Heart Surgery Forum 2024; 27(1): E068–E075 https://journal.hsforum.com/
doi: 10.59958/hsf.7001

Systematic Review

A Meta-Analysis for Postoperative Alternations of Aortic Coarctation

Yu Bao[1,2,3], Zhao Wang[1,2,3,*], Sibi Shan[1], Xiang Wang[1], Yuan Gong[1]

[1]Department of Cardiovascular Surgery, Yan'an Affiliated Hospital of Kunming Medical University, 65000 Kunming, Yunnan, China
[2]Key Laboratory of Cardiovascular Disease of Yunnan Province, 65000 Kunming, Yunnan, China
[3]Yunnan Province Clinical Medicine Center for Cardiovascular Disease, 65000 Kunming, Yunnan, China
*Correspondence: wangzhao_kmya@163.com (Zhao Wang)

Submitted: 15 November 2023 Revised: 25 December 2023 Accepted: 27 December 2023 Published: 21 January 2024

Abstract

Objective: To investigate postoperative vascular changes of patients with coarctation of the aorta (CoA). **Methods**: Literature review of updated articles was performed in June 2023 through the following databases: PubMed, Web of Science, EMBASE, Crohrane Library, CNKI and Wanfang database. All the case-control studies regarding the postoperative changes of vascular structure and function in patients with CoA were analyzed. **Results**: A total of 596 articles from the above databases were initially identified, with 10 articles being selected for meta-analysis. The analysis showed that weighted mean difference (WMD) of carotid intima-media thickness (cIMT) was 0.07 (95% CI = 0.01~0.13, $p < 0.01$) and WMD of flow mediated dilation (FMD) was –4.36 (95% CI = –7.49~–1.24, $p < 0.01$), respectively. The postoperative cIMT of CoA patients was higher than that of the control group, but the postoperative FMD was lower than that of the control group. **Conclusions**: The operation on CoA patients ameliorates anatomical deformity in the vascular structures. However, intima-media thickening and endothelial malfunction remain as the key postoperative issues.

Keywords

coarctation of aorta; carotid intima-media thickness; flow mediated vasodilation; meta-analysis

Introduction

Coarctation of the aorta (CoA) is characterized of congenital stenosis in the aortic isthmus, which is composed of thickened and convoluted aortic wall [1]. Among all hereditary cardiac disease, its prevalent ratio is from 5% to 8% and roughly 0.3% live-born neonates are diagnosed with it [2]. The anomalies of aortic arch or beginning of thoracic descending aorta arise alone or occur with cardiac deformity such as aortic and supraoptic stenosis, ventricular septal defect and hypoplastic left cardia. The advanced medical application, intravascular intervention or modern surgery, anatomical deformities of aorta are repaired, as well as the mortality of CoA patients are decreased. However, approximately 36% of CoA patients present postoperative complications, the most common of which are persistent hypertension, coronary atherosclerosis at early stage [3–5]. Besides, endothelial dysfunction and thicker intima-media of vessels appear, which could be potential mechanism for those postoperative complications [1]. CoA might be a systemic disease of cardiovascular system, not only reference to aortic isthmus.

The carotid intima-media thickness (cIMT) and brachial flow mediated dilation (FMD) are usually used to evaluate vascular structure and endothelial function for adults and children [6]. Compared with other vascular parameters, these two can be measured and recorded by ultrasound in a non-invasive and repeatable manner. A previous study reported that the median of FMD index is the better independent predictor of long-term cardiovascular adverse events in a cohort of 618 healthy subjects without heart disease history [7]. FMD of congenital heart disease (CHD) patients is less than that of healthy population. FMD is negatively correlated with cIMT value indicate the malfunction of vascular structures in CHD patients. In patients with different heart defects, the increase of cIMT value is most prevalent in children with CoA and transposition of the great arteries (TGA) [8–10]. It is valuable to clarify the changes of FMD and cIMT in postoperative CoA patients. This meta-analysis could provide reliable evidence to use FMD and cIMT to evaluate life quality of postoperative CoA patient.

Materials and Methods

The methods of this meta-analysis were applied by PRISMA guidelines [11]. The main and abstract checklist of PRISMA were completed (**Supplementary material**).

Search Strategy

Two authors searched the following databases independently: PubMed, Web of Science, EMBASE, Crohrane Library, Chinese National Knowledge Infrastructure (CNKI) and Wanfang Database. Articles were identified by using the following keywords individually and in various combinations: "Aortic Coarctation", "Coarctation of the Aorta", "Coarctation, Aortic", "endothelial function", "endothelial dysfunction", "Flow-mediated dilation", "Endothelium", "Intima-media thickness". The references included in the resulting literatures were perused manually. All the literatures from the databases were updated to June 2023.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) the patients were diagnosed with CoA after cardiac surgery as enrolled subjects, (2) case-control studies that compared the endothelial function and intima-media thickness between postoperative CoA patients and healthy controls as clinical trials were designed, (3) FMD of brachial artery and cIMT of anterior wall of common carotid artery were measured by ultrasound, and (4) the languages of the articles are limited to Chinese or English.

