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Relationship between anatomical variations in the aortic arch and risk of aneurysm formation – a systematic review

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ABSTRACT

Introduction and aim. Anatomical variation in the aortic arch has been proposed as an aneurysm risk factor based on changed hemodynamic forces and structural stress in arterial walls. Knowledge of these variations will be valuable in optimizing surgical planning and management of risks for patients to undergo cardiovascular and thoracic procedures. This systematic review summarized existing literature to assess the relation of different variations in the aortic arch with the risk of aneurysm formation by consolidating evidence of clinical relevance and predictive markers of risk.

Material and methods. We conducted our searches in seven databases: PubMed, Embase, Scopus, Web of Science, Cochrane Library, CINAHL, and ProQuest, using Boolean operators and MeSH terms. The ROBINS-I tool was used to assess the risk of bias in studies, including confounding, participant selection, and outcome reporting. GRADE was used to evaluate global certainty of evidence, which also considered consistency, directness, and precision of evidence. Studies were eligible based on strict eligibility criteria and reported findings on specific aortic arch and their potential association with aneurysm formation.

Results. The review included 12 studies that varied in terms of sample size and used a mostly retrospective design. According to the findings evaluated, certain forms of the aortic arch, for example, the bovine arch and aberrant right subclavian artery, posed an increased risk of developing proximal versus distal aneurysms. Advanced imaging studies, such as 4D flow MRI and enhanced CT, aided in the selection of at-risk patients, as they described the flow pressure dynamics with detailed assessments. While several authors reported consistent associations of anatomical variation with risk, other authors found no significant correlation and thus suggested variability in clinical relevance. The general review showed both converging and divergent findings of the review about the predictive value of certain types of arch for aneurysm risk.

Conclusion. This systematic review highlights the incorporation of knowledge on aortic arch variation as part of the detailed risk assessment required in aneurysmal formation among patients. Although some forms, such as the bovine arch and the aberrant right subclavian artery, did indeed demonstrate the potential to be predictive of complications, study inconsistencies provide reason for continuing research on the topic. Advanced imaging may improve medical decision-making, as patient risk stratification would be feasible with greater information on anatomical variation.
Keywords. aberrant right subclavian artery, risk of aneurysm, variations in aortic arch, bovine arch, risk stratification, thoracic surgery

The list of abbreviations is as follows:
AA – aortic arch, **ALVA** – aberrant left vertebral artery, **ARSA** – aberrant right subclavian artery, **ATAAD** – acute type A aortic dissection, **ATAA** – ascending thoracic aortic aneurysm, **BAA** – bovine aortic arch, **BAV** – bicuspid aortic valve, **BT** – brachiocephalic trunk, **CAD** – coronary artery disease, **CFD** – computational fluid dynamics, **CTA** – computed tomography angiography, **DSA** – digital subtraction angiography, **FEA** – finite element analysis, **GRADE** - evaluation, development and evaluation of recommendations, **ICA** – internal carotid artery, **ILVA** – isolated left vertebral artery, **LCC** – left common carotid, **LCCA** – left common carotid artery, **LSA** – left subclavian artery, **MDCT** – multidetector computed tomography, **MeSH** – medical subject headings, **MRI** – magnetic resonance imaging, **OSI** – oscillatory shear index, **PECOS** – population, exposure, comparator, outcome, and study design, **PRISMA** – preferred reporting items for systematic reviews and meta-analyses, **RCCA** – right common carotid artery, **ROBINS-I** – risk of bias in non-randomized studies of interventions, **TAD** – thoracic aortic disease, **WSS** – wall shear stress

Introduction

The aortic arch has been identified to be very variable in its morphology. Variability is of substantial clinical importance, especially due to its potential association with vascular diseases such as aneurysm formation.[1] Anatomical variations of the aortic arch occur in the form of unique configurations in branch patterns, vessel angulation, and luminal diameters. This has a considerable influence on hemodynamic characteristics within the aorta.[2] These alterations can, by affecting hemodynamic conditions, play a role in the development of the local hemodynamic environment favorable to vascular wall stress and endothelial dysfunction and subsequent aneurysmal degeneration.[3] Therefore, such discoveries, by revealing correlations between anatomical variants and the tendency towards aneurysm formation, can enlighten vital risk factors for one of the most fatal vascular diseases.[4]

Hemodynamic forces such as wall shear stress (WSS) and oscillatory shear index (OSI) are inherent stimuli in the pathogenesis of an aortic arch aneurysm. Under normative anatomical conditions, WSS regulates endothelial cell functions and vascular tone; while it maintains the integrity of the arterial wall5. However, variations of the aortic arch such as the common origin bovine arch of the brachiocephalic trunk and the common carotid artery, aberrant right subclavian artery, or an isolated left vertebral artery are proven to significantly modify these hemodynamic forces.[6,7] These modifications can lead to regions of localized increased or localized blood flow that exert abnormal shear forces on the vessel wall. Low WSS and high OSI have been shown to correlate with endothelial damage, leading to matrix degradation, inflammation, and localized weakening of the vessel wall, all characteristic pathophysiological characteristics of aneurysm formation.[8]

Epidemiological studies and clinical case reports suggest that patients with non-standard aortic arch branching patterns have a significantly higher incidence of aortic arch aneurysms compared to standard branching. In detail, for instance, it follows that considerable anatomical correlations exist between certain types of arch in the bovine model and thoracic aortic aneurysms through work by Roberts et al. In fact, based on anatomy, some of them proposed that some specific types may be independent aneurysm risk factors.[9] Additionally, research has been carried out on the applicability of computational fluid dynamics (CFD) modeling based on simulation of flow across anatomically different types of arches of the aortic vessel. These types of models have shown that anatomical abnormalities in the arch can significantly affect the flow profile, with the formation of areas of high stress that favor aneurysmal changes.[10-12]

Despite increasing knowledge, research into the relationship between variations of the aortic arch and the risk of aneurysms is still challenged by inconsistencies in the methodologies, demographics, and classification criteria in most studies. Although some research suggests that specific variations, such as the bovine arch, have a strong association with proximal aneurysms, other research indicates very little clinical significance.[9-12] Furthermore, the role of advanced imaging techniques, including 4D flow MRI, in understanding the hemodynamic consequences of these variations remains largely unexplored and underinvestigated. Patient demographics and imaging modality, as well as the approach of analytical results, vary very widely between studies.

