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Early and long-term outcome of surgery for cardiac myxoma: experience of a single cardiac surgical centre

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Abstract

Background: Outcome after surgery for cardiac myxoma is very good, although due to relatively low prevalence in general population there are only a few reports with long-term follow-up that involved large number of patients.

Aim: To evaluate short- and long-term outcome after myxoma removal in a single cardiac surgical centre.

Methods: The study involved 64 patients (42 women and 22 men) at the age ranging from 21 to 79 (mean 54.1 ± 18.8) years who were treated between 1981–2009 in our institution. All patients were operated on from median sternotomy and cardiopulmonary bypass. Additionally, in 6 (9.4%) patients coronary artery bypass grafting was performed (1 to 3 grafts were implanted) and in other 2 (3.1%) ostium secundum atrial septal defect was closed. Patient survival and complications rate were assessed using the Kaplan-Meier curves. Moreover, functional status at the last follow-up examination was evaluated.

Results: Two patients died in the perioperative period (in-hospital mortality 3.1%) and 4 during follow-up ranging from 5 to 320 months (median 81 months, cumulated follow-up period 5376 patient-months). Four other patients were lost from follow-up. One-year survival probability was 0.95 ± 0.03, 5-year — 0.88 ± 0.04 and 10-year — 0.84 ± 0.06. Estimated 10-year freedom from cardiac complications was 0.72 ± 0.08, hospital readmission 0.80 ± 0.07 and cardiac surgical reintervention 0.96 ± 0.03. None of the patients had tumour recurrence. At the last follow-up examination, 90.7% of patients were in functional NYHA classes I or II.

Conclusions: Surgery for cardiac myxoma is associated with low long-term mortality and morbidity. Functional status following operation improved significantly after surgery.

Key words: cardiac myxoma, surgery, long-term follow-up, survival, complications

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INTRODUCTION

Primary cardiac tumours are rare and their prevalence is estimated at 0.5 per million per year [1]. In the majority of cases, especially in adults, benign tumours are found, chiefly cardiac myxomas [2]. The only effective treatment providing a chance for radical cure is surgical removal, regardless of the histological type of the neoplasm [3, 4]. The majority of surgeons represent a view that the excision should closely follow the diagnosis, to prevent the potential serious complications [5, 6]. Statistical data show that cardiac tumour removal accounts for < 1% of the total number of operations performed in cardiac surgical centres for adult patients [7]. The results of surgical treatment of myxoma are good, but recurrences can occur, requiring reoperation [8]. Due to relatively low rates of primary cardiac tumours, there are only a few reports in the literature on large patient groups with follow-up of over 10 years.

The aim of the study was to assess the survival and complications in the early post-operative period and during the long-term follow-up in patients operated on due to cardiac myxoma in a single cardiac surgical centre.

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Table 1. Baseline patient characteristics

Age [years]	54.1 ± 18.8
Symptoms:	
Heart failure	40 (62.5%)
Embolic events	17 (26.6%)
Systemic symptoms	22 (34.4%)
Asymptomatic	11 (17.2%)
Time from symptom onset to diagnosis [days]	56.4 ± 12.8
Comorbidities:	
CAD, including:	12 (18.8%)
Angina	7 (10.9%)
History of MI	5 (7.8%)
Post PCI	1 (1.6%)
Post CABG	1 (1.6%)
Hypertension	11 (17.2%)
Diabetes	5 (7.8%)

CABG — coronary artery bypass grafting; CAD — coronary artery disease; MI — myocardial infarction; PCI — percutaneous coronary intervention

METHODS

Study group

Sixty four patients were included (42 women and 22 men) aged 21 to 79 (mean 54.1 ± 18.8) years operated on due to cardiac myxoma between 1981 and 2009 (Table 1).

Preoperative assessment

During history taking special attention was paid to the dominant symptom, time from symptom onset to diagnosis, functional status, and family history of cardiac tumours. Patients were selectes for surgery based on transthoracic echocardiographic examination (TTE) (Table 2). Pre-operative coronary angiography was performed in all patients older than 40 and in younger patients with suspected coronary disease (symptoms, ECG changes, regional wall motion abnormalities on TTE) or with coronary artery disease risk factors.

