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Review Article

The Relationship between the Permanent Trigeminal Artery and Cerebrovascular Disease: A Meta-Analysis

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Abstract

Background: We aimed to analyze the variability of the permanent trigeminal artery (PTA) and its relationship with cerebrovascular disease.

Methods: To analyze the variability of the PTA and its relationship with cerebrovascular disease by using the terms "primitive trigeminal artery", "persistent primitive trigeminal artery", " persistent trigeminal artery variant", "PPTA", "PTAV", "carotid- basilar anastomoses", "carotid-vertebrobasilar anastomoses", "persisting embryonic vessels" were used as keywords, and the English-language literature related to PTA and cerebrovascular diseases published in PubMed, EMBAS, and Web of Science databases from 2000 to 2022 were searched by using "subject terms + free words". A meta-analysis of the collected data was performed using stata14.0 statistical software to assess the relationship between the immortal trigeminal artery and cerebrovascular-related diseases.

Results: A total of 1908 relevant articles were initially retrieved for this study. Ten papers were initially screened according to the inclusion and exclusion criteria, while the literature was then read one by one to exclude duplicates, reviews, case reports, and conference abstracts, and six papers were finally included for meta-analysis. The six papers included in this paper were all cross-sectional studies with 39,355 subjects, of which 206 subjects had PTA, with a variation rate of approximately 0.52%, including 77 males and 129 females, 117 left-sided variants and 87 right-sided variants. In contrast, of the 206 subjects with a PTA, 52 had cerebrovascular disease, with an overall prevalence of approximately 25.24%.

Conclusion: The PTA could influence the development of cerebrovascular disease.

Keywords: Permanent trigeminal artery; Cerebrovascular disease; Variability; Internal carotid artery; Basilar artery

Introduction

During the human embryonic period, four transient anastomosing branches exist between the carotid artery and the basilar artery (1-4). As the embryo develops, the above four arterial anastomosing branches gradually degenerate until they completely disappeared at 11.5-14 mm of embryonic development.

However, due to developmental abnormalities, very few people still had the above four anastomosing branches in adulthood, of which the permanent trigeminal artery (PTA) variant was the most common (5, 6). PTA was first discovered and reported by Quain in 1844 through anatomical experiments (7). In recent years, with the rapid development of anatomical techniques, Magnetic Resonance Imaging (MRI), Computer Tomography (CT) and other diagnostic imaging techniques, the number of articles on anatomical and imaging studies related to PTA gradually increased (8-10). At the same time, previous study revealed that PTA variant might be associated with the occurrence of cerebrovascular diseases, such as cerebral hemangioma, cerebral infarction (11-15). However, no statistical studies on the relationship between PTA and cerebrovascular diseases were reported.

Therefore, we aimed to screen the previous literature on PTA and cerebrovascular diseases and to conduct a meta-analysis in order to clarify the interaction between them and to provide theoretical references for the prevention of PTA-related cerebrovascular diseases in the future.

Methods

Search Methods

According to the requirements of Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) specification, search and screen English literature related to PTA and cerebrovascular diseases in PubMed, Embas and Web of Science databases, the literature search time was set from 2000-2022, and the search strategy was the way of "subject words + free words". The search keywords were: “primitive trigeminal artery”, “persistent primitive trigeminal artery”, “persistent trigeminal artery variant”, “PPTA”, “PTAV”, “carotid-basilar anastomoses”, “carotid-vertebrobasilar anastomoses”, “persisting embryonic vessels”. References were traced by English search and manual screening.

Literature screening criteria

Inclusion criteria: (1 Literature types including cohort studies, case-control studies and cross-sectional studies; (2 Studies on the relationship between the PTA and cerebrovascular disease. Exclusion criteria: (1 Case reports, conference abstracts and review articles; (2 Literature with incomplete or irrelevant data from articles; (3 Studies conducted on fetuses; (4 Studies on patients with trigeminal neuralgia; (5 Duplicate literature.

