPECTS 4						
	CTP, then triage	Direct to EVT	Enroll in RCT	Medical management	MRI, then triage	*P* value
Overall	453 (35.61)	148 (11.64)	307 (24.14)	180 (14.15)	184 (14.47)	–
Specialty category						
Interventionist	129 (31.31)	61 (14.81)	103 (25.00)	58 (14.08)	61 (14.81)	0.0692
Noninterventionist	324 (37.72)	87 (10.13)	204 (23.75)	122 (14.2)	122 (14.20)	
Practice setting						
Comprehensive stroke center	412 (35.92)	119 (10.37)	293 (25.54)	162 (14.12)	161 (14.04)	<0.0001
Primary stroke center	30 (34.88)	14 (16.28)	13 (15.12)	14 (16.28)	15 (17.44)	
Nonstroke center	10 (26.32)	15 (39.47)	1 (2.63)	4 (10.53)	8 (21.05)	
Age						
≤50	385 (35.85)	121 (11.27)	256 (23.84)	158 (14.71)	154 (14.34)	0.6487
>50	68 (34.52)	26 (13.20)	51 (25.89)	22 (11.17)	30 (15.23)	
Income						
High income	341 (37.39)	78 (8.55)	277 (30.37)	116 (12.72)	100 (10.96)	<0.0001
Low or middle income	98 (30.72)	64 (20.06)	27 (8.46)	56 (17.55)	74 (23.20)	
Is advanced imaging available?						
	No, unavailable	No, weekdays only	Special request only	Yes, routinely	Yes, not immediate	*P* value
Overall	91 (6.31)	63 (4.37)	67 (4.64)	1020 (70.69)	202 (14.00)	
Specialty category						
Interventionist	21 (4.56)	17 (3.69)	18 (3.90)	339 (73.54)	66 (14.32)	0.2254
Noninterventionist	70 (7.14)	46 (4.69)	49 (4.99)	680 (69.32)	136 (13.86)	
Practice setting						
Comprehensive stroke center	53 (4.09)	40 (3.09)	51 (3.94)	973 (75.08)	179 (13.91)	<0.0001*
Primary stroke center	26 (26.00)	17 (17.00)	11 (11.00)	31 (31.00)	15 (15.00)	
Nonstroke center	12 (26.09)	6 (13.04)	5 (10.87)	15 (32.61)	8 (17.39)	
Age						
≤50	72 (5.98)	48 (3.98)	53 (4.40)	850 (71.29)	173 (14.36)	0.2628
>50	18 (7.59)	15 (6.33)	14 (5.91)	161 (67.93)	29 (12.24)	
Income						
High income	47 (4.47)	30 (2.85)	31 (2.95)	839 (79.75)	105 (9.98)	<0.0001
Low or middle income	38 (11.01)	31 (8.99)	30 (8.70)	159 (46.09)	87 (25.22)	

ASPECTS indicates Alberta Stroke Program Early CT Score; CTP, computed tomography perfusion; EVT, endovascular therapy; LVO, large vessel occlusion; MRI, magnetic resonance imaging; NIHSS, National Institute of Health Stroke Scale; and RCT, randomized controlled trial.

