CLINICAL DISCRIMINATORS BETWEEN ACUTE BRAIN HEMORRHAGE AND INFARCTION

A practical score for early patient identification

Ayrton R. Massaro[1], Ralph L. Sacco[2], Milberto Scaff[1], J.P. Mohr[3]

ABSTRACT - New treatments for acute stroke require a rapid triage system, which minimizes treatment delays and maximizes selection of eligible patients. Our aim was to create a score for assessing the probability of brain hemorrhage among patients with acute stroke based upon clinical information. Of 1805 patients in the Stroke Data Bank, 1273 had infarction (INF) and 237 had parenchymatous hemorrhage (HEM) verified by CT. INF and HEM discriminators were determined by logistic regression and used to create a score. ROC curve was used to choose the cut-point for predicting HEM (score ≤ 2), with sensitivity of 76% and specificity of 83%. External validation was done using the NOMASS cohort. Although the use of a practical score by emergency personnel cannot replace the gold-standard brain image differentiation of HEM from INF for thrombolytic therapy, this score can help to select patients for stroke trials and pre-hospital treatments, alert CT scan technicians, and warn stroke teams of incoming patients to reduce treatment delays.

KEY WORDS: cerebrovascular disorders, cerebral hemorrhage, cerebral ischemia, stroke, diagnosis.

Características clínicas diferenciais entre hemorragia e infarto cerebral: uma escala prática para identificação precoce do paciente

RESUMO - Novas perspectivas no tratamento do acidente vascular cerebral (AVC) requerem um método de triagem rápido para seleção dos pacientes. Nosso objetivo foi criar uma escala com informações clínicas simples para diferenciar hematoma intra-parenquimatoso (HEM) entre os pacientes com AVC. Estudamos 1.273 pacientes com AVC isquêmico (INF) e 237 com HEM do *Stroke Data Bank*. Variáveis independentes para o diagnóstico de INF e HEM foram determinadas pela análise de regressão logística e utilizadas para criar uma escala. Através da curva ROC foi escolhido o nível de corte para discriminar HEM (≤ 2), com sensibilidade de 76%, especificidade de 83%. Foi realizada validação externa utilizando os pacientes do estudo NOMASS. Embora o uso de uma escala de fácil aplicação pelas equipes de emergência não possa substituir os métodos de imagem na diferenciação entre INF e HEM para a indicação de trombolítico, a escala proposta pode ser útil para selecionar pacientes para estudos clínicos e tratamento pré-hospitalar, alertar técnicos de tomografia e as equipes médicas sobre a chegada de pacientes, contribuindo para reduzir atrasos cruciais no tratamento.

PALAVRAS-CHAVE: acidente vascular cerebral, hemorragia, isquemia.

New treatments for acute stroke require a rapid triage system, which minimizes treatment delays and maximizes selection of eligible patients[1]. Despite emergency physicians ability to accurately identify patients with acute stroke[2,3], the differentiation between acute brain hemorrhage (HEM) and infarct (INF) is more difficult and can only be confirmed by brain imaging. Time taken to obtain a CT may delay stroke treatment[4,5] ,therefore a pre-hospital screening stroke score which can help to differentiate INF and HEM patients may become a rational approach for acute stroke management.

Although there are some stroke score systems available[2,6-8] ,the Guy's Hospital Stroke (GHS) score[2] and the Siriraj Hospital Stroke (SHS) score[7] are the only two that have been largely validated[9-11], and only the SHS can promptly be used in the emergency room setting[7].

[1]Department of Neurology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [2]School of Public Health (Epidemiology) and the Sergievsky Center, Columbia University, New York, USA; [3]Department of Neurology, Neurological Institute of Columbia-Presbyterian Medical Center, New York, USA. This work was partially supported by grants from the National Institute of Neurological Disorders and Stroke R01 NS 27517 and R01 NS 29993.

Received 8 August 2001, received in final form 17 October 2001. Accepted 25 October 2001.

