Stroke and Transient Ischemic Attack in Takayasu's Arteritis: A Systematic Review and Meta-analysis

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Background: Cerebrovascular disease is one of the possible consequences of Takayasu's arteritis (TA). However, little is known about the prevalence of stroke/transient ischemic attack (TIA) or its related clinical features among these patients. We have performed a systematic review and meta-analysis to estimate the rate and risk factors of stroke/TIA in TA as well as to explore associations with poorer outcomes. *Methods:* MEDLINE and Embase were searched (October 2014) for observational studies of any design reporting prevalence rates of stroke/TIA among TA patients. Study selection, data collection, and quality assessment were done independently. Studies' results were pooled through random-effect meta-analysis. Heterogeneity was assessed with the I^2 test. *Results:* Twenty-one studies (16 studies were of cohort design) were included (n = 3269). The pooled stroke/TIA prevalence rate estimate was 15.8% (95% confidence interval [CI]: 10.7%-22.6%, I^2 = 94%). Sensitivity analysis, excluding 8 studies with poorer TA diagnostic criteria, yielded a similar estimate but without statistical heterogeneity (15.7%; 95% CI: 13.6%-18.1%, I^2 = 5.5%). Data were unavailable to explore possible associations between patients' characteristics and stroke/TIA prevalence. *Conclusion:* Our results document a high prevalence of stroke/TIA among TA patients. However, there is scarce information on the type of stroke, the characteristics of the affected individuals, and stroke-associated morbidity and mortality. Future studies should aim to further explore this disabling complication to find the best treatment and prevention strategies. **Key Words:** Takayasu's arteritis—stroke—TIA—cerebrovascular—aortitis—aortic arch syndrome—pulseless disease—large-vessel vasculitis.

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Received October 20, 2015; revision received November 30, 2015; accepted December 9, 2015.

Author contributions: J.C. is the guarantor. All authors contributed to the drafting of the manuscript, the development of the selection criteria, the risk of bias assessment strategy, and data extraction criteria. J.A. and R.S. developed the search strategy. M.D. and R.G. conducted the report screening, study inclusion, data extraction, and result interpretation and discussion. J.C. performed the statistical analysis, and conducted the result interpretation and discussion. R.G. and J.C. provided expertise on stroke and on methodology. All authors read, provided feedback, and approved the final manuscript.

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2015.12.005

Introduction

Takayasu's arteritis (TA) is a large-vessel vasculitis of unknown cause affecting mainly young women around the third decade of life.[1] It is more frequent in Asia[2-4] and has an estimated annual incidence in Europe of 0.4-1.3 per million.[5] Neurological manifestations are present in more than half of the patients during the course of the disease,[6,7] among which stroke can lead to the most catastrophic outcomes. Moreover, stroke/transient ischemic attack (TIA) can be a less typical initial presentation of TA, resulting in delayed diagnosis and treatment of this panarteritis.[8]

Despite its clinical relevance, the prevalence of stroke/TIA in TA can only be estimated to be around 10%-20%[4,6,9] based on relatively small series. With our work, we aimed to evaluate the prevalence of stroke/TIA through a systematic review and meta-analysis.

Additionally, TA's presentation shows a great variability among different geographic regions, which may result in distinctive clinical presentations.[10] However, differences between stroke in TA patients with different ethnical backgrounds remain poorly characterized. Other stroke characteristics, such as stroke type, location, and impact on disease morbidity and mortality, as well other features of the affected population (sex, age, therapy) are scarce. Because specific diagnostic, preventive, and therapeutic strategies may be required,[11] our secondary goals were to better characterize stroke and patient-associated factors.

Methods

This systematic review followed the Meta-analysis of Observational Studies in Epidemiology guidelines for reporting Meta-Analyses and Systematic Reviews of Observational Studies.[12] Reporting of statistical data followed the Statistical Analyses and Methods in the Published Literature guidelines.[13]

Eligibility Criteria

We included observational studies (cohort, cross-sectional, and case–control designs) wherein the individuals fulfilled the 1990 criteria proposed by the American College of Rheumatology (ACR) for TA (Table 1)[14] and in which both the presence and absence of episodes of cerebral ischemia (stroke/TIA) were documented. Studies including patients with TA not defined according to the 1990 ACR criteria were also considered for subsequent sensitivity analysis, providing that the number of patients with TA and the number of patients with TA suffering from stroke/TIA were available.

Bibliographic reviews, case reports, and studies containing data exclusively on a subgroup of TA patients (e.g., only patients who presented with ischemic events) or a special population (e.g., pediatrics), as well as studies where data were extracted postmortem (autopsy series), were excluded. We further excluded studies with unclear or incomplete data after having contacted the authors for data retrieval without success. When more than 1 publication for the same study was available, we used the one providing the most detailed information, the highest number of included subjects, or referring to the longest follow-up (for cohort designs), following this order. No studies were excluded a priori for weakness of design or data quality.

Table 1. *1990 criteria proposed by the ACR for classification of TA*[14]

	1990 ACR criteria for TA
1	Onset at age 40 years or younger
2	Claudication of an extremity
3	Decreased brachial artery pulse
4	Difference higher than 10 mm Hg in systolic blood pressure between arms
5	Presence of a bruit over the subclavian arteries or the aorta
6	Arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities

Abbreviations: ACR, American College of Rheumatology; TA, Takayasu's arteritis.

These 6 criteria hold a 90.5% sensitivity and 97.8% specificity when at least three are present.

Information Sources and Search Method

Potentially eligible studies were identified through an electronic search of bibliographic databases from inception to October 2014 (MEDLINE and Embase) and by extensive searching using cross-references from original articles and reviews. The strategy combined the terms "Takayasu arteritis" or "Takayasu disease" or "pulseless disease" or "Takayasu syndrome" or "aortitis syndrome" or "young female arteritis" or "aortic arteritis" with "cerebrovascular accident" or "transient ischemic attack" or "stroke" or "brain" or "cerebral" or "cerebrovascular" or "brainstem" or "brain stem" or "ischemia." All terms were searched as indexed and as free-text terms to increase sensitivity.

Study Selection and Data Collection Process

Titles and abstracts were screened. The selected references were assessed in full text. Data extracted from the included studies were used to fill in a detailed form that focused on topics related to study features, general and particular characteristics of the studied population, and stroke/TIA-specific characteristics, as listed on