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ORIGINAL ARTICLE

Outcomes of Video-assisted Minimally Invasive Cardiac Myxoma Resection

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Background Myxomas are the most frequent cardiac tumours. Their diagnosis requires prompt removal. In our centre, for valve surgery we use a minimally invasive approach. Here, we report our experience of cardiac myxoma removal through right lateral mini-thoracotomy (RLMT) with particular focus on its feasibility, efficacy and patient safety.

Methods Between February 2006 and January 2017, 30 consecutive patients (aged 66 ± 12.6 years, range 35–83 years) underwent atrial myxoma resection through video-assisted RLMT. Percutaneous venous drainage was performed in all patients and direct cannulation of the ascending aorta was performed in 28 out of 30 (93.3%). The diagnosis of atrial myxoma was confirmed by histology.

Results Complete surgical resection was achieved in all patients. The mean cardiopulmonary bypass (CPB) time was 76.5 ± 40.8 minutes and average aortic cross-clamping time was 41.5 ± 29.8 minutes. No patient suffered postoperative complications. Five patients (16.7%) received a blood transfusion. Mechanical ventilation ranged from 3 to 51 hours (median 6 hours), intensive care unit (ICU) stay ranged from 1 to 5 days (median 1 day). Total hospital length of stay (HLOS) was 5.6 ± 2 days. Home discharge rate was 56.7%. No in-hospital mortality was reported. During follow-up (55.6 ± 32.3 months; range 4–132 months), one tumour recurrence was observed. There were three late non-cardiac deaths. Overall survival was 100%, 85.7% and 85.7% at 1, 5 and 10 years, respectively.

Conclusions The use of video-assisted RLMT is an effective and reproducible strategy in all patients requiring expedited surgery for left atrial myxoma, independently of coexisting morbidity such as systemic embolisation or previous surgery. This technique leads to complete tumour resection, prompt recovery, early home discharge and high freedom from both symptoms and tumour recurrence.

Keywords Myxoma • Heart valves • Minimally invasive surgery • Outcomes

Introduction

Myxomas are the most common primary cardiac tumours in the cardiac surgery series [1,2]. The recognition of myxomas, although incidental in most cases, prompts expedited surgery, particularly in cases with systemic embolisation and/or intracardiac obstructive signs or symptoms [3]. In the past few decades, the conventional approach has been by median sternotomy. Since minimally invasive approaches have become the standard treatment in isolated valvular surgery in the last few years, many groups have also managed the tumour resection through this limited access [4–7]. In this

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study, we present our series of atrial myxomas resected by a minimally invasive approach through the right lateral mini-thoracotomy (RLMT).

Patients and Methods

The study (2013-22-412) was approved by the research ethics committee at our centre and consent was waived due to the retrospective nature of the study.

Patient Characteristics

Between February 2006 and January 2017, 30 consecutive patients (20 females, 66.7% — mean age 66 ± 12.6 years, range 35.5, 83 years) underwent surgical resection of cardiac myxoma using video-assisted RLMT (Table 1). This strategy is currently considered for ''all-comers''. Exclusion criteria consist of the presence of extensive thoracic adhesions or severe lung disease, an unclear diagnosis of myxoma, or because the suspected extension to other myocardial structures requires further diagnostic investigations and may represent a relative contraindication to RLMT.

