

Perioperative management of intracardiac leiomyomatosis

An observational cohort study

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Abstract

Intracardiac leiomyomatosis (ICLM) is a rare condition in which the benign tumor extends into the right heart chambers through inferior vena cava. The best surgical approach still remains unclear.

We present a retrospective cohort of 36 patients diagnosed with ICLM in Peking Union Medical College Hospital between 2002 and 2016.

The mean patient age was 44.5 (range 25–55) years. The clinical manifestations were various, including shortness of breath, chest tightness, edema of the lower extremities, palpitations, syncope, etc. Cardiac function of 30 patients (80%) remained mildly influenced, classified as New York Heart Association (NYHA) I-II. After careful preoperative evaluation, 19 patients underwent 1-stage operation while the other 17 patients underwent 2-stage operations. The original surgical plans were changed in 5 patients (14%) due to intraoperative transesophageal echocardiography (TEE) monitoring, with the tumor directly extracted through abdominal approach or right atrium without cardiopulmonary bypass and/or deep hypothermic circulatory arrest. Complete resection was achieved in 32 patients (89%). Despite increased volume of blood loss ($P < .05$), patients undergoing 1-stage operation had significantly shorter operation time, anesthesia time as well as hospital length of stay ($P < .05$), compared with 2-stage operations. The postoperative complication rates were not different between the 2 groups ($P = .684$). During mean follow-up time of 36.1 months, recurrence occurred in 7 patients (23%) but all are survived.

Precise and full-scale preoperative evaluation of both the tumor anatomy and the patient's tolerability to the surgery should be performed. TEE plays a crucial role in guidance of surgical decision making, and 1-stage extraction of tumor through either abdominal approach or right atrium may be possible.

Abbreviations: CPB = cardiopulmonary bypass, DHCA = deep hypothermic circulatory arrest, ICLM = intracardiac leiomyomatosis, ICU = intensive care unit, IVC = inferior vena cava, IVL = intravenous leiomyomatosis, LOS = length of stay, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography.

Keywords: intracardiac leiomyomatosis, perioperative management, transesophageal echocardiography

1. Introduction

Intravenous leiomyomatosis (IVL) is a rare condition characterized by progression of a histologically benign smooth muscle tumor from uterine vein directly to the venous channel, seldom invading the surrounding pelvic tissue. When the tumor extends

into the right heart chambers through inferior vena cava (IVC), it is commonly termed intracardiac leiomyomatosis (ICLM) and may pose greater threat to patients or even cause sudden death due to mechanical obstruction of the right ventricular outflow tract.^[1] Ever since the first case of ICLM was reported in 1974, there have only been approximately 200 cases published in the literature until May 2016,^[2] indicating the rarity of the disease. Previous studies have shown that incomplete resection of the tumor may lead to increased postoperative mortality.^[3] Therefore, complete surgical removal followed by antiestrogen therapy is the treatment of choice.^[4,5] However, it is sometimes not possible due to the difficulty of the procedure, with the rupture of IVC and catastrophic retroperitoneal hemorrhage being the biggest threat.^[6] Although some case reports demonstrated that the tumor could be directly pulled out through the incision of lower IVC,^[7,8] the best surgical approach remains undecided due to limited evidence. This study presents comprehensive and specific anesthetic management details and outcomes of 36 cases of ICLM in Peking Union Medical College Hospital from 2002 to December 2016, with highlights of some unique techniques utilized to enhance postoperative recovery of the patients.

2. Materials and methods

The medical records of all patients diagnosed with ICLM at Peking Union Medical College Hospital between 2002 and

