A Survey of Non-embolic Stroke in Adults under 50 Years of Age

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There have been many studies of non-embolic stroke in young adults from different parts of the world, including the USA[1-3], India[4,5], Kenya[6] and Scandinavia[7]. In spite of the widely differing populations studied and methods used, it is apparent that hypertension and age, as in older patients, are the most important identifiable risk factors. In all series a significant number of cases have no apparent cause. Surprisingly, at the time our investigation was begun, there had been no study in the UK of stroke specifically in young adults.

Methods

In an attempt to determine the causes of stroke in young adults we conducted a retrospective survey of completed stroke in patients under 50 years of age admitted to hospitals in the North East Thames Region between 1st January and 31st December 1980. The study was commissioned by the Research Group of the North East Thames Physicians Club.

All hospitals within the North East Thames Region, with one exception, co-operated in the study. Four hundred and fifty-three sets of case notes obtained through Hospital Activity Analysis under rubric codes 431-436 and 342 were reviewed and re-classified by us, excluding cases of subarachnoid haemorrhage, arteriovenous malformation, tumour and non-cerebrovascular disease. One hundred and thirty-three cases were excluded due to mis-coding, in addition to those admitted with an old stroke (48), transferred from a hospital outside the region (22), transferred to another hospital within the region (14) and those whose notes were unavailable (39). We also excluded 41 cases of transient ischaemic attacks, in which the neurological signs cleared within 24 hours, and 22 cases of cerebral emboli. The notes of 134 patients were available for further study at least one year after the stroke.

Patients were classified as hypertensive if this diagnosis was recorded or the diastolic blood pressure was greater than 110 mmHg on one reading, or greater than 100 mmHg on two readings. Information on possible risk factors, namely, smoking habits, high alcohol consumption, impaired glucose tolerance, hyperlipidaemia (fasting cholesterol > 6.7 mmol/litre, fasting triglyceride > 2.5 mmol/litre), high packed cell volume (men > 0.5, women > 0.45) and past history of cardiac and cerebrovascular disease were recorded if available.

Strokes were defined as haemorrhagic, thrombotic or of unknown type, depending on evidence from CAT brain scans, arteriography and postmortem information. A patient with a stroke and normal CAT brain scan was classified as having a thrombotic stroke.

Statistical analysis was by chi-squared tests.

Results

There were 88 males and 46 females who had suffered a stroke under 50 years of age. The estimated adult population served by the North East Thames Region hospitals (excluding the one not surveyed) is 1,669,300, which gives an annual incidence of 7.9/100,000 between 15-49 years. The number of cases increased as expected with each quintile, but the apparently more marked increase among the males, 45 per cent of whom were aged 45-49 years compared with 28 per cent of the women, was not significant (χ² = 3.73, P<0.1) (Fig. 1). Of the total, 56 patients (42 per cent) were hypertensive, 45 being men. The incidence of hypertension in men (51 per cent) was significantly greater than in women (24 per cent; χ² = 9.45, P<0.01). Hypertension had been previously diagnosed in 34 cases (61 per cent), 25 of the hypertensive men (56 per cent) and 9 of the hypertensive women (81 per cent), a difference that did not reach statistical significance (χ² = 2.55, P<0.2).

Analysis of 10 putative risk factors for stroke is recorded, comparing hypertensive and non-hypertensive groups (Table 1). The male to female ratio of hypertensive and non-hypertensive stroke in our study was 4.1:1.
unknown in 46 cases, 55 per cent of the hypertensive and 19 per cent of the non-hypertensive group ($\chi^2 = 18.88, P < 0.001$). There were in both groups, where the diagnosis was known, approximately twice as many cerebral infarcts as haemorrhage. At the time of study at least one year after the acute stroke there had been at least 28 deaths (21 per cent). There was no significant difference between the mortality of the hypertensive and non-hypertensive groups (22.2 per cent and 19 per cent respectively). However, of those known to have had a cerebral haemorrhage 10 (34.5 per cent) died compared with a mortality of 6 (10 per cent) for the cerebral infarction group ($\chi^2 = 5.1, P < 0.05$). Twelve (26 per cent) of the patients with unknown pathology also died.

**Discussion**

A study based on a retrospective survey of hospital case notes has obvious limitations, two major sources of error being death prior to admission and the management of milder cases at home. Nonetheless, our estimated incidence of stroke in those under 50 years of age of 7.9/100,000 is similar to that of 10.9/100,000 calculated from the figures of Brewis et al. [8], also based on case note review. In a more recent community-based study the incidence was 17/100,000 but this included patients up to 54 years of age as well as a small number of cases of subarachnoid haemorrhage [9]. In a recent study of stroke in people under 55 years of age based on in-patient records and death certificates, Arbuckle et al. [10] found annual age-specific hospitalisation rates of people aged under 35, 35-44 and 45-54 to be 3, 20 and 63 cases/100,000 respectively.