The exclusion criteria were as follows: (1) animal experiment or *in vitro* and *in vivo* cell experiment research, (2) case report, review or systematic review, (3) studies with repeated data from the same center or studies with missing and unavailable data, and (4) the articles with low quality design, data or analysis.

Data Extraction

Two authors independently extracted the data of the included literatures. Their discrepancies were resolved through consensus or a third reviewer. The following information of literatures were extracted: first author, the publication year and the region where the study was conducted. The variables were extracted from each article: sample size, age, sex, surgical methods, cIMT and FMD.

Quality Assessment

Newcastle-Ottawa Scale (NOS) was employed to evaluate the literature quality in that quality score include: the standard of case selection (0~4 scores), the comparability between case and control group (0~2 scores) and exposure factors (0~3 scores). The total sum of score is 9 and studies with a score $\geq$6 were considered as high-quality research.

Statistical Analysis

Heterogeneity test was carried out on the selected studies. When there was no significant heterogeneity among the studies, the fixed effect model was used to combine the effect sizes. If not, the random effect model shall be used to combine the effect sizes and the sensitivity analysis was performed. Quantitative analyses were expressed by Odds Ratio (OR), ratio (Odds) and 95% confidence interval (95% CI), and the measurement data were expressed by weighted mean difference (WMD) and 95% CI. The publication bias was assessed by funnel diagram and Egger's test. The statistical analysis were performed with R software (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria) and its package "meta" [12].

Results

Study Selection

A total of 596 literatures were initially identified. After eliminating duplicates, there were 300 remaining articles for further filtering. According to the preliminary screening of titles and abstracts, 34 literatures were selected for full text perusal, and the ones with data duplication or unavailable data were eliminated. The filtering process resulted in 10 English literatures for final data retrieval and analysis. Fig. 1 show the study selection process.

Characteristics and Quality Evaluation of Included Literatures

The study characteristics are summarized in Table 1 (Ref. [13–22]). Among the 10 studies included for meta-analysis, there were a total number of 744 enrolled subjects including 402 CoA cases in the patient group and 342 healthy subjects in the control group. FMD measurement was conducted in 9 studies and cIMT recording was performed in 6 studies. The evaluation of literature quality showed that the NOS scores of all studies were $\geq$6, indicating the high qualities of the included studies.

Changes of FMD Parameter after CoA Operation

A total of 8 studies reported FMD measurement in the postoperative patient. Heterogeneity test indicated that there was significant heterogeneity among the studies (I^2 = 96.78%, $p < 0.01$). Random effect model was adopted for meta-analysis. The results showed that WMD of FMD was –4.36 (95% CI = –7.49~–1.24, p <0.01) (Fig. 2A), suggesting that postoperative FMD of CoA patients was significantly lower than that of control group. Fig. 2B shows risk of bias in FMD changes in postoperative CoA.

Changes of cIMT Parameter after CoA Operation

Among the included studies, 6 reports after the operation and the heterogeneity test revealed a significant heterogeneity among the studies (I^2 = 76.34%, $p < 0.01$). Meta-analysis based on random effect model showed that the WMD of cIMT was 0.07 (95% CI = 0.01~0.13, $p < 0.001$) (Fig. 3A), indicating that the cIMT level of patients after CoA operation was significantly higher than that of healthy controls. The risk of bias summary plot in cIMT changes are presented in Fig. 3B.

