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ORIGINAL RESEARCH

Association Between Duration of Transient Neurological Events and Diffusion-Weighted Brain Lesions

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BACKGROUND: The relationship between duration of transient neurological events and presence of diffusion-weighted lesions by symptom type is unclear.

METHODS AND RESULTS: This was a substudy of SpecTRA (Spectrometry for Transient Ischemic Attack Rapid Assessment), a multicenter prospective cohort of patients with minor ischemic cerebrovascular events or stroke mimics at academic emergency departments in Canada. For this study we included patients with resolved symptoms and determined the presence of diffusion-weighted imaging (DWI) lesion on magnetic resonance imaging within 7 days. Using logistic regression, we evaluated the association between symptom duration and DWI lesion, assessing for interaction with symptom type (focal only versus nonfocal/mixed), and adjusting for age, sex, education, comorbidities, and systolic blood pressure. Of 658 patients included, a DWI lesion was present in 232 (35.1%). There was a significant interaction between symptom duration and symptom type. For those with focal-only symptoms, there was a continuous increase in DWI probability up to 24 hours in duration (ranging from ≈40% to 80% probability). In stratified analyses, the increase in probability of DWI lesion with increased duration of focal symptoms was seen in women but not men. For those with nonfocal or mixed symptoms, predicted probability of DWI lesion was ≈35% and was greater in men, but did not increase with longer duration.

CONCLUSIONS: Increased duration of neurological deficits is associated with greater probability of DWI lesion in those with focal symptoms only. For individuals with nonfocal or mixed symptoms, about one-third had DWI lesions, but the probability did not increase with duration. These results may be important to improve risk stratification of transient neurological events.

Key Words: diffusion-weighted imaging ■ focal symptoms ■ minor stroke ■ magnetic resonance imaging ■ symptom duration ■ transient ischemic attack

Recognition and treatment of transient cerebrovascular events is critical to lower the high early risk of recurrent ischemia and infarction.[1–3] Minor cerebrovascular events, including transient ischemic attack (TIA) and minor ischemic stroke, have a wide spectrum of symptomatology, making diagnosis challenging, and recurrent ischemic stroke risk is high for those with classic as well as atypical symptoms.[4] Therefore, it is important to identify markers of increased risk of recurrent ischemic stroke. Diffusion-weighted imaging (DWI) is the optimal imaging technique for the diagnosis of acute ischemic stroke,[5] with a sensitivity of 88% to 100% and specificity of 95% to 100%.[6–9] In a cohort of 1028 patients with

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CLINICAL PERSPECTIVE

What Is New?

- In those with transient events referred for urgent neurological assessment, the probability of having a diffusion-weighted imaging lesion on magnetic resonance imaging (indicating ischemic stroke) is high, and increased with the duration of the event in those with focal symptoms but not in those with mixed or nonfocal symptoms.

What Are the Clinical Implications?

- Although those with focal long-duration symptoms are at particularly high risk of a diffusion-weighted imaging–positive lesion, those with shorter-duration symptoms and with mixed-type or nonfocal symptoms still have a significant risk of diffusion-weighted imaging positivity.
- Symptom focality and event duration may be useful guides but cannot reliably distinguish those with and without ischemic stroke in clinical practice.

Nonstandard Abbreviations and Acronyms

DWI	diffusion-weighted imaging
SpecTRA	Spectrometry for Transient Ischemic Attack Rapid Assessment

lower-risk clinical events, there was a 6-fold higher risk of recurrent ischemic stroke in those who were DWI-positive, although this estimate is based on only 7 recurrent strokes in follow-up at 1 year.[10] In a cohort of 1033 patients with TIA or minor ischemic stroke, DWI positivity was associated with 2.2-fold increase in the hazard of 90-day recurrent ischemic stroke (14.5% versus 8.9%)[11] and therefore may be a useful test for prognostication. Nevertheless, magnetic resonance imaging (MRI) may not be readily available or done in a timely fashion in many settings, raising the importance of characterizing the association between key clinical factors and presence of DWI lesions to assist in early decision making.

Specifically, longer duration of event has been identified as a marker of ischemic stroke recurrence,[12,13] although information on DWI lesions is limited. Studies using binary time categories at the extremes of duration, such as 5 minutes[10] or 24 hours,[14] did not show a significant difference in DWI positivity. There was greater DWI positivity with symptom duration ≥1 hour compared with <1 hour in 1 study,[15] but not in 2 others.[14,16] However, a binary approach may miss important differences across the continuum of symptom duration.[17] Studies using multiple duration categories showed a numerically higher probability of DWI positivity with longer duration, ranging from 0% to 10% for episodes <5 minutes to 71% to 100% for episodes 12 to 24 hours.[18–20] These studies were small and did not assess changes in DWI positivity with continuous variation in event duration. Furthermore, the likelihood of permanent ischemic injury is related to both the duration and the severity of ischemia,[17] and therefore presenting symptom type may alter the time course of irreversible ischemia. We sought to characterize the association between duration of transient neurological events and presence of DWI lesions in relation to focality of presenting symptoms in a large group of patients referred for urgent neurological assessment.

METHODS

This is a substudy of SpecTRA (Spectrometry for Transient Ischemic Attack Rapid Assessment), a multicenter, prospective study aiming to identify a blood biomarker differentiating TIAs or minor ischemic strokes from stroke mimics in patients presenting within 24 hours of symptom onset and referred for an acute neurologic assessment.[21] Patients presented with acute transient or minor neurologic symptoms and were suspected of having experienced either a minor ischemic cerebrovascular event or a stroke mimic and were referred to stroke neurology for further evaluation. SpecTRA enrolled patients between December 2013 and March 2017. The SpecTRA study received institutional approvals from the participating hospitals' ethics review board for research using human subjects, and written informed consent was obtained from all patients enrolled. The data that support the findings of this study are available from the senior author upon reasonable request.

