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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Cardiac tumors in the pediatric population – surgical experience of four decades

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SUMMARY
Introduction/Objective Although cardiac tumors in the pediatric population are found infrequently, their occurrence is constant and with occasional variations.
The purpose of this study is to show our experience with surgical options of these masses in two leading national university-level pediatric centers over four decades.
Methods This retrospective study is presenting a total number of 24 surgically treated pediatric patients who have been operated on 1998–2020. There were 16 children with primary masses and eight children with metastatic cardiac tumors. Two patients with tumor-like intracardiac masses were not included in the series but had been mentioned as diagnostic challenges. Our patients did not have cardiac transplantation options.
Results The average age of our patients was five and a half years, and the most frequent operated tumor was the cardiac myxoma. Four children had neurological symptoms. There were two deaths, one in the primary tumor group and one metastatic patient misdiagnosed as a primary tumor in the early ages of our department. We had two recurrent cases, a girl with Carney complex, and an infant with an extremely rare form of cardiac malignancy after a myxoma extraction. One child required a permanent pacemaker insertion.
Conclusion Although rare, the pediatric cardiac tumors can be a source of different life-threatening conditions and lifelong sequelae. Therefore, special considerations should be paid to the diagnostic and surgical modalities of their treatment.
Keywords: cardiac tumors; pediatrics; surgical approach; follow up

INTRODUCTION

Primary cardiac tumors in the pediatric population are rare. They present with a variety of clinical presentations and different histological findings. Surgical strategies should be oriented towards the embologenic potential of the mass but also to the compression and obstruction symptoms. Benign tumors are dominant over malignant masses. Secondary cardiac tumors are less seen. The secondary (metastatic) tumors are more frequent in adults than in children [1, 2, 3], whilst the last national 30-years' series was published nearly a decade ago [4].

We present our series with modalities of surgical treatment and available follow up. Our results differ somewhat from the reported series so far.

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METHODS

Data collection / patients

The patient data was obtained by using institutional protocols (two tertiary pediatric cardiac surgery centers), operative notes, discharge summaries, histopathological reports and follow up reports. The Committee of Ethics of the Dr Vukan Čupić Institute for Mother and Child Health Care of Serbia has approved this investigation on March 24, 2021 (No 2263/1). Pre- and postoperative events (cardiac and non-cardiac), the operation itself and early and late complications had been analyzed. The starting date was September 1988 and the end date April 2020. The postoperative cardiac follow-up examinations (echocardiography [ECHO], and/or computed tomography [CT], nuclear magnetic resonance [NMR]) were performed at 15 days, three, six, 12, and 24 months respectively. One of the patients had a surgical reintervention abroad. The patients were transferred to adult medical care at the age of 18.

Background

Our paper encompasses a period of 32 years in which the population of Yugoslavia / Serbia decreased from 22 million to 7 million inhabitants in the current era. The majority of cases (20 out of 24) were operated after 1992. Individual referrals were accepted from surrounding

countries. Thus, the real incidence of the pediatric cardiac tumors cannot be adequately calculated and is limited to Caucasian population.

Sixteen cases of primary cardiac tumors were operated on a total of 11,840 cases in 38 years (0.135% of all operated cardiac cases).

One patient, initially presenting as a primary tumor in 1989, was excluded from the group of primary cardiac tumors and transferred into the secondary group. Intraoperative findings had shown a metastatic tumor with a complete occlusion of the inferior vena cava (IVC). This patient was the one of the two deaths in our series where the attempt of cannulating the IVC resulted in a fatal bleeding.

Metastatic cardiac tumors which were referred to our centers were eight children who were sent to our centers as metastatic Wilms' tumors and one child with non-Hodgkin lymphoma (NHL). Four children with Wilms' were inoperable with disseminated metastases and three were older adolescents who had minimal cardiac involvement but dominant infracaval expansion of the tumor. These children were referred to the vascular surgeons. The NHL patient was treated at the oncological department and was lost for follow up when he transferred to adult care.

Two secondary tumors were excluded from our study as the mass being non-tumorous. They shall be mentioned as masses which were initially thought to be metastases. The number of incidental findings at autopsies was one infant with a right ventricular rhabdomyoma who died of other causes. Four fetal discoveries of rhabdomyomas had been made in our series, one had been operated.

Our country has no pediatric cardiac transplant service and this option is not a feasible as a treatment modality.

