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Review

Uric acid in aortic dissection: A meta-analysis

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ABSTRACT

Background: Studies on the serum uric acid levels in patients with aortic dissection have yielded conflicting results.
Objective: To compare the difference in serum uric acid (SUA) levels between aortic dissection patients and controls by meta-analysis.
Methods: Electronic literature search was conducted in PubMed, Embase, CKNI, CBM, Wanfang, and VIP databases until January 31, 2018. All observational studies that investigated SUA levels in aortic dissection patients and controls were included. Weighted mean difference (WMD) with 95% confidence intervals (CI) was used to summarize the difference in SUA levels between aortic dissection and control group.
Results: A total of seven case-control studies involving 1197 patients and 1193 controls were included. Pooled analysis showed that SUA levels were significantly higher in aortic dissection patients compared with those in the controls (WMD 58.22 μmol/L; 95% CI 26.71–89.73) in a random effect model. No significant difference (WMD 9.94 μmol/L; 95% CI -17.89–37.76) was observed in SUA levels between Stanford type A and Stanford type B aortic dissection.
Conclusions: This meta-analysis provides evidence that SUA levels are significantly higher among patients with aortic dissection than those in controls. Elevated SUA levels may contribute to the pathogenesis of aortic dissection. Further large clinical studies to investigate whether SUA levels are an independently risk factor for aortic dissection are warranted.

1. Introduction

Aortic dissection is a life-threatening cardiovascular disease associated with high morbidity and mortality [1]. Increasing aortic dissection burden has been reported [2], particularly in developing countries [3]. The estimated incidence of acute aortic dissection is approximately 3 cases per 100,000 individuals per year [4]. The prevalence of aortic dissection after autopsy is estimated to be 1–3% [5, 6]. Certain biomarkers, such as D-dimer, C-reactive protein, matrix metalloproteinases, pro-brain natriuretic peptide, have served as additional tools for detecting aortic dissection [7]. However, these available biomarkers are not enough for the recognition and management of aortic dissection. Therefore, additional new biomarkers are still urgently needed.

Uric acid is an end-product of purine nucleotide degradation. Higher serum uric acid (SUA) levels were observed in patients with aortic dissection compared with those in the controls [8–13]. Hyperuricemia may be independently associated with the risk of aortic dissection [13, 14]. However, an association of elevated SUA levels with aortic dissection has been reported with conflicting findings [15, 16]. These inconsistent results may be correlated with the baseline characteristics of aortic dissection patients and the selected controls.

In this meta-analysis, we sought to compare the difference in SUA levels between aortic dissection patients and controls.

2. Methods

2.1. Literature search

We systematically searched the PubMed, Embase, CKNI, CBM, Wanfang, and VIP until January 31, 2018. The following keywords were applied: “aortic dissection” or “aortic dilation” and “hyperuricemia” or “urate” or “uric acid”. Our literature search was restricted to studies published in peer-review English and Chinese journals. The electronic literature search was supplemented by a manual search of the reference lists of relevant studies.

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2.2. Inclusion and exclusion criteria

The eligible studies included: 1) case-control studies that reported the SUA levels in aortic dissection patients and controls (healthy subjects or patients without aortic dissection); 2) providing mean values and standard deviation of SUA; and 3) aortic dissection was diagnosed by the ultrasonography, computed tomography, and magnetic resonance imaging. Studies lacking raw SUA levels or duplicated publications were excluded.

2.3. Data extraction and quality assessment

Two authors independently extracted the following data: first author's name, publication year, study design, sample sizes, type of aortic dissection, age, sex, SUA levels of aortic dissection patients and control group. The Newcastle–Ottawa Scale (NOS) for case–control study was used to assess methodological quality [17]. Studies with over 6 stars were regarded as good quality.

2.4. Statistical analysis

We used weighted mean difference (WMD) and 95% confidence intervals (CI) to summarize the statistical results for the SUA levels. The Cochran Q statistic and I^2 statistics were utilized to evaluate the heterogeneity across the included studies. In case of $I^2 > 50\%$ and/or Cochran Q statistic < 0.10, a random effect model was detected; otherwise, we applied a fixed-effect model. Sensitivity analyses were performed by leaving out one study at each time. Publication bias was explored by the Egger linear regression test [18] and Begg's rank correlation [19]. All the statistical analyses were conducted by STATA 12.0 (STATA Corp LP, College Station, TX, USA).

