

PREVENTION OF STROKE

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INTRODUCTION

Stroke is the largest single cause of adult disability and the third leading cause of death in the Western World. Every year in Ireland about 8,500 patients are admitted to hospital with stroke and it is likely that a further significant number, particularly those with mild strokes or posterior circulation symptoms, do not present at all to hospital services or general practitioners.

To illustrate the scale of the problem, about one in four women can expect to suffer a stroke between the ages of 45 and 85.

There are about 30,000 people in Ireland living with the after-effects of stroke and, typically, stroke patients occupy about one-fifth of acute hospital beds and a quarter of long-stay beds. A recent UK National Audit Office report found that care of stroke patients costs the UK economy approximately £7 billion a year. Figures for Ireland are not available.

While clearly some risk factors for stroke are not modifiable — such as age, race and family history — there are many risk factors that are amenable to intervention.

HYPERTENSION

The single greatest risk factor for stroke, both ischaemic and haemorrhagic, is hypertension. High blood pressure results in increased formation of atheroma, increasing the risk of large vessel thrombosis and rupture, and also causes damage to the cerebral microvasculature, resulting in smaller lacunar infarctions. From the point of view of primary prevention, the combination of the results of several large population studies (n=420,000) have shown that the risk of stroke roughly doubles with every 7.5mmHg rise in diastolic blood pressure. On the other hand, treatment studies have shown that an average reduction in blood pressure of 5.8mmHg can reduce the risk of stroke by 42%.

Even isolated systolic hypertension represents a risk for stroke. The Systolic Hypertension in the Elderly (SHEP) study, in particular, showed that treating systolic hypertension, the primary aim being to reduce systolic blood pressure by at least 20mmHg, resulted in a 36% reduction in stroke incidence, equivalent to preventing six strokes per year per 1,000 treated. These results have been confirmed by the subsequent Systolic Hypertension

in Europe (Syst-Eur) and Swedish Trial in Old People with Hypertension (STOP) trials.

The only potential concern with the treatment of systolic hypertension is in the very elderly (80-85 years+), where there is a little evidence of an increased morbidity and mortality associated with hypertensive control, although incidence of stroke is reduced. This has been demonstrated recently by the preliminary results of the Hypertension in the Very Elderly Trial (HYVET); however, the trial is ongoing.

In terms of secondary prevention, two studies have demonstrated that reducing blood pressure in patients following stroke using the thiazide diuretic, indapamide, 2.5mg daily reduces risk of stroke recurrence by 28%. Perhaps most surprisingly, the Perindopril Against Recurrent Recurrent Stroke Study (PROGRESS), using a combination of perindopril and indapamide, showed that reducing the blood pressure of normotensive (BP<130/80) individuals also significantly reduced the risk of recurrent stroke.

HYPERTENSION, STROKE AND DIABETES

One of the most important findings of the large UK Prospective Study (UKPDS) was the huge importance of addressing vascular risk factors in diabetic subjects. It showed that the biggest single risk factor for developing stroke in diabetes was hypertension. Diabetics have up to four times the risk of stroke of non-diabetics.

About one-fifth of stroke patients have diabetes and more than three-quarters of people suffering stroke in the 35-44 year age group have insulin-dependent diabetes. A large component of this greatly increased risk is the effect of hypertension in diabetics. Hypertension affects about 30% of type 1 diabetics and 20-60% of type 2 diabetics, depending on age, ethnicity and obesity, and is between 1.5 and three times more common than in age-matched non-diabetic subjects.

The UKPDS- Hypertension in Diabetes Study (HDS) sub study, which looked at 'tight' control of blood pressure (aiming for BP<150/85), showed a 44% decrease in stroke incidence during follow-up, compared to controls. Again, treating isolated systolic hypertension in diabetics is very important. The Syst-Eur study showed that diabetic subjects in the placebo group had a stroke rate double that of

the non-diabetics. This was equivalent to a 69% increase in stroke incidence in diabetic subjects with systolic hypertension.

Increasing emphasis is now being given to checking people's blood pressure and maintaining it within fairly strict limits. Guidelines in the UK are that non-diabetics should have their BP kept below 140/90mmHg and diabetics to 130/85mmHg, with UK general practitioners rewarded for meeting targets with respect to blood pressure control.

ATRIAL FIBRILLATION

Atrial fibrillation affects less than 1% of people under 65, but more than 10% of those over 85 years of age. It increases the risk of stroke in patients with rheumatic heart disease by 17-fold and in those without rheumatic heart disease by around five-fold. In large studies, about 15% of strokes have typically been associated with atrial fibrillation and about 35% of patients with untreated atrial fibrillation will eventually have a stroke.

The risk increases with age and with co-morbidities so that, in an extreme case, an over-75-year-old with atrial fibrillation and a history of previous stroke/transient ischaemic attack (TIA), diabetes and heart failure will have a risk of stroke in the next 12 months of 33%. The advice from both the American Heart Association and the British Heart Foundation for preventing stroke from atrial fibrillation is nearly identical. Patients under 65 years with uncomplicated atrial fibrillation should be started on aspirin; otherwise patients should be anticoagulated, unless contraindicated. Anticoagulation with warfarin (international normalised ratio [INR] 2.0-3.0) reduces the risk of stroke in patients with atrial fibrillation by about 70%. In comparison, aspirin reduces the risk by about 30%.

