

Demonstration of High Diagnostic Accuracy for Cerebral Ischemia in a Large Academic Hub-and-Spoke Telestroke Network

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Abstract

Objective: To determine the diagnostic accuracy of the initial telestroke consultation in a large academic hub-and-spoke telemedicine network.

Patients and Methods: This retrospective study includes all patients evaluated for cerebral ischemia through video telestroke consultation in a large academic hub-and-spoke telemedicine network from January 1, 2019 to December 31, 2020. A detailed chart review was conducted to identify the initial suspected diagnosis and final diagnosis. Cerebral ischemia was defined as acute ischemic stroke and transient ischemic attack. All other diagnoses were defined as stroke mimics. Data were organized into continuous and categorical variables. Sensitivity, specificity, positive predictive value, negative predictive value, accuracy, area under the curve (AUC), and likelihood ratio (LR+) for the telestroke-consultation diagnosis were calculated while using the final diagnosis as the gold standard diagnosis.

Results: A total of 1043 patients met the inclusion criteria. The final diagnosis of cerebral ischemia was made in 63.5% of all patients (539 of the 1043 with acute ischemic stroke, 123 of the 1043 with transient ischemic attack). Stroke mimic was diagnosed in 36.5% patients (381 of the 1043). The sensitivity and specificity of telestroke evaluation for diagnosis of cerebral ischemia were 97.1% and 81.4%, respectively. Positive predictive value was 90.1%, and negative predictive value was 94.2%. Overall diagnostic accuracy was 91.4%, with an LR+ of 5.21 and AUC of 0.89.

Conclusion: This study highlights the high diagnostic accuracy of telestroke providers in diagnosing cerebral ischemia. Further research exploring the application of teleneurology in the nonstroke setting and other medical subspecialties is warranted.

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Telestroke facilitates emergent assessment of patients with suspected acute ischemic stroke (AIS) to identify candidates for immediate therapeutic interventions.¹ The most recent guidelines for the early management of patients with AIS recommend the use of telemedicine for emergent evaluation of patients with suspected AIS to allow expert-guided time-sensitive interventions such as intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) when resources do not allow for in-person acute neurologic evaluations.²

The goal of our study was to determine the diagnostic accuracy of telestroke physicians in

diagnosing cerebral ischemia at the initial telestroke consultation in a large academic hub-and-spoke telemedicine network. In addition, we describe the use of IVT in cerebral ischemia and stroke mimic, and the recommendation of MT in patients found to have acute large vessel occlusions (LVOs) in our telestroke cohort.

METHODS

This is a retrospective study including all patients evaluated for cerebral ischemia through video telestroke consultation in a large academic hub-and-spoke telemedicine network from January 1, 2019 to December 31, 2020. The telestroke program at Mayo Clinic was

TABLE 1. Comparison of Initial Suspected Diagnosis Vs Final Diagnosis

Initial suspected diagnosis	Final Reference Standard Diagnosis (Gold Standard)		
	Stroke Mimic	Cerebral Ischemia	Total
Stroke mimic	310	19	329
Cerebral ischemia	71	643	714
Total	381	662	1043

established in 2007 to provide emergency care for suspected AIS cases in a hub-and-spoke model around comprehensive stroke centers in Minnesota, Florida, and Arizona. The program has grown to include 27 sites in 2021, of which 17 are Mayo Clinic Health System sites in rural Minnesota and Wisconsin. All sites have the ability to perform computed tomography (CT) angiography, but only 3 sites perform CT perfusion (CTP) studies. Telestroke activation criteria in our network include all patients presenting with acute neurologic deficits within 24 hours from previously known well. Other details concerning the structure, personnel, staffing, workflow, operations, administration, and technologies have already been published.³⁻⁵

All consecutive patients were included in the study within the predefined timeline. Patients were excluded if they were aged less than 18 years old, did not have video as a part of the consultation, did not have valid research authorization, or had intracerebral hemorrhage at the time of presentation.

