

## Research Article

# Pulmonary Artery Intimal Sarcoma: A Review of the Literature

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## Introduction

Pulmonary artery intimal sarcoma (PAIS) is a rare and aggressive tumor that is an unlikely cause of chronic pulmonary arterial obstruction [1] and is thus often misdiagnosed as thromboembolic disease. It has gone by several names, including intimal sarcoma, primary pulmonary artery sarcoma, and pulmonary sarcoma. Due to the paucity of data on the symptomology, diagnosis and prognosis of PAIS, this paper aims to help facilitate clinical recognition of PAIS through a comprehensive literature review and data analysis of the key clinical features of this tumor type.

Sarcomas of the pulmonary artery and cardiac vessels have been mistakenly classified as intimal sarcoma. In this paper, we focus on high grade spindle cell pulmonary artery sarcomas, including malignant fibrous histiocytoma (MFH), which is also known as undifferentiated pleiomorphic sarcoma (UPS) (Figure 1). Due to the similar clinical presentation of PAIS to chronic thromboembolic pulmonary hypertension (CTEPH), in combination with the paucity of this tumor, diagnosis is difficult and the prognosis is poor. Given the similarity to CTEPH, echocardiography studies are the first to be employed in patients with PAIS and often reveal pulmonary masses similar to thromboembolic disease. For patients who are stable enough to undergo further testing and evaluation, computed tomography or FDG-positron emission tomography scan is commonly implemented and are the imaging modalities of choice in diagnosing PAIS.

PAIS is a highly malignant tumor that most often affects the pulmonary trunk and thus commonly presents with pulmonary hypertension-like symptoms including dyspnea and chest pain. Many patients also exhibit hemoptysis due to a pulmonary embolus-like blockage, exertional syncopal episodes as well as symptoms mimicking myocardial infarction including chest pain with radiation to the shoulder and left arm and acute shortness of breath [2]. Less

common symptoms at presentation include back and lower leg weakness [3,4] lower extremity edema [5-7], syncope [7-11], chronic diarrhea [12], and pyrexia [13-15].

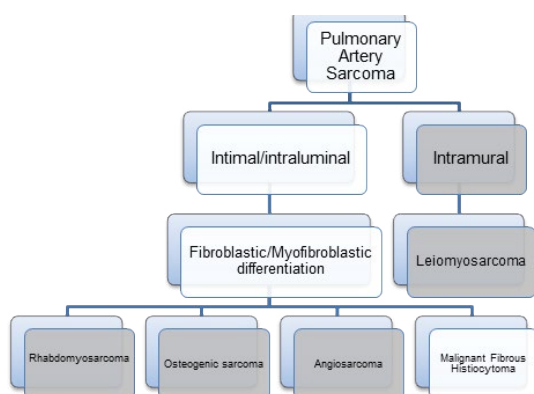
Due to its invasive nature, PAIS is often diagnosed at autopsy [16]. However, due to the initial presentation of cardiovascular-like disease, echocardiography is often used in preliminary workup. Several case reports specify finding right ventricle enlargement with hypokinesis and a severely enlarged right atrium, indicating findings similar to McConnell's sign seen in acute pulmonary embolus (PE) [7,17-20].

Further workup with computed tomography or FDG-positron emission tomography scan often reveals filling defects in the pulmonary arteries and elevated systolic pulmonary arterial pressure [7], as well as a mass most commonly involving the main pulmonary artery. Unfortunately, this disease often presents late in its course and imaging frequently reveals tumors metastases, contributing to the high mortality rate of this tumor type. The most common metastatic sites were noted to be in the lung, while rarer sites included the spleen, adrenals, femoral artery, and brain.

Due to the common misdiagnosis of pulmonary embolus in PAIS, patients are often prescribed anti-coagulants with little or no improvement in symptoms. At present, the most commonly implemented therapy is considered surgical resection of the tumor. Adjuvant chemotherapy with agents such as ifosfamide and doxorubicin [21] is often added to the regimen, with radiation therapy being the least common treatment method for PAIS. Despite these interventions, the aggressive nature of this tumor continues to result in high mortality rates.