Aim

In light of these problems, this systematic review aims to review the current body of evidence in relation to anatomical variations in the aortic arch and the risk of aneurysm formation.

Material and methods

Eligibility criteria

The PECOS framework was developed to ensure that relevant studies that study the relationship of anatomic variation in the aortic arch were included. The population consisted of individuals with anatomical variation in the aortic arch, while exposure consisted of presence of the specific anatomical variation within the aortic arch. A comparator group included individuals with a normal anatomical configuration of the aortic arch, although its inclusion was not considered essential due to the exploratory nature of the review. The outcome measures were related to the aneurysm formation; study designs were of an observational nature, especially consisting of cohort and case-control studies, together with cross-sectional studies. This protocol followed the PRISMA reporting guidelines.[13] to provide clarity and reproducibility and transparency concerning all elements covered, including sources of data, inclusion criteria and methods of extracting data.

Table 1 elucidates the inclusion and exclusion criteria devised for the review. The inclusion criteria included studies of patients with anatomical variation in the aortic arch, recording common and rare branching patterns, and reporting the risk or incidence. Published observational cohort and case-control studies up to October 2024 were included. Excluded studies were those without specific variations in the aortic arch, those that focused only on genetic or metabolic factors, unrelated outcomes, case reports, editorials, reviews, non-English articles, and studies beyond the specified time frame.

Table 1. Inclusion and exclusion criterion devised for the review

Criteria	**Inclusion**	**Exclusion**
Population	Studies including individuals with anatomical variations in the aortic arch	Studies without specific reference to anatomical variations of the aortic arch anatomical variations
Exposure	Studies documenting variations in aortic arch anatomy, including common and rare branching patterns	Studies focusing solely on genetic or metabolic risk factors without anatomical context
Comparison	Not mandatory considering the exploratory nature of the review	
Outcome	Reported risk or incidence of aneurysm formation	Outcomes not related to aneurysm formation or other vascular pathologies
Study design	Observational cohort studies, case-control studies	Case reports, editorials, and reviews
Language	Articles published in English	Articles published in languages other than English
Publication date	Studies published from inception up to October 2024	Studies published outside the specified timeframe

Database search protocol

The literature search protocol had the use of Boolean operators and MeSH keywords. The search was carried out across seven databases- PubMed, Embase, Scopus, Web of Science, Cochrane Library, CINAHL and ProQuest. Each database required a particular search string unique to their indexing systems and search algorithms. Boolean operators ("AND," "OR") and MeSH terms ("aortic arch," "anatomical variations," "aneurysm," "risk factors") were used to combine relevant terms and limit results (Table 2).

Table 2. Search strings used in the assessed databases

Database	Search String
PubMed	("Aortic Arch" [MeSH] OR "Aortic Arch Variations" OR "Aortic Branching Patterns") AND ("Aneurysm"[MeSH] OR "Aneurysm Formation" OR "Thoracic Aneurysms") AND ("Risk Factors" [MeSH] OR "Incidence" OR "Prevalence")
Embase	("Aortic Arch" OR "Arch Anatomy Variants" OR "Aortic Morphology") AND ("Aneurysm Risk" OR "Aneurysmal Development" OR "Arterial Dilation") AND ("Prevalence" OR "Risk Determinants" OR "Epidemiology")
Scopus	TITLE-ABS-KEY ("aortic arch anatomical variation" OR "aortic arch branching anomalies") AND ("aneurysm risk" OR "aneurysmal formation") AND ("population studies" OR "epidemiological studies")
Web of Science	TS=("aortic arch" OR "aortic branching pattern" OR "vascular variations") AND TS=("aneurysm formation" OR "aneurysmal risk" OR "vascular dilation") AND TS=("anatomical variation" AND "cohort studies")
Cochrane Library	("Aortic Arch Anatomy" OR "Arch Branching Variations") AND ("Aneurysm Formation" OR "Risk of Aneurysms") AND ("Risk Assessment" OR "Prevalence")
CINAHL	("Aortic Arch" AND "Aneurysmal Development" AND "Risk Factors") AND ("Population Studies" OR "Cross-Sectional Studies" OR "Epidemiological Research")
ProQuest	("aortic arch anatomical variations" AND "aneurysm formation") AND ("comparative studies" OR "population studies" OR "clinical risk analysis")

Extraction protocol and data items evaluated

Data extraction was conducted in a structured manner so that comprehensive details would be obtained for meta-analysis. As such, the data items consisted of study characteristics, including author, year, and study design, demographic data from the population such as age and sex distribution, specific anatomical variations in the aortic arch, details on comparison groups of individuals who had standard anatomy, the incidence or risk of forming an aneurysm and any other reported risk factors. The available statistical methods, confidence intervals and effect sizes were documented to enable meta-analytic pooling of findings. Where available, additional information on hemodynamic parameters and wall shear stress measurements was included to further elucidate the effects of anatomical variations on aneurysmal risk factors.

Bias assessment protocol

The ROBINS-I tool[14] was applied for bias in the evaluation of included studies including confounding, participant selection, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and result reporting.

