ejpmr, 2025, 12(6), 579-587

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ASSOCIATION BETWEEN AORTIC DISSECTION WITH CONCOMITANT CORONARY ARTERY DISEASE AND HEREDITARY CONNECTIVE TISSUE DISORDER: A META-ANALYSIS

Mohamed Nor Abubakar[a], Zhirong Lin[a], Shenghui Bi[b], Zhiye Wu[a] and Yanbin Cai[a,b,*]

[a]Guangdong Provincial Biomedical Engineering Technology Research Center for Cardiovascular Disease, Department of Cardiology and Laboratory of Heart Center, Zhujiang Hospital, Southern Medical University, Guangzhou, 510280, China.

[b]Department of Cardiovascular Surgery, Zhujiang Hospital, Southern Medical University, Guangzhou, 510280, China.

***Corresponding Author: Yanbin Cai**
Guangdong Provincial Biomedical Engineering Technology Research Center for Cardiovascular Disease, Department of Cardiology and Laboratory of Heart Center, Zhujiang Hospital, Southern Medical University, Guangzhou, 510280, China.

Article Received on 25/04/2025 **Article Revised on 15/05/2025** **Article Published on 09/06/2025**

ABSTRACT

Background*:** Aortic dissection is more common in individual with high blood pressure and atherosclerosis but most people with hypertension or atherosclerosis do not have dissection. Our aim is to identifying the association between aortic dissection and hereditary connective tissue disorders, as well as overlapping with genetic disorders linked to coronary artery disease. ***Methodology: We used databases based on PubMed, EMBASE and Scopus to cover almost all publications from 2000 to 2024. In the quality analysis, we created a number of tools, such as The Newcastle-Ottawa Scale and checklists are utilized to assess the validity of certain observational studies. ***Result:*** Based on four studies, aortic dissection occurrences were revealed in 414 participants, with 251 individuals having HCTD and 163 patients without HCTD (OR = 2.35, CL = 1.67–3.33, $p < 0.0001$). As shown by $I^2 = 31\%$ and P = 0.22, the study results exhibit no detectable heterogeneity, the findings demonstrated a strong association between HCTD and an elevated risk of AD when compared to non-HCTD. Our findings indicate that of the twelve identified CAD risk genes, genetic risk factors associated with aortic dissection elevate the probability of developing coronary artery disease. SMAD3, APOB, and COL4A1 exhibited an overlap in both aortic dissection and coronary artery disease. ***Conclusion***: This study establishes an outline for identifying the high-risk population for HCTD-associated AD and CAD, and helps to formulate preventive and therapeutic strategies and further investigation of genetic mechanisms particular observing the TGF-B pathway linked to AD may optimize risk assessment in the future.

KEYWORDS: Aortic dissection. Hereditary connective tissue disorder. Coronary artery disease.

INTRODUCTION

Aortic dissection (AD) generally is defined when the aortic media separates from the intima; this causes blood to collect in this area; the aorta wall will then eventually develop intimal tears and ultimately creates the real and false aortic lumens of two blood vessels.[1-4] AD patients are typically asymptomatic until the aorta wall ruptures catastrophically, which results in blood leaking into the aortic wall's layers and layer denudation; the disease has a high serious risk of morbidity and mortality.[5-7] Early diagnosis allows important decisions to be performed before acute dissection, which is likely to have better clinical outcomes and increases survival rate and decreases premature deaths from rupture or other dissection-related complications.[8] Patients with complain of mid-back and central chest pain, similar to a heart attack, when they approach the emergency room[9] and the incidences of AD in emergency departments range from 5.93/100,000 to 24.92/100,000.[10] Occasionally, the pain may be described as tearing or splitting and may radiate to the upper back or neck. In addition, that can mimic ischemia, resulting in a false diagnosis. The condition may deteriorate to the point where it affects the aortic branches and can spread both proximally and distally, resulting in a range of symptoms.[11,12] The coronary ostium may pressed by the enlarged false lumen in 10% to 15% of patients with type A dissection, leading to varying degrees of myocardial ischemia and infarction.[13] Equivalents in terms of electrocardiography (ECG) and clinical presentations and raises their chance of dying by double and increasing mortality may result from incorrect diagnosis or ineffective treatment of an AD.[4,13,14] Previous research indicated that aortic dissection patients had elevated rates of comorbidities, specifically hypertension (70.33%) and atherosclerosis (10.17%).[12,15] Hypertension is the most

common condition associated with aortic dissection. The majority of individuals with hypertension do not experience from dissections. Integrative functional analyses identified genes likely regulated in vascular smooth muscle cells related to extracellular matrix biology.[16,17] Numerous variants linked to aortic dissection display-contrasting associations with coronary artery disease suggesting that shared biological mechanism both conditions.[18] There are growing interest in discovering the hereditary connective tissue disorder resulting in medial degeneration of the aortic wall, as well as its association with genetic disorders related to coronary artery disease.

