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CASE REPORT

A Case Series Cadaveric Study on Acquired and Congenital Azygos Venous System Variations

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Abstract

The azygos venous system holds essential clinical relevance as it can provide collateral circulation in cases where the superior and inferior vena cava have become obstructed. Additionally, it is important in imaging and mediastinal procedures because variations in this system may be confused with pathology. In this study, the azygos system of 31 embalmed anatomy donors was dissected, analyzed, and classified according to the Anson McVay system and Dahran and Saomes subclassification. Out of 31 donors, one (3.22%) donor was classified as Type I, 27 (87.09%) were Type II, two (6.45%) were Type III, and one (3.22%) was unobservable. These values closely replicated values previously reported in literature. Four subjects, however, exhibited variations that are rare or not previously reported in literature. In this paper, we describe those rare cases and consider their development and clinical relevance.

Key Words: *Azygos venous system; Azygos system variation; Cardiopulmonary medicine; Cadaveric study; Hemiazygos vein; Accessory hemiazygos vein; Azygos vein*

Introduction

The azygos venous system (AVS) is a group of veins that forms an H-shape across the vertebral column along the posterior thoracic and upper abdominal region. The system is formed through connections of the azygos vein (AZY), hemiazygos vein (HAZY), accessory hemiazygos vein (AHAZY), and left superior intercostal veins (SIs) [1]. Collectively, these veins function to drain the posterior thoracic and abdominal wall. They also provide collateral circulation between the inferior vena cava (IVC) and the superior vena cava (SVC) [1].

The AZY most commonly originates near the IVC, from the union of the ascending lumbar and subcostal veins. The AZY often travels anterior to the lumbar vertebrae, it passes through the aortic opening of the diaphragm in its course from the abdominal cavity to reach the posterior mediastinum. This opening,

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bounded by the median arcuate ligament, allows the passage of two other tubes: the aorta and the thoracic duct. This ligament prevents the three important vessels from being affected by diaphragm contraction, making them passable all the time [2].The AZY drains the lower eight posterior intercostal veins (PIs) [3]. During its course, it receives the HAZY, AHAZY, and right SIs [1,3], allowing it to drain the posterior mediastinum into the SVC via the arch of the AZY (Figure 1). The arch of the AZY is the connection located superior to where the SVC drains into the right atrium at the level of the third costal cartilage [4]. Because of its origin at the IVC and drainage into the SVC, the AZY can function as a connection between these two great vessels. The AVS becomes essential in cases of obstruction of the IVC as it allows the lower half of the body to drain into the SVC instead [5,6].

