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Article

Efficacy of Surgical and Non-Surgical Treatments for Primary Cardiac Angiosarcoma

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Abstract

Background: This study aimed to investigate the optimal treatment strategy for primary cardiac angiosarcoma (PCAS) by evaluating the complications and survival outcomes associated with surgical and non-surgical treatment approaches. **Methods**: A retrospective cohort study was conducted to compare the clinical and pathological data of six patients who underwent surgical treatment (surgical treatment group) with those of five patients who received non-surgical treatment (non-surgical treatment group). These patients were hospitalized at the Department of Oncology, Chongqing University Cancer Hospital, and the Department of Cardiothoracic Surgery, Chongqing Kanghuazhonglian Cardiovascular Disease Hospital, between June 2014 and January 2024. The prognostic outcomes of both groups were analyzed. **Results**: Among the eleven patients diagnosed with PCAS (five males and six females, with a median age of 42 years), those who underwent surgical intervention exhibited greater improvement in cardiac function and quality of life scores at discharge compared to those who did not undergo surgery. Within 30 days of treatment, two patients died: One in the surgical group due to postoperative bleeding and another due to postoperative low cardiac output syndrome. Another patient from the non-surgical group also died as a result of tumor progression. The median follow-up period was 15 months (range, 2–44 months). The median overall survival (OS) in the surgical cohort was 344 days (range: 32–672), which was significantly shorter than the 458 days (range: 62–1341) observed in the non-surgical group ($p < 0.05$). Moreover, the median disease-free survival in the surgical group was 306 days (range, 273–672 days), whereas it was 396 days (range, 91–1341 days) in the non-surgical group ($p < 0.05$). **Conclusion**: For patients with advanced PCAS, non-surgical comprehensive treatment appears to be a more advantageous therapeutic option.

Keywords

heart; angiosarcoma; malignant tumor; surgical treatment; non-surgical treatment; efficacy

Introduction

Primary cardiac tumors are rare, with an incidence of 0.0017–0.0033%. Primary cardiac angiosarcoma (PCAS) is the most common type of malignant tumor [1]. However, the diagnosis and treatment of PCAS are challenging because of its rapid progression, advanced stage at diagnosis, and lack of specific clinical symptoms; treatment options include drug therapy, radiotherapy, and surgery [2]. Meanwhile, the number of people seeking medical consultation for PCAS is gradually increasing due to the development of perceptions of seeking medical treatment. Surgical intervention can relieve cardiac pressure and reduce venous distention, thereby enhancing cardiac function, alleviating discomfort, and improving quality of life. Notably, complete surgical resection is often unfeasible due to frequent late-stage diagnoses, resulting in high recurrence rates and only temporary symptom relief [3]. Additionally, the relief of intracardiac obstruction achieved through surgery is generally temporary [4].

Owing to potential surgical complications, including severe bleeding, low cardiac output syndrome, incomplete resection, metastasis, reduced cardiopulmonary function, and a significant deterioration in quality of life, treatment strategies for PCAS patients in clinical practice require optimization.

Therefore, this study aimed to retrospectively analyze previous cases of PCAS, documenting and evaluating the treatment approaches and clinical outcomes of surgical and non-surgical interventions. These findings provide valuable information for more optimized and effective treatment strategies for PCAS.

Table 1. Baseline clinicopathological characteristics of patients.

NO.	Gender	Age	Metastatic state	Grade	Tumor size	Date of diagnosis	Date of final follow-up
S-01	Female	43	Nonmetastatic	IV	7.1 × 5.6	2014.06	2015.05
S-02	Female	42	Nonmetastatic	IV	7.0 × 6.0	2014.10	2014.10
S-03	Female	42	Nonmetastatic	IV	4.5 × 5.5	2015.01	2016.05
S-04	Female	41	Nonmetastatic	IV	5.3 × 6.1	2021.03	2021.03
S-05	Female	41	Metastatic	IV	4.7 × 5.8	2022.04	2023.03
S-06	Male	43	Nonmetastatic	IV	4.0 × 5.2	2023.03	2025.01
N-01	Male	50	Involving the mediastinum	IV	5.4 × 6.0	2020.07	2021.09
N-02	Male	25	Nonmetastatic	IV	4.8 × 2.5	2021.05	2025.01
N-03	Male	36	Metastatic	IV	8.3 × 8.3	2022.04	2023.02
N-04	Female	43	Metastatic	IV	7.9 × 6.5	2022.12	2024.08
N-05	Male	39	Nonmetastatic	IV	4.3 × 2.7	2023.10	2025.01

Note: In the NO. column, S- represents surgical treatment, and N- represents non-surgical treatment.

