ONLINE APPENDIX

Part 1: Randomization Procedure for Selecting 70 Control Patients with No Vessel Occlusion

The 303 patients with no vessel occlusion were entered into an Excel spreadsheet (Microsoft). The "randomization" function in Excel was used to generate a random number for each patient. The Sort Data function was then used to order the patients according to the randomly assigned numbers, from lowest to highest. The first 70 patients were selected.

The same randomization procedure in Excel was used to determine the order in which the 140 patients included in the study were presented to the readers. The same order was kept for the first and second reads.

Part 2: NECT, CTP, and CTA Technique and Scan Parameters

Nonenhanced CT was performed in the helical mode with the following parameters: 0.625-mm section collimation, spiral pitch factor of 0.283, tube voltage of 120 kV(peak), and image matrix of 512 × 512. Images were reconstructed using a UB kernel at 1-mm overlapping sections, with axial, coronal, and sagittal multiplanar reconstructions performed at 4-mm section thickness.

For the CTP, 50 mL of nonionic contrast agent (350 mg of iodine/mL, iohexol, Omnipaque 350; GE Healthcare) was injected intravenously, followed by a 50-mL saline flush. A flow rate of 5 mL/s was used for both injections. The CTP acquisition parameters were as follows: 35 consecutive scans, 2.05-second mean temporal resolution, 80-kVp tube voltage, 160-mA tube current, 500-ms gantry rotation time, 80-mm z-axis coverage, 1.5-mm section collimation, and 512 × 512 acquisition matrix. Images were reconstructed using an iterative reconstruction (iDose4; Philips Healthcare) factor of 4 at 10-mm section thickness.

CTA was performed using 80 mL of the same nonionic contrast agent, injected intravenously at a rate of 5 mL/s, followed by a 40-mL saline flush at 6 mL/s. Acquisition parameters were as follows: craniocaudal coverage from the aortic arch to the vertex, 100-kVp tube voltage with tube current modulation, section collimation width of 0.625 mm, image matrix of 512 × 512, and spiral pitch factor of 0.618. We used the following reconstruction parameters: iterative reconstruction (iDose5) factor of 5 and convolution kernel B. Contrast bolus triggering was performed in the aortic arch.

Online Table 1: Patients with DVOs at 2 sites

	Occlusion Sites	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
		With Tmax	w/o Tmax	With Tmax	w/o Tmax	With Tmax	w/o Tmax	With Tmax	w/o Tmax
1	Left A3 ACA and left M3 MCA	1	0	2	1	2	1	2	2
2	Left P3 PCA and right P4 PCA	2	2	2	1	1	1	1	0
3	Right M2 MCA superior and inferior	2	1	2	1	2	2	1	1
4	Right M2 MCA and M3 MCA	1	1	1	1	1	1	1	1
5	Left P2 PCA and right PICA	1	1	1	1	1	1	1	1
6	Left M2 MCA superior division branch and inferior division trunk	1	0	2	2	2	1	2	2
7	Left M2 MCA and M3 MCA	1	1	2	1	1	1	1	1
8	Right P2 PCA and right SCA	1	1	2	2	2	1	1	1
9	Left M2 MCA and right M4 MCA	1	1	1	1	1	1	1	1
10	Right M2 MCA and right P4 PCA	1	1	2	1	1	1	1	1
11	Two right M4 MCA	1	0	2	2	1	1	1	1
12	Left M2 MCA inferior division trunk and superior division	2	2	1	1	2	2	2	1
13	Right P4 PCA and left M4 MCA	0	1	2	1	2	2	1	1
14	Left M2 and M3 MCA	0	1	2	1	2	2	1	1
Both occlusions correctly identified, number		3	2	10	3	7	4	3	2

Online Table 2: Readers' diagnostic performance for detection of a DVO on CTA on, with and without *Tmax* (expanded in Online Appendix and Online Table 3)