Surgical Technique

All patients were operated on through a right lateral mini-thoracotomy incision (5–8 cm) at the fourth intercostal space. A soft tissue retractor is placed into the surgical incision (Cardiovations, Edwards Life-sciences, Irvine, CA) and ribs were spread using a specifically designed retractor (Heart-port, Edwards Lifesciences Inc, Irvine, CA, USA). The pericardium was incised 4 cm above the phrenic nerve and 2/0 silk stay sutures were placed to expose the heart and isolate the lung from the surgical field. After full heparinisation, a Biomedicus® venous cannula (Medtronic, Minneapolis, MN, USA) or a double-stage 22-F or 25-F venous cannula (Estech, San Ramon, CA, USA) was then introduced with an ''over-the-wire technique''. In the case of a right-sided myxoma or anticipated tricuspid valve surgery, a 22-F or 25-F single stage femoral cannula (Cardiovations, Edwards Life-sciences, Irvine, CA) and a 14-F or 17-F DLP® jugular cannula (Medline Industries Inc., Mundelein, Illinois, USA) were used. Cardiopulmonary bypass (CPB) was instituted mostly by central cannulation using StraightShot Cannula (Cardiovations, Edwards Life-sciences, Irvine, CA, USA) or Easy-Flow® cannula (Estech, San Ramon, CA, USA). The surgical vision was enhanced by a 30° videoscope inserted through the 5.5 mm port. Resection of the left-sided myxoma was carried out by opening Sondergaard's groove. After opening the left atrium, a 2/0 silk suture is placed at the incision border of the interatrial septum; retracting this suture allows visualisation of the mass that usually ''pops out'' through the incision. A gentle grasp of the tumour stalk allows the excision of the mass along with a thin layer of endocardium, without fragmentation. In the case of a right-sided myxoma or tricuspid valve surgery, the right atrium was opened above the *sulcus terminalis*. Following the tumour resection, the excision of the implantation site was performed avoiding septum perforation. In case of tumour excision along with part of the inter-atrial septum, we used a Dacron patch with a running 4/0 polypropylene suture to close the atrial septal defect. The atrium was then closed and the patients routinely weaned off CPB. A transoesphogeal echocardiographic (TEE) assessment was then performed to evaluate the effectiveness of the tumour resection, the presence of iatrogenic atrial septal defects (ASDs), mitral/tricuspid valve function and cardiac wall motion.

Table 1 **Preoperative Data.**

Variable	Patients (no.)	Mean ± Sd	Percentage
Age	30	66 ± 12.6	100
Gender (female)	20		66.7
BMI	30	25.7 ± 4.3	
Hypertension	16		53.3
Diabetes mellitus	1		3.3
Cerebrovascular pathology	2		6.7
LVEF (%)	30	59.2 ± 4.7	
AF	6		20
NYHA class III	3		10
Redo Cases	2		6.7

Abbreviations: BMI: body mass index; LVEF: left ventricular ejection fraction; AF: atrial fibrillation; NYHA: New York Heart Association.

Histology

Histological analysis was performed on the atrial masses. The tumours were formalin fixed and paraffin embedded for routine histology. Immuno-histochemistry was performed on adjacent serial sections using specific antisera raised against calretinin, S100, Neuron Specific Enolase (NSE) and CD31 at appropriate dilutions and a Ventana automated immunostaining system according to the manufacturer's instructions (Ventana Medical Systems, Inc, Oro Valley, Arizona, USA).

Outcomes

We reported the intraoperative variables with emphasis on the cardiopulmonary bypass time and aortic cross-clamping time, associated valvular procedures, localisation and size of the myxoma. The occurrence of sternotomy conversion was also identified. Postoperative variables included hours of mechanical ventilation, days in ICU, transfusion, occurrence of complications (new-onset atrial fibrillation, new cerebrovascular event, bleeding requiring revision); total HLOS was reported along with 30-day death and home discharge rate. Follow-up was completed for all patients and events were collected via phone calls or last available out-patient or in-patient clinic contacts.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD); for non-normally distributed variables, the median value was reported. Dichotomous variables were expressed as percentages. The level of significance was set at $p < 0.05$. Survival analysis was performed using the

Kaplan-Meier method. Analyses were performed in R version 3.3.1 (2016-06-21) [8]. The package used for computation and the literate programming code for Kaplan-Meyer curve is reported in Supplement 1.