## Methods

Clinical data was obtained on tumor site (pulmonary artery, pulmonary vein, aorta, vena cava), tumor extension (endocardium, myocardium, pericardium), patient symptomology, disease recurrence, distant metastasis, and patient survival. The duration of follow-up ranged from 3 to 84 months with a median follow-up of 12 months. Progression-free survival (defined as time to local recurrence or metastasis), distant-metastasis free survival, and disease-specific survival curves and estimates were calculated using the Kaplan-Meier



**Figure 1:** PAS is subdivided into intimal and intramural sarcomas. Intimal sarcomas are further classified as fibroblastic/myofibroblastic differentiation, with several different subtypes. The four most common are listed here. In this paper, we focus on Malignant Fibrous Histiocytomas, also referred to as high grade spindle cell sarcoma, or undifferentiated pleiomorphic sarcoma (UPS).

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method. Comparison between survival outcomes for different strata was evaluated with the log-rank test. Univariate and multivariate analyses of the prognostic variables were calculated using the Cox

proportional hazards model. Statistical significance was set at  $P \leq 0.05$ . Statistical analyses were performed using SPSS for Windows version 20 (SPSS, Inc, Chicago, IL) software. (Table 1)

Table1

| Literature                  | Sex | Age (yrs) | Primary Tumor Location     | Sites            |                |       |    | Symptomology |            |                |       |                       |             |       | Treatment  |         |           | Outcome |         |                       |          |                    |
|-----------------------------|-----|-----------|----------------------------|------------------|----------------|-------|----|--------------|------------|----------------|-------|-----------------------|-------------|-------|------------|---------|-----------|---------|---------|-----------------------|----------|--------------------|
|                             |     |           |                            | Pulmonary artery | Pulmonary vein | Aorta | VC | Dyspnea      | Chest Pain | Chest pressure | Fever | Nocturnal Diaphoresis | Weight loss | Cough | Hemoptysis | Syncope | Back pain |         | Fatigue | Lower extremity edema | Diarrhea | Surgical Resection |
| 2016. Wang et al            | F   | 37        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2016. Kitajima et. al.      | F   | 42        | Pulmonary Artery           | X                |                |       |    |              |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2016. Kriz et. al.          | F   | 72        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     | X                     |             |       |            |         |           |         | X       | X                     | X        | NED                |
| 2016. Sakata et. al.        | F   | 77        | Pulmonary Artery           | X                | X              |       |    | X            |            |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | -                  |
| 2016. Chen et al            | F   | 36        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2015. Slorda et al          | M   | 59        | Pulmonary Artery           | X                |                |       |    |              |            | X              | X     | X                     | X           | X     |            |         |           |         | X       | X                     | X        | NED                |
| 2015. Li et al              | F   | 53        | Pulmonary Artery           | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | X        | NED                |
| 2015. Mori et al            | M   | 54        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | X        | AWD                |
| 2015. Xu et. al.            | F   | 40        | Pulmonary Artery           | X                |                |       |    |              |            |                |       |                       |             |       |            |         |           | X       | X       | -                     | -        | DOO                |
| 2015. Afzal et. al.         | F   | 52        | Inferior Vena Cava         |                  |                |       | X  | X            |            |                |       |                       |             |       |            |         |           | X       | X       | X                     | -        | NED                |
| 2015. Kaira et. al.         | M   | 58        | Right Pulmonary Artery     | X                |                |       |    | X            | X          |                |       | X                     |             |       |            |         |           | X       | X       | X                     | -        | NED                |
| 2015. Caraway et. al.       | M   | 78        | Right Pulmonary Artery     | X                |                |       |    |              |            |                |       |                       |             |       |            |         |           | X       | X       | X                     | -        | DOO                |
| 2014. Shomaf et al          | F   | 60        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 2014. Coskun et al          | F   | 60        | Pulmonary Valve            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2014. Ahmed et al           | M   | 77        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           | X       | X       | X                     | -        | NED                |
| 2014. Urmezawa et. al.      | F   | 84        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 2014. Inoue et. al.         | F   | 30        | Pulmonary Artery           | X                |                |       |    |              |            |                |       |                       |             |       |            |         |           |         | X       | -                     | X        | AWD                |