Ayrton Roberto Massaro, MD - Department of Neurology, Federal University of São Paulo - Rua Botucatu 740 - 04023-900 São Paulo SP - Brazil - E-mail: massaro@neuro.epm.br

Our aim was to create a score for assessing the probability of HEM among patients with acute stroke based upon simple, clinical information available prior to hospitalization which could be used by paramedics and emergency personnel.

METHOD

The Stroke Data Bank (SDB) was a prospective observational study, which collected acute care, clinical, and laboratory data on 1805 patients with stroke. The SDB entry criteria included patients with a sudden, nonconvulsive, focal neurological deficit persisting beyond 24 hours. Half the patients were admitted within 12 hours after stroke onset. The SDB excluded those patients in whom the stroke was coexistent with other severe illness such as tumor, hematological disease or head injury.

The collaborative study involved the Biometry and Field Studies Branch of the National Institute of Neurological Disorders and Stroke as the statistical coordinating center, and four academic hospital centers: Boston University, Boston; Michael Reese Hospital and Medical Center, Chicago; University of Maryland, Baltimore; and the Neurological Institute of Columbia-Presbyterian Medical Center, New York. A full description of the SDB can be found elsewhere[12].

Strokes were classified by causal mechanism into the following categories: (1) brain infarction (INF) which included infarction due to large artery atherosclerosis, lacune, cardioembolism, infarction with tandem arterial pathology and infarction of undetermined cause[13]; (2) parenchymatous hemorrhage (HEM); (3) subarachnoid hemorrhage; and (4) stroke from other causes. Each patient with acute stroke was examined by one of the SDB investigators and CT scan was used to confirm the diagnosis. The time from stroke onset to first CT scan ranged from 10 to 27 hours after onset[12]. For this analysis, all patients enrolled in the SDB with HEM and INF were eligible, while subarachnoid hemorrhage, and those patients classified as stroke from other causes, such as inflammatory arteriopathies and sickle cells disease, were excluded. Subarachnoid hemorrhage has a distinct clinical presentation. Whenever a patient arrives at the emergency room with headache, vomiting, decreased consciousness and nuchal rigidity without a focal neurological deficit suggesting subarchnoid hemorrhage, CT will be necessary. Even if CT is unremarkable, further investigation is usually required to rule out this condition.

The variables that were analyzed and compared in the HEM and INF groups included: (1) *demographics*: age, race, gender; (2) *historical stroke risk factors*: medical history of hypertension defined by prior hypertension in the physician notes or if the old chart revealed a systolic blood pressure ≥ 160mmHg and diastolic ≥ 95mmHg or if the patient was taking anti-hypertensive treatment prior to the admission; diabetes classified as treated with diet alone, oral agents, or insulin; prior symptomatic stroke or transient ischemic attack (TIA); cardiovascular disease consisted of the following: myocardial infarction, valvular heart disease, atrial fibrillation, other arrhythmia, angina, congestive failure, and claudication; alcohol intake within 24 hours of onset; (3) *clinical features at onset:* neurological symptoms or signs which presented upon awakening; severe headache with no features suggestive of migraine; seizures; vomiting; focal neurological deficit; coma within minutes of the onset of stroke and attributed to the effect of the stroke itself rather than metabolic causes; (4) *initial neurological examination:* level of consciousness (alert, lethargic, stupor, coma); motor and sensory deficits; extraocular movements and visual field abnormalities; ataxia; hemineglect; aphasia and presence of cervical bruit; (5) *clinical parameters:* first systolic and diastolic blood pressure measurements after admission to the hospital and initial Glasgow Coma Scale score. CT scan was performed to confirm the clinical diagnosis in all patients, but was not analyzed in this study, since the aim was to determine clinical predictors of the diagnosis.

