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Clinical and Surgical Implications of the Pulmonary Azygos Lobe: A Systematic Review

Implicaciones Clínicas y Quirúrgicas del Lóbulo Ácigos Pulmonar: Una Revisión Sistemática

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SUMMARY: Azygos lobe is one of the most common pulmonary variations. Although numerous studies discuss to the clinical and surgical implications of anatomical variations, there are few investigations about this topic. The aim of this study was to discuss the anatomy of the pulmonary azygos lobe and its possible clinical and surgical correlations. In this systematic review, a total of 48 results were found between 1968 and 2020. After application of eligibility criteria, 16 articles were included to analysis. Our results showed there were no reports of surgery complications in azygos lobe presence. In all articles that described the anatomical variation, the pulmonary azygos lobe received tertiary segmental branches. Among the surgical implications in the presence of the azygos lobe, complications are of low complexity. It is necessary to teach about this anatomical variation in medical schools in cadavers. Emphasizing the obvious morphological modifications in the superior mediastinum.

KEY WORDS: Anatomical variation; Clinical implications; Surgical outcomes.

INTRODUCTION

The azygos lobe is one of the most common pulmonary variations (Fig. I), with an estimated incidence of 0.4 % to 1 % (Sadikot *et al*., 1997; Arai *et al*., 2012; Ndiaye *et al*., 2012; Fukuhara *et al*., 2013). This anatomical variation was first described in 1777 by Heinrich August-Wrisberg, doctor and director of the Gottingen Anatomical Institute in Germany. In this description, an aberrant configuration of the path of the azygos vein was observed on the cadaver of a three-year-old child (Ndiaye *et al*.).

The azygos vein is responsible for the drainage of a great part of the internal thoracic wall and promotes, indirectly, a communication between the superior and inferior cava veins. This communication is extremely important, as the azygos system is an alternative pathway to the return of blood to the heart in case of obstruction of these great vessels. On its natural trajectory, the azygos vein has an intimate anatomical relation with the right lung up to its debouchment on the posterior part of the superior vena cava, at the height of the superior right lobe (Moore *et al*., 2014; Standring, 2010).

During normal embryonic development, the right lung bud passes inferior and laterally through an arch formed by the right posterior cardinal vein (Baumgartner, 2009; Moore *et al*., 2016). This arch must descend through the right paratracheal region until it reaches its final position between the superior right lobe and the main right bronchus (Maldjian & Phatak, 2008; Schoenwolf *et al*., 2015). If the lung bud fails on dodging the cardinal vein, which will posteriorly become the azygos vein, a fissure will form above the pulmonary hilum, resulting in an upper medial portion of the superior right lobe that is detached from the rest of the right lobe (Baumgartner; Fukuhara *et al*.). This detached lung portion became known as the azygos lobe, and its fissure, formed by parietal and visceral pleura, originates a

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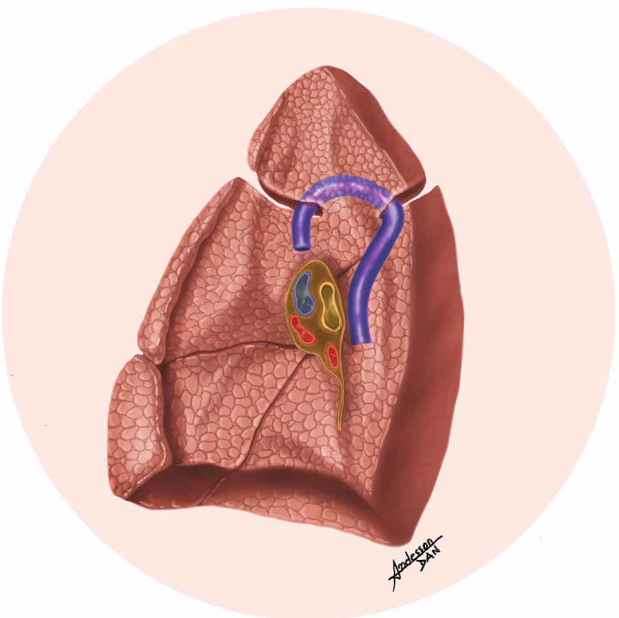

Fig. 1. Illustration of the Pulmonary Azygos Lobe in a medial view.

structure known as the mesoazygos web, which is structurally similar to the mesentery and contains the azygos vein in its inferior limit (Maldjian & Phatak; Standring).

