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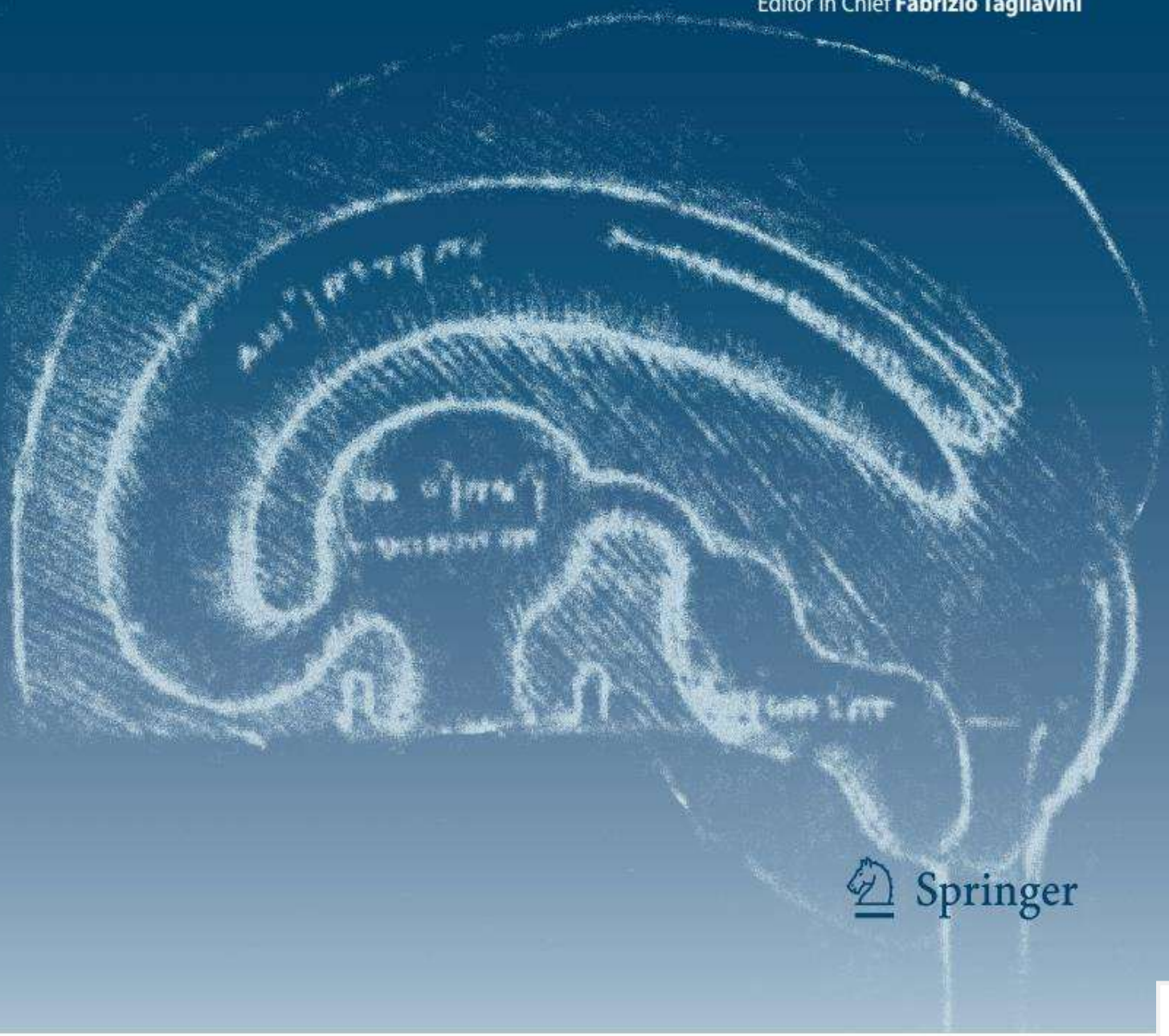

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ORIGINAL ARTICLE

Uric acid levels and their association with vascular dementia and Parkinson's disease dementia: a meta-analysis

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Abstract

Objectives To explore the association between uric acid (UA) levels and vascular dementia (VaD) and Parkinson's disease dementia (PDD), a meta-analysis was conducted.

Methods The relevant studies were identified by searching PubMed, Embase, Web of Science, and Cochrane Collaboration Database up to May 2022. Pooled analysis, sensitivity analysis, and publication bias examination were all conducted. All analyses were performed by using STATA 16.

Results Twelve studies with a total of 2097 subjects were included. The pooled analysis showed that UA levels were not associated with VaD (WMD = - 10.99 μmol/L, 95% CI (- 48.05, 26.07), $P = 0.561$) but were associated with PDD (WMD = - 25.22 μmol/L, 95% CI (- 43.47, - 6.97), $P = 0.007$). The statistical stability and reliability were evaluated using sensitivity analysis and publication bias outcomes.