Univariate Chi-square was used to compare the differences between the 2 groups (INF and HEM). The *t*-test was used to compare continuous variables. Continuous variables were categorized to maximize the distinction between the two groups. The value of $p < 0.01$ was used as a selection criteria for multivariate analysis. Variables which could be easily measured by emergency medical personnel were given preference. Multivariate logistic regression analysis was performed to assess the predictive potential of independent variables found to be different in the two groups (INF and HEM) by univariate test . Since we were concerned about the effect of many missing variables on the differentiation of INF from HEM we created a separate variable to identify those cases with more than one missing variable. This variable was inserted in our model. For the model, the set of potential factors was reduced by backward elimination until only those significant at the 0.01 level remained. Odds ratios (OR) and 95% confidence intervals (CI) were calculated based on the estimated ß coefficients and their standard errors. The ß coefficients of the final model were used to construct the components of a diagnostic scale. The product of each coded variable and its weight was assembled into a total diagnostic score. Receiver-operating-characteristic (ROC) curves were created and cut points in the calculated score were chosen to maximize the separation of INF from HEM.

For the external validation study, we applied this score system to the Northern Manhattan Stroke Study (NOMASS) cohort. The details of NOMASS have been described elsewhere[14,15]. Patients selected for this subanalysis were prospectively evaluated by the Stroke Service at the Presbyterian Hospital for first INF or HEM and were over age 39 years at stroke onset. The SDB score was calculated for patients in NOMASS based on the prospectively collected responses to the selected variables. A ROC curve was produced to demonstrate the sensitivity and specificity of the model in the NOMASS cohort. Using the same subset of patients, we also computed the Siriraj Hospital Stroke score and compared the classification of HEM and INF to the SDB score.

This study was approved by the National Institute of Neurological Disorders and Stroke and the local ethics committee.

RESULTS

Of 1805 patients with acute stroke enrolled in the SDB, 1273 were classified as INF and 237 as HEM. We excluded 243 patients with diagnosis of subarachnoid hemorrhage and only 52 who were classified as stroke from other causes. Patients with INF were older and less likely to be men than those with HEM (Table 1). There were no detectable ethnic differences between the 2 groups. Among stroke risk factors, hypertension was the most frequent in both groups. History of cardiovascular disease, diabetes, and TIA or stroke were more frequent among the INF group, whereas recent consumption of alcoholic beverages was more frequent in HEM patients. Among the clinical features presenting at onset, headache, vomiting, seizure, and decreased consciousness or

Table 1. Comparison of clinical features between acute brain hemorrhage and infarction in the Stroke Data Bank.

	Infarction	Hemorrhage	p*
Number of patients	1273	237	
Demographic features			
Mean age (± SD)	67 (± 0.37)	59 (± 1.06)	**0.001#**
Men	47.5%	56.5%	**0.010**
Race			0.076
White	34.4%	35.0%	
Black	57.7%	52.8%	
Other	7.9%	12.2%	
Historical stroke risk factors			
Hypertension	68.5%	66.1%	0.465
Diabetes mellitus	26.4%	9.3%	**0.001**
Myocardial infarction	18.9%	9.8%	**0.001**
Angina	17.4%	5.1%	**0.001**
Congestive heart failure	15.1%	8.2%	**0.007**
Valvular heart disease	4.7%	4.1%	0.660
Atrial fibrillation	10.1%	4.1%	**0.005**
Other arrhythmias	9.1%	0.9%	**0.001**
Prior stroke	25.7%	8.1%	**0.001**
Prior transient ishemic attack	18.1%	2.9%	**0.001**
Systemic emboli	1.2%	1.8%	0.465
Claudication	6.7%	2.7%	0.024
Alcoholic beverages in last 24 hrs	7.3%	21.3%	**0.001**
Clinical features at onset			
Severe headache	9.9%	51.0%	**0.001**
Vomiting	5.6%	34.0%	**0.001**
Seizure	2.1%	10.7%	**0.001**
Decreased consciousness	15.9%	60.7%	**0.001**
Coma	1.6%	21.7%	**0.001**
Deficit on awakening	30.6%	17.5%	**0.001**
Focal deficit	98.4%	83.0%	**0.001**
Initial neurological examination			
Alert	78.7%	36.3%	**0.001**
Cervical bruit	7.2%	0.9%	**0.001**
Motor deficit	88.0%	85.0%	0.215
Sensory deficit	54.6%	67.1%	**0.003**
Abnormal extraocular motility	29.2%	61.6%	**0.001**
Visual field deficit	27.2%	34.9%	0.065
Ataxia	20.0%	14.6%	0.167
Dysarthria	48.5%	37.9%	0.030
Hemineglect	32.3%	26.2%	0.316
Aphasia	30.9%	34.9%	0.395
Mean parameters on initial examination			
Systolic blood pressure mmHg	160	182	**0.001#**
Diastolic blood pressure mmHg	92	105	**0.001#**
Glasgow Coma Score	13	10	**0.001#**

