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Original article

## Factors affecting in-hospital mortality and likelihood of undergoing surgical resection in patients with primary cardiac tumors

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### ABSTRACT

**Background:** Previous studies on primary cardiac tumors were mainly based on small case series collected from a limited number of institutions. Contemporary data of patients with primary cardiac tumors treated with or without surgery in a nationwide clinical setting are limited.

**Methods:** Using the Diagnosis Procedure Combination database, we retrospectively identified 1317 patients hospitalized with a primary cardiac tumor (1023 myxomas, 63 non-myxomas, 72 sarcomas, 41 malignant lymphoma, 118 unspecified tumors) at 486 hospitals in Japan from July 2010 to March 2013. The outcome was overall in-hospital mortality, defined as in-hospital death occurring during the initial hospitalization or during rehospitalization. We examined the associations of baseline factors with overall in-hospital mortality and undergoing surgical resection using multivariable logistic regression analyses.

**Results:** Overall, 914 (69.4%) patients underwent surgery and 403 (30.6%) did not. The surgery group was younger (median age, 67 years vs. 71 years,  $p < 0.001$ ) and was more likely to be treated at an academic hospital (38.9% vs. 27.8%,  $p < 0.001$ ) than the no-surgery group. The surgery group also had a higher Barthel index and a higher conscious level and showed a lower frequency of extracardiac malignancies than the no-surgery group. The likelihood of undergoing surgery was associated with coexisting cerebral infarction [adjusted odds ratio (95% confidence interval), 1.96 (1.23–3.12)] and academic hospital [1.58 (1.20–2.09)]. Patients with lower Barthel index and coexisting extracardiac malignancies were less likely to undergo surgery. Overall in-hospital mortality was 2.1% and 13.4% in the surgery and non-surgery groups, respectively. Older age, lower Barthel index, lower consciousness level, coexisting metastatic extracardiac malignancy [2.95 (1.24–7.01)], and sarcoma [21.04 (8.28–53.42)] were associated with higher overall in-hospital mortality, while academic hospital [0.41 (0.20–0.84)] and surgical resection [0.39 (0.20–0.74)] were associated with lower mortality.

**Conclusions:** Several background factors were associated with prognosis and surgery in patients hospitalized with primary cardiac tumors.

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### Introduction

Primary cardiac tumors are rare, with a prevalence ranging from 0.001% to 0.030% in various autopsy series [1–6]. Cardiac tumors can be identified according to their constitutional

symptoms and cardiac complications, including systemic or pulmonary embolism, heart failure caused by circulatory obstruction, and cardiac dysfunction associated with direct tumor invasion [1,2,7–11]. Cardiac tumors can also be found incidentally in imaging studies such as echocardiography, computed tomography, and magnetic resonance imaging [8,12–14].

The Japanese annual national statistics of the Japanese Association for Thoracic Surgery (JATS) have shown that the number of surgically resected cardiac tumors has been increasing [15–19]. Possible reasons for this increase are greater awareness

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among physicians and wider availability of imaging modalities for cardiac tumors than in the past. However, previous studies investigating patient characteristics and outcomes of cardiac tumors have been largely restricted to single-center case series [6,11,20–23] or multicenter studies with limited study populations or small sample sizes [14,24–26]. In addition, patient data in most of the previous studies were collected for study periods of >10 years. Large contemporary multicenter studies of patients with primary cardiac tumors who were treated with or without surgery are lacking.

When a cardiac tumor is highly suspected, surgical resection is the mainstay of treatment for both benign and malignant cardiac tumors [1,2,7–10]. Most benign cardiac tumors are curable with complete resection [2,8,10,13], while malignant cardiac tumors are less likely to be completely resected and recur more frequently than benign tumors even after complete resection [20–24,27]. Although small benign tumors may be managed nonsurgically with echocardiographic follow-up, a recent observational study reported an increased risk of cerebrovascular complications and mortality in patients with suspected papillary fibroelastomas who did not undergo surgical resection [28]. Meanwhile, patients in poor general condition or with significant comorbidities may be nonsurgically treated irrespective of the type of cardiac tumor because of perioperative risk. No previous study has examined factors associated with the likelihood of undergoing surgical resection in patients with primary cardiac tumors. Although the prognosis of benign tumors is generally good, malignant tumors, especially cardiac sarcomas, have a rapidly fatal course even after surgery [20–24,27]. It remains unclear which patient factors are associated with poor in-hospital prognosis in patients with primary cardiac tumors. The objective of the present study was therefore to investigate factors associated with in-hospital mortality and the likelihood of undergoing surgical resection in patients hospitalized with primary cardiac tumors, using data from a large-scale inpatient database.

