

# Surgical treatment of cardiac metastatic melanoma



Robert Kwinta<sup>1</sup>, Katarzyna Kopcik<sup>2</sup>

<sup>1</sup>Municipal Hospital, Zabrze, Poland

<sup>2</sup>Regional Specialist Hospital, Częstochowa, Poland

Kardiochirurgia i Torakochirurgia Polska 2024; 21 (3): 172-176

## Abstract

Melanoma is an aggressive neoplasm mainly affecting the skin. It has a predisposition to metastasis and it presents the highest propensity to spread to the heart, mostly through the hematologic route. Cardiac metastases frequently remain asymptomatic, even though the metastatic process to other organs is described as an advanced stage of the melanoma. Treatment methods include conservative and surgical management. Surgeries should be preferably performed at the early stages of the disease, when physicians can achieve total resections with clear margins. In some cases palliative procedures are also implemented. In 26 patients analyzed in this review, eleven cases presented favorable results of the surgery. In majority of the patients the diffuse metastatic disease led to their decease despite the surgery.

**Key words:** melanoma, surgery, metastases.

## Introduction

Melanoma is an aggressive malignant neoplasm of the skin, the incidence of which increases linearly from the age of 25 to 50, and then the incidence decreases [1, 2]. Men are slightly more frequently affected than women, and the median age at which melanoma is detected and diagnosed is approximately 57 years old [1]. Recently, the incidence of melanoma has been increasing, especially in the Caucasian population [2].

Melanoma can spread to almost any organ, and the most common metastases are located in the skin, subcutaneous tissue, lymph nodes, lungs, brain, liver, and bone. This explains the different symptoms that happen depending on where the metastases are located [1, 3]. Among malignant tumors, melanoma has the highest propensity to metastasize to the heart, and this process occurs mainly through the blood route [4–6].

Melanoma metastases mainly affect the pericardium and myocardium, appearing as multifocal lesions, while the endocardium is rarely affected [5]. The metastasis may occur in any cavity of the heart, but typically, it is situated within the right atrium [1, 5, 7]. It appears that the identifi-

cation of cardiac metastases is an adverse prognostic factor associated with an increased mortality [1, 3].

The majority of melanoma metastases to the heart are asymptomatic and can only be diagnosed through post-mortem examination [1, 4, 5]. In contrast, ante-mortem diagnoses are incidental or symptomatic, with an estimated incidence of about < 2% of cases [1, 5].

Symptoms are usually related to the location in the heart, although some can cause systemic symptoms [7, 8]. Other factors influencing the clinical picture include the size of the metastasis, the propensity for embolization, invasiveness and the metastasis' association with other cardiac structures [7].

Cardiac symptoms typically manifest late in the course of the disease, after the cancer has already spread extensively throughout the body [5]. Only 20–30% of patients develop impaired cardiac function [6, 7, 9].

Selected symptoms of melanoma metastasis to the heart are shown in Table I [1, 4, 6–8].

When carrying out the diagnostic process for a suspected tumor present in the heart, it is important to consider the age of the patient at the time of reporting, epidemio-

**Table I.** Symptoms of melanoma metastasis to the heart

Systemic	Cardiac	Embolic
Fever	The effect of a mass on myocardial function or blood flow, leading to arrhythmias, conduction disorders, heart valve regurgitation and pericardial effusion. Other: dyspnea, chest discomfort, syncope or presyncope	Pulmonary or systemic thromboembolic processes
Joint pains		
Weight loss		
Fatigue		
Paraneoplastic syndromes		

**Address for correspondence:** Katarzyna Kopcik, Regional Specialist Hospital, Częstochowa, Poland, e-mail: [kopcik.katarzyna1@gmail.com](mailto:kopcik.katarzyna1@gmail.com)

**Received:** 19.06.2024, **accepted:** 11.08.2024, **online publication:** 29.08.2024.

logical and clinical probability, location of the tumor, laboratory tests, and imaging studies, including characteristics of cardiovascular magnetic resonance (CMR) images [7, 8].

Laboratory studies may reveal anemia, an increased erythrocyte sedimentation rate, and elevated levels of C-reactive protein and  $\gamma$ -globulin. Sometimes thrombocytopenia is also present [7].

Imaging studies used to determine cardiac involvement also include echocardiography and computed tomography (CT) [5, 7]. Contrast-enhanced transthoracic echocardiography (TTE) allows assessment of the perfusion of the mass, which can differentiate a tumor from a thrombus. Malignant tumors are often highly vascularized and show greater contrast enhancement than the adjacent myocardium [7]. If a tumor is located in the left ventricle, TTE should be performed to exclude the presence of a patent foramen ovale [5]. Of the imaging modalities, CMR shows the greatest utility in identifying masses in the heart [5, 7]. CMR makes it possible to determine topographic relationships, spread to surrounding structures, tissue characteristics, and specific patterns of enhancement (i.e., absent, early or delayed) after contrast agent administration [7]. The paramagnetic effect of T1-shortening melanin causes melanoma metastases in the heart to appear hyperintense on T1-weighted magnetic resonance (MR) images [8].