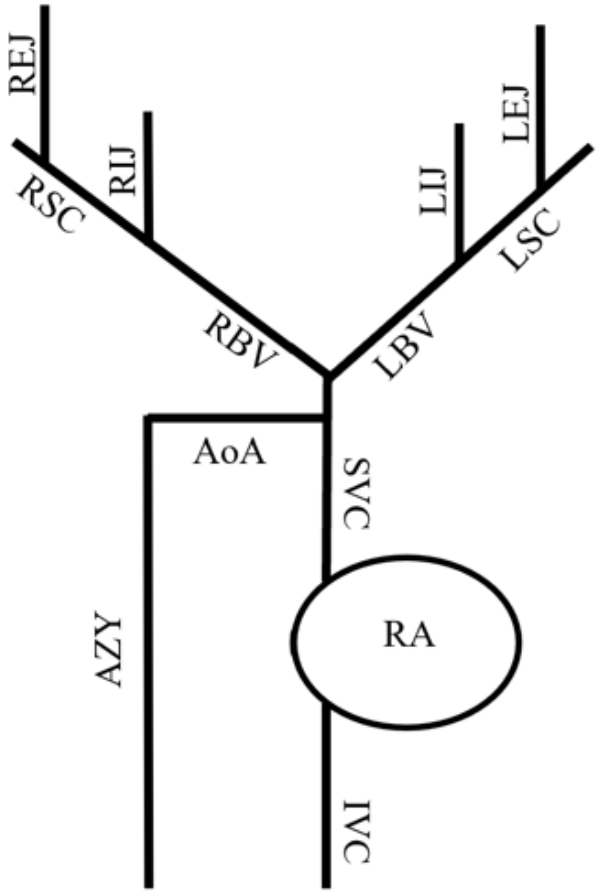

Figure 1) *Schematic depiction of the connection between the SVC and the azygos vein. In cases of SVC obstruction, the azygos venous system becomes clinically relevant as it provides collateral circulation between the SVC and IVC. RA=Right atrium, REJ=Right External Jugular vein, LEJ=Left External Jugular vein, RIJ=Right Internal Jugular vein, LIJ=Left Internal Jugular vein, LSC=Left Subclavian vein, RSC= Right Subclavian vein, LBV=Left Brachiocephalic vein, RBV=Right Brachiocephalic vein, AZY=Azygos vein, AoA=arch of the azygos vein.*

Beyond its importance in forming a connection between the IVC and SVC, the AVS has several other clinical implications. For instance, it may serve as a pathway for metastasis to travel from the esophagus [7]. Also, AVS abnormalities may be misinterpreted on imaging as aneurysms, mediastinal tumors, or enlarged lymph nodes. Cases in literature have described a rare course of the HAZY ascending obliquely between the aorta and the esophagus called interazygos. This transverse segment, crossing the midline, may be confused with different lesions situated at this level such as an aneurysm, tumor, or lymph node hypertrophy [8]. Knowledge of possible variants of the AVS is vital to prevent misdiagnoses.

Because of the high anatomical variation in the AVS, several studies have classified it, yet there remains no consensus on a single standardized classification. In this study, we apply one of the most frequently used classification systems, the Anson and McVay [9] classification with a Dahran and Saomes [5] subclassification when applicable, to investigate the variability of the AVS in 31 anatomical donors and relate the clinical importance of variation on rare cases that represent outlying variations.

Materials and Methods

This study included 31 preserved human donors. The donors were provided to the VCOM-Louisiana Anatomy Laboratory by the University of Texas Southwestern's Willed Body Program, with permissions for

teaching and research. The ages of the donors spanned from 53 to 94 years. The only health information provided by the willed body program was primary cause of death. Of the individuals, 23 (74.2%) were female and eight (25.8%) were male. The anterior thoracic wall, pericardium, heart, lungs, esophagus, anterior abdominal wall, and abdominal organs were removed during the regular anatomy course, exposing the posterior mediastinum and AVS for dissection. The aorta and diaphragm were left in situ but reflected as needed for further observation. Further dissection and cleaning of the involved structures were completed as needed. A schematic representation was drawn for each donor once the AVS was fully visible.

The AVS was classified according to the Anson and McVay system into three main types of AVS: primitive or embryological type I, transition type II, and single column type III [9]. This system classifies based on the vertical forms of the AZY and horizontal connections between the AZY, HAZY, and AHAZY.

Type I, or primitive type, consists of two separate, vertical, and often parallel AZYs with no retro-aortic connections. The right portion drains into the SVC and the left into the left brachiocephalic vein. Type II, or transitional subtype, is considered the typical presentation for the AVS. Type 2 consists of separate AZY, HAZY, and AHAZY. This type was divided further into groups A through E according to the number of retro-aortic communications from one (group A) to five or more (group E) as classified by Dahran and Saomes [6]. Type III, the single column type, consists of a single vein located in the midline, often called a unicolumnar vein [4] that drains both the left and right PIs.

Each individual was evaluated for origins and terminations of the azygos, hemiazygos, accessory hemiazygos, and right and left SIs. Measurements and photographs were taken when variations were observed that could not be found in previous publications and/or that might be associated with pathological processes instead of variations in embryological development.