## Methods

### Study design and data source

This was a nationwide retrospective cohort study using the Diagnosis Procedure Combination (DPC) database, which has been described in detail previously [29,30]. The Institutional Review Board of The University of Tokyo approved the study and waived the requirement for patient informed consent because all data were anonymized. The DPC database included approximately 18.3 million inpatient data from approximately 1000 Japanese hospitals for 33 consecutive months between 1 July 2010 and 31 March 2013, representing approximately 50% of all inpatient admissions in Japan [29,30].

The DPC database includes the following data: patient age and sex; diagnoses, comorbidities, and complications recorded with Japanese text and the International Classification of Diseases, 10th Revision (ICD-10) codes; status of activities of daily living, which can be used for calculation of the Barthel index [31]; consciousness level at admission measured with the Japan Coma Scale [30]; drugs and devices; surgical and nonsurgical procedures; length of hospital stay; discharge status (dead or alive); and unique hospital identifiers.

### Patient selection

From the DPC database, we selected patients with a confirmed diagnosis of a primary cardiac tumor using ICD-10 codes (Supplementary Table 1). Subtypes of benign cardiac tumors (myxoma, rhabdomyoma, fibroma, papillary fibroelastoma,

schwannoma, and lipoma) and malignant cardiac tumors (angiosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma, myxosarcoma, synovial sarcoma, and malignant lymphoma) were identified from the Japanese-text diagnoses in the DPC database. For cardiac myxomas, the tumor location (left atrium, right atrium, left ventricle, or right ventricle) was also identified according to the Japanese-text diagnosis. Non-myxomas included rhabdomyomas, fibromas, papillary fibroelastomas, schwannomas, and lipomas. Sarcoma included angiosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma, myxosarcoma, and synovial sarcoma. A primary cardiac tumor recorded without a specific Japanese-text diagnosis was defined as 'unspecified type of tumor' in the present study. Eligible patients with primary cardiac tumors were classified into patients who underwent surgical treatment for cardiac tumors (surgery group) and those who did not (no-surgery group). In the present study, surgical treatment for cardiac tumors included surgical resection of cardiac tumors with or without coronary artery bypass grafting or valve surgery (valvuloplasty or valve replacement).

### Baseline variables

Baseline variables included the following: patient age and sex; Barthel index at admission; Japan Coma Scale at admission; comorbidities already present at admission (primary extracardiac malignancy, metastatic extracardiac malignancy, cerebral infarction, congestive heart failure, pulmonary embolism, chronic pulmonary disease, chronic renal failure, and chronic liver disease); and type of hospital (academic or non-academic) (ICD-10 codes for comorbidities are shown in Supplementary Table 1).

### Outcome measures

The measured outcome was overall in-hospital mortality, which was defined as in-hospital death occurring during the initial hospitalization or during rehospitalization. For patients who underwent surgery, we also identified postoperative mortality, which was defined as in-hospital death occurring during the hospitalization in which surgical treatment was performed.

### Statistical analysis

Categorical variables are presented as numbers and proportions and were compared using the Chi-square test. Continuous variables are presented as median and interquartile range (IQR) and were compared using the Mann–Whitney *U* test or Kruskal–Wallis test. We examined factors associated with likelihood of undergoing surgical resection of cardiac tumors in a multivariable logistic regression model with adjustment for the following variables: age, sex, Barthel index at admission, Japan Coma Scale at admission, comorbidities at admission, and type of hospital. We also examined factors associated with in-hospital death in a multivariable logistic regression model with adjustment for the following variables: age, sex, Barthel index at admission, Japan Coma Scale at admission, comorbidities at admission, type of hospital, type of cardiac tumor (myxoma, non-myxoma, sarcoma, malignant lymphoma, or unspecified tumor), and performance of surgical resection.

All hypothesis tests had a two-sided significance level of 0.05. SPSS version 22 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

## Results

### Study population

We identified 1317 patients (1753 hospitalizations) with a primary cardiac tumor who were hospitalized at 486 acute-care

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