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Review article

A clinical study and meta-analysis of carotid stenosis with coexistent intracranial aneurysms

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A B S T R A C T

Carotid stenosis (CS) and intracranial aneurysms (IAs) may concur in one person. We studied the prevalence of IAs in CS patients in our retrospectively collected database and systematically reviewed this issue. Five hundred and fifty-seven CS (≥50%) patients confirmed by DSA in our hospital from 2010–06 to 2015–06 were screened for coexistent IAs. After searching the related literatures from English and Chinese journal literature databases, a meta-analysis was performed to pool the prevalence of CS with coexistent IAs. Subgroup analyses were performed to explore the causes of heterogeneity among studies. IAs were detected in 98(17.0%) out of the 577 CS patients. 12 literatures and the present study including a total of 6965 CS patients and 446 cases with coexistent IAs. The pooled prevalence of CS with coexistent IAs was 6.3% (95%CI: 4.2–8.3%) in all the CS patients. The pooled RR for female to male CS patients to have coexistent IAs was 1.67 (95%CI: 1.34–2.08, P = 0.000). 3 studies and the present study were carried out in Asian countries with a pooled prevalence of 10.8% (95%CI: 5.3–16.3%); 6 studies in European countries with 3.0% (95%CI: 2.2–3.7%); and 3 studies in USA with 6.0% (95%CI: 2.2–9.7%). There was a statistically significant difference between the three subgroups (P < 0.001). The prevalence of IAs in CS patients seems higher in our clinical study and the meta-analysis than in the general population and previously reported. The eastern and the women CS patients have a higher risk for coexistent IAs.

1. Introduction

Carotid stenosis (CS) and intracranial aneurysms (IAs) are the most frequently encountered diseases by neuro-interventional specialists. Carotid occlusive disease could be found in up to 20% of the patients with symptoms of cerebral ischemia [1]. IAs occur in 3–5% of the general population [2], and magnetic resonance imaging (MRI) studies of the general population aged 20–70 years revealed that unruptured intracranial aneurysms (UIAs) could be found in 0.1% to 1.8% of the participants [3,4]. On the other hand, subarachnoid hemorrhage (SAH) caused by aneurysm rupture is associated with high morbidity and mortality rate. Up to 40% of the patients die within 1 month and 30% of the survivors have persistent severe neurologic deficits [5]. It is reasonable for us to pay attention to the patients who have the both lesions. Recently, more and more patients having CS with coexistent IAs were reported due to the development of digital subtraction angiography (DSA), computed tomography angiography (CTA) and magnetic resonance angiography (MRA) [6–24]. But the prevalence was still unclear [6,8,10,12,15,16,19–24]. Heman et al. [15] reported the prevalence of IAs in patients with internal carotid artery (ICA) stenosis in their meta-analysis. But it had limitations such as the early study year and not including studies carried out in Asian countries. Thus, the aim of this study is to assess the prevalence of IAs in a retrospectively collected series of patients with CS. Furthermore, by performing a systemic literature review and meta-analysis, we try to obtain the overall prevalence of IA in the patients with CS.

2. Subjects and methods

2.1. Clinical research

2.1.1. Patients

We retrospectively reviewed all patients with concomitant diagnosis of CS and IA evaluated in the neurosurgical department of our hospital from June 2010 and June 2015. All IAs were diagnosed by DSA. The diagnosis of CS was determined with imaging methods including CTA, MRA, or DSA. We excluded patients who had arteriovenous malformation, Moyamoya disease, dural arteriovenous fistula, history of intracranial hemorrhage together with

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CS. In addition, patients whose carotid artery stenosis or occlusion was caused by other reasons except for atherosclerosis, such as fibro-muscular dystrophy were excluded. We screened for coexistent saccular IAs in this group of patients. Patients who had more than one aneurysm were counted as a single finding.

2.1.2. Methods

Conventional angiography was indicated for patients who were suspected of having CS after CTA or MRA and potentially needed intervention. It was performed using a biplane system via trans-femoral catheterization and selective injection of contrast media into the carotid and vertebral arteries. Three-dimensional image reconstruction following rotational angiography was applied to the patients when necessary. Images were read by experienced neurosurgeons.

The location and degree of the CS were recorded. The location of CS included common carotid artery, both extracranial and intracranial segment of internal carotid artery. The stenosis was accessed according to the criteria of the North American Symptomatic Endarterectomy Trial (NASCET) for extracranial artery stenosis, while for the intracranial artery stenosis the criteria of the Warfarin-Aspirin Symptomatic Intracranial Disease study (WASID) was used [25,26]. For the coexistent IAs, we recorded the location, number, size. Furthermore, only the largest size of the aneurysms was measured.

