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Case-control study of stroke and the quality of hypertension control in north west England

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Abstract

Objective: To examine the risk of stroke in relation to quality of hypertension control in routine general practice across an entire health district.

Design: Population based matched case-control study.

Setting: East Lancashire Health District with a participating population of 388 821 aged ≤ 80 .

Subjects: Cases were patients under 80 with their first stroke identified from a population based stroke register between 1 July 1994 and 30 June 1995. For each case two controls matched with the case for age and sex were selected from the same practice register. Hypertension was defined as systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 95 mm Hg, or both, on at least two occasions within any three month period or any history of treatment with antihypertensive drugs.

Main outcome measures: Prevalence of hypertension and quality of control of hypertension (assessed by using the mean blood pressure recorded before stroke) and odds ratios of stroke (derived from conditional logistic regression).

Results: Records of 267 cases and 534 controls were examined; 61% and 42% of these subjects respectively were hypertensive. Compared with non-hypertensive subjects hypertensive patients receiving treatment whose average pre-event systolic blood pressure was controlled to < 140 mm Hg had an adjusted odds ratio for stroke of 1.3 (95% confidence interval 0.6 to 2.7). Those fairly well controlled (140-149 mm Hg), moderately controlled (150-159 mm Hg), or poorly controlled (≥ 160 mm Hg) or untreated had progressively raised odds ratios of 1.6, 2.2, 3.2, and 3.5 respectively. Results for diastolic pressure were similar; both were independent of initial pressures before treatment. Around 21% of strokes were thus attributable to inadequate control with treatment, or 46 first events yearly per 100 000 population aged 40-79.

Conclusions: Risk of stroke was clearly related to quality of control of blood pressure with treatment. In routine practice consistent control of blood pressure to below 150/90 mm Hg seems to be required for optimal stroke prevention.

Introduction

The continuous relation between the blood pressure level and risk of subsequent stroke provides much of the impetus for measuring blood pressure in primary care.¹⁻⁵ Similarly, the benefit in reducing stroke in trials of treatment is that predicted from observational studies.⁶ However, to what extent that potential benefit is realised in routine clinical practice is much less clear. In hospital attenders blood pressure achieved with treatment rather than the initial blood pressure determined the risk of stroke.^{7,8} Few studies in routine primary care have examined either the question of what constitutes "hypertension" in relation to stroke or the quality of control of previously treated blood pressure in stroke cases.⁹⁻¹³ Both factors are likely to account for much of the population stroke risk that should be preventable on current evidence. Using a population based stroke register maintained fully for one calendar year, we tried to determine the relation between the risk of stroke and the quality of control of hypertension in routine general practice across an entire health district. The study setting in the community also allowed those stroke patients not admitted nor ever seen at a hospital to be included, so providing a representative sample in which to examine the link between stroke and blood pressure.

Subjects and methods

The study was in east Lancashire, a health district including the towns of Blackburn and Burnley, with a total population of 534 287 in the 1995 general practice register. Stroke cases were identified from a district wide, population based stroke register between 1 July 1994 and 30 June 1995 with 103 of 118 general practices participating. Cases from a further 10 (8%) practices were inconsistently notified or verified, so the total practice inclusion rate was 79% (93 practices). These practices served a population of 405 272, of whom 388 821 were under 80 years of age (161 978 aged 40-79 years), the denominator for the study.

A case-control design was used, restricted to patients aged under 80 with their first ever strokes because strokes below this age can be regarded as preventable.^{14,15} The main hypothesis was that there was a difference in risk of stroke between hypertensive patients who were treated but not well controlled and

those well controlled as well as subjects who were non-hypertensive. We used an arbitrary definition of hypertension ($\geq 160/95$ mm Hg)¹⁶ likely to be in routine use before the study and assumed the prevalence of treated hypertensive patients who were not well controlled ($\geq 150/90$ mm Hg) to be 14% of the population aged under 80. Applying these variables showed that 220 cases and 440 controls were required to detect an odds ratio of 2 compared with non-hypertensive subjects with 80% power when using a two sided α level of 5%. For each case two controls matched with the case for sex and age (within two years) and without a history of stroke were selected from the same practice register.

