ORIGINAL ARTICLES

Epidemiological Aspects of Referral to TIA Clinics in Glasgow

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ABSTRACT

A retrospective cohort study was carried out of new referrals to transient ischaemic attack (TIA) clinics in Glasgow. The aims of the study were to describe the profile of referrals and to assess the odds ratios for TIA, minor stroke or amaurosis fugax of both cardiovascular risk factors and clinical features.

In total, data were collected for 813 new referrals in a period of six months. Thirteen point eight percent of referrals were from other Health Boards. The overall referral rate among residents of Greater Glasgow NHS Board was 165.6 per 100,000 per year. About 20% of referrals were made by clinicians in secondary care. The specialties from which referrals were most commonly made were accident and emergency, general medicine, ophthalmology and geriatric assessment. The most common risk factors in patients referred were hypertension (52.9%), smoking (31.7%), ischaemic heart disease (22.7%) and former smokers (22.4%). The most common clinical features were hemiparesis (13.3%), weakness of an upper limb (8.7%), vertigo (7.9%) and dysphasia (7.3%). In 48.7% of cases, a non-cerebrovascular diagnosis was made.

Separate multivariate models were established for risk factors and clinical features. In the model for risk factors, five factors were significant for risk of TIA, stroke or amaurosis fugax. These were hyperlipidaemia, age over 64 years, hypertension, smoking and ex-smoking. In the model for clinical features, five factors were also significant. These were visual field defect, speech defact, facial weakness and hemiparesis.

Introduction

Stroke is an important problem in the public health of all western countries. Stroke accounts for more than 1,000 deaths in Glasgow each year and is now the second most important single cause of death.[1] A transient ischaemic attack (TIA) is defined as an episode of temporary and focal cerebral dysfunction of vascular (occlusive) origin that is rapid in onset and of variable duration, ordinarily lasting 2 to 15 minutes but rarely as long as one day.[2] In some cases, a minor stroke may occur in which the clinical features disappear rapidly, but last more than 24 hours. In about 15% of cases, a major ischaemic stroke is preceded by a TIA.[3]

The importance of recognising and treating TIA lies in the fact that the risk of a major ischaemic stroke is greatly increased in the aftermath of the more minor cerebrovascular event. In the Oxfordshire Stroke Study, the risk of stroke was estimated at 11% in the first year after a TIA and 5% in each succeeding year,[4] but considerably greater levels of risk have been described in more recent studies. Estimates of risk at 90 days after a TIA have ranged from 10 to 17%.[5,6,7] In one of these studies, the incidence of stroke was found to be as high as 8% in the first 7 days after a TIA.[6] These results underline the importance of rapid referral and assessment of patients who may have sustained a TIA.

Secondary prevention is an important component of a stroke service, and a range of effective interventions is currently available for the secondary prevention of stroke.[8] In addition, the requirement for secondary prevention has been recognised in the development of secondary prevention clinics, or TIA clinics,[9] designed specifically for the rapid assessment and treatment of patients who may have sustained a TIA. Although TIA clinics have now been established in most acute general hospitals, there have been relatively few studies of activity or of the epidemiological characteristics of referrals.[10] For this reason, a study was undertaken to describe overall patterns of activity and to identify the risk for TIA or minor stroke associated with both the cardiovascular risk factors and clinical features.

Methods

Ascertainment

The study was a retrospective cohort study of new referrals to any of the TIA clinics in Glasgow between 1st January 2003 and 30th June 2003. Cases were identified from lists of patients who had been appointed to the clinics. These lists were obtained either from consultant physicians or from hospital medical records departments.

Data Collection

Data were collected directly from case records and

recorded in a specially designed collection form. Data were collected about demographic factors, referral, risk factors, clinical presentation, investigations and diagnosis.

Data Preparation

The data were coded and keyed into a database in Microsoft Access. The ICD10 Classification of Disease[11] was used for coding both reasons for referral and diagnoses. Missing items of data were coded by allocating 'missing data' codes. The quality of the data was checked by manual comparison of each electronic record in Access with the corresponding data collection form. The final version of the dataset was later transferred to SPSS© for analysis.

Populations

The source of information about the population of Greater Glasgow NHS Board (GGNHSB) was the Registrar General's mid-year estimate of populations, derived from the Decennial Census of 2001.[12] The Carstairs Index[13] was used as the indicator of material deprivation. The Carstairs Index is derived from data collected in the Census, and has seven categories which range from 1 (most affluent) to 7 (most deprived). The code is applicable at the level of postcode sector.