*statistical tests using chi-square (k-1) *df* except where specified; # *t*-test; bold *p* values are considered significant.

coma were significantly more frequent in HEM patients. For those reporting deficits upon awakening or focal deficit at onset, the subtype was predominantly INF. Patients with HEM had more sensory and extraocular motility abnormalities on initial neurological examination, and greater mean blood pressures and lower level of consciousness measures by mean Glasgow Coma Scale score on the admission examination.

Six independent clinical variables distinguished INF from HEM by logistic regression: age greater than 55 years (Odds ratio - OR =1.7; 95% Confidence Interval-CI=1.1-2.4), history of angina (OR=3.4; CI=1.6-7.0), prior stroke or TIA (OR=3.1; CI=1.9-4.9), diabetes (OR=2.5; CI=1.4-4.3), deficit upon awakening (OR=1.8; CI=1.1-2.3), and presentation with focal deficit (OR=4.7; CI=2.4-8.9). Whereas, HEM was more likely among men (OR=1.6; CI=1.1-2.3) and those presenting with severe headache (OR=5.0; CI=3.3-7.5), vomiting (OR=3.7; CI=2.2-5.8), coma or decreased consciousness (OR=16.9; CI=8.0-37.0), or an initial blood pressure greater than 200/120mmHg (OR=3.8; CI=2.5-5.6). HEM was also favored if more than one of these clinical discriminators were unmeasurable (OR=2.9; CI=1.8-4.6). The latter blood pressure category was chosen to maximize the discrimination between INF and HEM.

Based on our final model, a score for the clinical diagnosis of INF or HEM was created ranging from -10 to +10 (Fig 1). We applied our model to the SDB cohort to create a ROC curve which shows the relationship between the sensitivity and 1-specificity for the diagnosis of HEM at various scores and can be used to select the best score cutpoint (Fig. 2). The more the curve is closer to the top left corner the better the sensitivity and the specificity. In the SDB cohort, the cutpoint which maximized sensitivity and specificity appeared to be 2.0. HEM was the most likely diagnosis with scores of 2.0 or lower (to -10), and INF was more likely with values of greater than 2.0 (to +10). Scores suggestive of HEM (-10 to 2.0) led to the correct classification of 76% of the HEM cases and misclassified only 17% of the infarct as HEM (sensitivity=76%; specificity=83%; positive predictive value for HEM=46%; negative predictive value for HEM=95%).

	No	Yes	Unknown	Score
Patient is more than 55 years old	0	+1.0	U	
Patient is a man	0	-1.0		
Has patient ever had a history of:				
TIA or Stroke	0	+2.0	U	
Angina	0	+2.0	U	
Diabetes	0	+1.5	U	
At the time of onset was there:				
Focal deficit	0	+2.5	U	
Deficit presented on awakening	0	+1.0	U	
Patient is not alert	0	-3.0	U	
Severe headache	0	-2.0	U	
Vomiting	0	-1.5	U	
Initial blood pressure higher than 200/120 mHg	0	-1.5		
More than one of previous questions answered unknown	0	-1.0		
TOTAL SCORE				
rating	-10 to +2 > 2 to + 10		BRAIN HEMORRHAGE BRAIN INFARCT	

Fig 1. Score derived from the Stroke Data Bank for clinical discrimination of acute brain hemorrhage from infarction.