A detailed chart review was conducted by 5 individuals of the study team: 3 medical students, 1 senior neurology resident, and 1 vascular neurologist. A second, complete review was done by the senior neurology resident to ensure initial and final diagnoses were correctly reported. The initial suspected diagnosis was extracted from the initial telestroke encounter. The final diagnosis from the discharge summary was supported by diagnostic studies and was taken as the gold standard diagnosis. In addition, demographic characteristic data, pre-existing vascular risk factors, pertinent medical history (seizure, migraine, and psychiatric history), and treatment recommendations such as IVT and MT were also recorded.

Cerebral ischemia was defined as AIS and transient ischemic attack (TIA), as these

diagnoses are difficult to differentiate at the time of telestroke encounter and both represent a continuum of neurovascular ischemia. All other diagnoses were defined as stroke mimics, which were subsequently coded into discrete categories.

Data were organized into continuous and categorical variables. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, area under the curve (AUC), and likelihood ratio (LR+) for the telestroke consultation diagnosis were calculated while using the final diagnosis as the gold standard diagnosis.

Kruskal-Wallis and Chi-Square tests were used to compare demographic characteristics and clinic risk factors by final diagnosis (cerebral ischemia vs stroke mimic). This study was reviewed and determined to be exempt by Mayo Clinic Institutional Review Board.

RESULTS

A total of 1073 patients' electronic records were manually reviewed. Twelve patients were excluded because of the presence of intracerebral hemorrhage on arrival, and 18 patients were excluded because their initial telestroke encounter did not have video. Therefore, 1043 patients met the inclusion criteria and were included in the final analysis.

Overall, the average age was 69.6 years (SD 16.6), 52.1% were women and 94.5% identified as White. The final diagnosis of cerebral ischemia was made in 63.5% of all patients (539 of the 1043 with AIS and 123 of the 1043 with TIA) (Table 1). Stroke mimic was diagnosed in 36.5% of patients (381 of the 1043). Table 2 displays the demographic characteristic data by final diagnosis.

Patients with a final diagnosis of cerebral ischemia were more likely to have pre-existing hypertension (78.5% vs 67.7%;

TABLE 2. Demographic Characteristics by Final Diagnosis^a

Characteristic	Final Reference Standard Diagnosis (Gold Standard)			P
	Stroke Mimic (n=381)	Cerebral Ischemia (n=662)	Total (N=1043)	
Age at Telestroke Consult				<.001 ^a
Mean ± SD	64.4±17.3	72.6±14.4	69.6±16.0	
Sex, n (%)				<.001 ^b
Man	152 (39.9%)	348 (52.6%)	500 (47.9%)	
Woman	229 (60.1%)	314 (47.4%)	543 (52.1%)	
Race, n (%)				.20 ^b
White	355 (93.2%)	631 (95.3%)	986 (94.5%)	
Black	7 (1.8%)	10 (1.5%)	17 (1.6%)	
Asian	5 (1.3%)	7 (1.1%)	12 (1.2%)	
American Indian or Native Alaskan	2 (0.5%)	1 (0.2%)	3 (0.3%)	
Pacific islander	0 (0.0%)	1 (0.2%)	1 (0.1%)	
Other	9 (2.4%)	4 (0.6%)	13 (1.2%)	
Unknown or choose not to disclose	3 (0.8%)	8 (1.2%)	11 (1.1%)	

^aKruskal-Wallis P-value^bChi Square P-value

$P \leq .001$), hyperlipidemia (68.4% vs 50.4%; $P \leq .001$), atrial fibrillation (23.7% vs 15.7%; $P = .0023$), and coronary artery disease (29.0% vs 22.8%; $P = .03$). Patients with a final diagnosis of stroke mimic were more likely to have a history of seizure (12.9% vs 5.4%; $P \leq .001$), migraine (20.5% vs 6.2%; $P \leq .001$), or psychiatric diagnosis (34.9% vs 18.1%; $P \leq .001$). There was no difference in diabetes mellitus (30.2% stroke mimic vs 30.1% cerebral ischemia; $P = .97$) or stroke history (19.4% stroke mimic vs 23.9% cerebral ischemia; $P = .10$) between the groups. Table 3 displays the baseline comorbidities by final diagnosis.