The acknowledgment of anatomical variations is essential to the medical practice, as the position of a vein on a non-habitual place, for example, can present a significant risk of bleeding secondary to an iatrogenic vascular lesion (Maldjian & Phatak). Although numerous studies discuss the clinical and surgical implications of anatomical variations, more substantial investigations on the subject are still scarce in the literature. Therefore, the objective of this work was to discuss the anatomy of the pulmonary azygos lobe and its possible clinical and surgical correlations, through a systematic review.

MATERIAL AND METHOD

This systematic review was developed according to PRISMA criteria, referring to scientific articles about the incidence of the pulmonary azygos lobe and its surgical and clinical applications. The electronic searches were carried out from October 8th of 2020 to May 31st of 2021 on the MEDLINE via PubMed and Latino-American and Caribbean Literature in Health Sciences (LILACS) databases. Furthermore, a complementary article obtained on the PubMed database and classical Anatomy and Embriology books were considered for analysis.

During the construction of the search strategies, descriptors and keywords were used for each database specifically. No MeSH terms related to the topic were found in the PubMed and LILACS databases. On PubMed, a simple search was conducted with English and Portuguese language filters, using the following descriptors: Azygos Lobe AND Anatomy AND Surgery. A total of 44 results was found between the years of 1968 and 2020. On LILACS, a simple search with no filters was conducted using the descriptors: "lobo ázigos" OR (azygos lobe) OR (lobus azygos). A total of 4 results was found between the years of 1996 and 2013.

Study selection. During the research, a total of 49 publications was found, of which 19 were excluded after the reading of the summary for not being related to the theme. Out of the 30 remaining publications, 12 were excluded after reading the entire text for not meeting the inclusion criteria. In the end, 18 publications were included in this review (Fig. 2).

For the description of the results of the selected articles, the present manuscript was organized into four items: Clinical implications; Surgical outcomes; Variations of the pulmonary azygos lobe malformation; Relation

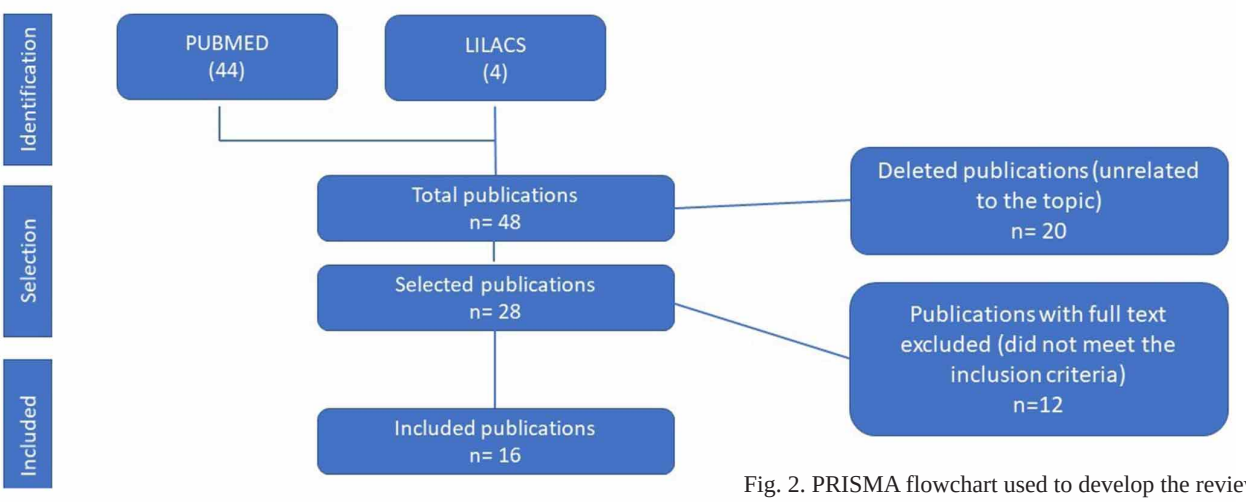

Fig. 2. PRISMA flowchart used to develop the review.

between the broncovascular tree and the pulmonary azygos lobe. The data obtained from the subjects of the selected articles regarding clinical and surgical implications were extracted and organized on a table.

