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Articles

Transient Neurological Attacks in the General Population

Prevalence, Risk Factors, and Clinical Relevance

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Abstract

Background and Purpose Patients with typical transient ischemic attacks (TIAs) have a higher

risk of stroke but a lower risk of cardiac events than patients with nonspecific transient neurological symptoms. We assessed the prevalences of typical TIAs and nonspecific transient neurological attacks (TNAs) and their determinants in the general population because such data are virtually absent.

Methods The Rotterdam Study is a population-based cohort study of 7983 subjects, aged 55 years and over, conducted in a district of Rotterdam, the Netherlands. At baseline examination, a history of episodes of disturbances in sensibility, strength, speech, and vision that lasted less than 24 hours and occurred within the preceding 3 years was determined by a trained physician. When such a history was present, information on time of onset, duration, and disappearance of symptoms and a detailed description of the symptoms (in ordinary language) were obtained. Subjects were classified by a neurologist as typical TIA or nonspecific TNA.

Results Prevalence of TNAs was 1.9% in subjects aged 55 to 64 years, 3.5% in subjects aged 65 to 74 years, 4.3% in subjects aged 75 to 84 years, and 5.1% in subjects aged 85 years or over. Prevalence figures for typical TIA were 0.9%, 1.7%, 2.3%, and 2.2% and for nonspecific TNA 1.0%, 1.8%, 2.0%, and 2.9%, respectively. Clinical parameters such as number of attacks, onset, duration, and disappearance of symptoms were similar for typical TIA and nonspecific TNA. Increased age, male sex, diabetes mellitus, low HDL cholesterol, Q-wave myocardial infarction on electrocardiogram, and carotid atherosclerosis were related to typical TIA, whereas increased age, hypertension, low HDL cholesterol, smoking, and angina pectoris were associated with nonspecific TNA.

Conclusions About half of the subjects with a TNA had symptoms that were not entirely typical for a TIA. Differences in associations with risk factors between typical TIA and nonspecific TNA point toward different underlying mechanisms of symptoms and may lead to different ancillary investigations and possibly treatment.

Key Words: cerebrovascular disorders • epidemiology • cerebral ischemia, transient • the Netherlands

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Introduction

It is well established that subjects with a TIA are at increased risk of stroke and coronary heart disease. ^{1 2 3} A TIA is commonly defined as an episode of temporary and focal cerebral dysfunction of vascular (occlusive) origin that is rapid in onset (no symptoms to maximal symptoms in less than 5 minutes and usually less than 1 minute) and of variable duration, ordinarily lasting 2 to 15 minutes but rarely as long as 1 day (24 hours).⁴ The resolution or disappearance of each attack is swift (ordinarily a few minutes at most). By definition, a TIA leaves no persistent neurological deficit. Despite this definition, it remains difficult to distinguish a TIA from other disorders such as migraine, epilepsy, syncope, or even neurosis because its diagnosis is commonly made on the basis of the history of the patient rather than from clinical observation. In the Dutch TIA trial among subjects whose TIA symptoms were well documented and clinically evaluated, a further distinction could be made in those with symptoms typical of TIA (81.7%) and those with atypical symptoms (18.3%). Subjects with atypical symptoms had a lower risk of stroke but a higher risk of cardiac events than subjects with typical attacks. On the basis of these observations, it has been suggested that these nonspecific TNAs may be due to cardiac abnormalities, such as arrhythmias. Although in several studies the prevalence of TIAs was addressed, information on typical TIA and nonspecific TNA and their determinants in the general population is virtually absent.

In the present study, we assessed the prevalences of typical TIA and nonspecific TNA and their determinants in a Dutch population-based cohort of 55 years and over.

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Subjects and Methods

Population

The Rotterdam Study is a single-center cohort study of 7983 subjects, aged 55 years or over, who live in the suburb of Ommoord in Rotterdam, the Netherlands. The study includes residents of six homes for the elderly (897 participants). The study was approved by the medical ethics committee of Erasmus University. Written informed consent was obtained from all participants. The rationale and design of the Rotterdam Study have been described elsewhere. Baseline measurements were collected from March 1990 through July 1993, comprising an extensive home interview, followed by two visits at the Rotterdam Study research center for clinical examinations. Overall response of those invited to participate was 78%.