DVO Detection on CTA	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax
Sensitivity (%)	60.0	80.0	77.1	95.7	71.4	90.0	74.3	95.7
95% CI	47.6–71.5	68.7–88.6	65.6–86.3	88.0–99.1	59.4–81.6	80.5–95.9	62.4–84.0	88.0–99.1
Specificity (%)	78.6	95.7	90.0	98.6	95.7	100.0	85.7	88.6
95% CI	67.1–87.5	88.0–99.1	80.5–95.9	92.3–100.0	88.0–99.1	94.9–100.0	75.3–92.9	78.7–94.9
AUC	0.693	0.879	0.836	0.971	0.836	0.950	0.800	0.921
95% CI	0.617–0.768	0.826–0.931	0.775–0.897	0.944–0.999	0.777–0.894	0.915–0.985	0.734–0.866	0.877–0.966
ΔAUC[a]	0.18		0.136		0.114		0.121	
95% CI	0.115–0.256		0.076–0.196		0.063–0.166		0.059–0.184	
P	<.001		<.001		<.001		<.001	

Note:—w/o indicates without.

[a] Determined using the DeLong algorithm.

Online Table 3: ROC analysis of diagnostic performance for detection of DVOs on CTA[a]

	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax
Sensitivity (%)	60.0	80.0	77.1	95.7	71.4	90.0	74.3	95.7
95% CI	47.6–71.5	68.7–88.6	65.6–86.3	88.0–99.1	59.4–81.6	80.5–95.9	62.4–84.0	88.0–99.1
Specificity (%)	78.6	95.7	90.0	98.6	95.7	100	85.7	88.6
95% CI	67.1–87.5	88.0–99.1	80.5–95.9	92.3–100.0	88.0–99.1	94.9–100.0	75.3–92.9	78.7–94.9
PPV[b] (%)	31.3	75.2	55.7	91.6	73.1	100	45.8	57.7
95% CI	21.9–42.6	50.0–90.2	38.1–72.0	60.9–98.7	47.0–89.2	NA	31.9–60.4	41.5–72.4
NPV[b] (%)	92.3	96.7	96.0	99.3	95.4	98.4	95.3	99.2
95% CI	89.8–94.3	94.8–97.9	94.0–97.4	97.9–99.8	93.4–96.8	96.8–99.2	93.1–96.9	97.7–99.7
AUC	0.693	0.879	0.836	0.971	0.836	0.950	0.800	0.921
95% CI	0.617–0.768	0.826–0.931	0.775–0.897	0.944–0.999	0.777–0.894	0.915–0.985	0.734–0.866	0.877–0.966
ΔAUC[c]	0.186		0.136		0.114		0.121	
95% CI	0.115–0.256		0.076–0.196		0.06–0.166		0.059–0.184	
Significance, *P*	<.001		<.001		<.001		<.001	

Note:—PPV indicates positive predictive value; NPV, negative predictive value; NA, not applicable.

[a] *n* = 140 (70 with a DVO, 70 without a DVO).

[b] PPV and NPV were calculated on the basis of the 14% (70/501) prevalence of a DVO in the population screened for the study. The NPV of CTA was high both with and without Tmax due to the low prevalence of DVOs.

[c] Determined using the DeLong algorithm.

Online Table 4: Readers' diagnostic performance for detection of a DVO on CTA, with and without Tmax, excluding 22 patients with proximal M2 MCA occlusion[a]

	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
DVO Detection on CTA	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax
Sensitivity (%)	47.9	72.9	66.7	93.8	64.6	85.4	64.6	93.8
95% CI	33.3–62.8	58.2–84.7	51.6–79.6	82.8–98.7	49.5–77.8	72.2–93.9	49.5–77.8	82.8–98.7
Specificity (%)	78.6	95.7	90.0	98.6	95.7	100	85.7	88.6
95% CI	67.1–87.5	88.0–99.1	80.5–95.9	92.3–100.0	88.0–99.1	94.9–100.0	75.3–92.9	78.7–94.9
AUC	0.632	0.843	0.783	0.962	0.801	0.927	0.751	0.912
95% CI	0.546–0.719	0.775–0.911	0.707–0.859	0.924–0.999	0.729–0.874	0.877–0.978	0.672–0.831	0.861–0.963
ΔAUC[b]	0.211		0.178		0.126		0.160	
95% CI	0.127–0.295		0.104–0.253		0.063–0.188		0.084–0.236	
P	<.001		<.001		<.001		<.001	

[a] *n* = 118; 48 with a DVO, 70 without a DVO.

[b] Determined using the DeLong algorithm.

