The ASPIRE Approach for TIA Risk Stratification

S.B. Coutts, P.N. Sylaja, Y.B. Choi, A. Al-Khathami, C. SivaKumar,
T.J. Jeerakathil, P.S. Sarma, M.D. Hill for the Calgary Stroke Program

ABSTRACT: *Background:* The risk of stroke after transient ischemic attack (TIA) is elevated in the days to weeks after TIA. A variety of prediction rules to predict stroke risk have been suggested. In Alberta a triage algorithm to facilitate urgent access based on risk level was agreed upon for the province. Patients with ABCD2 score ≥4, or motor or speech symptoms lasting greater than five minutes, or with atrial fibrillation were considered high risk (the ASPIRE approach). We assessed the ability of the ASPIRE approach to identify patients at risk for stroke. *Methods:* We retrospectively reviewed charts from 573 consecutive patients diagnosed with TIA in Foothills Hospital emergency room from 2002 through 2005. We recorded clinical and event details and identified the risk of stroke at three months. *Results:* Among 573 patients the 90-day risk of stroke was 4.7% (95% CI 3.0%, 6.4%). 78% of the patients were identified as high risk using this approach. In patients defined as high risk on the ASPIRE approach there was a 6.3% (95% CI 4.2%, 8.9%) risk of stroke. In patients defined as low risk using the ASPIRE approach there were no recurrent strokes (100% negative predictive value). In contrast, two patients with low ABCD2 scores (ABCD2 score < 4) suffered recurrent strokes.*Conclusion:* The ASPIRE approach has a perfect negative predictive value in the population in predicting stroke. However, this high sensitivity comes at a cost of identifying most patients as high risk.

RÉSUMÉ: L'approche ASPIRE pour la stratification du risque d'ICT. *Contexte :* Le risque d'accident vasculaire cérébral (AVC) après une ischémie cérébrale transitoire (ICT) demeure élevé dans les jours ou les semaines qui suivent l'ICT. Plusieurs méthodes de prédiction de l'AVC ont été suggérées. En Alberta, un algorithme de triage a été accepté dans toute la province, pour faciliter un accès hospitalier urgent basé sur le niveau de risque. Les patients dont le score ABCD2 est de 4 ou plus, ou qui ont des symptômes moteurs ou du langage, ou de la fibrillation auriculaire sont considérés comme étant à haut risque (approche ASPIRE). Nous avons évalué la capacité de l'approche ASPIRE à identifier les patients à risque d'AVC. *Méthodes :* Nous avons révisé rétrospectivement les dossiers de 573 patients consécutifs chez qui un diagnostic d'ICT avait été posé à l'urgence du Foothills Hospital de 2002 à la fin de 2005. Nous avons relevé en détail les informations cliniques et les informations concernant l'événement et nous avons identifié le risque d'AVC à trois mois. *Résultats :* Chez les 573 patients, le risque d'AVC était de 4,7% (IC à 95% : 3,0% à 6,4%) au cours des 90 premiers jours ; 78% des patients ont été identifiés comme étant à haut risque selon cette approche. Chez les patients considérés à haut risque selon l'approche ASPIRE, le risque d'AVC était de 6,3% (IC à 95% : 4,2% à 8,9%) et chez ceux considérés à faible risque selon cette approche il n'y a pas eu d'AVC (valeur prédictive négative de 100%). Par contre, deux patients ayant un score ABCD2 bas (score ABCD2 < 4) ont subi un AVC récurrent. *Conclusion :* L'approche ASPIRE a une valeur prédictive négative parfaite pour prédire l'AVC dans cette population. Cependant, le coût de cette sensibilité est d'identifier la plupart des patients comme étant à risque élevé.

The risk of stroke after transient ischemic attack (TIA) is elevated in the days to weeks after TIA.[1,2] To identify patients at highest risk for stroke is advantageous since in many health care settings not all patients can be urgently assessed. Using a combination of risk factors for recurrent stroke, clinical stratification tools, including the California[1], ABCD and ABCD2 scores[3,4] have been proposed to help identify patients at high risk of recurrent events, who could be urgently investigated further. Conversely, the scoring systems could identify patients at low risk, who could be managed less emergently and with lower cost to the system in the outpatient setting.