Operation and tumour location

After the final diagnosis was made, all patients were operated on as urgent cases (1 to 4 days after the diagnosis) from median sternotomy using the cardiopulmonary bypass with moderate hypothermia (26 to 28°C). Cold (4°C) cardioplegic solution prepared according to St Thomas formula was used.

In all cases, the myxoma was removed with adequate tissue margin, also when it was attached to valvular leaflets. In patients with anterior mitral leaflet (n = 2) and septal tricuspid leaflet (n = 1) involvement, the site of the removed stalk was covered with a small patch of autologous pericardium. The myxoma attached to the non-coronary aortic cusp had a very narrow stalk, hence its excision without the need for aortic valve replacement/repair was possible. Surgical completeness was confirmed by histopathology in all cases. After tumour excision, all cardiac chambers were inspected for fragments or additional foci of myxoma. Significant coronary artery stenoses were revascularised according to standard procedure, suturing the graft on the heart first with subsequent anastomosing to partially clamped aorta during the reperfusion period.

Early post-operative period and long-term follow-up

Patient survival and complication rates, both surgical and systemic, were analysed in the early (up to 30 days after surgery, regardless of the site of stay) and late post-operative periods. During the last follow-up visit, functional status assessment according to NYHA classification and TTE was performed.

Data presentation and statistical analysis

Continuous variables are presented as means ± SD. Complication rates in the early post-operative period were expressed as patient numbers, and during the long-term follow-up

Table 2. Echocardiographic assessment before and after the operation

	Before operation (n = 64)	After operation (n = 54)*	P
Ao [mm]	32.7 ± 2.5	32.8 ± 5.6	NS
LVEDD [mm]	44.0 ± 5.1	42.1 ± 8.1	NS
LVESD [mm]	28.7 ± 3.4	27.7 ± 7.3	NS
LA [mm]	39.9 ± 4.5	33.8 ± 4.7	< 0.05
RVD [mm]	26.8 ± 5.5	27.1 ± 5.3	NS
IVSD [mm]	10.8 ± 1.4	11.4 ± 2.2	NS
LVPWD [mm]	10.5 ± 1.0	11.2 ± 2.1	NS
LVEF [%]	60.4 ± 9.3	61.0 ± 7.8	NS

*Refers to the last follow-up visit; Ao — aortic annulus diameter; IVSD — interventricular septum, diastole; LA — left atrium; LVEDD — left ventricular end-diastolic diameter; LVEF — left ventricular ejection fraction; LVESD — left ventricular end-systolic diameter; LVPWD — left ventricular posterior wall diameter; RVD — right ventricle, diastole

Table 3. Intraoperative data referring to myxoma location and additional surgical procedures

ONE CHAMBER	60 (93.8%)
Left atrium:	47 (73.4%)
Interatrial septum	43
Free atrial wall	4
Right atrium:	5 (7.8%)
Interatrial septum	3
Free atrial wall	2
Left ventricle	3 (multifocal in 1 pt) (4.7%)
Right ventricle	1 (1.6%)
Heart valves:	4 (6.3%)
Mitral valve (anterior leaflet)	2
Aortic valve	1
Tricuspid valve	1
AT LEAST TWO HEART CHAMBERS	4 (6.3%)
Left and right atrium (through ASD)	2
Left and right atrium (no ASD)	1
Left atrium and right ventricle	1
MULTIFOCAL TUMOURS	3 (4.7%)
Left and right atrium (no ASD)	1
Left atrium and right ventricle	1
Left ventricle	1
ADDITIONAL PROCEDURES	8 (12.5%)
CABG	7 (10.9%)
Mitral valve repair	1 (1.6%)

ASD — atrial septal defect; CABG — coronary artery bypass grafting

— as percentages. Continuous variables with normal distribution (confirmed by Shapiro-Wilk W test) were compared by the Student t test for paired data. The remaining quantitative variables were analysed with the non-parametric Wilcoxon test. For qualitative data analysis, Kendall W concordance index was used. Long-term survival and complication rates were analysed by plotting Kaplan-Meier curves. In all tests, a p value < 0.05 was defined as statistically significant. The Statistica 9.0 package (StatSoft, Inc., Tulsa, USA) was used for data analysis.

