RUNNING HEAD: Supplement – Retrospective evaluation of a CDST

Supplement – Retrospective evaluation of a clinical decision support tool for effective CTA utilization in urgent brain imaging of suspected TIA/minor-stroke in the emergency department

Maximilian B. Bibok, PhD[1]; Kristine Votova, PhD[1,2]; Robert F. Balshaw, PhD[3]; Melanie Penn, RN[1]; Mary L. Lesperance, PhD, P.Stat[4]; Devin R. Harris, MD, MHSc[5]; Colin Sedgwick, BSc,[6] Madeline Nealis, BA[1]; Brian Farrell, MD[7]; John R. Mathieson, MD[8]; Andrew. M. Penn, MD[9]

Maximilian.Bibok@viha.ca; Kristine.Votova@viha.ca; Robert.Balshaw@umanitoba.ca; Melanie.Penn@viha.ca; mlespera@uvic.ca; Devin.Harris@interiorhealth.ca; colin.sedgwick@gmail.com; Madeline.Nealis@ucdenver.edu; Brian.Farrell@viha.ca; John.Mathieson@viha.ca; ampenn@mac.com

1. Department of Research and Capacity Building, Island Health Authority, 1952 Bay Street, Victoria, BC, V8R 1J8, Canada
2. Division of Medical Sciences, University of Victoria, PO BOX 1700 STN CSC, Victoria BC, V8W 2Y2, Canada
3. British Columbia Centre for Disease Control, 655 W 12th Avenue, Vancouver BC, V5Z 4R4, Canada
4. Department of Mathematics and Statistics, University of Victoria, PO BOX 1700 STN CSC, Victoria BC, V8W 2Y2, Canada
5. Department of Emergency Medicine, Kelowna General Hospital, 2268 Pandosy Avenue, Kelowna, BC, V1Y 1T2, Canada
6. Division of Medical Sciences & Island Medical Program, University of Victoria, PO Box 1700 STN CSC, Victoria, BC, V8W 2Y2, Canada
7. Department of Emergency Medicine, Island Health Authority, 1 Hospital Way, Victoria BC, V8Z 6R5, Canada
8. Department of Medical Imaging, Island Health Authority, 1 Hospital Way, Victoria BC, V8Z 6R5, Canada
9. Department of Neurosciences, Stroke Rapid Assessment Clinic, Island Health Authority, 1 Hospital Way, Victoria BC, V8Z 6R5, Canada

Corresponding Author:
Dr. Maximilian B. Bibok
Department of Research and Capacity Building
Island Health Authority 1952 Bay Street, Victoria, BC, V8R 1J8, Canada
Email: Maximilian.Bibok@viha.ca Phone: 250-882-6216

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Clinical Decision Support Tool

The clinical decision support tool (CDST) 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.<1> Activities involved in this study included ED workflow analysis and ED physician and nurse focus groups.

CDST Description and Operation

The CDST is electronically implemented as a form-fillable, JavaScript enabled, portable document format (PDF) document. The document consists of three pages (see Figure 1 below).

The first page is based upon the referral form to the Stroke Rapid Assessment Unit (SRAU) Victoria, BC,<2> and serves as the data entry instrument for the tool. As such, the first page may be printed after it has been completed and used as a referral form to the SRAU. Users enter patients' clinical information by way of mouse enabled form fields (checkboxes, date/time pop-ups, and on-screen keypads). Keyboard data entry is still possible, but not required. This design feature is meant to increase the speed at which the tool could be operated, as prior researchers have reported that speed is the number one concern of CDST end-users.<3>. After patients' clinical information has been entered, users click the calculate button located at the top of the page. The second page displays supporting Canadian stroke best practice guideline recommendations selected on the basis of the presenting symptoms entered on page 1. The third page is initially blank. If the tool determines a CTA is advisable, the third page is replaced with a pre-populated CTA requisition. This requisition may be printed and sent to the medical imaging department.

The calculate button calls underlying programming functions which then perform the following functions (see *Flowchart* section below). First, patient age, sex, and blood pressure values are checked for missing data. In the event of missing data, imputation is performed using mean substitution with values derived from the combined historical datasets (N = 7823) used to construct and internally validate a previously developed logistic regression model to differentiate TIA from stroke-mimic conditions (i.e., clinical classifier)<5> (age = 68.277 years; sex [male = 1] = 0.491; systolic BP = 141.606 mmHg; diastolic BP = 78.042 mmHg).<4> After correction for missing values, the estimated probability of TIA/minor stroke using the previously developed clinical classifier<5> is calculated (see *Clinical Classifier* section below for model coefficients).