Assessment of History of TNA

During the visit at the research center, a trained Rotterdam Study physician asked all participants, "Did you experience a short period with disturbances of sensibility in your face, arms, or legs, which lasted less than 24 hours over the last 3 years?" Similar questions were asked for disturbances in strength, speech, and vision. When answers were positive, time of onset, duration, and disappearance of symptoms and whether a general practitioner had been consulted were recorded. Additionally, a detailed description of the symptoms in ordinary language was obtained. On the basis of this information, one of the investigators, a neurologist (P.J.K.), classified subjects as typical TIA, nonspecific neurological attacks (atypical TIA), or no TIA.⁹ An attack was regarded as being a typical TIA according to the guidelines of the Ad Hoc Committee for the Classification and Outline of Cerebrovascular Disease⁴: ie, (1) weakness, clumsiness, or sensory alteration in one or both limbs on the same side, speech or language disturbance, loss of vision in one eye or part of the eye, or homonymous hemianopsia for symptoms that pertain to the carotid territory; (2) weakness or clumsiness (sometimes changing from one side to another), sensory alteration, complete blindness or homonymous hemianopsia, ataxia, imbalance, or unsteadiness not associated with vertigo; and/or (3) two or more of the following: diplopia, dysphagia, dysarthria, or vertigo for symptoms that pertain to the vertebrobasilar territory. 10 The attack was judged nonspecific if the subject had one or more of the following symptoms: disturbances of vision in one or both eyes consisting of flashes, objects, distorted-view tunnel vision, or image moving on change of posture; alteration of muscle strength consisting of tiredness or heavy sensation in one or more limbs, either unilateral or bilateral; sensory symptoms alone (unilateral or bilateral) or a gradual spread of sensory symptoms; brain stem symptoms and coordination difficulties consisting of isolated disorder of swallowing or articulation, double vision, dizziness, or uncoordinated movements; and accompanying symptoms including unconsciousness, limb jerking, tingling of the limbs or lips, disorientation, and amnesia. A reproducibility study in which 121 case histories were reclassified by the same neurologist, blinded for the initial diagnosis, revealed a weighted not 0.77 (P<.05), indicating a good reproducibility.

A second source of information on TIA came from those subjects who had replied affirmatively to the question "Did you ever suffer from a stroke?" Of these subjects, supplementary medical information, such as a copy of the hospital discharge records or a detailed description of the signs and symptoms, was obtained from the general practitioner. On the basis of the available information, these subjects were also classified by the same neurologist as having had a stroke, a (typical/nonspecific) TNA but not a stroke, or neither a TNA nor a stroke. As described elsewhere, 14% of the subjects were classified as having had a TNA but no stroke. The two sources were combined in the present analyses. In short, of all subjects with available information on the questions on TNA and stroke, negative answers on both questions were reported by 6830 subjects; 246 reported a stroke but not a TNA; 157 subjects reported no stroke but a TNA; and 70 reported both a stroke and a TNA. Of these 70 subjects, 36 were considered to have a typical TIA, 21 were considered to have had a stroke after the TNA, and 13 were considered to have had a nonspecific TNA.

Cardiovascular Risk Factors

In the Rotterdam Study, information on health status, medical history, current drug use, and smoking was obtained using a computerized questionnaire, which included a Dutch version of

