Monash Transient Ischemic Attack Triaging Treatment
Safety of a Transient Ischemic Attack Mechanism-Based Outpatient Model of Care

Lauren M. Sanders, MBBS; Velandai K. Srikanth, PhD; Damien J. Jolley, MSc(Stats); Vijaya Sundararajan, MD; Helen Psihogios, FACEM; Kitty Wong, MPH; David Ramsay, RN; Thanh G. Phan, PhD

Background and Purpose—Controversy surrounds the need for routine hospital admission for transient ischemic attack. The Monash Transient Ischemic Attack Triaging Treatment (M3T) model adopts rapid management in the emergency department followed by outpatient management prioritized by stroke mechanism. We compared safety and processes of care between M3T and the previous model of routine admission.

Methods—Study cohorts consisted of patients managed with M3T (2004–2007) and the previous model (2003–2004). We determined 90-day stroke outcome using clinical and medical record review and data linkage to the population level statewide hospital discharge morbidity database. We compared models of care using risk difference analysis, followed by logistic regression to adjust for previous indicators of risk. Secondary outcomes were proportions admitted, proportions undergoing carotid ultrasound, times to ultrasound and revascularization, and medication prescription.

Results—In M3T (mean age, 64.7±14.7) 85/488 (17.4%) patients were admitted compared with 117/169 (62.9%) in the previous model (mean age, 72.5±13.9). With near-complete follow-up, 90-day stroke outcome was 1.50% (95% confidence interval, 0.73%–3.05%) in M3T and 4.67% (95% confidence interval, 2.28%–9.32%) in the previous model (P=0.03). Compared with the previous model, the adjusted odds ratio of stroke for M3T was 0.46 (95% confidence interval, 0.12–1.68; P=0.24). M3T was associated with greater proportions undergoing carotid ultrasound (P<0.001) and receiving antiplatelet therapy (P=0.005).

Conclusions—The M3T system was associated with low 90-day stroke outcome in transient ischemic attack patients, providing proof of concept that these patients may be managed safely without routine hospital admission using a closely supervised protocol in the emergency department. (Stroke. 2012;43:2936-2941.)

Key Words: outpatient ■ stroke ■ transient ischemic attack

There is controversy regarding whether transient ischemic attack (TIA) patients can be managed safely without hospital admission.1-3 Although it has been proposed that hospitalization may improve access to thrombolysis in the event of recurrent ischemia,4 recent modeling indicates outpatient management may be more cost-effective.5 Post-TIA stroke rates are reported to be ≈5% at 7 days6 and as low as 1% to 3% at 90 days in settings of expedited treatment.7-12 The before and after study design of EXPRESS5 provided evidence that rapid clinic-based management was superior to delayed initiation of therapy in TIA patients not referred to an emergency department (ED). Low stroke rates were reported with a rapid nonadmission-based protocol in SOS-TIA (admission rate 26%),7 and the feasibility of protocol-driven evaluation based in an ED observation unit was later shown in unselected TIA patients presenting to hospital.12 In the Ottawa study,9 98.4% of patients were discharged from ED with medication management at the discretion of the ED physician, Doppler ultrasound was booked as an outpatient, and urgency of follow-up was triaged based on the ABCD2 score. In the TWO ACES study,10 patients were discharged from ED based on a low ABCD2 score11 (admission rate, 30%). However, a low ABCD2 score may miss patients with a modifiable high-risk mechanism such as atrial fibrillation or carotid stenosis.14,15 Management in an inpatient ward vs an ED setting (ED observation unit) has been evaluated in only...
1 randomized trial, although the primary outcome in this study was length of stay.\textsuperscript{11} It is uncertain whether nonadmission is safe compared with routine admission in unselected TIA patients if urgency of management is stratified based on vascular mechanism.