The purpose of this study is to find the association between aortic dissection and hereditary connective tissue disease, as well as to explore the overlap with genetic disorders involving coronary artery disease. The outcomes provide novel pathophysiological insights into artery integrity and establish an outline for future targeted therapeutics and preventive methods that could improve screening and diagnostic efforts with goal of lowering morbidity and mortality.

METHODS

Our methodology begins with an evaluation of the criteria for inclusion and exclusion, covering the definition of the research, the steps for data extraction, effect size (ES) calculation, and research quality rating. All procedures used in this meta-analysis and systematic review adhered to the PRISMA recommendations.

Strategy for data search

The following terms were used to build a search strategy: "aortic dissection" and "hereditary connective tissue disorder" or "aortic dissection and coronary artery disease." The analysis strategy was adjusted to fit the specifications of each database. The aim of the search was to acquire publications that evaluated the correlation between aortic dissection (AD) and hereditary connective tissue disorder (HCTD), as well as coronary artery disease (CAD) and HCTD. The reference lists of the included publications were reviewed for possibly useful information, and duplicate entries were removed using EndNote21 tool to assure completeness.

Selection and eligibility criteria for study

The inclusion criteria include quantitative research published in English, including cohort and controlled research, including clinical investigations examining the association of AD and HCTD or AD and CAD, with no restrictions on patient age, gender, ethnicity, or geographic origin. Exclusion criteria involve research that is irrelevant to AD and CAD in HCTD, in vitro studies, case series, systematic reviews, meta-analyses, non-human subjects, or studies that involve overlapping or duplicate data. Two investigators independently using their abstracts and titles reviewed the preliminary research. A third investigator was engaged for instances of disagreement.

Quality evaluation and publishing bias

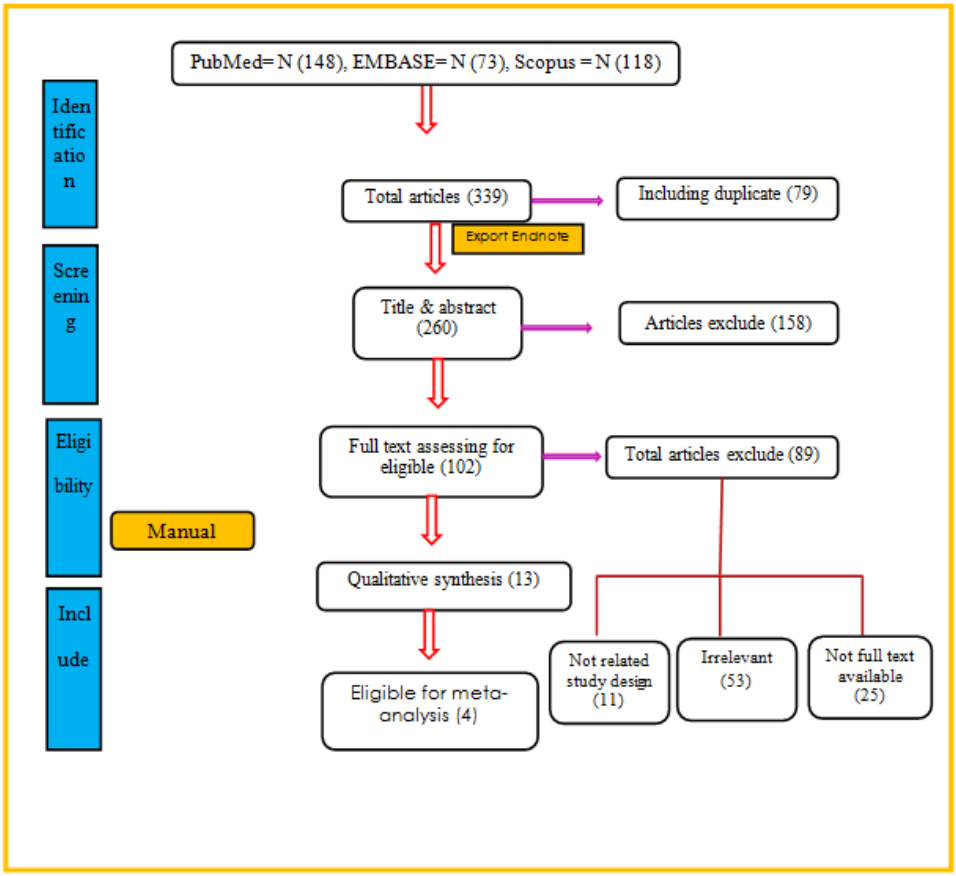
We selected scales that provide graded evaluations of research to determine the standard of the methodology, Thresholds for converting the Newcastle-Ottawa scales to standardize good, fair, and poor. Three aspects comprise the assessment of individual studies: participant selection, study group comparability, and identification of the associated exposure (case-control) or outcome (cohort and cross-sectional). Our studies are rated as follows: up to nine stars, when agreement is greater than 80%, low risk of bias, seven to eight stars moderate risk of bias, when agreement is between 51%–80% and six stars or less, high risk of bias, High when agreement is below 50%.