Next, from the symptom information entered, a binary variable is derived to indicate the absence or presence of characteristic TIA symptoms (0 = absent; 1 = present). This variable is coded as present if patients' clinical information indicate 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. Time since symptom onset is also determined.

An evaluation function then compares the estimated probability of TIA/minor-stroke against two threshold values. Both thresholds were empirically derived from the historical dataset (N = 4187) used to derive the clinical classifier.<5,6> The first threshold (≥ 0.516) was established as the value that maximized diagnostic accuracy; the second threshold (≥ 0.662) was the value that maximizes both sensitivity and specificity without trading one value off for the other (i.e., the point on the ROC curve closest to the (0,1) point).

The first threshold determines whether the entered case is to be considered TIA/minor-stroke, with cases greater than or equal to the threshold being scored as TIA/minor-stroke. That is, cases scored as TIA are considered to be "suspected TIA" in the context of the Canadian stroke best practice guidelines.<7> The second threshold determines whether the entered case should be scored as requiring emergent CTA. The second threshold was selected for decision on CTA requisition as it balances the need to image TIA patients with the aim of imaging as few stroke-mimic patients as possible.

Next the scored case is evaluated against the Canadian stroke best practice guidelines. Cases with estimated probabilities below the first threshold are considered stroke-mimics and the guidelines are not applied. If a case is scored as above the first threshold, but has no characteristic TIA symptoms, a recommendation is generated stating the case is ambiguous and for the user to consult neurology. If the case is above the second threshold, and has characteristic TIA symptoms, the guideline recommendations corresponding to the time since onset are displayed on the second page of the PDF document, and a CTA requisition is displayed on the third page, pre-populated with the clinical information entered on the first page.

If the case is above the first threshold, and less than the second threshold, and has characteristic TIA symptoms, a recommendation is generated indicating that the case falls below the threshold for emergent CTA, and displays the guidelines recommendations corresponding to the time since onset. An "override" button<3> is displayed to users in these instances by which they can generate a pre-populated CTA requisition if they still have a strong clinical suspicion about the case.

Density distributions of estimated probabilities for both TIA/minor-stroke and stroke-mimic patients, based upon the historical data (n = 4187) used to develop the prediction model, are also shown on Page 2. The current case under consideration is displayed as a green, vertical line, in order to visually contextualize the current case with respect to historical cases assessed at the SRAU. This feature is helpful for end-users when deciding on whether to employ the "override" button on cases below the CTA requisition threshold.

CDST Usability

The paper referral form upon which our CDST is based has a long and established history of real-world use. Since introduction of the referral form in November 2014 the SRAU has received over 8500 referrals from referring physician across southern and central Vancouver Island without any complaints regarding the length or complexity of the form. As our tool does not add any additional time demands upon ED physicians above that of completing the paper referral form, we believe its ease of use will facilitate its adoption by physicians.

Presently, the CDST PDF is being piloted in the EDs of Victoria General Hospital (VGH), BC, and Nanaimo Regional General Hospital (NRGH), BC. The PDF file is hosted on

the Island Health intranet and is accessible from any workstation. In the VGH ED, a dedicated mobile workstation has been established in the triage area of the ED to facilitate ED physician adoption of the tool. The NRGH ED has recently been modernized and features wired and mobile workstations in all examination rooms.

References

1. Lau F, Partridge C, Penn A, Stanley D, Votova K, Bibok M, 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.

2. VIHA. Vancouver Island Health Authority — ACVS assessment form. 2014. doi:10.5281/zenodo.810191.

3. Bates DW, Kuperman GJ, Wang S, Gandhi T, Kittler A, Volk L, 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.

4. Bibok MB, Votova K, Balshaw RF, Lesperance ML, Croteau NS, Trivedi A, et al. Reducing time-to-unit 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.