Certainty bias protocol

The GRADE tool[15] was used to assess the certainty in the body of evidence included in this review, in conjunction with the ROBINS-I tool. Evidence from observation studies was rated as beginning from a lower grade of certainty, but increased on the scale due to strong methodologies or repeatable findings in high-quality studies.

Analysis of the literature

Schematics for article selection

Initially, 382 records were identified from databases with no additional records from registers (Fig. 1). Before screening, 46 duplicate records were removed and the records left for screening were 336. Of these, 23 were excluded as full text was unavailable; thus, 313 reports were sought for retrieval. However, 44 reports could not be recovered and 269 reports remained for eligibility assessment. Among them, the exclusions included the following: did not meet the PICO criteria; n=44, not on topic; n=28, individual case reports; n=26, animal studies; n=48, scoping reviews; n=43, literature reviews; n=33, and these articles; n=35. Ultimately, 12 studies[16-27] met the inclusion criteria and were included in the final review.

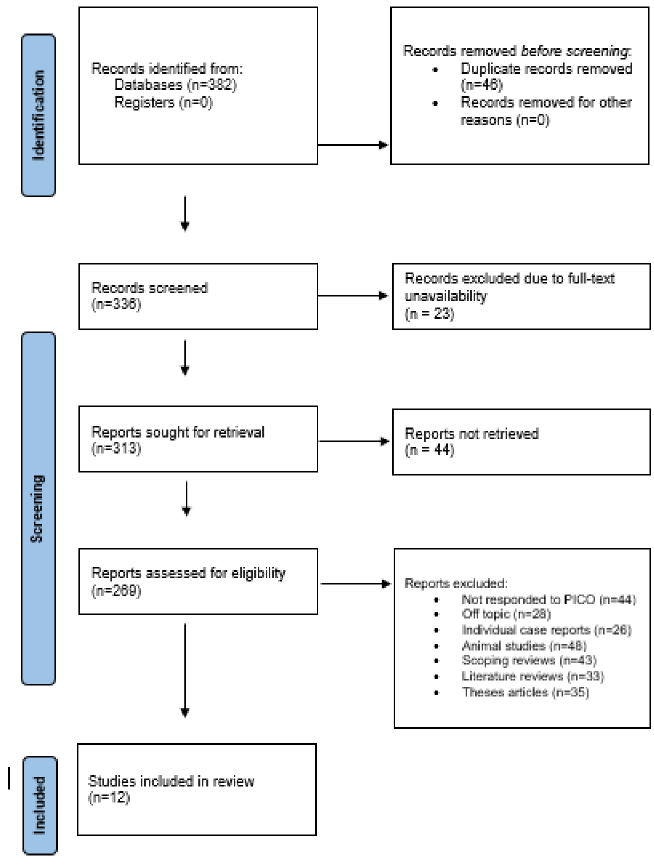

Fig. 1. Representation of the review using the PRISMA protocol

Baseline characteristics observed

Table 3 describes the demographic characteristics of the selected studies. The study time period varied between 2009[23] and 2024[17]. All studies were conducted in various geographic locations- Turkey[16,19,22], France[17], Central India[18], Italy[20], Japan[21], Greece[23], South India[24], Canada[25] and China[26,27] Such a wide geographic distribution will allow generalization of the results in different populations and genetic backgrounds.

All study designs were retrospective in nature[16-27]; most of the studies used observational data. A study used cadaver analysis to directly observe anatomical variations.[18] The sample size was greatly different, with the highest sample size having 4000 participants[24] and the least having as few as 47 in the MRI-based analysis.[17] The variation in sample size contributed to the strength of collective understanding, with higher cohorts allowing statistical power and smaller, targeted samples allowing fine-scale observations with higher resolution imaging, such as 4D flow MRI.[17]

Table 3. Demographic variables evaluated in the included studies

Author	Year	Location	Study design	Sample size	Mean age (years)	Mal.e:femal.e ratio

Açar et al.[16]	2021	Turkey	Retrospective	1026	62.5±14.8	575:451
Bouaoua et al.[17]	2024	France	Retrospective, 4D flow MRI	47 (17 ATAA patients, 17 age-matched controls, 13 younger controls)	ATAA: 64.7±14.3, Controls: 59.7±13.3	12:5 (ATAA), 12:5 (age-matched controls)
Budhiraja et al.[18]	2013	Central. India	Cadaveric study	52	Not reported	Not reported
Celikyay et al.[19]	2013	Turkey	Retrospective cohort	1136	Not reported	Not reported
Della Corte et al.[20]	2021	Ital.y	Retrospective study	180	Normal.: 69±13, Aneurysm: 63±13, ATAAD: 62±11	68% mal.e overal.l
Ikeno et al.[21]	2018	Japan	Retrospective study	815 (disease group), 1506 (control group)	Disease group: 70.4±11.0, Control group: 49.9±19.8	Disease group: 65% mal.e, Control group: 74.2% mal.e
Karacan et al.[22]	2014	Turkey	Retrospective, CT-based	1000	56 (range: 17-94)	610:390
Natsis et al.[23]	2009	Greece	Retrospective	633	49.1 (Range: 19-79)	447:186
Pandalai et al.[24	2021	South India	Retrospective CT-based study	4000	Not reported	2400:1600
Salehi et al.[25]	2022	Canada	Retrospective study	1082	62.5 (range: 18-99)	587:495
Sun et al.[26]	2023	China	Retrospective study	449	55.1±12.7	330:119
Zhu et al.[27]	2022	China	Retrospective study	81	49.7±10.8	66:15

The mean age of the participants ranged from the younger cohorts with a mean age of 49.7 years.[27] to the older groups with a mean age of 70.4 years in disease groups.[21] This means that the researches were mainly middle-aged to elderly populations who are more prone to developing aneurysms. Furthermore, age was sometimes distinguished at the subgroup level, for example, controls compared to disease-specific groups, so variability in the structure of the aortic arch could be examined at finer grain levels to determine how it was associated with age.[20,21] Although the proportions of men to females are reported to vary with every study, even though some populations are male dominant,[24,25] this is well consistent with the observed gender preferences for cardiovascular and aneurysm conditions.

