Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 113; No. 10; P198

The Incidence of Subsequent Stroke After Attending the Transient Ischaemic Attack (TIA) Clinic

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Abstract

Aim

A rapid access clinic for patients with recent (1-7 days) TIA and ABCD2 scores ≤4 is run in Cork University Hospital. However, the rate of stroke after attending the clinic is currently unknown. The overall aim was to evaluate recurrent 7-day, 90-day and 1-year stroke risk among the first 250 low-risk patients attending the TIA Clinic.

Methods

Data was collected from the iSoft Clinical Manager software, neuroimaging review, chart review and postal survey.

Results

Risk for recurrent stroke was 0% (n=0266) at 7-days, 0% (n=0266) at 90-days and 0.4% (n=1/266) at 1-year. Among patients with TIA, 8.7% (n=6/69) had a carotid endarterectomy and 5.8% (n=4/69) were commenced on anticoagulation therapy.

Conclusion

It is safe to see patients with ABCD2 scores of 0-4 at the TIA clinic as they are low risk for subsequent stroke following appropriate treatment/intervention. Despite low scores, 5.6% of all patients had a high-risk aetiology (symptomatic carotid stenosis) identified and treated.

Introduction

Transient ischaemic attack (TIA) is associated with considerable morbidity and mortality because it is a harbinger for the imminent development of stroke[1-3] with the majority of strokes occurring in the first 90 days post-TIA[3-6]. The subsequent stroke risk after TIA depends largely on clinical features, vascular risk factors and the underlying pathophysiology of the TIA[7], therefore stroke risk is not uniform, with the majority of patients experiencing a benign short-term prognosis[5]. However, because symptoms of TIA typically resolve, a serendipitous opportunity to commence treatment is presented, which may ultimately forestall the possible onset of debilitating brain infarction[8].

The EXPRESS study (Effect of urgent treatment of transient ischemic attack and minor stroke on early recurrent stroke) was a landmark study fuelling the change in the approach of the management of TIA[9]. Previously, symptoms of TIA tended to be ignored or minimised by patients, or not prioritised by physicians, largely because symptoms typically last only for a few minutes with apparent complete recovery[10]. The EXPRESS study showed an 80% reduction in subsequent stroke risk at 90-days in patients treated in a specialised TIA clinic with early assessment and urgent treatment initiation[9].

A rapid access stroke prevention (RASP) TIA clinic was established in Cork University Hospital (CUH) in 2013 to reduce stroke risk in patients with TIA in addition to reducing economic burden associated with unnecessary inpatient stay. The CUH TIA clinic accepts patients referred from primary care or the emergency department (ED) presenting with suspected TIA and $ABCD_2$ scores of ≤ 4 (see ***Table 1***). Patients with $ABCD_2$ scores of 5-7 are automatically re-directed for same day admission through the ED. Patients are seen by a stroke-trained doctor within 72 hours of referral and have a standard evaluation including blood tests, ECG, carotid duplex ultrasound, and brain imaging (typically MRI brain with diffusion weighted sequences).

Since early treatment post-TIA has been shown to significantly reduce the 90-day stroke risk[9], and the question remains as to how many people experienced a stroke after attending the CUH TIA clinic, the overarching aim of this investigation was to measure the incidence of subsequent stroke among the first 250 patients who attended the TIA clinic at 7-days, 90-days and 1-year. (***Table 1 next page***).

Parameters	$ABCD_2$ Score	$ABCD_3$-I
Age ≥ 60 years	1	1
Blood Pressure ≥ 140/90 mmHg	1	1
Clinical Features:		
Unilateral weakness	2	2
Dysphasia without weakness	1	1
Duration:		
≥60 min	2	2
10 - 59 min	1	1
Diabetes mellitus present	1	1
Dual TIA (< 7 days)	-	2
Imaging: Ipsilateral ≥ 50% stenosis of internal carotid artery	-	2
Imaging: Acute diffusion-weighted imaging hyperintensity	-	2
Total	**7**	**13**