In May 2004, we changed our model of TIA care, replacing an admission-based model with a nonadmission-based protocol, the Monash TIA Triaging Treatment (M3T) pathway. In M3T, rapid evaluation and management are initiated for all TIA patients in ED, in consultation with the stroke team, and urgency of TIA clinic follow-up is prioritized by vascular mechanism. Because the highest 90-day stroke risk is associated with large artery atherosclerosis and cardioembolism,\textsuperscript{16} such patients are given urgent clinic appointments. We present our experience of M3T during its first 4 years, comparing performance with the previous admission-based model to provide proof of concept for managing TIA patients safely without routine admission. We evaluated whether M3T would be no worse in safety compared with the previous model, hypothesizing that primary outcome (90-day stroke) would be similarly low for both models.

Materials and Methods

Samples and Descriptive Data

We adopted a before and after cohort design similar to EXPRESS.\textsuperscript{8} The primary cohort consisted of all patients with suspected TIA presenting to ED and managed in M3T from May 2004 to December 2007. TIA was defined as “acute loss of focal cerebral or monocular function with symptoms lasting <24 hours and that is thought to be due to inadequate cerebral or ocular blood supply as a result of arterial thrombosis or embolism.”\textsuperscript{12} We derived the comparison cohort from all patients presenting to ED from January 2003 to January 2004, who were assigned an International Classification of Diseases, 10th revision, Australian Modification TIA code G45.8 or G45.9. A stroke neurologist (T.P.) confirmed diagnosis after clinical consultation and/or review of medical records. In addition to presenting features, investigations, and treatment, we extracted data for potential confounding variables (preexisting vascular risk factors, medications before TIA) from hospital and clinic medical records. The Southern Health (Hospital) and Monash University Human Research Ethics Committees approved this study.

M3T Model

The M3T pathway (Figure) first requires emergency physician evaluation of suspected TIA patients, with decisions undertaken in consultation with the stroke team. Patients with persistent signs, recurrent/crescendo TIA, or other acute medical issues are admitted to the stroke unit. All other patients enter the nonadmission arm of M3T.

Our decision-making paradigm is driven by vascular mechanism, without dependence on the ABCD\textsuperscript{2} score\textsuperscript{13} or other risk-stratification tools. All patients receive urgent computed tomography brain imaging, ECG, and baseline blood tests in ED, with request forms marked “TIA Pathway” to expedite results. The radiology department facilitates same-day carotid ultrasound (anterior circulation symptoms) or next-day if patients present after usual working hours. After computed tomography review, antiplatelet therapy is immediately commenced or modified. If AF is identified and no contraindications exist for anticoagulation, then warfarin is commenced and titrated as an outpatient in conjunction with the patient’s general practitioner. Guidelines for antihypertensive and lipid-lowering therapies are included in the pathway.

When a patient enters the M3T pathway, ED physicians fax a standardized TIA referral to a daily TIA clinic to facilitate outpatient review. The stroke registrar and nurse triage referrals on a daily basis, with priority appointments for patients with ipsilateral internal carotid artery stenosis ≥50%, a conservative threshold chosen to avoid missing a critical stenosis attributable to ultrasound misclassification.\textsuperscript{14} For patients with ≥50% ipsilateral internal carotid artery stenosis, confirmatory computed tomography angiography or contrast-enhanced magnetic resonance angiography is arranged within 24 hours. Immediate referral for surgical intervention occurs for patients with confirmed symptomatic stenosis ≥70%. Patients with AF also receive priority review to assess anticoagulation. Patients without symptomatic internal carotid artery stenosis or AF are allocated less urgent appointments (usually within 4–6 weeks) given that antiplatelet therapy is commenced in ED. Optimization of other vascular risk factors occurs during clinic visits.
Pre-M3T Model of Care

During 2003, most TIA patients were admitted to hospital. For the few patients discharged directly from ED, management and referral for neurologist follow-up were at the discretion of the emergency physician. Outpatient neurology referral from ED was not routine.