| 2014. Evison et. al.        | F   | 61        | Pulmonary Artery           | X                |                |       |    | X            |            |                | X     | X                     |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2014. Tanaka et. al.        | M   | 61        | Metastatic                 | X                |                |       |    |              |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 2014. Min et. al.           | M   | 18        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     | X                     |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2013. Shinyogi et al        | M   | 63        | Pulmonary Artery           | X                |                |       |    |              |            |                |       | X                     |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 2013. Fukai et al           | F   | 57        | Right Pulmonary Artery     | X                |                |       |    | X            | X          |                | X     |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2013. Choi et. al.          | F   | 62        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | X        | NED                |
| 2013. Chen et al.           | F   | 54        | Pulmonary Artery           | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | AWD                |
| 2013. Hu et. al.            | F   | 43        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 2013. Lee et. al.           | M   | 58        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2012. Bohn et. al.          | F   | 36        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     | X                     |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 2012. Yamamoto et. al.      | F   | 39        | Pulmonary Artery           | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | X        | DOO                |
| 2012. Vasuri et. al.        | F   | 44        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2012. Hoicznyk et. al.      | F   | 76        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | X        | NED                |
| 2011. Chaachoul et al       | F   | 72        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2011. Xu et. al.            | F   | 55        | Superior Vena Cava         | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | AWD                |
| 2011. Zunick et. al.        | M   | 33        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2011. Fukuda et. al.        | M   | 61        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2011. Ote et. al.           | M   | 58        | Right Pulmonary Artery     | X                |                |       |    | X            | X          |                |       | X                     |             |       |            |         |           |         | -       | X                     | X        | AWD                |
| 2011. Shah et. al.          | M   | 65        | Pulmonary Artery           | X                | X              |       |    | X            |            |                | X     | X                     | X           |       |            |         |           |         | X       | X                     | X        | AWD                |
| 2011. Ebaugh et. al.        | M   | 87        | Superficial Femoral Artery |                  |                |       |    |              |            |                |       |                       |             |       |            |         |           |         | X       | -                     | X        | DOO                |
| 2011. Ramjee et al          | M   | 74        | Pulmonary Artery           | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2010. Halank et. al.        | M   | 64        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       | X                     |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2010. Scheidl et. al.       | M   | 40        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2009. Sheetha et al         | M   | 61        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 2009. Timmers et. al.       | M   | 82        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2009. Koch et. al.          | F   | 58        | Pulmonary Artery           | X                | X              |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | -                  |
| 2009. Schuler et. al.       | M   | 64        | Pulmonary Artery           | X                | X              |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | -                  |
| 2009. Hou et. al.           | F   | 38        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2009. Hou et. al.           | F   | 72        | Left Pulmonary Artery      | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | -                  |
| 2009. Dornas et. al.        | M   | 45        | Pulmonary Trunk            | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | -        | -                  |
| 2009. Hirose et. al.        | F   | 45        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | X        | DOO                |
| 2008. Terra et al           | F   | 77        | Right Pulmonary Artery     | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2008. Huwer et al           | M   | 63        | Pulmonary Trunk            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2008. Fernandez-Goffin      | F   | 43        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | -        | AWD                |
|                             | F   | 41        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
|                             | F   | 52        | Pulmonary Trunk            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
|                             | M   | 56        | Pulmonary Trunk            | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | -       | X                     | -        | AWD                |
| 2008. Jin et al.            | M   | 73        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 2008. Viana-Tejedor et. al. | F   | 48        | Pulmonary Artery           | X                | X              |       |    |              |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2008. Soltys et. al.        | M   | 75        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | X        | DOO                |