CIGARETTE SMOKING

Smoking is an independent risk factor for both ischaemic and haemorrhagic stroke, and also for the development of carotid stenosis. On average, it increases a person's lifetime risk of stroke by about 50%. Men who smoke more than 20 cigarettes per day have 3.3 times the risk of stroke as non-smokers. In women this risk is worse, being 3.9 times higher in smokers of more than 20 cigarettes per day compared to controls. The risk, however, is reversible. The Framingham study showed that, within five years of quitting, a person's risk of stroke and cardiovascular disease returns to that of the general population.

Tragically, while in print stopping smoking seems an easy means of reducing stroke incidence, the addictive effects of tobacco are such that, even after having a stroke, only 15% of smokers stop smoking. The truly effective intervention is probably

to increase measures to stop people smoking in the first place.



PHYSICAL ACTIVITY

Physical activity is associated with lower rates of stroke in both men and women. The Framingham study showed that moderate physical activity significantly reduced the risk of stroke by more than half. Other studies have shown a similar effect in women. The effect may be moderated through beneficial effects on blood pressure and lipid profile.

STATINS AND STROKE

The effect of lipid control in the prevention of stroke is far less dramatic than that for ischaemic heart disease. Patients with established coronary disease are at high risk of the same benefit from cholesterol-lowering therapy in terms of prevention, by about nine strokes prevented for 1,000 patients treated for five years. Primary prevention with statins outside high-risk groups has not been found effective in preventing strokes.

The treatment of stroke patients with statins does not appear to prevent further strokes, but there is evidence that tight control of cholesterol (total cholesterol <5.0mmol/l) may reduce total vascular events to a degree (70 vascular events per 1,000 people treated for five years) and current guidance would be to try and lower total cholesterol below 3.5mmol/l in patients who have suffered ischaemic strokes.

SECONDARY PREVENTION

The people at highest risk of having a stroke or TIA are probably those who have already had one.

Patients suffering a TIA have been shown to have an 8% risk of a stroke in the week after, rising to 17.3% at three months. The risk in patients with mild stroke is even higher, with an 11% risk at seven days and an 18% risk at three months. In light of this, it is important that patients with these symptoms be seen and assessed quickly, and possibly the most effective way of achieving this is through a rapid access TIA or neurovascular clinic.

Currently, common practice for patients with TIA or minor stroke is either admission, waiting an extended period for review in a clinic or not being seen at all. TIA clinics typically have rapid access to scanning facilities, especially Doppler ultrasound of the carotid artery and brain imaging (CT or MR) when necessary. The clinic has the facility to initiate anti-platelet or anti-coagulant therapy rapidly, and permits rapid medical review by colleagues in vascular surgery, allowing a more efficient use of their time.

Current guidance in the UK is that patients suffering TIA should be seen in clinic within one week. However, this may be too long for some people and recently a group in Oxford published the ABCD score as a means of identifying individuals with high risk of further events in the following week (see Table 1).

CAROTID ENDARTERECTOMY

Internal carotid artery stenosis represents a significant risk factor for stroke. About 15% of stroke/TIA patients have a significant (>70%) ipsilateral stenosis of their carotid artery. Carotid endarterectomy in patients with stenosis greater than 70%, who have suffered an ischaemic event in the distribution of the carotid is associated with a 65% relative risk reduction (17% absolute reduction)

in terms of further stroke.

The number needed to treat to prevent one stroke is about 17 patients. There are a number of innovations being trialled currently in the treatment of carotid stenosis.

An increasing number of centres are using carotid stenting for a proportion of patients. This is especially useful for patients with intracranial stenoses not amenable to surgical intervention or patients less fit for open surgery. A large number of centres have also begun to perform carotid endarterectomies under local anaesthetic. The advantage of this approach is that it enables the surgeon to identify problems with cerebral hypoperfusion while operating. However, this is at the cost of an often significantly prolonged procedure. Studies comparing the two methods are underway.

The evidence for operating on asymptomatic carotids is not as definite.

There is some evidence that patients may gain some benefit if the procedure is carried out in units with very low complication rates, but the risk benefit analysis is by no means as conclusively in favour of treatment as for symptomatic disease.

CONCLUSION

The high incidence of stroke in Ireland is associated with an enormous cost, not just to the health services, but also to the victims. If we apply UK figures to Ireland, every stroke may cost the State on average about €45,000 over five years and the total cost to the health service is about 50% more than the cost of treating heart disease. Facilities for prevention, TIA clinics and access to vascular surgery services around Ireland are at best patchy and greater investment is needed to develop services. It would be, without any doubt, money well spent.

Table 1. ABCD Score (From Rothwell PM et al. *Lancet* 2005; 366: 29-36)

A	Age >60 years	1 point
B	Blood pressure >140/90	1 point
C	Clinical features	
	Unilateral weakness	2 points
	Isolated speech disturbance	1 point
D	Duration	
	10 minutes, <60mins	1 point
	>60 minutes	2 points

A score of <5 is associated with a one-week risk of stroke of <0.5 %.

A score of >5 is associated with a one-week risk of >25 % and probably merits admission.

Caution: While this scale is a helpful guide to management of TIAs, it does not cover such important features as recurrent events and symptoms of carotid/vertebral dissection (e.g. neck pain, sudden onset Horner's) and does not replace careful history and examination.