Retrospective evaluation of a clinical decision support tool for effective computed tomography angiography utilization in urgent brain imaging of suspected TIA/ minor stroke in the emergency department

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CLINICIAN'S CAPSULE

What is known about the topic?

Canadian guidelines recommend that suspected transient ischemic attack (TIA) patients receive brain imaging in the emergency department; yet, high requisition rates for non-cerebrovascular patients exist.

What did this study ask?

What is the hypothetical impact that a clinical decision support tool (CDST) would have on computed tomography angiography (CTA) requisitions for suspected TIA patients.

What did this study find?

CDST use would have resulted in more TIA patients receiving CTA, while imaging fewer non-cerebrovascular patients.

Why does this study matter to clinicians?

A CDST could assist clinicians in applying the Canadian stroke guidelines as pragmatically as possible.

ABSTRACT

Objectives: The *Canadian Stroke Best Practice Recommendations* suggests that patients suspected of transient ischemic attack (TIA)/minor stroke receive urgent brain imaging, preferably computed tomography angiography (CTA). Yet, high requisition rates for non-cerebrovascular patients overburden limited radiological resources, putting patients at risk. We hypothesize that our clinical decision support tool (CDST) developed for risk stratification of TIA in the emergency department (ED), and which incorporates Canadian guidelines, could improve CTA utilization. **Methods:** Retrospective study design with clinical information gathered from ED patient referrals to an outpatient TIA unit in Victoria, BC, from 2015-2016. Actual CTA orders by ED and TIA unit staff were compared to hypothetical CTA ordering if our CDST had been used in the ED upon patient arrival.

Results: For 1,679 referrals, clinicians ordered 954 CTAs. Our CDST would have ordered a total of 977 CTAs for these patients. Overall, this would have increased the number of imaged-TIA patients by 89 (10.1%) while imaging 98 (16.1%) fewer non-cerebrovascular patients over the 2-year period. Our CDST would have ordered CTA for 18 (78.3%) of the recurrent stroke patients in the sample.

Conclusions: Our CDST could enhance CTA utilization in the ED for suspected TIA patients, and facilitate guideline-based stroke care. Use of our CDST would increase the number of TIA patients receiving CTA before ED discharge (rather than later at TIA units) and reduce the burden of imaging stroke mimics in radiological departments.

RÉSUMÉ

Objectifs: D'après les lignes directrices canadiennes sur les pratiques exemplaires en matière de prise en charge des accidents vasculaires cérébraux (AVC), il est recommandé de pratiquer d'urgence, dans les cas présumés d'accident ischémique transitoire (AIT) ou d'AVC léger, un examen par imagerie cérébrale, de préférence une angiographie par tomodensitométrie (TDM). Toutefois, le nombre élevé de demandes d'examen chez les patients exempts de lésions vasculaires cérébrales exerce une pression à la hausse sur les ressources disponibles en radiologie, d'où une augmentation

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du risque chez les patients concernés. Aussi l'étude visait-elle à vérifier si l'outil d'aide à la décision clinique (OADC) que l'équipe a élaboré pour l'évaluation du risque d'AIT au service des urgences (SU) et qui tient compte des lignes directrices en vigueur au Canada aurait permis une utilisation plus rationnelle de l'angiographie par TDM.

Méthode: Il s'agit d'une étude rétrospective reposant sur la collecte de renseignements cliniques, tirés de demandes d'examens faites par des SU à un service de consultations externes spécialisé dans le traitement des AIT, à Victoria, en Colombie-Britannique, de 2015 à 2016. Ont été comparés le nombre réel de demandes d'angiographie par TDM faites par le personnel de SU et du service spécialisé dans le traitement des AIT, et le nombre hypothétique de demandes d'angiographie par TDM si l'OADC avait été utilisé au SU, à l'arrivée des patients.

Résultats: Sur 1679 demandes de consultation, il y a eu 954 demandes d'angiographie par TDM faites par des cliniciens. Si l'OADC avait été appliqué, le nombre total d'angiographies par TDM se serait élevé à 977 chez les patients concernés, ce qui se serait traduit, dans l'ensemble, par une augmentation de 89 (10,1 %) demandes d'examens par imagerie chez les

patients ayant subi un AIT et une diminution de 98 (16,1 %) chez les patients exempts de lésions vasculaires cérébrales, sur la période de 2 ans. Ainsi, l'OADC aurait permis de faire une demande d'angiographie par TDM chez 18 (78,3 %) des patients ayant subi une récidive d'AVC, dans l'échantillon étudié.