All blood pressure readings with the dates and drug treatment before the index date of stroke were recorded from the notes or the practice computer. The classification of who met definitions of "hypertension" was conducted on computer blind to case or control status. Each set of notes was also systematically searched for other known prespecified risk factors.

Hypertension was defined as above blood pressure levels on two or more occasions within any three month period or a history of antihypertensive treatment at any time. Baseline blood pressure was either the average of these two readings if they met the criteria for hypertension or the blood pressure immediately before treatment first started if the criteria had not been met at that time. The quality of hypertension control was assessed by using the mean blood pressure recorded in the last one, three, and five years before the

index date. Treated hypertension was defined from the documented use (prescription) of drugs appropriate for hypertension.

Analysis—Matched case-control analysis was by conditional logistic regression,¹⁷ odds ratios being used to determine associations. Population attributable risk was calculated as the difference between overall risk in the population and the population risk that might be achieved if blood pressure were maintained at the "well controlled" level, divided by overall risk in the population. This was calculated in the population aged over 40 years because strokes are rare in people under 40.

Results

Stroke register—Of 1233 notifications from multiple sources, 932 were confirmed strokes. Of these, 642 were first ever strokes, 363 occurring in people under 80 (355 aged 40-79 years). Only the first 267 (74%) of the 363 formed the cases, as this number met power requirements and resources did not allow collection of two controls for the remaining 96 cases. However, these 96 cases were similar to the cases included: case fatality at 28 days was 25.1% for the 267 cases compared with 25.3% for the 363; age and sex distribution was also similar.

Prevalence—Comparing the characteristics of cases and controls showed a significantly higher prevalence of smoking, transient ischaemic attack, atrial fibrillation, and diabetes in cases (table 1). Occasional

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Table 1 Characteristics of cases and controls. Except where stated otherwise figures are numbers (percentages) of subjects

Characteristic	Cases (n=267)	Controls (n=534)	Crude odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)†
Mean (SD), median age (years)	67 (9.9), 69.0	67 (9.9), 69.5		
Mean (SD), median systolic/diastolic blood pressure in last five years (mm Hg)	151.0 (19.4), 151.0/85.1 (9.4), 85.0	145.6 (17.5), 144.5/82.6 (8.0), 82.5		
Non-smokers	72 (36.4)	203 (53.7)	1	1
Former smokers	48 (24.2)	79 (20.9)	1.7 (1.1 to 2.7)	1.5 (0.9 to 2.6)
Current smokers:				
<20 cigarettes/day	46 (23.2)	56 (14.8)	2.4 (1.5 to 3.9)	2.7 (1.5 to 4.9)**
≥ 20 cigarettes/day	22 (11.1)	23 (6.1)	2.7 (1.4 to 5.3)	2.9 (1.4 to 6.3)**
Amount unknown	10 (5.1)	17 (4.5)	1.6 (0.7 to 3.7)	1.4 (0.5 to 3.9)
Missing data on smoking	69 (25.8)	156 (29.2)	1.2 (0.8 to 1.9)	1.4 (0.8 to 2.5)
Non-drinkers	52 (44.5)	71 (22.8)	1	1
Occasional drinkers	30 (19.4)	96 (30.8)	0.4 (0.2 to 0.7)	0.3 (0.2 to 0.6)**
Regular drinkers:				
<20 U/week	39 (25.2)	108 (34.6)	0.5 (0.3 to 0.8)	0.4 (0.2 to 0.7)**
20-29 U/week	14 (9.0)	19 (6.1)	1.0 (0.5 to 2.2)	0.9 (0.4 to 2.2)
≥ 30 U/week	11 (7.1)	8 (2.6)	2.0 (0.7 to 5.2)	1.9 (0.6 to 5.8)
Amount unknown	9 (5.8)	10 (3.2)	1.2 (0.5 to 3.3)	1.4 (0.4 to 4.1)
Missing data on alcohol intake	112 (41.9)	222 (41.6)	0.7 (0.4 to 1.5)	0.8 (0.4 to 1.5)
Past medical history of:				
Transient ischaemic attack	29 (10.9)	14 (2.6)	4.6 (2.3 to 9.1)	4.1 (1.9 to 8.7)**
Myocardial infarction	28 (10.5)	32 (6.0)	1.9 (1.1 to 3.2)	1.3 (0.6 to 2.7)
Atrial fibrillation	32 (12.0)	12 (2.2)	6.6 (3.2 to 14.0)	5.4 (2.3 to 12.5)**
Diabetes	44 (16.5)	37 (6.9)	2.4 (1.6 to 3.8)	2.0 (1.2 to 3.4)**
Angina	53 (19.9)	73 (13.7)	1.6 (1.1 to 2.4)	0.9 (0.5 to 1.5)
Obesity	31 (11.6)	31 (5.8)	2.2 (1.3 to 3.8)	1.4 (0.7 to 2.6)
Migraine	23 (8.6)	32 (6.0)	1.5 (0.8 to 2.6)	1.2 (0.6 to 2.4)
Family history of stroke	18 (6.7)	44 (8.2)	0.8 (0.5 to 1.4)	0.9 (0.4 to 1.8)
Family history of myocardial infarction	27 (10.1)	47 (8.8)	1.2 (0.7 to 1.9)	1.2 (0.7 to 2.2)