Study Participants

A minor symptom was defined as a National Institutes of Health Stroke Scale score of 3 or lower. The SpecTRA study required a clinical evaluation by a neurologist with stroke expertise at least once between symptom onset and 90 days after onset as well as having brain MRI within 7 days of the event or computed tomography and computed tomographic angiography within 24 hours of the event. All other investigations and clinical follow-up were completed as was clinically routine. Our main analysis was restricted to those with transient neurological deficits, defined by self-report ("Does the patient feel all symptoms of any kind related

to this event have resolved [ie, focal symptoms or associated symptoms])?" We also evaluated those with no clinical deficits on neurological examination irrespective of self-reported symptoms, and those with resolved symptoms on self-report in addition to no new deficits on examination.

Symptom Type and Neurological Examination

We categorized symptoms as focal only or nonfocal/mixed. Focal neurologic symptoms included any motor, sensory, vision, or speech (aphasia or dysarthria) deficits. Nonfocal symptoms included the migration of symptoms that took longer than 2 minutes, symptoms affected by changes in head position, headache, neck pain, photophobia, eyelid droop, vertigo, unsteady gait, nausea, vomiting, feeling drunk, confusion, disorientation, difficulty concentrating, visuospatial difficulties, amnesia, fatigue, dizziness, involuntary movement, anxiety, or cardiac symptoms (shortness of breath, chest pain, palpitations, syncope, or presyncope). Symptoms were ascertained by study coordinators and investigators at the time of enrollment. A stroke neurologist documented whether the new neurological deficit had resolved on detailed examination.

Main Exposures

Our main exposures were symptom type and duration of neurological episode, as reported by the patient.

Outcome

The outcome was the proportion of participants with DWI lesions on brain MRI scans. Participants' MRI images were reviewed by a neuroradiologist. Assessment of interrater reliability for adjudicating MRI was not done in this study, but in prior studies interrater reliability of DWI lesions was excellent ($\kappa = 0.8$).[22]

Statistical Analysis

Because of the right-skewed distribution of event duration and of residuals, we computed the log-duration of the event as our main exposure. We chose log-duration because it resulted in a distribution of observations and of residuals nearest to a normal distribution compared with other transformations (Figure S1). We compared baseline characteristics between those with and without DWI lesions using *t* tests for continuous variables and the χ^2 test for categorical variables. To determine the association between event duration and DWI lesion by symptom type, we used logistic regression adjusting for age; sex; education; history of stroke, coronary artery disease, atrial fibrillation, hypertension, diabetes, and smoking; and systolic blood pressure in the emergency department. We included an interaction term between duration and symptom type. Using the fitted models, we generated predicted probability of DWI lesion across the range of event duration, stratified by symptom type. Duration was plotted on the original nontransformed scale. We stratified the analysis by sex. Any participant with missing data was removed from the logistic models through listwise deletion. We assessed model fit using the Hosmer-Lemeshow goodness-of-fit test.

In sensitivity analyses, we (1) excluded those who had an initial diagnosis of stroke mimic, (2) excluded those with a final adjudicated diagnosis of mimic, (3) divided the symptoms into 3 groups of focal, nonfocal, and mixed, (4) included only those with no clinical deficits on neurological examination irrespective of self-reported symptoms, and (5) included only those with resolved symptoms on self-report in addition to no new deficits on examination.

Because the median event duration was 1 hour, we also performed separate analyses replacing continuous duration with dichotomous duration at a threshold of 1 hour. We again checked for interaction by symptom type and produced odds ratios stratified by symptom type.

Analyses were performed in Stata 17.0 (StataCorp, College Station, TX).

RESULTS

There were 1054 patients with a resolved event (based on symptoms or exam) who had brain MRI (see Figure 1 for flowchart). Among them, there were 699 patients who had resolved symptoms based on self-report who comprised the main analytic sample. The mean age was 69.3 years (SD 14.9 years), 47.5% were women, 7.7% had prior stroke, 12.4% had atrial fibrillation, 55.1% had hypertension, 16.5% had diabetes, and 22.2% had focal-only symptoms. Median symptom onset to MRI time was 0 days (interquartile range [IQR] 0–1 day). A DWI lesion indicating acute infarct was present in 245 (35.1%) of participants. The shortest duration DWI lesion was seen in a patient who reported a 15-second episode. Those with DWI lesions were older and more likely to be men and to have prior stroke or atrial fibrillation (Table 1). The median duration of episodes was 1 hour (IQR, 0.25–3 hours), with 30.6% resolving within 30 minutes, 42.9% resolving within 1 hour, 57.9% resolving within 2 hours, and 42.1% resolving after >2 hours. Those with focal-only symptoms were more likely to be older and have hypertension (Table 2). One out of 5 patients with self-reported resolution of symptoms had a new clinical deficit on examination (143/693; 20.6%). For the sensitivity analyses, there were 905 patients who had no new deficits based on clinical examination, and 550 patients who resolved based on both self-reported symptoms and clinical examination (see Tables S1 and S2 for baseline characteristics).