Synthesis of data Statistical analysis was conducted with Review Manager Version 5.4 (e.g., Nordic Cochrane Centre, Copenhagen, Denmark). The pooled hazard ratio (HR) with a 95% confidence interval was calculated using the DerSimonian-Laird random effects model. The pooled hazard ratio for outcomes was evaluated using a multivariable model, adjusted for variables like age, sex, comorbidities, smoking, and socioeconomic status. Statistical significance was established if the 95% confidence interval for the pooled hazard ratio did not include the neutral value of "1" and the two-tailed p-value was less than 0.05. The Higgins I^2 metric was employed to evaluate statistical heterogeneity, classifying 25–50% as mild, 50–75% as moderate, and over 75% as severe heterogeneity. Sensitivity analysis was conducted to evaluate the influence of each study on the total effect estimate using the "leave-one-out method." The evaluation of publication bias indicated a p-value over 0.05.

RESULT

Selection of studies

The preliminary search found 339 appropriate articles. Following eliminating duplicates (n = 79), A first screening of 260 records was conducted. Following the evaluation of titles and abstracts, 158 articles were excluded. We found 102 articles received thorough full-text assessment, resulting in the removal for 89 for several reasons: incorrect results (n = 11), inadequate study population (n = 53) and insufficient publication form (n = 25). The internal validity of 13 papers was evaluated, four publications were incorporated into the conclusive meta-analysis. The PRISMA flowchart show the systematic literature and selection study methodology (Fig. 1).



Study and Participant Characteristics

The analysis included 414 patients who had aortic dissection, corresponding to 251 participants in the HCTD group and 163 in the non-HCTD. Using Data collected from 2018 to 2022. Four studies were conducted, with three in China.[7,19,20] and one in Poland.[21] The key features of all studies included in this meta-analysis [Table 1]**.** The hypertension group had a higher average start age for AD than the no hypertension group (49.51 ± 1.25 vs. 44.15 ± 1.94, p=0.02).[22] Older individuals may experience various comorbidities, such as diabetes mellitus and atherosclerosis.[23,24]

Table 1: The demographics and comorbidities associated with CAD and HCTD.

Author	Year	No. Patient	Mean age	Male gender	Disease	HCTD		Comorbidities disease			
						Positive Geno-type	Negative Geno-type	CAD	HT	DM	LD
Ponińska et al.	2022	132	44.9 ±14.2	92 (69.7%)	AD	79 (59.8%)	53(42%)	20 15.2%	73(55.3%)	10(7.6%)	37(28.0%)
Ying Li	2021	151	46.6	97 (80%)	AD	94 (62.3%)	57 (37.7)	37 (24.5)	88 (58.3)	16 (10.6)	0
PAN ET AL	2020	72	47.06 ± 9.79	50 (69.4%)	AD	39 (54.2)	33 (48.8)	13 (18.1)	48(66.7%)	0	0
Jinxiang Zheng	2018	57	40 ±12	33 (84.6)	AD	52 (91.2)	5 (8.8)	1(4.5)	31(79.5%)	2(5.1%)	8(20. 5%)

Quality evaluation and publications biases

We utilized the Newcastle-Ottawa Scale (NOS) for cohort studies to assess quality. the total score varied between six and nine (Table 2). The quality was high, and the probability of bias was low. There was no statistically significant publication bias (p = 0.24) as shown in Egger's regression test, which was based on a glance of the funnel plot (Table 2).

Table 2: Evaluation based on the Newcastle-Ottawa Quality Assessment Scale.

Research	Design				Comparison	Outcome			Total score	Agreement (%)	Risk of Bias
	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Demonstration	Comparability	Assessment of outcome	Follow-up	Adequacy of follow up of			
Ponińska et al 2022	*	*	*	*	*	*	*	*	9	100%	Low
Ying Li 2021	*	*	*	*	**	*		*	8	100%	Low
PAN ET AL 2020	*	*	*		*	*		*	6	100%	medium
Jinxiang Zheng 2018	*	*	*	*	**	*		*	8	100%	Low

Outcomes

All four studies indicated the risk of aortic dissection.[7,19-21] Individuals with hereditary connective tissue disorders demonstrate an elevated risk of aortic dissection (OR = 2.35, CL = 1.67–3.33, $p < 0.0001$). There was no heterogeneity across the study results, as shown by I^2 = 31% and $p = 0.22$. The effort to measure and control for variability is a fundamental goal of an M-A in order to ensure the M-A's reliability, the two types of variability—within-study and between-study—must be evaluated, and their impact must be reduced in the I^2 statistical analysis. The I^2 statistic was applied to evaluate heterogeneity among the included research, measuring the extent of variability in effect estimates attributable to genuine differences between studies rather than sampling error. An I^2 value of 25% indicates modest heterogeneity, 50% signifies moderate heterogeneity, and 75% denotes significant heterogeneity. This statistic helps determine whether pooling the study results is appropriate and guides the choice of model for meta-analysis [Fig 2].