Conclusion: L'application de l'OADC permettrait une utilisation plus rationnelle de l'angiographie par TDM, au SU, chez les patients atteints d'un AIT présumé, et faciliterait la prestation de soins fondés sur les lignes directrices dans les cas d'AVC. Ce faisant, il y aurait une augmentation du nombre d'angiographies par TDM pratiquées chez les patients souffrant d'un AIT avant le congé du SU (plutôt qu'après, dans les services de traitement des AIT) ainsi qu'une réduction du fardeau imposé par les affections simulant un AVC, quant au nombre d'examens par imagerie, sur les services de radiologie.

Keywords: clinical decision rule (CDR), clinical decision support tool (CDST), computed tomography angiography (CTA), transient ischemic attack (TIA)

INTRODUCTION

The management of transient ischemic attack (TIA)/ minor-stroke in the emergency department (ED) is challenging.¹ The risk of a recurrent stroke after TIA is greatest during the first 24 hours immediately following the event,^{2–5} with approximately 50% of recurrent strokes occurring during this period.⁴ The risk of a recurrent stroke after TIA, therefore, constitutes a medical emergency requiring urgent intervention to maximize positive outcomes. Early recognition of the

Table 1. Distribution of ED, SRAU, combined ED + SRAU, and CDST CTA requisitions for the 10 most frequent stroke-mimic diagnoses (N = 865)

Mimic classification	Ν	ED	SRAU	ED + SRAU	CDST
Migraine	117	52	17	69	35
Vestibulopathy	85	37	13	50	11
NYD	78	33	23	56	32
Other	58	18	8	26	32
Syncope	57	14	9	23	25
Neuropathy	46	18	6	24	30
TGA	37	12	4	16	3
Seizure	26	9	2	11	12
Constitutional	21	5	3	8	13
Psychogenic	19	7	0	7	9
CDST = clinical decision sur	port tool	FD = em	nergency de	partment: NYD = no	t vet

diagnosed; Other = non-typical minic diagnosis; SRAU = Stroke Rapid Assessment Unit; TGA = transient global amnesia. condition and initiating appropriate investigations and treatments are key to ensuring positive outcomes. The Canadian stroke best practice guidelines recommend that all patients with motor/speech deficits suspected of TIA who present to the ED less than 48 hours after symptom onset receive vascular imaging.^{6,7}

Suspected TIA patients with carotid stenosis, large vessel occlusion, and intracranial atherosclerosis are at greatest risk of stroke recurrence.⁸ Previous studies have demonstrated a high prevalence of these etiologies among TIA patients.^{9,10} Several guidelines^{6,7,11,12} recommend vascular imaging of suspected TIA patients in the ED for the early detection of these highrisk conditions, specifically carotid stenosis (Evidence Level A). Approximately 2% of TIA patients receive carotid endarterectomy (CEA),¹³ with the number needed to treat to prevent one recurrent stroke equal to 5 when performed within 2 weeks of the initial event.¹⁴ Computed tomography angiography (CTA) is recognized as a preferential vascular imaging investigation (Evidence Level C) to conduct when TIA/minor stroke is clinically suspected.^{6,7,15,16}

A challenge in adhering to the guidelines is the high prevalence of low-risk, non-cerebrovascular conditions (e.g., migraine; see Table 1) that mimic stroke in clinical presentations (i.e., stroke mimics), and which can account for 40% to 60% of patients referred to fast-track TIA units.^{1,17–20} Unnecessarily performing CTA

on stroke-mimic patients represents an inappropriate use of radiological resources and limits access to higherrisk patients. Further, to identify patients at highest risk of stroke recurrence, CTA investigations are recommended to be conducted in the ED prior to discharge. However, limited radiological resources means that the CTA decision for some patients must be delayed, with patients sent to outpatient TIA units. These patients represent an opportunity to improve TIA management.⁵ Finally, previous research has suggested that vascular imaging is frequently underutilized within Canadian EDs to assess suspected TIA patients.²¹ As such, present-day ED practices do not currently align with best practice recommendations. The gap between evidence-based guidelines and physician practice is widespread across medical specialties, and clinical decision support tools (CDSTs) have been suggested as a way of reducing this gap.^{22,23}

With our study, we hope to bridge the gap between stroke best practice recommendations and practicing ED physicians. Our group has developed an electronic CDST to assist in decision-making for CTA imaging of suspected TIA patients in ED settings. Our tool is based upon a logistic regression model (clinical classifier) that we previously developed and validated to identify TIA patients in the ED,^{24–26} and incorporates the Canadian stroke best practice guidelines.⁶ This decision support simplifies adherence to the guidelines, which contain numerous details and conditional logic. Our decision support tool thus assists ED physicians with decisionmaking by making the best pragmatic use of the guidelines and evidence-based care in an end-user informed format.