RESULTS

In 60 (93.8%) patients the tumour was confined to one chamber, and multiple tumours were found in 3 patients (Table 3). In the majority (62.5%) of the studied patients, heart failure (HF) was the dominant symptom and 11 patients had no symptoms prior to surgery and the diagnosis was made by chance (Table 1).

In-hospital deaths and early complications

Two patients died in the early post-operative period (in-hospital mortality 3.1%). One of them was a 52 year-old male patient with NYHA IV HF, with mechanical ventillatory support prior to surgery, with the mitral valve completely blocked by a huge tumour arising from interatrial septum. The patient deceased 72 h post-operatively due to multi-organ failure. The second patient, a 78 year-old woman with a tumour in the left ventricle, died of stroke on day 25 post-operatively.

In the early post-operative period complications were noted in 13 (20.3%) patients. In 7 (10.9%) atrial fibrillation (AF) occurred, successfully treated pharmacologically (potassium and magnesium supplementation as well as intravenous amiodarone administration), in one patient complete atrioventricular block was observed, requiring permanent pacemaker implantation on day 8 post-operatively. In the other 2 patients, hydrothorax was diagnosed which was evacuated by a single procedure of pleurocenthesis. One patient with the diagnosis of pneumonia was transferred to a pulmonology department where he remained for additional 3 weeks.

One patient required reoperation due to excessive post-operative drainage. In 2 (3.1%) patients, superficial wound infection was observed, successfully treated with targeted antibiotic therapy.

Post-discharge follow-up

The period of the long-term follow-up spanning 5–320 months (median 81, cumulated follow-up period of 5376 person--months) was completed by 93.8% patients. Four patients were lost to long-term follow-up. The other 5 died. The death cause were malignancies in 2 patients (4 and 10 years post-operatively), in single cases an acute coronary syndrome (3 months post-operatively), renal failure (after 1 year) and progressive HF (after 2.5 years). Based on the Kaplan-Meier curves, the proportion of patients surviving 1 year was estimated as 0.95 ± 0.03, 5 years as 0.88 ± 0.04 and 15 years as $0.84 \pm \pm 0.06$ (Fig. 1). It was lower ($p < 0.05$) in men (Fig. 2) than in women (Fig. 3), after 1 year as well as after 10 years of post--discharge follow-up (0.78 ± 0.13 *vs* 0.88 ± 0.06).

In one patient (42 year-old woman) a need for re-intervention occurred 12 months after surgical excision of the tumour and mitral valve repair. During second procedure mitral valve was replaced and tricuspid annuloplasty was performed with use of de Vega method. The estimated proportion of patients free of surgical reintervention was 0.96 ± 0.03.

During the long-term follow-up cardiovascular (CV) complications, chiefly supra-ventricular arrhythmia, were the most common (AF in 10 patients, and atrial flutter in 2). Ten patients were hospitalised for this reason (83% of the patients with CV complications). Atrial fibrillation was successfully managed pharmacologically in 7 patients. Electrical cardioversion was performed in 3 of the AF patients (including one unsuccessful) and in patients with atrial flutter. In one patient, sick sinus syndrome was diagnosed and permanent pacemaker was implanted 4 years after the operation. In 2 patients, coronary angiography was perfor-