RESULTS

Clinical implications. Amidst the searched articles, 7 manuscripts discussed that the presence of this anatomical variation presumably has no significant clinical importance (Sadikot *et al*.; Grismer & Read, 1998; Asai *et al*., 2005; Eradi & Cusick, 2005; Baumgartner; Arai *et al*.; Fukuhara *et al*.). However, cases of congenital lobar emphysema (Hill *et al*., 1988) and lung adenocarcinoma (Arai *et al*.) associated with the pulmonary azygos lobe were encountered. Nonetheless, according to Chabot-Naud *et al*. (2011) the accessory pulmonary lobe, formed by the azygos fissure, can be confused with pathological conditions such as abscesses, neoplasms, or subpleural emphysematous bullae on complementary exams such as radiography.

Surgical outcomes. Within the 17 articles of the main search, 14 (Hill *et al*.; Sadikot *et al*.; Sieunarine *et al*., 1997; Grismer & Read; Gill *et al*., 2004; Asai *et al*.; Eradi & Cusick; Reisfeld, 2005; Delalieux *et al*., 2006; Maldjian & Phatak; Baumgartner; Azoury & Sayad, 2011; Arai *et al*.; Fukuhara *et al*.) presented surgical cases that involved the azygos lobe, totalizing 37 patients (Table I). Most of the surgeries (n=26) were

Table I. Characteristics of the patients with a Pulmonary Azygos Lobe which underwent some type of surgical procedure.

PATIENT	SEX	AGE	CASE	SURGERY	OUTCOME
1	M	< 1	Congenital lobar emphysema	Right Thoracotomy	No complications
2	M	< 1	Tracheoesophageal fistula	Right Thoracotomy	No complications
3	F	< 1	Esophageal atresia	Right Thoracotomy	No complications
4	M	12	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
5	F	19	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
6	F	18	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
7	M	47	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
8	F	19	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
9	M	29	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
10	F	20	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
11	F	36	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
12	M	24	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
13	F	54	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
14	M	15	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
15	M	25	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
16	M	15	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
17	M	41	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
18	F	55	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
19	F	47	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
20	M	35	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
21	F	28	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
22	M	35	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
23	M	36	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
24	M	72	Adenocarcinoma of the lung	Lobectomy of the superior right lobe	Presence of complication
25	F	64	Adenocarcinoma of the lung	Lobectomy of the superior right lobe	No complications
26	M	25	Pneumothorax	Tubular Thoracotomy	No complications
27	M	69	Adenocarcinoma of the lung	Lobectomy of the azygos lobe	Presence of complication
28	M	71	Carcinoma of the distal esophagus	Right Thoracotomy	Presence of complication
29	M	22	Pneumothorax	Video-assited Thoracoscopy	No complications
30	F	15	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
31	M	74	Adenocarcinoma of the lung	Lobectomy of the azygos lobe	No complications
32	F	27	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
33	F	24	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
34	M	24	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
35	F	14	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
36	M	30	Hyperhidrosis	Thoracoscopic sympathectomy	No complications
37	M	20	Pneumothorax	Video-assited Thoracoscopy	Presence of complication

M = Male / F = Female

Thoracoscopic Sympathectomies for the treatment of diverse cases of hyperhidrosis. In addition, 4 lobectomies, 2 video-assisted thoracoscopies, 1 tubular thoracotomy, and 4 right thoracotomies were encountered. Out of the 37 patients, only 4 (11 %) presented some kind of surgical complication related or not to the pulmonary azygos lobe.

Variations of the pulmonary azygos lobe malformation. The anatomical variation in question suffers a lateral dislocation and converges between the folds of the parietal pleura, the mesoazygos web, which assumes a shape similar to a teardrop. In addition, the passage of the mesoazygos over the right lung provokes a remodeling of the superior lobe, creating an accessory fissure shaped like an inverted comma (Chabot-Naud *et al*.). The fissure which delimits the azygos lobe, located on the upper medial part of the right lung, showed a variety in its depth, ranging from 2,2 to 5 centimeters, and in its convexity, which could be lateral or medial (Çimen *et al*., 2005; Chabot-Naud *et al*.).

According to Ndiaye *et al*. three distinct types of the azygos fissure were found type A, B and C (Fig.3). In type A, the accessory fissure separates the lung apex from the superior lobe as it crosses superiorly and parallel to the horizontal fissure (47 %). In type B, the accessory fissure divides the apex into two halves as it crosses the apex vertically (26 %). In type C, the slit provoked by the accessory fissure, although considered vertical, is more medial and creates a detached lung portion in the lung apex (26 %) (Ndiaye *et al*.).

Furthermore, in most cases, the radiographic demonstration of the azygos lobe is not of great complexity, being portrayed through a pleural reflection represented by a straight line and a drop-shaped azygos vein (Sieunarine *et al*.).