In the present retrospective study, we aim to determine the hypothetical impact that the use of our CDST would have had on CTA requisitions at the institutional level if it had been available for use by ED physicians. We hypothesize that use of the CDST would have resulted in more TIA patients and fewer stroke-mimic patients receiving CTA imaging relative to the combined baseline CTA requisition patterns in three urban hospitals.

METHODS

Participants

servicing Vancouver Island (population: 799,400). The SRAU receives referrals from EDs, family practice, and specialists (e.g., ophthalmologists). The referral form for the unit is known as the ACVS (acute cerebrovascular syndrome) Assessment Form²⁷⁻²⁹ and has been in use since November 2014. We specifically developed the assessment form to capture all of the data elements required by our clinical classifier, as well as to improve referral triage within our unit.²⁶ Referral forms are entered verbatim by unit staff into the SRAU electronic medical record (EMR) system.

Neurological evaluation and diagnosis

Patients received standard of care treatment by unit neurologists upon arrival at the SRAU. Radiological investigations frequently include magnetic resonance imaging (MRI) and CTA. Unit neurologists diagnose patients on the basis of both clinical and radiological findings, the combination of which has been argued to represent the gold standard in stroke diagnosis.^{30,31} Possible diagnostic categories include "TIA/minor stroke," "stroke-mimic conditions," "not yet diagnosed" (NYD), and "hemorrhagic stroke."

TIA and minor stroke are grouped together because they both represent the lower end of the brain ischemia continuum,^{28,29} with TIA defined as a "brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction...[t]he corollary is that persistent clinical signs or characteristic imaging abnormalities define infarction — that is, stroke,"³² (p1715)</sup> with *minor stroke* defined as a stroke with a National Institutes of Health Stroke Scale (NIHSS) of < 4.³³

Stroke-mimic conditions are diagnosed when possible, with the most frequently identified being migraine, vestibulopathy, syncope, and neuropathy (see Table 1). Less common stroke-mimic diagnoses are classified as "Other" and include a variety of less common conditions, including congenital strabismus, and medication side effects.

A small portion of referred patients are not seen at the SRAU (i.e., "no shows"). Reasons for nonattendance include 1) patient refused appointment, 2) patient admitted to hospital with recurrent TIA/stroke, 3) patient seen by other physician/specialist, 4) inappropriate referral, 5) patient seen by inpatient neurology, and 6) death. For analysis purposes we created a patient classification variable that indicated either patients' SRAU diagnoses (e.g., TIA, stroke mimic, NYD, hemorrhagic stroke) or reason for unit non-attendance.

Clinical decision support tool

The CDST that we have developed was informed by data from a health informatics research study conducted to determine the operational requirements for the design of an electronic decision support tool to triage suspected TIA patients in the ED.³⁴ Activities involved in this study included ED workflow analysis and ED physician and nurse focus groups. A complete description of the CDST and clinical classifier can be found in the supplement.

Variables

Clinical variables consisted of the data elements from the ACVS Assessment Form.²⁷ Variables represented by checkboxes were treated as binary variables, with unchecked items interpreted as the absence of the given data element (0=absent; 1=present). Blood pressure was measured in millimeter of mercury (mm Hg), and patient age was recorded in years. Patient sex was treated as a binary variable (0=female; 1=male). CTA status (0=not done; 1=done), date of CTA investigation, and date of TIA unit arrival were also extracted from the SRAU EMR. CEA status was extracted from the regional hospital electronic health record system.

A variable representing institutional level CTAs (ED + SRAU) was also derived. The institutional level encompasses the entire patient care pathway for TIA management and includes both frontline, referring ED physicians and TIA unit staff and neurologists. We will use the term, *hospital clinicians*, henceforth, to refer to ED physicians and TIA unit neurologists who can requisition CTA for suspected TIA patients.

From the referral form information, we derived a binary variable to indicate the absence or presence of characteristic TIA symptoms (0=absent; 1=present), for example, language disturbance, speech disturbance, and face droop. Details are provided in the supplement.

Sample

The study sample consisted of ED patients consecutively referred from three urban EDs to the SRAU between January 2015 and December 2016. The three EDs (Victoria General Hospital, Royal Jubilee Hospital [Victoria, BC], Nanaimo Regional General Hospital) all have CTA imaging availability on-site. Upon extraction from the SRAU EMR, the sample consisted of 1,679 ED referred patients. Referral systolic and diastolic blood pressure readings were missing for 104 of these patients, with an additional 5 patients missing only referral diastolic blood pressure. Missing blood pressure values were imputed using mean substitution as described in the supplement (mean systolic = 142 mm Hg; mean diastolic = 78 mm Hg). Table 2 displays the demographic characteristics of the data set prior to corrections for missing blood pressure.