TABLE 6. Time to Obtain Advanced Imaging†

Question	n (column %)									
How long to obtain advanced images?										
		5 min	**10 min**	**20 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	***P* value**
Overall		307 (24.40)	428 (34.02)	254 (20.19)	155 (12.32)	53 (4.21)	42 (3.34)	11 (0.87)	8 (0.64)	–
Practice setting										
Comprehensive stroke center		295 (25.24)	408 (34.90)	235 (20.10)	139 (11.89)	43 (3.68)	34 (2.91)	8 (0.68)	7 (0.60)	<0.0001
Primary stroke center		11 (17.74)	16 (25.81)	15 (24.19)	9 (14.52)	4 (6.45)	4 (6.45)	2 (3.23)	1 (1.61)	
Nonstroke center		1 (3.85)	3 (11.54)	4 (15.38)	7 (26.92)	6 (23.08)	4 (15.38)	1 (3.85)	0 (0.00)	
Age										
≤50		268 (25.28)	348 (32.83)	212 (20.00)	140 (13.21)	41 (3.87)	36 (3.40)	10 (0.94)	5 (0.47)	0.0421
>50		39 (19.70)	80 (40.40)	42 (21.21)	15 (7.58)	12 (6.06)	6 (3.03)	1 (0.51)	3 (1.52)	
Income										
High income		286 (29.79)	357 (37.19)	188 (19.58)	87 (9.06)	27 (2.81)	9 (0.94)	5 (0.52)	1 (0.10)	<0.0001
Low or middle income		18 (6.82)	62 (23.48)	60 (22.73)	63 (23.86)	22 (8.33)	30 (11.36)	5 (1.89)	4 (1.52)	
How long is acceptable delay for advanced images?										
	0 minutes	5 minutes	10 minutes	20 minutes	30 minutes	45 minutes	60 minutes	90 minutes	120 minutes	*P* value
Overall	35 (2.78)	220 (17.46)	442 (35.08)	282 (22.38)	204 (16.19)	22 (1.75)	39 (3.10)	6 (0.48)	10 (0.79)	–
Specialty category										
Interventionist	12 (2.90)	79 (19.08)	147 (35.51)	80 (19.32)	65 (15.70)	8 (1.93)	15 (3.62)	3 (0.72)	5 (1.21)	0.6089
Noninterventionist	23 (2.72)	141 (16.69)	295 (34.91)	201 (23.79)	139 (16.45)	14 (1.66)	24 (2.84)	3 (0.36)	5 (0.59)	
Practice setting										
Comprehensive stroke center	33 (2.82)	211 (18.05)	415 (35.50)	257 (21.98)	185)15.83)	18 (1.54)	36 (3.08)	5 (0.43)	9 (0.77)	0.1122*
Primary stroke center	2 (3.13)	8 (12.50)	19 (29.69)	20 (31.25)	9 (14.06)	3 (4.69)	2 (3.13)	1 (1.56)	0 (0.00)	
Nonstroke center	0 (0.00)	1 (3.85)	8 (30.77)	5 (19.23)	9 (34.62)	1 (3.85)	1 (3.85)	0 (0.00)	1 (3.85)	
Age										
≤50	30 (2.82)	194 (18.27)	364 (34.27)	234 (22.03)	175 (16.48)	19 (1.79)	33 (3.11)	5 (0.47)	8 (0.75)	0.7840
>50	5 (2.53)	26 (13.13)	78 (39.39)	48 (24.24)	29 (14.65)	3 (1.52)	6 (3.03)	1 (0.51)	2 (1.01)	
Income										
High income	31 (3.23)	195 (20.33)	367 (38.27)	216 (22.52)	121 (12.62)	10 (1.04)	15 (1.56)	1 (0.10)	3 (0.31)	<0.0001*
Low or middle income	4 (1.50)	21 (7.87)	68 (25.47)	55 (20.60)	74 (27.72)	11 (4.12)	22 (8.24)	5 (1.87)	7 (2.62)	

†Percentages may not add to 100 due to rounding.

is required. The lower cost of plain CT (compared with CTP or MRI) and conservation of contrast for parenchymal selection may be other advantages to consider particularly for low- and middle-income countries, and in the setting of finite resources.[37,38]

This conflict was also evident in the responses in this survey when asked about imaging modalities for treatment decisions in clinical routine based on a patient case. Here, 67% of respondents would follow guidelines and perform perfusion imaging, while 1 quarter of respondents would forgo perfusion imaging. In view of the results of the CT for Late Endovascular Reperfusion studies,[19] nearly half of the respondents (42%) agreed that treatment decisions regarding reperfusion therapy should not be strictly based on advanced imaging and 25% of respondents would agree to base treatment decisions on CT/CTA only. Interestingly, if advanced imaging is not readily available, most respondents would refer patients to EVT based on CT scan only and only an estimated 20% would wait for advanced imaging, for example, if a technologist arrives on call to hospital, or refer patients to a center with advanced imaging. These results demonstrate the dissonance of clinical routine and adherence to guideline recommendation in view of limitations of timely advanced imaging, lack of 24/7 advanced imaging resources, but also in view of potential over-selection of patients and time delay due to the utilization of advanced imaging.

