# Adherence to Practice Guidelines for Transient Ischemic Attacks in an Emergency Department

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**ABSTRACT:** *Objective:* To evaluate the investigation and treatment of patients with a diagnosis of transient ischemic attacks (TIA) in the emergency department (ED) a tertiary care teaching hospital with a neuroscience referral program. *Methods:* A chart review was conducted in the hospital. Consecutive ED charts with a diagnosis of TIA were included; each was reviewed by independent coders using a standardized data form. *Results:* Two hundred and ninety-three TIAcharts were reviewed; the gender ratio was 1:1 with a mean age of 66 years. Most patients (75%; 95% CI: 70, 80) were evaluated by ED physicians; the remaining patients were seen directly by referral services. The median time from symptom onset to ED arrival was 2.9 hours and the duration of symptoms was 4.6 hours. Most patients received CT scans (81%; 95% CI: 73, 85), complete blood counts (74%; 95% CI: 68, 79), and electrocardiograms (75%; 95% CI: 70, 80) in the ED. In 16% (95% CI: 13, 22) a carotid doppler was performed and in 26% (95% CI: 21, 31) an outpatient doppler was booked. Among those who were discharged (75%; 95% CI: 70, 80), antithrombotic medications were not prescribed to 28% (95% CI: 22, 34). Conclusion: Practice variation exists with respect to the investigation and treatment of TIAs in this tertiary-care teaching hospital. Carotid doppler investigation and use of anti-platelet therapy for patients with TIAare suboptimal. Clinical practice guidelines and rapid assessment TIAclinics may change these results.

**RÉSUMÉ: Observance des lignes directrices sur la prise en charge à l'urgence des accès ischémiques transitoires cérébraux.** *Objectif:* Évaluer l'investigation et le traitement à l'urgence des patients ayant un diagnostic d'accès ischémique cérébral transitoire (ICT). *Méthodes:* Une révision des dossiers d'un hôpital de soins tertiaires ayant un programme de référence en neurosciences a été effectuée. Chaque dossier de l'urgence comportant un diagnostic d'ICT a été révisé par des examinateurs indépendants qui attribuaient un code selon un formulaire standardisé. *Résultats:* Deux cent quatre-vingt- treize dossiers de patients ayant reçu un diagnostic d'ICT ont été révisés; la proportion d'homme et de femmes était de 1:1 et l'âge moyen était de 66 ans. La plupart des patients (75%; IC 95%: 70 à 80) ont été évalués par des urgentologues; les autres patients ont été vus directement par les services de référence. L'intervalle médian du début des symptômes jusqu'à l'arrivée à l'urgence était de 2,9 heures et la durée des symptômes était de 4,6 heures. La plupart des patients ont subi une tomodensitométrie cérébrale (81%; IC 95%: 73 à 83), une formule sanguine complète (74%; IC 95%: 68 à 79), et un électrocardiogramme (75%; IC 95%: 70 à 80) à l'urgence. Chez 16% (IC 95%: 13 à 22), un Doppler carotidien a été fait et chez 26% (IC 95%: 21 à 31) un Doppler a été demandé en externe. Parmi ceux qui ont reçu leur congé de l'urgence (75%; IC 95%: 70 à 80), aucune médication antithrombotique n'a été prescrite chez 28% (IC 95%: 22 à 34). *Conclusion:* Il existe des variations quant à l'investigation et au traitement de l'ICT dans cet hôpital universitaire de soins tertiaire. L'investigation par Doppler carotidien et l'utilisation d'agents antiplaquettaires chez les patients présentant une ICT est sous-optimale. Des lignes directrices et des cliniques d'évaluation rapide de l'ICTpourraient modifier ces résultats.

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Stroke is the most common life-threatening neurological disorder and is the third leading cause of death in North America. The estimated economic consequence of stroke in the United States alone will reach approximately \$45.4 billion in 2001.<sup>1</sup> More importantly, stroke survivors experience a significant reduction in vocational function and socialization outside of the home. They are also more likely to experience a decrease in their interests and hobbies, develop dependence in mobility, and reside outside their family home.<sup>2</sup> Finally, 40% of the stroke patients and their family suffer from depression one year after the onset of the illness.<sup>3</sup> In spite of the advances in stroke treatments, rehabilitation, and family support programs, only

51% of the stroke victims return to work one year after their stroke.<sup>4</sup>

