

vious data, we have performed a Cox multivariate analysis of the probability of survival without stroke in 92 TIA patients with normal CT scan and in 24 TIA patients with cerebral infarct, followed during an average period of 21 months. Age, carotid lesions detected by ultrasonographic examination or angiography, and glycaemia level higher than 100 mg/dl were used as covariates since in a previous study we observed that these variables were related independently with the prognosis.⁴ Ninety nine per cent of the TIAs without infarct and 79% of the TIAs with infarct survived without suffering a major stroke (Mantel-Cox test, $p < 0.0001$). The probability of survival, free of stroke, was related with the presence of carotid atherosclerosis (odds ratio = 3.07, 95% confidence intervals = 1.27-7.40). Ischaemic lesions in the CT scan, age and glycaemia levels had no independent predictive value.

Our results suggest TIAs with cerebral infarct have a poorer outcome due to a higher frequency of atherosclerosis of the neck arteries.

ANTONI DÁVALOS
Unit of Neurology,
Hospital Dr Josep Trueta,
17007 Girona, Spain

- 1 Koudstaal PJ, van Gijn J, Frenken CWGM, et al. TIA, RIND, minor stroke: a continuum, or different subgroups? *J Neurol Neurosurg Psychiatry* 1992;55:95-7.
- 2 Calandre L, Gomara S, Bermejo F, Millan JM, Del Pozo G. Clinical-CT correlations in TIA, RIND, and strokes with minimum residuum. *Stroke* 1984;15:663-5.
- 3 Dávalos A, Matias-Guiu J, Torrent O, Vilaseca J, Codina A. Computed tomography in reversible ischaemic attacks: clinical and prognostic correlations in a prospective study. *J Neurol* 1988;235:155-8.
- 4 Dávalos A, Codina A. Factores de riesgo y variables pronósticas en los ataques isquémicos transitorios y en los infartos con residuo mínimo. Estudio comparativo multivariado. *Med Clin (Barc)* 1991;96:441-4.

Koudstaal and van Gijn reply:

We would like to thank Dr Dávalos *et al* for their comments on our study.¹ Their observation of a higher risk of stroke in TIA patients with a cerebral infarct on CT in a univariate, but not in a multivariate analysis, is very interesting.² We have recently completed a study of predictors of major vascular events in 3150 patients with a TIA or minor stroke who were entered into the Dutch TIA Study.³ In contrast to the findings of Dr Dávalos *et al*, we found that ischaemic abnormalities on CT scan were an independent risk factor for stroke and other vascular events, irrespective of the duration of the symptoms. In this multicentre study, however, it was impossible to collect objective information on the presence and degree of atherosclerotic abnormalities of the extracranial bloodvessels, which may explain the discrepancy between our findings and those of our Spanish colleagues.

PETER J KOUDSTAAL
University Hospital, Rotterdam

JAN VAN GIJN
University Department of Neurology,
Utrecht
The Netherlands

- 1 Koudstaal PJ, van Gijn J, Frenken CWGM, et al. TIA, RIND, minor stroke: a continuum or different subgroups? *J Neurol Neurosurg Psychiatry* 1992;55:95-7.
- 2 Dávalos A, Codina A. Factores de riesgo y variables pronósticas en los ataques isquémicos transitorios y en los infartos con residuo mínimo. Estudio comparativo multivariado. *Med Clin (Barc)* 1992;96:441-4.
- 3 The Dutch TIA Study Group. Predictors of major vascular events in patients with a

transient ischemic attack or minor ischemic stroke. *Stroke* (submitted for publication).

Diabetes and stress hyperglycaemia in stroke

Kiers *et al*¹ presented a prospective study on 176 stroke patients focused on stroke outcome in relation to hyperglycaemia and diabetes.¹ The patients were divided into four groups: 1) normoglycaemic patients with normal or marginally elevated glycosylated haemoglobin (HbA1c) level, without history of diabetes; 2) hyperglycaemic patients with normal HbA1c, without history of diabetes ("stress hyperglycaemia"); 3) new diabetics (hyperglycaemic patients with elevated HbA1c level, without history of diabetes) and 4) known diabetics. Stroke severity on admission was significantly worse in the patients with stress hyperglycaemia and in the known diabetics than in their normoglycaemic counterparts. In addition, hospital mortality was higher in the patients with stress hyperglycaemia, in the newly-diagnosed diabetics, and known diabetics compared with the normoglycaemic patients.

One of the conclusions was that there exists a relationship between diabetes and poor stroke outcome. This conclusion is hardly justified. It has been shown that reactive or "stress" hyperglycaemia is associated with poor stroke outcome in non-diabetics.^{2,3} In fact, this is one of the results of the authors as well. However, incorrect conclusions are readily made when diabetics are compared with non-diabetics after exclusion of the non-diabetics with stress hyperglycaemia. It is very probable that new or known diabetics with acute stroke cannot escape acute stress and reactive hyperglycaemia either. In one study, taking this aspect into consideration, in-hospital case fatality rate was 35% in diabetics with reactive hyperglycaemia but 0% without reactive hyperglycaemia.² When grouping the patients of Kiers *et al*¹ by HbA1c level, the case fatality rate (95% confidence interval) was 19.1% (11.0-27.2) for the 89 patients with normal HbA1c and 26.3% (14.9-37.7) for the 57 patients with elevated HbA1c. At present, studies based on HbA1c measurements suggest that no association exists between diabetes and poor short term (3 months) outcome in stroke.⁴ For Kiers *et al* point out that several animal studies have shown that hyperglycaemia increases ischaemic brain damage. However, in some studies of experimental cerebral ischaemia hyperglycaemia has been neuroprotective.^{5,6}