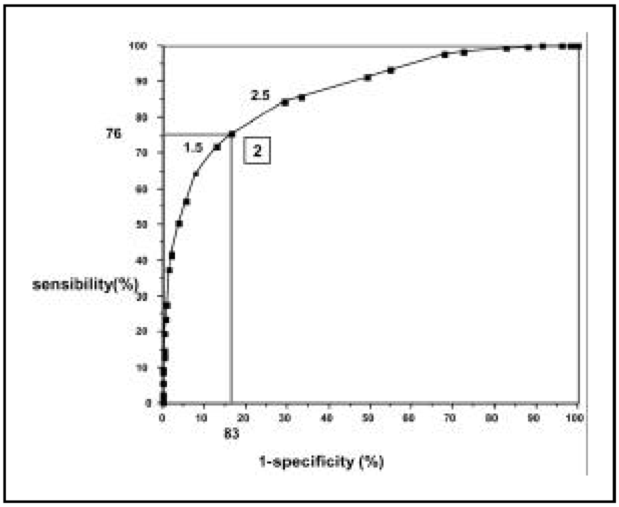

Fig 2. Receiver operating characteristic (ROC) curves show the relationship between the sensitivity and 1-specificity for the diagnosis of acute brain hemorrhage at various scores in the Stroke Data Bank. A cutpoint which maximizes sensitivity and specificity seems to be 2.0.

In the external validation of this score in the separate NOMASS cohort, the same score cutpoint of 2.0 led to the correct classification of 68% of the HEM cases and misclassified only 24% of the infarcts as HEM. Using the only other stroke score which can be used in the emergency room setting, the Siriraj Hospital Stroke score, led to a sensitivity of 24% and specificity of 97.4% for the classification of HEM cases from the NOMASS cohort. Among the 58 HEM patients in the NOMASS cohort the SHS score led to the correct diagnosis in only 14 patients.

DISCUSSION

Although the management of acute stroke requires institution of therapy within hours of stroke onset[16,17], recent surveys have demonstrated that there is often a delay among stroke patients in their presentation to medical personnel[5,18-21]. Part of the explanation may be based upon inadequate public and physician education of the signs and symptoms of acute stroke as was apparent for myocardial infarction in the past[22]. Treatment delays may be improved by better recognition of stroke symptoms, rapid patient transportation systems, and immediate emergency medical evaluation of the suspected stroke patient[20,23-25]. Emergency medical services (EMS) personnel are often the first medical contact for patients presenting with stroke[26], since most stroke events occur at home[27]. They represent a crucial link in the early triage and management of acute stroke patients. An early notification of stroke subtype by EMS to the receiving hospital may minimize the time delay to treatment by alerting and mobilizing the appropriate stroke-treatment personnel according to the possible stroke mechanism (HEM or INF).

The SDB practical classification may be a new tool to be used in the management of acute stroke patients. It was designed to use simple variables, which could be easily answered by EMS personnel. It has a reasonable sensitivity and specificity for differentiating HEM from INF in internal and external validation cohorts and it also permits the choice of different cutpoints to increase the score accuracy. In addition, clinical stroke subtype diagnosis with our score method appeared more accurate than the diagnosis made by the patient's physician at bedside prior to revealing the results of the CT in other studies[28]. Using our scoring system the clinician's may improve their clinical skills to differentiate HEM from INF[29].

It is well known that some risk factors are specific to either HEM or INF[30-32]. We have also detected demographic and stroke risk factor differences between patients presenting with HEM or INF. Hemorrhage has been observed in higher frequency in younger patients and in men[33-35]. Hypertension is a potent risk factor for both brain infarction and hemorrhage, however, as found by us, often does not discriminate between the two groups. In our study, as found by others[33,36], the level of the admitting blood pressure was more elevated in brain hemorrhage patients. Stroke patients with prior hypertension usually have the highest blood pressure levels compared to normotensives[37]. Diabetes and coronary artery disease were strongly associated with INF and they have been established as risk factors for brain infarction in numerous studies[31,32,38]. History of TIA and stroke have more often preceded a brain infarction than hemorrhage and contributed to the recurrence of infarction[35,36].