Literature quality screening and bias analysis

The included articles were independently screened by 2 investigators to extract information from the text including: patient age, gender, case source, affected side, disease duration, and type of concomitant cerebrovascular disease. The 2 investigators (G&C) compared the information after the extraction was completed. If there were differences in the data, they discussed and reviewed the literature again to re-extract the information. According to the different descriptions of the anatomy of the PTA in the references, variant blood vessels were defined as the following: 1. originating from the internal carotid artery and having anastomosing branches with only the basilar artery; 2. originating from the internal carotid artery and having anastomosing branches with at least one of the cerebellar arteries (inferior anterior cerebellar artery, superior cerebellar artery, and posterior inferior cerebellar artery). Literature bias analysis was performed using the JBI evaluation tool Appendix 7.3, which was a 10-question scale with a total score of 10.

Statistical analysis

A single-arm dichotomous variable meta-analysis of the data was performed using stata 14.0 statistical software to summarize the variability of the PTA and to analyze the relationship between the permanent artery and cerebrovascular disease. The heterogeneity of the results was tested qualitatively by chi-square test with a set test level of $P < 0.05$. I^2 statistics were used to quantify, with less than 25% representing low heterogeneity, 25%-50% representing moderate heterogeneity, and 75% representing high heterogeneity, using a fixed-effect model when $P \geq 0.05$ and $I^2 < 50\%$, and using a random-effects model when $P < 0.05$ and $I^2 \geq 50\%$.

Results

Literature screening results

A total of 1908 relevant literature was initially retrieved and ten papers were initially screened according to the inclusion and exclusion criteria. After excluding duplicates, reviews, case reports, and conference abstracts, six papers were finally included for meta-analysis (Fig. 1, Table 1).

