Epidemiological implications

- The risk of breast cancer is thought to be reduced by a past history of pregnancy
- Previous evidence suggests that a recent pregnancy (within three years) may transiently increase the risk of breast cancer
- A controlled study of over 2000 multiparous women aged 25-49 with newly diagnosed breast cancer has found no association between risk of breast cancer and time since last pregnancy

hospital based studies seem to show a transient increase in the relative risk of breast cancer related to a recent term pregnancy while the three population based studies found virtually no association.

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Comparability and validity of two clinical scores in the early differential diagnosis of acute stroke

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Abstract

Objective—To compare two available clinical scores for the differential diagnosis of cerebral ischaemia and haemorrhage in acute stroke patients.

Design—Prospective, multicentre study of acute stroke patients evaluated with computed tomography and Allen and Siriraj scores; the scores were tested for comparability (kappa statistic) and validity (sensitivity, specificity, positive and negative predictive values, diagnostic gain). The effect of a policy of using Allen and Siriraj scores to determine pathological type of stroke before computed tomography was calculated.

Setting—Three hospitals in Italy, all participating in the international stroke trial, with different access facilities to computed tomography.

Subjects—231 consecutive patients who were screened in the three hospitals for possible inclusion in the international stroke trial from 1 November 1991 to 31 May 1993.

Results—The prevalence of haemorrhage (diagnosed with computed tomography) was 14.7% (95% confidence interval 10.1% to 19.3%). Allen scores were "uncertain" in 44 cases and Siriraj scores in 38 cases; in the 164 cases with both the scores in the range of "certainty" kappa was 0.72. Sensitivity, specificity, positive and negative predictive values,

and diagnostic gain for haemorrhage were 0.38, 0.98, 0.71, 0.91, and 0.58 for Allen scores and 0.61, 0.94, 0.63, 0.93, and 0.48 for Siriraj scores; positive predictive values for infarction were 91% for Allen scores and 93% for Siriraj scores. According to these data, of 1000 patients with acute stroke, 680 would be correctly and 70 wrongly diagnosed as "ischaemic" with the Allen score; the figures would be 671 and 48 with Siriraj score.

Conclusion—When computed tomography is not immediately available and the clinician wishes to start antithrombotic treatment (or randomise patients in a clinical trial), the Siriraj score (and possibly the Allen score) can be useful to identify patients at low risk of intracerebral haemorrhage.

Introduction

Haemorrhagic and ischaemic stroke cannot be distinguished clinically with a simple clinical evaluation, and it is virtually impossible for all stroke patients to have a computed tomography scan immediately after admission. Thus, in small district hospitals as well as in large university centres a weighted clinical score may offer some advantages to physicians who are involved in stroke management and need to distinguish between haemorrhage and ischaemia for the purpose of treat-

ment. Two such scores are currently available.^{1,2} The Allen score has been validated in different European settings,^{3,4} and has a reasonably good (90%) accuracy when the suggested cutoffs (<4 for ischaemia and >24 for haemorrhage) are used; however, it requires several historical and clinical details to be registered (see Appendix) and cannot be used until 24 hours after the stroke. The Siriraj score is much easier to determine, and can be used immediately after the stroke; however, it has been tested only in Thailand, where the pretest probability of haemorrhage is higher than in Europe; as the positive predictive value depends on prevalence, the score needs to be validated in Europe to check the predictive values. We compared Allen and Siriraj scores in Italy.

Methods

Three centres were involved in this study: the university department of neurology in Perugia (24 hour access to computed tomography), the division of neurology in Trieste (daytime access to computed tomography), and the division of medicine in Cortona (no computed tomography in the hospital; patients sent by ambulance 30-50 km for computed tomography). All three hospitals are participating in the international stroke trial; physicians in these hospitals need to differentiate between haemorrhage and ischaemia to include patients with ischaemic stroke in that trial. From 1 November 1991 to 31 May 1993 all patients screened for potential inclusion in the international stroke trial (those with stroke onset within 48 hours) were evaluated with Allen and Siriraj scores, and submitted to computed tomography scan within 48 hours of inclusion in this study. Before being scanned, each patient was evaluated by one of the authors, who completed a form containing the variables of each score (answering yes or no to each question and reporting blood pressure) but did not calculate the scores (see Appendix). These forms, along with the computed tomography report, were sent to the neurology department in Perugia, where calculations and comparisons with the results of computed tomography were done only after all forms and reports had been received.