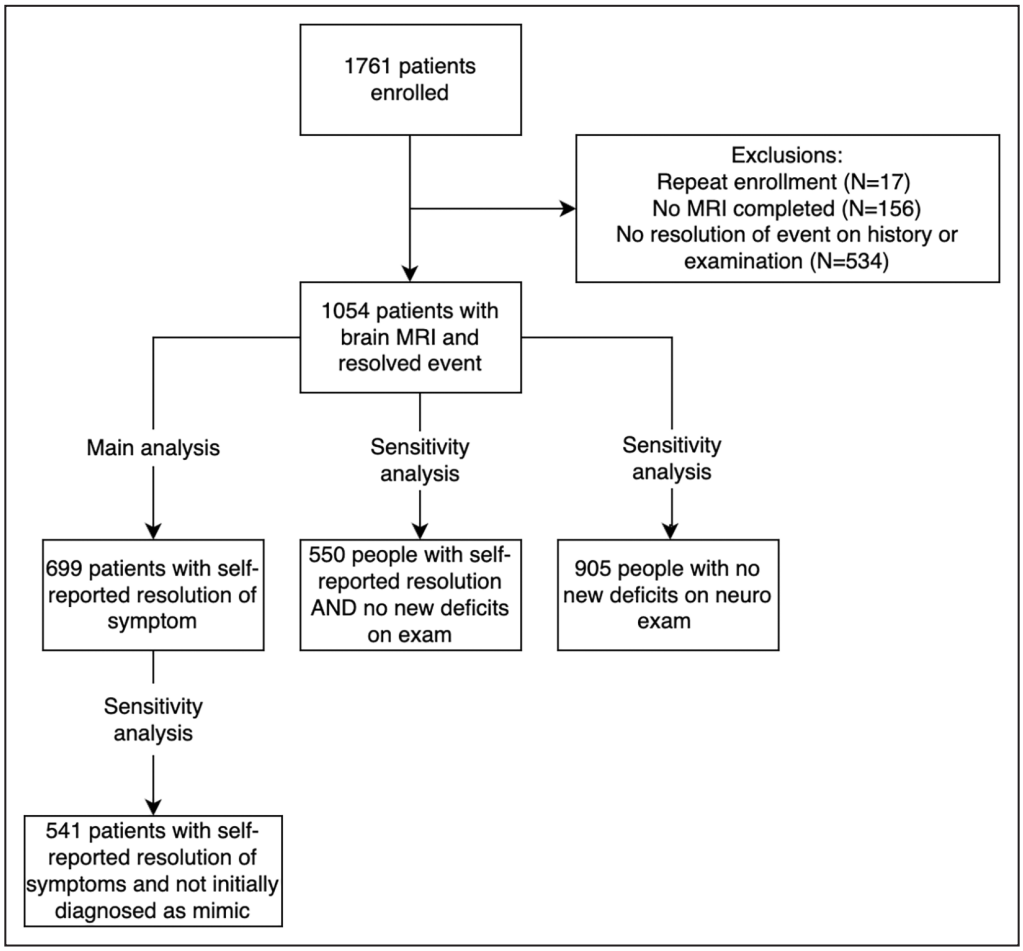

Figure 1. Study flowchart.
MRI indicates magnetic resonance imaging.

The logistic model was well fit as indicated by a Hosmer-Lemeshow *P* value of 0.22. Older age and atrial fibrillation were associated with higher odds, whereas female sex was associated with lowers odds, of DWI positivity (Table S3). There was a significant interaction between log-duration and symptom type (P_{int} =0.015; Figure 2A). The predicted probability of DWI lesion for focal-only symptoms increased continuously up to 24 hours duration, ranging between approximately 30% at very short durations and 72% near 24 hours. There was no apparent relationship between duration and DWI probability among those with mixed or nonfocal symptoms, which remained stable across durations at ≈35%. The results were similar in sensitivity analyses stratifying symptoms into 3 categories of focal, nonfocal, or mixed (Figure 2B), incorporating neurological examination (Figure 3), or excluding those with initial or final adjudicated diagnosis of mimic (Figure S2).

There was significant modification of the relationship of event duration and symptom type with DWI by sex (3-way interaction *P*=0.014). In the sex-stratified models, the interaction between symptom type and duration persisted for women (P_{int}=0.002) but not for men (P_{int}=0.9), in part because of the higher probability of DWI lesions with nonfocal symptoms in men (Figure 2C and 2D).

When dichotomizing event duration at 1 hour (the median), those with mixed/nonfocal symptoms had an unadjusted probability of DWI lesion of 33.9% (64/189) within 1 hour duration, and 35.5% (102/287) >1 hour duration, and those with focal-only symptoms had a probability of 28.8% (21/73) within 1 hour and 56.5% (35/62) >1 hour. In the logistic regression, there was a significant interaction between duration of 1 hour and symptom type (P_{int}=0.01). In those with focal-only symptoms, ≥1 hour duration was associated with 4-times higher odds of DWI lesion (adjusted odds ratio [OR], 4.0 [95% CI, 1.70–9.20]) compared with nonfocal/mixed symptoms where there was no significant association (adjust OR, 1.07 [95% CI, 0.71–1.61]).

DISCUSSION

In this prospective cohort of patients with transient neurological episodes, longer duration of event was a significant predictor of presence of a DWI lesion among people with focal symptoms only. Among

Table 1. Baseline Characteristics of Patients Stratified by Presence of a DWI Lesion