In Alberta at a consensus conference which took place in 2008, a triage algorithm for TIA risk stratification was agreed upon for the province. This approach was developed by consensus among experts and prior to examination of the data set described in this report. When the usual 'high risk' threshold ABCD2 score[4] of ≥6 is used to select patients for urgent

assessment, the ABCD2 scoring system has 44% sensitivity and 80% specificity to detect recurrent stroke. The low sensitivity from this commonly used threshold has led to criticisms of the score. However, rather than using a threshold score of ≥6, the

From the Calgary Stroke Program (SBC, MDH), Departments of Clinical Neurosciences (SBC, MDH), Radiology (SBC, MDH), Community Health Sciences (MDH), and Medicine (CSK, MDH), University of Calgary; Calgary; Division of Neurology (TJJ), University of Alberta, Edmonton, Alberta, Canada; Stroke Unit (PNS), Ananthapuri Hospitals and Research Institute; Sree Chitra Institute of Medical Sciences and Technology (PSS), Trivandrum, Kerala, India; St. Louis University Hospital (YBC), St. Louis, Missouri, USA; King Faisal Specialist Hospital and Research Centre (AAK), Riyadh, Saudi Arabia.

case can be made that using an ABCD2 score of ≥ 4 to define 'high risk' has excellent sensitivity and reduced but acceptable specificity for a triaging tool. In the pooled database of all ABCD2 patients (n>4800) use of this threshold has a sensitivity of 93% and a specificity of 35% to identify patients who later have recurrent stroke. Similarly, in the three cohorts studied in the original ABCD population[3] the presence of either speech or motor dysfunction demonstrates similar average sensitivity (96%) and specificity (40%).[3] Therefore the use of either an ABCD2 threshold score of ≥ 4 or speech or motor symptoms allows high sensitivity, which is important if considering use of either system for triaging purposes. Thus the consensus meeting identified patients with ABCD2 score ≥4, or motor/speech symptoms greater than five minutes, as high risk. Because atrial fibrillation is an eminently treatable condition with high stroke risk and complex management issues in the setting of cerebrovascular disease, it was additionally included.[5]

This risk stratification strategy is called the Alberta Stroke Prevention in TIAs and mild strokes (ASPIRE) approach and the recommendation was that a stroke specialist should assess these high-risk patients within 24 hours.[6] In this study our aim was to assess the accuracy of the ASPIRE approach to identify patients at high risk for recurrent stroke after TIA.

METHODS

Consecutive patients seen in Foothills Hospital Emergency room with a diagnosis of TIA between January 2002 and December 2005 had their in-patient and/or out-patient charts reviewed. The diagnosis of TIA was made clinically and the final diagnosis determined by the attending physician. The cases were identified using the administrative coding for TIA which we have shown to be good in our hospital.[7] Emergency physicians or a neurologist (or both) saw patients either in the emergency room or in the stroke prevention clinic. In few cases where the diagnosis was not clear these where were considered "possible" TIA. Clinical and event details were recorded for each patient. The total ABCD2 score, ranging from 0 to 7, relies on the summation of points assigned on the basis of: Age≥60, Blood pressure≥140/90 mmHg, Clinical features (motor or speech), Duration of symptoms and Diabetes mellitus and was collected for each patient based on chart review. During this time, the Calgary Stroke Program had begun instructing the Emergency physicians to identify patients with weakness and/or language disturbance as "high-risk" and to refer them to the Stroke Service. This process occurred over time and was becoming the local standard of practice during the course of this review.

Patients were classified as definite or possible TIA and the risk of stroke within 90-days was assessed. Follow-up assessment was from the three-month follow-up in the stroke prevention clinic. Where possible, patients who were not seen in follow up in clinic were contacted by telephone to determine stroke recurrence. Patients with prior stroke were included if the modified Rankin Scale (mRS) was ≤ 2. The ASPIRE approach to risk stratification defined high-risk patients as those with any one of the following components: ABCD2≥4; or motor or speech symptoms lasting longer than five minutes; or patients with atrial fibrillation.