3. Results

3.1. Characteristics of the included studies

A flow chart of the study selection process is shown in Fig. 1. A total of 96 articles were initially identified using the search strategy. After applying our inclusion criteria, 88 articles were subsequently excluded. One study [9] enrolling all kinds of hospital patients as controls was further excluded. Thus, seven case–control studies [8, 10–13, 15, 16] were finally included in the quantitative analysis. Table 1 summarizes the baseline characteristics of the included studies. These studies included 1197 aortic dissection patients and 1193 controls. The number of patients with aortic dissection in the included studies was 46 to 542.The mean age of patients was 47.1 to 65.2 years. Five studies [8, 10–12, 16] reported that patients with severe renal insufficiency were excluded from the enrolment. Control participants included health check-up participants and in-hospital patients with other confirmed diseases. Apart from one study [15] conducted in Japan,the others were performed in China. According to the NOS criteria, the score of included studies ranged from 5 to 7 stars.

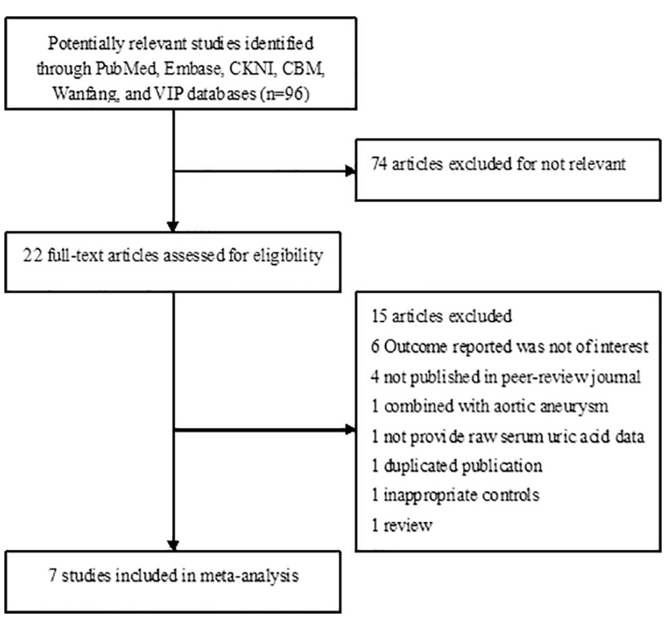

Fig. 1. Flow chart of study selection process.

3.2. Comparison of SUA levels between aortic dissection patients and controls

All included studies provided the SUA levels in aortic dissection patients and controls. As shown in Fig. 2, significant heterogeneity was observed among the seven studies; therefore, a random effect model was selected to combine effect size. A pooled summary showed that SUA levels in aortic dissection patients were significantly higher compared with those in controls (WMD 58.22 μmol/L; 95% CI 26.71–89.73). No significant publication bias was observed using Begg's rank correlation test ($p = 0.764$) and Egger's linear regression test ($p = 0.933$). Sensitivity analysis indicated that none of the individual study had a significant effect on the overall pooled results (Fig. 3). When two studies [13, 16] that exhibited no matching blood pressure were removed, a pooled analysis showed that SUA levels in aortic dissection patients were still significantly higher than those in controls (WMD 66.90 μmol/L; 95% CI 16.42–117.39; $I^2 = 94.3\%$, $p < 0.001$) in a random effect model. In addition, SUA levels in aortic dissection patients were significantly higher than those in controls (WMD 67.80 μmol/L; 95% CI 15.05–120.55) when we removed two studies [13, 15] that did not enroll the patients with severe renal insufficiency.

3.3. Comparison of SUA levels between Stanford type A and type B aortic dissection

Three studies [8, 11, 15] provided the SUA levels in patients with Stanford type A and type B aortic dissection. As shown in Fig. 4, there was no significant difference on SUA levels between type A and type B aortic dissection patients (WMD 9.94 μmol/L; 95% CI -17.89–37.76; $I^2 = 63.6\%$, $p = 0.064$) in a random effect model.

4. Discussion

The results of our meta-analysis show that SUA levels in aortic dissection patients are significantly higher than those in controls. This finding suggests that elevated SUA may play a role in the pathogenesis of aortic dissection. However, no significant difference in SUA levels between Stanford type A and type B aortic dissection patients was found.

Numerous risk factors including male gender, older age, smoking, and hypertension have been associated with aortic dissection [20]. Among these factors, hypertension is the most prevalent risk factor for acute aortic dissection [21]. However, our meta-analysis revealed that SUA levels in aortic dissection patients were still significantly higher than those in strictly matched gender, age and history of hypertension controls. Aortic dissection is frequently associated with some degree of acute kidney injury and elevated SUA can be an ‘effect of renal dysfunction in these patients. Our sensitivity analysis by removing two studies not considering of severe renal insufficiency in patients' enrolment also confirmed significantly higher uric acid levels in aortic dissection patients. These results revealed that our finding was not affected by severe renal insufficiency.

Jiang et al. 2016 [13] reported that the highest SUA levels significantly increased aortic dissection risk (odds ratios [OR] 1.76 for