Characteristic	Total, N=699	No DWI lesion, N=454	DWI lesion, N=245	*P* value
Age, y, mean (SD)	69.3 (14.9)	68.4 (15.4)	70.8 (13.6)	0.040
Female sex, n (%)	332 (47.5%)	230 (50.7%)	102 (41.6%)	0.023
Education, n (%)				0.35
Less than grade 12	118 (16.9%)	73 (16.1%)	45 (18.4%)	
Completed high school	151 (21.6%)	93 (20.5%)	58 (23.7%)	
Postsecondary, some or graduated	428 (61.2%)	287 (63.2%)	141 (57.6%)	
Prior stroke, n (%)	54 (7.7%)	25 (5.5%)	29 (11.8%)	0.003
CAD, n (%)	94 (13.4%)	64 (14.1%)	30 (12.2%)	0.49
Atrial fibrillation, n (%)	87 (12.4%)	48 (10.6%)	39 (15.9%)	0.041
Hypertension, n (%)	385 (55.1%)	250 (55.1%)	135 (55.1%)	0.99
Diabetes, n (%)	115 (16.5%)	69 (15.2%)	46 (18.8%)	0.22
Smoking, n (%)*	80 (11.4%)	50 (11.0%)	30 (12.2%)	0.63
Duration of event, h, median (IQR)	1 (0.25–3)	1 (0.25–3)	1.5 (0.5–4)	0.16
Systolic blood pressure, mean (SD)	159.2 (27.2)	159.6 (26.9)	158.4 (27.7)	0.56
Presentation type, n (%)				0.28
Mixed or nonfocal	544 (77.8%)	359 (79.1%)	185 (75.5%)	
Focal only	155 (22.2%)	95 (20.9%)	60 (24.5%)	
Right common/internal carotid artery stenosis, n (%)				0.45
None	270 (38.6%)	175 (38.5%)	95 (38.8%)	
<50%	203 (29.0%)	124 (27.3%)	79 (32.2%)	
≥50%	43 (6.2%)	24 (5.3%)	19 (7.8%)	
Left common/internal carotid artery stenosis, n (%)				0.044
None	276 (39.5%)	179 (39.4%)	97 (39.6%)	
<50%	210 (30.0%)	131 (28.9%)	79 (32.2%)	
≥50%	31 (4.4%)	13 (2.9%)	18 (7.3%)	
Recurrent stroke at 90 d, n (%)	21 (3.0%)	10 (2.2%)	11 (4.5%)	0.091

Missing data: N=2 for education, 5 for systolic blood pressure, 88 for duration of event, 183 for right carotid stenosis, 182 for left carotid stenosis. CAD indicates coronary artery disease; DWI, diffusion-weighted imaging; and IQR, interquartile range.

*Smoking is defined as regular use of cigarettes, cigars, chewing tobacco, or pipe within the past year.

these individuals, the predicted probability of a DWI lesion increased from 30% to 72% across 24 hours of event duration. Among those with nonfocal symptoms, the probability of a DWI lesion was ≈35% and did not change substantially with event duration.

DWI positivity implies irreversible damage and is a strong predictor of ischemic stroke recurrence.[10] However, MRI scanning may not be readily available in all settings. Our findings may have important implications in stratifying risk and prognosis of a potential cerebrovascular event using event duration and symptom type. First, there was an elevated probability of a DWI lesion in longer-duration events among those with focal symptoms compared with mixed or nonfocal symptoms, compatible with prior studies showing unilateral weakness was associated with DWI abnormalities.[23] Importantly, however, the rate of DWI lesions in those with mixed or nonfocal symptoms was substantial at ≈35%. Therefore, although the presenting clinical syndrome may indicate higher or lower probability of a DWI lesion, the presence of nonfocal symptoms cannot be relied upon to rule out a cerebrovascular event. This is in line with the prior evidence that low-risk events carry a substantive risk of DWI-positive brain imaging,[10] and is important to recognize because the presence of nonspecific symptoms may contribute to misdiagnosis.[24]

Second, in those with focal-only symptoms, there was an increase in probability of DWI-positive imaging over 24 hours of event duration. Prior studies on DWI positivity and duration of symptoms have been inconsistent. When dichotomizing at 1 hour, 1 study suggested a higher rate of DWI positivity (81% versus 39%),[15] whereas 2 others showed no statistical difference.[14,16] However, these studies were small and may have been underpowered to detect differences. Similarly small descriptive studies of <100 patients showed a higher proportion of DWI lesions with

Table 2. Baseline Characteristics of Patients Stratified by Presence of Focal Presentation

Characteristic	Total, N=699	Nonfocal or mixed, N=544	Focal, N=155	*P* value
Age, y, mean (SD)	69.3 (14.9)	68.2 (15.2)	72.8 (12.9)	<0.001
Female sex, n (%)	332 (47.5%)	259 (47.6%)	73 (47.1%)	0.91
Education, n (%)				0.34
Less than grade 12	118 (16.9%)	98 (18.0%)	20 (12.9%)	
Completed high school	151 (21.6%)	116 (21.3%)	35 (22.6%)	
Postsecondary, some or graduated	428 (61.2%)	329 (60.5%)	99 (63.9%)	
Prior stroke, n (%)	54 (7.7%)	41 (7.5%)	13 (8.4%)	0.73
CAD, n (%)	94 (13.4%)	73 (13.4%)	21 (13.5%)	0.97
Atrial fibrillation, n (%)	87 (12.4%)	61 (11.2%)	26 (16.8%)	0.064
Hypertension, n (%)	385 (55.1%)	288 (52.9%)	97 (62.6%)	0.033
Diabetes, n (%)	115 (16.5%)	86 (15.8%)	29 (18.7%)	0.39
Smoking, n (%)*	80 (11.4%)	61 (11.2%)	19 (12.3%)	0.72
Duration of event, h, median (IQR)	1 (0.25–3)	1.25 (0.33–3.50)	0.5 (0.17–2.33)	0.07
Systolic blood pressure, mean (SD)	159.2 (27.2)	158.2 (27.0)	162.7 (27.6)	0.072
MRI DWI lesion, n (%)	245 (35.1%)	185 (34.0%)	60 (38.7%)	0.28
Recurrent stroke at 90 d, n (%)	21 (3.0%)	15 (2.8%)	6 (3.9%)	0.47

Missing data: N=2 for education, 5 for systolic blood pressure, 88 for duration of event. CAD indicates coronary artery disease; DWI, diffusion-weighted imaging; IQR, interquartile range; and MRI, magnetic resonance imaging.