Another method is positron emission tomography computed tomography (PET-CT), which can be used simultaneously with MR imaging of the brain and CT scans of the chest, abdomen and pelvis [5]. Using fluoro-D-glucose (18F-FDG) in PET-CT, the malignancy and stage of the disease can be assessed. Furthermore, this test is used to detect tumor recurrence after surgery [7].

Non-surgical treatments consist of immunotherapy, targeted therapy, and radiation therapy [7]. Immune checkpoint inhibitors include ipilimumab (an antibody against CTLA-4) and nivolumab (an antibody against PD-1). They are used to improve the ability of T cells to fight cancer cells, thereby increasing the 5-year survival of patients treated with them [1, 3]. Targeted therapy targets BRAF and MEK, and the agents used include for example dabrafenib and trametinib [5]. Due to their direct immunomodulatory effects, BRAF and MEK inhibitors have long-term benefits; however, their side effect profile is higher than that of immune checkpoint inhibitors [3]. MR-guided stereotactic body radiotherapy (MRgSBRT) is used to treat metastatic tumors in the heart and pericardium. This method is most frequently performed for intracardiac lesions using real-time kinetic MR with respiratory gating or heart motion. MRgSBRT is currently evaluated as a reliable therapeutic option for patients with metastatic tumors in the heart [9].

The management of melanoma with cardiac metastases should be individualized depending on the patient's and tumor's characteristics [5]. Remission of metastatic melanoma in the heart can be achieved with appropriately selected treatment [1]. Positive prognostic factors include low or normal levels of LDH, a reduced tumor burden, and the presence of BRAF mutations [3]. Targeted therapy and

immunotherapy have been shown to enhance 5-year survival rates for metastatic melanoma, currently exceeding 50% [1].

BRAF and MEK inhibitors, and immunotherapy should be considered as the first-line treatment for multiple and/or infiltrating tumors or further spread of the disease not amenable to complete resection, especially with a confirmed BRAF mutation [5]. Targeted therapy has shown a high response rate with a short median response time in patients with symptomatic single or disseminated non-life-threatening metastases with positive BRAF mutations. This may lead to the regression of symptomatic lesions or the conversion of previously unresectable lesions into surgically resectable lesions [5]. Patients with symptoms and hemodynamic instability should undergo a complete surgical resection with margins of healthy tissue if possible [5].

## Material and methods

To provide this review, a manual search of PubMed database was held in June 2024. We used keywords “cardiac metastatic melanoma”, “melanoma metastases heart” and “cardiac metastases melanoma”. Thirty-nine studies were detected, 22 were excluded and finally we included 17 studies in our paper. The articles were evaluated by their titles, next by abstracts and then by full text. Papers were excluded if the case studies were focused on non-surgical treatment, if case studies and case series were based on autopsies or if no treatment was stated. We included case studies and case series that described surgical treatment of metastatic melanoma to the heart. The main aim of the paper is to summarize the topic of surgical treatment of metastatic melanoma to the heart.

## Cardiac metastatic melanoma and its surgical treatment

A brief summary of the cases describing cardiac metastatic melanoma is presented in Table II [5, 10–25]. The review contained 3 case series and 14 case studies, so 26 patients in general. 16 cases described male patients and 10 cases – female patients. The age of the patients varied from 31 to 80. The most common location of secondary melanomas seems to be the right atrium – fourteen cases described this location. The left atrium was involved in 2 cases. The left ventricle was disseminated in 3 patients, and the right ventricle in 4 cases. There was 1 case narrating the infiltration of both the left atrium and left ventricle, while the left ventricle and right side of the heart was described once, in a patient with patent foramen ovale. In one described patient, surgeons removed multiple masses located in the right atrium and right ventricle with dissemination of outflow tract. In the analyzed papers, patent foramen ovale was present in 2 patients. Bovine pericardial patch was used twice to provide accurate reconstruction of heart chambers. In 11 cases researchers described favorable results, while in 14 cases the patients died, mostly due to diffuse metastatic disease. Majority of cases presented described patients who had a history of malignant