Relation between the bronchovascular tree and the pulmonary azygos lobe. Out of the 36 cases of pulmonary azygos lobe reported on the 17 articles of the main esence of , anatomical variation. In the cases reported by Çimen *et al*. and Fukuhara *et al*. the pulmonary azygos lobe was supplied by the apical (BIa, AIa, VIa) and posterior (BIIa,AIIa,VIIa) segmentary branches of the bronchovascular tree of the superior right lobe (Fig. 4). While on the cases reported by Ndiaye *et al*. and Arai *et al*. the pulmonary azygos lobe was supplied only by the apical segmentary branches (BIa,AIa,Va) of the bronchovascular tree of the superior right lobe. None of the studies reported cases in which the azygos lobe was supplied by its own secondary lobar bronchus.

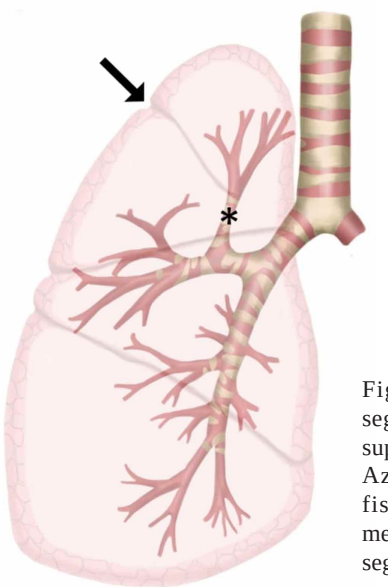

Fig. 4. Only the apical segmental bronchus (BI) supplying the Pulmonary Azygos Lobe. Azygos fissure (arrow) and medially displaced apical segmetar bronchus (*).

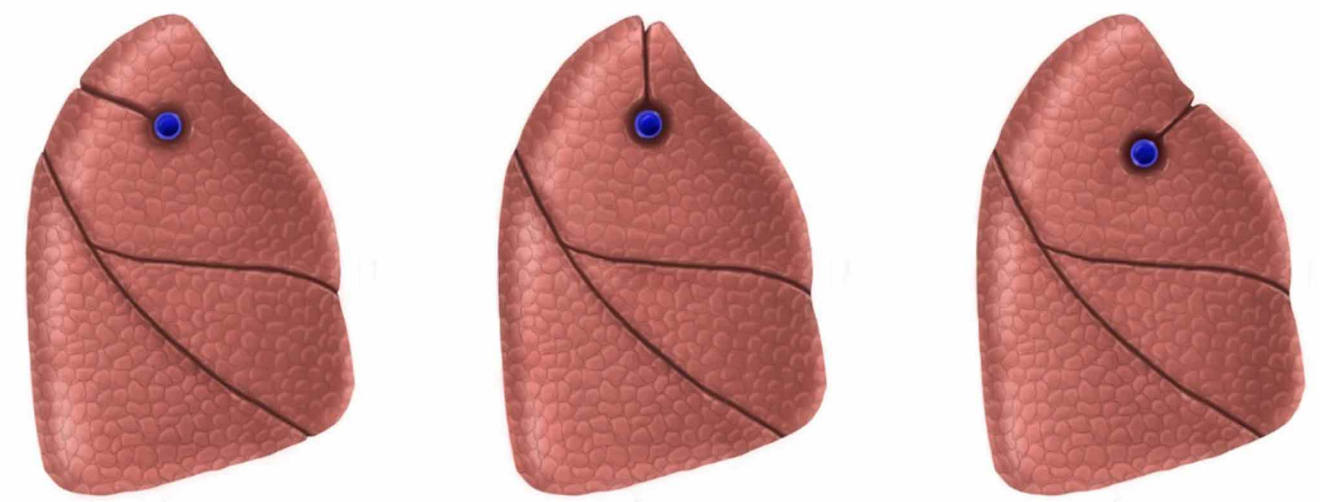

Fig. 3. Representation of azygos fissure types.

Moreover, 3 articles (Eradi & Cusick; Maldjian & Phatak; Sadikot *et al*.) mentioned that the pulmonary azygos lobe can receive apical and/or posterior segmentary branches of the bronchovascular tree and questioned the validity of the term "lobe" when referring to the azygos lobe anatomical variation.