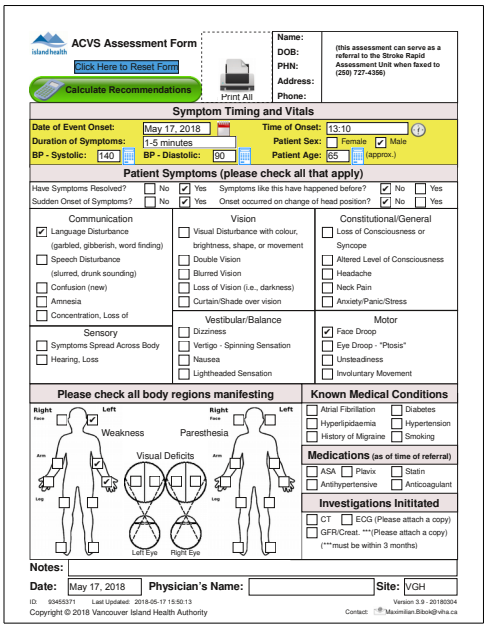
5. Bibok MB, Penn AM, Lesperance ML, Votova K, Balshaw R. Development of a multivariate clinical prediction model for the diagnosis of mild stroke/TIA in physician first-contact patient settings. bioRxiv. 2016;. doi:10.1101/089227.

6. Bibok MB, Penn AM, Lesperance ML, Votova K, Balshaw R. 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. doi:10.1177/1460458217747111.

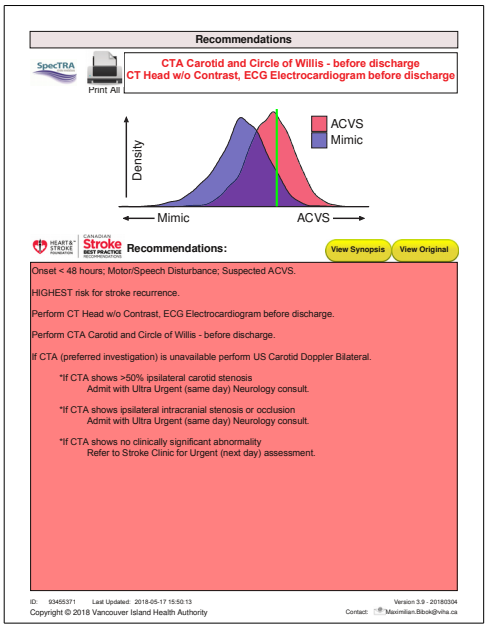
7. Coutts SB, Wein TH, Lindsay MP, Buck B, Cote R, Ellis P, et al. Canadian stroke best practice recommendations: secondary prevention of stroke guidelines, update 2014. Int J Stroke. 2014;10(3):282–91. doi:10.1111/ijs.12439.

Figure 1. Screen-captures of the TIA clinical decision support tool.

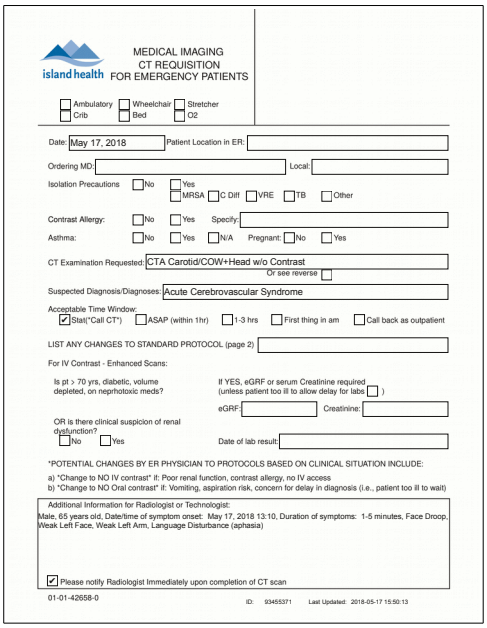
NOTE: The figures below are high-quality, vector-based images. Image details and legibility can be enhanced without pixelation by increasing the PDF reader's zoom/magnification level.