Regarding the time delay due to advanced imaging, several studies showed that advanced imaging led to longer door-to-puncture[12,18,19] and door-to-needle times.[35] In 1 report, time delays to treatment might not be as critical for functional outcome after thrombectomy in patients who present in the extended time window (6–24 hours) compared with patients in the early time window.[27] In this survey, 78% of respondents believed that a delay of 20 minutes or less was acceptable to obtain advanced imaging prior to thrombectomy. This is in discrepancy to the required time of advanced imaging in clinical practice which was often greater than 20 minutes. Importantly, about 1 quarter of respondents had a time delay greater than what they considered acceptable (Figure 2), which is important particularly in the view of studies demonstrating comparable clinical outcome with selection by NCCT.

As we evolve toward a paradigm of tissue rather than time based selection for EVT of patients with LVO,[41–43] the concept of time from symptom onset to treatment becomes less relevant, particularly in patients with the most severe presentation. While the notion of time is an important surrogate to estimate the degree of brain ischemia, these time thresholds were in place for optimizing the safety of IVT. In patients with symptomatic LVO, if one is presented with a good NCCT in a late window (ie, little early ischemic changes), this raises the question of the reliability of time, particularly in patients with unwitnessed or unknown onset of stroke. Because the notion of time may not be reliable, taking an additional 20 minutes to treat the patient (who may be a fast progressor)[44] may be unacceptable if it can be prevented.

Perhaps it would help to consider patients with severe symptoms from LVO as circulatory arrest patients, except that the arrest "only" affects half the brain. In this analogy, thrombectomy for LVO replaces cardiopulmonary resuscitation for cardiac arrest. There is no time to perform advanced imaging in patients who have had a cardiac arrest, whereas we may perform MRI to determine prognosis and select patients for continued support or withdrawal after the patient is resuscitated. In a patient presenting late with a severe stroke syndrome and LVO, the NCCT showing no major ischemic changes or good ASPECTS may have already done all the necessary screening work for decision-making to EVT. The DAWN and DEFUSE 3 trials may have over-selected late presenting patients (ie, the late window paradox),[45] as suggested by the better outcomes, greater difference in treatment effect, and their much lower number needed to treat compared with the trials of early LVO presentations.[46] It is unlikely that taking precious time to perform additional imaging with CTP or MRI will improve patient outcomes. Given the highly selective perfusion thresholds that were chosen for DAWN and DEFUSE 3, their very low number needed to treat, we are likely denying restoring circulation to many patients that could benefit as these trial criteria have been translated into guidelines with recommendations of "strict adherence."

Data from RCTs comparing simplified imaging modalities compared to medical management are important to provide evidence for patient selection in clinical routine for this patient population, particularly in areas with no or limited access to CTP or MRI. In this regard, 3 RCTs are in progress (the MR CLEAN LATE trial [Endovascular Treatment of Acute Ischemic Stroke in The Netherlands for Late Arrivals; ISRCTN19922220], the RESILIENT-Extended trial [Randomization of Endovascular Treatment in Acute Ischemic Stroke in the Extended Time Window; NCT04256096], and the NO CTP trial [A Randomized Trial of Imaging Selection Modalities for Stroke Thrombectomy; NCT05230914]).

Another unsolved question represents the efficacy of (EVT) in patients with large core infarcts. The RESCUE-Japan LIMIT trial demonstrated better functional outcome with EVT than with medical management alone in patients with LVO and ASPECTS of 3–5 within 6 hours after last being well or within 6–24 hours if no early changes were seen by MRI DWI-FLAIR mismatch.[47] In this survey, the management was asked for a patient