Online Table 5: ROC analysis of diagnostic performance for detection of DVOs on CTA, excluding patients with proximal M2-MCA occlusion[a]

	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax
Sensitivity (%)	47.9	72.9	66.7	93.8	64.6	85.4	64.6	93.8
95% CI	33.3–62.8	58.2–84.7	51.6–79.6	82.8–98.7	49.5–77.8	72.2–93.9	49.5–77.8	82.8–98.7
Specificity (%)	78.6	95.7	90.0	98.6	95.7	100	85.7	88.6
95% CI	67.1–87.5	88.0–99.1	80.5–95.9	92.3–100.0	88.0–99.1	94.9–100.0	75.3–92.9	78.7–94.9
PPV[b] (%)	19.9	65.4	42.6	87.9	62.6	100	33.4	47.7
95% CI	12.7–29.8	38.1–85.3	26.3–60.6	51.0–98.1	35.2–83.8	NA	21.4–48.1	32.1–63.7
NPV[b] (%)	93.1	97.0	96.0	99.3	96.1	98.4	95.6	99.2
95% CI	90.9–94.8	95.2–98.1	94.2–97.3	97.9–99.8	94.3–97.3	96.9–99.2	93.6–97.0	97.7–99.7
AUC	0.632	0.843	0.783	0.962	0.801	0.927	0.751	0.912
95% CI	0.546–0.719	0.775–0.911	0.707–0.859	0.924–0.999	0.729–0.874	0.877–0.978	0.672–0.831	0.861–0.963
ΔAUC[c]	0.211		0.178		0.126		0.160	
95% CI	0.127–0.295		0.104–0.253		0.063–0.188		0.084–0.236	
Significance, *P*	<.001		<.001		<.001		< 001	

Note:—PPV indicates positive predictive value; NPV, negative predictive value; NA, not applicable.

[a] *n* = 118 (48 with a DVO, 70 without a DVO). The prevalence of DVO in the screened population was 48/501 (10%).

[b] PPV and NPV were calculated on the basis of the 10% (48/501) prevalence of a DVO, excluding proximal M2 occlusions, in the population screened for the study. The NPV of CTA was high both with and without Tmax due to the low prevalence of DVOs.

[c] Determined using the DeLong algorithm.

Online Table 6: ROC analysis of diagnostic performance for detection of DVOs on CTA, excluding patients with M2-MCA and P2-PCA occlusions[a]

	Reader 1: Fellow		Reader 2: Scientist		Reader 3: Radiologist		Reader 4: Resident	
	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax	w/o Tmax	Tmax
Sensitivity (%)	29.6	66.7	48.2	88.9	44.4	77.8	48.2	92.6
95% CI	13.8–50.2	46.0–83.5	28.7–68.1	70.8–97.6	25.5–64.7	57.7–91.4	28.7–68.1	75.7–99.1
Specificity (%)	78.6	95.7	89.7	98.6	95.7	100	85.7	88.6
95% CI	67.1–87.5	88.0–99.1	79.9–95.8	92.3–100.0	88.0–99.1	94.9–100.0	54.3–92.9	78.7–94.9
PPV[b] (%)	6.8	45.0	19.8	76.6	35.3	100	15.1	29.9
95% CI	3.4–13.2	20.8–71.9	9.9–35.5	31.8–95.8	14.3–64.1	NA	8.1–26.2	18.0–45.2
NPV[b] (%)	95.5	98.2	97.0	99.4	97.0	98.8	96.9	99.6
95% CI	94.2–96.5	97.0–98.9	95.8–97.9	98.3–99.8	95.9–97.9	97.7–99.4	95.6–97.9	98.4–99.9
AUC	0.541	0.812	0.691	0.937	0.701	0.889	0.669	0.906
95% CI	0.441−0.641	0.718−0.906	0.588−0.793	0.875−0.999	0.602−0.799	0.809−0.969	0.565−0.774	0.843−0.966
ΔAUC[c]	0.271		0.247		0.188		0.237	
95% CI	0.166−0.376		0.14−0.349		0.094−0.282		0.133−0.340	
Significance, *P*	<.001		<.001		<.001		<.001	

Note:—PPV indicates positive predictive value; NPV, negative predictive value; NA, not applicable.