Patients' demographic and clinical data were collected using an electronic medical record system, including age, gender, comorbidities especially hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, chronic renal insufficiency, history of stoke, smoking and alcoholic status.

2.1.3. Statistical analysis

Continuous variables were presented as mean ± SD. Categorical variables were presented as percentages. All analyses were performed using the software (SPSS20.0).

2.2. Meta-analysis

The meta-analysis was done following the checklist proposed by Meta-analysis of Observational Studies in Epidemiology (MOOSE).

2.2.1. Search strategy

We searched the PubMed, EMBase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Chinese Scientific and Technological Journal databases (VIP) and Wanfang databases for studies that reported the prevalence of CS with coexistent IAs. The last search was performed on July 31, 2017. The search items were as follows: (intracranial or cerebral or berry or saccular and aneurysm*) and carotid stenosis. The reference lists of the articles included were further manually searched to identify any additional relevant studies.

2.2.2. Selection criteria

The following inclusion criteria were used to identify eligible studies. ① All observational studies, including cross-section, cohort and case-control studies, were included; ② All studies reporting the proportion of CS with coexistent IAs. ③ There were no publication date, language or publication status restrictions. ④ There were no restrictions for the imaging methods. The exclusion criteria were as follows. ① The patients' information were used or reported by the same author or by the similar articles made by other researchers in the same hospitals. ② The number of participants in the studies were <10 patients. ③ Case reports, reviews, comments, essays, and animal studies were excluded.

2.2.3. Data extraction

A data extraction sheet was developed that included the authors, publication year, country, eligibility criteria, period of enrollment, number of patients with CS, number of patients who had CS with coexistent IAs, the size and location of the coexistent IAs, and the prevalence in different gender.

2.2.4. Quality assessment

The methodological quality of the studies included was assessed using an 11-item checklist which was recommended by Agency for Healthcare Research and Quality (AHRQ). An item would be scored '0' if it was answered 'NO' or 'UNCLEAR'; if it was answered 'YES', then the item scored'1'. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4–7; high quality = 8–11.

2.2.5. Statistical analysis

The prevalence of CS with coexistent IAs in each study was combined to yield a pooled prevalence with a 95% confidence interval (CI) for all studies. Data were pooled using a random-effects model to generate a more conservative estimate of the prevalence. Heterogeneity between studies was assessed using the I^2 statistic and the χ^2-test ($I^2 > 50\%$ or $P < 0.10$ was considered to indicate statistically significant heterogeneity). We were unable to test for publication bias due to the non-comparative nature of the studies. To explore the causes of the heterogeneity among studies, subgroup analyses were performed according to the continent and publishing year. We used Pearson's chi-square test for group comparisons. $P < 0.05$ was considered statistically significant. The meta-analysis was performed by using the Stata12.0 software.

3. Results

3.1. Clinical study

3.1.1. Prevalence of CS with coexistent IAs

The study included 577 patients who had CS (469 men, mean age 66.7 ± 10.0). The prevalence of CS with coexistent IAs was 17.0% (98/577, 73men, mean age 68.8 ± 8.0). Among them, 63 patients had unilateral CS and 35 had bilateral stenosis. 68 patients had concomitant posterior circulation artery stenosis.

A total of 124 IAs were detected in 98 CS patients and 22 patients had multiple IAs. The locations of the IAs were as follows: internal carotid artery 65.3% (n = 81), middle cerebral artery 7.3% (n = 9), anterior cerebral artery/anterior communicating artery 4.0% (n = 5), posterior communicating artery 11.3% (n = 14), posterior circulation artery 12.1% (n = 15). The mean size of the aneur ysms ± SD was 3.4 ± 2.9 mm (range, 1.0–27.0 mm). Of the 124 aneurysms, 110 were <5 mm (88.7%), and 3 were >10 mm (2.4%). Furthermore, 81 were <3 mm (65.3%), and 16 aneurysms took endovascular treatment.

There were 344 CS patients who received carotid artery stenting, among which 48 patients had coexistent IAs. In addition, 8 patients underwent one stage coiling and carotid artery stenting. None of the patients experienced any immediate or delayed complication related to the coexistent IAs.

3.2. Meta-analysis

3.2.1. Description of the included studies

The search strategy identified 2545 potentially relevant studies (Fig. 1). Finally, 12 were eligible for the meta-analysis after the title/abstract/full-text screening [6,8,10,12,15,16,19–24]. All of these studies were published in full-text form. The detailed charac-