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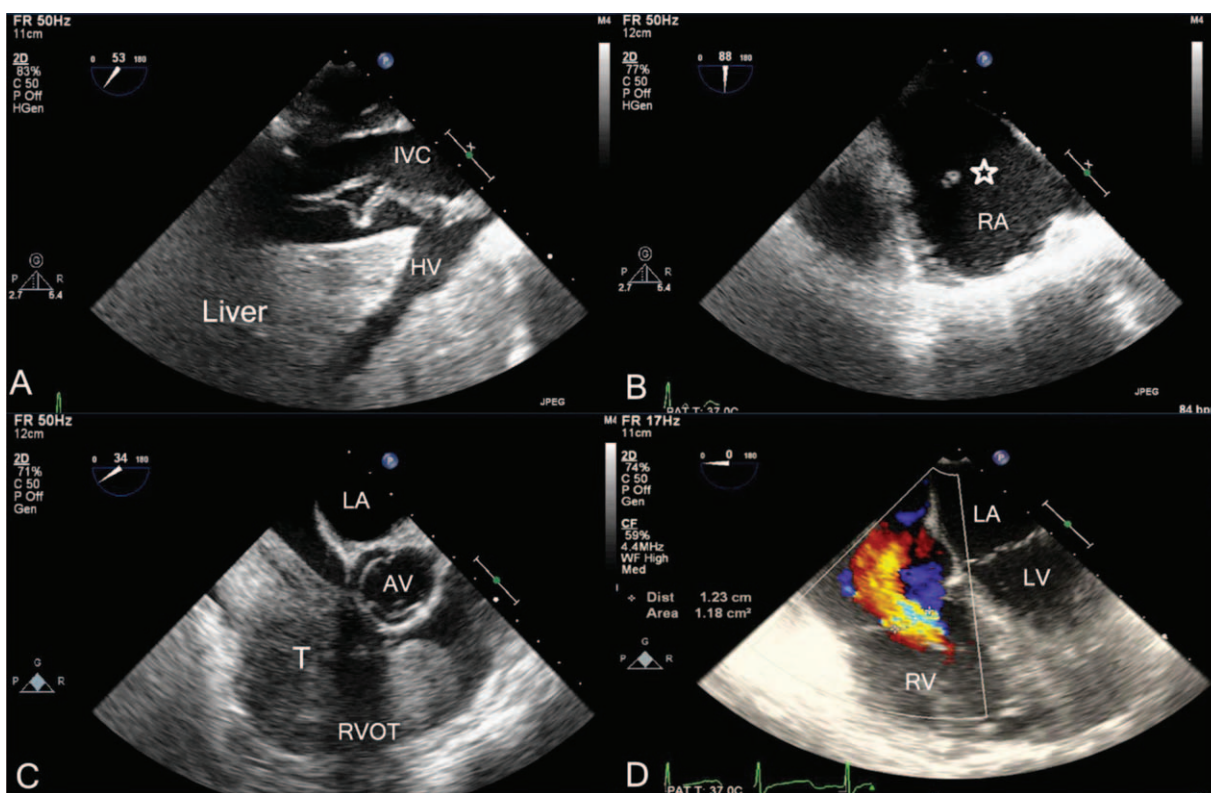


Figure 1. Intraoperative transesophageal echocardiography examination before surgical manipulation of the tumor. (A) A hepatic vein view of the intrahepatic inferior vena cava showing the tumor floating in the lumen and extending from the inferior vena cava to the opening of the right atrium. (B) A mid-esophageal bicaval view showing the thin tip of the tumor floating within the right atrium (indicated by ☆). (C) A mid-esophageal aortic valve short-axis view showing the end of tumor passing through the tricuspid valve and extending nearly toward the pulmonary valve. (D) A mid-esophageal four-chamber view showing a severe tricuspid regurgitation detected by color flow Doppler imaging. AV=aortic valve, HV=hepatic vein, IVC=inferior vena cava, LA=left atrium, LV=left ventricle, RA=right atrium, RV=right ventricle, RVOT=right ventricular outflow tract, T=tumor.

December 2016 were reviewed. The diagnosis of IVL was confirmed by at least 2 pathologists based on the classic findings of its histopathology. Whether there was intracardiac extension of the tumor was confirmed by both preoperative echocardiography and intraoperative surgical findings. As a result, 36 patients were included in this study. The study underwent ethics review and received approval from the Peking Union Medical College Hospital Review Board. The need for individual consent was waived by the board because of the retrospective nature of the study. Data from the entire perioperative process were collected, including patient age, symptoms on presentation, clinical features, imaging findings, surgical approaches, extent of resection, outcomes of the treatment, postoperative length of stay (LOS), and results of follow-up. The histopathologic data of all patients were also carefully reviewed.

Patients were carefully evaluated before operation. All 36 patients received imaging studies with ultrasonography, trans-thoracic echocardiography (TTE), computed tomography (CT), including CT angiography and CT urography, and magnetic resonance imaging (MRI). Twelve patients also received additional studies with venography and renal scan for renal blood flow determination. Since there were no established criteria, surgical plan of 1- or 2-stage operations was determined by the surgeon based on the above imaging findings and the general condition of the patients. Specifically, 1-stage operation consisted of intracardiac tumor resection, tumor thrombus resection from the IVC with primary repair, pelvic and abdominal mass resection, total abdominal hysterectomy or

removal of remaining cervix, and bilateral salpingo-oophorectomy via combined sternolaparotomy; 2-stage operations included sternotomy and removal of the tumor from the right heart chambers and the upper IVC (above the renal vein) in the 1st stage, and venotomy followed by tumor thrombus resection from the lower IVC (below the renal vein) as well as pelvic and abdominal mass resection in the 2nd stage. All operations were performed under multidisciplinary cooperation, including cardiac surgery, vascular surgery, gynecology, and anesthesiology. All patients were planned to receive the procedure under general anesthesia with cardiopulmonary bypass (CPB). Whether the patient necessitated deep hypothermic circulatory arrest (DHCA) was decided by the surgeon during the operation.