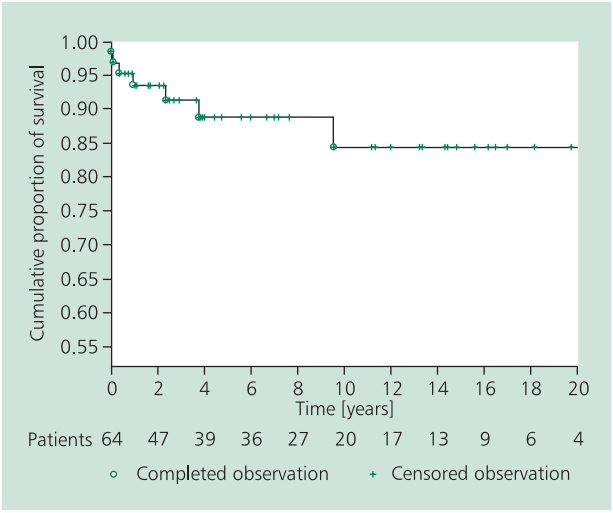

Figure 1. Cumulative proportion of survival after surgery for cardiac myxoma in studied population

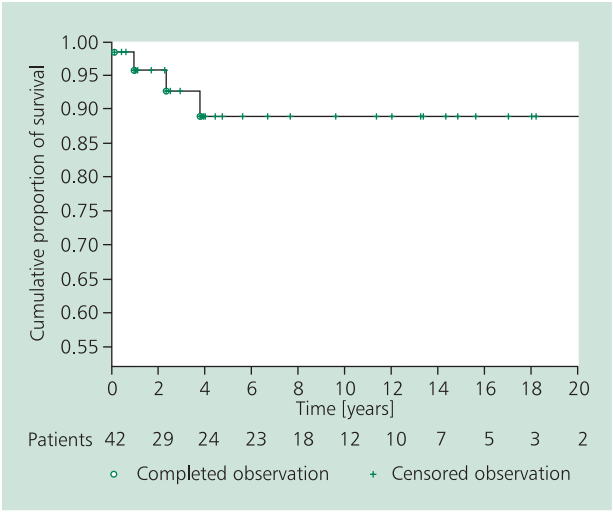

Figure 3. Cumulative proportion of survival — women

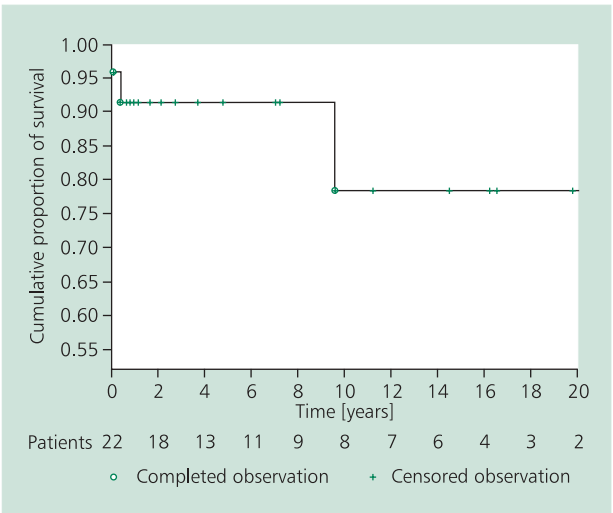

Figure 2. Cumulative proportion of survival — men

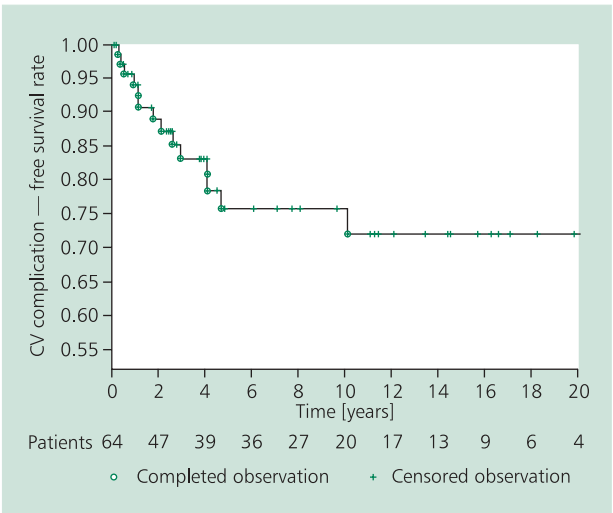

Figure 4. Cardiovascular (CV) complication rate

med due to angina, followed by successful angioplasty with stent implantation in the initially normal or insignificantly narrowed vessels.