†Odds ratios were adjusted for smoking, alcohol intake, past medical history of transient ischaemic attack, myocardial infarction, atrial fibrillation, diabetes, angina, obesity, migraine, family history of stroke, and family history of myocardial infarction.

** $P < 0.05$.

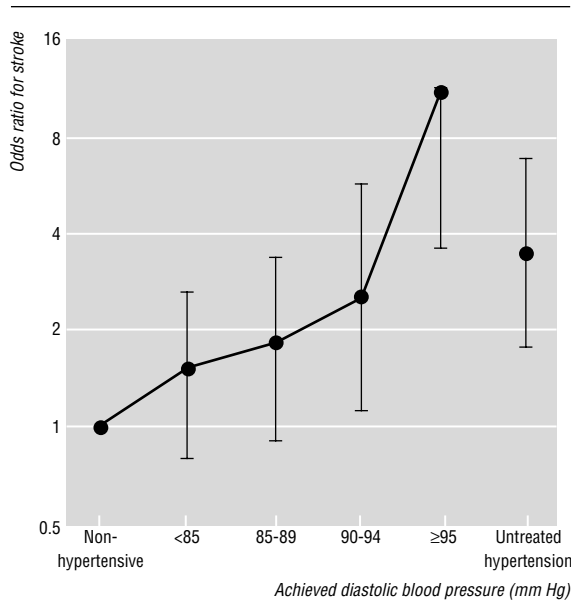


Fig 1 Odds ratios for stroke in relation to average diastolic blood pressures achieved with treatment in last five years before stroke (bars are 95% confidence intervals)

drinking and regular light drinking had protective effects. There was no significant impact of other recorded factors. Sixty one per cent (157/258) of stroke cases were hypertensive compared with 42% (212/499) of controls. The adjusted odds ratio for stroke due to hypertension was 2.5 (95% confidence interval 1.7 to 3.9). The prevalence of hypertension increased with age and was higher in women.