Conclusion UA levels are associated with PDD but not with VaD. This study will help to strengthen our knowledge of the pathophysiologies of VaD and PDD, and promote the development of prevention and treatment strategies.

Keywords Uric acid levels · Vascular dementia · Parkinson's disease dementia · Meta-analysis

Introduction

Dementia is characterized as a syndrome rather than a particular disease that can seriously affect an individual's work and life [1]. Because of its high prevalence, dementia has become a serious public health issue around the world [2]. Vascular dementia (VaD) and Parkinson's disease dementia (PDD) are both common types of dementia [3]. For a long time, factors related to VaD and PDD have attracted worldwide attention.

Previous studies have reported that dementia is influenced by many factors, including age, gender, educational level, obesity, and disease history [4–6]. Some researchers have demonstrated that neuronal injury can be caused by oxidative damage which might affect the pathophysiology of dementia [7–9]. Our previous study reported that low antioxidant capacity might be related to VaD, and treatment with antioxidants might mitigate cognitive impairment [10]. Similar results were also obtained in PDD [11].

As the most abundant endogenous antioxidant in blood, uric acid (UA) has been considered to exert neuroprotective effects by removing ROS and nitrite [12, 13]. However, studies have shown that high levels of UA can promote inflammation and oxidation in special environments and may cause neuronal injury [14, 15]. Many researchers have paid close attention to whether UA levels are associated with VaD and PDD, and several studies have been conducted. Nevertheless, no consistent conclusion has been reached on whether UA levels are related to VaD or PDD. Therefore, a meta-analysis was conducted in the study to investigate the association.

Methods

The study was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

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Search strategy

The PubMed, Embase, Web of Science, and Cochrane Collaboration Database were searched for all relevant citations up to May 2022. The following terms were used for searching: (uric acid OR UA OR urate OR hyperuricemia) AND (vascular dementia OR VaD OR Parkinson's disease dementia OR PDD OR dementia). No language or other restrictions were applied to the search strategy. References of the retrieved studies were also screened to identify available articles.

Inclusion and exclusion criteria

Criteria for study inclusion were based on the following: (1) the association between UA levels and VaD and/or PDD was