The proportion of patients free of CV complications during 10-years was estimated by Kaplan-Meier method as 0.72 ± ± 0.07 (Fig. 4) and free of admission for CV reasons: 0.80 ± ± 0.07. In none of the patients recurrence of the tumour was observed on follow-up TTE. At the last of the long-term follow-up visits the majority of patients (90.7%) were in NYHA class I or II (Fig. 5), and at the last TTE a significant reduction of the left atrial (LA) size compared to pre-operative period was demonstrated (Table 2).

DISCUSSION

Myxomas are by far the most common primary cardiac tumours. In 70% to 80% of the cases they occur in the LA cavity, mainly at the interatrial septum in the vicinity of the fossa ovalis. Ten to 20% are located in the right atrium and less than 10% in both atria as well as in the ventricles [9, 10]. On histopathology, myxomas are similar to embrional mesenchyma, hence it is believed that they develop from the non-differentiated multi-potential cells that are abundant in the vicinity of the fossa ovalis [6].

Cardiac myxomas cause three types of symptoms. Heart failure symptoms result from the disturbed blood flow (most

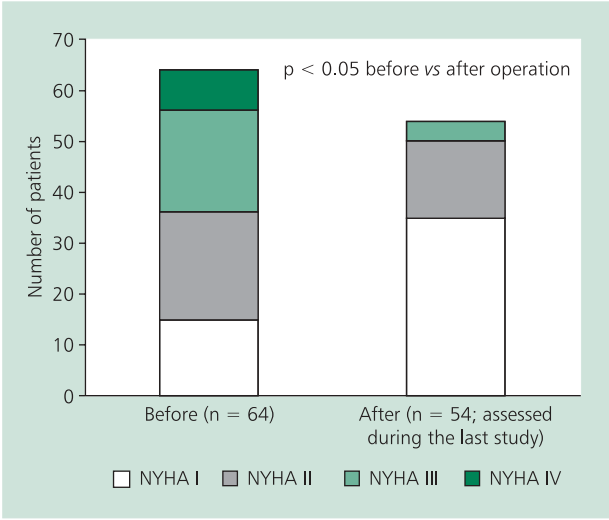

Figure 5. Cardiovascular status and NYHA before and after the operation

commonly through the LA), embolic events are related to the for tumour fragmentation and detachment. Lastly, in a proportion of patients systemic symptoms occur, such as fever, flu-like symptoms or symptoms suggestive of connective tissue diseases, weight loss, as a consequence of interleukin-6 release from the tumour cells [10, 11]. In one patient, the complete triad could be seen, but in the majority of cases one of these symptoms prevails. In our group, HF was the dominant symptom, less common were the systemic symptoms and in a little over 1/4 of the cases, embolic events occurred.

The emboli only sporadically caused irreversible nervous system damage. These results differ from series published to date [10]. It was also previously reported that the size and shape of the myxoma correlate with dominant symptomatology [10]. The largest tumours, exceeding 5 cm, more frequently cause symptoms suggestive of mitral valve disease and HF, whereas smaller tumours with irregular surface more commonly result in embolic events [12]. The relatively high proportion of asymptomatic patients should also be noted. A more detailed analysis per period (calendar year) in which the patients were operated on, demonstrated the increasing proportion of patients who underwent surgery before symptom occurrence or very early after symptom onset [13]. Also, uncommon locations of myxoma are increasingly diagnosed (Table 3). This is due to improving availability of imaging studies and higher expertise of the doctors performing echocardiography.