[a] *n* = 97 (27 with a DVO, 70 without a DVO). The prevalence of DVO in screened population was 27/501 (5%).

[b] PPV and NPV were calculated on the basis of the 5% (27/501) prevalence of a DVO, excluding M2 and P2 occlusions, in the population screened for the study. The NPV of CTA was high both with Tmax and without Tmax due to the low prevalence of DVOs.

[c] Determined using the DeLong algorithm.

Online Table 7: Shift analysis of change in diagnostic confidence with the addition of Tmax to CTA, using the Wilcoxon signed rank test

	Reader 1: Fellow	Reader 2: Scientist	Reader 3 :Radiologist	Reader 4: Resident
Wilcoxon signed rank test				
Patients with DVO, *P*	.001	.044	<.001	.003
Patients without DVO, *P*	.017	<.001	.009	.143

Online Table 8: Time taken (in seconds) to interpret CTA, with and without Tmax

	Reader 1: Fellow		Reader 2: Scientist	
	w/o Tmax	Tmax	w/o Tmax	Tmax
All patients				
Range	30–587	12–384	29–408	10–287
Median	138	86.5	161	49
95% CI	130–150	79–101	140–174	45–58
Interquartile range	88–213	61–130	107–211	37–90
P	<.001		<.001	
Patients without a DVO				
Range	30–464	13–276	40–408	10–176
Median	137	85	163	44
95% CI	120–156	76–97	145–177	37–48
Interquartile range	105–177	64–123	121–202	34–58
P	<.001		<.001	
Patients with a DVO				
Range	32–587	12–384	29–403	11–287
Median	140	88	149	68
95% CI	121–156	75–118	126–182	54–104
Interquartile range	86–223	60–146	88–218	42–122
P	<.001		<.001	

Online Table 9: Time taken (in seconds) to interpret CTA, with and without Tmax, for M2 (*n* = 38) versus M3- and M4-segment (*n* = 13) MCA occlusions

	Reader 1: Fellow		Reader 2: Scientist	
	M2 Occlusions	M3 and M4 Occlusions	M2 Occlusions	M3 and M4 Occlusions
Without Tmax				
Range	32–380	55–273	34–403	73–321
Median	136	159	159	230
95% CI	94–157	139–230	127–184	140–280
Interquartile range	87–187	142–224	110–213	143–273
P[a]	.27		.10	
With Tmax				
Range	12–310	36–384	11–227	41–287
Median	81	77	61	113
95% CI	68–126	61–157	42–102	60–161
Interquartile range	53–139	61–154	40–118	60–160
P[a]	.90		.03	

[a] Assessed using the Mann-Whitney *U* test given independent samples. The absence of a significant difference should be interpreted with caution given the small number of M3 and M4 occlusions.