Results

Two patients (6.7%) were redo cases with a previous history of mitral valve repair and mitral valve replacement associated with coronary artery bypass grafting (CABG). Two patients (6.7%) suffered from preoperative neurological dysfunction consisting of embolisation with stroke (n = 1) or transient ischaemic attack (n = 1), respectively. Most patients were in NYHA class $\leq$ II (90%). Mitral valve regurgitation was absent or mild in 91% of patients; only three patients (13.6%) showed tricuspid valve regurgitation $\geq$ 2+/4+. The atrial mass was confirmed and characterised by transthoracic echocardiography (TTE) or transoesophageal echocardiography (TTE). The tumour was localised to the left inter-atrial septum in 29 patients (96.7%) and to the right inter-atrial septum in the remaining patient. The average patient Logistic EuroScore was 6 $\pm$ 5.4%. Detailed intraoperative data are reported in Table 2. Femoro-femoral CPB was used in two cases (in a redo patient and in a subject with porcelain aorta and functioning CABG). A direct aortic clamping was performed in 29 patients (96.7%) by a Cygnet clamp (Novare Surgical Systems. Inc., Cupertino, CA, USA). In the remaining patient, the surgery was carried out without aortic cross-clamping due to a functioning bypass and porcelain aorta. Antegrade warm blood cardioplegia was administered in 24 patients (82.8%), while the remaining five patients received Custodiol® HTK cardioplegia. All the procedures were performed urgently because of tumour dimensions, severe left ventricular inflow impingement, likelihood of fragmentation or presence of congestive heart failure sign or symptoms. The average CPB time was 76.5 $\pm$ 40.8 minutes, with an aortic cross clamp time of 41.5 $\pm$ 29.8 minutes. The patient with right atrial myxoma underwent conversion to full sternotomy due to bleeding from the posterior aspect of the coronary sinus which could not be managed through the right lateral mini-thoracotomy (RLMT). Two patients underwent mitral valve repair (FutureBand®, Medtronic, Minneapolis, MN, USA) after tumour resection due to severe unmasked valvular regurgitation. One patient also had tricuspid valve repair with the Simplici-T band (Medtronic, Minneapolis, MN, USA). The postoperative and follow-up data are reported in Table 3. Median mechanical ventilation time was 6 hours (range 3–51 hours) and median intensive care unit (ICU) stay was 1 day (range 1–5 days). There were no in-hospital deaths. The majority of patients had a mitral regurgitation grade $\leq$ 1+/4+ (91%) and no tricuspid regurgitation (95.5%) at discharge. Discharge home rate was 56.7%, while the remaining patients were transferred to cardiopulmonary rehabilitation units. Histology confirmed the clinical diagnosis of cardiac myxomas in all cases. The average maximum tumour diameter was 43.6 $\pm$ 18.7 mm (range 15–80 mm). All tumours showed the typical features of cardiac myxomas consisting of polygonal *lepidic cells* [9] forming small nests, cord-like or perivascular structures and lacking mitotic figures, within a myxoid stroma (Figure 1A). The *lepidic cells* were positive for calretinin (Figure 1B), S100 and NSE. The surgical resection margin was microscopically free from tumour (R0) in all myxomas. The mean follow-up time was 55.6 $\pm$ 32.3 months (range 4–132 months). Survival was 100%, 85.7% and 85.7% at 1, 5 and 10 years (Figure 2); three non cardiac-related deaths

Table 2 Intraoperative Data.

Variable	Patients (no.)	Mean $\pm$ Sd	Percentage
CPB time (min)	30	76.5 $\pm$ 40.8	-
Cross-clamp time (min)	29	41.5 $\pm$ 29.8	96.7
Cardioplegia			
- Warm blood	24	-	80
- Cold Crystalloid	5	-	16.7
- No	1	-	3.3
Central Aortic Cannulation	28	-	93.3
Associated Procedures			
- Mitral Valve Repair	2	-	6.7
- Tricuspid Valve Repair	1	-	3.7
Myxoma Location			
- Left atrium	29	-	96.7
- Right atrium	1	-	3.3
Size of myxoma (mm)	30	43.6 $\pm$ 18.7	-
Conversion to sternotomy	1	-	3.3

Abbreviations: CPB = cardiopulmonary bypass.

Table 3 Postoperative and Follow-Up data.