Ethics statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Study approval (reference number H2009-114) was granted by the Health Research Ethic Board of the Vancouver Island Health Authority, Victoria, BC, Canada.

Statistical analysis

Our retrospective analysis compares the allocation of CTA requisitions by hospital clinicians among true TIA and stroke-mimic patients referred from the ED to our fast-track TIA unit, with the allocation that would have occurred had the CDST been available in the ED.

To compare the performance of our CDST for CTA requisition with hospital clinicians' CTA requisition baseline, we first applied the logistic regression model constituting the CDST (see the supplement for model coefficients) to calculate the estimated probability of TIA/minor stroke for each patient in the data set. Estimated probabilities were then filtered by the presence of characteristic TIA/minor-stroke symptoms: If the characteristic TIA symptoms variable was coded as absent, then the estimated probability remained unchanged. The estimated probability remained unchanged. The estimated probabilities were then dichotomized using two pre-established cutpoints (≥ 0.516 for flagging potential TIA cases, and ≥ 0.662 for recommending CTA). A discussion of the derivation and

	Mimic (36.2%)	TIA (52.4%)	Other (11.4%)	p value*	
N	608	879	192		
Patient age, mean (SD)	66.6 (15.4)	74.0 (12.2)	69.8 (15.6)	< 0.001	
Male, N (%)	284 (46.7)	450 (51.2)	94 (49.0)	0.234	
Positive symptom of TIA [†] , N (%)	425 (69.9)	784 (89.2)	148 (77.1)	< 0.001	
CT completed, N (%)	229 (37.7)	279 (31.7)	58 (30.2)	0.033	
CT/CTA completed, N (%)	329 (54.1)	558 (63.5)	68 (35.4)	< 0.001	
MRI completed, N (%)	147 (24.2)	227 (25.8)	20 (10.4)	< 0.001	
ASA, N (%) [‡]	145 (23.8)	203 (23.1)	14 (7.3)	< 0.001	
Clopidogrel, N (%) [‡]	18 (3.0)	25 (2.8)	1 (0.5)	0.152	
ASA + clopidogrel, N (%) [‡]	16 (2.6)	85 (9.7)	2 (1.0)	< 0.001	
Statin, N (%) [‡] , [§]	88 (14.5)	157 (17.9)	8 (4.2)	< 0.001	
ABCD2, N (%)					
0	15 (2.5)	8 (0.9)	5 (2.6)	< 0.001	
1	35 (5.8)	27 (3.1)	16 (8.3)		
2	110 (18.1)	94 (10.7)	36 (18.8)		
3	140 (23.0)	133 (15.1)	39 (20.3)		
4	181 (29.8)	255 (29.0)	45 (23.4)		
5	89 (14.6)	201 (22.9)	28 (14.6)		
6	32 (5.3)	136 (15.5)	21 (10.9)		
7	6 (1.0)	25 (2.8)	2 (1.0)		
Systolic BP, mean (SD) [¶]	151.1 (26.1)	156.7 (26.9)	152.3 (27.8)	< 0.001	
Diastolic BP, mean (SD) [¶]	80.8 (12.6)	81.8 (13.0)	82.2 (14.0)	0.278	
Hypertension, N (%)	317 (52.1)	567 (64.5)	72 (37.5)	< 0.001	
Hyperlipidemia, N (%)	219 (36.0)	338 (38.5)	38 (19.8)	< 0.001	
Atrial fibrillation, N (%)	63 (10.4)	170 (19.3)	24 (12.5)	< 0.001	
Diabetes, N (%)	87 (14.3)	182 (20.7)	28 (14.6)	0.003	
Smoking, N (%)	69 (11.3)	115 (13.1)	31 (16.1)	0.209	

*t and chi-square homogeneity test.

[†]Variable was coded as present if patients' referral data indicated any of the following symptoms: a) unilateral limb weakness; b) unilateral limb numbness; c) language disturbance (i.e., aphasia); d) speech disturbance (i.e., dysarthria); e) face droop; f) visual field deficits; g) unsteadiness (i.e., ataxia); h) diplopia; i) "curtain" descending over field of vision (i.e., amaurosis fugax); and j) vision loss.

*All medications referring to those that patients were currently taking or were prescribed in the ED at the time of their assessment in the ED;

[§]Any statin medication at any dose.

[¶]Values prior to mean substitution correction for missing blood pressure values.

ASA=acetylsalicylic acid; CT=computed tomography; CTA=computed tomography angiography; ED=emergency department; MRI=magnetic resonance imaging; Other=all patient classifications not *Mimic* or *TIA*.

rationale for these cutpoints can be found in the supplement.