Page 1



Page 2



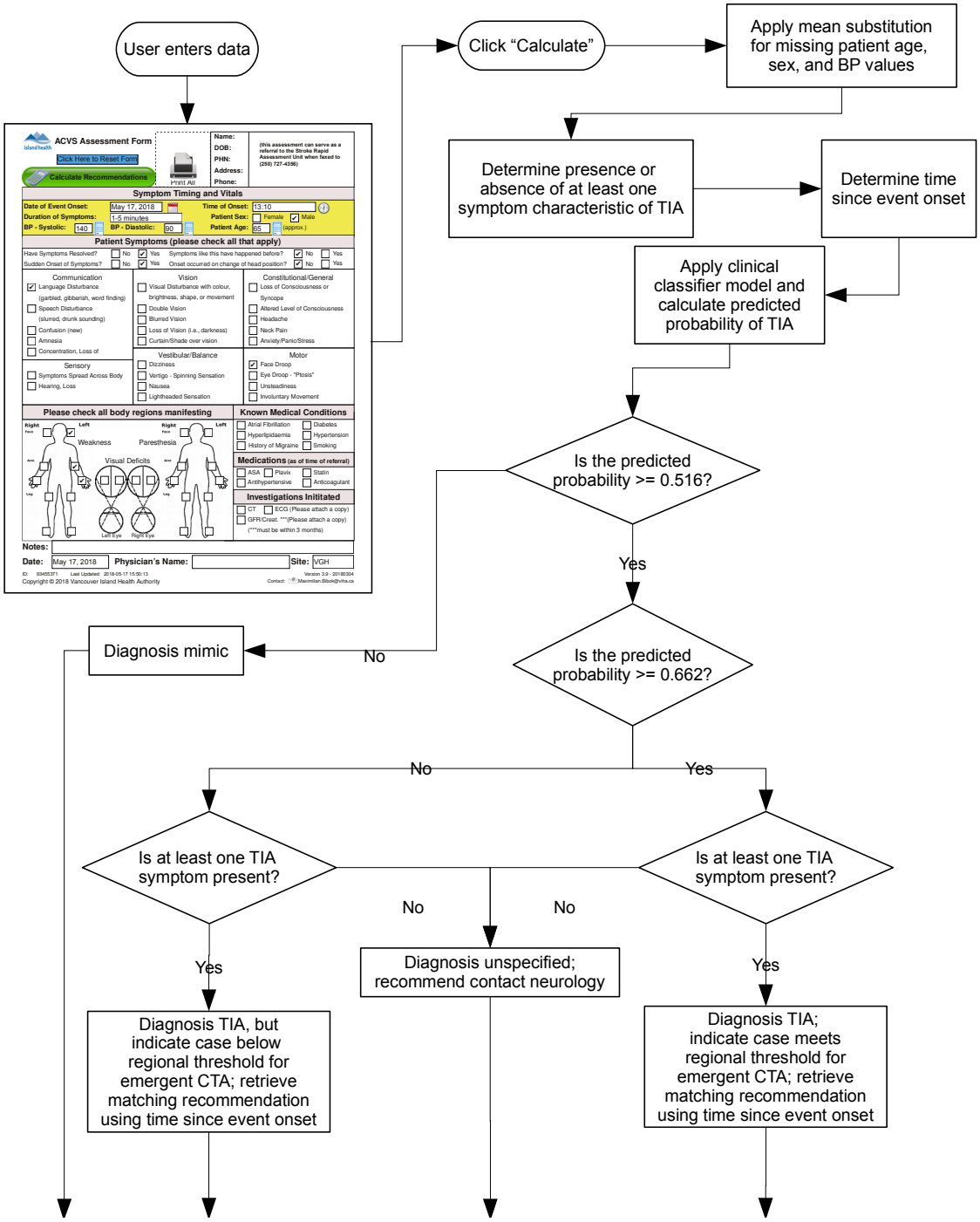
Page 3

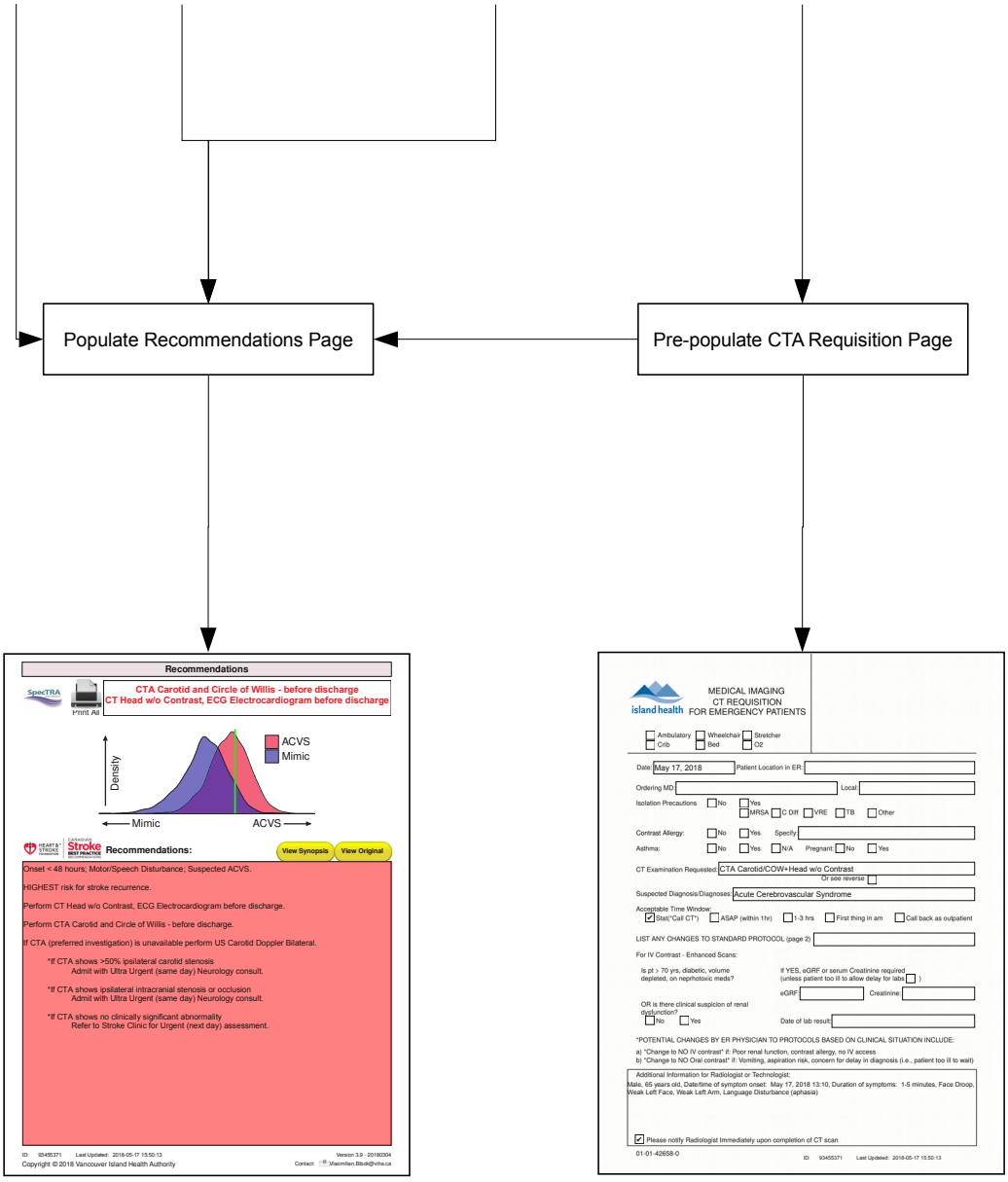
Figure 1. Screen-captures of the TIA clinical decision support tool.

Clinical Decision Support Tool - Flowchart

TIA/Minor-Stroke Clinical Decision Support Tool Flowchart

NOTE: The figures below are high-quality, vector-based images. Image details and legibility can be enhanced without pixelation by increasing the PDF reader's zoom/magnification level.