RESULTS

The mean age of our patients with primary cardiac tumors was 64.26 months (5.35 years), with female predomination (12:4). The dominant tumors in our series of operated children were myxomas (six children) with rhabdomyomas in the second place (four children). There were two patients with fibromas, three with intrapericardial teratomas and one with a hemangioma.

All the primary tumors were classified as benign. Because of the extension of myocardial involvement, one child with a fibroma was only biopsied and estimated as a patient with an unacceptable high surgical risk. There were two deaths, a neonate with a cardiac fibroma after a biopsy, and the first child in our series who was mistaken for a primary tumor in 1988.

Clinical presentations were varying. All of our patients have been diagnosed by clinical examinations, electrocardiogram, Chest X ray and transthoracic ECHO. Cardiac catheterization/angiography had not been utilized. CT and NMR imaging were readily available to all patients since 2006 [3, 5].

Table 1. Cardiac tumor demographics

Total number of patients	24		
Age (month, mean age)	64.3 (1 day – 220 months)		
Co-existing lesions	5		
Atrial septal defect Bicuspid aortic valve Patent ductus arteriosus	3 1 1		
Clinical signs			
Aortic regurgitation	1	Chest pain	2
Mitral regurgitation	2	Arrhythmias	5
Tricuspid regurgitation	1	LVOTO/RVOTO (> 30 mmHg)	2
Congestive heart failure	4	Pericardial effusion	3
Heart murmur	5	Tamponade	1
Dyspnea	4	Neurological symptoms	4
Cyanosis	1	Cerebrovascular Insults	3
Mode of diagnosis (heart and central nervous system)			
ECHO Cardiac catheterization CT NMR	16 (one prenatal) 0 7 6		
Type of tumor	Benign (16)	Malignant (8)	
	Myxoma 6 (37.5%) Rhabdomyoma 4 (25%) Fibroma 2 (12.5%) Teratoma 3(18.7%) Hemangioma 1 (6.25%)	Primary 0 Secondary 8 (100%) NH 1(12.5%) Wilms tumor 7 87.5%)	
Sex (male:female)	4:12	4:4	
Recurrent tumors	Myxoma – Carney complex (after six months) Myxoma – Myoepithelial carcinoma of the LV (after three months)		

CT – computerized tomography; ECHO – echocardiography; LV – left ventricle; LVOTO – left ventricular outflow tract obstruction; NMR – nuclear magnetic resonance; RVOTO – right ventricular outflow tract obstruction; NHL – non-Hodgkin lymphoma

All our patient cases had been presented at regular institutional heart team meetings. The timing and scheduling of the operation was in function of severity of symptoms and localization of the masses.

Concomitant cardiac lesions occurred as follows: five congenital heart lesions, a patent ductus arteriosus (one child), a secundum atrial septal defect (three children) and one competent bicuspid aortic valve. Atrial septal defects were not diagnosed in the patients who suffered stroke. All lesions had been corrected intraoperatively (ligation and closure) (Table 1).

There were four patients in our series with neurological symptoms. Three presented with stroke. The child most severely damaged by the brain tumor embolization was a teenager with a clinical history of migraines and participation in competitive sports. Postoperatively, she was diagnosed as Carney complex and had remained with devastating sequelae. The other two patients with myxomas had cerebral infarctions with concomitant hemiparesis. The older patient recovered completely, the infant had a recurrent malignant tumor and remaining sequelae. One patient with rhabdomyoma had convulsions which responded well to conventional therapy.

Initial treatment during the investigation of stroke etiology in our hospital is low

Table 2. Localization of the tumors

Type of tumor	Localization								Total
	RA	RA/LA	RV/RVOT	LA	LA/LV	LV/LVOT	RV/LV	OTHER	16
Myxoma	1			3	1	1			6
Rhabdomyoma			1			1	2		4
Fibroma							2		2
Teratoma								3	3
Hemangioma						1			1

RA – right atrium; RV – right ventricle; RVOT – right ventricular outflow tract; LA – left atrium; LV – left ventricle; LVOT – left ventricular outflow tract

molecular weight heparin. Since cardiac disease is complicated by stroke in a number of pediatric patients, but the cardiac tumors are extremely rare, the number of patients in whom the first clue to cardiac tumor diagnosis was the acute neurological deterioration is also small. This is the reason why the type and duration of anticoagulation treatment in this subgroup of cardioembolic patients could not be evaluated in a randomized prospective way. After the removal of cardiac tumor, in our opinion, the rationale is to continue either low molecular weight heparin or aspirin for at least three months. This approach could be modified according to the coexistence of underlying disease, as well as personal and family history for thrombophilia [6].

