LONG-TERM CLINICAL OUTCOME IN NORMAL VOLUNTEERS AND PATIENTS WITH CEREBRAL TRANSIENT ISCHEMIC ATTACKS

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Abstract - Detection and modification of the risk factors of stroke may be the most effective strategy for preventing its often irreversible consequences. A longitudinal prospective study was implemented to evaluate the effect of several risk factors on the course of cerebrovascular disease. The study groups were composed of 388 normal volunteers, and 308 patients with transient ischemic attacks. The two groups were followed for 4.2 (± 3.3) and 2.8 (± 2.9) years, respectively. Endpoints were defined as the occurrence of the following: transient ischemic attacks, stroke, multi-infarct dementia, dementia of the Alzheimer's type, or death. Stroke and death were 2.5 times more frequent in the second group. Hypertension was the single predictor of reaching the endpoints (P<0.014). By excluding the cases with dementia of Alzheimers type, no single predictor could be identified. This study suggests that ischemic events are significantly more frequent in patients with transient ischemic attacks. A dichotomous split was observed between neurogenic and cardiogenic endpoints.

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INTRODUCTION

Every year over half a million persons suffer a stroke in the United States and nearly a third of them die from their disease. There are a number of known risk factors and although some of these factors (such as age, family history and gender) cannot be modified, a great deal can be done for other factors such as hypertension, cardiac disease (especially atrial fibrillation), diabetes, hyperlipidemia, carotid artery disease, transient ischemic attacks (TIAs), smoking and alcohol abuse (1,2,3). Most strokes occur after the age of 65 (2,3), and after that age, hypertension is the most important risk factor (2,3). TIAs are defined as brief and reversible episodes of local neurological deficit lasting less than 24 hours, although most attacks last less than 30 minutes. As part of an ongiong fourteen year longitudinal study, the development of clinical endpoints including TIAs, stroke, multi-infarct dementia (MID), dementia of the Alzheimer's type (DAT) and death from presumed cardiac causes were compared among and between neurologically normal volunteers and patients with symptomatic TIAs who had no history of stroke. The objective of this study was to evaluate the development of disease in initially normal subjects, and to determine the role of brief ischemic episodes and concomitant risk factors in the progression and exacerbation of cerebrovascular disease.

MATERIALS AND METHODS

Subject groups were composed of 388 normal volunteers with and without risk factors for stroke (mean age at entry 63.8±10.7) and 308 TIAs patients (entry mean age 60.7±10.4). This is an ongoing study with subjects being added yearly. Control subjects have been followed up to 14.1 years, mean 4.2 years (±3.3). TIAs patients have been followed up to 13.8 years, mean 2.8 years (±2.9). All subjects were assessed via neurological and physical examinations, blood chemistries, review of history and tabulation of risk factors for cerebrovascular disease. Endpoints were determined by the occurrence of any of the following: TIAs, stroke, MID, DAT, or death. Recurrent events within a category were not considered to be endpoints, and were not tabulated. Endpoint episodes required a shift of categories with a marked change in severity. Therefore, patients who were initially in the TIAs

group and who only had recurrent episodes did not change categories.

RESULTS

In the normal volunteer group, 34 (9%) developed endpoints, the most common being TIAs (n=11), 9 developed MID, 4 had strokes without dementia and 6 developed DAT. Four died, 1 due to stroke and 3 due to presumed cardiac causes. Of the TIAs group, 22 (7%) developed endpoints (excluding recurrent TIAs). Eight developed MID, 7 had strokes without dementia, none DAT. Seven died, 3 due to stroke, 4 of presumed cardiac causes. Sixty four percent of all strokes and deaths occurred in the original TIA patients placing them at 2.5 times greater risk than normal volunteers.

Comparisons between the groups of volunteers and TIA patients who did not reach endpoints (Table 1) revealed that TIA patients were predominantly male ($p<0.001$) and had significantly higher risk factors for stroke including, hypertension, heart disease, diabetes mellitus, smoking (all $p<0.001$), hyperlipidemia ($p<0.004$), and alcohol consumption ($p<0.05$). Normal volunteers who developed cardiovascular endpoints (Table 2) compared to those who remained asymptomatic were older ($p<0.0001$), more frequently male ($p<0.05$), had greater incidence of heart disease ($P<0.005$) and smoking ($p<0.027$). For all patients who reached endpoints, the single predictor was the presence of hypertension ($p<0.014$). However, when DAT patients were excluded from the analysis no single risk factor could predict change of status between the changed volunteers and TIA patients. Among those patients initially presenting with TIAs, the strongest predictor for cardiovascular endpoints was advancing age ($p<0.026$).