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A transient ischemic attack (TIA) is an acute onset of brief focal neurological impairment or deficit due to a temporary disruption of blood supply to a region of the brain. This diagnosis is traditionally defined as neurologic symptom that resolves within 24 hours; however, the majority of deficits in these patients resolve within one hour.<sup>5</sup> Transient ischemic attack is a significant warning symptom for impending ischemic stroke. Patients experiencing their first episode of TIAhave 4 – 8% risk of stroke within the first month; this risk increases to 24 - 29%five years after the onset of symptoms.<sup>6</sup> In a recently published study, 10.5% of all patients suffered a stroke within 90 days after being diagnosed with a TIAin the emergency department (ED).<sup>7</sup> Among these stroke sufferers, one-fifth of them died and 64% suffered from disability. Consequently, the accurate diagnosis, identification of risk factors and treatment of TIAis an important issue in the delivery of emergency patient care.

Patients who experience symptoms compatible with TIA often present to the ED for initial evaluation. The management goals for patients presenting with TIAinclude rapid evaluation of possible risk factors and etiology and reduction of the risk of stroke either medically or surgically. The American Heart and Stroke foundation suggests that investigation should be individualized according to the possible etiology.<sup>6,8</sup> Other expert opinion suggests that computed tomography (CT) of the brain and a noninvasive vascular imaging study (i.e. carotid doppler) are important primary TIA investigations, especially in patients with hemispheric TIA.<sup>9</sup> At the present time, we have very little information regarding how patients presenting with TIA to the ED are being assessed and managed. The purpose of this study was to evaluate the investigation and treatment practices of physicians seeing patients with a discharge diagnosis of TIA in the ED.

## MATERIALS AND METHODS

**Design:** This was a retrospective chart review of consecutive patients seen in the University of Alberta Hospital (UAH) ED with a discharge diagnosis of TIA (ICD-9 code: 435.x).

**Setting:** The study was conducted in Edmonton, a northern Alberta city with a population of 820,000 (1996 Census, Statistics Canada). The UAH is the regional trauma and referral centre for burns, pediatrics, neurology, and other medical/surgical specialties within northern Alberta and Northwest Territories.

**Patients:** Emergency department charts from fiscal year 1997 with a primary ICD diagnostic code of TIA (435.x) were reviewed. The coding was based on the emergency physicians' written final diagnosis; no attempts were made in this study to validate the individual diagnosis of TIA. Emergency physicians (EP) and other specialty physicians were unaware the study was being conducted at the time of patient encounter. Patients who were aged 18 years, and presenting with focal neurological symptoms were eligible in the study. Patients with persistent symptoms (cerebrovascular accident; stroke), and isolated nonspecific symptoms (such as dizziness and lightheadedness), were excluded.

**Data Collection:** A standardized audit form was used to collect information regarding visits for TIA. Data were obtained from

patient records by one individual (EC or PK). Demographic (e.g., age, gender), hospital information (e.g., date and time of initial visit, location), mode of referral and transport, medical history (e.g., previous TIAor stroke, co-morbidities predisposing to development of TIA, etc), TIA description (e.g., location, duration, signs and symptoms), investigations (e.g., blood work, electrocardiogram, CT scan, carotid dopplers, angiograms), treatments (e.g., acetylsalicylic acid (ASA), warfarin, other agents) and disposition information were collected. The exact duration of symptoms was recorded when available; however, when the onset of symptom was documented as "morning", "afternoon" or "suppertime", estimations were made (time of onset as 08h00, 20h00 and 18h00, respectively). Neither standardized discharged instructions nor planning were available for patients during this study period.

**Data Validity:** A convenience sample of 30 consecutive charts was assessed independently by two researchers (EC, PK) to determine data validity. The agreement on major dichotomous outcomes was measured by simple agreement (SA) and kappa statistics (k); intraclass correlation coefficients (ICC) were used for continuous data.<sup>10</sup>

**Data Analysis and Statistics:** Data for all cases were analyzed using the SPSS-PC, Version 10.0, statistical software program (SPSS, Inc.; Chicago, IL). Categorical values are reported as counts and percentages (%), and continuous variables are reported as means and medians with their respective standard deviations or inter-quartile ranges (IQR).

**Subgroup Analyses:** In addition to analyses of descriptive data on demographic, history and symptom of presentation, investigations, treatment and disposition, two different subgroup analyses were conducted. These included the practice variation between patients that were initially seen by EP and neurologists, and the difference between patients with and without prior TIA or stroke.