The timing of the surgical procedure after stroke should be individualized, the embologenic potential of the remaining mass being the dominant factor for the urgent operation [5, 7].

Surgical approach

All of our patients have been operated via median sternotomy on cardiopulmonary bypass (CPB), except for the two children with intrapericardial teratomas where extracorporeal circulation was not initially utilized. One child had an intraoperative iatrogenic aortic tear which required the repair on CPB. Ascending aorta and bicaval cannulation, systemic hypothermic to normothermic temperatures (28–36°C), aortic cross clamp, crystalloid/blood cardioplegia were used, the technique being the surgeon's preference. No deep hypothermic circulatory arrest techniques were used [1].

Once on CPB, all of the tumors were approached initially through the right atriotomy. The left sided masses were approached via the atrial septum and in one case through aortotomy. The huge right ventricle (RV) fibroma required detachment and re-attachment of the septal tricuspid leaflet. The iatrogenic injury to the ventricular free wall had been managed by individual pledgetted sutures. In all patients with myxomas, additional circles of endocardial tissue were excised around the tumor (Table 2). Since 2003, transesophageal and/or epicardial echocardiograms were performed on all patients, after coming of CPB.

Myxomas

Myxomas were the most frequent tumors. Four patients (66.7%) were adolescents (12–16 years old). Two patients (33.3%) were younger than three years (three months, 18 months). They presented as pedunculated masses of different textures: two patients with myxomas had recurrence of the disease. A 13-year-old girl was operated after a stroke. A large myxoma was extracted from the left atrial septum, following all postulates of myxoma removal. A new mass was detected five months after the initial operation originating from the left atrial appendage. Genetic testing confirmed a *de novo* (nonfamilial) Carney complex [7, 8]. The patient had further multiple endocrine surgical procedures operations on her endocrine glands (thyroid, breast), polycystic ovaries and concomitant clinical depression.

One child had a right atrial myxoma with propagation into the IVC. Two patients had solitary peduncular myxomas in the left atrium attached to the superior wall of the chamber.

An unusual case was seen in a previously healthy infant with a sudden onset of afebrile convulsions and cerebral infarction. A large mass was found in the left ventricle protruding through the left ventricular outflow tract (LVOT) into the aorta. The mass originating from the posteromedial papillary muscle was completely surgically removed. The histological diagnosis of a myxoma was confirmed at our institution. Four months later, the child was reoperated for a rapid-growing recurrent mass abroad. A very rare malignant myoepithelial carcinoma was diagnosed and the child had been started on chemotherapy. The histological findings from the first operation had no presence of malignant cells [9] (Figure 1).

Rhabdomyomas

Although rhabdomyomas are the most frequent pediatric cardiac tumors, not all of them require surgical treatment [10]. Out of four operated children in our series one had positive family history. Female patients dominated (3:1). Tuberous sclerosis was confirmed in three cases (75%). One baby had prominences on the lateral ventricles of the brain without neurological symptoms. One infant had a solitary but obstructive tumor in the right ventricular outflow tract (RVOT), the other three were neonates with multiple masses in both ventricles and right atrium. The only child that developed postoperative moderate residual mitral regurgitation (detachment from the posteromedial papillary muscle) and was reoperated later in life (mitral valve reconstruction). Reduction of the masses was noted in two patients, six- and nine-months post-surgery.

An incidental finding of a RV rhabdomyoma was found on an autopsy of a child who died of other causes (Figure 2).

