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Aortic arch atheroma in transient ischemic attack patients

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ABSTRACT

Objective: Aortic arch atheroma (AAA) is associated with vascular risk factors and with stroke risk. Its prevalence and prognosis remain to be defined in patients with transient ischemic attack (TIA).
Methods: Using data from the SOS-TIA registry, we assessed the prevalence of AAA detected by transesophageal echocardiography (TEE). AAA was graded as moderate (<4 mm) or severe (≥4 mm). All patients had a standardized work-up investigation and were followed for 1 year.
Results: Between January 2003 and December 2008, 1850 patients with definite/possible TIA or minor stroke were enrolled and 1231 (67%) underwent TEE. Moderate AAA was found in 26% of patients ($n = 324$) and severe AAA in 14% ($n = 171$), giving an overall AAA prevalence of 40%. Among the 873 patients without identified cause of TIA, the prevalence of moderate and severe AAA were 24% and 12% respectively. Intracranial or extracranial stenosis ≥50% were detected in 21% of patients and were independently associated with AAA (adjusted odds ratio, 1.65, 95% confidence interval (CI), 1.23–2.22). At one-year, incidence of recurrent vascular events was 2.2% in patients without AAA, 4.1% in moderate AAA and 6.6% in severe AAA (log-rank, p for trend = 0.003). Using patients without AAA as reference, and after adjustment on vascular risk factors, the hazard ratio (95% CI) for moderate was 1.36 (0.62–2.99) and 2.08 (0.89–4.86) for severe (p for trend = 0.095).
Conclusions: These findings support a systematic identification of AAA in TIA patients to optimize risk stratification in this specific population.

1. Introduction

Aortic arch atheroma (AAA) is a source of cerebral emboli, known to be associated with vascular risk factors and an increased risk of vascular events and mortality [1,2]. AAA prevalence increases with age [3–5] and its progression is a dynamic process [5] which correlates with vascular events recurrence [6]. AAA is a specific risk factor for stroke [7–9] but its relevance in transient ischemic attack (TIA) patients has not been evaluated. Until now, AAA prevalence and prognosis was assessed in stroke patients in post-mortem studies [3,10,11], case series [12–17] or case-control studies [7,8,18] but AAA is not systematically evaluated in patients admitted for TIA, particularly by transesophageal echography (TEE). Therefore, the aim of this study was to evaluate AAA prevalence and the risk of recurrent vascular events in this population.

2. Methods

2.1. Patients

The design of the SOS-TIA registry and main results have been already described [19]. This report concerns all patients admitted to the SOS-TIA clinic between January 2003 and December 2008. Briefly, SOS-TIA is a TIA clinic with round-the-clock (24 h) access, located in a "day"-hospital (also open at night), nested in a neurology department that also has a stroke unit. Primary care physicians (i.e., general practitioners, cardiologists, neurologists, and ophthalmologists) and emergency department physicians in Paris and its administrative regions can contact the SOS-TIA clinic

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via a toll-free telephone number. Patients are admitted to the SOS-TIA clinic if the suspicion of TIA is confirmed by a trained nurse or vascular neurologist after a brief phone interview. After triage based on etiologic work-up performed in <4 h, patients are either discharged home from the day-hospital or further admitted to the stroke unit according to published criteria [19].

2.2. Data collection

Patient's characteristics, clinical information, examination findings, final vascular diagnosis, medications and follow-up information were collected using a structured questionnaire. TIA was defined as an acute loss of focal cerebral or ocular function attributed to inadequate blood supply with symptoms consistent with TIA lasting less than 24 h. If the brain computed tomography (CT) or magnetic resonance imaging (MRI) scans showed an acute infarction in an area corresponding to the symptoms, the patient was judged to have a TIA with a new lesion; if not, the event was classified as TIA without a new lesion. Cases with transient focal neurological symptoms whose clinical and radiological features did not allow designation as a definitive TIA were judged as possible TIA. Patients with an incomplete recovery were judged to have a minor stroke regardless of the brain imaging results.

The cause of TIA was defined using the ASCOD classification Grade 1. The ASCOD classification categorizes 5 predefined phenotypes: Atherosclerosis (A), Small vessel disease (S), Cardioembolism (C), Other causes (O), Dissection (D). Each of the 5 phenotypes is graded according to following categories: 1 when the disease is a potential cause of the index stroke, 2 when causality is uncertain, 3 when the disease is present but is unlikely a direct cause, 0 when the disease is absent, and 9 when the workup is insufficient to rule out the disease [20].