the Rose questionnaire for assessment of prevalent angina pectoris. 12 Determination of a history of myocardial infarction was based on the question "Did you ever suffer from a myocardial infarction for which you were hospitalized?" Diabetes mellitus was considered present when subjects were currently using oral blood sugar-lowering drugs or receiving insulin treatment. With respect to smoking, subjects were categorized into groups of current smokers, former smokers, and those who had never smoked. During two visits at the research center, several cardiovascular risk factors were measured. Height and weight were measured, and body mass index (kilograms per meter squared) was calculated. Sitting blood pressure was measured at the right upper arm using a random-zero sphygmomanometer. The average of two measurements obtained at one occasion, separated by a count of the pulse rate, was used in the present analysis. Hypertension was defined as a systolic blood pressure of 160 mm Hg or higher, a diastolic blood pressure of 95 mm Hg or higher, or current use of antihypertensive drugs for the indication hypertension. Carotid atherosclerosis was assessed using ATL Ultramark IV with a 7.5-MHz linear-array transducer. The common carotid artery and the carotid bifurcation were evaluated on-line for the presence (yes/no) of atherosclerotic lesions on both the near and the far wall of the carotid artery. Atherosclerosis was considered present when one or more plaques were seen during ultrasonography as described elsewhere. 13 Plaques were defined as a focal widening relative to adjacent segments, with protrusion into the lumen composed of either calcified deposits only or a combination of calcification and noncalcified material. No attempt was made to quantify the size or extent of the lesions or the percentage of stenosis of the carotid arteries. An ECG was made in 6579 subjects, and the presence of a myocardial infarction (Q-wave) and arrhythmia was assessed using an automated diagnostic classification system of the Modular Electrocardiogram Analysis System (MEANS). 14 15 Because of the limited number of subjects with cardiac arrhythmias, we defined arrhythmia as either atrial flutter (0.2%), atrial fibrillation (2.9%), atrial arrhythmia (0.5%), or atrioventricular arrhythmia (1.0%). A nonfasting venous blood sample was taken as described elsewhere. ¹⁶ Serum total cholesterol was determined using an automated enzymatic procedure. HDL cholesterol was measured similarly, after precipitation of the non-HDL fraction with phosphotung state magnesium.

Data Analysis

Subjects of the Rotterdam Study pilot phase were excluded (n=384) because of differences in the questionnaire. No information was available on the TNA symptom questions in the interview of 245 subjects. Complete self-reported information was therefore available for 7354 subjects. Results on prevalence are presented by age and sex. The age on the day of participation (interview) was used in the analysis of prevalence. Logistic regression was applied to study the association between cardiovascular risk factors and both typical TIA and nonspecific TNA. ORs were calculated as measures of strength of the association, and results are expressed with a corresponding 95% CI.

Results

General characteristics of the study population are given in Table 1 +. The prevalence of TNAs, typical TIA, and nonspecific TNA increased gradually with age (Table 2+). No major differences in the relative prevalence of typical TIA and nonspecific TNA were seen among age groups. The prevalence of typical TIA was slightly but significantly higher in men than in women (Table 3 +).

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View this table: Table 1. General Characteristics of Study Population

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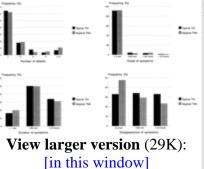
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View this table: Table 2. Prevalence (%) of Typical TIA and Nonspecific TNA by Age

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View this table: Table 3. Prevalence (%) of Typical TIA and Nonspecific TNAs by

No difference in frequency of general clinical characteristics such as number of attacks, time of onset of symptoms, and disappearance of symptoms was found between typical TIA and nonspecific TNA (Fig 1 +). The proportion of subjects with disappearance of the symptoms "at once" was clearly higher in those with nonspecific attacks than in those with typical attacks (47.5% versus 33.0%). Results were similar for men and women and across age groups. Of the subjects with TIA, 74.0% consulted a general practitioner for their symptoms, and 71.3% of those with a nonspecific TNA did also (P=.65, for the age- and sex-adjusted difference). Unfortunately, information on whether or not a patient had been referred to a neurologist was not collected.



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Figure 1. Several clinical characteristics of typical TIA and nonspecific TNAs.

Analyses with adjustments for age and sex revealed that typical TIA was significantly and positively associated with age (OR per year, 1.04; 95% CI, 1.02 to 1.06), male sex (OR, 1.36; 95% CI, 1.06 to 1.64), diabetes mellitus (OR, 2.21; 95% CI, 1.22 to 3.99), Q-wave myocardial infarction (OR, 1.75; 95% CI, 1.06 to 2.91), and carotid plaques (OR, 2.16; 95% CI, 1.27 to 3.68) and inversely with HDL cholesterol (OR per mmol/L, 0.43; 95% CI, 0.23 to 0.80). Analyses for nonspecific TNA showed significant associations with age (OR, 1.04; 95% CI, 1.02 to 1.06), hypertension (OR, 1.66; 95% CI, 1.13 to 2.43), current smoking (OR, 1.73; 95% CI, 1.15 to 2.60), and angina pectoris (OR, 2.06; 95% CI, 1.20 to 3.53) and inverse associations with HDL cholesterol (OR, 0.46; 95% CI, 0.26 to 0.83). In a multivariate logistic model including all these risk factors, increasing age and presence of carotid plaques remained independent predictors of typical TIA, whereas hypertension, smoking, and angina pectoris proved to be independent predictors of nonspecific TNA (Table 4*). Cardiac arrhythmia was not related to either typical TIA or nonspecific TNA: age- and sex-adjusted ORs (95% CI) were 1.24 (0.59 to 2.61) and 1.20 (0.57 to 2.53), respectively.