Table II. Cases of surgically treated cardiac metastatic melanoma

Study	Patient data	Treatment	Follow-up	Comments
Bortolotti <i>et al.</i> , 1990	49, M	Pericardiocentesis with 600 ml of hemologic fluid drainage; then sternectomy with drainage of 500 ml of hemologic fluid. Invasion of the aorta, RA and pulmonary artery was observed – surgical treatment was discontinued	The patient died 2 months after the surgery	
Chen <i>et al.</i> , 1996	56, F	RA mass was surgically removed with no septal or valvular involvement; the patient received systemic therapy after surgery	Favorable effects of the surgery	History of resected MM on the right elbow
Mousseaux <i>et al.</i> , 1998	46, M	Surgical drainage of heart tamponade without tumor resection; tumor located in LA and LV	Died despite the chemotherapy	History of MM on the left thigh
	67, M	Successful surgical ablation of LV tumor	Recovered and alive 5 years after the surgery	History of MM on the left thigh
	63, F	Surgical drainage of heart tamponade without tumor resection; tumor located in LA	Died due to diffuse metastatic disease after brief remission	
	50, F	Successful surgical ablation, infiltration of SVC and RA walls	No symptoms after 1 year of treatment	History of MM on the neck
Prabhakar <i>et al.</i> , 1998	65, M	RA mass resection with 30 ml of hemologic fluid drainage; RA reconstruction with autologic pericardium	Resected brain metastases. Uneventful postoperative periods with improved life quality	History of the excised scalp lesion. Presence of patent foramen ovale
Gibbs <i>et al.</i> , 1999	46, F	RA mass not completely resected as the operation was palliative and total resection would lead to RA reconstruction, which was not considered	Symptoms – dyspnea, palpitations – were relieved	
Wood <i>et al.</i> , 2010	7 cases (4 F, 3 M) 31–79 years	Surgical resection or biopsy in all cases, but no further description	All patients died due to diffuse metastatic disease, one lost to follow-up	RA invasion in 4 cases, RV – 2 cases, LV – 1 case
Onan <i>et al.</i> , 2010	31, M	RA tumor surgically removed, pericardium and endocardium were not infiltrated	No recurrence after 1 year	Unknown primary lesion
Lee <i>et al.</i> , 2012	59, F	Pericardial window operation with biopsy of pericardial mass, followed by chemotherapy	The patient survived 14 months after the surgery	RA invasion with pericardium and ascending aorta involvement
Demondion <i>et al.</i> , 2013	80, M	Median sternectomy with incomplete removal of LV mass in multiple pieces, closure of patent foramen ovale; intraoperatively tumor invasion in the right heart was observed. Next step – systemic therapy	Uneventful postoperative period	History of right ocular MM with enucleation
Noel <i>et al.</i> , 2014	64, F	Median sternectomy with incomplete removal of the RV mass attached to the septum; then systemic adjuvant therapy	Uneventful postoperative period, occurrence of the right bundle block branch	History of ulcerated melanoma removal from the right arm
Kuriakose <i>et al.</i> , 2015	54, M	Surgical removal of RA mass with pericardial patch reconstruction, followed by systemic therapy	Heart function was normal with moderate tricuspid valve regurgitation	Presence of liver metastases with no primary lesion
Velho <i>et al.</i> , 2017	41, M	Surgical resection of LV mass via mini-thoracotomy, annuloplasty of the mitral valve, followed by systemic therapy	Uneventful postoperative period with partial response to chemotherapy	
Carillio <i>et al.</i> , 2018	50, M	Surgical excision of LA mass, followed by systemic therapy	Bone and cephalic metastases with disease progression. Died 3 years after surgery	
Burazor <i>et al.</i> , 2018	> 50, M	Resection of RA mass	Single brain metastasis removed by radiosurgery a year after the surgery. After 5 years the patient is alive and symptom-free	History of MM
Babar <i>et al.</i> , 2020	57, M	Total resection of the RV mass with RV free wall and outflow track reconstruction with bovine pericardial patch, then immunotherapy	Resolution of metastatic disease	History of resected MM on the right shoulder
Spilopoulos <i>et al.</i> , 2021	71, M	Resection of multiple tumors from RA, RV and outflow vascular system with stabilization of tricuspid valve, followed by systemic therapy	The patient suddenly died 42 days after the surgery	History of multiple excisions of MM of the breast
Schmidbauer <i>et al.</i> , 2023	57, M	RA mass level R2 resection due to preservation of the right coronary artery, reconstruction of RA with bovine pericardium, tricuspid valve reconstruction with annuloplasty	Lung, liver and brain metastases. Died 1 month after the surgery due to diffuse metastatic disease	Mobile RA lesion connected to the tricuspid valve; history of MM removed from the right leg

F – female, M – male, RA – right atrium, LA – left atrium, RV – right ventricle, LV – left ventricle, SVC – superior vena cava, MM – malignant melanoma.

melanoma in the past in various locations, including ocular melanoma or scalp lesions. In some cases – primary lesions were never detected.

