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Stroke mortality risk increased by hyperglycaemia

It is well recognised that the presence of diabetes increases the risk of coronary heart disease, more so in females than in males (Juutilainen et al, 2004). Controversy, however, continues to reign as to whether hyperglycaemia, in particular diabetes, contributes to risk of new and recurrent stroke.

A number of epidemiological studies have supported a notion that diabetes is a major risk factor for new and recurrent stroke (Tuomilehto et al, 1996; Hillen et al, 2003). In keeping with this notion, other studies demonstrated increasing incidences of stroke with elevation of blood glucose levels in patients without diabetes (Fuller et al, 1983). However, other studies have not been confirmatory of these findings (Rastenyte et al, 1996; Qureshi et al, 1998). A well-conducted systematic analysis examining mortality from ischaemic heart disease and stroke attributed to higher than optimal glucose values suggested that elevation of blood glucose levels measured by fasting glucose are significantly associated with stroke mortality (Danaei et al, 2006). Some of the controversy has been based on studies that have insufficient power in terms of patient numbers and cardiovascular endpoints, and indeed follow-up periods, to provide a more definitive examination of the link between hyperglycaemia and stroke mortality.

Stroke mortality in individuals with differing levels of hyperglycaemia, and indeed in the fasting or 2-hour post-glucose status, have been evaluated by the DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study group (Hyvärinen et al, 2009). The study was examining 11 800 men and 9860 women in 13 European cohorts, followed for a median of 10.5 years. Data were examined in terms of fasting, as well as 2-hour post-75 g oral glucose values. The analysis demonstrates that in people without a prior history of diabetes, a 1 standard deviation increase in fasting plasma glucose level causes an increase in their varied, adjusted, Cox proportional hazard ratio for stroke to 1.02 (95% confidence interval [CI] 0.83–1.25) and 1.52 (95% CI 1.22–1.88) in men and women respectively. For the 2-hour plasma glucose value the hazard ratio increased to 1.21 (95% CI 1.06–1.38) and 1.3 (95% CI 1.06–1.61), again in men and women respectively. Predictive value for stroke mortality was significantly increased in men with the addition of a 2-hour plasma glucose value to fasting glucose, but not in women. The addition of fasting plasma to 2-hour glucose value increased stroke mortality in women but not in men.

This analysis demonstrates that in people without diabetes an elevated 2-hour post-challenge glucose value is a better predictor than fasting plasma glucose in men, whereas fasting plasma glucose is better than 2-hour post-challenge glucose value in women as a predictor of stroke mortality. The results clearly demonstrate that diabetes, defined either by a fasting plasma glucose or a 2-hour glucose concentration, increases risk of stroke mortality. Thus, the data appear to provide more clear evidence for an increase in stroke mortality with hyperglycaemia, similar to that observed for coronary heart disease.

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- Danaei G, Lawes CM, Vander Hoorn S et al (2006) Global and regional mortality from ischaemic heart disease and stroke attributable to higher-than-optimum blood glucose concentration: comparative risk assessment. *Lancet* **368**: 1651–9
- Fuller JH, Shipley MJ, Rose G et al (1983) Mortality from coronary heart disease and stroke in relation to degree of glycaemia: the Whitehall study. *Br Med J (Clin Res Ed)* **287**: 867–70
- Hillen T, Coshall C, Tilling K et al (2003) Cause of stroke recurrence is multifactorial: patterns, risk factors, and outcomes of stroke recurrence in the South London Stroke Register. *Stroke* **34**: 1457–63
- Hyvärinen M, Qiao Q, Tuomilehto J et al (2009) Hyperglycemia and stroke mortality: comparison between fasting and 2-h glucose criteria. *Diabetes Care* **32**: 348–54
- Juutilainen A, Kortelainen S, Lehto S et al (2004) Gender differences in the impact of type 2 diabetes on coronary heart disease risk. *Diabetes Care* **27**: 2898–904
- Qureshi AI, Giles WH, Coft JB (1998) Impaired glucose tolerance and the likelihood of nonfatal stroke and myocardial infarction: the Third National Health and Nutrition Examination Survey. *Stroke* **29**: 1329–32
- Rastenyte D, Tuomilehto J, Domarkiene S et al (1996) Risk factors for death from stroke in middle-aged Lithuanian men: results from a 20-year prospective study. *Stroke* **27**: 672–6
- Tuomilehto J, Rastenyte D, Jousilahti P et al (1996) Diabetes mellitus as a risk factor for death from stroke. Prospective study of the middle-aged Finnish population. *Stroke* **27**: 210–15