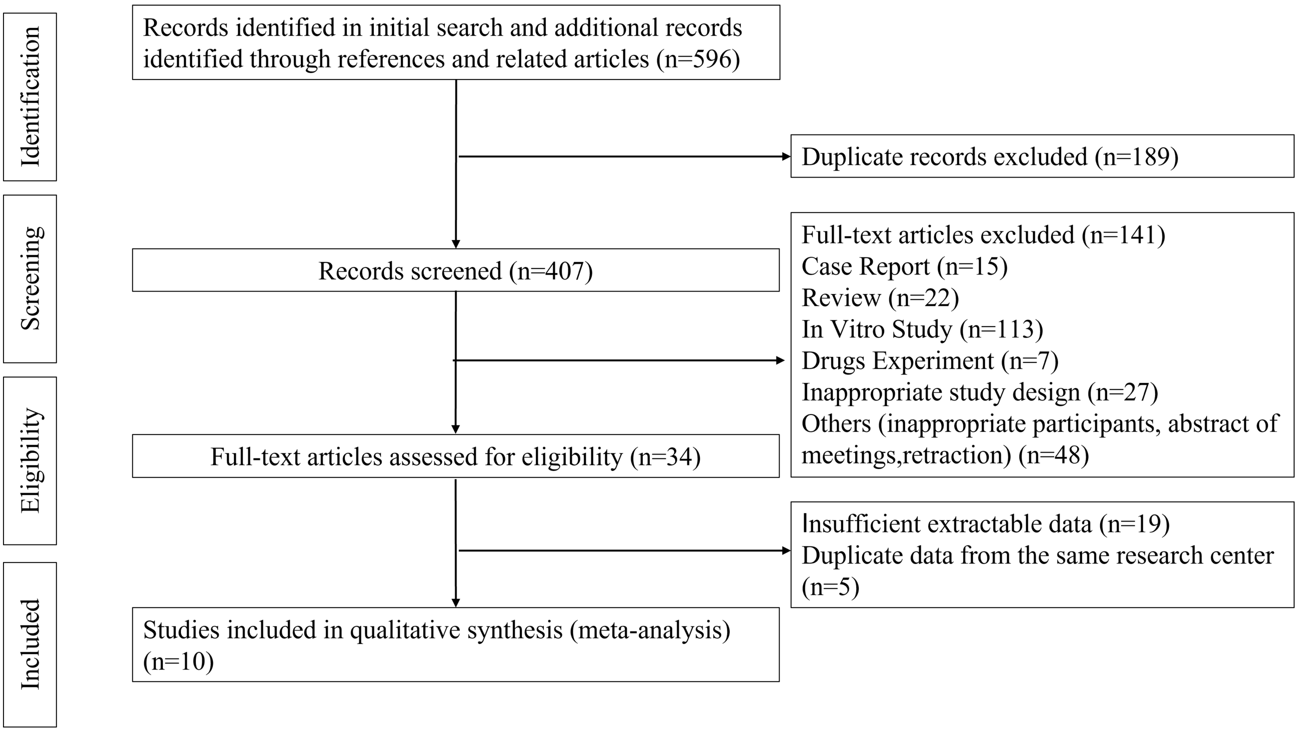

Fig. 1. Flowchart of clinical trials selection.

Sensitivity Analysis

To assess the influence of each study on the final analysis result, we eliminated each study at once and performed the sensitivity analysis. The elimination of FMD-related studies showed no significant effect on the total effective seize, indicating a robustness and consistency among the studies. In cIMT related studies, if Wybraniec *et al.* [22] 2014 was eliminated from the data, the heterogeneity of combined effect was abolished ($I^2 = 0.0\%$). However, there was no significant change in combined effect size (WMD = 0.10, 95% CI = 0.08~0.12, $p < 0.001$). Collectively, the elimination of each study did not show significant impact on total effect size, which indicates the robustness of data in these studies.

Publication Bias

The funnel diagram and Egger's test were employed to evaluate the publication bias for included studies. As shown in Fig. 4, the funnel diagram displayed a roughly symmetrical inverted funnel shape, suggesting no obvious publication bias. The results of Egger's test revealed a t value = –1.01 ($p = 0.3493$) in FMD (Fig. 4A) and t value = –1.33 ($p = 0.2534$) in cIMT (Fig. 4B), indicating publication bias of both indicators were not significant.

Discussion

Previous studies suggested that although CoA patients show postoperative improvement of the anatomical structures in the aorta, they are still prone to progressive damage of vascular structure and function, which is the plausible cause of complications and cardiovascular disorders in postoperative CoA patients. These findings highlight the importance of lifelong follow-up after CoA operation [22–24]. FMD and cIMT are commonly used indicators for evaluating the structural and functional damages in vascular system, which provide valuable information for the prognosis of cardiovascular diseases.

CIMT is one of the significant indexes for early cardiovascular diseases, which is related to the progression of hypertension and atherosclerosis. It was found that cIMT value was elevated in CoA patient at all ages, especially in children predisposed to coronary heart disease [18,24]. It is generally believed that the change of cIMT in CoA results from fetal congenital vascular structural abnormality and hypertension [25], among which hypertension includes the cases with high blood pressure in general measurement and the abnormal blood pressure detected during exercise [5]. A recent study indicates that altered anatomical structure of aortic arch is one of the major factors affecting cIMT [19]. However, there is discrepancy in the literatures with the above notion. Previous studies showed that normal cIMT was maintained in patients after CoA recovery [20,26–28]. In order to analyze the changes of cIMT in CoA patients

Table 1. Characteristics and quality evaluation of included literatures.