Outcome and Follow-Up

Primary outcome was stroke at 90 days. Stroke was defined as “rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting >24 hours or leading to death, with no apparent cause other than of vascular origin.”20 We determined stroke events by face-to-face neurologist consultation for the majority of patients. We used a sensitive and validated telephone questionnaire20 in patients who declined consultation, or we searched medical records if they were deceased or unable to be contacted. Methods of outcome ascertainment may vary by physician, method of interview, or in recording of data in medical files. To limit this possible bias, we also captured stroke events within 90 days of TIA by data linkage of both cohorts to International Classification of Diseases, 10th revision, Australian Modification TIA codes). Of these, 41 were neurologist-confirmed TIA. We identified 169 patients treated in the previous model between January 2003 and January 2004, with a presenting diagnosis of TIA (based on International Classification of Diseases, 10th revision, Australian Modification TIA codes). Of these, 41 were TIA “mimics,” leaving 128 with confirmed TIA.

Statistical Analysis

We used 2-tailed t tests and χ2 tests to compare groups for baseline characteristics and to assess distribution of potential confounders.22 We calculated 95% confidence intervals (CI) for observed proportions (p) of stroke at 90 days using the Wilson method.23 To evaluate our hypothesis of similarly low stroke outcome in both models, we calculated the risk difference (risk difference=Previous model−M3T) and constructed confidence limits using the method of variance estimates recovery.24 In cases of no true difference between groups, the risk difference CI would be expected to include zero.25

We controlled for potential confounding using established methods of multivariable logistic regression.22 We first evaluated the effect of each potential confounding variable on stroke outcome using univariable logistic regression. Variables with P≤0.20 were included in multivariable logistic regression to generate an adjusted odds ratio of 90-day stroke outcome for M3T compared with the previous model. We did not adjust for differences in treatment after presentation, because these are components of the model of care undergoing evaluation. We also compared stroke in M3T with proportions reported in other published nonadmission-based TIA management studies24,25 using χ2 test.

Additionally, we assessed M3T for noninferiority against the previous model and other rapid-care models (1-tailed; α=0.10). We assumed admission to represent “optimal treatment” and proposed that an increase of >3 strokes per annum in M3T would be unacceptable. Based on an average of 84 patients per annum presenting with a definitive TIA in M3T, this would equate to 3.6% absolute increase in 90-day stroke rate, which we rounded down to a conservative noninferiority margin (b) of 3.0%. Noninferiority is inferred if the 90-day stroke rate in M3T is not >3.0% higher than that in the previous model.

Because of skewed distribution of times to carotid ultrasound and revascularization, we evaluated differences in the interquartile ranges using interquartile range, adjusting for baseline confounding factors. Proportions admitted were compared using χ2 test. Although we did not use ABCD2 score11 to enable decision-making, we compared stroke outcome between those who would have been assigned ABCD2 scores 0 to 3 vs >3. All statistical analyses were undertaken using Stata (version 11.0; Stata Corporation).

Results

We treated 488 patients in M3T between May 2004 and December 2007. Of these, 187 patients were TIA “mimics,” leaving 301 with neurologist-confirmed TIA. We identified 169 patients treated in the previous model between January 2003 and January 2004, with a presenting diagnosis of TIA (based on International Classification of Diseases, 10th revision, Australian Modification TIA codes). Of these, 41 were TIA “mimics,” leaving 128 with neurologist-confirmed TIA. Table 1 details comparison of patient characteristics between M3T and the previous model. Patients in M3T were younger, less likely to have atrial fibrillation and carotid stenosis, or to be former smokers (all P<0.05), but they were similar with respect to sex and other vascular risk factors. There were no significant differences in antiplatelet (P=0.08), antihypertensive (P=0.47), or statin (P=0.85) use before TIA.