Variable	Patients (no.)	Median	Percentage
Mechanical ventilation (hours)	30	6 (range 3–51)	-
Intensive care stay (days)	30	1 (range 1–5)	-
Hospital stay (days)	30	5 (range 3–12)	-
Blood transfusion	5	-	16.7
Bleeding	1		3.3
Stroke	0		0
Atrial fibrillation	4		13.3
In-hospital death	0		
Home discharge rate	17	-	56.7
Follow-up time (months)	30	59 (range 4–132)	-

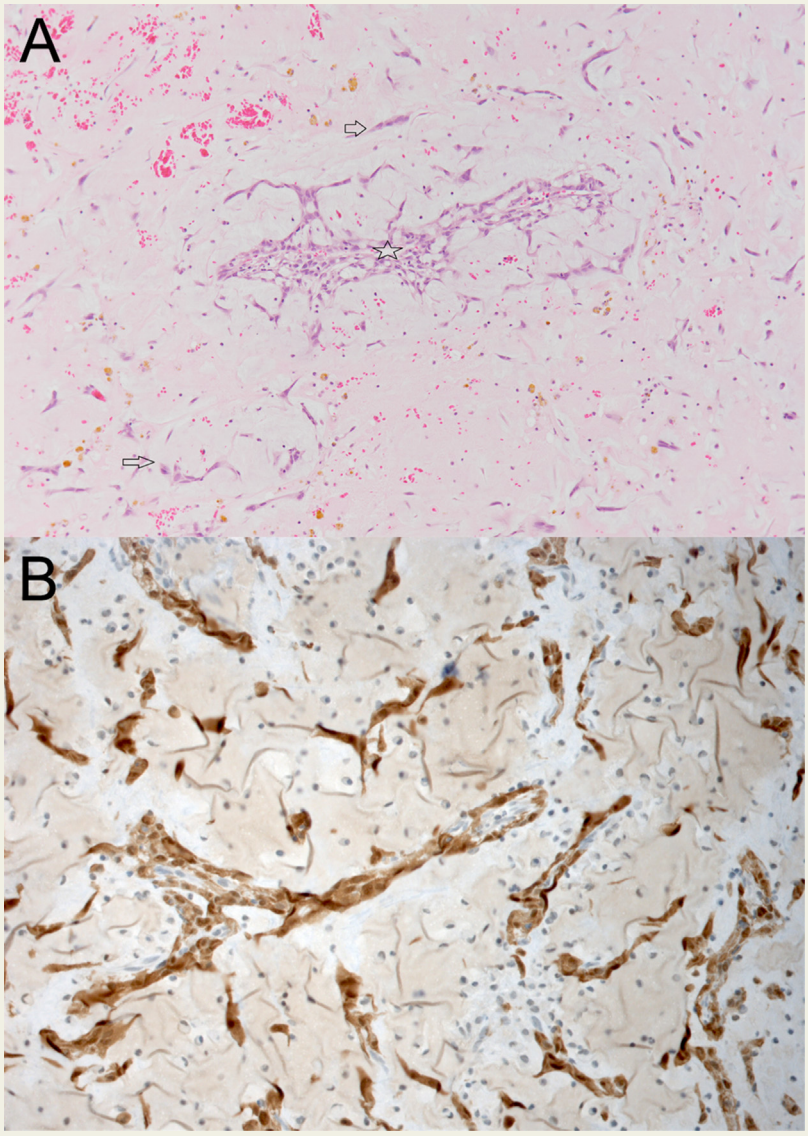

Figure 1 A) Neoplastic myxoma cells (so-called *lepidic cells*) are evidenced within the myxoid stroma as a perivascular structure (star) or small solid nests (arrows) (haematoxylin and eosin; original magnification 10x). B) The *lepidic cells* show strong calretinin immunoreactivity (avidin-biotin complex, haematoxylin counterstaining; original magnification 25x).

occurred during follow-up (one colorectal cancer, one lung cancer and one cerebral haemorrhage). One patient had recurrence of the left atrial myxoma. Due to her history of post-cardiotomy pericarditis, this patient was reoperated on by median sternotomy. Complete pericardiectomy and tumour resection were performed. In this case the inter-atrial septum was excised and replaced with a Dacron patch. No further recurrence was noted during follow-up.

Discussion

In this study we presented the application and the outcomes of minimally invasive cardiac surgical technique in the resection of myxomas. They represent biologically benign tumours that are often diagnosed incidentally, whose clinical features are determined by their location, size and mobility, potentially causing life-threatening symptoms and even sudden death. The occurrence of one or more of the triad of embolism, intra-cardiac obstruction and constitutional symptoms warrants surgical resection [1,2,10].