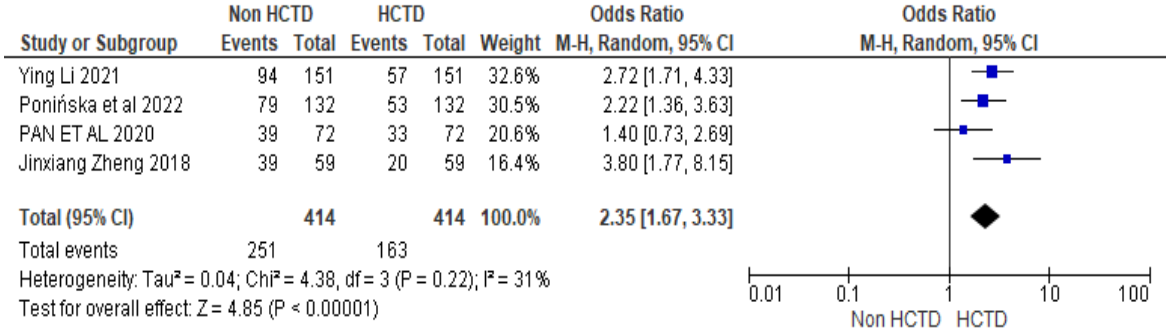


Figure 2: Forest layout for the association between HCTD and non-HCTD in random effects model.

In our meta-analysis of individuals with aortic dissection (AD), we found 16 pathogenic/likely pathogenic (P/LP) mutations as potential related genes. The findings conclude that the genes listed are definitively associated to a greater probability of aortic dissection. [Table 3]. Pathogenic variants are identified as predispositions for heritable connective tissue disorders, while likely pathogenic variants may be essential for the precise diagnosis of individuals with thoracic aortic enlargement; however, variants of uncertain significance (VUS) are not considered to substantially elevate the risk of progression to aortic dissections. Uncertain genes are those that have just been published, have little information, and no clear classification. It remains viable until additional data are available.

Table 3: Genes on the list show major predicting genes in HTAD associating with the risk of aortic dissection.

Number	Name of Genes	Inherited	Related Syndrome	Routes Affected
1	ACTA2	AD	Smooth muscle dysfunction syndrome	SMC contraction
2	APOB	AD		
3	ABCC6	AD		
4	COL3A1	AD	Vascular Ehlers-Danlos syndrome	ECM
5	FBN1	AD	Marfan syndrome	ECM
6	F5	AD		
7	MYLK	AD		SMC c
8	MYH11	AD		SMC
9	SMAD3	AD	Loeys-Dietz syndrome	TGF-β
10	SMAD6	AD	Loeys-Dietz syndrome	TGF-β
11	TGFBR2	AD	Loeys-Dietz syndrome	TGF-β
12	TGFBR1	AD	Loeys-Dietz syndrome	TGF-β

13	LOX	AD	Marfan syndrome	
14	LTBP3	AD	MFS	ECM
15	HCN4	AD		
16	B3GAT3	AD		

Abbreviation: AD implies aortic dissection; ECM signifies extracellular matrix; TGF stands for transforming growth factor; HCTD indicates heritable connective tissue disorder; SMC represents smooth muscle cell. Aortic disease or other vascular problems may be present in individuals with deleterious mutations in these genes who also do not show syndromic manifestations. This is based on current data.[12,25]

We reviewed the existing research on coronary artery disease and heritable connective tissue disorders. We identified 12 genes with mutations classified as P/LP, indicating their probable role as causative factors. The research demonstrates that the specified genes significantly increase the risk of CAD (Table 4).[16,17,26-29] Coronary artery disease has a complex etiology, primarily involving a combination of traditional risk factors.[17] Dyslipidemia and hypertension are common risk factors; however, they are insufficient for identifying high-risk asymptomatic individuals and do not encompass all cases of coronary artery disease (CAD).[16] Genetic factors account for 40% to 50% of cases of susceptibility to coronary artery disease.[26]

Table 4: Frequent Genes Influencing coronary artery disease.

Num.	Genes	Potential Functions of Possible Significance to CAD	Odds Ratio
1	SORT1	Modulate apoB secretion and LDL metabolism	1.11
2	PDE5A,	Unknown	1.06
3	LDLR,	Low-Density Lipoprotein clearance	1.08
4	PCSK9	Regulation of LDL receptor recycling	1.08
5	APOB	Principal apolipoprotein of low-density lipoprotein	1.07
6	LPA	Intracellular hydrolysis of cholesteryl esters	1.07
7	ADAMTS7	Proliferative response to vascular injury Downstream modulator of the TGF-β signalling pathway	1.08
8	SMAD3	Downstream mediator of TGF-β signaling pathway	1.07
9	HHIPL1,	Unknown	1.04
10	COL4A1/A2	Type IV collagen chain of the basal membrane	
11	GUCY1A1	Signaling via nitric oxide	1.06
12	ANGPTL3	Unknown	1.05