Clinical features at onset may also help to discriminate between brain infarction and hemorrhage[36]. The high frequency of severe headache at onset in brain hemorrhage has also been reported by others[33,35,36,39]. The occurrence of headache varies by stroke subtype and may be an important indicator of stroke mechanism[39-41]. Vomiting, decreased consciousness and coma were also found to be more predictive of hemorrhage as have been observed in other clinical series[33,35,36]. In our study, the occurrence of a deficit upon awakening was more predictive of INF than HEM. Previous reports have identified a circadian rhythm to the onset of brain infarction[42].

Other clinical scores have been developed to help discriminate brain infarction from hemorrhage. The

Kyushu University score included 16 clinical items of various different weights to arrive at the stroke subtype[6]. Other than the items mentioned in this analysis, this score included conjugated eye deviation, anisocoria, light reflex, corneal reflex, speech disorder, neck stiffness, sensory deficit, and cerebrospinal fluid. Six factors were found to predict hemorrhage among a sample of cases in Rochester, NY: coma, vomiting, severe headache, marked hypertension (systolic blood pressure greater than 220 mmHg), new hyperglycemia (serum glucose level greater than 170 g/dL), and warfarin therapy[43]. Unfortunately, this model included results of testing that could cause treatment delays. Besson et al.[8] developed a scoring system to identify nonhemorrhagic infarct patients based on 8 variables that included history of hyperlipidemia, alcohol consumption, plantar response and atrial fibrillation on admission using electrocardiogram. Although it gives a high positive predictive value, this scoring system cannot be applicable as a pre-hospital screening score to all stroke patients. The Guy's Hospital Stroke score included 8 variables that were obtained not only by clinical history but also using clinical examination and chest X-rays[2]. In addition, some variables can only be calculated 24 hours after the stroke, such as level of consciousness and diastolic blood pressure, so it cannot be used in acute stroke treatment trials. This score achieved a sensitivity for the diagnosis of hemorrhage of 81% and 88% in patients from Oxford and London, respectively[9]. The Siriraj Hospital Stroke score is simpler and can be calculated immediately after stroke at bedside[7]. This score uses five variables: level of consciousness, vomiting, headache, diastolic blood pressure, and atheroma markers. The validation study of the Siriraj Hospital Stroke score in Thailand revealed higher sensitivities for supratentorial hemorrhage (89.3%) and infarction (93.2%)[7]. The difference in prevalence of hemorrhagic stroke may explain the lower diagnostic accuracy of the Siriraj Hospital Stroke score in the NOMASS cohort. More recent evaluations of the Guy's Hospital Stroke and Siriraj Hospital Stroke scores conclude that such scoring systems are not useful in routine clinical practice[44,45], although they may be used in large scale epidemiological studies[9,10].

The limitations of the scoring system should be understood. It is not possible to achieve total separation of all patients with HEM from those with INF using clinical features, particularly in those cases with small deep HEM that mimic the clinical features of INF. Due to this fact, some scoring systems[2,7] have created an uncertain group that will effectively increase the sensitivity and specificity of the final calculation[45]. The use of an uncertain group, however, will not achieve the goal of the acute stroke score which is to classify all incoming patients with acute stroke. If a large percentage of the patients fall into the uncertain category, then the utility of the score is weakened.

The variables needed to calculate a stroke score should be available when management decisions are being made and take into account the possibility of missing information. There are diagnostic problems caused by the lack of complete information in some patients when the GHS and SHS scores were used[44,45]. For this reason, we designed a model to be performed by non-neurologists with minimal reliance on any laboratory testing and most of the information could be obtained by direct observation, interviewing the patient or the family members, and measurement of blood pressure. Our score could be calculated easily and a presumptive diagnosis could be made prior to the CT scan. Most of the inaccuracies to differentiate HEM from INF arise in the diagnosis of HEM, because many of the variables used in these scoring systems (level of consciousness at onset, early headache, vomiting) discriminate in favor of hemorrhage. If a patient or relative cannot give a clear description of the symptom at the stroke onset, the score will tend to overestimate the likelihood of INF. Taking into account all these considerations, our score has included a new variable to account for the inability to ascertain specific information (one or more missing variable).