We achieved 90-day follow-up in 468/488 (95.9%) patients in M3T and 150/169 (88.6%) patients in the previous model. Stroke outcome at 90 days was 1.50% (7/468; 95% CI, 0.73%–3.05%) in M3T compared with 4.67% (7/150; 95% CI, 2.28%–9.32%) in the previous model (P=0.03). All stroke events occurred in patients with neurologist-confirmed TIA: 2.36% (7/296; 95% CI, 1.15%–4.80%) in M3T compared with 6.14% (7/114; 95% CI, 3.01%–12.13%) in the previous model (P=0.06). Using data linkage, 90-day outcome was available for 93.3% of cases (M3T: 460/488, 94.3%; previous model: 154/169, 91.1%). This approach identified 17 stroke events overall, and proportions of patients
Importantly, by guest on July 14, 2017 http://stroke.ahajournals.org/ Downloaded from M3T 7/296 2.36 1.15–4.80 . . .

Table 2. Comparison of 90-Day Stroke Outcome Between Monash Transient Ischemic Attack Triaging Treatment and Previously Published Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>90-Day Stroke</th>
<th>n/N*</th>
<th>%</th>
<th>95% CI, %</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>M3T</td>
<td></td>
<td>7/296</td>
<td>2.36</td>
<td>1.15–4.80</td>
<td>. . .</td>
</tr>
<tr>
<td>EXPRESS (phase 1)††</td>
<td></td>
<td>32/310</td>
<td>10.32</td>
<td>7.41–14.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EXPRESS (phase 2)†</td>
<td></td>
<td>6/281</td>
<td>2.14</td>
<td>0.98–4.58</td>
<td>0.85</td>
</tr>
<tr>
<td>SOS-TIA†</td>
<td></td>
<td>13/770</td>
<td>1.68</td>
<td>0.99–2.87</td>
<td>0.47</td>
</tr>
<tr>
<td>Ottawa†</td>
<td></td>
<td>31/882</td>
<td>3.16</td>
<td>2.23–4.45</td>
<td>0.48</td>
</tr>
<tr>
<td>TWO ACES†</td>
<td></td>
<td>2/116</td>
<td>1.72</td>
<td>0.47–6.07</td>
<td>0.69</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; M3T, Monash Transient Ischemic Attack Triaging Treatment; TIA, transient ischemic attack.
†TIA patients with 90-d follow-up.
††EXPRESS (phase 1) did not have an associated accelerated protocol for investigation and management.

Discussion

Our results indicate that the nonadmission-based M3T system is safe when compared with routine hospital admission for TIA patients. Stroke rates in M3T were low and comparable with those observed in other rapid-care TIA models.2–12 Compared with the previous model, M3T was associated with greater use of antiplatelet medication and carotid ultrasound. The ABCD² score did not predict outcome in either M3T or the previous model of care. Our findings suggest that a well-structured and supervised model focused on rapid investigation and initiation of treatment in ED, coupled with prioritized clinic follow-up based on stroke mechanism, is an acceptable alternative to hospital admission for TIA patients.

The stroke rate at 90 days in M3T was low and similar to rates associated with structured nonadmission-based TIA management in EXPRESS,8 SOS-TIA,7 and Ottawa5 studies. However, unlike our study, there was no comparison with admitted patients in these studies. In the TWO ACES study,10 30% of patients were admitted based on risk stratification using the ABCD² score.11 The M3T protocol, in contrast, is applied to unselected TIA patients, successfully avoiding admission in the majority of patients. The M3T protocol differs from other published pathways in several components. Unlike SOS-TIA7 and EXPRESS,8 it does not require the presence of neurologists at first assessment but requires initiation of treatment by ED physicians based on a structured pathway developed by stroke neurologists. Clinic follow-up urgency, in contrast to Ottawa5 and TWO ACES,10 is not based on the ABCD² score, but rather on underlying vascular mechanism. We recently have shown in our setting that a low ABCD² score may miss a modifiable high-risk mechanism.15 Importantly, admitting M3T patients based on ABCD² score would have resulted in a dramatically higher admission rate (65%) with resultant implications for resource utilization.