Reference	Region	Sample size		Gender (male)		Age		Operational procedure	Indicator of vascular function and structure	NOS score
		T	C	T	C	T	C			
Baykan 2018 [13]	Turkey	20	20	4	5	14.2 ± 3.9	13.7 ± 2.7	SI	cIMT	7
Cuypers 2013 [14]	Norway	10	8	5	4	20.4 ± 3.2	20.9 ± 4	SU	FMD	9
de Divitiis 2001 [15]	England	64	45	43	-	19 ± 1.9	20 ± 8.1	SU, SI	FMD	6
Gardiner 1994 [16]	England	25	50	16	32	19.6 ± 3.2	19.6 ± 5.1	SU	FMD	6
Heger 2005 [17]	Austria	36	25	25	12	28 ± 9	28 ± 6	SU, SI	FMD	6
Jesus 2016 [18]	Brazil	21	21	13	13	15 ± 8	15 ± 7	SI	FMD, cIMT	8
Meyer 2005 [19]	Germany	28	30	20	12	12 ± 11	14 ± 6	-	FMD, cIMT	8
Ou 2007 [20]	France	63	63	34	33	15.9 ± 6.3	14.0 ± 6	SU	FMD, cIMT	7
Trojnarska 2011 [21]	Poland	85	30	53	18	34.6 ± 10.3	33.6 ± 8.2	SU	FMD, cIMT	6
Wybraniec 2014 [22]	Poland	50	50	31	31	33 ± 14	29 ± 13	SU	cIMT	8

T, CoA group; C, Control group; SU, Operation; SI, Interventional Surgery; NOS, Newcastle-Ottawa Scale; cIMT, Carotid intima-media thickness; FMD, flow mediated dilation.

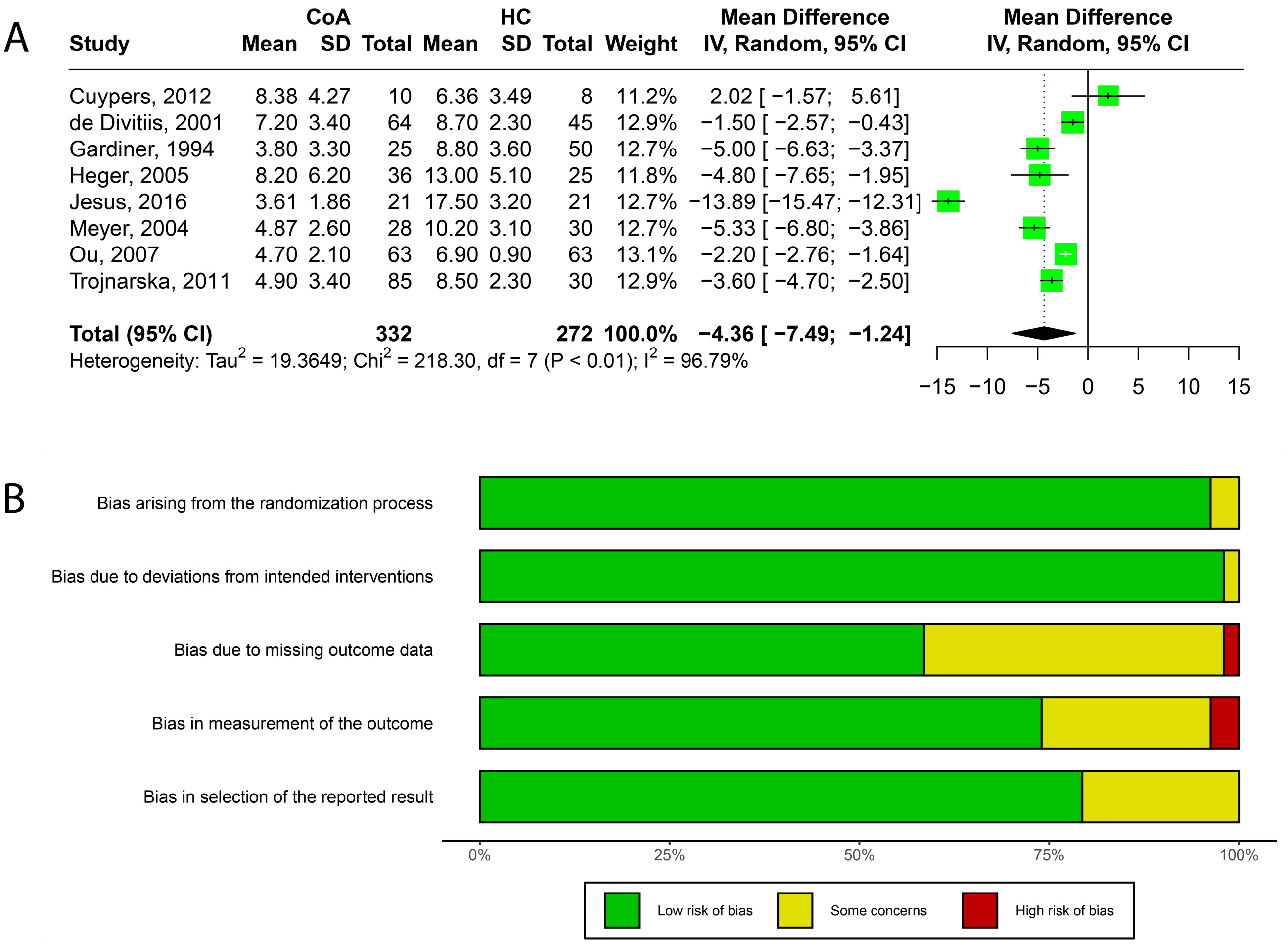

Fig. 2. Forest diagram of FMD changes after Coarctation of the aorta (CoA) operation (A) and its risk of bias (B). FMD, flow mediated dilation.