Effects of blood pressure control—Compared with non-hypertensive subjects, hypertensive patients whose average systolic blood pressure in the last five years before the index date was well controlled to below 140 mm Hg or fairly well controlled to 140-149 mm Hg had insignificantly raised odds ratios (table 2). Hypertensive patients whose systolic blood pressure was moderately controlled (150-159 mm Hg) or poorly controlled (≥ 160 mm Hg) or untreated had progressively raised risks. Odds ratios for well controlled diastolic pressure (< 85 mm Hg), fairly well controlled diastolic pressure (85-89 mm Hg), moderately controlled diastolic pressure (90-94 mm Hg), and poorly controlled (≥ 95 mm Hg) and untreated diastolic pressure were generally similar to those for systolic pressure in size and trend (fig 1). Risk was also similar for blood pressure levels achieved in the last one and three years before the index date (data not shown) but was strongest and most consistent in the last five years. Patients with no blood pressure readings recorded in the last five years had over five times the risk for stroke with wide confidence intervals. Systolic and diastolic blood pressures were highly correlated. After adjusting each for the effect of the other adjusted odds ratios for systolic pressures of 150-159 mm Hg and ≥ 160 mm Hg were significantly raised at 1.7 and 2.0 compared with non-hypertensive subjects and for diastolic pressures ≥ 95 mm Hg were 5.4.

Baseline blood pressure—The risk of stroke with achieved blood pressure was also examined in relation to baseline pressure before treatment (table 3). This showed a trend of increasing risk with poor control (that is, a trend across rows) in almost all groups

Table 2 Relation between risk of stroke and blood pressure control in last five years before stroke

Category of systolic blood pressure	Mean (SD)	No of cases (n=267)	No of controls (n=534)	Crude odds ratio (95% confidence interval)	Adjusted odds ratio† (95% confidence interval)	P value
	systolic pressure in last five years (mm Hg)					
Not hypertensive	140.0 (17.1)	101	287	1	1	
Treated hypertensive patients' blood pressure in last five years before index date (mm Hg):						
<140	131.4 (7.7)	23	43	1.7 (0.9 to 3.1)	1.3 (0.6 to 2.7)	0.559
140-149	144.3 (2.8)	22	41	1.9 (1.0 to 3.5)	1.6 (0.7 to 3.3)	0.251
150-159	154.5 (2.7)	31	38	2.7 (1.6 to 4.7)	2.2 (1.1 to 4.4)	0.023
≥ 160	164.3 (2.8)	49	55	3.0 (1.8 to 4.9)	3.2 (1.8 to 5.6)	<0.001
Hypertensive but untreated	178.8 (9.1)	28	32	2.9 (1.6 to 5.3)	3.5 (1.8 to 6.9)	<0.001
No blood pressure readings in period		4	3	4.0 (0.9 to 19.0)	5.6 (1.1 to 28.2)	0.036
No blood pressure record at all		9	35	0.7 (0.3 to 1.6)	0.9 (0.4 to 2.1)	0.771

†Adjusted as in table 1. Significance of trend in odds ratios for systolic blood pressure P<0.01.

Table 3 Effect of achieved blood pressure in treated hypertensive patients in last five years before stroke and baseline blood pressure. Results expressed as odds ratios (95% confidence intervals) adjusted as in table 1 (numbers of cases, controls). Non-hypertensive subjects served as reference

Baseline systolic blood pressure (mm Hg)	Systolic blood pressure in last five years (mm Hg)			Baseline diastolic blood pressure (mm Hg)	Diastolic blood pressure in last five years (mm Hg)		
	< 150	150-159	≥ 160		< 85	85-89	≥ 90
<160	1.5 (0.7 to 3.3) (20, 32)	1.4 (2.2 to 8.3) (3, 6)	3.1 (0.5 to 21.3) (3, 4)	<95	2.0 (1.0 to 4.1) (31, 40)	2.1 (0.9 to 5.1) (19, 18)	3.4 (0.7 to 17.5) (4, 6)
160-169	1.0 (0.4 to 2.6) (11, 28)	2.0 (0.5 to 7.0) (6, 10)	4.8 (1.4 to 16.4) (7, 7)	95-99	2.2 (0.7 to 7.4) (8, 11)	0.8 (0.2 to 2.9) (5, 13)	1.1 (0.2 to 4.8) (3, 12)
170-179	1.3 (0.4 to 4.3) (8, 14)	3.0 (1.0 to 8.7) (12, 10)	6.7 (2.5 to 17.9) (18, 11)	100-104	0.8 (0.2 to 3.0) (5, 18)	2.0 (0.6 to 7.1) (7, 9)	8.9 (1.5 to 51.1) (7, 5)
≥ 180	1.5 (0.4 to 6.1) (6, 10)	1.6 (0.5 to 4.7) (10, 12)	1.7 (0.8 to 3.7) (21, 33)	≥ 105	0.6 (0.2 to 2.0) (7, 21)	2.1 (0.6 to 7.0) (7, 10)	5.5 (2.3 to 13.2) (22, 14)