Cases and Controls

The univariate and multivariate analyses were carried out by defining case and control subjects. Cases were defined to be patients with a new diagnosis of TIA, stroke or amaurosis fugax, and controls were defined to be patients with all other diagnoses.

Statistical Analysis

Standardisation of rates and calculation of univariate odds ratios were carried out in the Microsoft Excel package. Multivariate logistic regression was carried out in the SPSS package. Standardisation of referral rates was carried out by the indirect method. This allows calculation of a standardised referral ratio, which is analogous to the commonly-used standardised mortality ratio (SMR). The referral ratio allows the referral experience in different populations to be compared with that in the standard population, in this case, the population of Greater Glasgow NHS Health Board (GGNHSB). The referral ratio in Glasgow is, by definition, 100.

Results

Referrals

In total, 840 new referrals were made to TIA clinics in Glasgow in the first six months of 2003. Of these, 15 patients failed to attend and the notes were not available for 12 other patients. Case notes were available for 813 of the 825 patients who attended the clinic, an ascertainment rate of 98.5%. A correction factor of 1.033 was applied globally to calculate the absolute referral rates cited in the report.

Together, the age-groups 45-64 years and 65-84 years accounted for about 35.5% and 48.8% respectively of all referrals. In total, 13.8% of all referrals were from the populations of boards other than GGNHSB. The importance of this is that only referrals from the defined population of GGNHSB could be used to calculate referral rates. The overall referral rate was 165.6 referrals per 100,000 per year (Table 1). The referral rate was greatest, 610 per 100,000 per year, in the population aged 65 to 84 years.

Table I Referral Rate (per 100,000) to TIA Clinics

Age	Males	Females	Total
<25	0.0	7.6	3.8
25-44	41.5	51.0	46.5
45-64	260.0	248.1	253.9
65-84	701.4	548.6	610.1
>84	693.1	369.3	447.8
Total	**162.7**	**168.3**	**165.6**

The difference in level of referral between the more and less deprived areas of the population may be expressed as a ratio. The value of the ratio for the entire population would be 100. Referral ratios standardised for age and sex were calculated for the population of GGNHSB respectively in deprivation categories 1 to 4 and 5 to 7. The ratio for categories 1 to 4 was 83.1, and the confidence interval was (72.7, 93.5). The ratio for the three most deprived categories was 112.6, and the confidence interval was (102.2, 124.0).

Source of Referral

Of the total number of attendances, 655 (81%) resulted from direct referral by a primary care physician. The remaining 158 attendances (19%) were the result of referral by doctors in hospital specialties. The five specialties which accounted for most of the referrals from hospital were accident and emergency (28.5%), general medicine (24.1%) ophthalmology (20.9%), geriatric assessment (12%) and neurology (5.6%).

Risk Factors

The risk factor that was most prevalent in patients referred

to TIA clinics was history of hypertension. About 53% of all patients had a history of either treated or untreated hypertension. The four next most frequent risk factors were smoking (31.7%), hyperlipidaemia (17.2%), ischaemic heart disease (22.7%) and previous smoking history (22.4%). Other risk factors were history of previous stroke or TIA (20.7%), diabetes mellitus (11.7%), alcohol abuse (9.5%), atrial fibrillation (7.0%), peripheral vascular disease (6.0%) and history of other cardiac disease (4.4%).

Clinical Presentation

Patients presented to TIA clinics with a wide range of clinical presentation. The commonest presentations were hemiparesis (13.3%), weakness of an upper limb (8.7%), vertigo (7.9%), dysphasia (7.3%) and hemiparaesthesia (4.7%).

Diagnosis

A diagnosis of TIA, stroke or amaurosis fugax was made in only 51.4% of referrals (Table II). In almost half of the referrals, an alternative diagnosis was made. The most common alternative diagnoses included migraine, syncope, neuropathy, seizure and anxiety (Table III).

Table II Diagnostic Categories by Health Board of Residence

Category	Health Board of Residence		
	GGNHSB	Other	Total
TIA	198	19	217 (26.8%)
Stroke	150	16	166 (20.5%)
Amaurosis fugax	28	5	33 (4.1%)
Other	324	71	395 (48.7%)
Total	**700**	**111**	**811 (100%)**

Univariate Odds Ratios

Both univariate and multivariate analyses were carried out by defining cerebrovascular cases as patients with a new diagnosis of TIA, stroke or amaurosis fugax. All others were defined as controls. The univariate odds ratios and associated confidence intervals for risk factors are shown in Table IV. The odds ratios were greater than one and significant for peripheral vascular disease, hyperlipidaemia, age, hypertension, atrial fibrillation, smoking, history of stroke or TIA, ex-smoking history and male sex. The risk factors for alcohol excess, diabetes and history of other cardiac disease were not significant.