after operation, we included 6 literatures to quantitatively assess cIMT. The results showed that compared with the control group, cIMT was increased in CoA patients after operation. Based on the heterogeneity of cIMT studies, sensitivity analysis was used to screen each study and it was found that I^2 decreased to 0.0% after Wybraniec *et al.* [22] was eliminated. After further evaluating this study, there were a small number of systemic hypertension patient in the control group, which may be the main cause of the loss of combined effect the heterogeneity.

FMD damage is associated with the progression of early cardiovascular disorders, and long-term monitoring

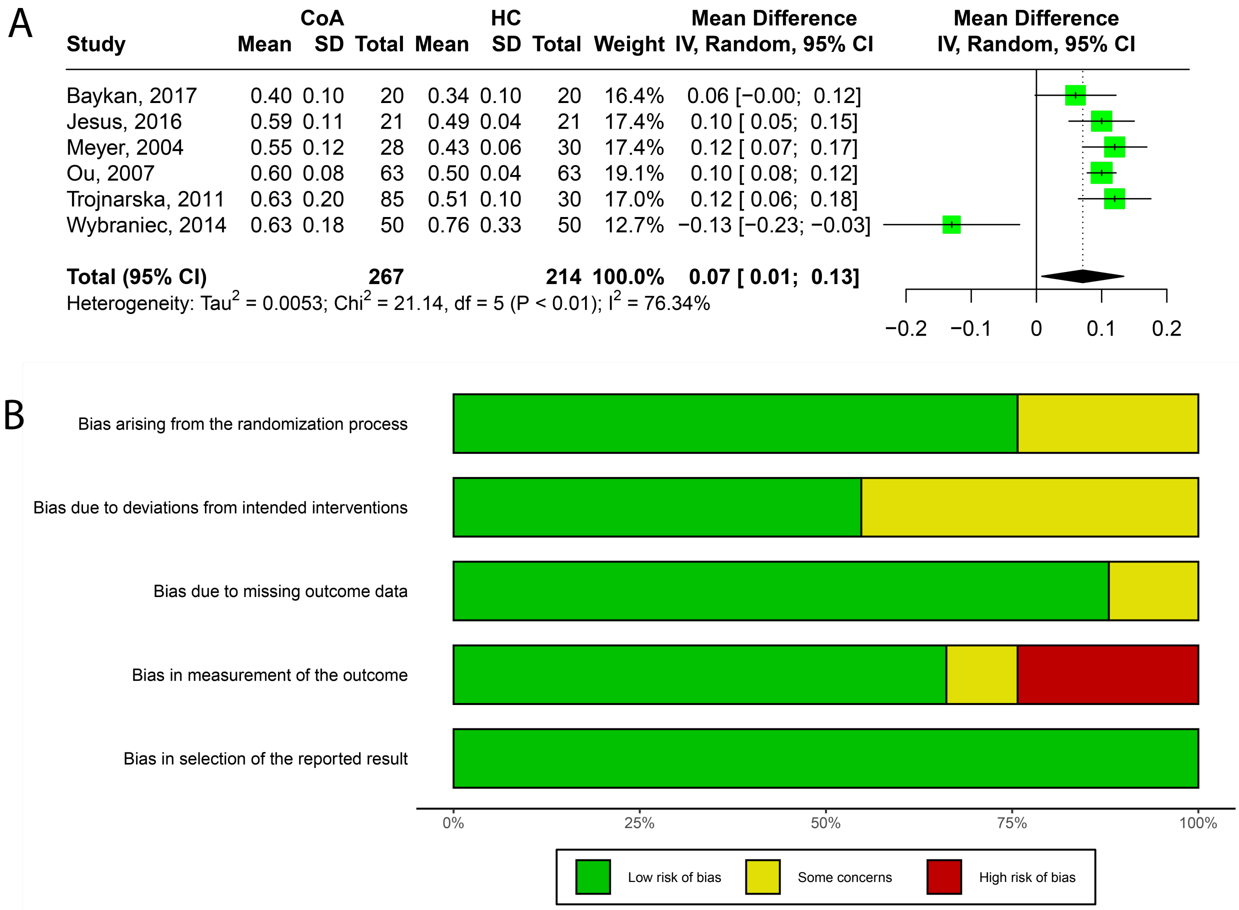

Fig. 3. Forest diagram of cIMT changes after CoA operation (A) and its risk of bias (B).