Results

Results are presented in Table 1. Type I is designated as the primitive type because it resembles the AZYs in fetal development prior to the formation of connections between the right- and left-sided structures. Type I was found in one 77-year-old male donor (1/31; 3.22%). In this donor, the right PIs drained into the right AZY and then into the SVC. The left intercostal veins drained into a separate left AZY and then into the left brachiocephalic vein without connecting to the AZY on the right.

Type II was observed in 27 donors (27/31; 87.09%). Type IIA was present in three donors (3/31; 9.67 % of the total) where only one retro-aortic communication was observed. In all three of the Type IIA donors, the communication consisted of the HAZY traversing the vertebral column between vertebral levels T6 to T8. Type IIB was observed in 11 donors (11/31; 35.48%) with two retro-aortic communications between the AZY and the left-sided HAZY and AHAZY respectively. Type IIC (three retro-aortic communications) was observed in eight donors (8/31; 25.8 %). For the purposes of classification, the most inferior was designated as the HAZY and the most superior as the AHAZY. Type IID was observed in three donors (3/31; 9.67 %) with four retro-aortic communications and Type IIE in two donors (2/31; 6.45%) containing five retro-aortic communications in one donor and seven in the other.

TABLE 1

Comparison of results across some of the most common azygos venous system variation studies.

Author (year)	Number of Cadavers	Type I (%)	Type II (%)		Type III (%)
Mouawad et al. (present study)	30 (31 but 1 non observable)	3.22	87.09	A=9.67 B=35.48 C=25.8 D=9.67 E=6.45	6.45
Patra et al. (2017) [17]	30	3.3	90	A=10 B=40 C=30 D=6.67 E=3.33	6.7
Dahran & Soames (2016) [6]	30	3.3	86.7	A=12 B=35 C=7 D=15 E=12	10
Kotoglu et al. (2012) [3]	48	2.1	92	Subclassification system not yet available	2.1
Anson McVay (1984) [8]	100	1	98	Subclassification system not yet available	1
Seib (1934) [18]	200	1-2	93-94	Subclassification system not yet available	5

Two Type III variations were observed in this study. In these donors, there were no distinguishable AZY and HAZY observed. Instead, a unicolumnar vein beginning at vertebral level T8 or T9 was observed in the midline. This single vein drained the right and left PIs into the SVC directly (Figure 2).

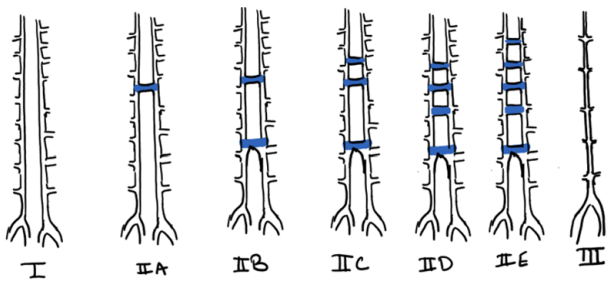

Figure 2) *Schematic representation of the Anson McVay subtypes. Type I shows separate parallel longitudinal azygos veins. Type II A-E show 1-5 retro-aortic communications respectively between the left and right sides of the azygos venous system and finally Type III depicts a unicolumnar midline azygos vein draining both the left and right posterior intercostal veins.*

Atypical Variants

In addition to those types that fit into previously described categories, there were four variants (4/30, 13.3%) observed in our dissections that are rarely, if ever, described in published literature. The presentation and potential clinical implications for each will be described below.