KARI MURROS
RAINER FOGELHOLM
Department of Neurology,
Central Hospital of Central Finland,
40620 Jyväskylä, Finland

- 1 Kiers L, Davis SM, Larkins R, et al. Stroke topography and outcome in relation to hyperglycaemia and diabetes. *J Neurol Neurosurg Psychiatry* 1992;55:263-70.
- 2 Melamed E. Reactive hyperglycaemia in patients with acute stroke. *J Neurol Sci* 1976;29:267-75.
- 3 Candelise L, Landi G, Orazio EN, Boccardi E. Prognostic significance of hyperglycaemia in acute stroke. *Arch Neurol* 1985;42:661-3.
- 4 Murros K, Fogelholm R, Kettunen S, Vuorela A-L, Valve J. Blood glucose, glycosylated haemoglobin, and outcome of ischemic brain infarction. *J Neurol Sci* 1992; (in press).
- 5 Zasslow MA, Pearl RG, Shuer LM, Steinberg GK, Lieberman RE, Larson Jr. CP. Hyperglycaemia decreases acute neuronal ischemic changes after middle cerebral artery occlusion in cats. *Stroke* 1989;20:519-23.

- 6 Kraft SA, Larson Jr CP, Shuer LM, Steinberg GK, Benson GV, Pearl RG. Effect of hyperglycaemia on neuronal changes in a rabbit model of focal cerebral ischemia. *Stroke* 1990;21:447-50.

Kiers, Davis, Larkins *et al* reply:

We thank Drs Murros and Fogelholm for their comments. The relationships between diabetes, stress hyperglycaemia and stroke outcome are indeed complex. In our study design, we attempted to examine separately the effects of diabetes and stress hyperglycaemia on stroke outcome, compared with the euglycaemic non-diabetic state, using the four groups categorised on the basis of history, fasting glucose and glycosylated haemoglobin.¹ We acknowledge that stress hyperglycaemia was also likely to be present in some of the diabetic patients, but these subjects could not be identified.

Our study¹ demonstrated significantly higher mortality in the combined diabetes groups (as well as the stress hyperglycaemia group) compared with the euglycaemic, non-diabetic subjects, but we would agree that this adverse effect could have been due to stress hyperglycaemia in a proportion of the diabetic patients.

We are aware that there have been animal studies of cerebral ischaemia which have suggested that hyperglycaemia may be protective,^{2,3} but there is also substantial evidence to the contrary.^{4,5} What has been clearly shown by the results of our study, and previous human investigations,^{6,7} is that elevated blood glucose is associated with a worse outcome after stroke. This association was even present within our euglycaemic group. As discussed in our paper, it is not possible to conclude whether this is a causal relationship or whether the degree of hyperglycaemia reflects the severity of the acute event. Until the mechanism of the association can be resolved, however, glucose infusions should be avoided in acute stroke.⁸

STEPHEN DAVIS
Department of Neurology,
Clinical Neuroscience Centre,
The Royal Melbourne Hospital,
Victoria 3050, Australia

- 1 Kiers L, Davis S M, Larkins R, Hopper J, Tress B, Rossiter S C, Carlin J, Ratnaik S. Stroke topography and outcome in relation to hyperglycaemia and diabetes. *J Neurol Neurosurg Psychiatry* 1992;55:263-70.
- 2 Kraft S A, Larson Jr C P, Shuer L M, Steinberg G K, Benson G V, Pearl B C. Effect of Hyperglycaemia on Neuronal Changes in a Rabbit Model of Focal Cerebral Ischemia. *Stroke* 1990;21:447-50.
- 3 Zasslow M A, Pearl R G, Shuer L M, Steinberg G K, Lieberman R E, Larson Jr C P. Hyperglycemia Decreases Acute Neuronal Ischemic Changes After Middle Cerebral Artery Occlusion in Cats. *Stroke* 1989;20:519-23.
- 4 Pulsinelli W A, Waldman S, Rawlinson D, Plum F. Moderate hyperglycaemia augments ischemic brain damage: a neuropathologic study in the rat. *Neurology* 1982;32:1239-46.
- 5 Siemkowitz E, Gjedde A. Post-ischemic coma in rat: effect of different pre-ischemic blood glucose levels on cerebral metabolic recovery after ischemia. *Acta Physiol Scand* 1980;110:225-32.
- 6 Pulsinelli W A, Levy D E, Sigsbee B, Scherer P, Plum F. Increased damage after ischemic stroke in patients with hyperglycaemia with or without established diabetes mellitus. *Am J Med* 1983;74:540-4.
- 7 Gray C S, Taylor R, French J M, et al. The prognostic value of stress hyperglycaemia and previous unrecognised diabetes in acute stroke. *Diabetic Medicine* 1987;4:237-40.
- 8 WHO Task Force on Stroke and Other Cerebrovascular Disorders. Stroke-1989. Recommendations on Stroke prevention, diagnosis, and therapy. *Stroke* 1989;20:1407-31.