Historically, the median sternotomy was the approach of choice, ensuring fast access to the mediastinum, control over the heart and the great vessels without any limitations in the use of different techniques; the choice was also dictated by the era and the lack of technological advances for reducing the surgical trauma.

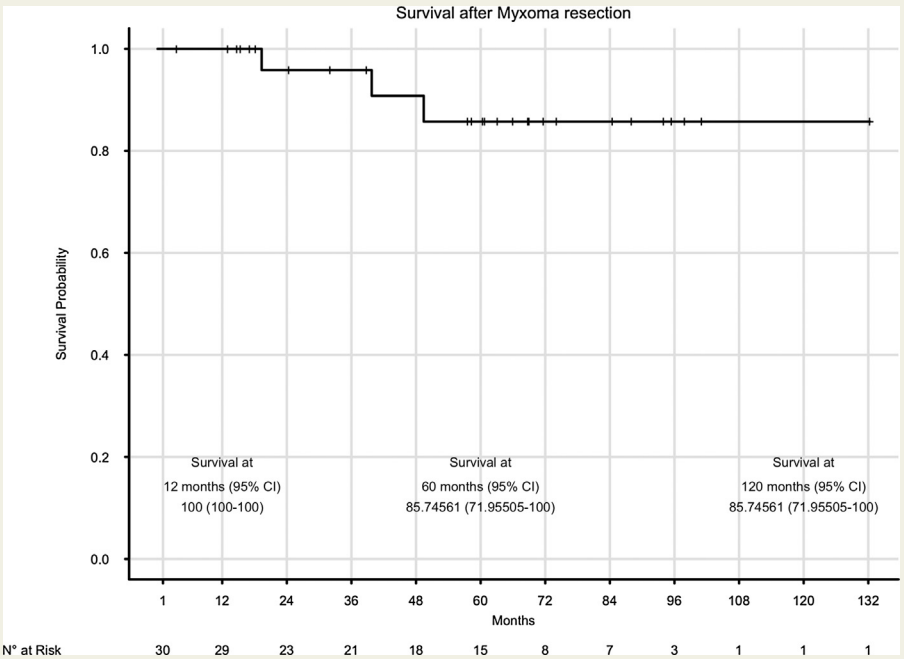

Figure 2 Kaplan-Meier curve of survival after myxoma resection.

The increasing burden of evidence regarding an equivalent perioperative mortality, a reduced need for reoperation and a trend towards shorter hospital stays for minimally invasive mitral valve surgery compared to sternotomy [11], led to an adaptation of the minimally invasive techniques on cardiac tumours surgery. Since the first report of minimally invasive resection of a cardiac myxoma in 1998 using a right parasternal approach or sub-mammary incision [12], many centres adopted the upper [13] or the j-shaped mini-sternotomy [5].

Since 2003, also our Institution focussed on developing a comprehensive program of minimally invasive cardiac surgery. Currently, it is the most widely used approach for valvular procedures at our centre and was therefore applied to tumour resection.

In the attempt to resect these cardiac masses, the surgeon must consider the clinical presentation, the presumptive nature of the mass and the degree of myocardial infiltration which is only accurately determinable on the operating table, and the need to ensure a complete tumour excision, offering also a procedure with low mortality and morbidity.

In our study, all patients were operated on an emergency basis to relieve the obstructive symptoms and to prevent fragmentation and/or embolisation of the mass. Two patients presented with neurological impairment (one stroke and one TIA), but were not excluded from the minimally invasive treatment.

A comprehensive imaging assessment before operation, using TEE, a computed-tomography scan (CT-scan) and/or magnetic-resonance imaging (MRI) in a step-wise fashion according to the degree of urgency, is mandatory to characterise the mass. Also, clinical integration with anamnestic data is crucial, since, together they can identify masses of different nature or a more widespread disease. We recently published a case report of colonic cancer metastasis to the right inter-atrial septum mimicking atrial myxoma which was resected by the means of RLMT without complications. This was possible since it had a well defined tumour stalk and no evidence of infiltration of the surrounding structures; reviewing the literature of this case, we found that only well-defined atrial metastases, and thus atrial masses in general, are more likely to be resected [14]; therefore we recommend the use of RLMT only if the tumours fulfill these criteria.