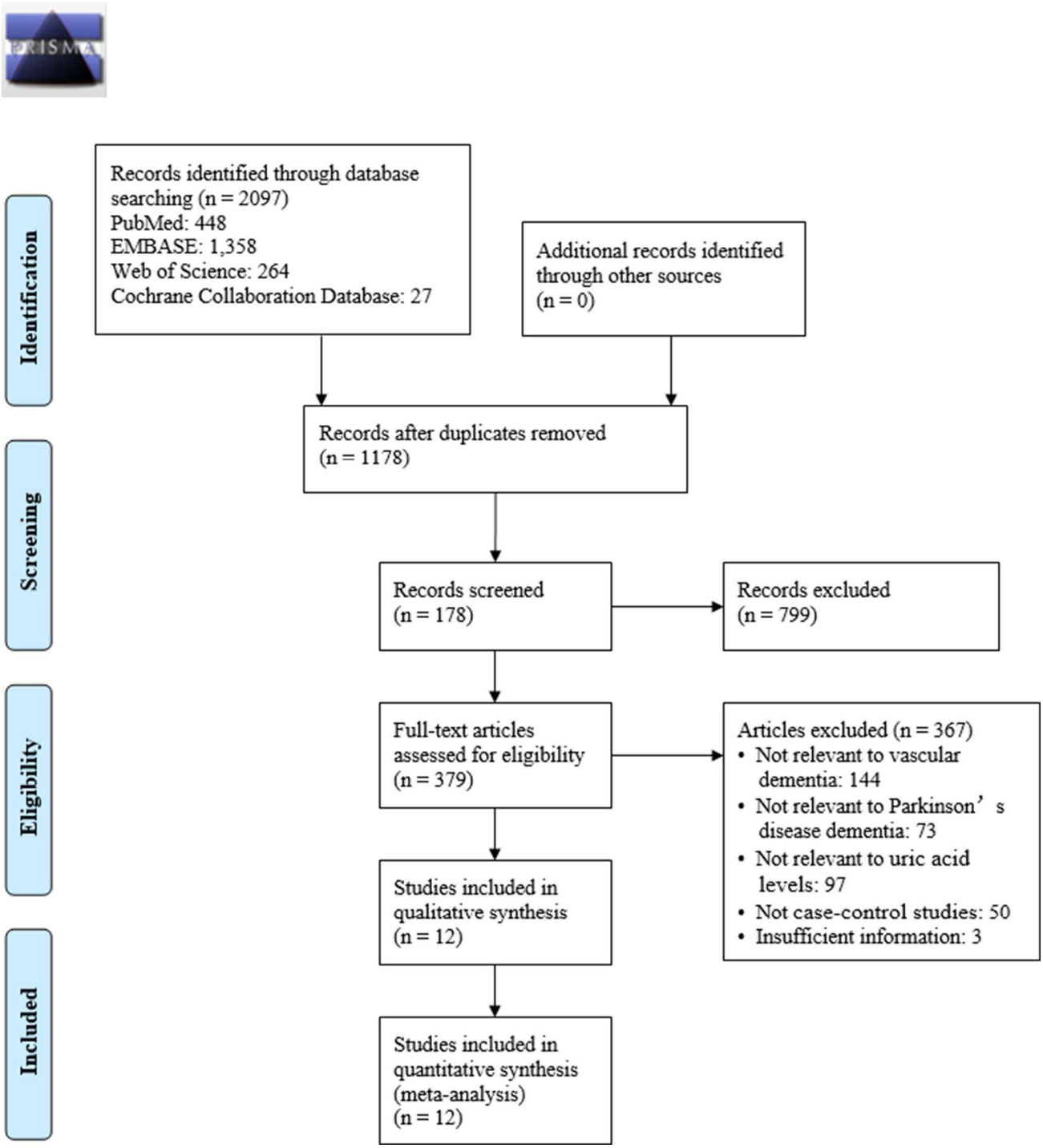


Fig. 1 Flow diagram of study selection

Table 1 Characteristics of the included studies

First author, published year	Country	Continent	Mean age (yr)	Male percentage (%)	Sample		Uric acid (μmol/L)		Dementia types	NOS score
					Case	Control	Case	Control		
Serdarevic N, 2020 [21]	Bosnia and Herzegovina	Europe	71.7	100.0	100	100	321.3 ± 85.8	263.0 ± 62.5	VaD	7
Liu HX, 2020 [22]	China	Asia	65.6	70.5	111	79	360.0 ± 110.0	348.0 ± 86.0	VaD	6
Tuven B, 2017 [23]	Turkey	Europe	NA	NA	16	1119	376.0 ± 181.5	343.9 ± 108.3	VaD	6
			NA	NA	15	1119	277.3 ± 111.9	343.9 ± 108.3	PDD	
Xu Y, 2016 [24]	China	Asia	67.7	53.8	127	81	300.1 ± 110.5	336.6 ± 103.6	VaD	8
Hatanaka H, 2015 [25]	Japan	Asia	82.8	47.5	27	53	323.1 ± 74.4	338.6 ± 100.0	VaD	7
Cervellati C, 2014 [26]	Italy	Europe	78.6	38.2	54	48	363.2 ± 94.8	317.0 ± 118.5	VaD	7
González-Aramburu I, 2014 [27]	Spain	Europe	64.2	57.0	72	271	299.9 ± 101.2	318.3 ± 83.3	PDD	8
Maetzler W, 2011 [28]	Germany	Europe	62.7	61.5	20	76	285.6 ± 83.3	303.5 ± 54.5	PDD	7
Polidori MC, 2004 [29]	Italy	Europe	76.4	35.9	23	55	193.6 ± 46.6	312.9 ± 82.3	VaD	8
Foy CJ, 1999 [30]	UK	Europe	75.9	53.7	37	58	266.7 ± 92.4†	300.0 ± 106.4†	VaD	6
			74.5	55.3	18	58	268.9 ± 80.4†	300.0 ± 106.4†	PDD	
Tohgi H, 1993 [31]	Japan	Asia	68.5	NA	15	14	283.0 ± 91.0	303.0 ± 70.0	VaD	7
Maesaka JK, 1993 [32]	America	North America	77.9	NA	6	11	330.0 ± 20.0	350.0 ± 30.0	VaD	7

NA, not available; *NOS*, Newcastle-Ottawa quality assessment scale; *VaD*, vascular dementia; *PDD*, Parkinson's disease dementia