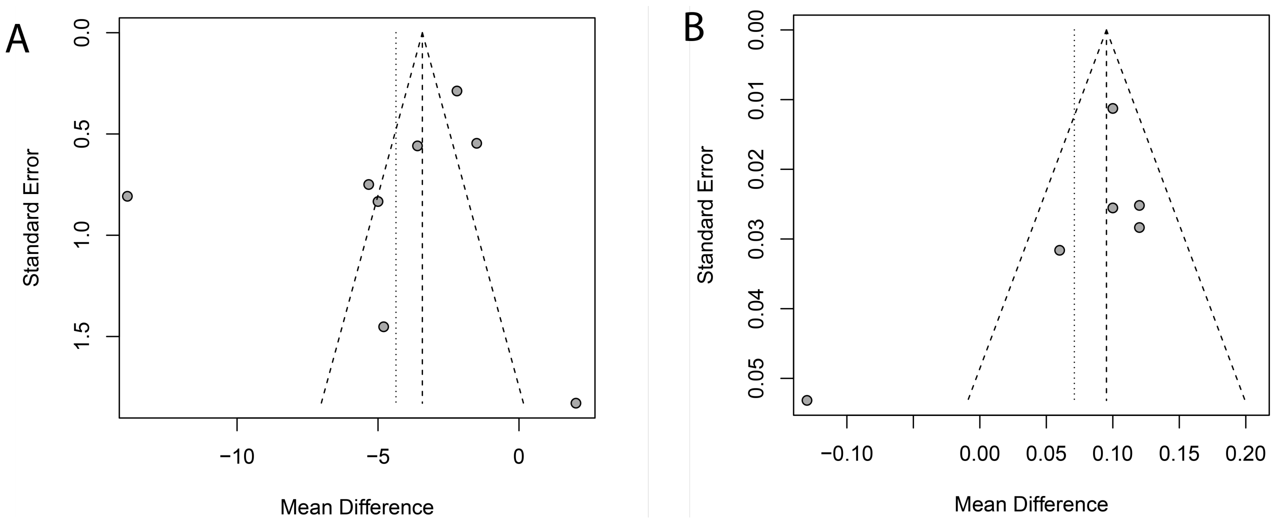

Fig. 4. Funnel diagram analysis of the included studies for FMD (A) and cIMT (B).

is necessary for evaluating the prognosis of cardiovascular diseases [19]. The alterations of vascular endothelial function are controversial in the postoperative study of CoA patients. Cuypers *et al*. [14] reported that there was no difference in vascular endothelial function between control group and CoA patients after operation. Other studies indicated that even after anatomical malformation is improved, postoperative CoA patients could still suffer from persistent vascular endothelial function damage. The pathological mechanisms underlying the change are inconclusive. It is generally believed that the increase of collagen deposition and the decrease of smooth muscle content in the upper aorta of primary coarctation may account for the impairment of arterial wall [14,17,18]. The defects in endothelial function may also result from long-term hypertension caused by Coarctation, which culminates in irreversible changes in arterial wall [13,26,29–31]. In addition, the influence of age on postoperative endothelial recovery is controversial. de Divitiis *et al.* [15] suggested that FMD was significantly reduced in patients undergoing repair surgery above 9 years old, suggesting that age-related recovery is a key determinant in postoperative vascular endothelial function. In contrast, other studies failed to show significant correlation between age and postoperative endothelial repair. Neonatal who had undergone CoA surgery in the first few months may still develop endothelial malfunction, which may be caused by the abnormal hemodynamics in the first few weeks after birth [20,32]. Therefore, the influence of recovery age on vascular endothelial injury warrants more validation. In our analysis, FMD values from 8 compliant studies showed that the level of FMD in patients after CoA operation was lower than that of the control. The elimination analysis showed no significant effect on total effective size. Therefore, our analysis supports the notion that vascular endothelial injury occurs in patients after CoA operation.

Several inherent limitations of this meta-analysis. First, only eight literatures were included, which would increase the level of Type II error and contribute less power in meta-analyses. Second, inherent publication bias refers to publish studies with positive findings than negative those. Third, there is a discrepant mean of the age among group from different publication. CoA present in infancy or dose not present until later life, in consequence, various treatments and follow-up duration would be chosen. Last, unequal sample size and gender distributions also caused high heterogeneity leading to the justification for an integrated result becomes more difficult.

This meta-analysis also demonstrated the intima-media thickening and endothelial function impairment in CoA patients after the recovery from anatomical malformations. Few studies employed FMD and cIMT as indexes to assess the association between diffuse vascular injury and complications after CoA operation. Therefore, we were not able to retrieve a prospective cohort study to define the relationship between vascular changes and the postoperative complications in CoA patients. In addition, we adopted the case-control analysis mode which has its own limitations and needs to be interpreted with caution.