Online Table 10: False-negatives for a DVO on CTA, with and without Tmax

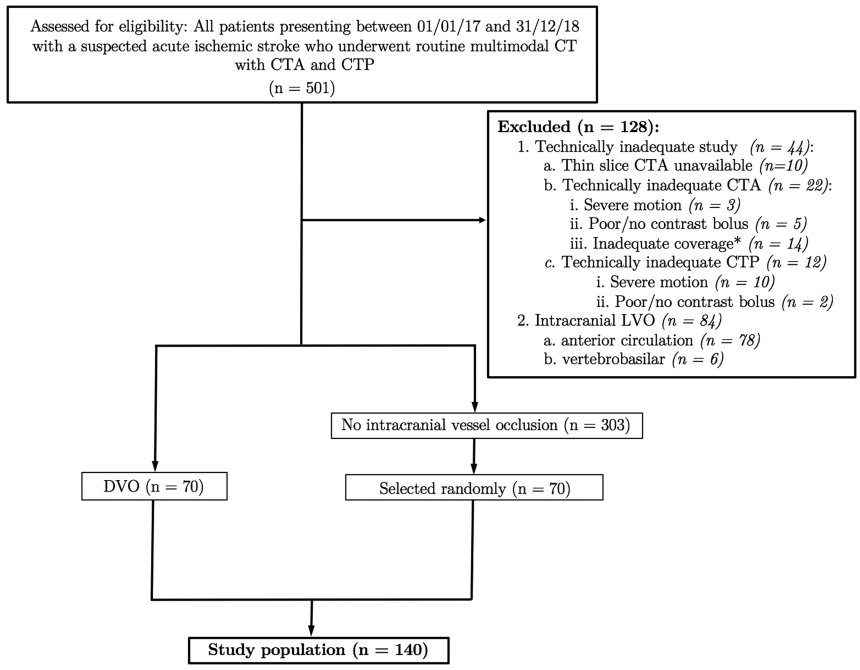
	With Tmax				Without Tmax			
	Reader 1: Fellow	Reader 2: Scientist	Reader 3: Radiologist	Reader 4: Resident	Reader 1: Fellow	Reader 2: Scientist	Reader 3: Radiologist	Reader 4: Resident
All DVOs ($n = 70$)	14	3	7	3	28	16	20	18
"Distal" DVOs, ie, excluding M2 and P2 ($n = 27$)	9	3	6	2	19	14	15	14
MCA: M2 segment ($n = 38$)[a]	5	0	1	1	9	2	5	4
Proximal ($n = 22$)	1	0	0	0	3[b]	0	3[b]	1[b]
Distal ($n = 16$)	4	0	1	1	6	2	2	3
MCA: M3-segment ($n = 5$)	0	1	0	0	4	3	1	2
MCA: M4 segment ($n = 8$)	6	1	5	2	7	5	8	7
ACA: A3 or A4 segment ($n = 3$)	2	0	0	0	3	2	2	2
PCA: P2 segment ($n = 5$)	0	0	0	0	0	0	0	0
PCA: P3 or P4 segment ($n = 8$)	0	0	0	0	3	3	2	2
PICA ($n = 2$)	1[b]	1[b]	1[b]	0[b]	2	1	2	1
SCA ($n = 1$)	0	0	0	0	0	0	0	0

[a] Four proximal M2 occlusions were missed on CTA without Tmax: Two were missed by both the radiologist and the fellow; 1, by both the resident and the radiologist; and 1, by the fellow alone. Three of these involved the dominant or codominant M2 division, and 2 were on the left.

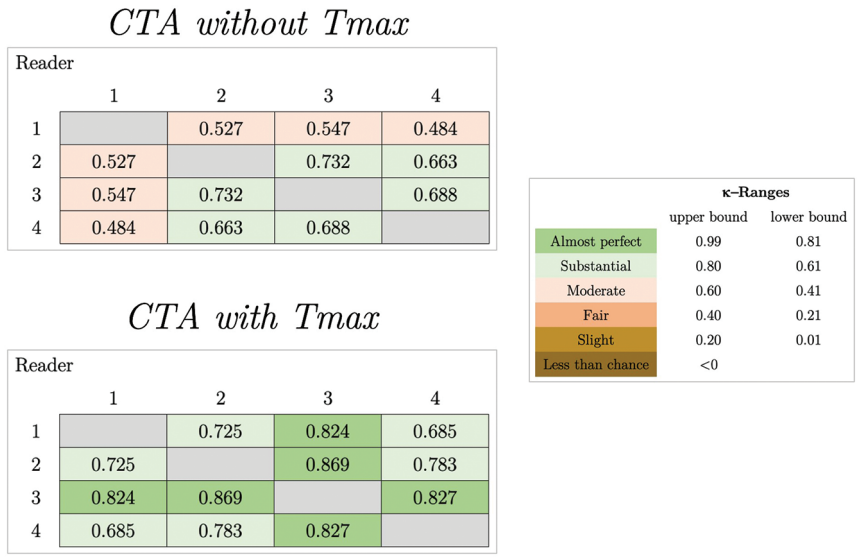
[b] A distal posterior inferior cerebellar artery occlusion associated with a small area of delay was detected only by the resident.