DISCUSSION

Surgical complications. The surgical complications can be avoided if the surgeon has previous knowledge regarding the azygos lobe anatomical variation. This is enough to conduct the surgery in the best possible way and avoid delicate situations (Reisfeld). During thoracoscopic sympathectomies, performed in cases of hyperhidrosis, the azygos vein and the mesoazygos web hindered or prevented the visualization of the sympathetic chain in the superior part of the thorax. In most of these cases, the web has to be perforated, creating a window that allowed access to the previously obscured sympathetic ganglia, as well as a better mobilization of the vein and web if needed (Sieunarine *et al*.; Gill *et al*.; Reisfeld; Baumgartner). Sympathectomies were also performed outside the margins of the web or after its dissection from the costal head, without perforation (Baumgartner). There were no reports of complications in none of the cases related to this procedure.

After the resection of a superior sulcus adenocarcinoma on an azygos lobe, using a transcervical-transmanubrial approach, the patient developed a post-operatory infection on the incision site caused by Staphylococcus capitis (Delalieux *et al*.). During another adenocarcinoma resection, a robot-assisted lobectomy of the azygos lobe and mediastinal lymph node dissection, the azygos vein was not fixated to the mediastinum, and was well mobilized with no difficulty, as was the azygos lobe, and the venous drainage that branched from the azygos vein was identified and divided (Fukuhara *et al*.). In a distal esophageal carcinoma case, the right lung was deflated to allow the esophageal dissection. Although the azygos vein was not directly manipulated during this procedure, the patient's post-operatory thoracic radiography showed that the vein had dislocated to its usual paramediastinal position and escaped the azygos fissure (Maldjian & Phatak).

The presence of an azygos lobe modifies the mediastinal anatomy, possibly removing all membranous support of the membranous part of the trachea, leaving it unprotected, and dislocating the trachea and the esophagus to the left (Grismer & Read). During a thoracotomy performed on a patient with cancer on the superior right lobe of the lung, a tracheal rupture occurred during surgery after inflating a tracheal balloon of 10mL. Both tracheobronchial lacerations and the presence of an azygos lobe are atypical findings, it is not possible to affirm that they are related. However, the fact that the patient did not present either common risk factors for tracheal rupture indicated that there might be a greater risk of this event in the presence of an azygos lobe (Grismer & Read).

For the correction of a case of esophageal atresia with distal tracheoesophageal fistula, a right lateral thoracotomy with extra-pleural approach was performed. After the parietal pleura was reflected medially, the appearance of the azygos vein emerging from the intercostal extra-pleural plane made it impossible to reflect the pleura further and access the posterior mediastinum without dividing the vein. In another case of esophageal atresia, the reflection of the pleura was more difficult from the start, as the azygos vein presented an abnormal arched shape, invading the anterior face of the superior lobe of the right lung. In both cases, the division of the azygos vein was necessary in order to finish the procedure (Eradi & Cusick).

While attempting to perform a video-assisted thoracoscopy in a case of right pneumothorax, dense adhesions were found surrounding the azygos fissure, preventing the access to the lung apex. As this access was necessary and the dissection of the adherences was considered a potential hazard due to risk of bleeding from the azygos vein, the procedure was converted to a thoracotomy. The azygos vein was then sectioned and the fissure walls were resected in order to access the lung apex (Sadikot *et al*.).

Clinical difficulties associated with the azygos lobe. The obtained data regarding the clinical aspects associated with the azygos lobe are contradictory. While a considerable amount of studies support the thesis that the presence of this anatomical variation has no clinical relevance (Sadikot *et al*.; Grismer & Read; Asai *et al*.; Eradi & Cusick; Baumgartner; Rai *et al*., 2012; Fukuhara *et al*.) other articles associate this condition with clinically important pathologies (Hill *et al*.; Azoury & Sayad; Arai *et al*.).

Amidst the articles reporting clinical difficulties associated with the azygos lobe, stands out the report of a 10-week-old baby who presented respiratory distress and, during the complementary examination, an azygos lobe was found associated with congenital lobar emphysema. Considering this, clinical studies support the idea that various pathological conditions and associations of congenital anomalies can occur in/or close to an azygos lobe (Hill *et al*.). Furthermore, Azoury & Sayad suggests that the

distortion of the bronchi due to the curvature or bending caused by the azygos fissure may predispose the azygos lobe to air trapping, with subsequent evolution to emphysema, bronchiectasis, or atelectasis.