Abbreviation: CAD signifies coronary artery disease; EC, endothelial cells; HIF1A, hypoxia-inducible factor 1A; IL, interleukin; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; LncRNA, long noncoding RNA; MAPK, mitogen-activated protein kinase; MEF2 refers to myocyte enhancer factor 2; MMP denotes matrix metalloproteinase. Nuclear interacting partner of anaplastic lymphoma kinase (NIPA); Odds ratio (OR); PC refers to phosphatidylcholine. PDGF denotes platelet-derived growth factor; PE signifies phosphatidylethanolamine; REST, RE-1 Silencing Transcription Factor; SMC refers to smooth muscle cell.[30]

DISCUSSION

We discovered that the average event-free survival was lower in those with triple variations or higher than in those with single and double variants, respectively.[12] It showed that patients with triple or more AD mutations had a higher chance of developing the disease early than those with a limited number of variations, and that patient with three or more mutations in AD typically experienced more severe symptoms.[31] The amount of variants a individual carries is a crucial factor in risk stratification, and is used to predict and diagnose disease in patients.[32] Aortic root syndromic symptoms and age under 45 years are predictor the chance of having a P/LP variant.[33] with regard to the first author Ying Li discovered that people with LP/P v, which was younger than those with VUSs (48.5 years) and those without any variant (53.0 years) in South China.[34]

In contrast, Duan et al. interestingly found that P/LP variants were more likely to be found in younger individuals, for P/LP carriers it was 31.5 years, for VUS carriers it was 57 years and for the NV group it was 57 years, these were the median ages at testing in East China.[35]

Patients Individuals with P/LP variations exhibited a median maximal aortic size of 5.25 cm while patients without P/LP variants had a median size of 5.1 cm, according to Ruwan Weerakkody et almost 50% of the P/LP variations found were caused by mutations in FBN1, most of which affected functionally important areas of the gene.[36,37] The fact that the disease is located in the ascending aorta as opposed to the descending aorta signifies that the ascending aorta's known greater hereditary etiology of AD.[38] Type A dissection patients are often younger than type B dissection patients, and

Aortic dissection generally manifests in individuals below 40 years of age with connective tissue disorder.[14,39] Intentional coronary angiography has been linked to increased readmission rates from the intensive care unit (30.0% vs. 7.7%), as well as a trend toward longer stays in the intensive care unit (e.g., 92.0 hours versus 63.5 hours) and the hospital (e.g.,18 days versus 13 days), which suggested a more difficult recovery process.[40] We also frequently forego CAG prior to surgery if the coronary arteries are very clear of calcified plaques, which would be evident in the high-resolution CT scan, even in the absence of coronary CT angiography.[41] In these three Criteria should be considered, firstly, it is important to take into account the possibility of aortic ectasia, which is frequently seen in patients tissue disorders such as Marfan's. A modified Bentall approach is advised in this case, Secondly, the presence of an impaired coronary ostium, which often requires removal, is a consideration. Finally, the absence of an ostial rupture was noted as an additional suggestions, contingent upon specific coronary dissection anatomy.[42] Specific care of coronary involvement in AD is still debatable with recommendations by Neri and Chen; some studies advocate employing CABG in all cases, while others suggest utilizing only local in repairing in cases of type A coronary dissection.[14] We identified the level of pleiotropy in CAD by looking for links between all known CAD genes shared with the aorta dissection. Pleiotropy is a trait that many CAD risk variations share; it means that similar biological processes may play a role in many diseases. This helps us understand how diseases start and makes the genotype-phenotype relationship clearer.