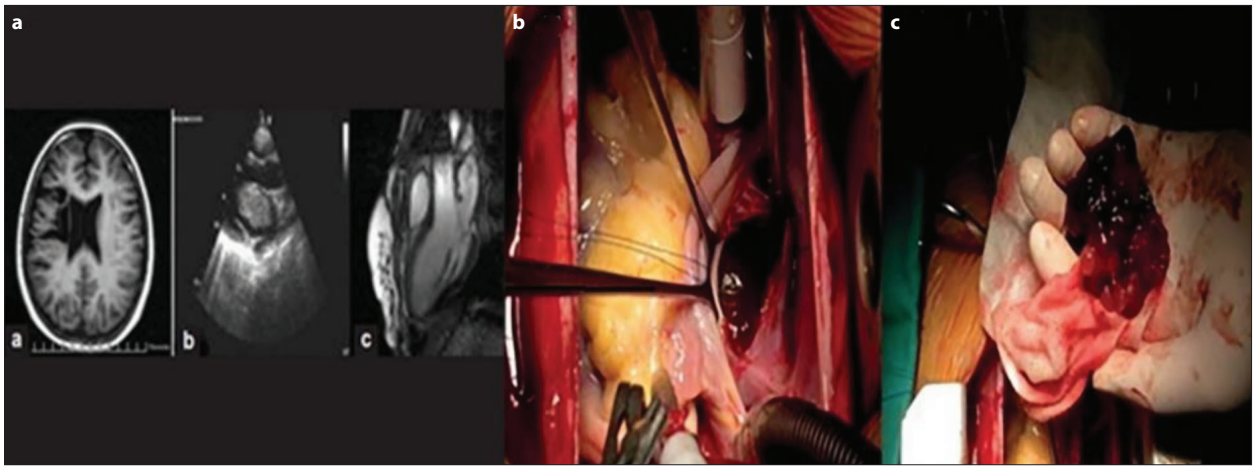

Figure 1. Preoperative and intraoperative myxoma findings; a – preoperative brain and heart computed tomography scans of a huge myxoma in a patient with Carney complex; b – intraoperative finding of a myxoma; c – the tumorous mass after enucleation

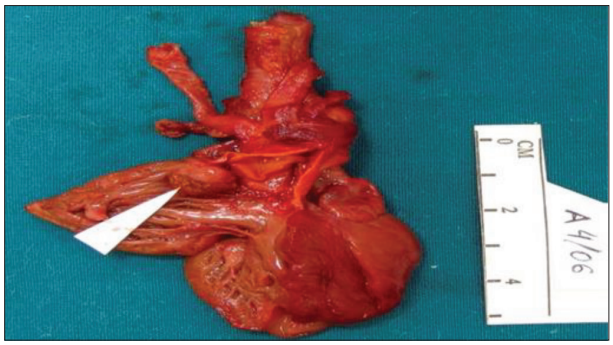

Figure 2. Rhabdomyoma in the right ventricle – incidental finding at an autopsy

Fibromas

The two patients with fibromas were approached by biopsy and relief of RVOT obstruction (RVOTO). The hemodynamically compromised premature neonate weighing 1400 grams, was biopsied with a fatal postoperative outcome. The myocardium was completely invaded by fibrous tissue. The second child had a significant right ventricular involvement with RVOT protrusion. The flow through the pulmonary artery was laminar and sufficient to maintain adequate oxygenation of the child but the patient developed arrhythmias and dyspnea. The clinical symptoms and distant place of residence pushed us towards the attempt of extracting the tumor. Intraoperatively, the septal tricuspid valve leaflet was found to be incorporated and adherent over the fibroma. The leaflet was mobilized, detached, repaired with autologous pericardium, and subsequently reattached during surgery. The fibroma was originating from the RV free wall which was damaged during the enucleation, and had to be sutured with interrupted pledgetted sutures. The child required an insertion of a permanent pace maker ten days after the surgery for complete atrioventricular block, in spite of sinus rhythm in the immediate postoperative period [11, 12] (Figure 3).

Teratomas

Two intrapericardial teratomas in our series were diagnosed in the neonatal age and one in infancy. Both neonates presented with signs of severe respiratory distress after birth [13, 14]. The intrapericardial teratomas were adherent to the right atrium and the adventitia of the ascending aorta, and to the aorta in the second case. The third case with the aortic attachment was an infant who was operated by a general pediatric surgeon. During the operation, the aortic wall was damaged with profuse bleeding. The aorta had been repaired on CPB with a good outcome (Figure 4).