The mean systolic blood pressure overall at presentation was 154.7 (SD 27.1) mmHg, and diastolic blood pressure overall was 86.6 (SD 16.8) mmHg. Systolic blood pressure was significantly higher in the cerebral ischemia group ($P = .0047$), although diastolic blood pressure was similar between the groups. The mean blood glucose overall was 183.7 mg/dL (SD 72.9) and was similar between the groups ($P = 0.24$).

The median National Institute of Health Stroke Scale score at presentation was 3 (interquartile range, 1-8) and was significantly higher in the cerebral ischemia group ($P \leq .001$).

Overall Diagnostic Accuracy of Cerebral Ischemia

The sensitivity and specificity of telestroke evaluation for the diagnosis of cerebral ischemia were 97.1% and 81.4%, respectively. The PPV was 90.1%, and NPV was 94.2% (Table 4). Overall diagnostic accuracy was 91.4%, with an LR+ of 5.21 and an AUC of 0.89 (Table 5).

Intervention Recommendations

Intravenous thrombolysis was recommended for 20.6% (215 of the 1043) patients overall during the initial telestroke encounter. Ultimately, 93.0% (200 of the 215) had IVT administered. Notably, 90% (180 of the 200) of patients who had IVT administered had a final diagnosis of cerebral ischemia. Reasons for not administering included minor nondisabling deficits (7 of the 15), patient preference (4 of the 13), medical decompensation (2 of the 15), or being beyond the established time window for thrombolysis (2 of the 15). Of the patients who received IVT as part of acute stroke treatment, 90.0% (180 of the 200) had a final diagnosis of cerebral ischemia, and 10.0% (20 of the 200) were diagnosed as a stroke mimic at discharge. Of these, only 1 patient had a final diagnosis of TIA (99.4%

TABLE 3. Baseline Comorbidities by Final Diagnosis

Comorbidity	Final Reference Standard Diagnosis (Gold Standard)			P
	Stroke Mimic (n=381)	Cerebral Ischemia (n=662)	Total (N=1043)	
Hypertension, n (%)	258 (67.7%)	520 (78.5%)	778 (74.6%)	≤.001 ^a
Hyperlipidemia, n (%)	192 (50.4%)	453 (68.4%)	645 (61.8%)	≤.001 ^a
Diabetes mellitus n (%)	115 (30.2%)	199 (30.1%)	314 (30.1%)	.97 ^a
Tobacco use, n (%)				.002 ^a
Former	112 (29.5%)	249 (37.7%)	361 (34.7%)	
Current	89 (23.4%)	105 (15.9%)	194 (18.6%)	
Atrial fibrillation, n (%)	60 (15.7%)	157 (23.7%)	217 (20.8%)	.002 ^a
Stroke history, n (%)	74 (19.4%)	158 (23.9%)	232 (22.2%)	.10 ^a
Coronary artery disease, n (%)	87 (22.8%)	192 (29.0%)	279 (26.7%)	.03 ^a
Seizure history, n (%)	49 (12.9%)	36 (5.4%)	85 (8.1%)	≤.001 ^a
Migraine history, n (%)	78 (20.5%)	41 (6.2%)	119 (11.4%)	≤.001 ^a
Psychiatric history, n (%)	133 (34.9%)	120 (18.1%)	253 (24.3%)	≤.001 ^a

^aChi square P-value.

[179 of the 180] AIS vs 0.6% [1 of the 180] with TIA). The most common stroke mimic diagnosis among patients who received IVT was functional neurological disorder (6 of the 20, 30%).