Populate Recommendations Page
Pre-populate CTA Requisition Page
Recommendations
SpecTRA
Print All
CTA Carotid and Circle of Willis - before discharge
CT Head w/o Contrast, ECG Electrocardiogram before discharge
Density
ACVS
Mimic
Mimic
ACVS
Canadian Stroke Best Practice Recommendations
Recommendations:
View Synopsis
View Original
Onset < 48 hours; Motor/Speech Disturbance; Suspected ACVS.
HIGHEST risk for stroke recurrence.
Perform CT Head w/o Contrast, ECG Electrocardiogram before discharge.
Perform CTA Carotid and Circle of Willis - before discharge.
If CTA (preferred investigation) is unavailable perform US Carotid Doppler Bilateral.
*If CTA shows >50% ipsilateral carotid stenosis
Admit with Ultra Urgent (same day) Neurology consult.
*If CTA shows ipsilateral intracranial stenosis or occlusion
Admit with Ultra Urgent (same day) Neurology consult.
*If CTA shows no clinically significant abnormality
Refer to Stroke Clinic for Urgent (next day) assessment.
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Contact : Maximilian.Bibok@viha.ca
island health
MEDICAL IMAGING
CT REQUISITION
FOR EMERGENCY PATIENTS
Ambulatory
Wheelchair
Stretcher
Crib
Bed
O2
Date: May 17, 2018
Patient Location in ER:
Ordering MD:
Local:
Isolation Precautions
No
Yes
MRSA
C Diff
VRE
TB
Other
Contrast Allergy:
No
Yes
Specify:
Asthma:
No
Yes
N/A
Pregnant:
No
Yes
CT Examination Requested: CTA Carotid/COW+Head w/o Contrast
Or see reverse
Suspected Diagnosis/Diagnoses: Acute Cerebrovascular Syndrome
Acceptable Time Window:
Stat("Call CT")
ASAP (within 1hr)
1-3 hrs
First thing in am
Call back as outpatient
LIST ANY CHANGES TO STANDARD PROTOCOL (page 2)
For IV Contrast - Enhanced Scans:
Is pt > 70 yrs, diabetic, volume depleted, on nephrotoxic meds?
If YES, eGRF or serum Creatinine required (unless patient too ill to allow delay for labs)
eGRF
Creatinine:
OR is there clinical suspicion of renal dysfunction?
No
Yes
Date of lab result:
*POTENTIAL CHANGES BY ER PHYSICIAN TO PROTOCOLS BASED ON CLINICAL SITUATION INCLUDE:
a) "Change to NO IV contrast" if: Poor renal function, contrast allergy, no IV access
b) "Change to NO Oral contrast" if: Vomiting, aspiration risk, concern for delay in diagnosis (i.e., patient too ill to wait)
Additional Information for Radiologist or Technologist:
Male, 65 years old, Date/time of symptom onset: May 17, 2018 13:10, Duration of symptoms: 1-5 minutes, Face Droop, Weak Left Face, Weak Left Arm, Language Disturbance (aphasia)
Please notify Radiologist Immediately upon completion of CT scan
01-01-42658-0
ID: 93455371 Last Updated: 2018-05-17 15:50:13

Clinical Classifier to Differentiate TIA/Minor-Stroke and Stroke-Mimic Patients

Adapted from Table 2 of,

Bibok MB, Penn AM, Lesperance ML, Votova K, Balshaw R. Development of a multivariate clinical prediction model for the diagnosis of mild stroke/TIA in physician first-contact patient settings. bioRxiv. 2016;. doi:10.1101/089227.

Variable names in the table reproduced below have been changed to match the text descriptions on page one of the clinical decision support tool.

Table 2. Full clinical logistic regression model (Age, Systolic BP and Diastolic BP standardized). B=coefficient estimate, OR=odds ratio, CI=confidence interval.

Variable	B	OR	95% CI
Intercept	-0.489	0.613	0.476–0.789
Patient age (years, center = 60, sd = 10)	0.301	1.351	1.248–1.463
Patient sex	0.441	1.554	1.320–1.829
History of hypertension	0.335	1.398	1.189–1.643
History of hyperlipidaemia	0.121	1.128	0.964–1.321
Smoking	0.470	1.600	1.266–2.023
History of atrial fibrillation	0.224	1.251	0.977–1.602
History of diabetes	0.082	1.086	0.885–1.332
History of migraine	-0.474	0.623	0.454–0.853
Dizziness	0.006	1.006	0.817–1.239
Headache	-0.324	0.723	0.590–0.887
Systolic BP (mmHg, center = 140, sd = 10)	0.055	1.056	1.006–1.109
Diastolic BP (mmHg, center = 90, sd = 10)	0.026	1.026	0.934–1.127
Face droop*	0.673	1.960	1.431–2.685
Weak face left	-0.206	0.814	0.459–1.443
Weak face right	-0.700	0.497	0.277–0.892