On the other hand, in addition to the azygos lobe not having any significant clinical relevance for some articles in the search (Sadikot *et al*.; Grismer & Read; Asai *et al*.; Eradi & Cusick; Baumgartner; Rai *et al*., 2012; Fukuhara *et al*.), it is speculated that the mesoazygos web, could limit the size of any subsequent pneumothorax due to its strong adherence (Sadikot *et al*.).

The anatomical certainty obtained by this systematic review is that the early anterior curvature of the azygos vein over the right pulmonary apex, promotes, indeed, important modifications in the superior mediastinum (Speckman *et al*., 1981). Therefore, great caution is needed when examining a thoracic radiography to rule out false diagnoses induced by the azygos lobe (Chabot-Naud *et al*.) and avoid iatrogenic events.

Azygos lobe or pseudolobe?. The term "lobe" is repeatedly questioned by some of the searched articles, putting its validity in doubt when used to name the pulmonary azygos lobe. In the classical literature (Standrig, 2010; Moore *et al*., 2014), a part of the lung is considered a lobe when it receives its own secondary lobar bronchus. Anatomically, each primary bronchus, originated from the division of the trachea, divides into secondary lobar bronchi, two to the left and three to the right, and each of them supplies a pulmonary lobe. Each lobar bronchus divides itself into many tertiary segmentary bronchi, supplying the bronchopulmonary segments. Arteries and veins follow the same logic of division to form the bronchovascular tree.

In all articles that described the anatomical variation, the pulmonary azygos lobe received tertiary segmental branches, contradicting the anatomical foundations. Çimen *et al*. and Fukuhara *et al*. showed that the azygos lobe was supplied by the apical (apical segmental bronchus – BIa; apical segmental artery – AIa; apical segmental vein – VIa) and posterior (posterior segmental bronchus – BIIa; posterior segmental artery – AIIa; posterior segmental vein – VIIa) segmentary branches of the bronchovascular tree of the right superior lobe. While in the articles (Arai *et al*.; Ndiaye *et al*.), it was supplied only by the apical segmentary branches (BIa, AIa, VIa). Following the anatomical reasoning, the azygos lobe is closer to a bronchopulmonary segment than to a pulmonary lobe (Standring; Moore *et al*., 2014). As a limitation of the study, the small number of articles regarding the subject, which made further analysis difficult, stands out.

CONCLUSION

Among the surgical implications in the presence of the azygos lobe, complications are of low complexity. According to the information obtained, the surgeon's prior knowledge about the anatomical variation is enough to overcome surgical complications and adopt another approach. However, reports of life risk regarding clinical implications were found during this review.

Regarding clinical implications, some difficulties that put the patient's life at risk were encountered, although much was affirmed about the clinical irrelevance of the azygos lobe, demonstrating inconsistency in the scientific literature. Given this fact, a broad clinical study should be sought to clarify these doubts. Therefore, it is necessary to teach about this anatomical variation in medical schools in cadavers. Emphasizing the obvious morphological modifications in the superior mediastinum.

BUSTAMANTE, L. O.; GUALBERTO, V. H. A.; SOUZA, C. F. S.; DOS SANTOS, A. S.; TORRES, D. F. M. & SILVA, J. G. Implicaciones clínicas y quirúrgicas del lóbulo ácigos pulmonar: Una revisión sistemática. *Int. J. Morphol., 40(2)*:442-448, 2022.

RESUMEN: El lóbulo ácigos es una de las variaciones pulmonares más comunes. Aunque numerosos estudios discuten las implicaciones clínicas y quirúrgicas de las variaciones anatómicas, existen pocas investigaciones sobre este tema. El objetivo de este estudio fue discutir la anatomía del lóbulo ácigos pulmonar y sus posibles correlaciones clínicas y quirúrgicas. En esta revisión sistemática se encontraron un total de 48 resultados entre los años 1968 y 2020. Después de la aplicación de los criterios de elegibilidad, 16 artículos fueron incluidos para análisis. Nuestros resultados mostraron que no hubo informes de complicaciones quirúrgicas en presencia del lóbulo ácigos. En todos los artículos que describieron la variación anatómica, el lóbulo ácigos pulmonar recibió ramas segmentarias terciarias. Dentro de las implicaciones quirúrgicas en presencia del lóbulo ácigos, las complicaciones son de baja complejidad. En las escuelas de medicina es necesaria la enseñanza en cadáveres de esta variación anatómica, destacando las evidentes modificaciones morfológicas en el mediastino superior.

PALABRAS CLAVE: Variación anatómica; Implicaciones clínicas; Resultados quirúrgicos.

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