| 2008. Rashid et. al.        | F   | 38        | Pulmonary Trunk            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | AWD                |
| 2008. Long et. al.          | F   | 54        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | X        | DOO                |
| 2008. Scheffel et. al.      | F   | 38        | Pulmonary Trunk            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2008. Chappell et. al.      | M   | 02        | Pulmonary Trunk            | X                | X              |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2008. Austin et. al.        | M   | 44        | Pulmonary Artery           | X                |                |       |    | X            | X          |                | X     |                       |             |       |            |         |           |         | X       | X                     | X        | DOO                |
|                             | M   | 53        | Pulmonary Trunk            | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 2007. Ishiguro et al        | F   | 53        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2007. Chong et al           | M   | 29        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2007. Hsing et. al.         | M   | 51        | Pulmonary Trunk            | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2007. Coli et. al.          | F   | 36        | Pulmonary Artery           | X                |                |       |    | X            |            |                | X     | X                     |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2007. Nakajima et. al.      | F   | 44        | Left Pulmonary Artery      | X                |                |       |    | X            |            |                | X     |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2007. Ozbek et. al.         | M   | 42        | Pulmonary Artery           | X                | X              |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2006. Levy et al            | F   | 65        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2006. Dimitrakakis et al    | F   | 62        | Right Pulmonary Artery     | X                |                |       |    | X            | X          |                |       | X                     |             |       |            |         |           |         | X       | X                     | X        | NED                |
| 2006. Alsoufi et. al.       | M   | 76        | Pulmonary Trunk            | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | NED                |
| 2006. Strobel et. al.       | M   | 40        | Left Pulmonary Artery      | X                |                |       |    | X            |            |                | X     | X                     | X           | X     |            |         |           |         | X       | -                     | -        | -                  |
| 2005. Kunimura et. al.      | M   | 44        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | X        | DOO                |
| 2005. Kerr et. al.          | F   | 40        | Pulmonary Artery           | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | AWD                |
| 2005. Miura et. al.         | F   | 68        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | X        | DOO                |
| 2005. Uchida et. al.        | F   | 63        | Pulmonary Trunk            | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 2004. Choi et. al.          | F   | 64        | Right Pulmonary Artery     | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | -                  |
| 2002. Dennie et. al.        | F   | 34        | Pulmonary Artery           | X                |                |       |    | X            |            |                | X     | X                     | X           |       |            |         |           |         | X       | -                     | -        | DOO                |
| 2000. Kaplinski et al       | M   | 42        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
|                             | F   | 33        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | -                     | -        | DOO                |
| 1999. Weijmer et al.        | F   | 89        | Left Pulmonary Artery      | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 1993. Gosalbez et al        | M   | 35        | Pulmonary Artery           | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | DOO                |
| 1992. Head et al            | F   | 48        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | X       | X                     | -        | NED                |
| 1991. Waller et al          | M   | 75        | Pulmonary trunk            | X                |                |       |    | X            | X          |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 1990. Pandit et al          | F   | 25        | Pulmonary Artery           | X                |                |       |    | X            |            |                |       |                       |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 1990. Fitzmaurice et al     | M   | 67        | Aorta                      | X                |                |       |    | X            | X          |                | X     | X                     |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 1976. Murthy et al          | F   | 49        | Pulmonary Trunk            | X                |                |       |    | X            | X          |                | X     | X                     |             |       |            |         |           |         | -       | -                     | -        | DOO                |
| 1973. Altman et al          | F   | 64        | Pulmonary Artery           | X                |                |       |    |              |            |                | X     | X                     |             |       |            |         |           |         | X       | -                     | -        | DOO                |

