

# Review: Stress hyperglycemia after ischemic stroke indicates a greater risk for death in patients without diabetes

Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients. A systematic overview. *Stroke*. 2001 Oct 1;32:2426-32.

## QUESTION

In patients who have had a stroke, what are the differences in all-cause mortality and functional outcomes for different blood glucose levels and diabetes status?

## DATA SOURCES

Studies were identified by searching MEDLINE (1966 to December 2000) and Science Citation Index (1980 to December 1999). Bibliographies of relevant articles were reviewed, and experts in the field were contacted to identify unpublished studies.

## STUDY SELECTION

English-language studies were selected if the design was a cohort study, an inception cohort of patients with stroke was used, blood glucose level was measured within 24 hours of admission,  $\geq 80\%$  of the patients had follow-up to hospital discharge or to 1 month, and outcomes were reported in relation to blood glucose levels at admission. Exclusion criteria included exclusive reporting on subarachnoid hemorrhage, transient ischemic attack, and nonstroke causes of focal neurologic deficits.

## DATA EXTRACTION

Data were extracted on sample size, type of stroke (ischemic or hemorrhagic), definition

of stress hyperglycemia, percentage of patients with stress hyperglycemia, and outcomes. Outcomes included in-hospital or 30-day all-cause mortality and poor functional recovery.

## MAIN RESULTS

31 articles describing 32 cohort studies met the selection criteria. 4 of the 32 studies presented data separately for patients with ischemic or hemorrhagic stroke; 11 studies included only patients with ischemic stroke; and 17 studies either combined data for patients with ischemic or hemorrhagic stroke or did not state the subtype of stroke. In nondiabetic patients with stroke, the risk for in-hospital or 30-day all-cause mortality (short-term mortality) was 3-fold greater in patients with stress hyperglycemia than in those without it (relative risk [RR] 3.07, 95% CI 2.5 to 3.79). In patients with diabetes, stress hyperglycemia was not associated with short-term mortality after stroke (RR 1.3, CI 0.49 to 3.43). Subgroup analysis showed that in nondiabetic patients with ischemic stroke, the risk for short-term mortality was 3-fold greater in patients with a glucose level  $> 6.1$  to  $7.0$  mmol/L at admission than in those with a glucose level  $\geq 6$  mmol/L at admission (RR 3.28, CI 2.32 to

4.64). In patients with diabetes who had ischemic stroke, stress hyperglycemia was not associated with short-term mortality (RR 2.00, CI 0.04 to 90). Stress hyperglycemia was also not associated with short-term mortality after hemorrhagic stroke. In 5 studies, the risk for long-term mortality (3 mo to 1 y) was greater in patients with hyperglycemia than in those without it. In patients without diabetes, the risk for poor functional recovery up to 6 months after stroke was greater in patients with stress hyperglycemia than in those without hyperglycemia on admission (RR 1.41, CI 1.16 to 1.73).

## CONCLUSION

In patients without diabetes who have had ischemic stroke, stress hyperglycemia is associated with an increased risk for in-hospital or 30-day all-cause mortality.

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## COMMENTARY

In the timely review by Capes and colleagues, stress hyperglycemia after a stroke, which occurs in 20% to 50% of patients, half of whom are nondiabetic (1), was associated with an increased risk for in-hospital mortality and poor functional recovery in nondiabetic but not diabetic patients. On the surface, these findings might have resulted from better glycemic control in diabetic patients and could imply that glucose-lowering interventions should be considered in nondiabetic patients.

The findings from this review, however, are not conclusive. First, stress hyperglycemia was not uniformly defined. Second, the effect of cointerventions was not assessed. Third, the reported RRs were not adjusted for such baseline prognostic factors as the extent of stroke, deterioration within 48 hours of presentation, or hypertension.

Large prospective cohort studies of unselected patients with stroke, which are better suited to address the prognostic importance of baseline clinical and physiologic indices, have provided mixed results for the association between glucose level and outcome. In a study of patients with ischemic stroke (2), hyperglycemia was a questionable risk factor for mortality when adjusted for baseline prognostic factors (odds ratio = 1.007, CI 1.004 to 1.01). In another study of similar patients, the adjusted risk for a poor functional recovery increased by 28% for every 100-mg/dL increase in blood glucose levels ( $P = 0.03$ ) (3).

Clinical trials of glucose-lowering interventions in nondiabetic patients with stroke and stress hyperglycemia are ongoing. In the meantime, what should clinicians do when faced with a nondiabetic patient presenting with a stroke and hyperglycemia? It is reasonable to limit the use of glucose-containing intravenous fluids and investigate patients for impaired glucose tolerance or diabetes. Glucose-lowering therapy should be used with caution because inadvertent hypoglycemia can worsen a stroke and decrease the seizure threshold (4).

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