Surgical removal of myxoma is related with a low risk of mortality and early complications, and patients experience substantial improvement (the majority are in NYHA class I or II) [14]. This finding was confirmed in our study with a large group of patients included and a long-term follow-up (over 90% of patients were in NYHA class I or II). Peri-operative mortality ranges from 0% to 7.5% [6, 8, 15], hence the rate reported in our study did not differ from the previously published. In patients who died in the peri-operative period, urgent/emergent operation and history of embolic events were more frequent [6]. In the long-term follow-up, the leading causes of death are not related to CV disease [8]. Similarly, in our group only 2 (40%) deaths were attributed to CV causes, i.e. myocardial infarction and progressive HF. The changing profile of the patients referred for surgery due to myxoma (ageing patients with more comorbidities including CV disease [13, 15]) can contribute to worsening of the long-term results as well as higher proportion of CV deaths.

The most common post-operative complication, in-hospital as well as post-discharge, was arrhythmia, especially supra-ventricular premature contractions and AF [10, 16]. In our group, these were diagnosed in as many as 7 patients during hospitalisation and additionally in 8 patients at long term follow-up. Our study showed that these are the most common reasons for readmission in the long-term follow-up. Additionally, the possibility of embolic events during follow-up should be taken into account, chiefly due to AF occurrence [9, 16]. In our group, no late thromboembolic complications were observed. In all patients who had arrhythmia post-operatively, routine anticoagulation treatment was recommended, with close international normalised ratio monitoring.

Despite the fact that myxomas are generally considered benign, tumour recurrences and malignant forms have been also described. The recurrence rate is estimated as 5% and usually this happens up to 5 years post-operatively [17, 18]. Tumour recurrence is possible in cases of incomplete resection, implantation of tumour cells during tumour excision as well as regrowth in another location [6, 18]. To avoid this, open heart chambers were examined carefully and the manipulations during the procedure minimised. It is believed, that the risk of tumour recurrence is higher in younger patients, in familial forms of myxoma (hence the importance of detailed family history) and in multi-locular myxomas [19]. A separate and extremely rare type is the familial, autosomal dominant Carney syndrome, where cardiac myxoma is accompanied by skin changes, endocrinological disturbances and schwannomas [20, 21]. In our group, no familial type was found and in 4 cases of multi-locular myxoma the excision was done with wider margins of macroscopically healthy tissues. Moreover, in this last patient group TTE was performed more frequently (e.g. every 3 months) than in the remaining patients.

CONCLUSIONS

In summary, our study performed on a group of over 60 patients with long-term follow-up demonstrated that surgical excision of myxoma is related to low risk of death and complications in the early and long-term follow-up and, what is even more important, offers a complete cure option.

Conflict of interest: *none declared*

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Wczesne i odległe wyniki leczenia chirurgicznego śluzaków serca — doświadczenia własne

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Streszczenie

Wstęp: Wyniki leczenia operacyjnego śluzaków serca są dobre, ale ze względu na dość rzadkie występowanie niewiele jest obserwacji trwających kilkanaście lat i obejmujących dużą grupę osób.

Cel: Celem pracy była analiza przeżycia i występowania powikłań we wczesnym okresie pooperacyjnym i w obserwacji odległej u chorych operowanych z powodu śluzaków serca w jednym ośrodku kardiochirurgicznym.

Metody: Badaniem objęto 64 chorych (42 kobiety i 22 mężczyzn) w wieku 21–79 lat (średnio 54,1 ± 18,8 roku) leczonych w latach 1981–2009. Chorych do operacji kwalifikowano na podstawie badania echokardiograficznego. Wszystkich operowano w trybie pilnym ze sternotomii pośrodkowej w krążeniu pozaustrojowym i w hipotermii umiarkowanej (26–28°C). U 6 (9,4%) chorych dodatkowo wykonano 1–3 pomostów aortalno-wieńcowych, u 2 (3,1%) zamknięto ubytek w przegrodzie międzyprzedsionkowej typu otworu wtórnego. Przeżycie chorych i częstość występowania powikłań zarówno chirurgicznych, jak i narządowych analizowano we wczesnym okresie okołooperacyjnym (do 30 dni po zabiegu, niezależnie od miejsca pobytu) i w obserwacji odległej. Podczas ostatniej wizyty w obserwacji odległej oceniano wydolność układu sercowo-naczyniowego i wykonano przezklatkowe badanie echokardiograficzne.