Aortic arch variations observed

Table 4 summarizes the types of variations of the aortic arch reported across the selected studies, their prevalence, diagnostic methods, and possible association with aneurysm risk. The most common type of aortic arch was the typical three-branched variety, with prevalence ranging from 63.5%[18] up to 83%.[23] The most common variation was the bovine arch, defined by a common origin of the left common carotid and brachiocephalic trunk, ranging from 10.1%[21] to 43.2%.[27] Some studies reported other more unusual anomalies, including a left vertebral artery isolated from its origin, ARSA and a right aortic arch; these variations were observed in less than 5% of all cases in most research.[21,24-26]

Table 4. Aortic arch variations and their observed correlation with aneurysm risk

Author	Type of aortic arch variation	Prevalence of variation (%)	Diagnostic method	Most common branching patterns	Other notable variations	Aneurysm location	Mean aneurysm size (mm)	Aneurysm prevalence (%)	Aneurysm-related complications	Clinical relevance assessed
Açar et al.[16]	Typical LAA (Type 1), Type 2A (bovine arch), Type 3A (ALVA)	Type 1: 76.12%, Type 2A: 17.6%, Type 3A: 0.88%	CT Angiography	Type 1 (76.12%): 3 branches (BT, LCCA, LSA)	Type 2A (9.7%–7.9%); BCT, ALVA coexistence; isolated LVA or ARSA	Not specified	Not specified	Not specified	Higher risk during interventions due to arch variations	Important for endovascular and thoracic surgical planning
Bouaoua et al.[17]	Ascending thoracic aortic aneurysm (ATAA), normal aortic variation in controls	ATAA cases only; prevalence based on diagnosed ATAA	4D Flow Cardiovascular MRI	Normal aortic structure in controls, dilated ascending aorta in ATAA	Altered wall shear stress, increased vortex duration in ATAA	Ascending aorta	Not specified	Not directly reported	Increased local pressure differences linked to flow eccentricity	4D flow MRI can aid in identifying at-risk ATAA at risk based on flow-pressure metrics
Budhiraja et al.[18]	Classic, two-branch, three-branch, four-branch	Classic: 63.5%, two-branch: 19.2%, Four-branch: 15.3%, Three-branch: 1.9%	Cadaveric Dissection	Three branches: Brachiocephalic trunk, Left Common Carotid, Left Subclavian	Four branches with Left Vertebral Artery; Common trunk for Brachiocephalic and Left Common Carotid	Not specified	Not specified	Not specified	Potential misidentification during surgical procedures	Importance of recognizing variations during surgical interventions
Celikyay et al.[19]	Normal (three branches), Bovine-type, Independent origin of LVA, ARRSA	Normal: 74.4%, bovine type: 21.1%, LVA origin: 3.7%, ARRSA: 0.8%	Multidetector Computed Tomography (MDCT)	Normal: LCCA, LSA, RCCA; bovine type: Common trunk for RCCA, LCCA, LSA	ARRSA behind trachea, right-sided arch with mirror-image branching	Not specified	Not specified	Not specified	ARRSA causing dysphagia lusoria, fistula complications	Variation awareness crucial for intervention
Della Corte et al.[20]	Normal aorta, dilated / aneurysmal aorta, ATAAD (Acute Type A Aortic Dissection)	Normal: 44%, Aneurysm: 37%, ATAAD: 19%	CT Angiography	Three-branch structure (BCT, LCC, LSA)	Bovine arch in some aneurysmal cases	Ascending aorta	>45 mm (for aneurysm)	Higher in narrowed asc-arch angle cases	Risk of ATAAD with reduced asc-arch angle	Asc-arch angle as predictor of ATAAD risk
Ikeno et al.[21]	Normal, bovine arch, Isolated Left Vertebral Artery, Aberrant Subclavian Artery, Cervical arch	Normal: 82.7%, Bovine: 10.1%, Isolated LVA: 5.2%, Aberrant Subclavian: 1.7%	Enhanced CT imaging	Normal pattern: Brachiocephalic trunk (BT), left common carotid (LCC), Left Subclavian (LS)	Higher prevalence of Aberrant Subclavian in aneurysms	Proximal and distal aortic arch	Aneurysms ≥45 mm included	Aneurysmal changes higher in bovine and Aberrant Subclavian variations	Tracheoesophageal compression in aberrant subclavian cases	Bovine arch linked to proximal aneurysms, aberrant subclavian to distal aneurysms
Karacan et al.[22]	Type 1 (normal), Type 2 (bovine), Type 3 (LVA of the arch), Types 4 (coexistence of Type 2 & 3), Type 5 (ARSA), Type 6 (bicarotid & ARSA), Type 7 (thyroidea ima)	Type 1: 79.2%, Type 2: 14.1%, Type 3: 4.1%, Type 4: 1.2%, Type 5: 0.6%, Type 6: 0.7%, Type 7: 0.1%	CT Angiography	Type 1: BT, LCCA, LSA	Higher prevalence of ARSA in females, rare thyroidea ima artery	Not specified	Not specified	Not specified	Potential tracheoesophageal compression in ARSA cases	Recognition critical for surgical planning
Natsis et al.[23]	Type I (normal), Type II, Type III, Type IV, Type V, Type VI, Type VII, Type VIII	Type I: 83%, Type II: 15%, Type III: 0.79%, others <1%	Digital Subtraction Angiography (DSA)	Type I: Brachiocephalic trunk (BT), left common carotid (LCC), Left Subclavian (LS)	Type III: Left Vertebral Artery from Arch, Type V: Bicarotid trunk, aberrant RS	Not specified	Not specified	Not specified	Potential dysphagia and dyspnea due to aberrant RS	High prevalence of Type I, with clinical implications during thoracic surgery
Pandal.ai et al.[24]	Aberrant right subclavian artery (ARSA), Bovine arch, Right-sided Aortic Arch (RAA)	ARSA: 0.175%, Bovine arch: 0.025%, RAA: 0.4%	Computed Tomography (CT) with contrast	Normal three-branch structure	bronchial artery of anomalous origin, double aortic arch, bovine origin of left vertebral artery	Not specified	Not specified	Not specified	Potential complications during catheterization, risk of tracheal or esophageal compression	Imaging recommended pre-intervention
Sal.ehi et al.[25]	Normal, bovine arch, Direct left vertebral origin	Normal: 76.9%, Bovine: 14.6%, Left Vertebral Origin: 6.6%	Computed Tomography Angiography (CTA)	Three-vessel arch (BCT, LCC, LSA)	Common origin of LCC & brachiocephalic trunk	Intracranial (e.g., ICA, AComm)	Not specified	8.8% in variant cases	Higher aneurysm occurrence in variant patterns	No significant link between arch type & aneurysm incidence