*Smoking is defined as regular use of cigarettes, cigars, chewing tobacco, or pipe within past year.

longer event duration, ranging from 0% to 10% for <5 minutes, 33% to 71% for within 1 hour, and 38% to 100% for 12 to 24 hours.[15,18–20] We therefore took the approach of evaluating duration of resolved symptoms as a continuous variable, made possible by our large sample size. We also accounted for symptom focality in the analysis, given that it may be a marker of severity of ischemia and could modify the time course of DWI positivity. We found that longer event duration was associated with higher probability of DWI lesion only in those with focal symptoms. We also did not find a clear threshold of duration that could be used to stratify risk, but rather a continuous graded increase with a steeper early curve. Even short-duration events carried a clinically relevant probability of DWI lesion in our study. Crisostomo et al[15] described a patient with a pathological DWI and a TIA lasting only 40 seconds. In our study, the shortest duration of event with a DWI lesion was 15 seconds. The progressive time course of DWI positivity for focal symptoms only may be because of severity of ischemia with focal symptoms, differences in collaterals between anterior and posterior circulation, or the presence of mimics in the nonfocal group despite adjudication, which may dilute the association between duration and DWI lesion. Overall, our results suggest that using short duration of event or a particular threshold in time is inadequate to exclude a cerebrovascular event.[15] In other words, there may be substantial interindividual variability in the duration of ischemia required for infarction. Using the tissue-based paradigm, where stroke is defined by imaging evidence rather than duration, our results are in line with a statement from the American Heart Association/American Stroke Association that does not support the use of fixed time thresholds in differentiating stroke or TIA[17] when modern imaging is available. When there is uncertainty, particularly for symptoms deemed low-risk or brief-duration events, brain MRI can be useful to make a definitive diagnosis. In the Diagnosis of Uncertain-Origin Benign Transient Neurological Symptoms study, the final diagnosis was revised in 30% of patients after undergoing brain MRI among patients with lower-risk symptoms.[10]

Third, the continuous increase in probability of DWI lesion for focal-only symptoms over the course of 24 hours event duration raises the possibility of preventing permanent parenchymal damage with rapid interventions, including the use of reperfusion therapies and anti-thrombotics. The Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke trials demonstrated that the risk of recurrent stroke was lower when dual antiplatelet therapy was given in the first 24 hours.[3] It is possible that early therapies may prevent development of initial or recurrent DWI lesions, but this is speculative and remains to be tested. Lastly, future studies assessing variables associated with the risk of DWI lesions should

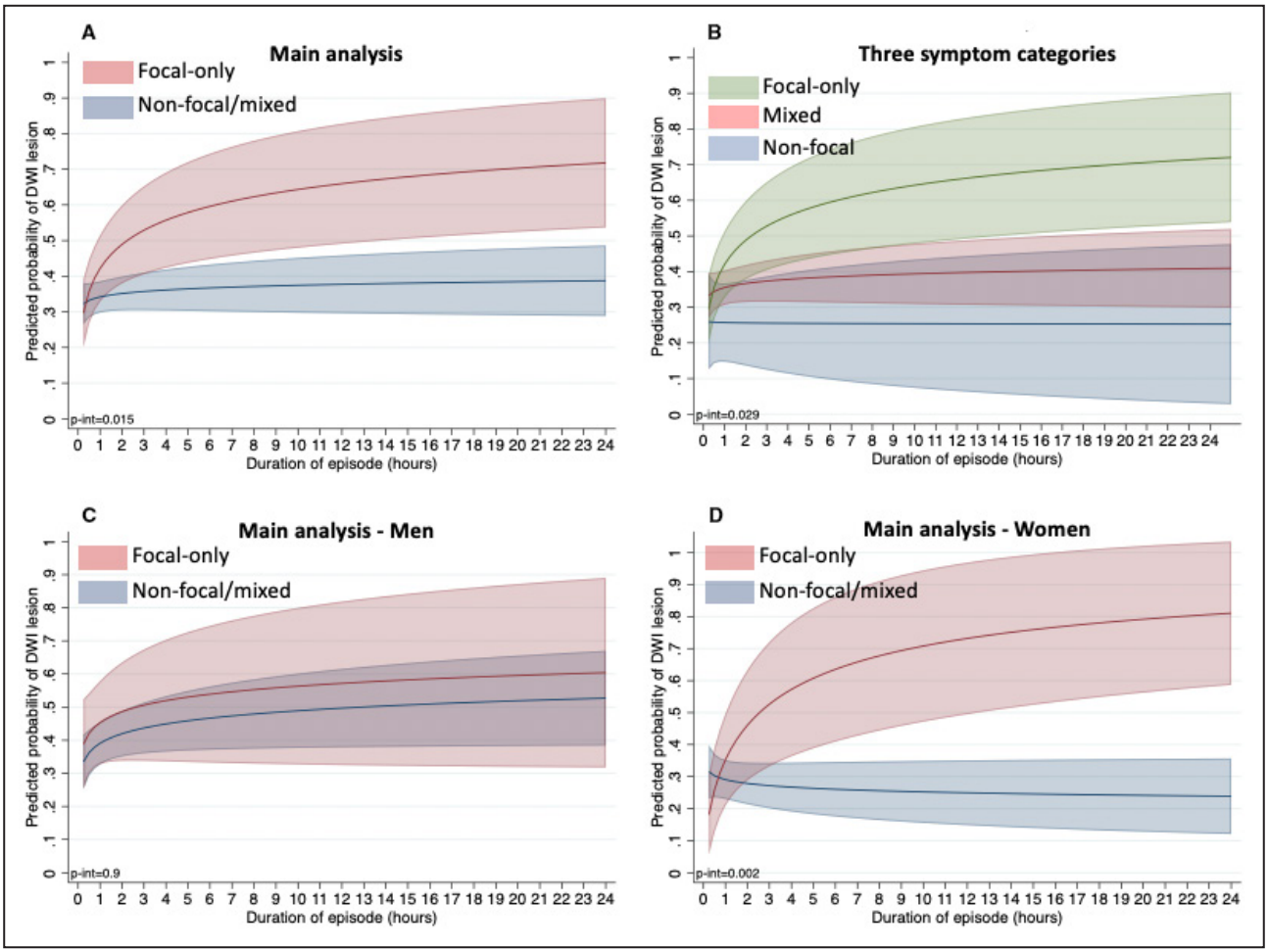

Figure 2. Predicted probability of DWI lesion as a function of event duration and symptom type among those with self-reported symptom resolution.
Results are shown for the main analysis (**A**), with all 3 symptom categories (**B**), among men only (**C**), and women only (**D**). DWI indicates diffusion-weighted imaging.

incorporate the complex interaction of event duration, symptom type, and sex. Sex was a significant modifier of the relationship between event duration and symptom type, in part because of the higher DWI probability of nonfocal or mixed symptoms among men.