Hypertension is recognised as the single most important risk factor for stroke at all ages in both sexes of all racial groups studied [11,12]. The risk is graded according to blood pressure throughout its range. Not surprisingly, in view of differing populations and diagnostic criteria, the incidence of hypertension reported in series of stroke in young adults varies widely, from 19 per cent in India [5] to 41 per cent and 78 per cent in cerebral infarction and haemorrhage respectively in a largely black population in the USA [13]. Of our cases 56 (42 per cent) were hypertensive by our criteria, 34 of them (25 per cent of the total series) being previously known to have a raised blood pressure before the stroke, a figure close to that of 21 per cent noted by Arbuckle et al. [10], who did not record newly diagnosed hypertension. In an earlier prospective study 54 per cent of acute stroke patients in a hospital in the North East Thames Region were hypertensive and a majority (32 of 35) were previously diagnosed and in a large part poorly controlled [14].

Several risk factors (Table 1) apart from hypertension and age have been implicated in non-embolic stroke and have been recently reviewed by Kurtzke [15]. There is considerable controversy about which, if any, are dependent and important factors in stroke production and Kurtzke dismisses the evidence that body weight, blood cholesterol, lipids and the contraceptive pill are implicated. Sex appears to play a small part, the incidence of stroke, especially in younger age groups, being higher in

**Table 1. Risk factors.**

|                  | Hypertensive n = 56 | Non-hypertensive n = 78 |
|------------------|---------------------|-------------------------|
| Smoking          | 31/45 (69%)         | 38/64 (59%)             |
| Diabetes mellitus| 5/51 (10%)          | 7/75 (9%)               |
| High PCV         | 7/48 (15%)          | 9/67 (13%)              |
| High cholesterol | 1/16 (6%)           | 3/19 (16%)              |
| High triglyceride| 4/16 (25%)          | 2/19 (11%)              |
| Previous cerebrovascular disease | 12/53 (23%) | 14/73 (19%) |
| Previous cardiovascular disease | 3/54 (7%) | 11/73 (15%) |
| Alcohol*         | 14/56 (25%)         | 12/78 (13%)             |
| Age 40–49 years  | 49/56 (88%)         | 41/78 (53%)             |
| Male:female      | 45:11               | 43:35                   |

*Alcohol intoxication or known regular large consumption of alcohol.

*(P<0.001) and 1.2:1 (P<0.1) respectively. Of the hypertensive patients 88 per cent were between 40 and 49 years, significantly more than in the non-hypertensive group (53 per cent, P<0.001). Although the data base is incomplete there was no obvious difference in the prevalence of any other single factor between the two groups and no suggestion that the non-hypertensive patients had an excess of these factors. Information was not available on the number and distribution of different racial groups in the analysis of these risk factors. A diagnosis of syphilitic arteritis was made in two male patients and sarcoidosis and an unspecified connective tissue disorder in two others. In one patient leukaemia resulted in a cerebral haemorrhage.

A pathological diagnosis was made in 88 cases (66 per cent) on the basis of CAT brain scans (77 cases), arteriography (34 cases) and postmortem. The diagnosis was
men than women[15]. This is apparent also from the Framingham data[16], the incidence of stroke in the 45-54 age group being 1.8:1 male:female. In this study there were four times as many men as women in the hypertensive group but no sex difference in the non-hypertensive group. The hypertensive group was also older than the normotensive group. However, there was no significant difference between the other putative risk factors composing the hypertensive and non-hypertensive groups. We believe that, in the non-hypertensives, the nature of the vascular disease is unclear and cannot be dismissed as atherosclerotic. As Warlow[17] states in his review of the causes of stroke in young people, 'there is a proportion of stroke patients in whom no cause can be demonstrated and it is better to be honest and admit this than to talk vaguely about premature degenerative arterial disease'.

In two studies from the USA[3,18] this proportion amounted to about 20 per cent of cases of acute brain infarction when all known hypertensive, cardiac, oestrogen-related and systemic diseases had been excluded. Critchley[19] has recently reviewed the many non-atherosclerotic, non-hypertensive causes of stroke, only five of which were diagnosed in our series.

The contribution of alcohol intake to stroke by a hypertensive or other mechanism is of current interest[20,21]. A history of alcoholism or acute alcohol intoxication at presentation was noted in one in five of our cases with a higher, but not significantly so, incidence in the hypertensive patients. However, the importance of alcoholism in acute stroke in young (and older) patients will only be determined in prospective studies.

This study highlights the need for better control as well as earlier diagnosis of hypertension, especially in men[22]. It also identifies another large group of patients who do not have any obvious underlying risk factors. A clearer knowledge of the underlying pathology obtained by modern non-invasive techniques and detailed studies of the contribution of coagulation and haemorrhage disorders, is needed in this group of patients.

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