Wyniki: Dwóch chorych zmarło we wczesnym okresie pooperacyjnym (śmiertelność szpitalna 3,1%): 52-letni mężczyzna z powodu niewydolności wielonarządowej i 78-letnia kobieta w wyniku powikłań neurologicznych (udar). We wczesnym okresie operacyjnym u 13 (20,3%) pacjentów wystąpiły powikłania, głównie kardiologiczne, w tym u 7 (10,9%) osób migotanie przedsionków. Z powodu całkowitego bloku przedsionkowo-komorowego w 2 przypadku wszczepiono stymulator. Jeden chory wymagał ponownej operacji ze względu na zwiększony drenaż pooperacyjny, w 2 przypadkach obserwowano powierzchowne zakażenie rany, skutecznie leczone antybiotykoterapią. Czterech pacjentów utracono z obserwacji odległej trwającej 5–320 miesięcy (mediana 81 miesięcy, skumulowany okres obserwacji 5376 osobomiesięcy). Pięciu chorych zmarło w późnym okresie pooperacyjnym, przyczyną były nowotwory złośliwe (n = 2), w pojedynczych przypadkach ostry zespół wieńcowy, postępująca niewydolność serca i niewydolność nerek. Prawdopodobieństwo przeżycia 1 roku oszacowano na 0,95 ± 0,03, 5 lat — na 0,88 ± 0,04, a 10 lat — na 0,84 ± 0,06; istotnie mniejsze ($p < 0,05$) dla mężczyzn niż dla kobiet, zarówno po roku (0,90 ± 0,06 *v.* 0,95 ± 0,04), jak i po 10 latach obserwacji poszpitalnej (0,78 ± 0,13 *v.* 0,88 ± 0,06). W 1 przypadku u 42-letniej chorej 12 miesięcy po operacji usunięcia guza i plastyce zastawki mitralnej zaszła konieczność ponownej interwencji kardiochirurgicznej, podczas której wymieniono zastawkę mitralną i dodatkowo wykonano anuloplastykę trójdzielną metodą de Vegi. Oszacowany odsetek chorych bez interwencji kardiochirurgicznych w obserwacji 10-letniej wyniósł 0,96 ± 0,03. W obserwacji odległej najczęściej stwierdzano powikłania kardiologiczne, głównie nadkomorowe zaburzenia rytmu serca (migotanie przedsionków u 10 osób, trzepotanie przedsionków u 2 osób). Dziesięciu chorych z tego powodu hospitalizowano (83% pacjentów z powikłaniami kardiologicznymi). U 2 osób ze względu na bóle stenokardialne wykonano koronarografię, a następnie skuteczną angioplastykę z wszczepieniem stentów w uprzednio prawidłowe lub nieistotnie zwężone tętnice wieńcowe. Dziesięć lat po operacji odsetek chorych bez powikłań kardiologicznych wyniósł 0,72 ± 0,08, a bez hospitalizacji — 0,80 ± 0,07. U nikogo nie stwierdzono nawrotu guza. W ostatnim badaniu w trakcie obserwacji odległej większość chorych (90,7%) znajdowało się w I lub II klasie wydolności wg NYHA, natomiast w ostatnim badaniu echokardiograficznym zaobserwowano istotne zmniejszenie lewego przedsionka w porównaniu z okresem przedoperacyjnym (z 39,9 ± 4,5 mm do 33,8 ± 4,7 mm; $p < 0,05$).

Wnioski: Leczenie operacyjne chorych ze śluzakami serca jest obarczone niewielkim ryzykiem zgonu i powikłań we wczesnym okresie pooperacyjnym oraz w obserwacji odległej. Chirurgiczne usunięcie guza stwarza możliwość pełnego wyleczenia chorych.

Słowa kluczowe: śluzak serca, operacja, obserwacja odległa, przeżycie, powikłania

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