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#### Review

# Stroke and rheumatic heart disease: A systematic review of observational studies



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#### ABSTRACT

Ischemic stroke is a severe complication of rheumatic heart disease (RHD), but data about its incidence and case-fatality in RHD patients' population is unclear. We aimed to perform a systematic review of the literature to better define the incidence, prevalence and case-fatality of stroke in patients with RHD, and to estimate the proportion of RHD in stroke population. We searched Ovid Medline, EMBASE, CBM, CNKI and VIP for observational studies published in English or Chinese reporting the association of stroke and RHD until April 2011. Two authors independently assessed each study for eligibility based on predefined criteria in a two-step approach and then made a final decision. Twenty-one studies, involving 26 994 participants, were deemed eligible (albeit of low quality) and included in our analysis. Two studies reported stroke incidence in RHD patients' population, which was 4.5 per 100 patient years in America by 1978 and 5.9 per 100 patient years in China 30 years later. Eight studies reported stroke prevalence in RHD patients' population. It ranged from 0.37% to 12.6% in Asia in last 30 years. Ten studies reported the proportion of RHD in stroke patient. The proportion of RHD in patients with ischemic stroke ranged from 3.4% to 23.2% in Asia and 1.8% to 2.0% in Europe and Northern America during the past 3 decades. Six studies reported case-fatality in stroke patients with RHD. It was 49.2% in America by 1951, and ranged from 8.5% to 47.4% in Asia during last 3 decades. These data suggest that stroke due to RHD remains a hidden burden that cannot be ignored in developing areas such as Asia.

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#### 1. Introduction

Rheumatic heart disease (RHD) is the most common form of cardiac disease that affects people of low socioeconomic status [1]. Globally, 97% of all cases of RHD occur in developing countries and other populations living in poverty, such as indigenous peoples from New Zealand and Australia [2]. RHD has not been a common topic in recent years since its burden has waned in high-income countries. However, RHD remains an ongoing problem, especially in Asia, and its burden may still be increasing. It is conservatively estimated that 15.6 million people in the world have RHD, with approximately 282 000 new cases diagnosed and 233 000 resultant deaths each year [3]. The persistently high rates of acute rheumatic fever (ARF) in some developed countries, also highlight the need to remain aware of ARF and RHD in all populations [4].

Worldwide, 15 million people suffer a stroke each year and stroke accounts for 5.7 million deaths annually, nearly 10% of all deaths worldwide [5]. It is estimated that 3-7.5% of all strokes in less developed countries are related to RHD, which represents 144 000-360 000 strokes and 108 000-269 000 stroke related deaths each year, and 640 000-1.6 million stroke survivors in less developed countries [3]. These data show that RHD is of sufficient importance as a cause of stroke to warrant the attention of research communities, especially in developing countries. However, less importance has been placed on the association of stroke and RHD in the last decades due to the fact that most stroke research takes place in high-income countries where RHD is becoming rare. The knowledge about stroke incidence and case-fatality in RHD patients' population is scarce and confusing and there have been no recent attempts to collate such information. Thus, RHD might be an underestimated cause of stroke in low- and middle-income areas such as Asia.

Therefore, we systematically reviewed existing studies to estimate the incidence, prevalence and case-fatality of stroke in patients with RHD, and the proportion of RHD in stroke population.

#### 2. Methods

#### 2.1. Data sources and searches

The search strategy was developed according to the recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [6] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7]. We performed a comprehensive search of Ovid Medline (from 1948 to April 2011), EMBASE (all years to April 2011), China Biological Medicine Database (CBM from 1978 to April 2011), China National Knowledge Infrastructure (CNKI from 1915 to April 2011) and Chinese Science and Technique Journals Database (VIP from 1989 to April 2011) using the search strategy in Appendix 1. References from all eligible studies, relevant reviews and guidelines were manually searched for additional studies.

#### 2.2. Inclusion criteria

Studies were selected if they met any the following entry criteria: (1) observational studies examining the association between

stroke and RHD; (2) reported stroke incidence, prevalence, or case-fatality; reported stroke or RHD proportion or stroke outcomes as count data; or reported quantitative estimates of relative risks (RR) or odds ratios (OR) and 95% confidence intervals (CI) for stroke associated with RHD; (3) were published in English or Chinese language. Both population-based studies and hospital-based studies were eligible. Studies not meeting these criteria or focusing on the effects of surgical valvular repair or replacement for RHD were excluded.

In case of multiple publications from same study population, we only included data from the article with greatest amount of information.

#### 2.3. Study selection and data extraction

We identified eligible studies using a two-step selection process. Firstly, two investigators screened the titles and abstracts to exclude studies that did not meet any of the pre-specified criteria. Secondly, the same investigators evaluated full text articles of the remaining studies, then excluded studies that did not meet the inclusion criteria. Disagreements were resolved by discussion and consensus.

The following data were extracted from studies: authors and titles, year of publication, study design, study size, enrollment period, source of RHD population, age range and sex of the participants, duration of follow-up, extent of loss to follow-up, investigated outcomes (for example, total stroke, ischemic stroke, hemorrhagic stroke), and count data or RR or OR with 95% CIs for each of the associations investigated. All data were extracted from published studies. We did not contact authors to obtain additional information

#### 2.4. Data analysis

Adapted from the updated criteria for ideal study of stroke incidence and/or mortality suggested by Feigin [8], we predefined the following two criteria to assess the quality of each study: (1) prospective design; and (2) use of standardized definitions [i.e., WHO definition of stroke or similar definition, in at least 80% of cases the diagnosis had to be verified either by head computed tomography (CT) or magnetic resonance imaging (MRI)]. We calculated the incidence of stroke per RHD patient-years, if possible. We also evaluated stroke prevalence in RHD patients, proportion of RHD in stroke patients, case-fatality of stroke patients with RHD, and risk of stroke associated with RHD. We used the MetaAnalyst software [9] to conduct a meta-analysis of the combined data.

#### 3. Results

A total of 13 910 relevant publications were initially identified through electronic search. Of these, 19 studies were included after the two-step selection processes (Fig. 1). Two additional studies were identified by manually screening references from relevant studies, reviews, and guidelines. Therefore, a total of 21 studies, with 26 994 participants, were included in this analysis.

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