Of the 12 CAD risk gene discovered demonstrated substantial relationships with conventional variables, with certain gene displaying multiple associations (e.g., SMAD3, APOB, and COL4A1).[17,43-45] Particularly, these genes exhibit overlap with loci associated with the risk of AD with similar by Webb and colleagues found 38.7% found these genes interlaced risk for AD and CAD.[46] According to what Chesmore et al. found, 50% of CAD risk loci were linked to various diseases including migraines, cancer, and height.[18] There are at least two ways that genes that control the role of vascular smooth muscle cells in influencing atherosclerosis.[47] One strategy involves regulating vascular tone and blood pressure.[48] The second way is through local processes like inflammation and vascular remodeling, which can either make the plaque more stable or less stable.[49] As anticipated, there exists considerable genetic correlation between these two qualities, as significant example is the nitric oxide signaling system.[50] Cyclic guanosine monophosphate, a second messenger, stimulates vascular smooth muscle cells and this leads to the relaxation of vascular smooth muscle cells. Mice lacking the nitric oxide receptor in vascular smooth muscle cells display a hypertensive phenotype.[51] Human genomics identified ADAMTS7, a non-lipid etiology of coronary artery disease.[46] This discovery elicited considerable interest in elucidating the underlying mechanism. This difference is connected to a 19% rise in the number of people who have CAD, which is defined as a main coronary canal that is more than 50% narrowed. Many people wanted to know more about how this variation works, especially since it has nothing to do with blood cholesterol levels or other known risk factors for CAD.[52] ACTA2 is often located in smooth muscle cells that border the arteries, facilitating arterial constriction to regulate blood pressure and flow.[29] We identified a novel pathway to atherosclerosis, rendering our discovery distinctive. This elucidates why statins are generally accepted for their role in preventing heart attacks in healthy people, including those with normal blood cholesterol levels. Statins inhibit cholesterol synthesis by stressed smooth muscle cells in individuals with ACTA2 mutations.[47] the ACTA2 mutation made a protein that stressed the cells in the artery wall.[28] Now, aortic dissection and other coronary artery disease risk factors are being studied to see if they can cause cellular stress and start this new pathway.[53] Genetic risk scores have been studied in detail, which has helped us learn a lot about how genes affect CAD and what role each different locus plays. Nonetheless, the role of most genetic variants in disease pathways remains unrecognized. The existence or lack of a conventional risk factor may affect the degree to which a genetic factor contributes to disease. It is imperative to focus on alleviating and controlling traditional risk factors until the impact of genetic risk scores is thoroughly clarified.

CONCLUSION

Our results indicate that aortic dissection with concomitant coronary artery disease and hereditary connective tissue disorder are related, and that having two or more gene Variations were linked to an increased risk of both aortic dissection and coronary artery disease compared to having none at all. Our comprehension, this meta-analysis is the initial show a link between HCTD and AD and CAD risk. It is recommended that family members who began the disease early (< 50 years), have a family history of the condition, and have never had hypertension be tested. In an effort to lower morbidity and mortality, the finding of particular genes in aortic dissection with concomitant CAD may help improved patient treatment and surveillance, predictor risk classification and prognosis, as well as cascade screenings for relatives whose might be in hazard factors. In order to potentially get the best results. We ultimately found innovative therapeutic targets, including PCSK9, ANGPTL4, ANGPTL3, and GUCY1A1.[27] Thus, our findings provide a robust basis for the future formulation of tailored treatment approaches, however, since decades of a thorough desire for efficient medicinal interventions for AD have failed to provide positive results recognizing the core genetics of disease presents the greatest opportunity of finding a successful, biologically based medical therapy in the future.

Prospective future

Patients with inherited connective tissue disorders who have aortic dissection and concomitant coronary artery disease have a promising future ahead of them due to various areas of active research and possible advancements. More accurate genetic testing and screening methods for hereditary connective tissue diseases will be developed, which will aid in the early identification of high-risk people.

Limitations of research

The quality of the studies incorporated in the meta-analysis may differ; certain studies may exhibit methodological deficiencies (e.g., limited sample sizes, absence of controls), which can bias the results. Publication bias is another concern, as studies with significant or Positive outcomes are more likely to be disseminated. Variations in study design, population, interventions, and outcome measures across studies can lead to heterogeneity. This can make it difficult to draw a clear, consistent conclusion across studies and may require additional statistical methods (e.g., random-effects models) to account for this variability.

Declaration of generative AI in academic papers

AI is not currently being used for writing.

CRediT authorship contribution statement

Mohamed Nor Abubakar: The conceptualisation, Methodology, Original Draft Composition, Writing – review & editing, Project administration. **Zhirong Lin:** Validation, Formal analysis, Data curation. **Shenghui Bi:** Methodology, Validation, Investigation. **Zhiye Wu:** Validation, Supervision, Conceptualization. **Yanbin Cai:** Writing-review & editing, Supervision, Funding acquisition, Conceptualization.

Statement of conflicting interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement of assistance from grants

The writers assert that they have not received any grant support from individuals, funding agencies, or institutions.