Table 1: *ABCD2 and ABCD3-I scores are prognostic scores proposed to estimate the short-term risk of stroke after TIA. The ABCD2 score allocates points based on age, blood pressure, clinical symptoms, duration and diabetes (range 0-7). The ABCD3-I score (range 0-13) was developed to enhance decision-making in secondary care setting and holds promise to significantly improve risk stratification post-TIA due to the incorporation of three additional markers of unstable vascular disease associated with stroke; dual TIA (the index TIA plus at least one other TIA in the preceding 7 days); positive diffusion-weighted brain imaging (DWI MRI); and carotid stenosis.*

Methods

Data was collected from patients who attended the TIA clinic in a retrospective cohort analysis format using the iSoft Clinical Manager (iCM) software, city-wide neuroimaging platforms (AGFA Impax 6), chart review and postal survey. $ABCD_2$ and $ABCD_3$-I scores were calculated for each patient and retrospectively applied. Subsequent stroke status was identified by electronic discharge letter review, postal survey review, chart review and neuroimaging review.

Stroke was considered the primary endpoint with secondary endpoints being myocardial infarction (MI), any vascular event, and all-cause death.

Patients eligible for inclusion were the first 250 patients who attended the TIA clinic with fully completed electronic TIA clinic discharge letters. Alternatively, if patients were admitted to hospital upon presentation, and no TIA clinic discharge letter was available, they were still considered eligible if standard electronic discharge letters or dictated letters were completed.

Exclusion criteria were incomplete or missing TIA clinic discharge letters. Some patients died in the interim, given the relatively older profile of persons with TIA, therefore patients who died were followed up electronically only.

Ethical approval was granted by the Clinical Research Ethics Committee (CREC) on 13th March 2017.

Statistical analysis was performed using the SPSS statistical package (version 23). Using a time to event approach, Kaplan-Meier estimator was used to calculate the cumulative probability of any subsequent event and the log-rank and Breslow tests were used to compare event-free survival between groups.

Results

The first 250 patients referred to the TIA clinic who met both inclusion and exclusion criteria received surveys, of which 77 were returned fully completed (equating to a 30.8% overall response rate for the follow-up survey). An additional 16 patients were included in the study but excluded from the postal survey as they had died prior to commencing the study.

Baseline Population Characteristics

Mean age was 62.2 years (± 15.3 years; n=266), 139 (52.3%) patients were female and 127 were male (47.7%). TIA was diagnosed in 69 (25.9%) patients, stroke in 15 (5.6%), and non-TIA events in 182 (68.5%) (see ***Figure 1***).