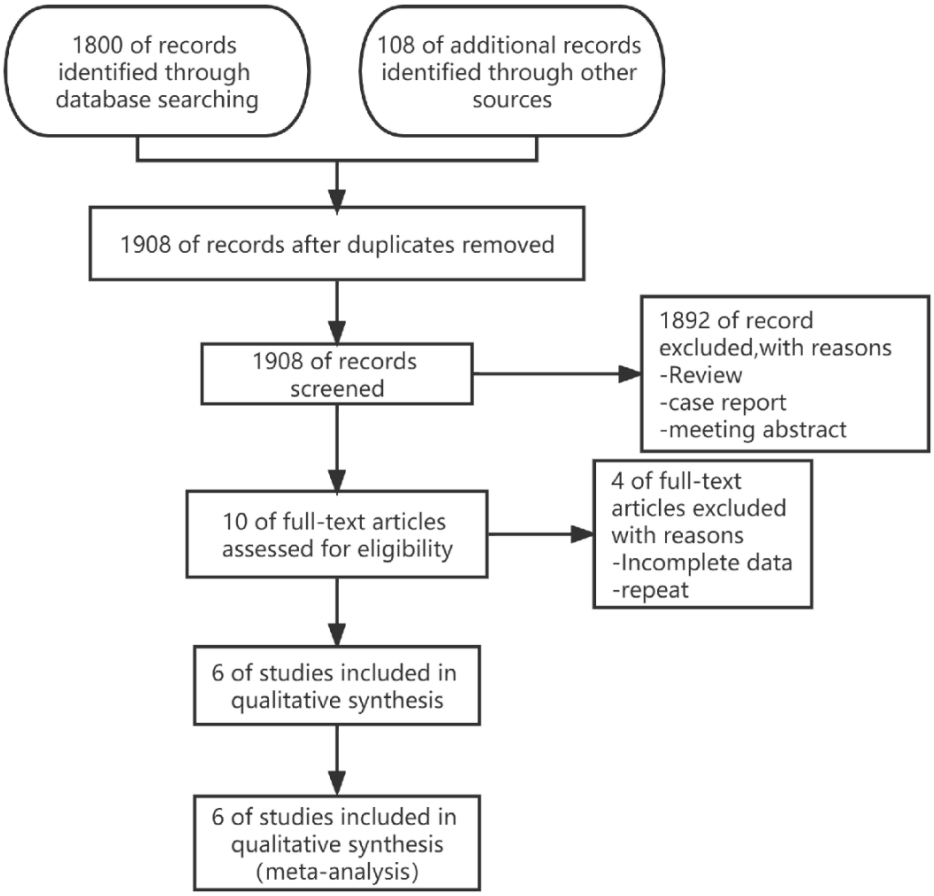

Fig. 1: Flow chart of literature screening

Table 1: Table of literature characteristics

Reference No.	*Date of publication (years)*	*Total cases*	*PTA cases*	*Gender*		*The affected side*		*Category of cerebrovascular diseases*				*Appendix Score*
				Male	Female	Left	Right	Intracranial Aneurysm	Moyamoya	Cerebral Infarction	Arteriarctia	
(16)	2013	2488	19	8	11	12	7	8	0	0	0	6
(17)	2011	7329	24	7	17	15	9	9	10	0	0	6
(18)	2011	4650	25	5	20	12	13	4	0	3	0	7
(19)	2013	6063	26	10	16	9	15	1	0	0	6	5
(20)	2016	2410	9	2	7	6	3	2	0	3	0	8
(21)	2010	16415	103	45	58	63	40	5	0	0	0	6

Meta analytic result

Basic information of literature

Six papers included in this study were all cross-sectional studies, including 39,355 subjects, among which 206 PTA subjects (77 males and 129 women) and a variation rate of about 0.52%, including 117-left variant and 87-right variant. Among the 206 PTA subjects, 52 subjects had cerebrovascular disease, and the overall prevalence was about 25.24%. The results of the randomized controlled experimental risk of bias assessment were shown in Fig. 2. Literature quality was scored according to the NOS assessment scale, and the total scores were 8,5,8,8,7 and 7, respectively, suggesting reliable literature quality.