Patients and Methods

Patients

This study used a retrospective cohort design. The inclusion criteria were as follows: (1) patients with malignant PCAS hospitalized at the Department of Oncology, Chongqing University Cancer Hospital, or at the Department of Cardiothoracic Surgery, Chongqing Kanghuazhonglian Cardiovascular Disease Hospital; (2) histopathological confirmation of PCAS; (3) patients who are currently alive and have a follow-up period of at least one year.

Based on these criteria, we retrospectively collected clinical data from 11 patients diagnosed with PCAS and hospitalized between June 2014 and January 2024. The cohort comprised five males and six females, with a median age of 42 years (range, 25–50 years). All patients received multidisciplinary consultations, with treatment decisions—whether surgical or non-surgical—made based on patient preferences, expected survival prognosis, surgical safety assessments, and the feasibility of surgery as determined by imaging results. Among the eleven patients, six underwent surgery or exploratory surgery (surgical treatment group), whereas five received non-surgical treatment (non-surgical treatment group). The baseline data for the two groups were comparable (all $p > 0.05$; Table 1). This study adhered to the ethical standards of the Declaration of Helsinki. Written informed consent was obtained from all patients or their family members. Although some non-surgical patients had more advanced diseases (e.g., mediastinal involvement), these patients experienced improved progression control, possibly due to the systemic nature of therapy.

Treatment

Surgical treatment group: Six patients underwent cardiac tumor resection and atrial repair. The surgical group included patients who underwent tumor resection only (n = 4) and those who received surgery followed by chemotherapy (n = 2).

Non-surgical treatment group: four patients received a combination of puncture biopsy of metastatic lesions, chemotherapy, and targeted drug therapy.

In the surgical treatment group, two patients died early in the perioperative period and were not administered additional treatment. Owing to tumor recurrence, the remaining patients transitioned to non-surgical treatment, which included chemotherapy, targeted therapy with antiangiogenic agents, and symptomatic supportive care. The specific drug regimens used included the following:

Paclitaxel + Gemcitabine + Anlotinib;

Docetaxel + Gemcitabine + Bevacizumab;

Ifosfamide + Etoposide;

Vincristine + Doxorubicin + Cyclophosphamide.

Observation Indicators and Follow-up

The pre-treatment and post-treatment conditions were compared between the two groups. The following factors were assessed: tumor size before treatment, 30-day mortality rate after diagnosis, tumor progression time, changes in cardiopulmonary function. Regarding the scoring method of the cardiopulmonary exercise testing (CPET), we selected several indicators including peak VO_2, VE/VCO_2 slope, anaerobic threshold (AT), blood pressure (BP), heart rate (HR) and electrocardiogram (ECG) changes to score the cardiopulmonary function of patients. After combining the scores of various indicators, the evaluation results are presented using a 4-point scale: 4: malignant arrhythmia; blood pressure drops during exercise ($\geq$10 mmHg); AT $<$11 mL/min.kg; VE/VCO_2 slope $\geq$45; peak VO_2 $\leq$10 mL/min.kg; 3: no malignant arrhythmia; blood pressure maintain stability during exercise; AT $<$11 mL/min.kg; 45 $>$ VE/VCO_2 slope $\geq$ 36; 10 $<$ peak VO_2 $\leq$ 15 mL/min.kg; 2: no malignant arrhythmia; blood pressure maintain stability during exercise; AT $\geq$11 mL/min.kg; 36 $>$ VE/VCO_2

Table 2. Treatment and disease progression after diagnosis.

NO.	Treatment subtype	CPFS before surgery	CPFS post-surgery	KS before surgery	KS post-surgery	Date for disease progression	Date of death	Cause of death
S-01	Surgical only	3	2	60%	50%	2015.03	2015.05	Tumor progression
S-02	Surgical only	3	_	60%	_	Perioperative death	2014.10	Circulatory failure
S-03	Surgical + chemotherapy	3	2	60%	60%	2016.03	2016.05	Tumor progression
S-04	Surgical only	3	_	50%	_	Perioperative death	2021.03	Circulatory failure
S-05	Surgical only	4	3	40%	50%	2023.02	2023.03	Tumor progression
S-06	Surgical + chemotherapy	3	2	60%	80%	No progression	Survival	_
N-01	Untreated	4	4	40%	40%	_	2021.09	Tumor progression
N-02	Chemotherapy only	3	2	60%	80%	No progression	Survival	_
N-03	Chemotherapy only	3	3	60%	70%	2022.07	2023.02	Tumor progression
N-04	Chemotherapy only	3	3	60%	70%	2023.11	2024.08	Tumor progression
N-05	Chemotherapy only	3	3	60%	70%	No progression	Survival	_