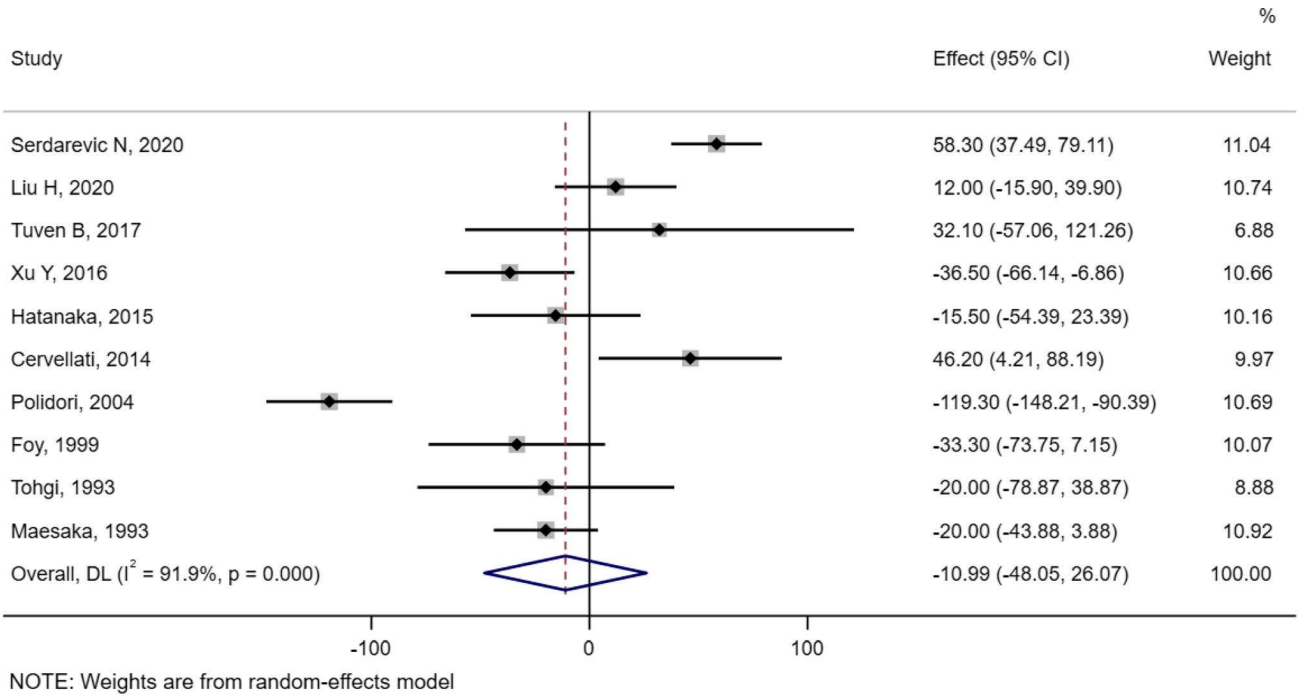
†Mean ± standard deviation estimated by median (interquartile range)

involved; (2) it should be a case-control study; (3) subjects in the case group were VaD or PDD patients, while the control group was not; and (4) the study should provide mean and standard deviation (SD) values of UA for each group. When only the median and interquartile ranges were provided, the mean and SD were estimated according to the formula [16].

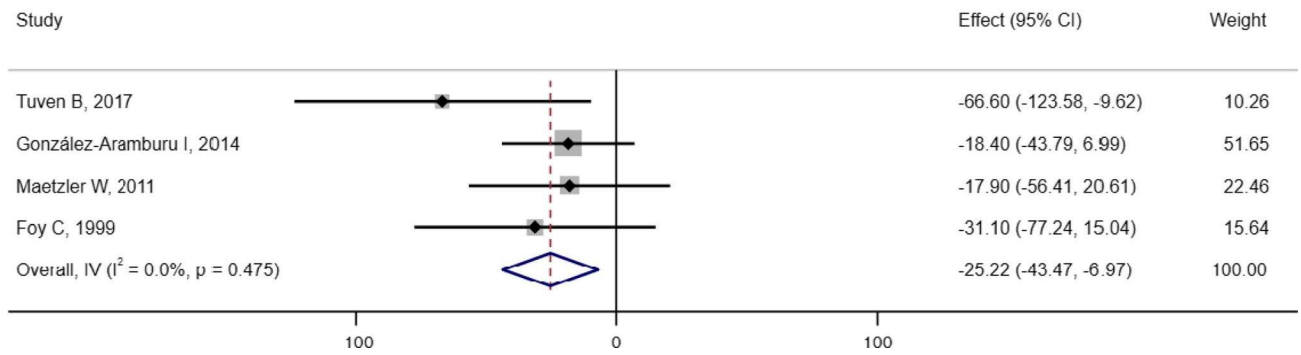
Studies were excluded according to the following criteria: (1) reviews, case reports or letters; (2) animal or cell studies; and (3) repeated publication of data from the same population.

Data extraction

All data were recorded for further evaluation separately by two reviewers, and any discrepancy was resolved by the third investigator. The following baseline data were collected: first author's name, year of publication, country, mean age, male percentage, number of patients in the case and control groups, and mean and SD values of UA in each group. Corresponding author was contacted for studies with inadequate information.



(a) Vascular dementia



(b) Parkinson's disease dementia

Fig. 2 Forest plot of weighted mean difference of vascular dementia and Parkinson's disease dementia associated with uric acid levels