Ethics: This study was approved by the combined Research Ethics Review Committee of the University of Alberta. No informed consent was obtained, records remained stored in a secure area, and only aggregate data are reported. Follow-up contacts were not possible in this study.

### RESULTS

**Sample:** Two hundred and ninety-three charts were identified as a TIA and included in the study; all charts were recovered and reviewed. Of the charts reviewed, excellent agreement between the data abstractors was obtained for demographic and event details. Other more important outcomes such as age (ICC = 1.0), previous TIA (SA = 90%), stroke scale (ICC = 0.34), investigations (k = 0.67), and disposition (kw = 0.55) indicate mostly good to excellent agreement.

**Patient Demographics:** Gender distribution was equal (50%). The average age of the patients was 66 years; 175 (60%) patients had no previous TIAor stroke history. One hundred and eighteen (40%) patients reported having at least one episode of TIA or stroke in the past. Apart from being older (69 vs 65 years; p =

| Table 1: Patient demographics and characteristics |  |
|---|--|
|---|--|

| Factors                                  | n      | %             |
|--|--------|---------------|
| Male                                     | 147    | (50%)         |
| Age (mean years)                         | 66     |               |
| Age Range (years)                        | 25-100 |               |
| Marital Status                           |        |               |
| Married                                  | 191    | (65%)         |
| Mode of Transportation                   |        |               |
| Ambulance                                | 114    | (39%)         |
| Own vehicle                              | 159    | (54%)         |
| Others                                   | 4      | (1%)          |
| Past Medical History                     |        |               |
| Stoke or TIA                             | 118    | (40%)         |
| Hypertension                             | 167    | (43%)         |
| Valvular heart disease                   | 10     | (3%)          |
| Atrial fibrillation                      | 22     | (8%)          |
| Coronary artery disease                  | 53     | (18%)         |
| Hypercholesteroemia                      | 55     | (19%)         |
| Diabetes mellitus                        | 37     | (13%)         |
| Hormone replacement                      | 25     | (9%)          |
| No antiplatelet or anticoagulant therapy | 177    | (60%)         |
| Assessment and Treatment                 |        |               |
| Directly seen by EP                      | 213    | (73%)         |
| Time to be assessed by EP                | 46     |               |
| after triage (minutes)                   |        | (IQR: 26, 80) |
| Discharged from the ED                   | 218    | (75%)         |
| Oxford Stroke Classification             |        |               |
| Upper extremity weakness                 | 144    | (49%)         |
| Lower extremity weakness                 | 95     | (32%)         |
| Facial weakness                          | 84     | (29%)         |
| Dysphasia                                | 68     | (23%)         |
| Brainstem sign                           | 46     | (16%)         |
| Visual-spatial disorder                  | 23     | (8%)          |
| Homonymous hemianopsia                   | 13     | (4%)          |

0.007), there were no demographic or historical differences between patients with and without a history of a previous event. Among other known cerebrovascular risk factors, 167 (43%) had hypertension, 55 (19%) had hypercholesterolemia, 53 (18%) had coronary artery disease, 37 (13%) had diabetes mellitus, 25 (9%) were on hormone replacement therapy, 22 (8%) had atrial fibrillation, and 10 (3%) had valvular heart disease. Ninety-nine patients (34%) reported being lifetime nonsmokers; however, history of smoking was not documented in many (26%) charts. At presentation to the ED, the majority of patients (177 [60%]) were not receiving any form of antiplatelet or anticoagulation therapy (Table 1).

**ED** Assessment and Treatment: The majority of patients arrived to the ED using private transportation (159 [54%]) and 114 (39%) arrived by ambulance. Most patients (213 [75%]) were initially evaluated by EP. The average time lapse from the time of symptom onset to ED presentation was available for 193

**Table 2:** Investigations performed and ordered by physicians on

 293 patients presenting with TIA to an emergency department

 divided into Emergency Medicine and Neurology specialties.

| Er                  | nergency Physician<br>(n = 213) | Neurologist<br>(n =72) | Totals<br>(n = 293) |
|---------------------|---------------------------------|------------------------|---------------------|
| Carotid Doppler     | 38%                             | 58%                    | 42%                 |
| CT Scan             | 79%                             | 88%                    | 81%                 |
| Echocardiogram      | 6%                              | 7%                     | 6%                  |
| CXR                 | 22%                             | 14%                    | 20%                 |
| Electrolytes        | 73%                             | 67%                    | 72%                 |
| Complete Blood Cour | nt 75%                          | 69%                    | 74%                 |
| Cardiac Enzymes     | 23%                             | 12%                    | 21%                 |
| Coagulation Profile | 34%                             | 35%                    | 33%                 |
| ECG                 | 76%                             | 72%                    | 75%                 |
| No Discharge Meds   | 26%                             | 33%                    | 28%                 |

Note: CTscan = computed tomography scan; CXR = chest radiography; ECG = electrocardiograph; numbers do not total 293 due to missing information.