Note: (1) In the NO. column, S- represents surgical treatment, and N- represents non-surgical treatment; (2) cardiopulmonary function classification was performed according to the New York Heart Association (NYHA) cardiac function classification. (3) The life ability score was determined via the Karnofsky functional status score standard. CPFS, cardiopulmonary function score (low score means better cardiopulmonary function); KS, Karnofsky score (high score means better cardiopulmonary function).

slope $\geq$ 30; 16 $<$ peak VO_2 $\leq$ 20 mL/min.kg; 1: no malignant arrhythmia; blood pressure raise during exercise ($\geq$10 mmHg); AT $\geq$11 mL/min.kg; VE/VCO_2 slope $<$30; peak VO_2 $>$20 mL/min.kg). Karnofsky performance status scores were employed to assess changes in quality of life (100%: normal, no complaints; no evidence of disease): 90%: Able to carry on normal activity; minor signs or symptoms of disease; 80%: Normal activity with effort; some signs or symptoms of disease; 70%: Cares for self; unable to carry on normal activity or to do active work; 60%: Requires occasional assistance, but can care for most of his personal needs; 50%: Requires considerable assistance and frequent medical care; 40%: Disabled; requires special care and assistance; 30%: Severely disabled; hospital admission is indicated, although death is not imminent; 20%: Very sick; hospital admission necessary; active supportive treatment necessary; 10%: Moribund; fatal processes progressing rapidly; 0%: dead, progression-free survival (PFS), and overall survival (OS).

Disease progression was defined as radiological enlargement of the tumor, appearance of new metastatic sites, or clinical deterioration. Causes of death were classified as tumor progression, perioperative complications, or cardiopulmonary failure.

Patients were followed up through outpatient visits and telephone calls every month until January 31, 2025, to monitor and compare PFS and OS between the two groups.

Statistical Methods

All data were analyzed using SPSS 19.0 software (SPSS Inc., Chicago, IL, USA). Categorical data are expressed as frequencies and percentages, with intergroup comparisons performed using the χ^2 test. Continuous data that followed a normal distribution according to the Shapiro–Wilk test are expressed as the mean $\pm$ standard deviation ($\bar{x} \pm s$), and intergroup comparisons were performed via *t*-tests for independent groups. Kaplan–Meier survival curves were generated, and log-rank analysis was performed to compare survival rates between the two groups. All differences were considered statistically significant at $p < 0.05$.

Due to the small sample size and the retrospective, non-randomized design, this study may be subject to selection bias. As such, all findings should be interpreted with caution. A formal power calculation was not conducted due to the limited number of cases. Therefore, *p*-values are interpreted as exploratory rather than confirmatory.

Results

Treatments and Outcomes

In the surgical treatment group, all six patients underwent tumor reduction surgery, including cardiac tumor resection and atrial repair. Among them, two patients died during the perioperative period. The remaining four patients developed recurrence and metastasis at 11–22 months post-surgery. Despite receiving further treatment, three patients died at 11, 11, and 16 months after diagnosis. Of the two patients who received surgery followed by chemotherapy, one survived long-term. This suggests a potential benefit of combined therapy in selected patients.

Among the five patients in the non-surgical treatment group, one was unable to tolerate antitumor treatment due to severe illness and died from tumor progression within two months of diagnosis. This patient received only symptomatic supportive care, including drainage of pleural effusions. The other four patients, who received chemother-