Online Table 11: False-positives for a DVO on CTA, with and without Tmax

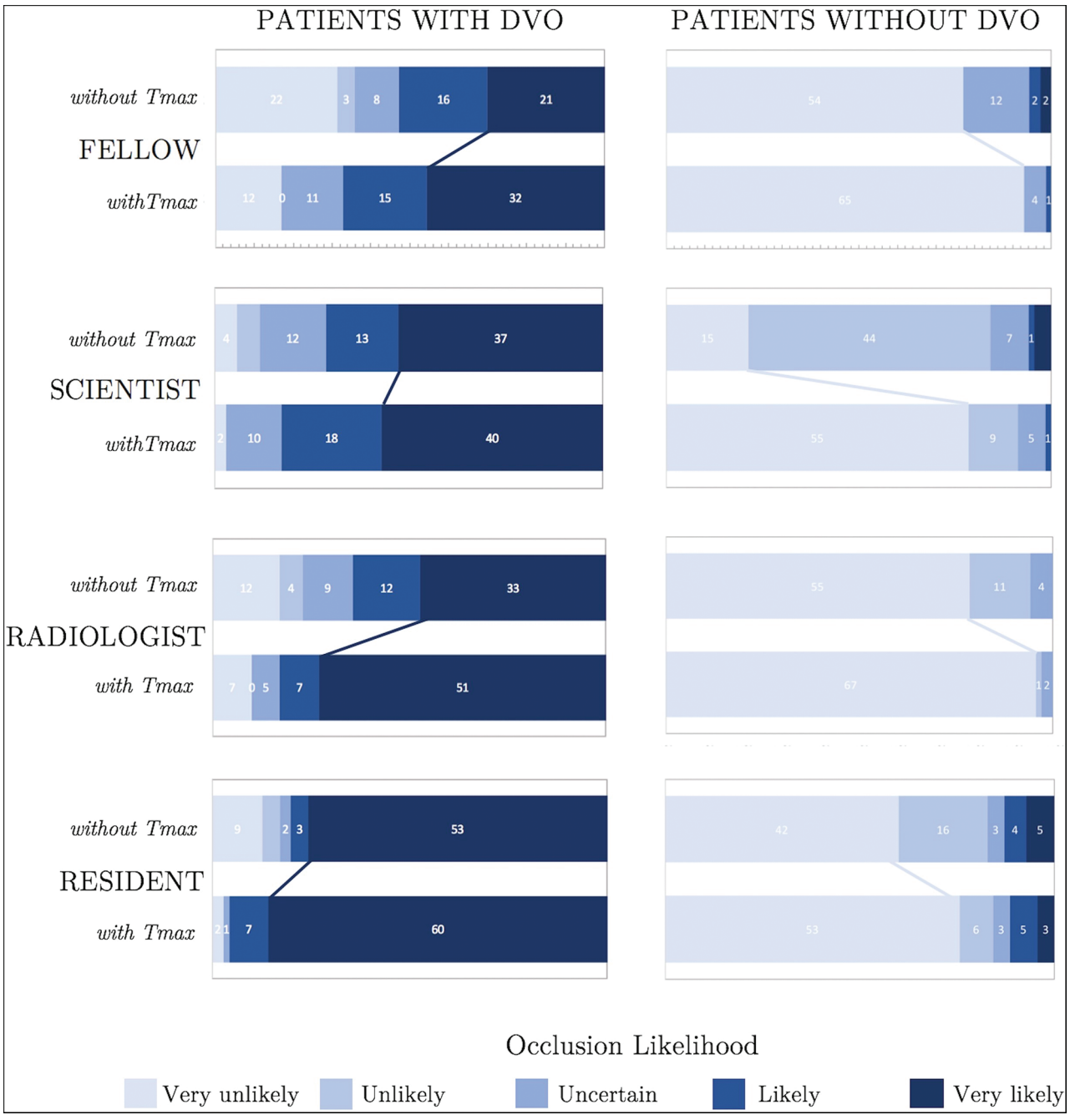
	With Tmax		Without Tmax	
	No.	Causes	No.	Causes
Reader 1: Fellow	3	Prolonged Tmax due to a developmental venous anomaly that did not conform to an arterial territory ($n = 1$) Borderzone Tmax delay ($n = 2$)	15	Small-caliber distal branches and distal branch points
Reader 2: Scientist	1	Motion artifacts causing apparent M4-MCA Tmax delay ($n = 1$)	7	
Reader 3: Radiologist	0		3	
Reader 4: Resident	8	Prolonged Tmax due to a developmental venous anomaly in the distal ACA territory ($n = 1$) (Online Fig 4*A–C*) Hemispheric Tmax delay, more pronounced in the anterior and posterior external watershed areas, due to hemiplegic migraine (Online Fig 4*D*) Borderzone Tmax delay ($n = 6$)	10	