(66%) cases; patients waited a median of 2.9 hours (IQR: 1.1, 6.8) following symptom onset before presenting to the ED. The median time from triage to physician assessment was 46 minutes (IQR: 26, 80). Seventy-two (25%) patients were seen directly by other specialty services, of which the majority (n=67; 93%) were neurologists.

**TIA Description:** When patient's clinical symptoms were categorized into the Oxford Stroke Classification, <sup>11</sup>, 144 (49%) had upper extremity weakness, 95 (32%) had lower extremity weakness, 84 (29%) had facial weakness, 68 (23%) had dysphasia, 46 (16%) had brainstem sign(s), 23 (8%) had visual-spatial symptom (e.g., diplopia), and 13 (4%) experienced homonymous hemianopsia. Carotid bruits were not detected in 152 patients; however, this clinical finding was not documented in 42% of the charts.

**ED Investigations:** The majority of the patients with symptoms of TIAhad a CTscan of the head (231 [81%]), electrocardiogram (221 [75%]), complete blood count (216 [74%]), electrolytes (210 [72%]), coagulation profile (98 [33%]), cardiac enzymes (61 [21%]), and/or chest radiography (59 [20%]). Carotid dopplers were performed in the ED or deferred to an outpatient investigation in only 47 (16%) and 77 (26%) patients, respectively (Table 2). Only two (1%) patients received echocardiogram in the ED; however, 16 (6%) echocardiograms were ordered as an outpatient procedure. Emergency department investigations were similar for patients with and without a previous history of TIA or stroke.

**Outcomes:** Most patients (218 [75%]) were discharged from the ED; those who were admitted remained hospitalized for a median of one day (IQR: 1, 2). Acetylsalicylic acid was the most common discharge medication (Table 3); 28% of these patients

| Table 3: Discharge medications ordered by physician  | s on 293 |
|--|----------|
| patients presenting with TIAto an emergency departme | nt.      |

| 0   |
|-----|
| 59% |
| 4%  |
| 6%  |
| <1% |
| 2%  |
| <1% |
| 28% |
|     |

Note: ASA= acetylsalicylic acid.

were not discharged with a documented treatment employing either antiplatelet or anticoagulation agents.

**Specialty Comparisons:** When we compared the variation in investigations and treatments between the patients who were seen by an EP or neurologist directly, neurologists and EPs ordered CT scans (88% vs. 79%; p = 0.11) and ECGs (67% vs. 73%; p = 0.08) in similar percentages of patients (Table 2). However, neurologists ordered more carotid doppler studies (58% vs. 38%; p = 0.0026) while EPs ordered more cardiac enzymes (23% vs. 12%; p = 0.05). The admission rate of patients who were directly seen by neurologists was higher than those who were seen initially by an EP (p = 0.01). Among those who were discharged from the ED, 26% and 33% of the patients suspected of having a TIAwere not prescribed either antiplatelet or anticoagulation agents by EPs or neurologist, respectively (p = 0.18).

# DISCUSSION

This single-centre study identifies a consecutive sample of patients diagnosed with TIA after presenting to a major neurological centre in Canada over a one-year period. The results suggest that TIA patients receive a varied approach to investigation by both EP and their neurology colleagues. Moreover, the outpatient treatment of these patients varies with respect to the use of antiplatelet and anticoagulant agents. Since recent evidence suggests that patients with this diagnosis are at a higher risk of stroke than previously recognized, these results suggest education of staff and adherence to practice guidelines are urgently required.

In a convenience survey of neurologists, Johnston<sup>12</sup> demonstrated that there was a significant variation in management of TIA particularly in patients presenting with anterior TIA with clinical signs of carotid stenosis. Comprehensive computerized searching (Medline [1966 – 2001] and EMBASE [1988 – 2000]) using the keywords "transient ischemic attack" and "physician's practice pattern" did not produce any other studies that evaluated the practice variation of TIA in an ED setting. Consequently, this study represents new information about the approach to this diagnosis in an important treatment location.