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Table 4. Association Between Cardiovascular Risk Factors and Typical TIA and Nonspecific TNA

Discussion

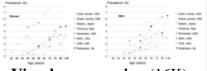
The prevalence of TNAs increased gradually with age in men and women. About half of the subjects with a TNA had symptoms that were not entirely typical for a TIA. We observed some differences in magnitude and significance of associations with risk factors between typical TIA and nonspecific TNA.

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In cross-sectional studies, several factors may lead to an underestimation of the true prevalence. In the present study, subjects living in homes for the elderly were included, whereas subjects residing in nursing homes were not included. Exclusion of these usually very old subjects with a high prevalence of disabling disease may have led to an underestimation of the TIA prevalence. Similarly, information on subjects who declined the invitation to participate in the Rotterdam Study (22%) is missing. In this group, the prevalence of TIA might have been higher than in the participating subjects. Also, other subjects, in particular those with impaired cognitive function, may have been "missed" because of false-negative answers to the screening questions; the extent of this, however, cannot be ascertained. Available prevalence estimates for the Netherlands are very limited and come from studies among general-practitioner practices. A direct comparison is, however, not possible because of lack of age-and sex-specific prevalence data.

A limited number of population-based studies on the prevalence of TIA have been performed in industrialized countries. $^{19\ 20\ 21\ 22\ 23\ 24\ 25\ 26}$ Because frequency of occurrence of TNA is a function of the population cardiovascular risk profile, which is known to differ across countries, prevalence estimates of TNAs are likely to vary across studies. Furthermore, the studies differed in methods used to assess TNAs (ie, a questionnaire only, a questionnaire combined with physical examination, a questionnaire combined with an examination by a neurologist), in population size, in time period, and in extent of nonresponse. These factors limit comparison of the findings across studies. Consequently, the findings of the prevalence studies show considerable variation (Fig 2 +).



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Figure 2. Prevalence of TIA according to some selected population-based studies among men (right) and women (left).

Several factors have been put forward as causes of TIAs, of which extracranial atherosclerosis, predominantly in the carotid artery, and cardiac disease (acute myocardial infarction, valvular disease, arrhythmias) are the most frequent. In the present study, we observed that indicators of large-vessel atherosclerosis, such as Q-wave myocardial infarction and presence of carotid

plaques, were more strongly related to typical TIA than to nonspecific TNA. This may suggest that typical symptoms are more likely to be of atherosclerotic origin. The higher cardiac event rate among those subjects with nonspecific TNAs in the Dutch TIA trial generated the hypothesis that some of the nonspecific atypical attacks may be due to cardiac arrhythmia. Because long-term ECG monitoring was not performed in the present study, we could not confirm or refute the hypothesis. As in the Dutch TIA trial, baseline ECG abnormalities did not differ between typical and nonspecific TNA. The association between atypical symptoms and angina pectoris in the present study may imply that in some of the subjects with atypical symptoms, the attack may initially have been angina pectoris followed by anxiety-induced hyperventilation with associated sensory symptoms.

The distinction between typical and nonspecific TNA may be important for diagnostic procedures and possibly treatment of these patients presenting at the clinic. If our findings are confirmed in future studies, it may be recommended that subjects with nonspecific attacks should be carefully evaluated by a neurologist.⁹

In conclusion, about half of the subjects with TNAs had symptoms that were not entirely typical for a TIA. Differences in associations with risk factors between typical TIA and nonspecific TNA point toward different underlying mechanisms of symptoms and may lead to different ancillary investigations and possibly treatment.

Selected Abbreviations and Acronyms

CI = confidence interval

ECG = electrocardiographic, electrocardiogram

OR = odds ratio

TIA = transient ischemic attack

TNA = transient neurological attack

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Footnotes

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