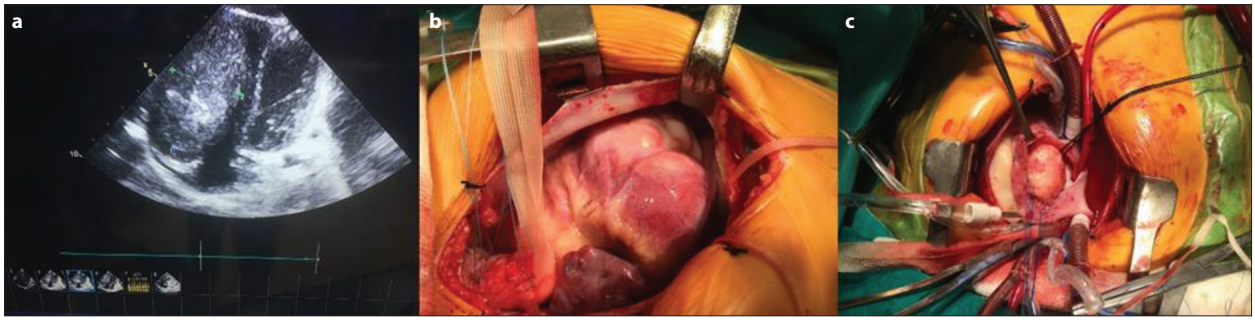

Figure 3. Fibroma; a – echocardiographic view of the tumor; b – macroscopic view of the heart with a huge fibroma; c – "delivery" of the egg-shaped fibroma through the tricuspid valve

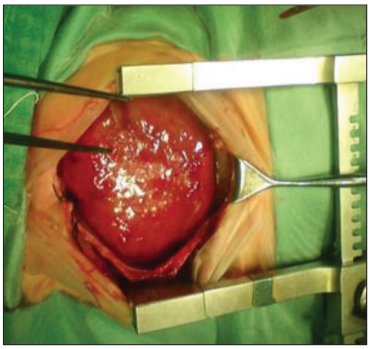

Figure 4. Intrapericardial teratoma adherent to the right atrium and ascending aorta

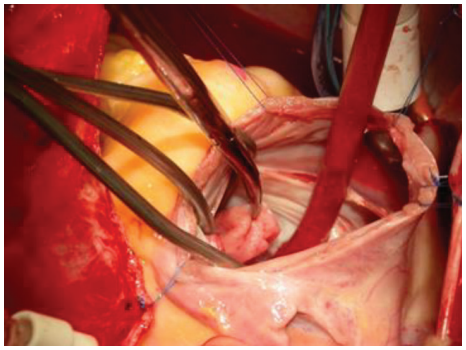

Figure 5. Transseptal and transmittal removal of a hemangioma

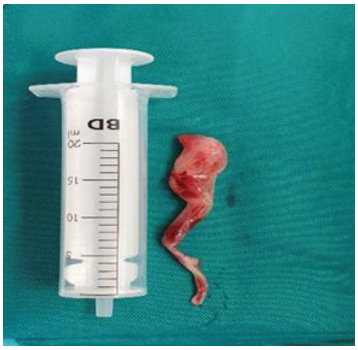

Figure 6. White thrombus originating from the superior vena cava in a patient operated from epipharyngeal rhabdomyosarcoma

Hemangiomas

Cardiac hemangiomas are very rare [15, 16]. Solitary case of a left ventricular hemangioma was diagnosed and surgically removed from an 18-year-old girl who complained of migraines six months prior to the diagnosis. Intraoperatively, the pedunculated multicystic formation was partially attached to the posteromedial papillary muscle and the ventricular free wall. No residual clinical or echocardiographic sequelae were seen (Figure 5).

Secondary cardiac tumors

Seven patients with secondary cardiac tumors were metastatic Wilms' tumors and one had been an adolescent with a NHL [17, 18].

Wilms' tumors

All Wilms' tumor patients with intracardiac involvement were referred from other centers after unsuccessful treatment with chemotherapy and radiation [18]. The first patient in our Wilms' series was mistaken for a primary right atrial tumor. This operation was performed in the early 1980s as our first cardiac tumor operation. The problems with cannulating the IVC resulted with the vein tear and fatal abdominal bleeding. Three patients in critical conditions (Wilms' tumor grade III/IV) were denied surgery. The remaining three patients were referred to the adult cardiovascular centers. One child was operated and died on the second postoperative day due to hepatorenal failure.

Non-Hodgkin lymphoma

The NHL patient had an incidental finding of his condition after a car accident and diagnosis of a pericardial effusion with a threatening tamponade. After draining more than 1 liter of serosanguinous fluid from the pericardium, layers of white fragile tissue were found to be incorporated in the epicardium. Biopsies of both pericardium, pericardial effusion and the epicardial layers of the heart confirmed the diagnosis of NHL. The echocardiographic examination showed intracardiac opacity and thickening of the right ventricular cavity but with no hemodynamic compromise. He was transferred and treated by hematology oncologists. The regression of both extracardiac and intracardiac components after chemotherapy was decisive to abandon the intracardial biopsy attempt. He went into remission and was transferred into adult care.