A significant advantage of models such as M3T is the ability to improve hospital bed availability with the potential for cost-savings to the hospital system. An Australian survey reported that 96% of TIA patients managed in a hospital setting initially present to ED, and 65% of surveyed hospitals reported a policy of admission for either all or “high-risk” TIA.28 With a national average of just 2.6 public hospital beds per 1000 population and hospital occupancy commonly >90% capacity, hospital beds are a limited resource.27 In 2006/2007, the average bed-day cost for TIA in Victoria, Australia, was approximately 1000 Australian dollars (AUD$). Based on the median length of stay for TIA patients with stroke were 1.74% (8/460; 95% CI, 0.88%–3.39%) in M3T compared with 5.84% (9/154; 95% CI, 3.1%–10.73%) in the previous model (P=0.007). The absolute risk difference between M3T and the previous model was 3.17% (95% CI, 0.32%–8.17%) among all patients and 3.78% (−0.19% to 9.89%) among those with definite TIA. Using a threshold of P≤0.20 in univariable logistic regression, age, sex, atrial fibrillation, carotid stenosis, ever-smoking, and previous statin use were considered for adjustment in multivariable logistic regression. The adjusted odds of stroke in M3T tended to be lower than in the previous model when all patients were considered (odds ratio, 0.46; 95% CI, 0.12–1.68; P=0.24) and among only those with definite TIA (odds ratio, 0.431 95% CI, 0.12–1.59; P=0.21), although neither reached statistical significance. Stroke outcome at 90 days in M3T was similar to that reported in other published rapid TIA management models (Table 2). At the prespecified δ of 3.0%, M3T was noninferior to the previous model, EXPRESS (phase 2),8 SOS-TIA7 and Ottawa5 studies (Supplementary Table I). However, the noninferiority comparison with the previous model was powered below the recommended 95%,25 whereas comparison with SOS-TIA7 was adequately powered at 97% (Supplementary Table I).

In M3T, 417/488 (85.5%) underwent carotid ultrasound compared with 79/169 (47.9%) in the previous model (P<0.001). Median time to ultrasound, adjusted for differences in demographics, was similar in both groups (M3T: 1 day, interquartile range 0–3; prior model: 1 day, interquartile range 0–2; P=0.09). Of the patients with ipsilateral internal carotid artery stenosis ≥50%, 14/39 (35.9%) and 8/19 (42.1%) underwent carotid revascularization in M3T and the previous model, respectively. Median time to revascularization was 17.5 (interquartile range, 4–44) days in M3T and 26.5 (interquartile range, 6.5–149.5) days in the previous model (P=0.59). Compared with the previous model, more TIA patients in the M3T cohort were discharged with antplatelet therapy (92.2% vs 82.0%; P=0.005), but there were no differences in proportions of patients discharged with statins (42.2% vs 46.3%; P=0.47) or antihypertensive agents (46.1 vs 50.5%; P=0.44). Admission to a hospital bed occurred in 85/488 (17.4%) and 117/169 (69.2%) patients in M3T and the previous model, respectively (P<0.001). Within M3T, there was no difference in stroke outcome between admitted (2/85; 2.35%) and nonadmitted (5/403; 1.24%) patients (P=0.43). Stroke outcome at 90 days in patients with ABCD² score ≥3 was 1.27% (5/297; 0.74%–3.96%) for M3T and 4.76% (4/84; 1.87%–11.61%) for the previous model. In patients with ABCD² score 0 to 3, the respective proportions were 1.05% (2/191; 0.29%–3.74%) and 3.53% (3/88; 1.21%–9.87%). There was no significant difference in stroke outcome between those with ABCD² score 0 to 3 and ≥3 within either cohort (M3T: P=0.56; previous model: P=0.68).
in our study (2 days) and ≈160 TIA presentations per year to our center, the annual bed-cost alone would be as high as AUD$320 000 for 100% admission, AUD$256 000 for 80% admission, and only AUD$64 000 for 20% admission. For a median 4-day admission, as seen in our previous model of care and in SOS-TIA, the respective values would be AUD$640 000, AUD$512 000, and AUD$128 000 per annum. However, these are only estimates, and further detailed cost evaluation with attention to microcosting of elements may be required to determine cost-effectiveness.