Several analyses were carried out. The scores were compared in terms of "certain" results (that is, percentages of cases in which the scores predicted ischaemia or haemorrhage, according to the cutoffs suggested in the original papers^{1,2}; a result was considered to be certain when the Allen score was <4 or >24 or the Siriraj score was <-1 or >1. The kappa statistic was determined for agreement between the two scores (all cases and "certain" cases). The two scores were compared with the results of computed tomography, and sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic gain (the difference between post-test and pretest probability of disease) were calculated. We used the kappa statistics program⁵ for comparability tests, EPISTAT for McNemar's test, CIA for 95% confidence intervals,⁶ and an ad hoc program, based on widely described calculations,⁷ for the validation tests.

Results

In 231 cases, the prevalence of haemorrhage (diagnosed with computed tomography) was 14.7% (95% confidence interval 10.1% to 19.3%). The overall comparability of the Allen and Siriraj scores was fair ($\kappa=0.4$) (table I). The Allen score was uncertain in 44 cases, and the Siriraj score was uncertain in 38 ($P=0.49$; McNemar's test); however, the kappa statistic showed a worse comparability between the two scores in terms of certain results ($\kappa=0.23$) (table II).

TABLE I—Comparison of Allen and Siriraj scores

	Siriraj score		
	Haemorrhage	Ischaemia	Uncertain
Allen score:			
Haemorrhage	10	1	3
Ischaemia	6	147	20
Uncertain	11	18	15

$\kappa=0.397$.

TABLE II—Certain and uncertain results with Allen and Siriraj scores

	Allen score	
	Certain	Uncertain
Siriraj score:		
Certain	164	29
Uncertain	23	15

$P=0.49$, McNemar's test; $\kappa=0.23$.

When only the results that were within the diagnostic range with both the scores (164 cases) were considered, the agreement in diagnosing infarction and haemorrhage was high ($\kappa=0.72$) (table III). When computed tomography scan results are used as a standard (tables IV and V), the diagnostic gain for detecting haemorrhage was 0.58 with the Allen score and 0.48 with the Siriraj score; however, for the detection of infarction, besides a poor diagnostic gain (0.05 and 0.08), the positive predictive value was 91% for the Allen score and 93% for the Siriraj score. In the 157 patients in whom the two scores were both certain and in agreement, when the combined result was compared with results of computed tomography, accuracy was slightly better (0.92), and the diagnostic gain was 0.6.

TABLE III—Diagnostic agreement of Allen and Siriraj scores

	Allen score	
	Haemorrhage	Ischaemia
Siriraj score:		
Haemorrhage	10	6
Ischaemia	1	147

$\kappa=0.72$.

TABLE IV—Comparison of Allen score with results of computed tomography

	Computed tomography	
	Haemorrhage	Ischaemia
Allen score:		
Haemorrhage	10	4
Ischaemia	16	157

Sensitivity=0.38; specificity=0.98; positive predictive value=0.71; negative predictive value=0.91; accuracy=0.89; diagnostic gain=0.58.

TABLE V—Comparison of Siriraj score with results of computed tomography

	Computed tomography	
	Haemorrhage	Ischaemia
Siriraj score:		
Haemorrhage	17	10
Ischaemia	11	155

Sensitivity=0.61; specificity=0.94; positive predictive value=0.63; negative predictive value=0.93; accuracy=0.89; diagnostic gain=0.48.

Using these data, we calculated that, out of 1000 patients with acute stroke, 750 (693 to 805) would be diagnosed as ischaemic with the Allen score; of those, 70 (40 to 110) would be wrongly diagnosed (that is, computed tomography would show haemorrhage); in addition, 17 (4 to 43) further patients would be wrongly diagnosed as haemorrhagic (computed tomography would show ischaemia) and 190 (140 to 241) could not be diagnosed because of an uncertain score