In conclusion, the use of our stroke score system as a screening score by emergency personnel can help select patients for stroke treatments, alert CT scan technicians, and warn teams of incoming patients to reduce treatment delays. New variables may be identified in further studies, which certainly will optimize our scoring system to differentiate acute brain hemorrhage from infarction. At present, we are not advocating the use of this score to replace the gold-standard brain image differentiation of HEM from INF for thrombolytic therapy. However, as we develop other safe and effective acute stroke treatments, such as the recently recommended use of early aspirin for suspected acute ischemic stroke when CT scan in unavailable[46], the SDB score may become a useful tool in acute stroke triage settings.

Acknowledgments - We thank Xun Chen for her skillful statistical support.

REFERENCES

1. Adams HP Jr, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: a supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 1996;27:1711-1718.
2. Allen CMC. Clinical diagnosis of the acute stroke syndrome. Q J Med 1983;52:515-523.
3. Kothari RU, Brott T, Broderick JP, et al. Emergency physicians: accuracy in the diagnosis of stroke. Stroke 1995;26:2238-2241.
4. Barsan WG, Brott TG, Olinger CP, et al. Identification and entry of the patient with acute cerebral infarction. Ann Emerg Med 1988;17:1192-1195.
5. Timerding BL, Barsan WG, Hedges JR, et al. Stroke patient evaluation in the emergency department before pharmacologic therapy. Am J Emerg Med 1989;7:11-15.
6. Hatano S. Variability of the diagnosis of stroke by clinical judgement and by a scoring method. Bull WHO 1976;54:533-540.
7. Poungvarin N, Viriyavejakul A, Komontri C. Siriraj stroke score and validation study to distinguish supratentorial intracerebral haemorrhage from infarction. BMJ 1991;302:1565-1567.
8. Besson G, Robert C, Hommel M, et al. Is it clinically possible to distinguish nonhemorrhagic infarct from hemorrhagic stroke? Stroke 1995;26:1205-1209.
9. Sandercock PAG, Allen CMC, Corston RN, et al. Clinical diagnosis of intracranial haemorrhage using Guy's Hospital score. BMJ 1985;291: 1675-1677.
10. Celani MG, Ceravolo MG, Duca E, et al. Was it infarction or haemorrhage? A clinical diagnosis by means of the Allen score. J Neurol 1992; 239:411-413.
11. Celani MG, Righetti E, Migliacci R, et al. Comparability and validity of two clinical scores in the early differential diagnosis of acute stroke. BMJ 1994;308:1674-1676.
12. Foulkes MA, Wolf PA, Price TR, et al. The Stroke Data Bank: design, methods, and baseline characteristics. Stroke 1988;19:547-554.
13. Mohr JP, Barnett HFM. Classification of ischemic strokes. In Barnett HJM, Mohr JP, Stein BM, Yatsu FM (eds.) Stroke: pathophysiology, diagnosis, and management. New York: Churchill Livingstone, 1986:281-291.
14. Gan R, Sacco RL, Gu Q, et al. Lacunes, lacunar syndromes, and the lacunar hypothesis: the Northern Manhattan experience. Neurology 1997;48:1204-1211.
15. Sacco RL, Boden-Albala B, Gan R, et al. Stroke incidence among White, Black and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. Am J Epidemiol 1998;147:259-268.
16. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995; 333:1581-1587.
17. Broderick JP, Adams HP Jr, Barsan W et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 1999;30:905-915.
18. Alberts MJ, Bertels C, Dawson DV. An analysis of time of presentation after stroke. JAMA 1990;263:65-68.
19. Herderscheê D, Limburg M, Hijdra A, et al. Timing of hospital admission in a prospective series of stroke patients. Cerebrovasc Dis 1991;1:165-167.
20. Bratina P, Greenberg L, Pasteur W, et al. Current emergency department management of stroke in Houston, Texas. Stroke 1995;26:409-414.