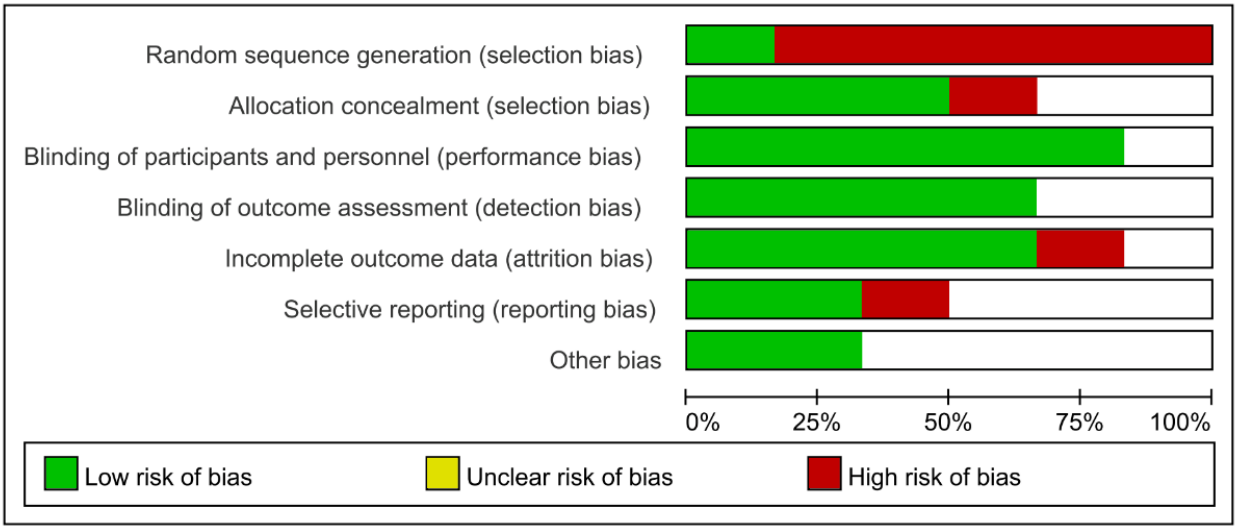

Fig. 2: Risk of bias summaries for all trials

Meta-analysis of random effects

A meta-analysis based on random effects yielded a pooled effect size of 0.324 with a 95% confidence interval of 0.16-0.58 and statistical significance for the six studies, $Z = 1.243$, $P < 0.01$, suggesting a 34% increased risk of cerebrovascular disease in patients with a PTA (Fig. 3).

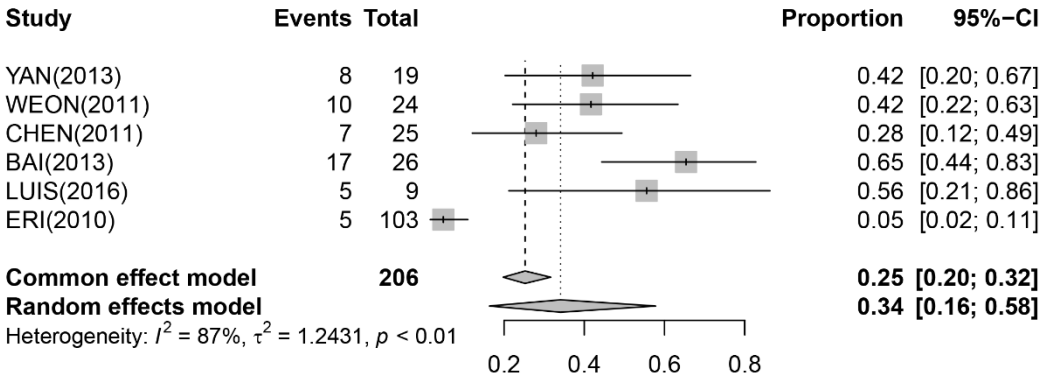

Fig. 3: Forest plot of the relationship between PTA and cerebrovascular diseases

Heterogeneity test

The literature included in this paper was tested for heterogeneity with , I^2=87% > 50% , P < 0.1, suggesting a high degree of heterogeneity and continued sensitivity analysis.

Sensitivity analysis

After sensitivity analysis, among the six included articles, those published by ERI greatly interfered with the results, suggesting that this article might be the source of heterogeneity in this study (Fig. 4).