## Discussion

Although metastatic melanomas are common, the cases of this malignant tumor metastasizing to the heart are rare, such as cardiac metastases in general [10]. On the other hand, it is worth remembering that primary cardiac tumors are significantly more rare than metastatic growths [19, 26, 27]. The incidence of metastatic tumors is estimated as 100-times higher than occurrence of primary tumors [28]. Metastases in the heart are caused by hematogenous spread and may be located in every part of the heart, including its walls [6, 7, 15, 26]. Other routes of spread are direct extension or lymphatic dissemination [7, 8, 29, 30]. Infiltration of pericardium and myocardium usually originates from coronary artery blood flow, and multifocal dissemination can be spread through vena cava [31]. Secondary tumors may present as small or large masses or as infiltrative disease [1]. The right side of the heart is in general more frequently affected and the most common location is the right atrium – the occurrence is estimated as 46% [5, 15, 32]. 18% of melanomas are located in the right ventricle and 18% in the left atrium [32]. It is vital to remember that in cases of metastatic tumors located on the left side of the heart, patent foramen ovale needs to be ruled out [5, 24]. Pericardium and myocardium are also commonly infiltrated, while endocardium or valves are rarely involved [5, 15, 26, 31]. Myocardium involvement is usually connected with infiltration of the left ventricle wall and septum [32]. Endocardium dissemination is typically linked with intracavitary masses [32]. In some cases, there is a need of differential diagnosis towards hypertrophic cardiomyopathy if the wall seems to be thickened, what may occur for example when the melanoma infiltrates ventricular apex [33]. It is particularly important in patients with a previous history of melanoma [33]. Among the valves, the tricuspid valve is most commonly affected [34].

When discussing the diagnostic approach for suspected cardiac tumors, it is essential to consider several factors. The patient's age, epidemiological and clinical probability, and tumor location are crucial in forming an initial assessment [7, 8]. Laboratory tests may reveal unspecific markers such as anemia, elevated erythrocyte sedimentation rate, C-reactive protein, and  $\gamma$ -globulin levels, with occasional thrombocytopenia [7]. Imaging modalities play a pivotal role, with echocardiography, CT, and CMR being fundamental [5, 7]. CMR is particularly valuable in characterizing tissue and surrounding cardiac and extracardiac structures. Furthermore, PET-CT can assess malignancy, stage the disease, and detect recurrences post-surgery, offering a comprehensive diagnostic toolset for managing cardiac tumors [7].

Surgical treatment should be preceded by critical evaluation of this decision and proceeded only if R0 resection level can be obtained, so no cancer cells are visible macroscopically and microscopically at all margins [5, 10]. Resection should be followed by chamber reconstruction providing

accurate. Favorably, the operation should be performed at the early stages of the disease [20]. Unfortunately, the literature points out that heart dissemination of malignant melanoma is typically connected with advanced phases of the disease and low survival chances as it is described as stage IV melanoma [6, 35, 36]. 5-year survival rates are estimated as 15% to 20% [36, 37]. It is believed that the median interval between primary diagnosis of cardiac metastases of melanoma and death is approximately 2 years [1]. The main aim of the surgeries, both radical and palliative, is prevention of heart failure, heart tamponade, circulation obstruction, superior vena cava syndrome or dysrhythmias [20, 38]. It is worth mentioning that in cases of cardiac cancer spread, the heart is rarely the only location of tumor secondary growth [10]. Diffuse spread of the melanoma usually excludes patients from surgical management [29]. In some cases, surgeries are implemented due to reduction of the size of the tumor prior to the chemotherapy, or to mitigate symptoms and to prevent heart failure [20, 38]. Among potential complications one can distinguish myocardial destabilization or myocardial rupture [1]. Radical surgeries for metastatic melanoma should be performed in experienced cardiac surgery centers that provide the whole range of heart surgeries [16]. Besides cardiac surgeons, cardiologists, oncologists, radiologists, radiation oncologists and nuclear medicine doctors should be involved in the therapeutic process [16, 32, 39].

It is important to provide the patients with an individual approach regarding their management options. Surgical treatment should be a method of choice if the cardiac mass is solitary and the surgeon is able to perform total excision with clear margins [5, 17]. In cases of multiple tumors and generalized disease diffusion, systemic management should be implemented as the option of choice [5].

In the study held by Balinski *et al.*, among 23 patients with cardiac metastases out of 1231 patients with melanoma, three (15%) underwent cardiac surgery [1]. Other methods implemented were radiation, immunotherapy and targeted therapy [1].

Aggressive therapy may lead to good outcomes in managing cardiac metastatic melanomas, but longitudinal studies are necessary to confirm that. The rarity of the disease, combined with the special circumstances needed to perform total resection of the tumor masses is the main limitation for providing studies on large groups of patients. Another limitation is that cardiac metastatic melanomas are often recognized post-mortem during autopsies as the disease often remains asymptomatic or diagnosed at a very late stage when the patient's condition is too serious to provide an extensive diagnostic process.

## Funding

No external funding.

## Ethical approval

Not applicable.

## Disclosure

The authors report no conflict of interest.

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