REFERENCE

1. Mikulski MF, Well A, Mery CM, et al. Outcomes of thoracic aortic interventions in Marfan syndrome in the state of Texas over 11 years. *Interdisciplinary CardioVascular and Thoracic Surgery*, 2023; 37(2).
2. Gawinecka J, Schnrath F, von Eckardstein A. Acute aortic dissection: pathogenesis, risk factors and diagnosis. *Swiss Medical Weekly*, 2017.
3. Tsai TT, Trimarchi S, Nienaber CA. Acute Aortic Dissection: Perspectives from the International Registry of Acute Aortic Dissection (IRAD). *European Journal of Vascular and Endovascular Surgery*, 2009; 37(2): 149-159.
4. Sayed A, Munir M, Bahbah EI. Aortic Dissection: A Review of the Pathophysiology, Management and Prospective Advances. *Current Cardiology Reviews*, 2021; 17(4).
5. Lai1 P. The 100 most-cited articles on aortic. *BMC Cardiovascular Disorders*, 2017; 17: 30: 1.
6. Lai P, Liu YH, Xue JH, He PC, Qiu YQ. The 100 most-cited articles on aortic dissection. *BMC Cardiovasc Disord*, Jan 17, 2017; 17(1): 30.
7. Pan M, Chen S, Wang H, et al. Exploring the genetic pathogenicity of aortic dissection from 72 Han Chinese individuals using next-generation sequencing. *Clin Genet*, May 2020; 97(5): 704-711.
8. Wang JX, Xue YX, Zhu XY, et al. The impact of age in acute type A aortic dissection: a retrospective study. *J Cardiothorac Surg*, Mar. 19 2022; 17(1): 40.
9. Fujiyoshi T, Minatoya K, Ikeda Y, et al. Impact of connective tissue disease on the surgical outcomes of aortic dissection in patients with cystic medial necrosis. *J Cardiothorac Surg*, Nov. 23, 2017; 12(1): 97.
10. Ke1 C. Clinical features and risk factors 2021.
11. Ke C, Wu H, Xi M, Shi W, Huang Q, Lu G. Clinical features and risk factors of postoperative in-hospital mortality following surgical repair of Stanford type A acute aortic dissection. *BMC Cardiovasc Disord.*, Aug. 12. 2021; 21(1): 392.
12. Chou E, Pirruccello JP, Ellinor PT, Lindsay ME. Genetics and mechanisms of thoracic aortic disease. *Nat Rev Cardiol.*, Mar. 2023; 20(3): 168-180.
13. Sayed A, Munir M, Bahbah EI. Aortic Dissection: A Review of the Pathophysiology, Management and Prospective Advances. *Curr Cardiol Rev.*, 2021; 17(4): e230421186875.
14. Kayali F, Jubouri M, Al-Tawil M, et al. Coronary artery involvement in type A aortic dissection: Fate of the coronaries. *J Card Surg*, Dec. 2022; 37(12): 5233-5242.
15. Dennis J, Sealock J, Levinson RT, et al. Genetic risk for major depressive disorder and loneliness in sex-specific associations with coronary artery disease. *Mol Psychiatry*, Aug. 2021; 26(8): 4254-4264.
16. <Large-scale association analysis identifies 13 new.pdf>.
17. <Partitioningtheheritabilityofcoronary.pdf>.
18. <mcpherson2016 (1).pdf>.
19. Zheng J, Guo J, Huang L, et al. Genetic diagnosis of acute aortic dissection in South China Han population using next-generation sequencing. *Int J Legal Med.*, Sep. 2018; 132(5): 1273-1280.
20. Li Y, Fang M, Yang J, et al. Analysis of the contribution of 129 candidate genes to thoracic aortic aneurysm or dissection of a mixed cohort of sporadic and familial cases in South China. *Am J Transl Res.*, 2021; 13(5): 4281-4295.
21. Ponińska JK, Bilińska ZT, Truszkowska G, et al. Good performance of the criteria of American College of Medical Genetics and Genomics/Association for Molecular Pathology in prediction of pathogenicity of genetic variants