STATISTICS

Sensitivity, specificity positive predictive value and negative predictive value of the ASPIRE approach and its individual components to predict recurrent stroke within 90-days was calculated. The predictive accuracy of the ASPIRE approach and the three individual components of the ASPIRE approach were quantified by the Area Under the Curve (AUC) from Receiver Operating Characteristic (ROC) analysis using binomial regression analysis with a log link. Values of AUC range from 0·5 (chance prediction) to 1·0 (perfect prediction).

RESULTS

Five hundred and seventy-three patients were identified with a diagnosis of TIA who met the inclusion criteria. An emergency room physician alone assessed 100 patients and a neurologist or stroke neurologist either assessed the remaining. Table 1 shows a comparison of definite and possible TIAs. Follow up was unavailable in 82 patients. Overall there were 28 strokes in follow-up so that the 90-day risk of stroke was 4.7% (95% CI 3.0%, 6.4%), 5.1% in patients with definite TIA and 2.1% in possible TIA cases. The difference in risk between definite and possible TIA was numerically doubled but not statistically different RR 2.5 (0.3-17.8, p=0.500) and thus these two categories are considered together for the rest of the results. Similarly there was no difference in stroke recurrence rates according to whether the patient was initially seen and managed by an Emergency physician compared to a neurologist (p=0.609). Using ABCD2≥4 to identify high-risk correctly identified 26/28 cases of recurrent stroke, 2/28 (7%) cases of recurrent stroke would be missed by this method. This results in a sensitivity of 93% and specificity of 30% (PPV 6%, NPV 99%). Using motor and speech symptoms of any duration only missed one case (4%) of recurrent stroke (Se = 96%, Sp = 29%,
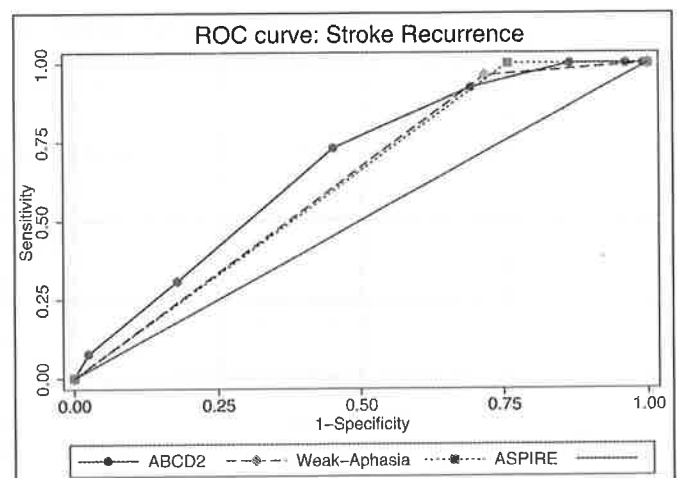

Figure: *ROC curves illustrating the predictive accuracy of the ABCD2 score (ABCD2), weakness and speech greater than five minutes duration (WA5min), weakness and speech of any duration (WA) and the ASPIRE approach. The AUC's for ABCD2 score (ABCD2), weakness and speech of any duration (WA) and the ASPIRE approach were 0.67, 0.66, and 0.62 respectively.*

PPV = 7%, NPV = 99%). Using motor and speech symptoms lasting longer than five minutes, one case was missed. However, specificity was marginally increased (Se = 96%, Sp = 38%, PPV = 7%, NPV = 99%). In contrast, the presence of atrial fibrillation on its own was not substantially predictive, identifying 4/28 strokes (14%).

Seventy-eight percent of patients were identified as high risk using the ASPIRE approach. In patients defined as high risk on the ASPIRE approach there was a 6.3% (95% CI 4.2%, 8.9%) risk of stroke. In patients defined as low risk using the ASPIRE approach there were no recurrent strokes (100% negative predictive value). The addition of atrial fibrillation to the other components of the ASPIRE approach resulted in the identification of one additional stroke over the other clinical components. The Figure shows the ROC curves illustrating the predictive accuracies of these various triage strategies. Note that ABCD2 has more gradations (7 points) than the others, which are dichotomous and this raised the ROC AUC.

Using motor and speech symptoms or using ABCD2≥4 to identify high-risk patients identifies a similar, but not identical population as high risk. We found that 52 patients with ABCD2≥4 did not have weakness or aphasia and 54 patients with weakness or aphasia did not have ABCD2≥4.