Case 1: A congenital atypic variant related to the formation of the HAZY

The AVS in a 77-year-old male with a history of nontraumatic cerebral brain hemorrhage, lung transplant, diabetes mellitus type 2, and chronic kidney disease presented with a unique variation that does not belong to any Anson-McVay subgroups. In this case, we observed

three tributaries connecting the left-sided venous structures with the right-sided azygos vein (Figure 3a, b). The most superior vein on the left side was identified as the accessory HAZY, draining to the AZY across the vertebral column at approximately vertebral level T7. The lower two tributaries cross the vertebral column at approximately vertebral level T10. Instead of a continuous path ascending the thorax with isolated retro-aortic veins, there are three intercostal veins draining into these two tributaries, which are connected by a vertical connection to the left side of the vertebral column. While the AHAZY was simpler to find and describe, the two potential HAZYs forming a loop are more complex. A similar atypical case was reported previously [4]. However, the prior study described a venous anastomosis that was observed higher in the thoracic region at the level of the AHAZY rather than HAZY, as was observed in our case. Another similar case was reported where an intercostal vein ascended from the 6th to the 8th thoracic vertebra and formed an anastomotic venous circle on the right side of the lower thoracic vertebra [10]. The current case is unique because the anastomosis of two potential HAZYs on the left was lower, at the level of the 10th thoracic vertebra, than previously described by previous literature.

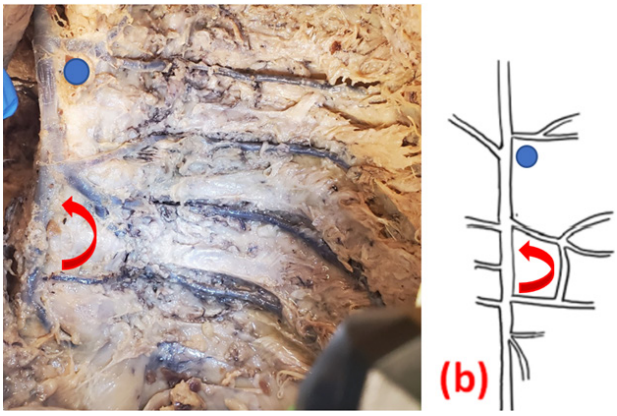

Figure 3) ***(a)*** *Atypic variant of the azygos venous system. The most superior vein to the left of the azygos vein is identified as the accessory hemiazygos vein (blue dot) and the second branch as the hemiazygos vein. When ascending from the lumbar region, it branches to receive three intercostal veins before looping back to drain into the azygos vein (red arrow).* ***(b)*** *Schematic representation.*

Case 2: A possible acquired variation of the AVS as a function of arthritic change.

We present a unique and possibly acquired variation on an 89-year-old female who died of heart failure, a unique and possibly acquired variation was presented. Upon initial dissection, the AVS appears as a Type I variant as one can easily distinguish the two longitudinal and separate AZYs. However, this case is not considered a typical Type I variant because there are remarkable osteophytic growths on the right side of the mediastinum from vertebral levels T7 to T10, where retroaortic communications indicate this case should be considered as a Type II variant instead. These growths are likely the result of age-related arthritic changes. They tend to occur around the left and right AZYs, making the veins appear to dive into the bone at the levels of T8-T9 respectively (Figure 4). Additionally, the right PIs appear to terminate into the bone rather than into the right longitudinal vein. Upon closer observation, in this case the PIs are embedded in the bone and are deep and brittle to dissect. This case is interesting as cases where ossification impacts the AVS are rare. For example, similar variants were observed in only one case out of 1479 patients using CT imaging studies as ossifications usually do not impact the surrounding azygos vasculature [11]. However, the veins traveling into the bone have yet to be described in literature.

Case 3: An enlarged azygos venous system

This case involves a 69-year-old female whose documented cause of death was complications of advanced chronic obstructive pulmonary disease (COPD). This case was classified as a variant of Type IIB under the Anson McVay system. Unlike the standard Type IIB described, the AHAZY drained directly to the left brachiocephalic vein rather than to the AZY (Figure 5a). Additionally, the AZY and AHAZY

appeared significantly enlarged compared to the size expected for this donor and the average reported in previous literature. In this donor, the diameter of the AZY was 14.5 mm as opposed to a mean of 8.558 ± 1.2569 mm (Figure 5b) [4]. The diameter of the AHAZY was 8.5 mm, compared to the reported mean of 5.471 ± 1.1740 mm (Figure 5c) [4].