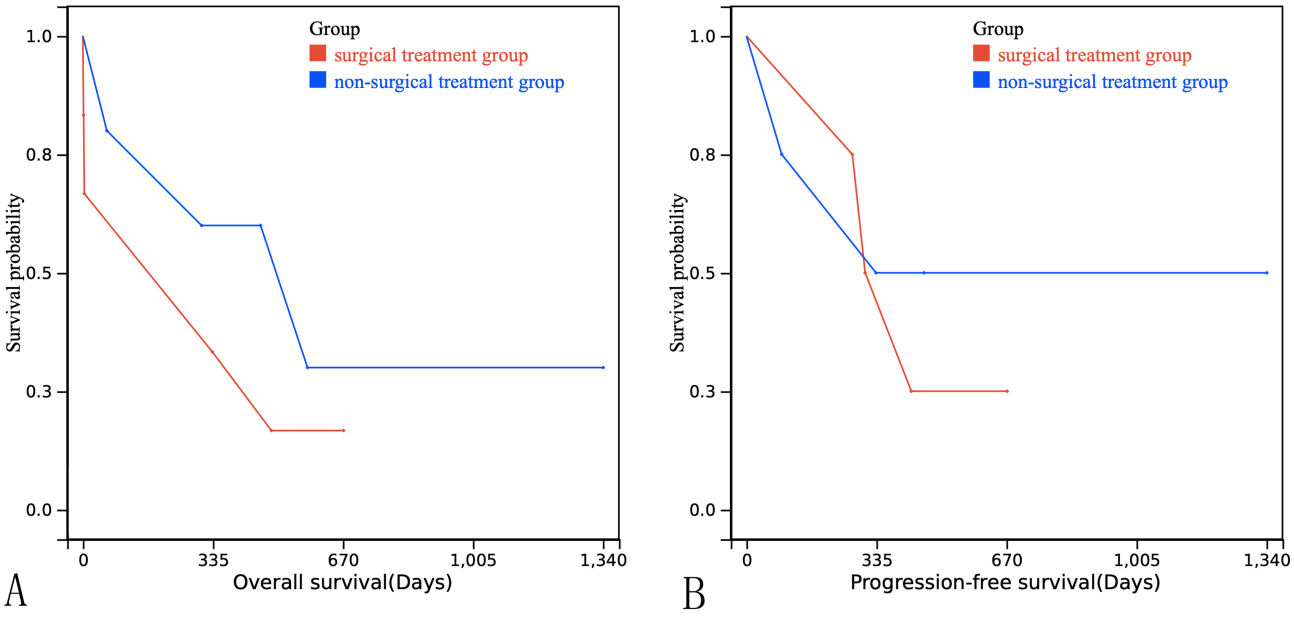

Fig. 1. Outcomes of primary cardiac angiosarcoma (PCAS) patients treated with surgical or non-surgical methods. (A) Overall survival (OS) of patients in the surgical treatment group and the non-surgical treatment group; (B) Progression-free survival (PFS) curves of patients in the two groups.

apy and antiangiogenic drug therapy, experienced significant symptom relief. The other two patients died after 10 and 20 months of diagnosis. The remaining patients had stable physiological functions and achieved long-term survival.

Regarding cardiopulmonary function, patients in the surgical treatment group showed significant improvement after treatment ($p < 0.05$). Conversely, the non-surgical treatment group had significantly improved outcomes in terms of the 30-day mortality rate, tumor progression time, and changes in Karnofsky performance scores before and after treatment (Table 2).

Follow-up

Patients were followed up monthly after diagnosis and treatment, with no patients lost to follow-up. The median follow-up duration for the cohort was 15 months (range, 2–44 months). In the surgical treatment group, the median PFS and OS were 306 days (range, 273–672 days) and 344 days (range, 32–672 days), respectively. In comparison, the non-surgical treatment group had a median PFS of 396 days (range, 91–1341 days) and a median OS of 458 days (range, 62–1341 days). The difference between the groups was significant ($p < 0.05$) (Table 2; Fig. 1).

Discussion

Primary cardiac tumors are rare, with malignant cardiac tumors accounting for about 25% of cases [5]. PCAS is the most common form of primary malignant cardiac tumor, accounting for approximately 37% of all malignant cardiac tumors [1,6,7]. Owing to the rarity of PCAS, no standardized treatment protocol is available. Surgical resection is the primary treatment approach, with adjunctive therapies, such as drug therapy and radiotherapy, often used to prolong survival [8]. Mayer *et al.* [9] reported that palliative resection can significantly alleviate symptoms such as heart failure and pericardial tamponade in patients with tumors that severely affect hemodynamics. However, Coli *et al.* [10] reported that patients with cardiac synovial sarcoma who were administered only regular radiotherapy and chemotherapy exhibited improved survival outcomes. Our findings were similar to those reported in previous studies, suggesting that while surgical treatment can significantly improve cardiopulmonary function, non-surgical treatment offers distinct advantages regarding multifactorial mortality, functional performance assessments (e.g., Karnofsky score), PFS, and OS. All patients who underwent chemotherapy experienced adverse side effects, regardless of whether the patient had also undergone surgery, whereas those who did not require chemotherapy following surgical intervention did not experience these effects.