Conclusions

Irreversible vascular changes after CoA operation may be the cause of persistent hypertension and early onset of coronary artery diseases. Long-term monitoring of vascular structure and function in postoperative CoA patients is necessary. In the future, the heart center need to conduct multicenter prospective studies to verify whether these indexes could serve as prognostic indicators for postoperative cardiovascular complications.

Abbreviations

FMD, flow mediated dilation; NOS, Newcastle-Ottawa Scale; CNKI, Chinese National Knowledge; OR, Odds Ratio; CHD, congenital heart disease; WMD, weighted mean difference.

Availability of Data and Materials

The data involved in the study can be found in contact the corresponding author of this article.

Author Contributions

ZW designed the research study; YB performed and analyze data of this study. Both authors participated in the writing the manuscript of the study and confirmed the final manuscript. SS and XW independently extracted valuables from included literatures. Their discrepancies were resolved through consensus or a third reviewer YG. YG also assessed risk of bias for literatures. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This work was supported by Yunnan Province Clinical Medicine Center for Cardiovascular Disease-Research Platform Construction and the key technology of Diagnosis and Treatment for Cardiovascular Diseases (Grant ID: 202102AA310003-15).

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7001.

References

[1] Kim YY, Andrade L, Cook SC. Aortic Coarctation. Cardiology Clinics. 2020; 38: 337–351.

[2] Ding P, Chen F, Qi J, Peng W, Wu K, Ding J, *et al*. Perioperative Brain Injury in Children with Aortic Arch Anomalies: A Retrospective Study of Risk Factors and Outcomes. Pediatric Cardiology. 2023. (online ahead of print)

[3] Ungerleider RM, Pasquali SK, Welke KF, Wallace AS, Ootaki Y, Quartermain MD, *et al*. Contemporary patterns of surgery and outcomes for aortic CoArctation: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. The Journal of Thoracic and Cardiovascular Surgery. 2013; 145: 150–157.

[4] Rajbanshi BG, Joshi D, Pradhan S, Gautam NC, Timala R, Shakya U, *et al*. Primary surgical repair of CoArctation of the aorta in adolescents and adults: intermediate results and consequences of hypertension. European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2019; 55: 323–330.

[5] Yogeswaran V, Connolly HM, Al-Otaibi M, Ammash NM, Warnes CA, Said SM, *et al*. Prognostic Role of Hypertensive Response to Exercise in Patients With Repaired CoArctation of Aorta. The Canadian Journal of Cardiology. 2018; 34: 676–682.

[6] Lo MH, Lin IC, Lu PC, Huang CF, Chien SJ, Hsieh KS, *et al*. Evaluation of endothelial dysfunction, endothelial plasma markers, and traditional metabolic parameters in children with adiposity. Journal of the Formosan Medical Association. 2019; 118: 83–91.

[7] Shechter M, Shechter A, Koren-Morag N, Feinberg MS, Hiersch L. Usefulness of brachial artery flow-mediated dilation to predict long-term cardiovascular events in subjects without heart disease. The American Journal of Cardiology. 2014; 113: 162–167.

[8] Sabri MR, Daryoushi H, Gharipour M. Endothelial function state following repair of cyanotic congenital heart diseases. Cardiology in the Young. 2015; 25: 222–227.

[9] Reiner B, Oberhoffer R, Häcker AL, Ewert P, Müller J. Carotid Intima-Media Thickness in Children and Adolescents With Congenital Heart Disease. The Canadian Journal of Cardiology. 2018; 34: 1618–1623.

[10] Remmele J, Willinger L, Oberhoffer-Fritz R, Ewert P, Müller J. Increased carotid intima-media thickness and reduced health-related physical fitness in children and adolescents with coarctation of the aorta. International Journal of Cardiology Congenital Heart Disease. 2022; 8: 100390.

[11] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical Research Ed.). 2021; 372: n71.

[12] Jiang WH, Chen BW, Zheng JG, Li J. Application of R language meta-package in meta-analysis. Evidence-Based Medicine. 2011; 11: 305–309.

[13] Baykan A, Demiraldi AG, Tasci O, Pamukcu O, Sunkak S, Uzum K, *et al*. Is hypertension the fate of aortic CoArctation patients treated with Cheatham Platinum (CP) stent? Journal of Interventional Cardiology. 2018; 31: 244–250.

[14] Cuypers J, Leirgul E, Larsen TH, Berg A, Omdal TR, Greve G. Assessment of vascular reactivity in the peripheral and coronary arteries by Cine 3T-magnetic resonance imaging in young normotensive adults after surgery for CoArctation of the aorta. Pediatric Cardiology. 2013; 34: 661–669.

[15] de Divitiis M, Pilla C, Kattenhorn M, Zadinello M, Donald A, Leeson P, *et al*. Vascular dysfunction after repair of CoArctation of the aorta: impact of early surgery. Circulation. 2001; 104: I165–I170.

