

## **Evidence Based Medicine**

### **What modifiable risk factors lead to strokes in our part of the world?**

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#### **The Interstroke Study**

##### **Why is this study important and noteworthy?**

Stroke is the second leading cause of death worldwide and the leading cause of disability the world over. In the low and middle income countries like ours, stroke burden is the highest and it tends to affect a younger age group of individuals leading to a greater number of Disability Adjusted Life Years (DALYs) and hence a greater burden on an already strained health system. Therefore it is important to prevent these events from happening and for this a sound understanding of the risk factors for this devastating illness is necessary.

The INTERSTROKE study is the first of its kind designed to establish the association of traditional and emerging risk factors with stroke (and primary stroke subtypes) in countries of high, middle, and low income. It is an international multi center case control study.

##### **Who were the participants?**

Participants were recruited from 84 centers in 22 countries. A total of 3000 cases were recruited and there were 3000 controls. Cases were patients admitted to hospital with

first acute stroke. They were included if they presented within the first 5 days of onset, had imaging planned within one week of presentation and gave informed consent or surrogate informed consent. They were excluded if they had a non vascular cause for stroke, if they had a concomitant acute coronary syndrome or if consent could not be obtained.

Controls were based in hospital or community and had no history of stroke. They were age and sex matched and in some regions the ethnic origins were also matched. Hospital based controls were either patients admitted with diseases other than stroke or TIA or their relatives or visitors. Sources of community bases controls were not prespecified.

South East Asia contributed 1146 patients and India contributed 958 out of these 3000 cases. There were 422 cases from high income countries and 323 from Africa. Therefore there was a very good representation from this part of the world.

##### **What were the parameters of interest?**

Structured questionnaires were administered and physical examinations were undertaken to assess key risk factors in a similar manner for both groups of people. Risk factors that were assessed included waist hip ratio, Body

mass Index (BMI), hypertension (self reported as well as measured), Diabetes, Physical activity, alcohol intake, smoking status, Atrial fibrillation, flutter, and depression. For those who consented blood samples were taken to measure biochemical parameters.

### What were the findings?

Of the 3000 cases 2337 (78%) had ischaemic stroke and 663 (22%) had intracerebral haemorrhagic stroke. In all regions ischaemic strokes were more common than haemorrhagic strokes. About a seventh of the patients were less than 45 years of age with the highest proportion in Africa. Presumed primary etiology was small vessel disease in most of the patients. Cardioembolic cause accounted for a small proportion of patients in India and Southeast Asia, but a much larger proportion in high income countries and Africa.

Self reported history of hypertension was the strongest risk factor for stroke and the association was stronger for haemorrhagic strokes than for ischaemic strokes. The population attributable risk was 34.6% and increased further to 51.8% when the definition of hypertension included either self report or a BP value of >160/90. This association was even stronger in individuals younger than 45 years as compared to those older than 45 years.

The other important risk factors identified were smoking, abdominal obesity, sedentary lifestyle, Diabetes, alcohol intake, and abnormal lipids. The odds ratios and population attributable risk for each of these risk factors are given in the table.

Ratio of non- HDL to HDL cholesterol was associated with increased risk of ischaemic stroke but reduced risk of

intracerebral haemorrhagic stroke. Ratio of ApoB to ApoA1 was a stronger predictor of ischaemic stroke than was ratio of non-HDL to HDL cholesterol.

### What were the conclusions?

This study showed that five risk factors: hypertension, current smoking, abdominal obesity, diet, and physical activity accounted for greater than 80% of the global risk of all strokes. Hypertension was the most important risk factor for all stroke subtypes, and a more potent risk factor for intracerebral haemorrhagic stroke than for ischaemic stroke and especially important in people of 45 years or younger. There was a strong association between stroke risk and waist to hip ratio, but not with BMI. These investigators also report a consistent association between physical activity and reduction in risk of all strokes. There was a dose response association between number of cigarettes smoked and stroke risk particularly for ischaemic strokes. Their findings also suggest that risk rapidly reduces following smoking cessation.

This study provides new information on the relationship between apolipoproteins and stroke risk. There was a reduction in the risk of ischaemic stroke associated with increased ApoA1 and HDL cholesterol that was larger than the increase in risk associated with increased ApoB or non-HDL cholesterol.

### How does this impact our clinical practice?

The study provides important insight into the major risk factors for both ischaemic and haemorrhagic strokes. Its findings are particularly applicable to us as our region contributed large numbers to the study population. The study has identified the major targets for secondary stroke prevention for us. These include, in order of decreasing importance, hypertension, abdominal obesity, and sedentary lifestyle, abnormal lipids, particularly low HDL and smoking. By taking care of these major risk factors we can bring down the risk of strokes significantly in our part of the world.

### Recommended Reading

1. O'Donnell MJ, Xavier D, Liu L, et al, on behalf of the INTERSTROKE investigators. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet* 2010; published online June 18. DOI:10.1016/S0140-6736(10)60834-3.

Table.

Variable	Odds Ratio (95% CI)	Population Attributable Risk (95% CI)
Hypertension	3.89 (3.33-4.54)	51.8% (47.7-55.8)
Current Smoker	2.09 (1.75-2.51)	18.9% (15.3-23.1)
Waist to Hip Ratio	1.65 (1.36-1.99)	26.5% (18.8-36)
Regular Physical Activity	0.69 (0.53-0.90)	28.5% (14.5-48.5)
Diabetes Mellitus	1.36 (1.10-1.68)	5.0% (2.6-9.5)
>30 Drinks Per Month	1.51 (1.18-1.92)	3.8% (0.9-14.4)
Cardiac Causes	2.38 (1.77-3.20)	6.7% (4.8-9.1)
Ratio of Apo B to Apo A1	1.89 (1.49-2.40)	24.9% (15.7-37.1)