PCAS is typically found in the right atrium and epicardium, although PCAS can occasionally involve the right ventricle, left atrium, left ventricle, or pericardium [11,12]. PCAS presents with no specific clinical symptoms, with manifestations largely influenced by the location of the tumor, the extent of infiltration, and the effect on cardiac function. In the early stages, hemodynamic disturbances are minimal, leading to subtle clinical symptoms or the ab-

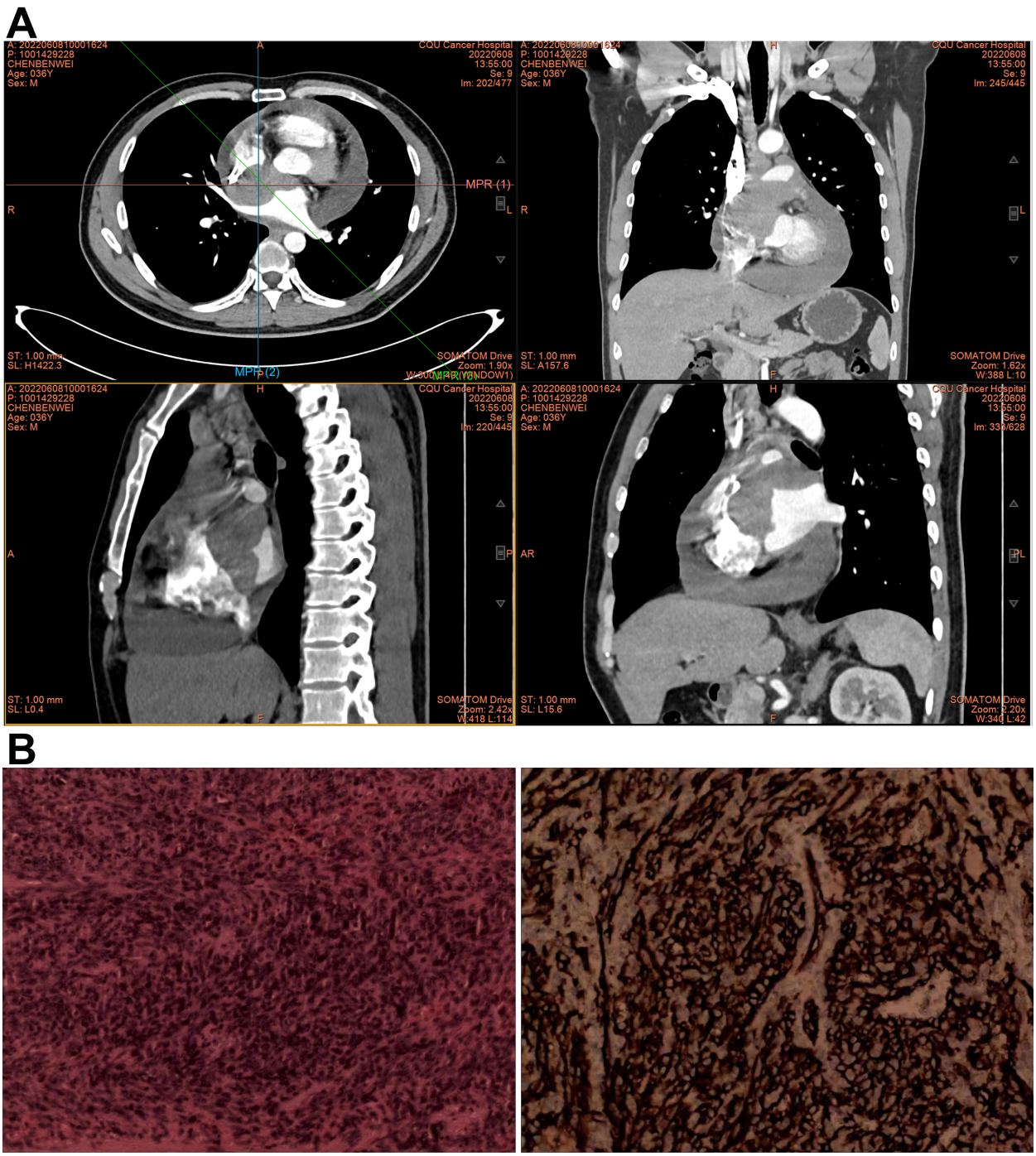

Fig. 2. Imaging and pathological examination of a typical case of PCAS. (A) MR image of a right atrial mass involving the pericardium. (B) The tumor infiltrated the myocardial tissue, and the tumor tissue formed an irregular vascular cavity-like structure that was interconnected. The cavity was lined with highly proliferative tumor endothelial cells. Tumor cells with immature vascular cavities and fibrosarcoma-like solid areas were found locally.