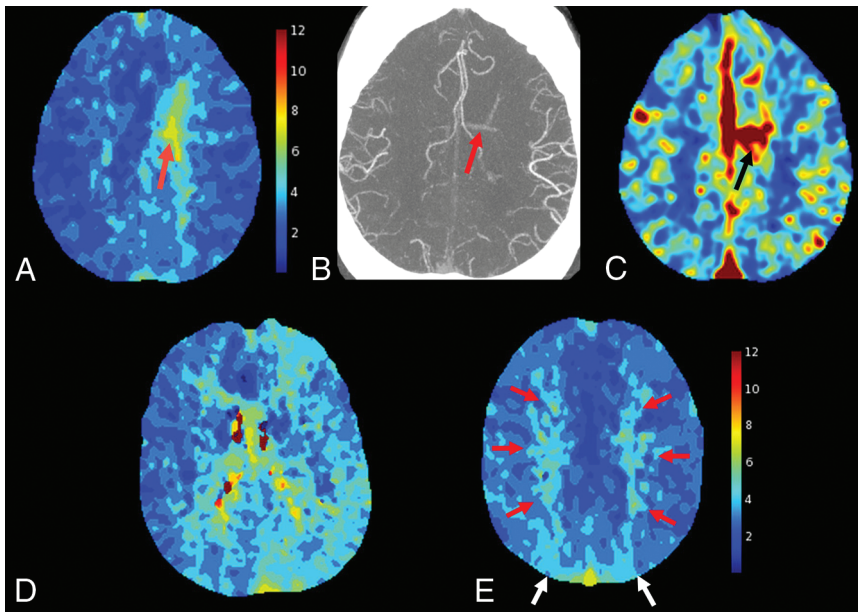
ON-LINE FIG 1. Patient selection flow chart. All patients who had presented to our institution with a suspected acute ischemic stroke and who had been within the endovascular thrombectomy window (and otherwise had met clinical eligibility criteria) underwent emergent multimodal CT with nonenhanced CT, CTA, and CTP as standard of care. CTA did not extend to the vertex; therefore, the anterior cerebral artery A4 and A5 segments were not covered. LVO indicates large-vessel occlusion.



ON-LINE FIG 2. Interreader agreement between pairs of readers regarding the presence of a DVO on CTA, with and without Tmax, determined using Cohen κ statistics. Without Tmax, agreement between readers was either moderate or substantial. Agreement increased with use of Tmax, to either substantial or almost perfect for all pairs of readers.



ON-LINE FIG 3. Shift analysis of diagnostic confidence. When analysis was confined to patients with a DVO (on the reference standard), there was a positive shift in confidence for all readers. More patients were identified as "very likely" to have an occlusion. In patients without a DVO (on the reference standard), confidence in the absence of a DVO increased. More patients were considered very unlikely to have an occlusion.



ON-LINE FIG 4. Tmax delay not due to a DVO. This led to false-positives for the trainees. *A*, Tmax delay of >6 seconds is seen in the left distal ACA territory (*arrow*) on this selected section from the Tmax maps of an 83-year-old woman who presented with sudden-onset right-sided weakness. *B*, The CTA shows venous structures, in keeping with a developmental venous anomaly (*arrow*) in the corresponding area. No distal ACA occlusion was evident. *C*, Relative cerebral blood volume map shows a blood pool (*arrow*) within the venous anomaly. The experienced readers recognized the cause of Tmax delay and dismissed a DVO. *D*, Left-hemispheric Tmax delay, more pronounced in the external watershed, in a 70-year-old man who presented with a transient right-sided weakness and speech disturbance. The patient developed a headache, but no infarct on follow-up imaging. The presentation was ascribed to a hemiplegic migraine. *E*, Borderzone Tmax delay is a pattern that involves the deep white matter watershed (*red arrows*) as well as the external watershed (the MCA-PCA watershed is indicated by *white arrows*). It results from contrast bolus dispersion, which causes delayed arrival of contrast in the most distal arterial territories. Causes for bolus dispersion include a proximal (eg, internal carotid artery) arterial stenosis or occlusion, poor cardiac output, and a poor contrast bolus injection.