Our study had some limitations. Patients were recruited from the emergency departments of academic centers, and all patients were referred to the neurology service acutely. Patients without obvious neurologic symptoms may not have been referred to the neurology service and therefore not captured in SpecTRA, which may limit the generalizability of our findings to the population of general emergency departments. In the main analysis, we relied on patient report of resolution of symptoms, which may underestimate residual mild or unrecognized symptoms. However, our results were robust in sensitivity analyses when including those with both self-reported and examination-based resolution of deficits. Although we adjusted for a number of potential confounders, there remains the possibility of residual measured or unmeasured confounding. We did not have information on how patients were treated after their event. However, current guidelines do not recommend differences in treatment depending on DWI positivity for those suspected of having TIA or minor stroke; therefore, we do not believe clinical care would have differed significantly or would have influenced the results. Lastly, although DWI is a sensitive marker for acute ischemic stroke and the positive predictive value is 99.8%,[6] DWI-negative acute stroke has been observed in 6.8% of cases, primarily for posterior circulation ischemia.[25]

In a prospective study of patients with transient neurological events, longer duration was associated with greater probability of DWI lesion for focal, but not mixed or nonfocal symptoms, with a continuous increase over 24 hours. However, a third of patients with nonfocal/mixed symptoms had DWI lesions. Event duration or symptoms at presentation cannot be used to exclude a cerebrovascular event, although

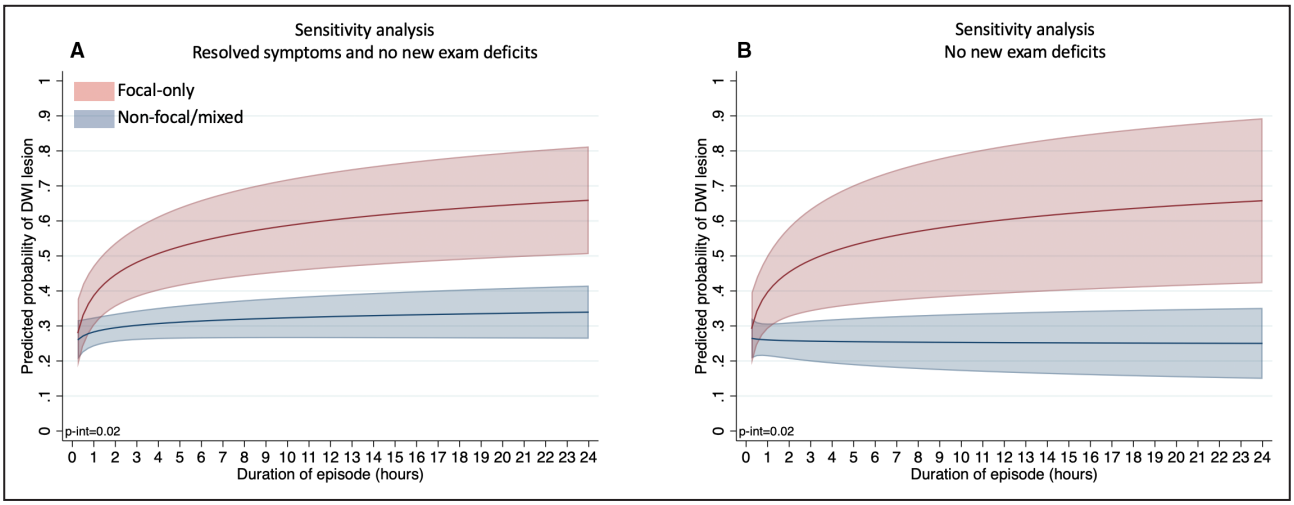

Figure 3. Predicted probability of DWI lesion as a function of event duration and symptom type among those with no new deficits on clinical examination (A) and those with both self-reported symptom resolution in addition to no new deficits on examination (B).
DWI indicates diffusion-weighted imaging.

information from both may be used together for risk stratification.