sence of such symptoms (Fig. 2). Consequently, diagnosis often occurs at advanced stages, when treatment options become limited and assessing clinical benefits becomes more challenging [2,13]. During diagnosis, complete tumor resection is frequently unachievable due to local invasion or distant metastasis. Meanwhile, in some cases, partial tumor resection is performed to alleviate hemodynamic complications. However, non-surgical or palliative treatment approaches are generally considered when tumors are large, highly invasive, or involve multiple metastases, or when the condition of the patient does not permit surgical intervention.

We did not conduct randomized controlled trials, as the risks were high for patients in the non-surgical treat-

ment group, who generally had larger tumors and a higher incidence of metastasis at baseline ($p < 0.05$). Multiple metastases are associated with poor prognosis in patients with malignant tumors [14]. Despite this, our study revealed that, except for patients receiving palliative care, disease progression was better controlled in patients who received non-surgical treatment. The tumors did not significantly enlarge, and no new metastatic lesions were detected during the observation period. These patients experienced significantly prolonged PFS compared with those in the surgical treatment group, which may be attributed to surgery-related hematogenous metastasis, the additional burden on cardiopulmonary function, and the systemic effects of surgical trauma. Unexpectedly, the non-surgical group demonstrated longer median survival. This may reflect improved systemic control through chemotherapy or the detrimental impact of surgical complications, including perioperative mortality and cardiopulmonary stress. However, given the small cohort and the non-random allocation of treatment, the results of this study are hypothesis-generating and may not be generalizable.

Open-chest cardiac surgery presents significant risks, necessitating meticulous perioperative management. The physiological demands on patients are considerable, with sudden circulatory failure frequently occurring in the early postoperative period. Additionally, surgery-induced tissue damage and functional decline can be substantial [8,15]. When tumors invade critical structures such as the coronary artery or a large portion of the ventricle, complete resection may not be feasible, increasing the risk of local recurrence, distant metastasis, and poor prognosis [16].

In contrast, non-surgical approaches, including chemotherapy, radiotherapy, immunotherapy, and targeted therapy, impose a lower physiological burden on cardiopulmonary function, making these approaches viable options for a broader patient population [17,18]. The clinical application of these treatment techniques has advanced, with established protocols for managing side effects and improving patient outcomes. Through a comprehensive evaluation of risks and benefits, clinicians can develop individualized non-surgical treatment plans, either as monotherapies or in combination, which are generally easier to manage and provide stable therapeutic effects.

Overall, we suggest that non-surgical treatments aimed at controlling and alleviating the disease may offer better clinical outcomes for many patients. To better support our findings, further studies involving larger cohorts are needed. Although the number of cases in this study was limited, all patients underwent multidisciplinary consultations and received treatment based on a comprehensive assessment of various factors. The findings of this study can provide valuable clinical insights and inform individualized decision-making and treatment planning for patients with PCAS.

Conclusions

The feasibility of surgical intervention should be carefully evaluated for rapidly progressing PCAS, which is often diagnosed at an advanced stage and frequently involves metastasis or important anatomical structures.

Abbreviations

PCAS, primary cardiac angiosarcoma; PFS, progression-free survival; OS, overall survival.

Availability of Data and Materials

All data points generated or analyzed during this study are included in this article.

Author Contributions

JF, YW, and YMW contributed to the design of this work. HWM and ZC contributed to the interpretation of data, drafted the work, and were responsible for data visualization. XDC and XXF analyzed the data, and were responsible for data visualization. HWM, ZC, JF, YW, YMW, XDC and XXF revised critically for important intellectual content. All authors read and approved the final manuscript. 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.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki. This study has been reviewed and approved by the Ethics Committee of Chongqing Kanghuazhonglian Cardiovascular Disease Hospital, with the reference number 000389. Written informed consent was obtained from all patients and their family members.

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Conflict of Interest

The authors declare no conflict of interest.

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