Neurologists in the outpatient clinic obtained follow-up information on the occurrence of any vascular events or death during face-to-face interviews or by research nurses via telephone calls. In cases of reported of any vascular event, medical records were obtained whenever possible. Adjudication of predefined endpoints (stroke, myocardial infarction and vascular death) was validated by consensus between two neurologists (PL and PA).

2.3. Investigations

All patients had an initial standardized evaluation including medical history, physical examination, routine blood biochemistry and diagnostic testing. Brain imaging was performed immediately (either MRI or a default CT scan). Cervical duplex ultrasonography and transcranial Doppler were performed systematically and immediately by a fully trained senior vascular neurologist. Other form of vascular imaging (magnetic resonance angiography or computed tomography angiography) were also performed in majority of cases (86%). Cardiac evaluation included 12 lead-EKG, and transthoracic echocardiography (TTE) and TEE. Echocardiography was performed the same day in case a high-risk cardiac source of embolism was clinically suspected, and later in other cases. TTE and multiplane TEE were conducted according to standard practice guidelines using commercially available ultrasonographic instruments. TEE was performed with the patient in the left lateral decubitus position, after premedication and with topical anesthesia (lidocaine) and sedation for most of patients (intravenous midazolam). The aorta was imaged in short- and long-axis views and plaques in the thoracic aorta were defined as irregular intimal thickening with increased echogenicity. Plaque thickness was measured as the maximal thickness of the intimal and medial layers and graded as no, moderate (<4 mm) or severe (≥4 mm) with the criteria of Amarenco et al. [7].

2.4. Statistical analysis

To assess the selection bias related to absence of transesophageal examination of the aortic arch, we compared the clinical characteristics between the included and the non-included TIA and minor stroke patients using the Chi-square test for categorical variables and Student's t test for continuous variables. Further statistical analysis was based on the 1231 included TIA and minor stroke patients, divided into three groups according to the severity of AAA (no AAA vs. moderate vs. severe). We calculated the prevalence of AAA (overall and for each severity grade) in all study sample, by age decade and by final vascular diagnosis. Prevalence of AAA were compared between age-groups using the Chi-square test for trend and between the final vascular diagnosis using logistic regression analysis adjusted on age. Vascular risk factors, TIA symptoms and measurements of extra and/or intracerebral artery atherosclerosis were compared between AAA groups using analysis of variance for continuous variables and chi-squared test for categorical variables. To evaluate the independent associations of vascular risk factors with AAA, the vascular risk factors with values of $p < 0.20$ in univariate analyses were entered into a multivariate ordinal logistic regression analyses taking to account the severity grade of AAA (i.e. the dependent variable coded as 0 for no AAA, 1 for moderate AAA and 2 for severe AAA). We also used multivariate ordinal logistic regression analyses to assess the associations of TIA symptoms and cerebral artery atherosclerosis measures with AAA after adjustment for independent risk factors of AAA. The proportional odds assumption, inherent in ordinal logistic regression analysis, was checked with Score test for all models. Finally, we compared the composite outcome (i.e. stroke, myocardial infarction or vascular death) and all-cause mortality at one-year follow-up between AAA groups using the log-rank test (global and trend tests). For vascular-event free survival analyses, patients who died from causes other than vascular disease were censored at the time of death. Using patients with no AAA as the reference group, we estimated the crude and age-adjusted relative risks for moderate and severe AAA by Cox proportional hazards regression analyses (after examining the log–log survival plots to appreciate the proportional hazards assumption). An additional adjustment was performed by including the other risk factors associated with AAA into the Cox proportional-hazards model. Statistical testing was done at the two-tailed α level of 0.05. Data were analyzed using the SAS software package, release 9.1 (SAS Institute, Cary, NC).

3. Results

From January 2003 to December 2008, 2398 patients with a suspected TIA were admitted at the SOS-TIA clinic of whom 1850 had a definite/possible TIA or minor stroke. Among them, 1231 (67%) underwent a TEE examination of the aortic arch (see Supplemental Fig. 1). As compared to the 619 non-included TIA or minor stroke patients in whom TEE was not performed, the 1231 included TIA or minor stroke patients were younger, more frequently men, had less often hypertension and history of atrial fibrillation (see Supplemental Table 1).

3.1. Prevalence of aortic arch atheroma

The overall prevalence of AAA was 40% (95% confidence interval [CI], 37–43; $n = 495$). According to severity grades, moderate AAA was found in 26% (95%CI, 23–29; $n = 324$) of patients and severe AAA was found in 14% (95% CI, 11–16; $n = 171$). As shown in Supplemental Table 2, the overall prevalence of AAA increased gradually with increasing age, ranged from 3% in patients <40 years