APPENDIX

SpecTRA Study Group

Investigators of the SpecTRA Study Group are all affiliated with institutions in Canada and are Alison Nikolejsin, RN, of Island Health Neurosciences and Research Department, Victoria, British Columbia; Amy Y. X. Yu, MD, of University of Toronto, Toronto, Ontario; Andrew M. Penn, MD, Anurag Trivedi, MD, Jaclyn Cook, RN, Jaclyn Morrison, RN, Kaitlin Blackwood, BA, Karen Richards, RN, Kristine Votova, PhD, Madeline Nealis, MA, Maximilian B. Bibok, PhD, Melanie Penn, RN, Pavla Beattyova, RN, Priya Rosenberg, BSc, and Sheilah Frost, RN, of Island Health, Neurosciences and Research & Capacity Building Department, Victoria, British Columbia; Carolyn Grant, RN, Janka Hedgedus, MD, Sarah Grant, RN, Tim Watson, MD, and Viera Saly, MD, of Island Health, Neurosciences Department, Victoria, British Columbia; Colin Sedgwick, BSc, of Island Medical Program, University of British Columbia, Victoria, British Columbia; Mary L. Lesperance, MSc, of University of Victoria, Department of Mathematics and Statistics, Victoria, British Columbia; Nicole S. Croteau, MSc, of Island Health, Neurosciences and Research & Capacity Building Department, University of Victoria, and of the Department of Mathematics and Statistics, Victoria, British Columbia; Ramana Appireddy, MD, of Queen's University, Ontario; Robert F. Balshaw, PhD, of University of Manitoba, Winnipeg; Thalia S. Field, MD, of University of British Columbia; Veronique Dubuc, MD, of Hôpital Sacré-Coeur, Montreal, Québec; and Andrew M. Demchuk, MD, Anitha Jambula, MSc, Anne Le, BSc, Bijoy K. Menon, MD, Carly Calvert, BSc, Carol Kenney, RN, Charlotte Zerna, MD, Davar Nikneshan, MD, Eric E. Smith, MD, Evgenia Klourfeld, MD, Gabrielle Wagner, BSc, Gary Klein, MD, Heidi Aram, RN, Jamsheed Desai, MD, Karla Ryckborst, RN, Lisa Bilston, BSc, Michael D. Hill, MD, Mohammed Almekhlafi, MD, Nathan Godfrey, BSc, Oje Imoukheude, MD, Peter Stys, MD, Philip A. Barber, MD, Phillippe Couillard, MD, Prasanna Eswaradas, MD, Privia Rhandawa, BSc, Shelagh B. Coutts, MD, Simerpreet Bal, MD, Steven Peters, MD, Supriya Save, PhD, Suresh Subramaniam, MD, Tapuwa Musuka, MD, Teri Stewart, RN, and Zachary M. Hong, BSc, of University of Calgary, Alberta.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Tables S1–S3
Figures S1, S2

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Association between duration of transient neurological events and diffusion-weighted brain lesions

SUPPLEMENTAL MATERIALS

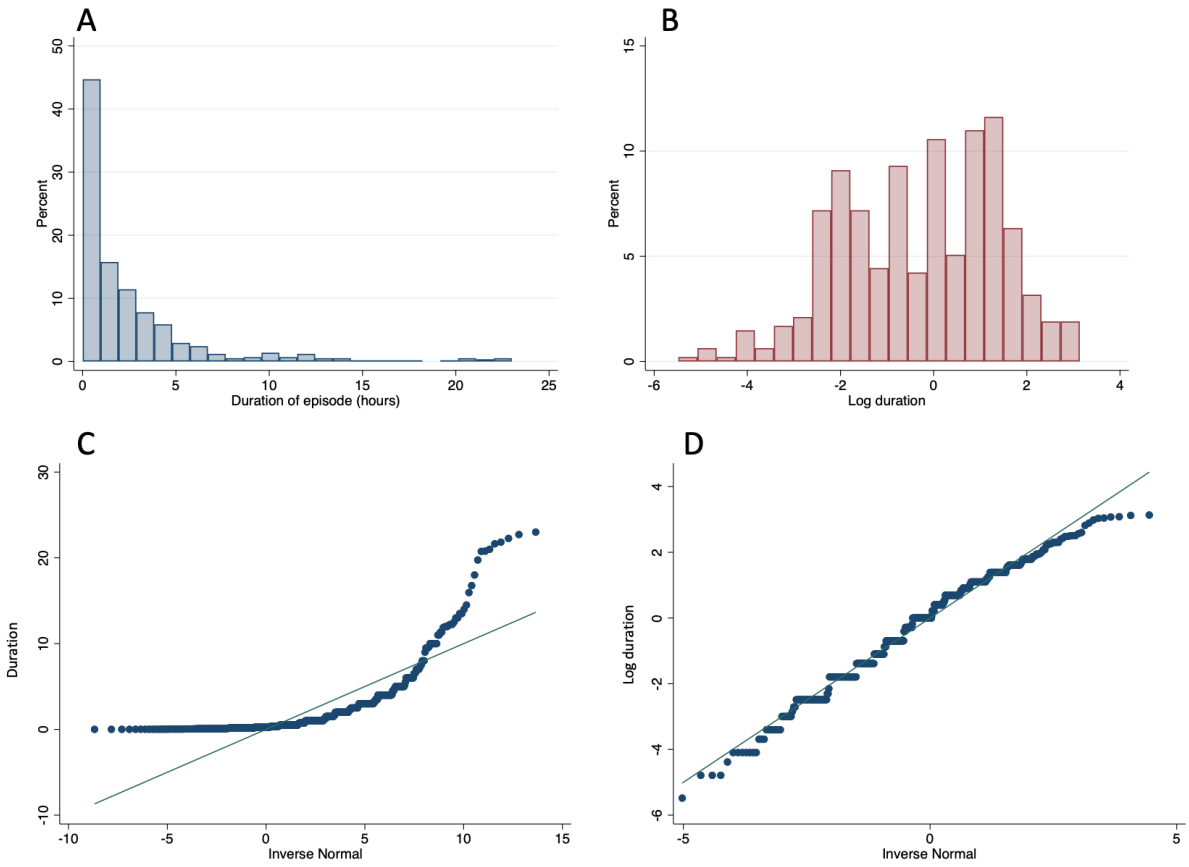

Figure S1. Comparing duration of episode versus log-duration. The distribution of duration is right skewed (A) and the residuals are not normally distributed in a quantile plot (C). After log-transformation, the data (B) and the residuals (D) are more normally distributed.