False alarms

Two patients were referred to the cardiac team as children with masses in the right atrium after previous treatments for malignant diseases: NHL and oropharyngeal rhabdomyosarcoma. The boy who was treated for NHL developed a mass around the long-standing Hickman catheter. Although we were confident that the mass was not of tumorous origin, macroscopically the mass did not resemble a thrombus. The histopathology confirmed a thrombus.

The second patient had an epipharyngeal rhabdomyosarcoma surgically removed three months before a mass appeared in the right atrium. The cardiac examination followed after a systolic murmur was heard during a routine auscultation. The child did not have previously cannulated neck vessels, yet intraoperatively, we found a mass originating in the superior vena cava on a thin peduncle, extending and free-floating into the right atrium. Histopathology confirmed to be a white thrombus (Figure 6).

Postoperative course, outcomes, and follow-up

All operated patients were easily weaned off CPB. The inotrope protocols changed and decreased over time. Nowadays, inotropes are used only if needed in younger patients. The extubation protocol is individualized and dependent on the status of the patient. Three patients were extubated on the operating table, 12 were transported to the Intensive Care Unit intubated. The mean intubation time was 15.7 hours, SD 19.5 (3–48 hours). No patient needed reintubation.

Postoperative bleeding / thoracic drainage was not significant. All thoracic drains were removed within 72 hours.

The patient with a right ventricular fibroma developed a complete atrioventricular block after initial postoperative

period of sinus rhythm. A permanent transvenous pacemaker was implanted on the 10th postoperative day.

The girl with a huge atrial myxoma and stroke had an early recurrence of the myxoma. The rapidly growing mass was noted five months after the initial operation. The patient reported generalized pruritus as main complaint and the characteristic "cafe au lait" spots became visible only at the time of the tumor recurrence. She was consequently operated from a thyroid adenoma, breast adenoma, and a ovarian torsion. She was under psychiatric care for depression.

We had only one case of early mortality; neonate who was biopsied for a cardiac fibroma. Except from the myxoma recurrence that was treated surgically again abroad, all other patients were free of reintervention.

The patients who are still in our care receive no medical treatment.

We had seen no late mortality. All the patients exceeding the pediatric age group, were not under our care and we have not included the latter findings.

The mean follow up was 43.13 months (SD 34.001 months), while one patient moved abroad two months after the operation.

Limitations of the study

This is a retrospective study of a 32-year-long period hallmarked by demographic changes of our country and heavy regional displacement, different availability of diagnostics and approaches to data collection. Until 1998, no uniform system was present nationally, yet data were collected per surgeons' training. Regrettably, we have limited knowledge of the patient follow-up in the adult care. The absence of a national data base and limited possibilities of fetal screening in our country decreases the prenatal detection of intracardial masses.

DISCUSSION

Cardiac tumors in the pediatric age group are a rare entity [19]. The first patient who survived a cardiac mass operation was a child in whom Crafoord removed a myxoma on CPB in 1954.

The true incidence of cardiac tumors is children is not known, but it can be quoted that is between 0.0017 and 0.28%. The majority of cardiac tumors in the pediatric population are primary masses.

In our series, the exact tumor incidence could not be calculated due to geopolitical changes in our country. We can state that cardiac tumor operations make 0.13% of all operated cases. The female to male ratio is inverse in our series compared to the data reported in other series. Female patients were dominantly more affected, 12 compared to four males.

We had one accidental finding of a rhabdomyoma on an autopsy of an infant who had died from non-cardiac causes. Fetal examinations have also discovered four hearts with rhabdomyomas, but as the adequate fetal scans are limited only to high volume centers this number is probably larger. There are currently 12 patients with rhabdomyomas under our care, who do not need surgical treatment. Central nervous involvement is seen in more than 50% of the cases.

All the primary masses in our series were benign except for one recurrent tumor. Our series differs from the majority of papers by the dominance of operated myxomas. Myxomas have been seen in children as young as three and 18 months. The child who was initially operated at the age of three months as a left ventricular myxoma had an early recurrence of a rare malignant form of myoepithelial carcinoma. It is difficult to postulate that this child had two different tumors in such a short period of time, but the pathohistological specimens of the first removed had no malignant cells and were typical of a benign myxoma. The early recurrent mass was malignant. This type of recurrence has not been described so far.