[16] Gardiner HM, Celermajer DS, Sorensen KE, Georgakopoulos D, Robinson J, Thomas O, *et al*. Arterial reactivity is significantly impaired in normotensive young adults after successful repair of aortic CoArctation in childhood. Circulation. 1994; 89: 1745–1750.

[17] Heger M, Willfort A, Neunteufl T, Rosenhek R, Gabriel H, Wollenek G, *et al*. Vascular dysfunction after CoArctation repair is related to the age at surgery. International Journal of Cardiology. 2005; 99: 295–299.

[18] Jesus CA, Assef JE, Pedra SRFF, Ferreira WP, Davoglio TA, Petisco ACGP, *et al*. Serial assessment of arterial structure and function in patients with CoArctation of the aorta undergoing stenting. The International Journal of Cardiovascular Imaging. 2016; 32: 729–739.

[19] Meyer AA, Joharchi MS, Kundt G, Schuff-Werner P, Steinhoff G, Kienast W. Predicting the risk of early atherosclerotic disease development in children after repair of aortic CoArctation. European Heart Journal. 2005; 26: 617–622.

[20] Ou P, Celermajer DS, Mousseaux E, Giron A, Aggoun Y, Szezepanski I, *et al*. Vascular remodeling after ”successful” repair of CoArctation: impact of aortic arch geometry. Journal of the American College of Cardiology. 2007; 49: 883–890.

[21] Trojnarska O, Mizia-Stec K, Gabriel M, Szczepaniak-Chicheł L, Katarzyńska-Szymańska A, Grajek S, *et al*. Parameters of arterial function and structure in adult patients after CoArctation repair. Heart and Vessels. 2011; 26: 414–420.

[22] Wybraniec MT, Mizia-Stec K, Trojnarska O, Chudek J, Czerwieńska B, Wikarek M, *et al*. Low plasma renalase concentration in hypertensive patients after surgical repair of Coarctation of aorta. Journal of the American Society of Hypertension: JASH. 2014; 8: 464–474.

[23] Ghorbannia A, Maadooliat M, Woods RK, Audi SH, Tefft BJ, Chiastra C, *et al*. Aortic Remodeling Kinetics in Response to Coarctation-Induced Mechanical Perturbations. Biomedicines. 2023;11: 1817.

[24] Zeng Jiemin, Huang Ping, Wang Hongying, Yuan Jia, Zhang Li, *et al*. Short-term and medium-term follow-up of vascular endothelial function after correction of aortic CoArctation. 2016; 32: 1247–1249.

[25] Brown ML, Burkhart HM, Connolly HM, Dearani JA, Cetta F, Li Z, *et al*. CoArctation of the aorta: lifelong surveillance is mandatory following surgical repair. Journal of the American College of Cardiology. 2013; 62: 1020–1025.

[26] Vriend JWJ, de Groot E, Bouma BJ, Hrudova J, Kastelein JJP, Tijssen JGP, *et al*. Carotid intima-media thickness in post-CoArctectomy patients with exercise induced hypertension. Heart (British Cardiac Society). 2005; 91: 962–963.

[27] Luijendijk P, Bouma BJ, Vriend JWJ, Groenink M, Vliegen HW, de Groot E, *et al*. Beneficial effect of high dose statins on the vascular wall in patients with repaired aortic CoArctation? International Journal of Cardiology. 2014; 176: 40–47.

[28] Trojnarska O, Szczepaniak-Chicheł L, Mizia-Stec K, Gabriel M, Bartczak A, Grajek S, *et al*. Vascular remodeling in adults after

CoArctation repair: impact of descending aorta stenosis and age at surgery. Clinical Research in Cardiology: Official Journal of the German Cardiac Society. 2011; 100: 447–455.
[29] Swan L, Kraidly M, Vonder Muhll I, Collins P, Gatzoulis MA. Surveillance of cardiovascular risk in the normotensive patient with repaired aortic CoArctation. International Journal of Cardiology. 2010; 139: 283–288.
[30] Thijssen DHJ, Bruno RM, van Mil ACCM, Holder SM, Faita F, Greyling A, *et al*. Expert consensus and evidence-based recommendations for the assessment of flow-mediated dilation in humans. European Heart Journal. 2019; 40: 2534–2547.
[31] Vogt M, Kühn A, Baumgartner D, Baumgartner C, Busch R, Kostolny M, *et al*. Impaired elastic properties of the ascending aorta in newborns before and early after successful CoArctation repair: proof of a systemic vascular disease of the prestenotic arteries? Circulation. 2005; 111: 3269–3273.
[32] Leeson CP, Whincup PH, Cook DG, Donald AE, Papacosta O, Lucas A, *et al*. Flow-mediated dilation in 9- to 11-year-old children: the influence of intrauterine and childhood factors. Circulation. 1997; 96: 2233–2238.