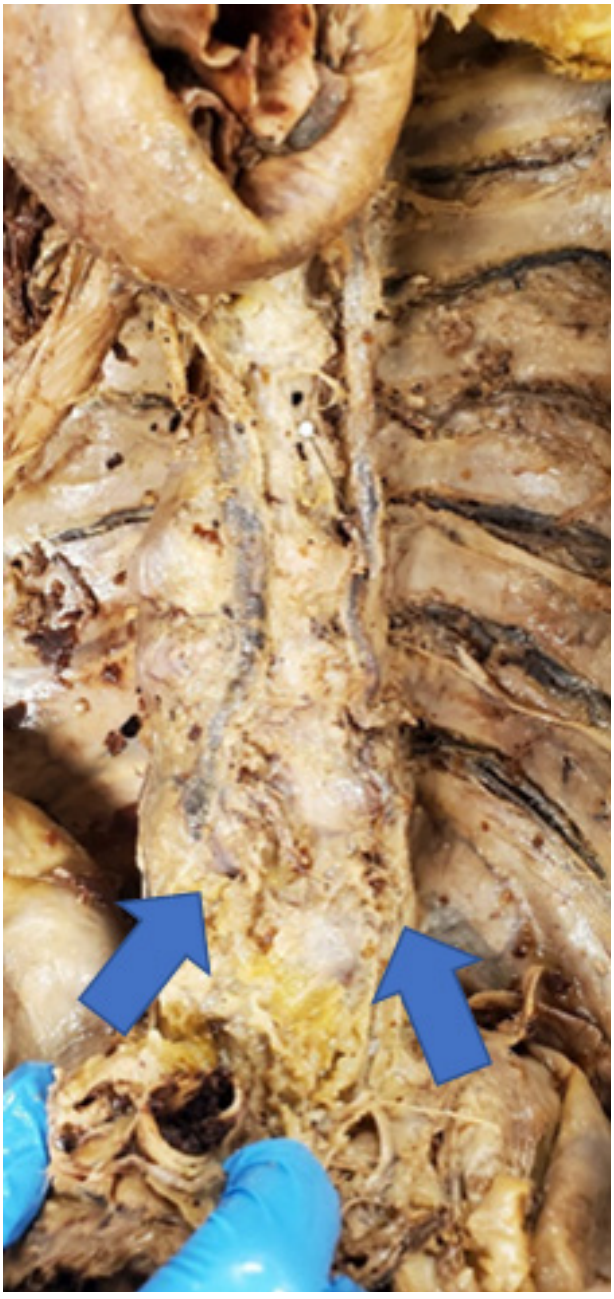

Figure 4) *Osteophytic growths to the right of the mediastinum making the longitudinal veins appear as if they dive into the bone at the T8-T9 level (blue arrows).*

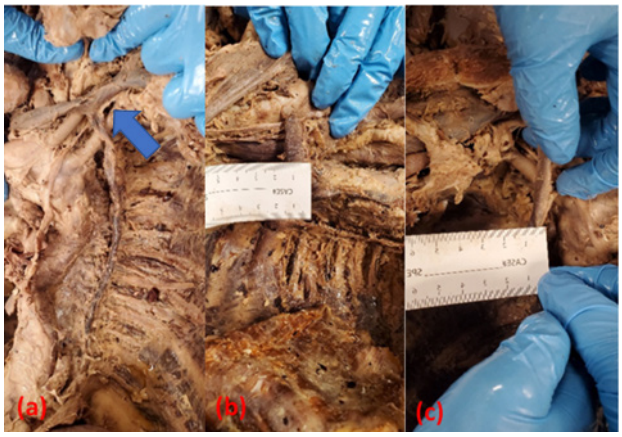

Figure 5) ***(a)*** *Rare variation showing the accessory hemiazygos vein draining into the left brachiocephalic vein directly rather than connecting to the azygos vein (blue arrow);* ***(b)*** *Azygos vein measuring 14.5mm in diameter, which is enlarged compared to the mean of 8.55mm [3];* ***(c)*** *Accessory hemiazygos vein measuring 8.5mm in diameter, which is enlarged compared to a mean of 5.47 mm[3].*

Case 4: A possible congenital abnormality related to the formation of the aorta.