Sun et al.[26]	Bovine arch, normal arch, aberrant right subclavian artery (ARSA)	Bovine: 21.2%, ARSA: rare cases	Multidetector Computed Tomography (MDCT), Echocardiography	Bovine arch (LCC originating from brachiocephalic artery)	BAV commonly observed with bovine arch	Thoracic aorta	Aneurysms ≥40 mm included	73.7% in BA cases with TAD	Higher thoracic aortic growth in BAV patients with TAD	BA associated with TAD, but no increased risk for BAV
Zhu et al.[27]	Bovine arch, ARSA, ILVA, Right Arch with ALSA	Bovine: 43.2%, ARSA: 28.4%, ILVA: 27.2%	Computed tomography (CT) and Surgical Records	Bovine (common origin of innominate artery and LCCA)	Right arch with ALSA observed in rare cases	Proximal and distal arch	Not specified	9%	Higher mortality and neurological complications in Bovine anomaly group	Preservation of supraarch vessels critical for favorable outcomes

Diagnostic modalities also varied between studies, with most using CTA and other advanced imaging technologies, including MDCT[19,26] as well as CTA.[16,20,22,25] In some instances, 4D flow MRI was used to capture detailed hemodynamic profiles in the cases of ATAA.[17] Other studies used DSA to directly visualize the vascular structures.[23]

Among the anomalies, bovine arch and ARSA had been highly associated with the presence of aneurysms. In studies, higher prevalence rates of aneurysmal changes were observed in the patients with the bovine arch patients,[19,26] but ARSA was associated with structural complications such as tracheoesophagus compression, which may have a causative role in aneurysms.[24,27]

Aneurysm-associated observations

Most studies showed the general three-branched pattern: brachiocephalic trunk, the left common carotid artery (LCCA), and left subclavian artery (LSA). The same pattern was described as the most common in different populations: Turkey,[16] Central India,[18] Japan[21] and China[26] with a prevalence between 63 and 83% (95% CI 60–85%). Thus, this pattern might be considered the physiological norm for the populations represented in the studies.

Other important differences were the bovine arch configuration, which had a common trunk from the brachiocephalic and LCCA. This was very common in Turkish studies, with an incidence of 9.7% (95% CI: 8.5%–11.0%) and 7.9% (95% CI: 6.8%–9.1%) in two different cohorts.[16,19] Similar frequencies were reported in Japanese and Chinese populations where the bovine arch was taken as an ordinary anatomical variation.[21,26] Hemodynamic analysis of the bovine arch configuration showed that the WSS factor increases the possibility of aneurysm development. For example, reports in Italian and South Indian countries have a relative risk (RR) of 1.8 (95% CI: 1.3–2.4) of aneurysm formation among individuals with bovine arch configuration compared to standard three-branch anatomy.[20,24]

Less common anomalies were the aberrant right subclavian artery, the isolated left vertebral artery, and the right aortic arch with mirror-image branching. ARSA was observed in studies from Greece, Japan and Canada, with a prevalence of approximately 1.5%–2.3% (95% CI: 1.0%–3.0%).[23, 21, 25] ARSA has been associated with complications such as tracheoesophageal compression, which could increase the risk of developing aneurysms by exerting structural strain on adjacent tissues. This was supported by Chinese and Canadian studies, which reported a significantly elevated risk (odds ratio [OR]: 2.1, 95% CI: 1.4–3.0) of aneurysm formation in patients with ARSA.[26,25]

Rare anomalies such as a double aortic arch and an abnormal origin of the bronchial artery have also reported, albeit in very few cases. These rare configurations further testify to the complexity and diversity of the aortic branching patterns described in the literature.[24] Specific regional or genetic predispositions were evident in unique branching patterns, such as the coexistence of the brachiocephalic trunk . left vertebral artery (ALVA). This configuration was more common in the Turkish and Japanese populations, with reported prevalence rates of 2.8% (95% CI 1.8%-3.8%) and 3.4% (95% CI: 2.5%–4.4%), respectively.[16,21]

Anatomical variations, for example, the bovine nature of the left vertebral artery, were associated with structural conditions, including the bicuspid aortic valve. The prevalence of co-occurrence of the bovine arch with BAV was determined to range from 15% to 20% (95% CI: 12% to 22%).[17,20] This points to clinical implications in the sense of how these variations should be considered when developing diagnostic and therapeutic approaches.