The myxomas were, in spite of their benign nature, tumors with the worst general outcomes: only one patient did not have a prior stroke. Unfortunately, the symptoms usually have a sudden onset in children who are healthy or have no other comorbidities. The Carney complex, hereditary or *de novo*, is an absolute indication for additional and more detailed and frequent postoperative examinations as they are inevitably linked to other medical conditions.

Rhabdomyomas were the second most frequent tumors in our series. The dominant clinical symptoms had been of obstruction and compression. The majority have confirmed tuberous sclerosis. The greatest challenge is the extensiveness of the surgical resection. Our approach is to remove only the hemodynamically compromising mass. These patients are younger than the others and have a potential for tumor regression. Over aggressive surgery has the potential of myocardial injury and damage of vital structures.

Fibromas are rare but from the surgical point of view the most demanding cases and tumors where cardiac transplantation is the most feasible option. Therefore, in one of our two cases, extensive resection was recognized as an option of treatment because of threatening obstruction and the dysrhythmias. These tumors do not regress and are incorporated in the myocardium itself beside the intracavitary formations. Risks of valvular or myocardial injuries are recognized risks.

The secondary tumors in the pediatric population are less frequent than in adults. Our series comprised of seven patients with Wilms' tumor and one with an accidentally discovered NHL. The patients with Wilms' tumor who have an intracardiac (right atrial) propagation through the IVC are often in the end-stage disease with unfavorable outcome. Although authors report successful extraction of tumor masses and/or thrombus, our experience with this type is nonexistent except for one case in the early stages of our department who had a fatal outcome after mistaking the metastatic tumor for a primary mass. The solitary case of NHL cardiac involvement in our series had been an incidental finding. We had operated on two children (treated for other malignancies) with right atrial masses, but both tumors proved to be organized intracardiac thrombi.

CONCLUSION

Our study illustrates that despite the benign histology of most primary pediatric cardiac tumors there is a significant associated comorbidity and occasional mortality. Clinicians should keep in mind that although these tumors are rare, they have a wide and unusual spectrum of presentations. Total resection is not always the therapeutic aim; an important factor is the restoration of the best possible hemodynamic cardiac function without additional cerebrovascular or pulmonary embologenic accidents. Stroke should be treated medically like any other etiology. Although intrapericardial teratomas might attract general surgeons, our hospital policy is that all thoracic tumors should be operated by cardiac surgeons. The absence of a pediatric cardiac transplant program can push the surgeon towards palliative interventions (partial obstruction relief).

Conflict of interest: None declared.

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Тумори срца у педијатријској популацији – хируршко искуство од четири деценије

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САЖЕТАК

Увод/Циљ Мада су тумори срца у педијатријској добној групи ретки, њихова инциденција је константна са повременим варијацијама.

Намера ове студије је да покаже искуства и хируршка решења лечења тумора срца у два водећа национална универзитетска педијатријска центра у распону од четири деценије.

Методе Ова ретроспективна студија укључује 24 хируршки лечена болесника који су оперисани у периоду између 1988. и 2020. године. Било је 16 деце са примарним масама и осморо са метастатским туморима у срцу. Два болесника са масама у срцу које нису биле тумори нису укључени у серију, али су представљени као дијагностички изазови. Болесници нису имали могућности за трансплантацију срца.

Резултати Просечан узраст наших болесника је био пет и по година, а најчешће оперисан тумор је био миксом срца. Четворо деце је имало неуролошке симптоме. Била су два смртна исхода – један у групи примарних тумора и један случај где је код болесника метастаза погрешно дијагностикована као примарни тумор. Пријављујемо и два рекурентна случаја – девојчицу са Карнијевим комплексом и одојче са екстремно ретком формом малигнитета срца после примарне екстракције миксома. Један болесник је захтевао уградњу трајног пејсмејкера.

Закључак Иако ретки, тумори срца у дечјој популацији могу бити узрок различитих животно угрожавајућих стања, као и доживотних последица. Стога, посебну пажњу треба обратити како на дијагностичке тако и на хируршке врсте лечења.

Кључне речи: тумори срца; педијатрија; хируршко лечење; период праћења