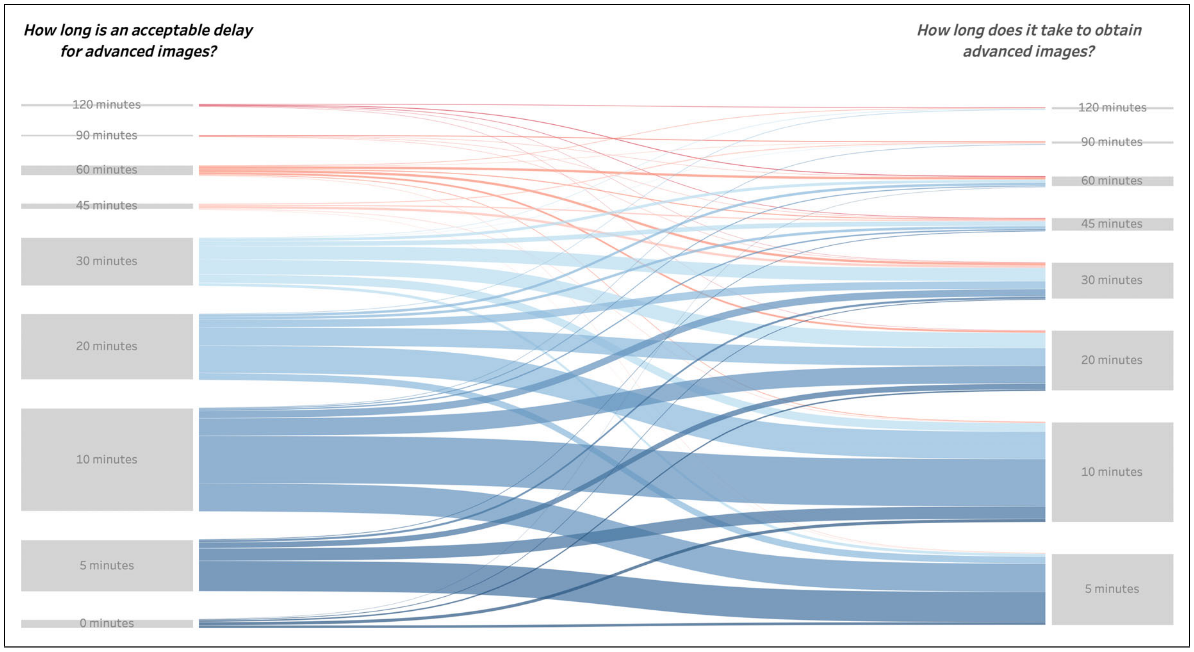

FIGURE 2. Sankey flow chart of physician perception of acceptable time delay to obtain advanced imaging compared and physician estimate of time to perform the study. In 340 (27.13%) respondents, time delay in image acquisition at their center was greater than what the respondent believed to be an acceptable time delay to obtain advanced imaging data.

who presented 7 hours after symptom onset with an M1 occlusion and a CT ASPECTS of 4. Half of the respondents would perform CTP or MRI, while 12% would refer directly to EVT, 14% would treat with medical management only, and 24% would randomize into an ongoing large core infarct trial. These responses indicate that management for patients with large infarct core in the extended time window remains unclear and further RCTs about imaging modality for patient selection but also about efficacy of EVT are needed.[48,49]

Limitations

While this survey included responses from a large number of practicing physicians and these responses represent current clinical practice, surveys cannot be used to determine the best treatment of patients. Physicians from PSCs and from low- and middle-income countries were under-represented. The survey captures physician experience by responder, rather than by center. As it was not possible to dissect response by center, responses from multiple persons from the same center may overestimate (or underestimate) the availability of imaging resources.

This survey did not address late window imaging selection for basilar artery occlusion patients to EVT,[44] therefore these findings are not generalizable to the posterior circulation. In ATTENTION (Endovascular Treatment for Acute Basilar Artery Occlusion)[45] and BAOCHE (Basilar Artery Occlusion Chinese Endovascular Trial),[46] patients presenting with basilar artery occlusion were selected mainly by CT with PC ASPECTS in the late window up to 24 hours from estimated symptom onset. As detection of early ischemic changes is known to be more difficult to discriminate in the posterior circulation with CT,[47] the results of these 2 basilar artery occlusion trials, which were predominantly based on CT PC ASPECTS,[48,49] may lower thresholds to utilization of CT paradigms for late window selection of patients for EVT.

CONCLUSIONS

This late window thrombectomy survey demonstrated that among respondents, predominantly from CSCs and high-income countries, advanced imaging was available and used for thrombectomy selection of patients presenting in the late time windows. Access to advanced imaging was lower in PSCs and middle-income countries compared with CSCs and high-income countries, respectively. Although most respondents would follow guidelines, a substantial number of respondents would base reperfusion therapy decisions on CT imaging only or make individualized decisions. Most respondents considered a delay of 20 minutes or less acceptable to obtain advanced imaging. However, the time required to obtain these images was often longer than deemed acceptable. If advanced imaging is not readily available, most respondents would refer patients to EVT based on CT scan only. These findings suggest the current guideline recommendations for imaging in the selection of patients for EVT in the late window do not match the opinions of practicing physicians and support ongoing RCTs analyzing simplified imaging selection modalities in this patient population.

ARTICLE INFORMATION

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Supplemental Materials

Supporting Information

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