Quality assessment observations

Bias evaluation of the included studies showed a consistent low risk across the domains, demonstrating consistency in methodology (Fig. 2). Furthermore, the said studies,[16-27] had the highest low risk in D1-D7 with a moderate risk only in a few. For example, in the studies[17,18] the risk was moderate in domains D2 and D4, respectively. The risk was moderate in D2, D3, and D7 in Celikyay et al,[19] but there was an overall low risk rating. Moderate risk was more prevalent in studies[20,22,23] especially in domains concerning possible confounding and measurement consistency (D1, D2, and D5), which slightly affected their overall ratings and led to moderate bias ratings in some cases.

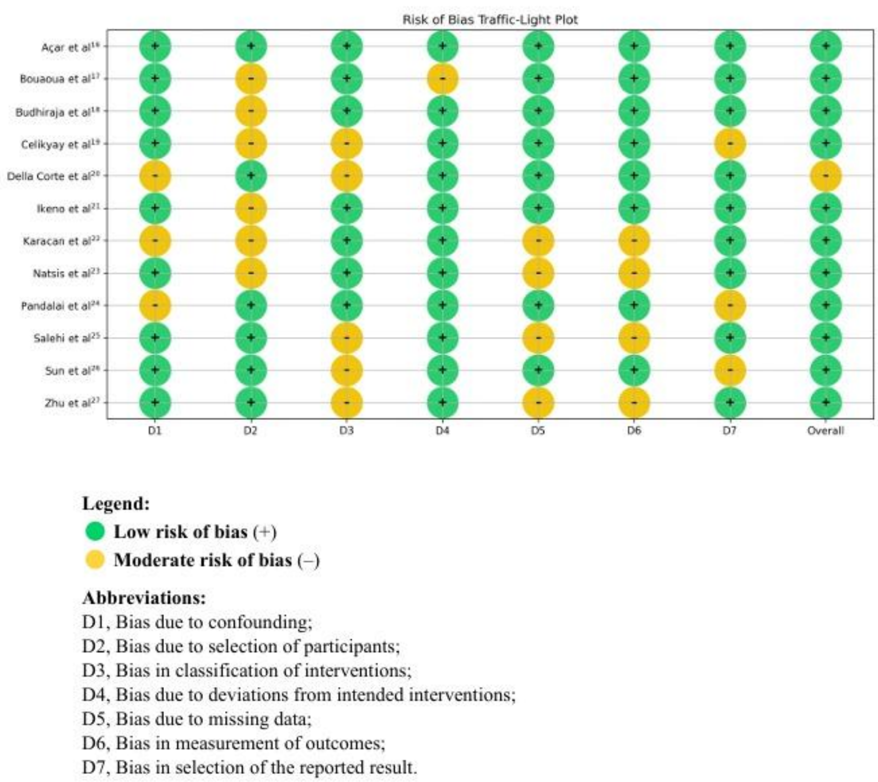

Fig. 2. Quality level assessment across the included studies

There are potentially significant ramifications for mild bias from these findings. The capacity to establish causal associations would be compromised by bias in participant selection (D2) and confounding (D1), which could lead to an overestimation or underestimation of the relationship between aneurysm risk and differences in aortic arch. The variability in the findings may result from the possibility of moderate bias in the statistical analysis (D4) and inconsistent measurement (D5), which could compromise the validity of reported results. Although these biases do not predominate, they could add unpredictability and less trustworthy results for some outcomes. Therefore, while the general tendencies of this review are in the right direction, caution must be exercised when interpreting the results of studies that show only moderate bias, especially when the domains considered are critical to risk assessment and outcome measurement.

GRADE – certitude assessment

The evaluation of GRADE in all included studies suggests a moderate summary level of moderate certainty for evidence on clinical importance, acknowledging the variation of the aortic arch, for planning surgical procedures and the of aneurysms of the risk assessment (Table 5). The majority consisted of retrospective studies at low-to-moderate risk of bias with moderate consistency within the findings; they highlighted how arch variations would play into procedural planning and risk prediction for aneurysm.[16-26] The lone cadaveric study pertained but its design did hinder this study from having maximum utility, meaning the degree of evidence was not particularly strong in regard to straight clinical application due to possible lack of context applicability in this case.[18] Studies with more advanced imaging techniques, especially by MRI and CT, clearly demonstrated their use in the exploration of specific arch types and, therefore, related hemodynamics such as flow-pressure changes. With a risk of bias at a low to moderate level, low precision was achieved due to the very small number of only imaging-based studies, which however were all relevant to the clinical area.[17,27]

Table 5. GRADE certainty assessment

Study approach	Count of studies	Common finding	Bias risk	Consistency	Applicability	Precision	Additional factors	Overall certainty
Retrospective	9	Importance of aortic arch variations in surgical planning and prediction of aneurysm risk prediction[16,17,19-22,24-26]	Low to moderate	Moderate	Direct	Low	Potential publication bias	Moderate
Cadaveric analysis	1	Relevance of anatomical awareness during interventions[18]	Low	High	Direct	High	Limited by single study design	Low
Advanced imaging	2	MRI and CT-based metrics for identifying risk profiles in specific arch variations[17,27]	Low to moderate	Moderate	Direct	Low	Flow-pressure dynamics important	Moderate