21. Fogelholm R, Murros K, Rissanen A, et al. Factors delaying hospital admission after acute stroke. Stroke 1996;27:398-400.
22. Leitch JW, Birbara T, Freedman B, et al. Factors influencing the time from onset of chest pain to arrival at hospital. Med J Aust 1989;150:6-10.
23. Kothari R, Hall K, Brott T, et al. Early stroke recognition: developing an out-of-hospital NIH Stroke Scale. Acad Emerg Med 1997;4:986-990.
24. Dávalos A, Castillo J, Martinez-Vila E, for the Cerebrovascular Diseases Study Group of the Spanish Society of Neurology. Delay in neurological attention and stroke outcome. Stroke 1995;26:2233-2237.
25. Jørgensen HS, Nakayama H, Reith J, et al. Factors delaying hospital admission in acute stroke: the Copenhagen Stroke Study. Neurology 1996;47:383-387.
26. Kothari R, Barsan W, Brott T, et al. Frequency and accuracy of prehospital diagnosis of acute stroke. Stroke 1995;26:937-941.
27. Kelly-Hayes M, Wolf PA, Kase CS, et al. Temporal patterns of stroke onset: the Framingham Study. Stroke 1995;26:1343-1347.
28. von Arbin M, Britton M, de Faire U, et al. Accuracy of bedside diagnosis in stroke. Stroke 1981;12: 288-293.
29. Chimowitz MI, Logigian EL, Caplan LR. The accuracy of bedside neurological diagnoses. Ann Neurol 1990;28:78-85.
30. Davis PH, Dambrosia JM, Schoenberg BS, et al. Risk factors for ischemic stroke: a prospective study in Rochester, Minnesota. Ann Neurol 1987;22:319-327.
31. Jørgensen HS, Nakayama H, Raaschou HO, et al. Intracerebral hemorrhage versus infarction: stroke severity, risk factors, and prognosis. Ann Neurol 1995;38:45-50.
32. Sacco RL, Benjamin EJ, Broderick JP, et al. Risk factors. AHA conference proceedings. Stroke 1997;28:1507-1517.
33. Aring CD, Merritt HH. Differential diagnosis between cerebral hemorrhage and cerebral thrombosis: a clinical and pathologic study of 245 cases. Arch Intern Med 1935;56:435-456.
34. Harrison MJG. Clinical distinction of cerebral haemorrhage and cerebral infarction. Postgrad Med J 1980;56:629-632.
35. Bogousslavsky J, van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1000 consecutive patients with first stroke. Stroke 1988; 19:1083-1092.
36. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: a prospective registry. Neurology 1978;28:754-762.
37. Britton M, Carlsson A. Very high blood pressure in acute stroke. J Intern Med 1990; 228:611-615.
38. Mortel KF, Meyer JS, Sims PA, et al. Diabetes mellitus as a risk factor for stroke. South Med J 1990;83:904-911.
39. Melo TP, Pinto AN, Ferro JM. Headache in intracerebral hematomas. Neurology 1996;47:494-500.
40. Gorelick PB, Hier DB, Caplan LR, et al. Headache in acute cerebrovascular disease. Neurology 1986;36:1445-1450.
41. Jørgensen HS, Jespersen HF, Nakayama H, et al. Headache in stroke: the Conpenhagen Stroke Study. Neurology, 1994;44;1793-1797.
42. Gallerani M, Manfredini R, Ricci L, et al. Chronobiological aspects of acute cerebrovascular disease. Acta Neurol Scand 1993;87:482-487.
43. Panzer RJ, Feibel JH, Barker WH, et al. Predicting the likelihood of hemorrhage in patients with stroke. Arch Intern Med 1985;145:1800-1803.
44. Weir CJ, Murray GD, Adams FG, et al. Poor accuracy of stroke scoring systems for differential clinical diagnosis of intracranial haemorrhage and infarction. Lancet 1994;344:999-1002.
45. Hawkins GC, Bonita R, Broad JB, et al. Inadequacy of clinical scoring systems to differentiate stroke subtypes in population-based studies. Stroke 1995;26:1338-1342.
46. Chen Z, Sandercock P, Pan H, et al. Indications for early aspirin use in acute ischemic stroke: a combined analysis of 40 000 randomized patients from the Chinese Acute Stroke Trial and the International Stroke Trial. Stroke 2000;31:1240-1249.