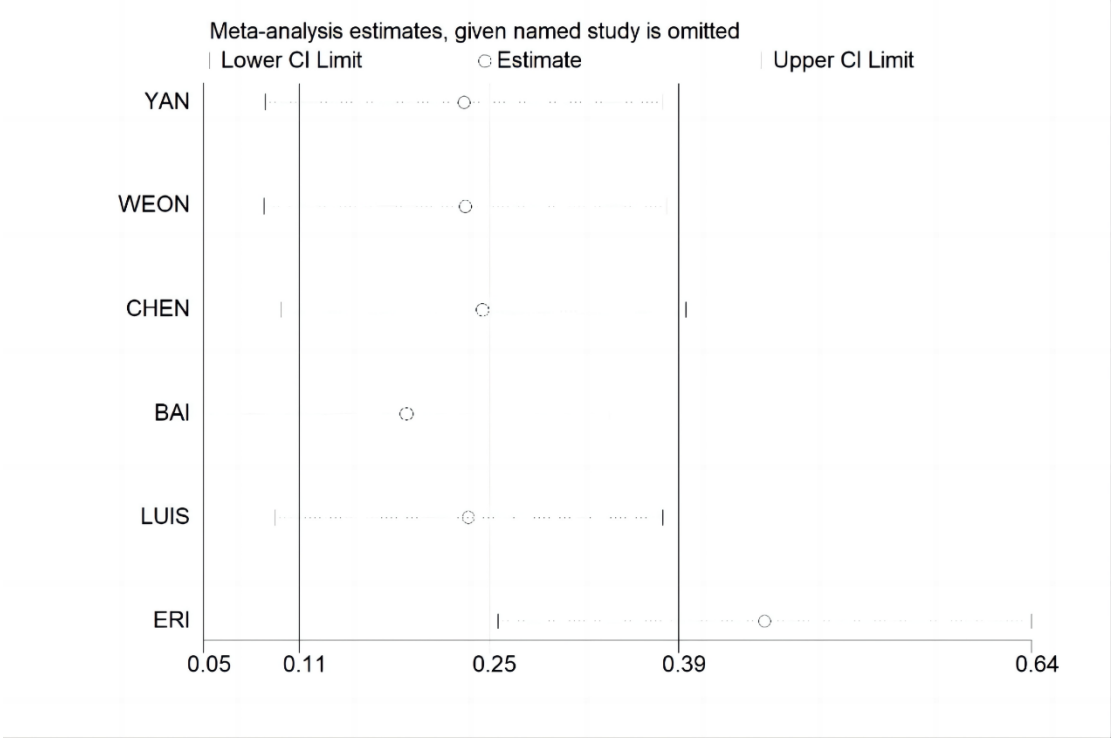

Fig. 4: Sensitivity Analysis Plot

The bias test

Since the small inclusion of literature, the study was investigated for publication bias by Egger linear regression method. According to the test results, P=0.992> 0.05, so it could be judged that the literature of this study did not have publication bias (Fig.5).