To evaluate the effect of the CDST on the number of imaging requisition, we compared the total number of CTA orders by hospital clinicians with those of the CDST for all consecutively referred ED patients, regardless of diagnosis. To evaluate the performance of the CDST's recommendations on CTA requisitions, we restricted the sample to only those patients who received a diagnosis of TIA or stroke mimic at the SRAU. We calculated the diagnostic odds ratio (DOR)³⁵ of hospital clinicians and the CDST with respect to ordering CTA for TIA patients. We compared the sensitivity, specificity, and accuracy of hospital clinicians CTA orders with those of the CDST using McNemar tests.³⁶ The diagnostic performance of the CDST (i.e., flagging possible TIA cases) is also presented, although no comparisons with hospital clinicians are possible because the referring physicians by definition will have 100% sensitivity for TIA patients in this sample of referred patients.

Analyses were completed using the ROCR (v1.0.7),³⁷ pROC (v1.12.1),³⁸ Hmisc (v4.1.1),³⁹ and rms (v5.1.2)⁴⁰ libraries in the R statistical language (v3.4.4).⁴¹

RESULTS

Table 3 summarizes the frequencies of patient classifications for the 1,679 patients referred to the SRAU. Of the patients referred to the SRAU, 1,537 (91.5%) attended the unit and were assessed by unit neurologists; 142 referred patients did not attend the unit (i.e.,

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Patient classification	N	MRI		СТ		СТА			
		ED	SRAU	ED	SRAU	ED	SRAU	ED + SRAU	CDST
Patients seen in SRAU									
TIA	879	14	213	200	79	372	186	558	647
Mimic	608	12	135	160	69	235	94	329	231
NYD	31	0	10	9	3	11	6	17	11
No diagnosis recorded	16	1	2	1	4	3	0	3	11
Hemorrhagic stroke	3	0	2	0	1	1	1	2	2
Patients not seen in SRAU ("no show")									
Refused	77	0	0	0	0	24	0	24	33
Admitted – recurrent TIA/stroke	23	1	0	12	0	10	0	10	18
Other reasons	42	1	0	5	0	11	0	11	24

"no show"). Of "no show" patients, the reason for unit non-attendance was unknown for 2 patients.

A total of 23 patients were admitted to the hospital with recurrent TIA/stroke prior to their SRAU appointment. The mean time to TIA/stroke recurrence from the initial ED visit to hospital admission was 35.5 hours (range, 5.8-91.2); 10 (43.5%) of recurrent events occurred within 24 hours. Of recurrent TIA/ strokes, 7 (30.4%) resulted in persistent deficits.

A total of 23 patients (3% of TIA patients) received CEA in relation to their condition (none with recurrent stroke). Of the patients (N = 1,537) who attended the unit, 1,487 (96.7%) received a definite diagnosis (i.e., TIA or stroke mimic). A total of 3 patients were diagnosed with a hemorrhagic stroke at the SRAU. Neurologist diagnoses were unknown for 16 patients. The median time from ED referral to unit arrival was 3.2 days (interquartile range 1.6-5.4 days).

Table 3 summarizes the number of CTA requisitions by ED physicians, the SRAU, hospital clinicians (ED + SRAU), and the CDST, stratified by patient classification. Out of the 1,679 ED referrals, hospital clinicians ordered 954 CTAs. Over the 2-year period, mean of CTA requisitions per day by ED physicians was 0.91 (range, 0-5). The total volume of CTAs ordered over the 2-year period remained relatively constant between hospital clinicians and the CDST (954 v. 977). Overall, the CDST would have ordered 23 additional CTAs over the 2-year period and increased the number of imaged-TIA patients by 89 (10.1%), while imaging 98 (16.1%) fewer stroke-mimic patients. For the 2-year period, the mean of CTA requisitions per day by the CDST would have been 1.34 (range, 0-7). Of the 23 recurrent TIA/stroke patients admitted to the hospital before arriving at the SRAU, 10 (43.5%) received CTA during their initial ED visit. The CDST would have requisitioned CTA for 18 (78.3%) of the 23 recurrent TIA/stroke patients; 9 of the CDST requisitions overlapped with the 10 CTA orders that took place during the initial ED visit. Of the 7 recurrent patients with persistent deficits, 4 received CTA during their initial ED visit; the CDST would have requisitioned CTA for all such cases.

Of the 23 CEA patients, 7 (30.4%) received CTA during their initial ED visit, and 11 (47.8%) during their SRAU visit. The CDST would have requisitioned CTA for 22 (95.7%) of the 23 CEA patients.

Table 1 summarizes the number of CTAs for diagnosed mimic patients, stratified by the 10 most frequent strokemimic diagnoses. Of the stroke-mimic subdiagnoses, the CDST would have requisitioned fewer CTAs for migraine and vestibulopathy patients. These two stroke-mimic diagnoses represent the most frequently occurring stroke-mimic diagnoses encountered at the SRAU.