Vascular imaging was completed in 658 of the 1043 cases, and acute LVO was identified in 18.7% (123 of the 658) of cases. This was defined as occlusion in the internal carotid artery, middle cerebral artery segment 1, middle cerebral artery segment 2, posterior cerebral artery segment 1, or basilar artery. Any intracranial vascular occlusion was identified in 22.5% (149 of the 658) of patients (internal carotid artery/middle cerebral artery segment 1/middle cerebral artery segment 2/M3/A1/A2/basilar/vertebral/P1/P2). Of those with LVO, 40.3% (60 of the 149) underwent MT with most patients achieving thrombolysis in cerebral infarction 2b reperfusion or higher (82.0%, 50 of the 61). The most common reasons for MT not being performed in patients with vessel occlusion identified was lack of LVO identified on repeat imaging of cerebral angiogram (36.8%, 32 of the 75) followed by large, identified core on CTP (11.5%, 10 of the 75). Computed tomography perfusion was ordered as part of the initial telestroke encounter in 3.2% of all cases (33 of the 1035). Thirty-two patients with a final

diagnosis of cerebral ischemia (n=662) received both IVT and MT.

Stroke Mimics

The most common stroke mimics were metabolic encephalopathy (13.7%, 52 of the 381), migraine (10.8%, 41 of the 381), and seizure (10.5%, 40 of the 381). A detailed breakdown of all stroke mimics can be found in [Supplementary Table 1](#), available online at <https://www.mcpcdigitalhealth.org/>, with the 10 most common stroke mimics highlighted in [Figure](#).

DISCUSSION

This study highlights the ability of vascular and critical care neurologists to accurately diagnose cerebral ischemia in patients presenting with acute stroke syndromes through video-based telemedicine platforms, as the overall diagnostic accuracy of predicting cerebral ischemia in our study was 91.4%. Moreover, 90% of the patients who received IVT were diagnosed with cerebral ischemia at discharge, indicating excellent diagnostic reasoning and appropriate recommendations in this setting. Our study is in line with previous research investigating the diagnostic accuracy of telestroke. Poon et al⁶ describe a high diagnostic agreement for stroke and TIA when comparing the initial telestroke

TABLE 4. Statistical Analysis of the Diagnostic Accuracy of Cerebral Ischemia at the Initial Telestroke Encounter

Statistic	Calculation	Rate	95% CI Lower	95% CI Upper
Sensitivity	643/662	97.13	95.55	98.26
Specificity	310/381	81.36	77.09	85.15
PPV	643/714	90.06	87.62	92.15
NPV	310/329	94.22	91.13	96.49
Accuracy	953/1043	91.37	89.50	93.00

NPV, negative predictive value; PPV, positive predictive value.

encounter with discharge diagnosis (88%), similar to our diagnostic accuracy of 91.4%. By contrast to our data, the cohort from Poon et al⁶ is smaller (n=404) and does not have clear guidelines for activation of a telestroke consult (ie, previously known normal and objective neurological deficit) but rather encourages activation if the activating provider believes the patient is within the timeframe for IVT or MT. Our cohort is similar in that we both include only video encounters completed by vascular or critical care neurologists. Our work also supports the literature by Escola et al,⁷ who report a high sensitivity of diagnosis of cerebrovascular disease (95.2%) at the initial telestroke encounter, similar to our sensitivity of 97.1%. Their cohort differs in that it includes a larger number of stroke mimics, with 48% of final diagnoses being noncerebrovascular. Notably, telestroke activation criteria are not disclosed in their paper, and therefore, a lack of clear activation criteria may help explain this difference, resulting in a higher number of inappropriate telestroke activations. It is important to note that their initial cohort before exclusion (lack of full source data) was larger (n=1500) than the current data presented, although, it differs in that their initial telestroke consultations were performed by various physicians, including an important portion being completed by