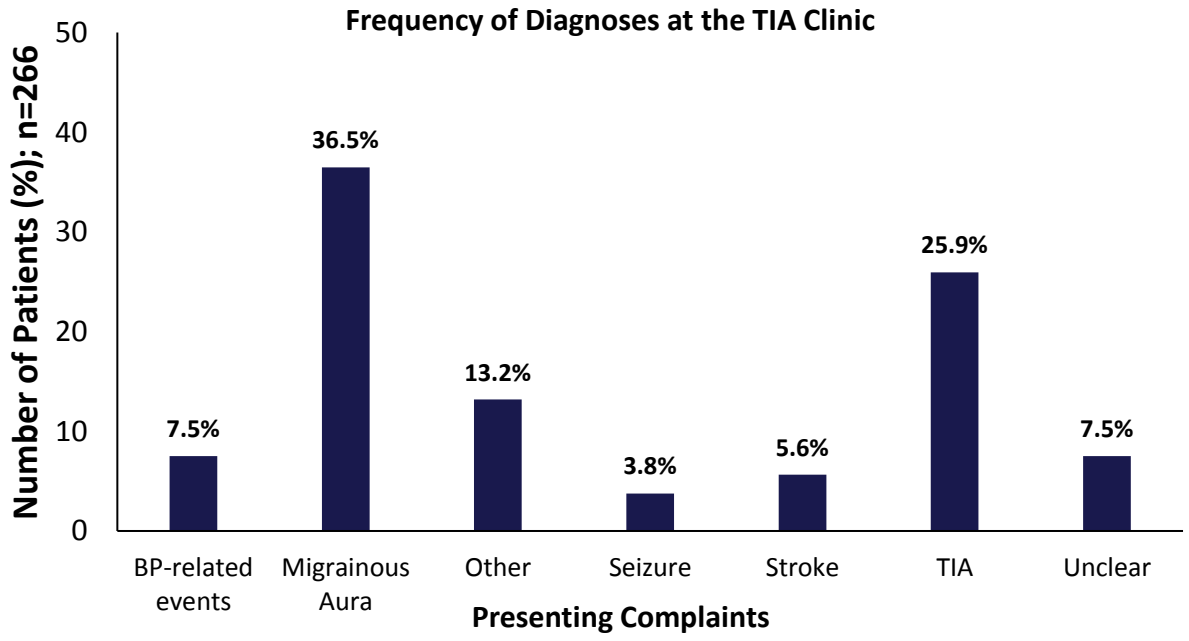

Figure 1: *Frequency of Events Presenting at the TIA Clinic. Non-specific or "other" symptoms included altered levels of consciousness, amnesic episodes, syncopal events and musculoskeletal symptoms.*

Cardiovascular Risk Factors for Stroke

The prevalence of cardiovascular risk factors for stroke among this cohort is highlighted in ***Table 2***. The most prevalent risk factor for stroke was hypercholesterolaemia with 82.1% (n=55/67) of TIA patients, 73.3% (n=11/15) of stroke patients and 53.9% (n=98/182) of non-TIA patients afflicted.

Cardiovascular Risk Factors	TIA Status					
	TIA		Stroke		Non-TIA	
	%	N = 69	%	N = 15	%	N = 182
Hypercholesterolaemia	82.09	55/67	73.33	11/15	53.85	98/112
Hypertension	63.24	43/68	60	9/15	50	91/182
Coronary Artery Disease	19.12	13/68	6.67	1/15	10.44	19/182
Diabetes Mellitus	11.94	8/67	40	6/15	6.04	11/182
Atrial Fibrillation	11.76	8/68	14.29	2/14	4.42	8/182
Coagulopathy	0	0/67	7.14	1/14	0.55	1/182
Aneurysm	0	0/67	0	0/14	2.75	5/182
Cardiomyopathy	4.47	3/67	0	0/14	1.1	2/182
Smoker	8.87	6/69	33.33	5/15	12.64	23/182
Ex-Smoker	42.03	29/69	33.33	5/15	41.21	75/182
Previous TIA (>7 days)	16.18	11/68	6.67	1/15	4.95	9/182
Previous Stroke	5.88	4/68	7.14	1/14	9.89	18/182
Previous MI	4.41	3/68	0	0/15	1.65	3/182
Peripheral Vascular Disease	2.99	2/67	0	0/14	1.65	3/182
Valvular Heart Disease	8.95	6/67	0	0/14	2.75	5/182

Table 2: *Cardiovascular risk factors for stroke among all three cohorts. Patients with missing data were excluded from the analysis.*

Average ABCD2 and ABCD3-I Score by TIA Status

Each individual was awarded a score between 0-7 and 0-13 according to the $ABCD_2$ and $ABCD_3$ –I score respectively. Overall, 92.8% (n=64/69) of TIA patients had a low-risk $ABCD_2$ score of ≤4 and 82.6% (n=57/69) of TIA patients had a low-risk score when re-stratified with the $ABCD_3$-I score.

Medication Changes at the TIA Clinic

After attending the clinic, 33.3% (n=23/69) of TIA patients were commenced on aspirin therapy and 23.2% (n=16/69) were commenced on clopidogrel and 5.8% (n=4/69) were commenced on a direct oral anticoagulant (DOAC). Additionally, 29% (n=20/69) of this cohort were started on either a statin or a fibrate.

Rate of Neuroimaging and Carotid Endarterectomy

We found that 85% of all patients received neuroimaging, 89% of all patients received carotid imaging, 7.5% were discussed for CEA with 5.6% of all patients having a CEA carried out within one month. Despite being referred to the "low-risk" clinic, 8.8% (n=6/68) of TIA patients had a CEA carried out within one month.

Subsequent Events

Kaplan–Meier plots of all-cause morbidity and mortality stratified by diagnosis are shown in ***Figure 2***. Two patients from the TIA group had a subsequent stroke; one at 22-months; and one at 23-months. Additionally, ten patients died; one from MI (5-weeks), three from cancer. The cause of death for the remaining six is unknown.