Univariate odds ratios and associated 95% confidence intervals for clinical features are shown in Table V. The odds ratios were greater than one and significant for speech defect, visual field defect, facial weakness and hemiparesis, and less than one and significant for blurred vision, vertigo and visual disturbance. The risk factors for hemiparaesthesia, diplopia and ataxia were not significant.

Table III Diagnostic Categories other than TIA, Stroke or Amaurosis Fugax

Diagnosis	No.	%
Migraine	35	8.9
Syncope	30	7.7
Peripheral neuropathy	17	4.3
Seizure	16	4.1
Postural hypotension	14	3.6
Cervical spondylosis	14	3.6
Anxiety	13	3.3
Dementia	11	2.8
Middle ear disease	11	2.8
Brain tumour	9	2.3
Transient global amnesia	8	2.0
Occluded retinal artery	7	1.8
Arrythmia	5	1.3
Sequelae previous stroke	4	1.0
Motor neurone disease	3	0.8
Multiple sclerosis	3	0.8
Parkinson's disease	3	0.8
Asymptomatic stenosis of carotid artery	3	0.8
Benign paroxysmal positional vertigo	2	0.5
Epilepsy	2	0.5
Depression	1	0.3
Oversedation	1	0.3
Trigeminal neuralgia	1	0.3
Others	179	45.7
Total	**392**	**100.0**

Table IV Odds Ratios for Risk Factors (Univariate Analyses)

Risk factor	Point estimate and 95% Confidence interval
History of PVD	2.88 (1.51, 5.48)
Hyperlipidaemia	2.10 (1.54, 2.88)
Age over 64 years	2.03 (1.53, 2.69)
Hypertension	2.00 (1.51, 2.64)
Atrial fibrillation	1.85 (1.04, 3.41)
Smoking	1.66 (1.23, 2.25)
History of TIA or stroke	1.60 (1.13, 2.27)
Ex-smoker	1.47 (1.05, 2.05)
Male sex	1.42 (1.07, 1.88)
History of IHD	1.30 (0.93, 1.81)
Alcohol excess	1.17 (0.73, 1.89)
Diabetes	1.15 (0.74, 1.79)
History of other cardiac disease	0.90 (0.45, 1.79)

Multivariate Regression

Separate multivariate logistic regression models were constructed for risk factors and clinical features respectively. Only the variables that had been found to be significant in the univariate analysis were included in multivariate models. The results of these models are shown in Tables VI and VII. In the multivariate model for risk factors, five of the original variables were found to be

Table V Odds Ratios for Clinical Features (Univariate Analyses)

Clinical feature	Odds ratio (95% confidence interval)
Speech defect	4.15 (2.73, 6.33)
Visual field defect	3.96 (1.58, 9.90)
Facial weakness	3.33 (1.78, 6.22)
Hemiparesis	2.57 (1.68, 3.93)
Blurred vision	0.42 (0.19, 0.91)
Vertigo	0.36 (0.23, 0.57)
Visual disturbance	0.28 (0.13, 0.59)
Hemiparaesthesia	1.65 (0.95, 2.78)
Diplopia	0.52 (0.21, 1.32)
Ataxia	0.50 (0.17, 1.47)

Table VI Odds Ratios for Risk Factors (Multivariate Analyses)

Variables	Odds ratio (95% confidence interval)
Hyperlipidaemia	2.34 (1.67, 3.28)
Age over 64 years	2.37 (1.73, 3.24)
Hypertension	1.67 (1.24, 2.26)
Smoking	2.65 (1.86, 3.78)
Ex-smoking	2.08 (1.42, 3.05)

Table VII Odds Ratios for Clinical Features (Multivariate Analyses)

Variables	Odds ratio (95% confidence interval)
Visual Field Defect (VFD)	5.56 (2.05,15.05)
Speech defect	4.24 (2.70, 6.68)
Facial Weakness	3.38 (1.71, 6.69)
Hemiparesis	2.96 (1.89, 4.64)

significant. These were hyperlipidaemia, age over 64 years, hypertension, smoking and ex-smoking. In the multivariate model for clinical features, four of the original variables were also found to be significant. These were speech defect, visual field defect, facial weakness and hemiparesis.

Discussion

The case-records were available for 98.5% of the 825 patients who attended the clinic. In 15 cases, the patient did not attend at all, although multiple appointments were offered. In general, non-attendance at clinics is often viewed as an administrative problem whose main consequence is waste of clinic time, but in regard to TIA clinics, non-attendance may have more serious implications. In one study,[5] about one half of the strokes that occurred within 90 days of a TIA were within the first three days. This underlines the need for rapid assessment and treatment after a TIA. Patients who fail to attend, or who fail to attend for the first appointment offered, may incur a greater risk of a disabling stroke.