Table 1. Distribution of risk factors for stroke among changed and unchanged subjects subjects who changed (n=56)

	CONTROLS (N=34)	TIAs(N=22)	P
Age (±SD)	72.00 (10.32)	65.45 (10.89)	P<.027*
Sex (M/F)	20/14	13/9	NS
Hypertension	44%	77%	P<.014
Heart disease	44%	46%	NS
Hyperlipidemia	15%	27%	NS
Diabetes Mellitus	12%	23%	NS
Smoking	62%	73%	NS
Alcohol	77%	68%	NS
subjects who remained unchanged (N=640)			
	CONTROLS (N=34)	TIAs(N=22)	P
Age (±SD)	62.96 (10.42)	60.38 (10.23)	P<0.002*
Sex (M/F)	148/206	193/93	P<0.00001**
Hypertension	33%	63%	P<0.00001**
Heart Disease	18%	47%	P<0.00001**
Hyperlipidemia	18%	31%	P<0.0004**
Diabetes Mellitus	05%	21%	P<0.00001**
Smoking	42%	70%	P<0.00001**
Alcohol	75%	67%	P=0.05**

*t-test; **Chi-square analysis of frequency distributions

Table 2. Distribution of risk factors for stroke among normal volunteers and TIA patients volunteer subjects (N=388)

	Changed (N=34)	UNCHANGED (N=354)	P
Age (±SD)	72.00 (10.32)	62.96 (10.42)	P<0.0001*
Sex (M/F)	20/14	148/206	P=0.05**
Hypertension	44%	33%	NC
Heart disease	44%	18%	P<0.0005**
Hyperlipidemia	15%	18%	NS
Diabetes Mellitus	12%	05%	NS
Smoking	62%	42%	P<0.0269**
Alcohol	77%	75%	NS
TIA SUBJECTS (N=308)			
	Changed (N=22)	UNCHANGED (N=286)	P
Age (±SD)	65.49 (10.89)	60.38 (10.23)	P<.026*
Sex (M/F)	13/9	193/93	NS
Hypertension	77%	63%	NS
Heart disease	46%	47%	NS
Hyperlipidemia	27%	31%	NS
Diabetes Mellitus	23%	21%	NS
Smoking	73%	70%	NS
Alcohol	68%	67%	NS

*t-test; **Chi-square analysis of frequency distributions

DISCUSSION

In one study, TIA was found to be a strong predictor for stroke, with an annual stroke risk of 1-15% (14). The average annual risk of stroke, myocardial infarction or death was found to be over 7.5% in hospital - referred patients. The greatest risk occured in the first year after TIA (4). In another study, 20% of infarcts occured within a month after the first attack (5). In another prospective study of 390 patients with focal TIAs, 5 year cummulative rate of fatal or nonfatal cerebral infarction was 23%. Myocardial infarction in these groups especially in those with carotid lesion was seen in 21% (6). In keeping with the results of the above mentioned studies, this present one confirms the importance of control of the risk factors in prevention and management of cerebrovascular disease. It is of note that even though they were classified at the mildest level of ischemic events, TIA patients were at significantly greater risk for stroke as indicated by the increased presence of hypertension, heart disease, diabetes mellitus, smoking, hyperlipidemia and alcohol consumption. Normal volunteers who developed cardiovascular endpoints compared to those who remained asymptomatic were older, more frequently male, and had greater incidence of heart disease and smoking. The strongest predictor for endpoints among those patients initially presenting with TIA was advancing age, suggesting that prolonged duration of risk factors increases the likelihood of severe and fatal cardiovascular outcomes. Moreover, TIA patients were 2.5 times more likely than normal volunteers to have strokes and/or die from cardiac causes. The presence of hypertension significantly predicted endpoint categorization only when the DAT patients were included, but dropped out of the equation when DAT patients were excluded from the analysis. This indicated a dichotomous split between endpoints of neurogenic vs. cardiogenic origin. The lack of development of DAT from the original TIAs group may indicate that CVD signs override the more insidious nature of DAT and mask the early presence of DAT, or that those conditions which produce DAT are indeed not present in those with cerebrovascular disorders.

REFERENCES

1. Wolf PA., D'Agostino RB. and Belanger AJ. Probability of stroke, a risk profile from the Framingham study on stroke 1991: 22: 312 - 318.

2. Sacco RL. Ischemic stroke in Handbook of Neuroepidemiology, NewYork, 1994: 77 - 119.

3. Wolf PA., Cobb JL. and D'Agostino RB. Epidemiology of Stroke, NewYork, Churchill livingston, 1992: 3 - 27.

4. Howard G; Evans GW. and Crouse JR. A prospective reevaluation of TIAs as a risk factor for death and fatal, or nonfatal cardiovascular events. Stroke. 25: 342 - 45; 1993.

5. Whisnant JP., Matsumoto N. and Elveback LR., TIAs in a Community, Rochester, Minnesota, 1955-1969, Mayo Clin. proc. 48: 194; 1993.

6. Heyman A., Wikinson WE. and Heyden S. Risk of ischemic heart disease in patient with TIA. Neurology. 34: 626; 1984.