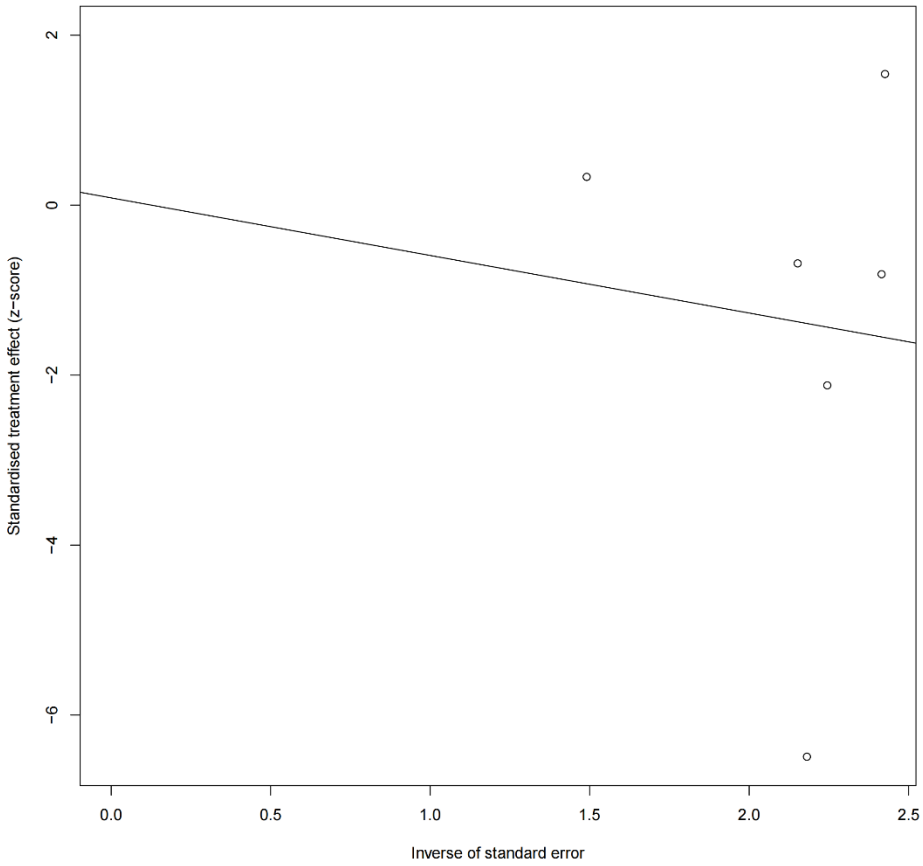

Fig. 5: Literature bias analysis

Discussion

PTA aberration rate

PTA was a relatively rare congenital vascular developmental anomaly, which was a permanent internal carotid artery-basilar artery anastomosis. PTA developed gradually in adulthood without degeneration of the communicating branches of the internal carotid artery and the basilar artery during embryonic life (22). The variant of PTA was mostly unilateral and less bilateral (23). Currently, this variant reported in the extensive literature in the form of disease case reports. Of the 6 PTA studies included in this study, with 39,355 subjects which 206 subjects had a PTA. The total variation rate was about 0.52%, which was consistent with the overall variation rate reported in previous literature of 0.1% -0.6% (24-26). Studies showed (27-29) that the prevalence of PTA was similar on the left and right sides, and there was no significant relationship with gender. However, the results of this study showed that the number of women with the disease was significantly higher than that of men, and that more PTA was present on the left side than on the right side. The reason for the difference in results might be related to the PTA as a rare disease. Therefore, further studies were needed to explore the difference of the disease in different populations.

PTA variants had a higher risk of cerebrovascular disease

The correlation between the presence of PTA and cerebrovascular disease described in previous literature. Yang et al (30) suggested that the presence of PTA might contribute to the development of posterior circulation cerebral infarction, which might be due to the "bridging effect" of

PTA. Dislodged thrombus in the internal carotid artery often caused the development of anterior cerebral circulation infarction. However, the presence of PTA allows the existence of a bridge vessel between the internal carotid vein and the basilar artery, through which the dislodged thrombus could enter the posterior circulation and cause blockage of the posterior circulation vessels, which in turn causes ischemic necrosis of the brain tissue. This view was recognized in the study of He Dongruo (31). Of the literature included in this study, only LUIS reported the presence of cerebral infarction in patients with PTA and concluded that the occurrence of cerebral infarction is strongly associated with the presence of PTA.

In addition to cerebral infarction, intracranial aneurysms were the most common in PTA patients, accounting for 55.7% of all cerebrovascular diseases caused by PTA. The presence of intracranial aneurysms in PTA patients not only increased the risk of cerebral hemorrhage, but also made it very easy for surgeons to cause serious intraoperative hemorrhage if the presence of this variant was not detected preoperatively. Bechri et al (32) reported that due to the thin vascular wall of PTA, aneurysm rupture was occur in the blood pressure of the internal carotid artery and basilar artery, which leaded causes cerebral hemorrhage. Yilmaz et al (33) also found that PTA patsients often produced aneurysms in the cavernous sinus, which could not only caused dizziness and headache due to the space occupying effect, but also produced symptoms of intracranial nerve paralysis due to compression of the trigeminal nerve. More importantly, carotid cavernous fistula or subarachnoid hemorrhage occurred due to the acute rupture of hemangioma. In addition to the above diseases, cerebrovascular diseases associated with PTA include Alzheimer's disease, smoker's disease, and internal carotid artery dysplasia or occlusion, but these diseases were only described in a few case reports and their incidence was extremely low. Therefore, they were not included in the analysis of this study. Therefore, the type of previous literature was mostly case reports and lacks epidemiological statistics for larger sample sizes. Thus, there were some implications for the accuracy of the study results.

Conclusion

Although PTA was a rare disease, the presence of PTA could significantly increase the risk of cerebrovascular disease. Therefore, in future clinical work, further examination need to exclude the presence of PTA before receiving cerebral infarction, cerebrovascular aneurysm and performing cranial surgery.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

The authors declared that there was no conflict of interest.

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