For the stroke group, one patient died of a subsequent stroke at 35-months, one had a further TIA within 3-months, and one had an MI at 22-months.

For the non-TIA group, three patients had a subsequent stroke; two were fatal (9-months and 15-months) and one non-fatal (14-months), one patient had a TIA at 4-months, and one had an acute MI at 19-months. Additionally, four patients died of cancer.

Overall, for any subsequent event, survival curves were not significantly different when compared using both the log-rank test=2.743 (p=0.254) and the Breslow test=1.213 (p=0.545).

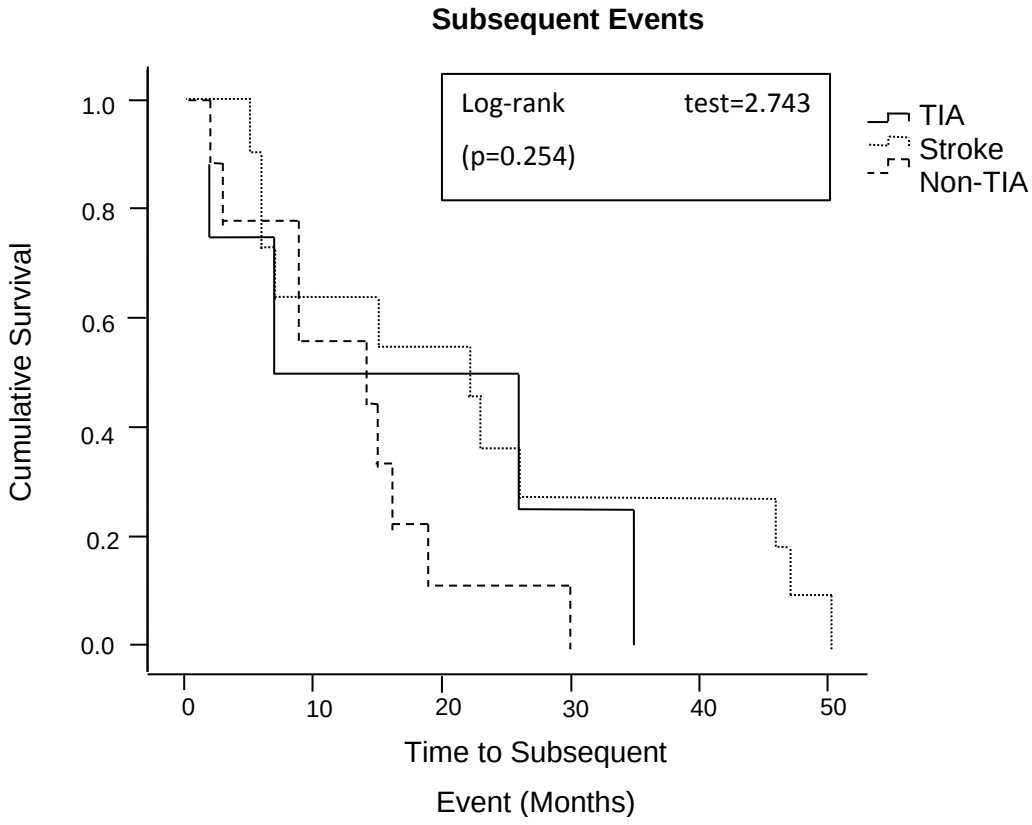

Figure 2: *Kaplan-Meier Survival Curve stratified according to TIA status.*

7-Day /90-Day /1-Year/2-Year Stroke Recurrence

The overall risk for recurrent stroke was 0% at 7 days and 90 days, 0.4% at 1 year and 2.3% at 2 years. Broken down into their respective groups, this equated to a 0% risk of stroke at 7-days/90-days/1-year and 2.9% at 2 years for the TIA group. For the stroke group, there was a 0% at 7-days/90-days/1-year/2-years stroke recurrence rate. Finally, for the non-TIA group, the subsequent stroke risk was 0% at 7-days and 90-days, 0.6% at 1-year and 1.7% at 2-years.