Restricting the sample to only those patients with a diagnosis of TIA or stroke mimic, the CDST demonstrated a sensitivity of 83% (95% CI, 80%, 85%), specificity of 48% (95% CI, 44%, 52%), and diagnostic accuracy of 69% (95% CI, 66%, 71%), when using the diagnostic threshold (≥ 0.516) to identify TIA patients. The DOR of the CDST at this threshold was 4.48 (95% CI, 3.54, 5.68).

When the second threshold for determining CTA requisition (≥ 0.662) was used, the CDST demonstrated a sensitivity of 74% (95% CI, 71%, 76%), specificity of 62% (95% CI, 58%, 66%), and diagnostic

accuracy of 69% (95% CI, 66%, 71%). The DOR of the CDST at this threshold was 4.54 (95% CI, 3.64, 5.67).

Figure 1 displays the discriminant predictive performance of hospital clinicians (ED + SRAU) and the CDST for requisition of CTA imaging for patients referred from the ED and diagnosed at the SRAU as either TIA or stroke mimic (N = 1,487). Hospital clinicians CTA requisitions had a sensitivity of 63% (95% CI, 60%, 67%), specificity of 46% (95% CI, 42%, 50%), and diagnostic accuracy of 56% (95% CI, 54%, 59%). The DOR of hospital clinicians was 1.47 (95% CI, 1.19, 1.82).

The CDST was found to have a significantly higher sensitivity (74% v. 63%), specificity (62% v. 46%), and diagnostic accuracy (69% v. 56%) than hospital clinicians' baseline CTA ordering (each, p < 0.001). The DOR of the CDST was significantly greater than that of hospital clinicians (4.54 v. 1.47), as indicated by non-overlapping confidence intervals.

DISCUSSION

The results of our study suggest that use of the CDST could have had a beneficial impact on CTA requisitions at the institutional level. Critically, the use of our CDST would have increased the number of TIA patients (particularly, recurrent stroke and CEA candidate patients) receiving CTA imaging before ED discharge (rather than later at TIA units; median time from referral to unit arrival 3.2 days), which is in keeping with the Canadian stroke best practice guide-lines. Earlier detection and treatment of high-risk TIA

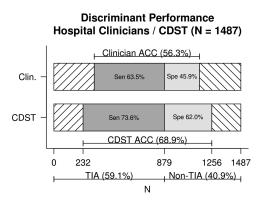


Figure 1. Discriminant performance of hospital clinicians v. CDST for TIA and stroke-mimic patients referred from the ED and diagnosed at the SRAU. ACC = diagnostic accuracy; CDST = clinical decision support tool; Clin. = hospital clinicians; Sen = sensitivity; Spe = specificity.

patients may improve outcomes by reducing the number of recurrent strokes occurring within 24 hours.⁵ Use of our CDST in the ED would have increased the mean number of ED CTAs per day for suspected TIA patients by 0.42, while keeping the institutional number of CTAs ordered relatively constant. As such, our CDST has the potential to improve the effectiveness of existing CTA usage without overutilization of the resource above current levels.

We anticipate our tool being particularly helpful in support of medical decision-making, regarding transport/referral from rural/remote communities to larger centres for brain imaging. In these situations, the decision to transport/refer will be based solely on the patient's presenting history. Focus group discussion and demonstration of the CDST in rural settings, thus far, have been strongly received and supportive; further study is planned.

A limitation of the current study is that we have no way of ascertaining the number of TIA patients missed by ED physicians and, therefore, not referred to the TIA unit. Our results, therefore, should not be interpreted as making any statement regarding the diagnostic accuracy of referring ED physicians.

An additional limitation of the current study is its retrospective design. As such, it represents a best-case scenario, assuming full adoption of the tool by front-line physicians. As well, the study is based on referral data, and it is likely that physicians report positive TIA symptoms with greater frequency than less referral-relevant mimic symptoms (e.g., confusion). This would decrease specificity of the CDST to identify stroke-mimic patients. Interactive use of the tool may change physician reporting behaviour, by increasing the clinical relevance of mimic symptoms for decision-making. A prospective evaluation of the tool will be required to determine its clinical utility and rate of adoption by ED physicians, and to determine tool performance in real-world settings.

CONCLUSION

Our CDST has the potential to increase the institutional effectiveness of CTA requisition among clinically suspected TIA/minor-stroke patients. Specifically, a greater number of TIA patients would receive CTA imaging, with that imaging occurring before ED discharge rather than later at outpatient TIA units. In this way, use of our CDST would permit healthcare institutions to provide greater patient care and financial value out of each CTA conducted for suspected TIA patients, all the while improving institutional adherence to the Canadian stroke best practices guidelines. Further prospective validation of the CDST is necessary, however, before it can be adopted into clinical practice.