Weak arm left	0.470	1.600	1.137–2.251
Weak arm right	0.568	1.765	1.233–2.528
Weak leg left	0.277	1.319	0.864–2.014
Weak leg right	0.420	1.523	0.948–2.446
Weakness (motor, any indication)**	0.426	1.532	1.247–1.881
Numb face left	0.503	1.653	1.192–2.292
Numb face right	0.220	1.246	0.847–1.832
Numb arm left	0.205	1.227	0.915–1.646
Numb arm right	0.165	1.179	0.837–1.661
Numb leg left	0.498	1.646	1.100–2.462
Numb leg right	0.442	1.556	0.950–2.548
Numbness (any indication)**	-0.019	0.981	0.778–1.236
Bilateral (numbness or weakness)***	-0.551	0.576	0.417–0.798
Eye droop (ptosis)	-0.030	0.971	0.432–2.180
Visual field deficit (either side)	0.366	1.442	1.018–2.041
Neck pain	-0.509	0.601	0.373–0.968
Nausea	-0.435	0.647	0.482–0.870
Unsteadiness	0.256	1.292	1.074–1.553
Curtain/Shade over vision	0.411	1.509	0.986–2.308
Loss of consciousness or Syncope	-0.595	0.552	0.386–0.789
Lightheaded Sensation	0.021	1.021	0.695–1.500
Vertigo – Spinning Sensation	-0.871	0.419	0.294–0.596
Confusion (new)	-0.585	0.557	0.452–0.687
Amnesia	-1.569	0.208	0.085–0.512
Language Disturbance (garbled, gibberish, word finding)	0.450	1.568	1.246–1.973
Speech Disturbance (slurred, drunk sounding)	0.769	2.157	1.767–2.633

Visual Disturbance with colour, brightness, shape or movement	-0.866	0.421	0.321–0.551
Onset of occurred on change of head position?	-0.407	0.665	0.270–1.638
Double Vision[2]	0.525	1.690	1.228–2.326
Loss of Vision (i.e., darkness)	0.686	1.986	1.370–2.879
Concentration, Loss of[5]	-0.885	0.413	0.233–0.731
Sudden Onset of Symptoms?	0.191	1.211	1.006–1.456
Symptoms Spread Across Body	-0.623	0.536	0.317–0.908
Involuntary Movement	-0.712	0.491	0.338–0.713
Anxiety/Panic/Stress	-0.657	0.518	0.382–0.702
Patient age (years, center = 60, sd = 10) × Concentration, Loss of	0.354	1.424	0.968–2.095
Patient age (years, center = 60, sd = 10) × Headache	0.159	1.173	1.038–1.324
Patient sex × Nausea	0.239	1.270	0.815–1.980
Patient sex × “Onset of occurred on change of head position?”	-0.871	0.418	0.127–1.382
Confusion (new) × Amnesia	1.479	4.390	1.297–14.861
Dizziness × “Lightheaded Sensation”	-0.764	0.466	0.285–0.761
Headache × “Lightheaded Sensation”	0.615	1.850	1.102–3.104
Headache × “Vertigo – Spinning Sensation”	0.674	1.962	1.109–3.469
Neck Pain × Language Disturbance	1.325	3.763	1.015–13.950
“Lightheaded Sensation” × “Speech Disturbance”	-0.907	0.404	0.243–0.671
“Vertigo – Spinning Sensation” × “Speech Disturbance”	0.786	2.195	1.126–4.277
“Face droop” × “Eye droop (ptosis)”	-1.129	0.323	0.100–1.047

In the coding rules below, “0” indicates the corresponding checkbox is unchecked; “1” indicates checked. Weak and Numb hand and feet indicators do not factor into the calculations for the variables below.

*Face droop is coded as present if:

```
“Face Droop” = 1  and/or
[(Weak face left = 1 & Weak face right = 0) or
 (Weak face left = 0 & Weak face right = 1)]
```

**Weakness (any indication) is coded as present if:

```
Weak face left = 1 or Weak face right = 1 or
Weak arm left  = 1 or Weak arm right  = 1 or
Weak leg left  = 1 or Weak leg right  = 1
```

Numbness (any indication) is comparably coded using the indicators for numb face, arm, and legs.

***Bilateral (numbness or weakness) is coded as present if:

```
(Weak face left = 1 & Weak face right = 1) or
(Weak arm left  = 1 & Weak arm right  = 1) or
(Weak leg left  = 1 & Weak leg right  = 1) or
(Numb face left = 1 & Numb face right = 1) or
(Numb arm left  = 1 & Numb arm right  = 1) or
(Numb leg left  = 1 & Numb leg right  = 1)
```