The AVS in an 89-year-old female with a cause of death of senile degeneration of the brain was classified as Type IIC using the Anson McVay system. This donor exhibited a curved AZY that follows a curve in the aorta, as opposed to the expected straight shape (Figure 6a, b). This donor's marked tortuosity and curve in the aorta and paralleling AZY has not been reported in previous literature in the absence of scoliosis, aneurysms, and/or history of heart failure. While we acknowledge that this donor may have had history of some of these conditions that were not documented in the postmortem paperwork, we argue that this abnormality may be congenital. Previous literature has documented that congenital abnormalities in the aorta may lead to paired variations in the AVS in cases, such as right-sided aortic arches [12], aortic branch variations [13], and left-sided Scimitar syndrome [14]. In this case, the AZY curvature followed the contours of the aorta, further hinting at a possible congenital variation. Moreover, the AHAZY in this donor drains directly to the left brachiocephalic vein

(Figure 6c), which is another rare variation in the system [15].

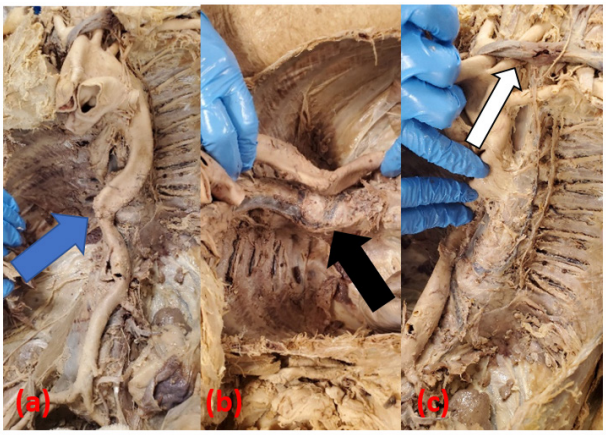

Figure 6) ***(a)*** *Marked aortic tortuosity with aortic curve to the right in the descending aorta at the level of T8 (blue arrow);* ***(b)*** *Azygos system variation following aortic tortuosity (black arrow);* ***(c)*** *Accessory hemiazygos vein draining into the left brachiocephalic vein (white arrow).*

Discussion

The widespread variation in the AVS is often explained by processes occurring during embryological development. Nevertheless, while multiple studies in current literature argue that most AVS variants result from congenital causes, few describe variations in the AVS that are acquired as part of pathological processes [16]. In this section, we explore both congenital and acquired variants while discussing the atypical variations found in this study.

During weeks 5 to 7 of embryogenesis, transverse anastomotic channels divert venous blood from the left to the right side, after which the veins on the left side shrink in size [17]. Hence, a principal AZY on the right side is found most of the time paired with a structure at least alluding to a HAZY and AHAZY on the left [16]. Most variations are observed on the left side, including aplasia of the HAZY and AHAZY or poorly defined left-sided structures [18]. At other times the HAZY and AHAZY might fuse to form a distinct left-sided AZY paralleling the right-sided AZY, creating the form discussed earlier as primitive Anson McVay Type I. In other instances, communications between the AZY and its left-sided counterparts are variable. The number of these communications, which often lie behind the aorta, determine the subgroup of Type II of the Anson McVay system using the Dahran and Soames system [6]. And lastly, when a single mid-line AZY occurs, it is classified as Type III in the Anson McVay system.