Discussion

The formation of an aneurysm in the aortic arch has significant clinical implications. In this location, aneurysms are risky because the environment is high pressure in the aorta and can cause catastrophic hemorrhage with a high mortality rate if not treated.[28] Furthermore, surgical intervention on the aortic arch is complicated by the structure and anatomical positioning of the aortic arch. Therefore, the need to prevent the development of aneurysm lies in the early identification of at-risk populations.[29] Although genetic predispositions, metabolic factors, and lifestyle influences are considered to contribute to the formation of aneurysms, anatomical variation is increasingly recognized as a potential factor, but remains under-explored in the existing literature.[30]

With the advent of advanced imaging modalities, such as MRI and CT, and CFD and FEA, researchers can now visualize the precise geometry of the aortic arch in unprecedented detail. In so doing, these technologies surpass the mere correct classification of anatomical variations to reveal their hemodynamic implications. These imaging studies and calculations measure the high-risk anatomical variants and quantify the hemodynamic parameters associated with aneurysm formation so that risk stratification becomes more complete and individualized clinical management strategies are taken into account.[31-33]

The clinical relevance of AA differences in relation to aneurysm formation, surgical planning, and perioperative treatment is highlighted by the evaluated research taken together. However, a more thorough review of the literature identifies some significant gaps in our understanding of these relationships. First, the included research ranges from sophisticated CFD analyses to retrospective cohorts, demonstrating a significant degree of variation in study designs and methodology. Despite the fact that 4D flow MRI and CTA have significantly enhanced our capacity to evaluate the architecture and hemodynamics of AA, published research is very inconsistent due to the lack of imaging procedure standardization and a definition of what constitutes “high risk.” For example, researchers have documented a positive association, negative association, or no association of risk in developing aneurysm among their groups when using two alternative thresholds to calculate wall shear stress or oscillatory shear index.[17,21,32]

The issue of generalization is exacerbated by population differences. Many studies focus on specific geographic or ethnic groups; for example, the existence of an abnormal right subclavian artery is an AA anomaly that is commonly observed in East Asians.[20,29] Despite their usefulness, these results cannot be applied consistently to populations with different genetic and environmental origins. The lack of a standardized method for determining the risk associated with certain anatomical variations is another issue. Configurations such as the bovine arch are linked to aneurysms and strokes in some studies, but not in others. This is likely due to variations in sample numbers, power, and controls for confounding factors such as smoking and hypertension. This requires larger-scale, more thorough research.[26,31,36]

There is a great deal of literature in this regard to incorporate their findings into predictive models for clinical use, despite the general recognition of the promise of sophisticated imaging techniques and computer models. Most analyses continue to be descriptive, restricting their applicability for tailored interventions and risk classification. There is also little research on the perioperative and procedural outcomes in patients with AA variants. Although carotid artery stenting for individuals with bovine arch morphology has been associated with technical challenges, there is a lack of quantitative information on long-term success and neurological problems.[33,34]

All the included studies in our review showed both converging and divergent results as far as clinical relevance for the variation of the aortic arch. Some studies' results are almost similar to each other, while others provide some individuality. Many of them suggested that awareness of variations is crucial in the management plan and interventions during surgical operations, especially in endovascular and thoracic procedures.[16,18,19,22,23] Studies that used very advanced imaging techniques, such as 4D flow MRI, highlighted the potential of such modalities in the detection of high-risk patients by flow-pressure metrics, particularly in ATAAs.[17]

Some studies identified particular anatomical variations that have been shown to predict aneurysm risk, including the angle between the ascending aortic arch (asc-arch) and ATAAD[20], as well as the association of bovine arch configurations with proximal aneurysms and aberrant subclavian arteries with distal aneurysms.[21,26] These results aligned with those that indicated high clinical relevance for preoperative imaging to direct surgical plans and minimize the risk of complications in anatomically variant patients.[24,27] Other studies were different in showing no considerable association between specific arch types and aneurysm prevalence, suggesting a more conservative approach in terms of clinical relevance.[25]

A larger-scale study is necessary to establish whether specific patterns of branching of AA influence the lateralization of hemispheric stroke and whether the bovine arch configuration predisposed to cardioembolic stroke.[33] Further research has indicated that anatomical variations in AA, including BAA, preferentially result in left-sided embolic events, often implicating the left cerebral hemisphere in approximately 30% of cases.[34] With a frequently poorer prognosis associated with strokes originating from the left-sided cerebral sites, it may also be seen whether BAA anatomy presents a worse prognosis as opposed to that of the standard architecture of AA. Findings of this nature would possibly increase the awareness and incorporation of AA anatomy within anticoagulation schemes used in patients at risks for cardioembolic stroke.

Other studies suggest that the flow dynamics of the AA branches may be further studied to explain mechanistic pathways toward ischemic stroke in AA variation of AA, especially BAAs.[29] Other recommendations were also made on routine assessment of AA in carotid imaging, especially in the younger population of stroke patients, as well as highlighted in a preventive approach.[31]

A higher rate of adverse neurological events and mortality was observed among individuals with BAA configurations during the perioperative period, compared to those with other AA patterns, although more research with larger cohorts is required to determine the effect of specific AA variations on perioperative outcomes.[32] Evidence also supported that carotid artery stenting with transradial or transbrachial approaches is safe and effective for patients with BAAs; CTA imaging before the procedure has helped determine the best vascular access approaches to patient-specific anatomy of the Aas.[33] Additionally, findings pointed out that catheter handling the catheter was one of the most important outcome determinants for CAS and careful planning in advance regarding procedural details could reduce even further the amount of time spent on catheter management and, thereby, safety in CAS; this implies technical delicacy.[34]

The general prevalence of the three-branched aortic arch model including the brachiocephalic trunk, the left common carotid artery, and the left subclavian artery observed in this review were comparable to the findings by Popieluszko et al.[35] The prevalence was generally high (between 63.5% and 83%), which is well established with the findings reported in Popieluszko et al. for 80.9%. Both studies mentioned the bovine arch as an anatomical variation that is present in the population, but our review covered a greater range of prevalence of 10.1% to 43.2% as opposed to 13.6% by Popieluszko et al. The two studies indicated that there was a higher risk of hemorrhagic and ischemic events during thoracic surgery in patients with such variations, which indicates the importance of preoperative planning.