Clinical implications

- It is not possible for all stroke patients to have a computed tomography scan immediately after admission to differentiate between haemorrhage and ischaemia
- The Allen and Siriraj clinical scores have been proposed to help clinicians in making decisions while waiting for results of computed tomography
- In this study, the accuracy of both scores when compared with computed tomography was 89%
- The Siriraj score is simpler, can be used immediately after the stroke, and has a 93% positive predictive value for ischaemia
- When clinicians wish to start antithrombotic treatment (aspirin or subcutaneous heparin) while waiting for the scan results, they can rely on the Siriraj score

(between 4 and 24). With the Siriraj score 719 (661 to 777) patients would be diagnosed as ischaemic, with 48 (24 to 84) wrong diagnoses (computed tomography would show haemorrhage), and 43 (21 to 78) wrongly diagnosed as haemorrhagic (computed tomography would show ischaemia); in addition, 165 patients (117 to 212) could not be diagnosed because of an uncertain score (between -1 and 1).

Discussion

Our study shows that the Allen and Siriraj scores do not diagnose the same cases as being certain infarction or certain haemorrhage. The scores should be considered comparable only when both show certainty and point to the same side of the scale. Using both scores may slightly increase the accuracy, but the Allen score can be calculated only after 24 hours, so the combined use should be restricted to few patients; furthermore, the variables used in the Siriraj score are all present in the Allen score, making an additional effect unlikely. Thus, this time consuming double procedure does not seem clinically sound. Different cutoffs might be used to increase the accuracy, or different variables might be added to obtain a better accuracy; there is some research in this direction but results have not been published, so we must rely on the published and validated cutoffs.

When the doctor needs to ascertain ischaemic stroke (to immediately start antithrombotic treatment in a clinical trial), the positive predictive value of both the scores is good, and given the characteristics of the calculations, the Siriraj score could be used at bedside. When the problem is to detect a haemorrhage (to ask for a neurosurgical opinion), the Allen score is probably better, as there is a low pretest probability of this disease. We have already suggested practical applications of these scores.⁴ In addition, when computed tomography is not immediately available and the doctors wish to start antithrombotic therapy (or randomise patients in the international stroke trial,⁶) if the Siriraj score (and possibly the Allen score) is low enough to convince them of the presence of an ischaemic stroke, one or two doses of aspirin or subcutaneous heparin can be given, or the patient randomised, while waiting for computed tomography. These drugs can be withdrawn immediately if the scan

shows a small, deep haemorrhage, and a few patients with haemorrhage entered in a trial of ischaemic stroke treatment. In this way the sample size of a clinical trial can be increased and—more importantly—treatments tested in hospitals, where stroke patients are acutely admitted, and where it is rather difficult to always obtain a computed tomograph quickly. Furthermore, it would be possible to test the advantage of early treatment of cerebral ischaemia as opposed to the risk of giving a few doses of antithrombotic drugs to a patient with a small haemorrhage.

Appendix

Calculation of Siriraj score

Variable	Clinical feature	Score
Consciousness ($\times 2.5$)	Alert	0
	Drowsy, stupor	1
	Semicoma, coma	2
Vomiting ($\times 2$)	No	0
	Yes	1
Headache within two hours ($\times 2$)	No	0
	Yes	1
Diastolic blood pressure ($\times 0.1$)		
Atheroma markers ($\times 3$)	None	0
Diabetes, angina, intermittent claudication	One or more	1
Constant		-12

Calculation of Allen score

Variable	Clinical feature	Score
Apoplectic onset:		
Loss of consciousness	None or one	0
Headache within two hours	Two or more	21.9
Vomiting		
Neck stiffness		
Level of consciousness (24 hours after admission)	Alert	0
	Drowsy	7.3
	Unconscious	14.6
Plantar responses	Both flexor or single extensor	0
	Both extensor	7.1
Diastolic blood pressure (24 hours after admission) ($\times 0.17$)		
Atheroma markers		
Diabetes, angina, intermittent claudication	None	0
	One or more	-3.7
History of hypertension	Not present	0
	Present	-4.1
Previous event	None	0
Transient ischaemic attack	Any number of previous events	-6.7
Heart disease	None	-4.3
	Aortic or mitral murmur	-4.3
	Cardiac failure	-4.3
	Cardiomyopathy	-4.3
	Atrial fibrillation	-4.3
	Cardiomegaly	-4.3
	Myocardial infarct within six months	-4.3
Constant		-12

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