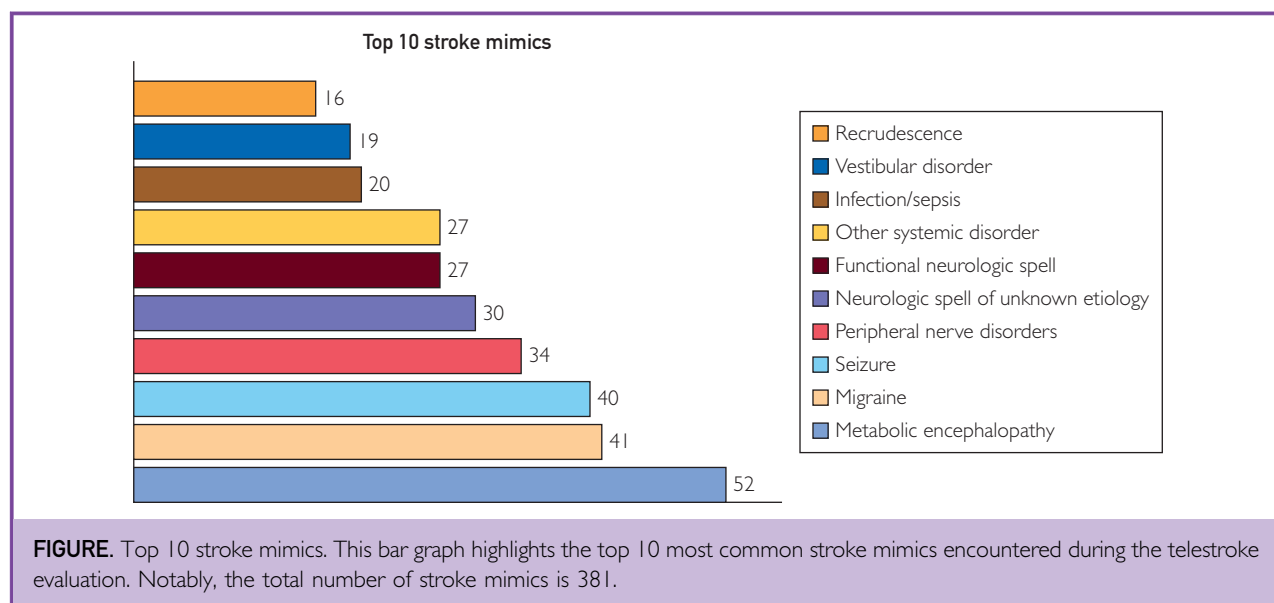
residents and internal medicine consultants.⁷ This contrasts with our data, in which initial telestroke consultations are only completed by board-certified neurologists, specifically vascular or critical care-trained neurologists.

Despite the high overall accuracy, there are opportunities for improvement. Although the sensitivity for cerebral ischemia is very high (97.1%), the specificity is less robust (81.4%), which may expose patients to excess risk by IVT administration, invasive diagnostic workup, excessive or costly evaluations, and resource utilization. To assist in the detection of stroke mimics, many predictive models have been proposed, including the TeleStroke mimic score by Ali et al.⁸ The TeleStroke mimic score was developed as a prediction model for identifying stroke mimics in telestroke evaluations and is on the basis of factors independently associated with stroke mimics including younger age, being less likely to have hypertension, atrial fibrillation, heart failure, and more likely to have a history of seizure.⁸ In this original study, the TeleStroke mimic score was retrospectively applied to 13,897 patients being evaluated for cerebral ischemia and was found to have a ROC (receiver operative characteristic curve) of 0.75 in the derivation cohort.⁸ This was validated by Carlin et al⁹ in a retrospective study where the TeleStroke mimic score was applied retrospectively in 339 patients who

TABLE 5. Additional Statistical Analysis of the Diagnostic Accuracy of Cerebral Ischemia at the Initial Telestroke Encounter

Other Statistics	Calculation	Estimate	95% CI Lower	95% CI Upper
LR+	0.9713/(1-0.8136)	5.21		
LR-	(1-0.9713)/0.8136	0.04		
AUC	Logistic Regression	0.8925	0.8719	0.9131

AUC, area under the curve; LR, likelihood ratio.



underwent telestroke evaluation for cerebral ischemia, and the area under the ROC curve was found to be 0.78, higher than the original study. We also note that our study found that patients with stroke mimic are more likely to have a history of seizure, migraines, and psychiatric disorders.