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Competing interests: None declared.

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/cem.2018.449

REFERENCES

- Prabhakaran S, Silver AJ, Warrior L, et al. Misdiagnosis of transient ischemic attacks in the emergency room. *Cerebrovasc Dis* 2008;26(6):630-5, doi:10.1159/000166839.
- Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of scores to predict very early stroke after transient ischaemic attack. *Lancet* 2007;369 (9558):283-92, doi:<u>10.1016/S0140-6736(07)60150-0</u>.
- Rothwell P, Giles M, Flossmann E, et al. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. *Lancet* 2005;366(9479):29-36, doi:10.1016/s0140-6736(05)66702-5.
- Chandratheva A, Mehta Z, Geraghty OC, et al. Populationbased study of risk and predictors of stroke in the first few hours after a TIA. *Neurology* 2009;72(22):1941-7, doi:<u>10.1212/wnl.0b013e3181a826ad</u>.
- Coutts SB, Modi J, Patel SK, et al. CT/CT angiography and MRI findings predict recurrent stroke after transient ischemic attack and minor stroke: results of the prospective CATCH study. *Stroke* 2012;43(4):1013-7, doi:10.1161/ strokeaha.111.637421.
- Coutts SB, Wein TH, Lindsay MP, et al. Canadian stroke best practice recommendations: secondary prevention of stroke guidelines, update 2014. *Int J Stroke* 2014;10(3):282-91, doi:10.1111/ijs.12439.
- Casaubon LK, Boulanger J-M, Blacquiere D, et al. Canadian stroke best practice recommendations: hyperacute stroke care guidelines, update 2015. *Int J Stroke* 2015;10(6):924-40, doi:<u>10.1111/ijs.12551</u>.
- Purroy F, Montaner J, Molina CA, et al. Patterns and predictors of early risk of recurrence after transient ischemic attack with respect to etiologic subtypes. *Stroke* 2007;38 (12):3225-9, doi:<u>10.1161/strokeaha.107.488833</u>.
- Sheehan OC, Kyne L, Kelly LA, et al. Population-based study of ABCD2 score, carotid stenosis, and atrial fibrillation for early stroke prediction after transient ischemic attack: the North Dublin TIA study. *Stroke* 2010;41(5):844-50, doi:<u>10.1161/strokeaha.109.571844</u>.

- Smith WS, Lev MH, English JD, et al. Significance of large vessel intracranial occlusion causing acute ischemic stroke and TIA. *Stroke* 2009;40(12):3834-40, doi:<u>10.1161/</u> strokeaha.109.561787.
- 11. Jauch EC, Saver JL, Adams HP, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals. *Stroke* 2013;44 (3):870-947, doi:10.1161/str.0b013e318284056a.
- 12. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals. *Stroke* 2009;40(6):2276-93, doi:10.1161/strokeaha.108.192218.
- Rappeport Y, Simonsen L, Christensen H, Boysen G. Prevalence of significant carotid artery stenosis in patients with transient ischaemic attack. *Med Sci Monit* 2002;8(5):CR317-20.
- Rothwell P, Eliasziw M, Gutnikov S, et al. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet* 2004;363(9413):915-24, doi:<u>10.1016/s0140-6736(04)15785-1</u>.
- Graham BR, Menon BK, Coutts SB, et al. Computed tomographic angiography in stroke and high-risk transient ischemic attack: do not leave the emergency department without it! *Int J Stroke* 2018;174749301876417, doi:10.1177/1747493018764172.
- BCGuidelines.ca. Stroke and transient ischemic attack acute and long-term management; 2015. Available at: https://www2.gov.bc.ca/gov/content/health/practitionerprofessional-resources/bc-guidelines/stroke-tia (accessed May 18, 2018).
- 17. Ferro J, Falcão I, Rodrigues G, et al. Diagnosis of transient ischemic attack by the nonneurologist: a validation study. *Stroke* 1996;27(12):2225-9, doi:<u>10.1161/01.str.27.12.2225</u>.
- Quinn TJ, Cameron AC, Dawson J, et al. ABCD2 scores and prediction of noncerebrovascular diagnoses in an outpatient population: a case-control study. *Stroke* 2009;40 (3):749-53, doi:10.1161/strokeaha.108.530444.
- Sheehan OC, Merwick A, Kelly LA, et al. Diagnostic usefulness of the ABCD2 score to distinguish transient ischemic attack and minor ischemic stroke from noncerebrovascular events. *Stroke* 2009;40(11):3449-54, doi:10.1161/strokeaha.109.557074.
- Fonseca AC, Canhão P. Diagnostic difficulties in the classification of transient neurological attacks. *Eur J Neurol* 2010;18(4):644-8, doi:<u>10.1111/j.1468-1331.2010.03241.x</u>.
- 21. Hosier GW, Phillips SJ, Doucette SP, et al. Transient ischemic attack: management in the emergency department and impact of an outpatient neurovascular clinic. *CJEM* 2016;18(05):331-9, doi:10.1017/cem.2016.3.
- Bates DW, Kuperman GJ, Wang S, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. *J Am Med Inform Assoc* 2003;10(6):523-30, doi:10.1197/jamia. m1370.
- Sim I, Gorman P, Greenes RA, et al. Clinical decision support systems for the practice of evidence-based medicine. *J Am Med Inform Assoc* 2001;8(6):527-34, doi:10.1136/ jamia.2001.0080527.
- 24. Bibok MB, Penn AM, Lesperance ML, et al. Development of a multivariate clinical prediction model for the diagnosis of mild stroke/TIA in physician first-contact patient settings. *bioRxiv*. 2016;1-36, doi:10.1101/089227.