Odds ratios for 60 subjects with untreated blood pressure and 51 with no readings (including seven without blood pressure readings in last five years) were 3.4 (1.7 to 6.7) and 1.3 (0.6 to 2.7) for systolic blood pressure, and 3.2 (1.6 to 6.2) and 1.2 (0.6 to 2.5) for diastolic blood pressure respectively.

defined by their baseline pressure. However, there was no consistent trend from low to high baseline pressures (that is, down columns), suggesting that after treatment baseline pressures no longer influenced the risk of stroke. To test this proposition more formally models which included achieved and baseline blood pressures were fitted. Adding the achieved pressure variable to a model including baseline significantly improved the fit ($P=0.04$ for systolic; $P<0.001$ for diastolic) whereas adding the baseline pressure variable to a model including achieved pressure did not ($P=0.192$; $P=0.388$). We also considered whether the effect of achieved blood pressure varied with the baseline pressure by fitting an interaction variable to the model; this was not significant ($P=0.282$; $P=0.146$).

Population attributable risk—When moderately controlled, poorly controlled, or untreated hypertension was reduced to well controlled levels ($<150/90$ mm Hg) population attributable risk was 21% in the population aged 40-79 years after adjusting for the total age and sex specific population. Thus every year 75 (21% of 355) first strokes in a population of 161 978 aged 40-79 years could have been prevented by good control, a rate of some 46 events per 100 000 population aged 40-79 years. The number of poorly controlled and untreated hypertensive patients requiring good control to below 150/90 mm Hg (that is, the “numbers needed to treat”) to prevent one stroke was 86 for five years in the population aged 40-79 years.

Discussion

This population based case-control study examined the relation between the risk of stroke and the quality of hypertension control in people aged under 80. To our knowledge this is the first study to do so after ascertaining all stroke events in routine care in a whole community rather than selected (hospital or volunteer) cases.

The study had potential limitations. Firstly, clinical diagnosis of stroke made by doctors was usually not confirmed by computed tomography. The clinical diagnosis of a stroke having occurred or not is reliable.^{18 19} As the diagnosis of stroke types without computed tomography is unreliable,¹⁹ all types of stroke were combined. Secondly, though hypertension data were missing in only 5% of notes, the proportion missing for smoking and alcohol consumption was large. However, we analysed the effect of these missing values, which illustrated their potential risks. Our results also showed an impact on stroke from other major risk factors—twofold for known diabetes and nearly threefold for smoking, similar to results of cohort studies.^{20 21}

Though hypertension detection was much better than the rule of halves, achieving adequate control for patients so detected was not. The rule was operating in the United Kingdom in the 1980s^{11 22} and continues in the most recent analyses in terms of control.^{23 24} This is particularly important for communities at high cardiovascular risk with most to gain—for instance, older adults and particular ethnic groups. Trial results have shown unequivocal evidence in favour of hypertension treatment reducing all cardiovascular events, dating back to 1985 for older adults,²⁵⁻³⁰ illustrating the difficulty of convincing doctors and possibly patients that not just treatment but optimal control is what matters.