AWD: alive with disease, DOO: dead of disease, NED: no evidence of disease

## Results

Kaplan-Meier survival plots did not indicate statistically significant correlations between mean survival and tumor location; however, metastasis and tumor recurrence showed statistical significance in correlation with mean survival time ( $P=0.21$ ,  $P=0.31$  respectively; figure 2). Chi-squared values indicated tumor location in the pulmonary valve and aorta were significant factors in mean survival time ( $P=0.004$ ,  $P=0.23$  respectively, figure 2), as well as metastasis and tumor recurrence ( $P=0.003$ ,  $P=0.001$  respectively). (Figures 2-4)

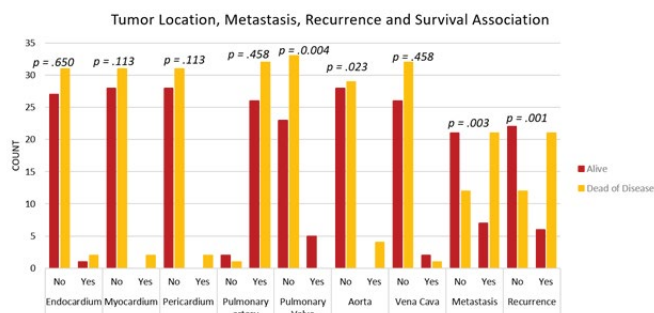


Figure 2

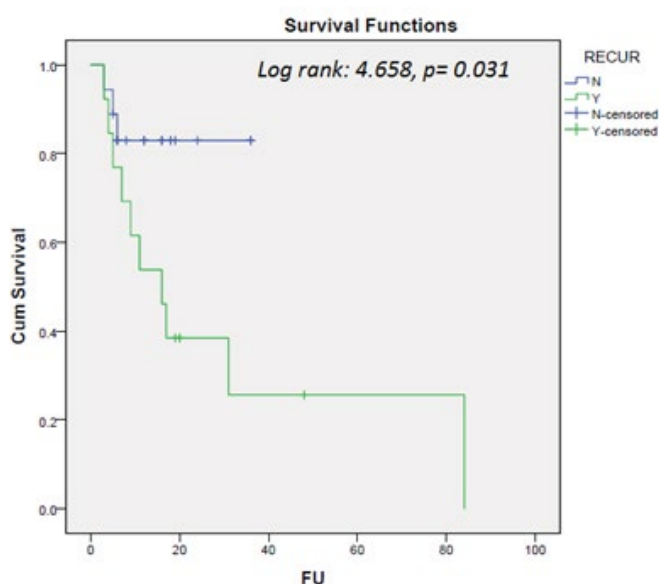


Figure 3: Kaplan-Meier survival curve in patients with/without tumor recurrence. FU = follow up (months).

## Discussion

Pulmonary artery intimal sarcoma, also commonly referred to as pulmonary artery sarcoma and intimal sarcoma, was first described by Mandelstamm in 1923 [22]. It is a highly malignant tumor type that is often diagnosed at autopsy and most commonly arises in the main pulmonary arteries or pulmonary valve. Patients typically present with symptoms of PE or CTEPH, most frequently dyspnea with additional chest pain, cough and hemoptysis [7]. Although the mean age of presentation for this tumor type is 52 years old [7], there has been one pediatric case reported of a 2-month old infant with poor feeding, tachypnea, and a heart murmur [22]. Statistical analysis of over sixty case reports indicated that patients with metastasis, tumor recurrence, or chest pain on initial presentation show a statistically significant correlation with survival time.

The principal method of diagnosis is through imaging, including

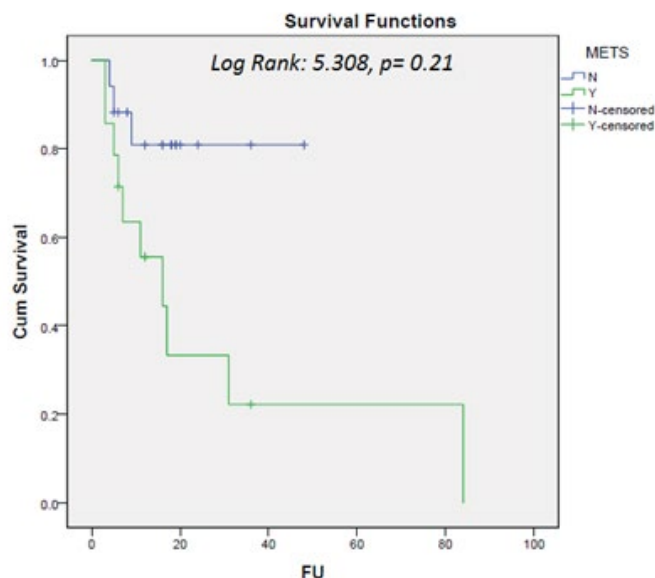


Figure 4: Kaplan-Meier survival curve in patients with/without metastatic PAIS. FU = follow up (months).