There is very little evidence to suggest that urgent evaluation and treatment of TIA prevents a stroke in the acute phase of the illness and this may partially explain the results found in this cohort. Until recently, most EP felt initiating treatment for TIA should be a role assumed by the patient's primary care provider. However, a recent study<sup>7</sup> demonstrated a trend in reducing the risk of stroke within the first 90 days after TIA symptoms when antiplatelets or anticoagulatants were started in the ED. Consequently, the role of the EP in TIA treatment is changing, particularly when several other studies demonstrate the potential seriousness of this diagnosis.13 Moreover, there are a number of modifiable conditions that can be treated to lower the risk of future stroke.<sup>14</sup> In this study many patients presented with at least one cerebrovascular risk factor and most had several which were easily identifiable. Attention to screening for and treating these conditions is important in reducing stroke morbidity and mortality.

Both medical and surgical treatments are now available for patients with documented TIAs; both treatment modalities have been shown to reduce the risk of stroke for patients who experience a TIA. Antiplatelet agents such as aspirin has been shown to reduce the risk of stroke, myocardial infarction or vascular death by 16% in patients who had prior stroke or TIA.15 Investigators demonstrated that ticlopidine provides a further 21% relative risk reduction for stroke when compared to aspirin.<sup>16</sup> Clopidogrel, a newer antiplatelet agent, has also been shown to reduce the risk of achieving a composite end-point (e.g. stroke, myocardial infarction or vascular death) by 7.3% when compared to aspirin.<sup>17</sup> The combination treatment of ASA and dipyridamole has also been shown to reduce the recurrence of TIAs and decrease the proportion of patients who progress to stroke.<sup>7,18</sup> Finally, anticoagulants, such as warfarin, have been shown to reduce the risk of stroke by 68% in patients who have nonrheumatic atrial fibrillation.<sup>19</sup> Thus, it is surprising that chart documentation of this important treatment approach was missing in so many patients in this series.

From the surgical perspective, several possible options exist for TIA patients. In the North American Symptomatic Carotid Endarterectomy Trial study, carotid endarterectomy was shown to reduce the risk of stroke for patients with carotid artery stenosis greater than 70%; this surgical procedure also reduced the risk of stroke, albeit by a smaller percentage, for patients with symptomatic carotid stenosis between 50% - 69%.<sup>20,21</sup> Consequently, decisions in the ED by both neurologists and EPs may have important implications for patients in the sub-acute and long-term periods following their TIAevent. Once again, the failure of physicians to obtain carotid imaging, while in the ED or immediately thereafter, to determine if stenosis was an etiological factor in the TIAis alarming.

Since this is a retrospective chart review, the main limitations of this study are missing data bias and charting accuracy. We assumed that the investigation had not been performed or the treatment had not been initiated if chart documentation was missing. This may underestimate the rate of investigation performed in patients diagnosed with TIA in the ED. However, given the gravity of the diagnosis, failure to document both carotid imaging and antiplatelet therapy is concerning.

Another limitation of this study is the lack of follow-up information for TIA patients. For example, we cannot provide additional and comprehensive data on subsequent TIA or stroke events following the ED visit, patient adherence with medications and the subsequent referral and work-up of patients. Due to the retrospective nature of this study, such outcomes were unavailable. Further research in follow-up care is required to substantiate the alarming findings reported in a recent study.<sup>7</sup>

Finally, the generalizability of this study needs to be discussed. The data in this study were collected from a single tertiary care center. Given a population of 820,000, the annual incident of TIA in Edmonton would be expected to be greater than 400 cases. Clearly, patients with TIApresented to one of the other six EDs in the Capital Health Region. Consequently, these results may only reflect the practice pattern of the local area. Additional research involving other referral and nonreferral centres is required for comparison; however, it is unlikely that practice would be more aggressive in busier, nonacademic ED settings.

We were particularly surprised to discover that carotid doppler studies were not ordered by physicians, especially given the potential benefits of carotid endarterectomy in the setting of critical stenosis. Moreover, it is alarming that patients with suspected TIAwere not prescribed antiplatelet or anticoagulation therapy. Interestingly, the proportion of patients who were not prescribed any stroke prophylactic treatment was the same irrespective of whether the patient was seen by an EP or neurologist. A possible explanation for this is poor documentation. However, it is also possible that the physician was not strongly convinced that the symptoms were truly TIA despite the diagnosis written on the chart. Alternatively, the physician may have felt the responsibility for this preventive treatment lies with the primary care provider.