- Bibok MB, Penn AM, Lesperance ML, et al. Validation of a multivariate clinical prediction model for the diagnosis of mild stroke/transient ischemic attack in physician first-contact patient settings. *Health Inform J* 2017;1-10, doi:<u>10.1177/</u> 1460458217747111.
- Bibok MB, Votova K, Balshaw RF, et al. Reducing time-tounit among patients referred to an outpatient stroke assessment unit with a novel triage process: a prospective cohort study. *BMC Health Serv Res* 2018;18(142):1-9, doi:10.1186/s12913-018-2952-x.
- VIHA. Vancouver Island Health Authority ACVS assessment form; 2014. Available at: https://zenodo.org/record/ 810191 (accessed June 16, 2017).
- Albers GW. Acute cerebrovascular syndrome: time for new terminology for acute brain ischemia. *Nat Clin Pract Cardiovasc* 2006;3(10):521, doi:<u>10.1038/ncpcardio0679</u>.
- Kidwell CS, Warach S. Acute ischemic cerebrovascular syndrome: diagnostic criteria. *Stroke* 2003;34(12):2995-8, doi:10.1161/01.str.0000098902.69855.a9.
- Whiteley W, Tseng M-C, Sandercock P. Blood biomarkers in the diagnosis of ischemic stroke: a systematic review. *Stroke* 2008;39:2902-9, doi:10.1161/STROKEAHA.107.511261.
- Whiteley W, Wardlaw J, Dennis M, et al. Blood biomarkers for the diagnosis of acute cerebrovascular diseases: a prospective cohort study. *Cerebrovasc Dis* 2011;32:141-7, doi:10.1159/000328517.
- Albers GW, Caplan LR, Easton JD, et al. Transient ischemic attack – proposal for a new definition. N Engl J Med 2002;347(21):1713-6, doi:10.1056/nejmsb020987.

- Fischer U, Baumgartner A, Arnold M, et al. What is a minor stroke? *Stroke* 2010;41(4):661-6, doi:<u>10.1161/strokeaha.</u> <u>109.572883</u>.
- Lau F, Partridge C, Penn A, et al. Sociotechnical design of an electronic tool for managing transient ischemic attack in the emergency department. *Stud Health Technol Inform* 2015;208:242-7, doi:10.3233/978-1-61499-488-6-242.
- Glas AS, Lijmer JG, Prins MH, et al. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol* 2003;56(11):1129-35, doi:<u>10.1016/s0895-4356(03)00177-x</u>.
- McNemar Q. Note on the sampling error of the difference between correlated proportions or percentages. *Psychometrika* 1947;12(2):153-7, doi:10.1007/BF02295996.
- Sing T, Sander O, Beerenwinkel N, Lengauer T. ROCR: visualizing classifier performance in R. *Bioinformatics* 2005;21(20):3940-1, doi:10.1093/bioinformatics/bti623.
- Robin X, Turck N, Hainard A, et al. pROC: an open-source package for R and S+to analyze and compare ROC curves. BMC Bioinformatics 2011;12(1):77, doi:10.1186/1471-2105-12-77.
- Harrell FE Jr, Dupont C. Hmisc: Harrell miscellaneous; 2016. Available at: https://CRAN.R-project.org/package= Hmisc (accessed April 4, 2017).
- 40. Harrell FE Jr. rms: Regression modeling strategies; 2016. Available at: https://CRAN.R-project.org/package=rms (accessed April 4, 2017).
- 41. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2016. Available at: https://www.R-project.org (accessed December 23, 2016).