Some propose that admission would expedite access to thrombolysis, which may confer cost-savings given projected decreases in stroke-associated morbidity and mortality. Authors of a cost modeling study reported borderline cost-effectiveness for 24-hour admission of all TIA patients assuming a 24-hour stroke risk of 4.2% and a presumed higher rate of thrombolytic administration in hospitalized patients. However, results of a more recent decision analysis indicated early stroke rates of 20% were necessary to achieve cost-effectiveness. In our study, 2-day stroke outcome in M3T was only 0.85% with similarly low early rates seen in other rapid assessment pathways. To date, clinical evidence is lacking to support the hypothesis that admission of TIA patients leads to timely thrombolysis.

We recognize that different health systems and economic factors may influence TIA care models. For example, other Australian investigators have observed higher stroke rates in patients discharged directly from their ED compared with those admitted, concluding that delay or omission of appropriate investigations and treatment, in the absence of a structured rapid-care pathway, contributed to their findings. In our center, strong collaborative links between ED and stroke and radiology departments were integral to the successful implementation of our M3T protocol. Conversely, a Spanish study reported difficulties implementing timely investigations and treatment, leading the authors to conclude that hospital admission was necessary in their setting.

The strengths of our study include the high rate of follow-up, multiple sources of outcome ascertainment, and comparison with the model of care immediately preceding M3T. To minimize possible measurement bias associated with use of a historical cohort, we applied standardized definitions for TIA and stroke and a neurologist confirmed TIA diagnosis. Beyond searching hospital medical records for stroke outcome, we used data linkage with the Victorian hospital discharge morbidity database to detect patients presenting to another institution with stroke. These data, although dependant on the accuracy of International Classification of Diseases, revision, Australian Modification coding, provide another avenue by which the 2 groups could be compared and minimize potential bias attributable to loss of follow-up. In the unlikely event of stroke in all M3T patients lost to follow-up, and no additional stroke in the previous model, there would still be no significant difference in outcome ($P_{=0.48}$).

There are limitations to this study. We did not perform a randomized comparison of TIA models, but used a before and after study design similar to EXPRESS. However, to design a randomized trial comparing models for noninferiority with conservative δ values of 3%, 2%, and 1%, we would require >600, >1400, and >5600 patients per arm, respectively, posing significant logistic challenges to conduct such a trial in a timely fashion at a single institution. Although the comparison of M3T with the previous Monash model was underpowered to definitively confirm noninferiority, it was clearly noninferior to the SOS-TIA model (a large study with the lowest 90-day stroke rate). Furthermore, we used a conservative noninferiority margin. The low stroke rate (1.50%) in M3T presented with robust and conservative CI along with superior system process indicators (eg, uptake of antiplatelets, proportions receiving ultrasound) add credence to the safety of M3T.

In summary, our study provides proof of concept that a well-organized nonadmission-based TIA model of care such as M3T is likely to be safe. The key component in any TIA model of care probably lies in mobilization of resources to expedite essential investigations and management based on vascular mechanism.

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Disclosures
None.

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Monash Transient Ischemic Attack Triaging Treatment (M3T): safety of a TIA mechanism-based outpatient model of care

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Supplementary Table S1: Non-inferiority comparisons between M3T model and other models (δ=3.0%)

<table>
<thead>
<tr>
<th>Comparison group*</th>
<th>95% CI for non-inferiority (1 tailed; α=0.10)</th>
<th>Power (1-β)</th>
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</thead>
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<td>Prior Monash Model (n=114)</td>
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<td>EXPRESS(^1) phase 2 (n=281)</td>
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<td>0.88</td>
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<td>0.97</td>
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<td>TWOACES(^4) (n=116)</td>
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<td>0.72</td>
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*TIA patients with 90-day follow-up

References