causing thoracic aortic aneurysms and dissections. *J Transl Med.*, Jan 25, 2022; 20(1): 42.
22. Hibino M, Otaki Y, Kobeissi E, et al. Blood Pressure, Hypertension, and the Risk of Aortic Dissection Incidence and Mortality: Results From the J-SCH Study, the UK Biobank Study, and a Meta-Analysis of Cohort Studies. *Circulation*, Mar 2022; 145(9): 633-644.
23. Hassan R, Miller RJH, Howlett JG, White JA, Fine NM. Prevalence, incidence and clinical outcomes of epicardial coronary artery disease among transthyretin amyloidosis cardiomyopathy patients. *BMC Cardiovasc Disord*, Mar. 8, 2023; 23(1): 124.
24. Li W, Luo S, Lin W, et al. Coronary artery disease as an independent predictor of short-term and long-term outcomes in patients with type-B aortic dissection undergoing thoracic endovascular repair. *Front Cardiovasc Med.*, 2022; 9: 1041706.
25. Pinard A, Jones GT, Milewicz DM. Genetics of Thoracic and Abdominal Aortic Diseases. *Circ Res.*, Feb. 15, 2019; 124(4): 588-606.
26. <Large-scale association analysis identifies new risk loci for.pdf>.
27. <LargeScaleAssociationAnalysisIdentifiesThree.pdf>.
28. <erdmann2018.pdf>.
29. <khera2017.pdf>.
30. McPherson R, Tybjaerg-Hansen A. Genetics of Coronary Artery Disease. *Circ Res.*, Feb 19 2016; 118(4): 564-578.
31. Baumann S, Behnes M, Sartorius B, et al. Follow-up of iatrogenic aorto-coronary "Dunning" dissections by cardiac computed tomography imaging. *BMC Med Imaging*, Dec 21 2017; 17(1): 64.
32. Akutsu K. Etiology of aortic dissection. *General Thoracic and Cardiovascular Surgery*, 2019; 67(3): 271-276.
33. Liu O, Li J, Xin Y, et al. Association of MMP-2 gene haplotypes with thoracic aortic dissection in chinese han population. *BMC Cardiovasc Disord*, Jan 14, 2016; 16: 11.
34. Zheng J, Guo J, Huang L, et al. Genetic diagnosis of acute aortic dissection in South China Han population using next-generation sequencing. *International Journal of Legal Medicine*, 2018; 132(5): 1273-1280.
35. Duan Y, Xiong J, Lai Z, et al. Analysis of the genetic contribution to thoracic aortic aneurysm or dissection in a prospective cohort of patients with familial and sporadic cases in East China. *Orphanet J Rare Dis.*, Aug 29, 2023; 18(1): 251.
36. Stengl R, Bors A, Agg B, et al. Optimising the mutation screening strategy in Marfan syndrome and identifying genotypes with more severe aortic involvement. *Orphanet J Rare Dis.*, Oct 15 2020; 15(1): 290.
37. Sun L, Chang Y, Jiang P, Ma Y, Yuan Q, Ma X. Association of gene polymorphisms in FBN1 and TGF-beta signaling with the susceptibility and prognostic outcomes of Stanford type B aortic dissection. *BMC Med Genomics*, Mar 20 2022; 15(1): 65.
38. Akutsu K, Morisaki H, Okajima T, et al. Genetic analysis of young adult patients with aortic disease not fulfilling the diagnostic criteria for Marfan syndrome. *Circ J.*, May 2010; 74(5): 990-997.
39. Hashiyama N, Goda M, Uchida K, et al. Stanford type B aortic dissection is more frequently associated with coronary artery atherosclerosis than type A. *J Cardiothorac Surg*, Jun 27 2018; 13(1): 80.
40. <TGFB1 genetic polymorphisms and coronary heart.pdf>.
41. Huang EW, Peng LY, Zheng JX, et al. Investigation of associations between ten polymorphisms and the risk of coronary artery disease in Southern Han Chinese. *J Hum Genet*, May 2016; 61(5): 389-393.
42. Bai B, Zhang M, Zhuang Y, et al. The pregnancy-associated spontaneous coronary artery dissection in a young woman with a novel missense mutation in NOTCH1: a case report. *BMC Med Genet*, Jun. 1, 2020; 21(1): 119.
43. Cury M, Zeidan F, Lobato AC. Aortic Disease in the Young: Genetic Aneurysm Syndromes, Connective Tissue Disorders, and Familial Aortic Aneurysms and Dissections. *International Journal of Vascular Medicine*, 2013; 2013: 1-7.
44. Patel JV, Dwivedi S, Hughes EA, Lip GY. Premature coronary artery disease: an inferred cardiovascular variant or a South Asian genetic disorder? *Thromb Haemost*, Jun. 2008; 99(6): 991-992.
45. Keravnou A, Bashiardes E, Michailidou K, Soteriou M, Moushi A, Cariolou M. Novel variants in the ACTA2 and MYH11 genes in a Cypriot family with thoracic aortic aneurysms: a case report. *BMC Med Genet*, Dec. 7, 2018; 19(1): 208.
46. <main.pdf>.
47. Adlam D, Berrandou TE, Georges A, et al. Genome-wide association meta-analysis of spontaneous coronary artery dissection identifies risk variants and genes related to artery integrity and tissue-mediated coagulation. *Nat Genet*, Jun. 2023; 55(6): 964-972.
48. Carss KJ, Baranowska AA, Armisen J, et al. Spontaneous Coronary Artery Dissection: Insights on Rare Genetic Variation From Genome Sequencing. *Circ Genom Precis Med.*, Dec. 2020; 13(6): e003030.
49. Goel K, Tweet M, Olson TM, Maleszewski JJ, Gulati R, Hayes SN. Familial spontaneous coronary artery dissection: evidence for genetic susceptibility. *JAMA Intern Med.*, May 2015; 175(5): 821-826.
50. Joy G, Eissa H. Spontaneous Coronary Artery Dissection in a Patient with a Family History of Fatal Ascending Aortic Dissection: Case Report and Discussion of Diseases Causing Both Presentations. *Case Rep Cardiol*, 2019; 2019: 7218480.
51. Grond-Ginsbach C, Engelter ST. Genetics of Spontaneous Coronary Artery Dissection Gains New Momentum. *Circ Genom Precis Med.*, Apr. 2018; 11(4): e002148.

52. Brownstein AJ, Kostiuk V, Ziganshin BA, et al. Genes Associated with Thoracic Aortic Aneurysm and Dissection: 2018 Update and Clinical Implications. *Aorta (Stamford).* Feb., 2018; 6(1): 13-20.
53. Aday AW, Kreykes SE, Fanola CL. Vascular Genetics: Presentations, Testing, and Prognostics. *Curr Treat Options Cardiovasc Med.*, Nov. 13. 2018; 20(12): 103.