An additional future area of exploration includes the application of advanced neuroimaging in the acute setting to assist with hyperacute management decisions, such as CTP within the telestroke setting. Tran et al¹⁰ aimed to determine if CTP provided benefit to clinical assessment alone in distinguishing between stroke and stroke mimic. This retrospective analysis included 1513 patients being evaluated in the Northern New South Wales Telestroke service in Australia where CTP was routinely ordered as part of the acute telestroke assessment. They found that AUC on the ROC was found to be 0.91 when using the absence of ischemic lesion on CTP in addition to clinical features, whereas the AUC was lowered to 0.71 when using clinical features alone to distinguish stroke from stroke mimic.¹⁰ This study supports the use of CTP to help differentiate the stroke from mimic, although the overall performance is similar to our study (AUC 0.89) despite low CTP utilization in our study (3.2% of all encounters). Given the limited data regarding CTP in our study, it is unclear if it provided clinically meaningful information

in the acute setting for decision-making regarding administration of IVT or recommendation of MT. Future studies investigating the use of CTP and acute MRI at the initial telestroke encounter should investigate if these advanced imaging options ultimately help preserve cost and resources in the long run because of providing early, useful diagnostic information that may prevent unnecessary transfers and invasive workup and treatment. Given the high diagnostic accuracy of cerebral ischemia despite the low utilization of advanced imaging such as CTP in our study, inaccessibility to CTP should not prevent decision-making regarding immediate treatment and diagnosis in the initial telestroke encounter at this time.

Overall, our data may support the potential expanded use of acute teleneurology to assist with other neurologic emergencies,¹¹ such as seizure,¹² coma,¹³ intracranial hemorrhage,¹⁴ vision loss,¹⁵ brain death,¹⁶ and neuroprognostication.¹⁷ Research has shown that critically ill neurological patients admitted to a neurointensive care unit have improved outcomes;^{18,19} however, neurocritical care remains a growing field and is often absent in most hospitals, particularly in the rural and underserved parts of the United States.²⁰ Tele-neurology may help fill this gap and allow neurointensivists to assess patients by video and provide recommendations to intensivists

who may not have specialized training in neurology. We also acknowledge that this shortage of neurological care may be felt even more abroad, where there are only 3 per 10 million people in low income countries.²¹ Therefore, the application of teleneurology for consultation of conditions other than AIS should be further investigated and applied, as it may have life-changing outcomes both within the United States and beyond.²² More research is needed to assess the accuracy of telemedicine-based assessment of other acute neurologic conditions.

CONCLUSION

This study represents the largest academic cohort of video-based telestroke evaluations by vascular and critical care neurologists used to determine the diagnostic accuracy of cerebral ischemia. This study builds on previous literature and shows the consistent ability to provide high-quality recommendations through telemedicine. Although telestroke has been validated and endorsed in acute stroke guidelines, this study highlights further opportunities to expand teleneurology beyond AIS assessment, where there remains a shortage of acute neurologic expertise. Future research should focus on determining how to accurately diagnose and distinguish stroke mimic from cerebral ischemia, with the goal of reducing administration of unnecessary treatments and diagnostic procedures to our patients and preserving resources.

POTENTIAL COMPETING INTERESTS

Given his role as Editorial Board member, Dr Bart Demaerschalk, reported no involvement in the peer-review of this article and has no access to information regarding its peer-review. The remaining authors report no disclosures.

ACKNOWLEDGMENTS

We would like to acknowledge Ms Charisse Nord, Ms Emily Pahl, and all our telestroke providers (Dr Kevin Barrett, Dr Felix Chukwudelunzu, Dr Bart Demaerschalk, Dr Oana Dumitrascu, Dr Stephen English, Dr Kelly Flemming, Dr William Freeman, Dr Courtney Hrdlicka, Dr Josephine Huang, Dr Zafer Keser, Dr James Klaas, Dr Gyanendra Kumar, Dr Michele Lin, Dr Elizabeth Mauricio, Dr Bayan

Moustafa, Dr Deena Nasr, Dr Cumara O'Carroll, Dr Alejandro Rabinstein, Dr Lindsay Williams, and Dr Micah Yost) for their ongoing support and contributions to the telestroke network clinical operations, administration, and clinical consultations.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <https://www.mcpcdigitalhealth.org/>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: AIS, acute ischemic stroke; AUC, area under the curve; CTP, computed tomography perfusion; IVT, intravenous thrombolysis; LR+, likelihood ratio; MT, mechanical thrombectomy; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating curve; TIA, transient ischemic attack

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