In the current study, the distribution of the classifications is comparable to those reported in previous studies, and most of the donors could be classified into the existing classification system subgroups. This study yielded one (1/31; 3.22%) Type I, 27 (27/31; 87.09%) Type II, and two (6.45%) Type III AVSs. The AVS was unobservable for one (1/31; 3.22%) donor. Further breakdown of the Type II subgroups according to the Dahran and Soames system yielded Type IIA in 3 donors (3/31; 9.67 %), Type IIB in 11 donors (11/31; 35.48%), Type IIC in 8 donors (8/31; 25.8 %), Type IID in 3 donors (3/31; 9.67%) and Type IIE in 2 donors (6.45%). A comparison of these results to similar previous studies in literature is listed in Table 1. However, two of the four abnormal variants described above show drainage of the AHAZY into the left brachiocephalic vein. This amounts to approximately 7% of the donors in this study having this potentially rare variant. This suggests that this variant is either not as rare as reported, or that this study exhibits a biased sample given small sample sizes.

The likely connection between AVS variation and embryogenesis aids in the classification and understanding of these systems. In most cases, the variations observed are consistent with patterns of venous system development and change during embryological development. For example, Cases 1 and 4 both exhibit variations in the AVS that can be explained by embryological

development, such as the development of the HAZY in Case 1 and in the aorta in Case 4.

However, the applied classification systems fail to acknowledge variation in cases that may have been acquired. Some variations that are attributed to acquired underlying pathology include enlargement from hemodynamic changes such as fluid overload, increase in right atrial pressure, fibrosing mediastinitis, and caval syndrome. Others are due to tumors or other processes that cause compression or intraluminal filling defects [16]. An example of a fluid overload case was described in Case 3 above, where a COPD patient presented with an abnormal dilation of the blood vessels in the AVS, possibly from venous stasis [19]. COPD patients are at an increased risk for venous thromboembolism (VTE) because of immobilization, heightened systemic inflammation, cigarette smoking, and venous stasis [20]. VTE, however, remains under-diagnosed in COPD patients because its symptoms mimic a COPD exacerbation [21]. In the absence of signs of congestive heart failure, an abnormal prominence of the AZY suggests the possible presence of cor pulmonale (i.e., abnormal enlargement of the right side of the heart as a result of disease of the lungs or the pulmonary blood vessels), which could favor the diagnosis of thromboembolism [22]. However, while it is possible that VTE played a part in this individual's death in addition to the diagnosed COPD, there was no evidence of abnormal size or structure of the donor's heart during dissection. Additionally, in Case 2 we described an individual that initially appeared to have a Type I AVS variant under the Anson McVay system. The subsequent arthritis changes described in this case might be included in variations in the AVS that could be caused by processes that could compress the vessels. In this donor, we observed arthritic osteophytic growth in the posterior mediastinum with neovascularization in the bone growth and absorption of the AZY and HAZY into the bone causing a varying expression of the AVS.

Conclusion

While AVS variations are common, they are often overlooked as they are deemed clinically insignificant. However, knowledge of these variations may prevent misdiagnosis in imaging studies. In this paper, we studied the expression of AVS in 31 donors. The variations in our study support patterns and distributions described by previous studies that often result from embryological processes. In addition to classifying according to pre-existing systems, we also described variations not yet described in literature.

Ethical Approval

IRB review was confirmed as not required by the Edward Via College of Osteopathic Medicine's Institutional Review Board as it involves cadaveric research.

Informed Consent

All donors provided general research consent under their donation to the University of Texas Southwestern's Willed Body Program. Permission for research was obtained by this program.

Author Contribution

SN and CC provided substantial contributions to conception and design. MM provided substantial contributions to acquisition, analysis, interpretation of data as well as clinical correlations; MM also drafted the article. SN and CC revised the article and data critically for important intellectual content, gave final approval of the version of the article to be published; and all authors

agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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