chest CT and echocardiography. Chest CT findings often indicate filling defects of the main PA, left PA, and right PA with or without a visible mass. Echocardiographic findings are similar to those of pulmonary embolus with RA/RV dilation and blockage of the right ventricular outflow tract [7,17-20,23]. PA pressures up to 157 mmHg have also been reported on echocardiography indicating pulmonary hypertension in these patients [5,7-9,19,23-28]. PET scans have been valuable for identifying metastases as well differentiating PE from PAIS as PAIS is more metabolically active and shows increased FDG activity than thrombi. Metastases have been reported largely to be in the lungs but have also been present in the adrenal glands [12,13,29,30], liver [29,31,32], brain, intestines [13,33], and an isolated case of metastasis to the chin [34]. Although employed less commonly due to misdiagnosis of PE, cardiac MRI has been implemented in some cases for confirmation of diagnosis [1,3,6,10,11,19,22,28,35-38]. T1 weighted images characteristically show a low-density mass, while T2 weighted images present a high-density mass, as representative of most tumor types [7], which is beneficial for distinguishing between thrombi and PAIS. In one particular case, cardiac MRI confirmed tumor recurrence 24 months after initial diagnosis and surgical resection [11], however, the patient expired 1-month post-recurrence.

As mentioned previously, PAIS is a highly malignant and invasive tumor, with nonspecific radiological characteristics making it difficult to diagnose [7]. Furthermore, diagnosis is made once patients are symptomatic which often indicates poor prognosis and high risk of mortality [7]. Due to the nonspecific manifestations of this tumor type with striking similarities to PE, anti-coagulant therapy is often implemented when patients first present with symptoms refractory to therapy, leading to further work up and diagnosis of PAS [7]. Therapeutic strategies consist of radiotherapy, chemotherapy, surgical intervention, or combination of these three (Table 1). The most commonly implemented therapeutic strategy is surgical resection of the tumor (Table 1), followed by chemotherapy. Chemotherapeutic agents most frequently employed include doxorubicin, dacarbazine, ifosfamide, and interferon (Table 1). One patient, a 52-year-old female with an undifferentiated intimal sarcoma of the IVC, was treated with surgical resection of the tumor and chemotherapy; she developed encephalopathy on dual doxorubicin/dacarbazine therapy, which was then changed to dual gemcitabine/docetaxel therapy with complete remission of the tumor and no evidence of disease at 19 months follow up. Radiation therapy is the least implemented and is often



combined with adjuvant chemotherapy and/or surgical intervention [5,16,20,27,30,35,38-43]. In one particular case, radiation therapy was implemented with local tumor recurrence, although treatment was unsuccessful and the patient expired 11 months after initial diagnosis [29]. Thus, surgical resection and chemotherapy remain the most common therapeutic strategies in treating PAIS, with radiation therapy being the least common. Extensive surgical resection of the tumor has been proposed to prolong survival [44].

The pathological origin of PAIS is assumed to be of mesenchymal origin from the pluripotent intimal cells of large vessels, including the aorta and pulmonary arteries [7]. Although exceedingly rare, pulmonary artery intimal sarcoma is twice as common as intimal sarcomas arising from the aorta and can manifest in other large blood vessels such as the IVC [44]. Conversely, pulmonary artery leiomyosarcomas arise from the vascular media and are so named mural sarcomas (Figure 1). Amplification of MDM2 are rare in cases of intimal sarcoma (<3% of cases). No unifying histopathologic or clinical correlations emerged from this or other studies of intimal sarcomas with MDM2 amplifications. MDM2 amplifications in intimal sarcoma are associated with increased protein expression by immunohistochemistry. The functional correlate of protein expression is unknown. Future studies are necessary to determine the possible functional, diagnostic or therapeutic significance of MDM2 amplification in intimal sarcoma.

Thus, while PAIS is a rather rare tumor type with an insidious onset and is often misdiagnosed as PE, clinicians treating patients for suspected PE that is refractory to anti-coagulant or thrombolysis therapy should have a high level of clinical suspicion for PAIS. Echocardiography followed by PET scans are the most useful tools for diagnosis, along with Cardiac MRI. Surgical resection and chemotherapy to prevent metastasis or recurrence of the tumor are the most commonly employed tactics to treat PAIS. Factors that correlate with reduced survival time are chest pressure, metastasis and recurrence of the tumor and thus aggressive treatment should be employed.

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