Almost one half of the patients were aged 65 to 84 years and 35.5% were aged 45 to 64 years. This demographic profile reflects the fact that cerebrovascular disease is primarily a condition of the elderly population, and that age is one of the most important non-modifiable risk factors for stroke and TIA.[14]

Source of Referral

About 80% of all new referrals were made by primary care physicians. This reflects the most common method of presentation, in which patients initially consult a primary care physician. In the remaining 20% of cases, the referral was made by a clinician in secondary care. The hospital specialties from which referrals were most commonly made reflect alternative modes of presentation and the diversity of clinical presentation associated with stroke or TIA. For example, a substantial number of patients attend an A&E department after a TIA, instead of making an appointment to see a primary care physician, and most of the referrals from ophthalmology reflect the frequency of amaurosis fugax and other ocular symptoms in presentations associated with TIA or stroke. These factors may result in circuitous pathways of referral, in which an initial referral to a hospital specialty is followed by a second referral to a TIA clinic. The delay in referral may be important in view of the risk of a second cerebrovascular event soon after an initial TIA.[5]

Clinical Features

Patients presented to TIA clinics with a wide range of clinical features. These reflected not only the classical presentations of TIA and stroke but also the symptoms of a wide range of other pathology. Hemiparesis, weakness of the upper limb, vertigo, dysphasia and hemiparaesthesia were the commonest presenting features. Although these are among the classical presentations of stroke,[15] they are non-specific. Some patients presented with other clinical features that are uncommon features of TIA or stroke, including headache and loss of consciousness.

Diagnosis

A diagnosis of TIA, stroke or amaurosis fugax was made in only 51.4% of referrals. In almost half of the referrals, an alternative diagnosis was made. This reflects the range of pathology in the group of patients referred, a finding that has been reported in other studies of referrals to TIA clinics.[10] The pathology included relatively common conditions, for example, migraine, and also small numbers of cases of less common conditions, for example, motor neurone disease and multiple sclerosis. This underlines the

degree of clinical suspicion that is necessary for medical staff in TIA clinics to maintain.

Risk Factors and Clinical Features

In this study, a case-control methodology was employed to calculate both univariate and multivariate odds ratios for TIA, stroke or amaurosis fugax for vascular risk factors and clinical features. The most serious methodological limitation of the case-control methodology is bias due to differential recall of information of possible prognostic importance by case and control subjects. This is unlikely to have been significant in the present study, either in respect of clinical features or risk factors, for a number of reasons. Most importantly, the period between the event and attendance at the clinic was relatively brief, usually not more that a few weeks, so that recall of clinical features was likely to have been accurate. Information about clinical features was also supplied by primary care physicians and other referring clinicians by whom patients were usually seen soon after the event. Lastly, most referrals were made because of neurological features of some kind. There was no reason to assume differential recall on the part of patients who subsequently fell into different diagnostic groups. It was considered that information about different risk factors was unlikely to be a source of bias, because information was available in the referral notes and case-records as well as from patients themselves.

The significance of the two types of analysis was different. The aim of the analysis in relation to risk factors was to define the epidemiological importance of each factor for the risk of TIA, stroke or amaurosis fugax. The aim of the analysis in relation to clinical features was to assess the degree of association of the features with the presence of a new lesion.

In the univariate analysis of risk factors, eight risk factors were found to significantly increase the risk of an ischaemic lesion, but only five remained significant in the multivariate analysis. These were hypertension, hyperlipidaemia, age over 64 years, smokers and former smokers. The results of the multivariate analysis were broadly similar to those of previous studies.[16, 17] For example, the estimates of odds ratio associated with hypertension in the current study and in the study by Whisnant et al were respectively 1.67 and 1.80. Differences in these estimates may reflect different methods of selection of cases and controls. In the current study, both cases and controls were represented by patients referred to a TIA clinic. In the Whisnant study[16], cases and controls were selected from a population register so that both groups represented approximately a random sample from case and control subjects.

In the univariate analysis, seven clinical features were found to be significantly associated with a diagnosis of TIA, stroke or amaurosis fugax. Only four of these remained significant in the multivariate analysis. These were visual field defect, speech defect, facial weakness and hemiparesis. This appears to be the first study set in a TIA clinic in which odds ratios have been calculated for clinical features. The probability of a TIA-related diagnosis would be different in patients with different combinations of clinical features, so that groups could be defined in which the proportions of TIA-related diagnoses could be expected to be high, average or low.

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