Baz Rao et al.[36] also showed that TAD and complications associated with the intervention were correlated with the bovine arch. Although both reviews discussed advanced imaging such as CTA and 4D flow MRI in evaluating the hemodynamic consequences of aortic arch variations, Baz Rao et al.[36] specifically drew a link of the bovine arch with complications of coarctation of the aorta (CoA) and stroke; our review covered the potential impacts of different arch anomalies, including the angle of the ascending arch and aberrant subclavian artery, on the risk of aneurysm.

Our findings were consistent with the review by Lazaridis et al.[37] in the presence of rare abnormalities, including a left vertebral artery that originated from the aortic arch, which makes these patients prone to cerebrovascular complications. However, Lazaridis et al. focused specifically on VA origin anomalies and their implications for endovascular procedures, while our literature review covered a more extensive spectrum of aortic arch anomalies, including the bovine arch and ARSA, in relation to the risk of aneurysm and perioperative complications.

Ahmad et al.[38] discussed endovascular repair techniques for the aortic arch and provided some results of the approaches of ChTEVAR SM TEVAR, and custom-made devices. Our review looked at anatomical variations and how these would affect procedural risks. Ahmad et al. reviewed the efficacy and safety of endovascular techniques in patients with complex aortic anatomy. Although our review stressed anatomical knowledge for planning, Ahmad et al. presented quantitative procedural outcomes that clearly demonstrated technique-dependent differences. Both studies supported the individualized approach in patients with aortic arch anomalies, and Ahmad et al.[38] specifically emphasized endovascular interventions.

The limitations of the selected research are also reflected in the limits of this review. Retrospective designs are significantly overrepresented, which restricts causal inference and introduces selection bias. Crossstudy comparison is difficult due to the lack of a consensus classification scheme for AA variants, and definitions of "bovine arch" vary. The technological diversity creates factors of poor replicability and diagnostic variability.[35,36] Since the majority of the studies were single-center research, generalizations would be more challenging due to the limited variety of population variety and expertise variability of experience that would be present in multicenter studies. Despite being commonly associated with AA abnormalities, stroke risk has not been thoroughly investigated in terms of mechanisms such as haemodynamic changes or embolic routes.[31,37]

Standardization in methodology, such as uniform imaging techniques and classification systems, should be the main focus of future research. To validate the results and guarantee a wider application across various populations and therapeutic situations, prospective multicenter studies are required. Developing predictive tools for aneurysm risk and procedure outcomes can be made easier by integrating complex computer models, such as CFD and finite element analysis.[17,38] Long-term follow-up studies would be helpful in providing important information on the durability of treatments and the natural history of aneurysms in patients with AA abnormalities. A deeper understanding of these interactions may also be gained by researching the mechanistic links of AA variants with stroke, which integrate imaging data with genetic profiles and biomarkers. For individuals with anomalies of the aortic arch, this would close a gap in the literature and offer different approaches to diagnosis and therapy.[29,30,33]

Study limitations

This study was weakened by heterogeneity in the study designs and sample size, which thereby introduced heterogeneity in assessing aneurysm risk and variations in the aortic arch. Also, the study is retrospective with an overwhelming predominance, potentially compromising control over a number of confounding variables, thus allowing scope for inconsistency in findings of association. The heterogeneity due to the lack of uniformity in the advanced imaging techniques that contribute to the accuracy was one of the critical weaknesses this study had. Anatomical variation, as such, was necessarily complicated and perhaps too subtle in its classification for certain types of interpretation, which were variable from study to study. All these factors narrowed the generalizability potential of any findings.

Clinical recommendations

According to the findings evaluated in this review, it becomes apparent that the clinical examination will include modern imaging techniques of CT and MRI to amplify the specificity of the diagnosis along with the detection of risk aortic arch variations prone to aneurysmal development. Standardized imaging and classification protocols for different types of aortic arches will increase the reproducibility of the risk detected in patients. Further prospective studies with well-defined controls for confounders are warranted to establish more strongly the relationship between certain arch types and the risk of aneurysms. Finally, interprofessional collaboration between vascular surgeons, radiologists, and cardiologists will ensure optimal risk stratification and surgical planning in patients with anatomy variations.

Conclusion

The results indicated a specific anatomical variation related to the aortic arch, such as a bovine arch and the aberrant right subclavian artery, which is reportedly associated with increased apparent risks of developing aneurysm formation. However, in view of the consistent association, through all study populations, the influence of the specific anatomical variation upon the other factors can differ. It emphasizes the need to include detailed imaging assessments within the clinical evaluation, and future research will be required to establish a definitive relationship between these variations and to explain the predictive value that may exist for aneurysm development.

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Authors' contributions

Conceptualization, S.K.J. and S.S.; Methodology, S.S.; Software, S.S.; Validation, S.K.J. and S.S.; Formal Analysis, S.K.J.; Investigation, S.S.; Resources, S.K.J.; Data Curation, S.S.; Writing – Original Draft Preparation, S.S; Writing – Review & Editing, S.K.J.; Visualization, S.S; Supervision, S.K.J.; Project Administration, S.S.; Funding Acquisition, S.K.J.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Data availability

The availability is not applicable to this article, as no new data were generated or analyzed during the current study.

Ethics approval

Ethical approval was not required for this study, as it is a review of previously published literature.

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