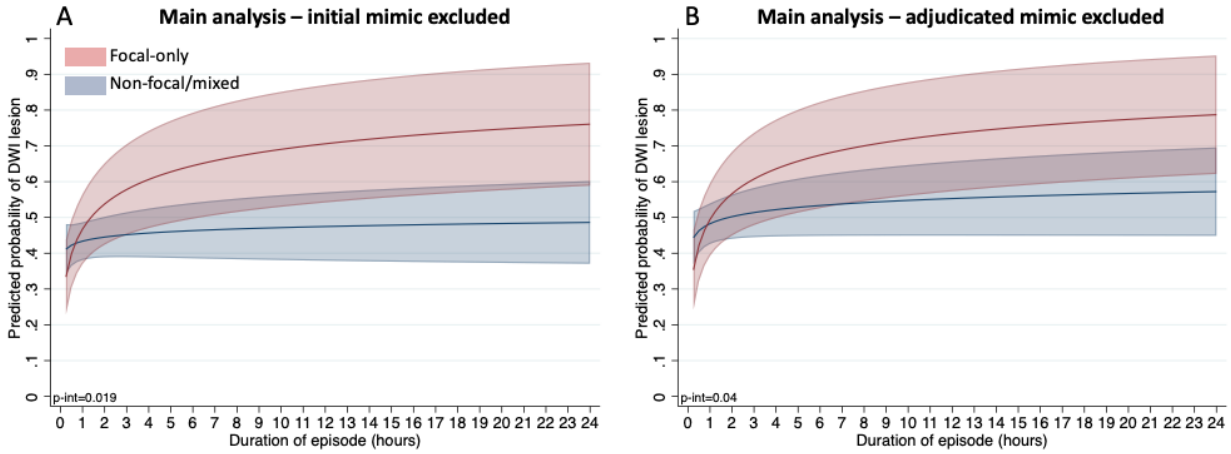

Figure S2. Predicted probability of DWI lesion as a function of event duration and symptom type among those with self-reported symptom resolution, excluding those with (A) initial diagnosis of mimic and (B) final adjudicated diagnosis of mimic.

Table S1. Baseline characteristics of patients in sensitivity analysis who had no new deficits on clinical examination, stratified by presence of DWI lesion

	Total N=905	No DWI lesion N=636	DWI lesion N=269	P-value
Age	68.1 (15.6)	67.3 (16.3)	70.0 (13.7)	0.014
Female sex	442 (48.8%)	324 (50.9%)	118 (43.9%)	0.052
Education				0.48
Less than grade 12	139 (15.4%)	92 (14.5%)	47 (17.5%)	
Completed high school	209 (23.1%)	146 (23.0%)	63 (23.4%)	
Some or graduated post-secondary	552 (61.0%)	394 (61.9%)	158 (58.7%)	
Prior stroke	61 (6.7%)	36 (5.7%)	25 (9.3%)	0.046
Coronary artery disease	125 (13.8%)	90 (14.2%)	35 (13.0%)	0.65
Atrial fibrillation	112 (12.4%)	70 (11.0%)	42 (15.6%)	0.054
Hypertension	475 (52.5%)	329 (51.7%)	146 (54.3%)	0.48
Diabetes	134 (14.8%)	85 (13.4%)	49 (18.2%)	0.060
Smoking	96 (10.6%)	61 (9.6%)	35 (13.0%)	0.13
Duration of event in hours, median (IQR)	2 (0.42-6)	2 (0.33-5.4)	2.5 (0.5-8.5)	0.01
Systolic blood pressure, mean (SD)	157.3 (26.8)	157.2 (26.3)	157.6 (27.8)	0.84
Presentation type				<0.001
Mixed or non-focal	713 (78.8%)	524 (82.4%)	189 (70.3%)	
Focal-only	192 (21.2%)	112 (17.6%)	80 (29.7%)	

Table S2. Baseline characteristics of patients in sensitivity analysis who were resolved on self-report and had no new clinical deficits, stratified by presence of focal presentation

	Total N=550	No DWI lesion N=393	DWI lesion N=157	P-value
Age	69.1 (14.9)	68.1 (15.4)	71.5 (13.3)	0.016
Female sex	268 (48.7%)	197 (50.1%)	71 (45.2%)	0.30
Education				0.45
Less than grade 12	91 (16.5%)	61 (15.5%)	30 (19.1%)	
Completed high school	116 (21.1%)	81 (20.6%)	35 (22.3%)	
Some or graduated post-secondary	341 (62.0%)	250 (63.6%)	91 (58.0%)	
Prior stroke	38 (6.9%)	23 (5.9%)	15 (9.6%)	0.12
CAD	76 (13.8%)	56 (14.2%)	20 (12.7%)	0.64
Atrial fibrillation	71 (12.9%)	42 (10.7%)	29 (18.5%)	0.014
Hypertension	301 (54.7%)	219 (55.7%)	82 (52.2%)	0.46
Diabetes	81 (14.7%)	53 (13.5%)	28 (17.8%)	0.19
Smoking	60 (10.9%)	45 (11.5%)	15 (9.6%)	0.52
Duration of event in hours, median (IQR)	1 (0.25-3)	1 (0.25-3)	1 (0.33-3)	0.8
Systolic blood pressure, mean (SD)	158.7 (26.6)	159.2 (26.4)	157.5 (26.9)	0.52

Table S3. Results of main logistic regression model showing associations between baseline factors and DWI positivity on MRI*

Variable	Odds ratio	Lower 95% CI	Upper 95% CI	P-value
Age (per year of age)	1.01	1.0	1.03	0.046
Female sex	0.59	0.41	0.84	0.004
Education (reference= less than grade 12)				
Completed high school	1.33	0.75	2.38	0.33
Some or graduated post-secondary	1.14	0.68	1.91	0.63
Prior stroke	1.70	0.88	3.27	0.11
Coronary artery disease	0.58	0.33	1.02	0.057
Atrial fibrillation	1.90	1.12	3.21	0.017
Hypertension	0.86	0.58	1.27	0.45
Diabetes	1.40	0.86	2.26	0.17
Systolic blood pressure	1.0	0.99	1.0	0.46
Smoking	1.57	0.91	2.73	0.11

***Model includes an interaction term between focal symptoms and duration of event, p_{int}=0.015.**