Since this study was conducted, a new Stroke Prevention Clinic has been established at this institution. This clinic is staffed by neurologists and stroke fellows, who have strong interests in the prevention and treatment of cerebrovascular diseases. They have rapid access to carotid doppler, transcranial doppler, and the latest preventative treatments. Since not all TIA patients are referred to this clinic after discharge from the ED, particularly when their initial visits was not at the UAH, it may be possible to study whether this specialized clinic provides improved assessment and management of patients diagnosed with TIA in the ED.

# CONCLUSION

Transient ischemic attacks commonly present to this emergency department. This study described some of the risk factors and predisposing conditions of TIA in a large urban setting and compared its findings to past studies. Although most patients completely resolve their symptoms prior to ED discharge, investigative and treatment concordance with current recommendations among ED physicians and consultants was low. These results indicate that there may be a role for the development of clinical practice guidelines. In addition, these data suggest that programs such as rapid stroke clinic referral, improved access to diagnostic imaging and improved prevention programs need to be linked to such patients in order to provide better care for patients with TIA. Further research is required to evaluate all of these options.

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#### Statistical review

Statistical review was conducted by Dr. Kelly, PhD who was associated with the Division of Emergency Medicine, Faculty of Medicine and Dentistry, University of Alberta at the time of the research.

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#### **Competing interests**

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#### References

- 1. Economic cost of cardiovascular disease. American Heart Association. 2001.
- Gresham GE, Phillips TF, Wolf PA. Epidemiological profile of long term stroke disability: the Framingham Study. Arch Phys Med Rehab 1979;60:478.
- Kotila M, Numminen H, Waltirno O, Kaste M. Depression after stroke - results of the FINNSTROKE study. Stroke 1998;29:368-372.
- Wozniak MA, Kittner SJ, Price TR, et al. Stroke location is not associated with return to work after first ischemic stroke. Stroke 1999;30:2568-2573.
- Levy DE. How transient are transient ischemic attacks? Neurology 1988;38:674-677.
- Feinberg WM, Albers GW, Barnett HJM, et al. Guidelines for the management of transient ischemic attacks. Circulation 1994;89:2950-2965.
- Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. JAMA 2000;284:2901-2906.
- Albers GW, Hart RG, Lutsep HL, Newel DW, Sacco RL. Supplement to the guidelines for management of transient ischemic attack. Stroke 1999;30:2502-2511.
- Culebras A, Kase CS, Masdeu JC, et al. Practice guidelines for the use of imaging in transient ischemic attacks and acute stroke. Stroke 1997;28:1480-1497.
- Kramer MS, Feinstein AR. Clinical biostatistics. LIV. The biostatistics of concordance. Clin Pharmacol Ther 1981;29:111-123.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet 1991;337:1521.
- Johnston SC, Smith WS. Practice variability in management of transient ischemic attacks. Eur Neurol 1999;42:105-108.
- Dennis M, Bamford J, Sandercock P, Warlow C. Prognosis of transient ischemic attacks in the Oxfordshire community stroke project. Stroke 1990;21:848-853.
- Goldstein LB, Adams R, Becker K, et al. Primary prevention of ischemic stroke - statement for healthcare professionals from the stroke council of the American Heart Association. Circulation 2001;103:163-182.
- Algra A, Gijn J. Aspirin at any dose above 30 mg offers only moderate protection after cerebral ischemia. J Neurol Neurosurg Psychiatr 1996;60:197-199.
- 16. Hass WK, Easton JD, Adams HP Jr, et al. A randomized trial

comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. N Engl J Med 1989;321:501-507.

- 17. CAPRIE Sterring Committee. A randomized, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events. Lancet 1996;348:1329-1339.
- Diener HC, Cunha L, Forbes C, et al. European stroke prevention study 2: dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurosci 1996;143:1-13.
- 19. Hart RG, Benavente O, McBride R, Pearce LA. Antithrombotic

therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med 1999;131:492-501.

- North American Symptomatic Carotid Endarterectory Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. N Engl J Med 1991;325:445-458.
- Barnett HJM, Meldrum HE, Eliasziw M, for the North American Symptomatic Carotid Endarterectomy Trial (NASCET) Collaborators. The appropriate use of carotid endarterectomy. Can Med Assoc J 2002;166:1169-1175.