The majority of myxomas are located in the left side of the heart; although the presence of a right atrial tumour has been reported as a possible contraindication for a minimally invasive approach [15], we observed no fragmentation during surgery for the case in our series, which was accomplished by both a jugular and femoral venous vacuum-assisted drainage.

Regarding the completeness of resection, not only is the mini-thoracotomy not inferior to sternotomy, but also the latter does not ensure a 100% success rate. In fact, in the retrospective study from the Mayo Clinic spanning over 50 years, the authors observed a recurrence rate of 5.6% (11 patients); in most cases the recurrence site was the same as the primary tumour, mostly occurring within 10 years from the first surgery in young and female patients. Interestingly, there was no difference in tumour recurrence based on resection margin, namely, endocardial resection versus base of stalk resection [16]. In our series, we routinely used base stalk resection, although endocardial excision with patching is feasible and not limited by the approach. Also, all myxomas were sent for histopathological analysis and showed

stalk margins that were free from tumour (R0). Over a decade, we had only one recurrence in a 53-year-old female, occurring 24 months after surgery. Our rate of 3.3% is in line with the published data reporting the same percentage [17]. Since the literature shows that the risk of myxoma recurrence is independent of surgical access and resection technique, this reinforces the effectiveness of RLMT, while reducing the surgical trauma. Also, in the event of a redo procedure, RLMT is feasible with a low risk, lower than expected in the case of sternal re-entry.

The major criticism against minimally-invasive cardiac surgery is its association with a longer CPB and cross-clamp time compared to the median sternotomy approach as highlighted by many reports and meta-analyses [11,18]. In addition, the cross-clamp time is independently associated with mortality, despite the preoperative contractile function and whether the patient belongs to a low- or high-risk group [19,20].

In papers comparing the minimally invasive approach to standard sternotomy for myxomas resection, no differences in terms of cross-clamp time [21–24] and CPB time [21–23] were found. These results are also consistent with the findings in a very recent case-control study [25]. In our series, the CPB and cross-clamp time were shorter than all the other series published.

The RLMT theoretically decreases the surgical trauma and beneficially affects the postoperative course: the median ICU stay of our patients was 1 day, which is in line with other studies for a right anterior mini-thoracotomy (35.6 ± 20.6 hours) [7,21–23,26] and especially lower than sternotomy patients, which ranged from 46 to 60 hours [21–23]. Furthermore our patients' median HLOS was 5 days, which is exactly the same value reported in other minimally invasive series [21–24], again significantly shorter than patients operated on by median sternotomy.

The home discharge rate was high (56.7%), although our patients were older (66 ± 12.6 years) compared to those in other series (52.4 ± 2.8 years and 57 ± 17 years, respectively) [22–24]. The remaining patients were sent back to the referring hospital or to cardiac rehabilitation centres depending on the postoperative functional status. The recovery from surgery was uneventful in all patients, even in those presenting with neurological symptoms, with no in-hospital deaths or major complications.

At follow-up we observed three non-cardiac related deaths. We did not observe any progression of tricuspid or mitral valve regurgitation. Apart from one recurrence, all patients remained asymptomatic. This reinforces the concept that, after removal of the tumour, the life expectancy realigns with that of age- and gender-matched subjects [16,27].

Conclusion

In conclusion, the minimally invasive video-assisted approach for myxoma removal was feasible, effective and generally safe. This was also the case in patients with critical presenting symptoms and unsuitable anatomy, without sacrificing the completeness of surgical resection. Due to the rarity of right-sided myxomas and the presence of one case in our series that required sternotomy conversion, further data are needed to support the same conclusions. The overall results were excellent, with ICU and hospital LOS comparable and even shorter than those reported through standard sternotomy; no early or long-term cardiac-related deaths were observed. In centres dedicated to minimally invasive surgery, after careful and complete imaging and assessment of the tumour extension, this approach should be a choice for prompt and effective myxoma removal.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2017.11.010.

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