Discussion

There was a low incidence (25.9%) of TIA at presentation to the clinic. This figure is considerably lower than the 32-65% incidence reported in previous studies[11-15]. One possible explanation may be that, previously, studies reported poor public understanding and awareness of the symptoms of both TIA and stroke, and implementation of public health campaigns to promote education was desperately needed[10, 12, 15-17].

Consequently, in 2010, the Irish Heart Foundation launched the mass-media public health campaign "Act F.A.S.T.", an acronym designed to help people remember the major symptoms of stroke (facial weakness, arm weakness, speech impairment, "time" to call the emergency response)[16]. Even after reports revealed success in increasing public awareness in Ireland[16], there remained a lower than expected incidence of TIA at presentation to the clinic, compared to previous studies[11-15]. Several non-TIA events often mimic stroke, therefore, it is likely that misdiagnosis by the referring physician is why so many non-TIA events and so few TIA/stroke events were observed[6, 11-15].

Thus, it remains an unanswered question whether this low incidence of TIA combined with high incidence of non-TIA events is because most patients were referred by non-neurologists who frequently misdiagnose TIA[11, 18] or if it is due to the inherent flaw of the "Act FAST" campaign whereby posterior circulation strokes, visual disturbance, dysphagia *etc.* are potentially missed by patients/referring physicians because these symptoms do not fall into the criteria defined by "Act FAST".

Prevention of acute stroke takes a multipronged approach starting with recognising the risk factors and establishing effective primary and secondary treatment strategies[19]. Several studies have advocated for the use of aspirin, anti-hypertensive agents, statins, anticoagulation for atrial fibrillation, and carotid endarterectomy for $\geq$70% symptomatic carotid stenosis[9, 20-22] in the approach to long-term prevention of stroke after TIA. Early initiation of a combination of these interventions in suitable patients have shown reductions in long-term risk of recurrent stroke by 80-90%[9].

Since 2003, the risk of subsequent stroke after TIA has been persistently decreasing[1-5, 14] primarily due to major advancements in patient care, including, urgent care in specialised units[9, 11-13]; immediate investigations[9, 11, 12]; and rapid initiation of treatment with anti-platelet and other stroke preventing agents.

The low rate of subsequent stroke in this study is likely also explained by the successful implementation of these superior secondary stroke prevention strategies in contemporary TIA clinics compared to the classical evaluation of TIA patients that often resulted in treatment delays because of lack of access to immediate care facilities[9, 12, 14, 23].

Current guidelines for TIA management recommend triage of patients based on stroke risk as defined by the $ABCD_2$ score[22, 24]. $ABCD_2$ scores of ≥4 indicates urgent care within 24 hours of symptom onset[17, 22, 24]. However, scores of ≤4 don't necessarily identify all patients needing immediate treatment[25]. Results from our study support this finding as, despite low scores, almost 10% of TIA patients had ≥70% carotid stenosis, a well-established risk factor for stroke, identified and subsequently treated. Thus, early detection of medical conditions with a high risk of early stroke occurrence likely contributes to the low subsequent stroke occurrences in our study.

This study was limited by design and the its performance in a single centre with a small sample size. Failure to identify all outcomes was a considerable confounding factor in this study, as follow-up was only possible for those patients who re-attended at CUH or Mercy University Hospital (MUH). The postal survey was distributed in an attempt to overcome this predicament and capture the health status of all patients who attended the clinic but response rates from postal surveys are generally low. Despite a moderate response (30.8%), our stroke recurrence rate may still be falsely low.

Thus, our results may represent a true effect of improved awareness in conjunction with urgent evaluation and treatment or perhaps all outcomes were not ascertained due to limitations in our methodology or, a combination of both factors.

In conclusion, this study helps to shed light on the growing evidence that management of patients with TIA is safe in an outpatient clinic but is largely dependent upon swift referral, rapid assessment and timely diagnosis[9, 11-13]. However, the caveat must be inserted that $ABCD_2$/$ABCD_3$-I scores ≤4 does not necessarily exclude all high-risk cases as 8.8% of apparent low-risk TIA clinic patients had a high-risk aetiology (symptomatic carotid stenosis or AF) identified and, successfully, treated.

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Declaration of Conflicts of Interest:
The authors declare that they have no conflicts of interest.

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