DISCUSSION

The ASPIRE approach has a perfect negative predictive value in a tertiary care hospital referral population in predicting stroke. However, this high sensitivity comes at a cost by declaring roughly 80% of patients in this population as high risk. In risk stratifying patients with TIA or minor stroke, we have to assess the objectives of risk stratification to properly use existing tools. The low specificity is of lesser concern if the goal is screening patients with transient neurological symptoms for subsequent urgent evaluation – it is not expected that all or even the majority of high-risk patients will actually have a stroke event.

The ABCD2 score overall has moderate discriminative value, and is not of much help for patient triage, unless a cut point that includes both moderate (score 4-5) and high risk patients (score 6-7) is used. Indeed, a majority of patients who suffer a recurrent stroke will have a mid-ranged ABCD2 score. We found that simply using the presence of motor and speech symptoms (with or without duration) was as accurate at predicting recurrent stroke as the ABCD2 score (see Figure). In general, we see that that the majority of currently available clinical risk stratification tools have similar characteristics; the corollary is that there is still much to improve upon and additional markers including imaging, will be required to best stratify patients.[8]

Patients with definite TIA were much more likely to have risk factors, but these did not predict recurrent stroke risk. In particular, atrial fibrillation was not found to be an important risk factor for predicting early recurrent stroke.[9] Risk is predicted by the clinical presentation and therefore, TIA or minor stroke patients need a detailed assessment by someone with an expertise in transient neurological events to determine risk.

This study has the limitation of being a retrospective chart review with all the potential biases that this entails. The major limitation is that we were unable to obtain follow-up information in 14% of patients. Thus it is possible that the recurrent stroke risk is higher than described in this study since we know empirically that patients who do not show up to clinic are most likely the ones who have suffered recurrent events. Another limitation is that it is possible that simply identifying patients at high risk for stroke and treating them would not reduce their risk of recurrent stroke, but given the results of the FASTER[10], SOS-

Table: Comparison of vascular risk factors and symptoms between definite and possible TIA patients

	Definite TIA (n=525) % (n)	Possible TIA (n=48) % (n)	p
Age	71 (sd 13	64 (sd 17)	0.0005
Female Sex	49.5 (260)	62.5 (30)	0.058
Hypertension	69.7 (366)	56.3 (27)	0.073
Diabetes	16.6 (87)	8.3 (4)	0.153
Smoker (current)	12.6 (66)	18.4 (5)	0.821
Coronary artery dx	24.8 (130)	6.3 (3)	0.002
Valvular heart dx	2.7 (14)	4.2 (2)	0.636
Hyperlipidemia	33.0 (173)	25.0 (12)	0.333
Congestive heart failure	2.7 (14)	0 (0)	0.620
Atrial fibrillation	10.3 (54)	4.2 (2)	0.211
Prior stroke	12.6 (66)	10.4 (5)	0.821
Prior TIA	16.6 (87)	10.4 (5)	0.311
ICA disease	7.2 (38)	0 (0)	0.063
Past DVT	1.1 (6)	0 (0)	1.000
Antiplatelet tx	48.4 (254)	41.7 (20)	0.451
Baseline glucose (mM)	6.4 (sd 2.1)	6.0 (1.7)	0.204
$ABCD^2$ score Median (range)	4 (0-7)	3 (0-6)	<0.0001
Weakness and/or speech disturbance	74.9 (393)	39.6 (19)	<0.0001

TIA[11] and EXPRESS[12] studies, this seems unlikely. The ASPIRE approach also uses a second component for triage – time. Patients are only classified as high risk if they present with 48 hours of symptom onset.[6] In this dataset we did not collect this information and so are unable to assess the accuracy of this component of the ASPIRE approach.

CONCLUSIONS

The ASPIRE approach has a perfect negative predictive value in a tertiary care referral centre population in predicting stroke. If such a tool as the ASPIRE approach is used to further define who requires urgent cerebrovascular imaging or admission, then high sensitivity is critical. Whether the negative and positive predictive value of the ASPIRE approach will change when the system is applied to a more general population of TIA patients province-wide remains to be seen and this study is now underway. As a result of our philosophical decision to mitigate all stroke after TIA, a triage tool that has perfect or near perfect sensitivity, even at the expense of low specificity is a necessity.

ACKNOWLEDGEMENTS

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