Key messages

- A case-control study based on the community stroke register and practice records showed a prevalence of hypertension of 61% for stroke patients and 42% in controls
- Quality of control of blood pressure was clearly related to the risk of stroke, independent of baseline blood pressure
- Detection and treatment rates of hypertension were high but control of blood pressure to below 150/90 mm Hg in treated hypertensive patients was only 33% in cases and 42% in controls
- When achieving optimal control of hypertension (to $<150/90$ mm Hg) in the most at risk and treatable age range (40-79 years) 86 hypertensive patients currently not well controlled need to be treated over five years to prevent one stroke

Over half of the hypertensive stroke cases (51%; 80/157) had either untreated or poorly controlled blood pressure in the last five years before the index date compared with 42% (88/212) of non-stroke hypertensive patients. The gap between routine practice and evidence from other studies may partly be due to the doctors' beliefs—for example, that these were research populations and therefore less relevant to their practice—or due to the slow acceptance of new knowledge. As our study was based on practitioners' own medical records in routine primary care the results would be highly relevant not only to them but also to health purchasers, as general practitioners are the gatekeepers of medical care in the NHS.

The most appropriate way of expressing these results for routine practice has been discussed.^{31 32} For primary care teams and purchasers perhaps the most useful is in relation to the age group at high risk—say, 40-79 years. For those hypertensive patients in our study who were receiving treatment, achieving good control to below 150/90 mm Hg reduced the risk of stroke by 53% with a continuing favourable trend below this level. Some 46 first strokes per 100 000 population aged 40-79 years could be avoided yearly. Hence the number needed to treat was 86 such hypertensive patients required to have changed from poorly controlled to well controlled blood pressure levels (maintained at that average level over five years) to have prevented one stroke, and within this age range the older the patient the greater the absolute benefit.

Finally, other studies may have overestimated the role of diastolic pressure by not adjusting for the simultaneous systolic value^{1 2 5 6} and smoking.⁵ In a recent large prospective study³³ and an earlier study³⁴ the impact of diastolic pressure on risk of stroke was much reduced when systolic pressure was taken into account. However, in our study the effect of one pressure when adjusted for the other was still impressive with the size of risk reduced only slightly. Thus in routine practice our data suggest that, independent of baseline level, blood pressure achieved with treatment in the few years before a stroke was the

important predicting factor. This has important implications for hypertension management policy, requiring patients with hypertension to have their blood pressure treated and maintained below the specified target levels rather than just being given treatment.

Conclusion

The risk of stroke was clearly related to the quality of blood pressure control with treatment. In routine practice, together with detecting untreated subjects, consistent control to target levels below 150/90 mm Hg rather than just starting treatment seems to be required for optimal stroke prevention.

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Conflict of interest: None.

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ONE HUNDRED YEARS AGO

The bicycle and the appendix

The bicycle is taking the place of the cigarette as a pathological scapegoat. When so heavy and so complex a burden of diseases has been laid upon it, one more might seem to be of little importance, were it not that this last straw is—appendicitis. Yet as everyone rides a bicycle nowadays, and as (if we may believe some modern authorities) nearly everyone has had or will have appendicitis, the wonder is that the connection between the two series of phenomena has not been perceived sooner. The discovery, it is scarcely necessary to say, comes from America, where there is, we are assured, a "boom" in appendicitis. The condition is caused, it is alleged, by the contractions, too frequent or too violent, of the psoas-iliacus which bicycling involves. Hence results contusion of the appendix, followed by the desquamation

of its mucous membrane; this makes a breach through which infective agents find their way into the walls of the appendix and set up inflammation. The straining caused by going uphill makes the danger all the greater. In persons who have already suffered from appendicitis, bicycling may easily lead to rupture of adhesions and to the development of an acute condition. Some little time ago an American practitioner was so impressed by the dangers to which the possession of a vermiform appendix exposed mankind that he suggested its systematic removal in childhood as a prophylactic measure. In these days, when bicycling is so fashionable, this proposal may perhaps have to be taken into serious consideration. (BMJ 1897;ii:872.)