Transesophageal echocardiography (TEE) was routinely performed as standard intraoperative monitoring, and its effects on surgical decision making were specified. TEE examination was applied 3 times throughout the surgery. The 1st TEE was applied during preresection phase to verify the information of the tumor obtained before surgery and to provide the last opportunity to revise the surgical plan if this occurs (Fig. 1). The 2nd TEE was applied to provide real-time visualization of the tumor during surgical manipulation of the tumor, especially in off-pump cardiac cases. TEE was used for the 3rd time during the postresection phase to detect the residual tumor blood flow inside the lumen of IVC is visualized and evaluate the surgical results.

Outcome measurements including volume of blood loss, time of operation, allogeneic transfusion rates, postoperative complication rates, intensive care unit (ICU) LOS, and hospital LOS

Table 1
Summary of clinical details of intracardiac leiomyomatosis (n = 36).

Clinical data		No of patients, %
Age, y	20–29	1 (3%)
	30–39	4 (11%)
	40–49	25 (69%)
	50–59	6 (17%)
Presenting symptoms	Shortness of breath	11 (30%)
	Chest tightness	11 (30%)
	Edema of the lower extremities	10 (28%)
	Palpitation	6 (17%)
	Abdominal distension	5 (14%)
	Syncope	4 (11%)
	Pelvic mass	6 (17%)
	Fatigue	2 (6%)
	Hypermenorrhea	2 (6%)
	Asymptomatic	9 (25%)
ASA classification	ASA II	15 (41%)
	ASA III	19 (53%)
	ASA IV	2 (6%)
NYHA classification	NYHA I	12 (33%)
	NYHA II	17 (47%)
	NYHA III	7 (20%)
Extent of involvement	Right atrium	19 (53%)
	Right ventricle	11 (30%)
	Pulmonary artery	6 (17%)

ASA = American Society of Anesthesiologists, NYHA = New York Heart Association.

were compared between the groups of 1- and 2-stage operations. The aforementioned data from the 2-stage operation group was measured as the sum of both 2 procedures. Finally, the recurrence rates retrieved from follow-up data were also compared and analyzed.

SPSS 17.0 software was used for statistical analysis. The means of blood loss during operation, anesthesia and operation times, ICU LOS, and hospital LOS were compared with nonparametric statistical method of Mann–Whitney *U* test for independent variables and Wilcoxon rank test for 2 related variables. The blood transfusion rates and postoperative complication rates were compared with Fisher exact test. *P* < .05 was considered statistically significant.

3. Results

Of the 36 patients with ICLM who underwent surgical treatment, the mean age was 44.5 years (range: 25–55 years). Thirty-three patients (92%) had history of uterine leiomyoma and 29 patients (81%) had prior hysterectomy or myomectomy. The clinical manifestations were various, including shortness of breath (30%), chest tightness (30%), edema of the lower extremities (28%), palpitations (17%), abdominal distension (14%), and syncope (11%) (Table 1). American Society of Anesthesiologists (ASA) and New York Heart Association (NYHA) classification were utilized to describe the general condition and functional status of the patients. Based on preoperative TTE findings, the proximal end of the tumor extended to the right atrium in 19 patients (53%), to the right ventricle in 11 patients (30%), and to the pulmonary artery in 6 patients (17%). Due to mechanical obstruction of blood flow in the IVC and the right heart chambers, 7 patients (19%) received the treatment of warfarin, 4 patients (11%) received furosemide, 1 patient (3%) received hydrochlorothiazide, and 2 patient (6%) received both warfarin and furosemide before the operation. All the patients were treated

with appropriate dosages of the above medications according to their symptoms.

Surgical approach was determined primarily according to the characteristics of the tumor on preoperative TTE and the general condition of the patients. Of all the 36 patients, 31 (86%) underwent the surgery with CPB and 23 (64%) with DHCA. Moreover, 19 patients (53%) underwent 1-stage operation while the other 17 patients (47%) underwent 2-stage operations. Interestingly, 4 out of the 19 patients undergoing 1-stage operation were spared from sternotomy and CPB altogether, because the size of the tumor measured on the preresection TEE was smaller than on the preoperative TTE, and the tumor was free from attachment to either the right atrium or the IVC (Fig. 2). The tricuspid valve apparatus was also intact in all 4 cases, with only slight regurgitation. Therefore, based on these findings, the surgeons made the decision to perform only laparotomy and extract the mass through IVC under live TEE visualization. By means of gentle pressure, the tumor was successfully extracted without vein injury or retroperitoneal hematoma. Postresection TEE of the heart and the IVC confirmed complete removal of the tumor. Additionally, TEE monitoring also changed the surgical decision in another patient, when preresection TEE showed that the IVC was not completely occluded and still had blood flow, while preoperative TTE showed a complete occlusion. Consequently, CPB was initiated but without cardiac arrest, and the tumor was extracted from the right atrium. Therefore, taken together, there were 5 patients (14%) whose surgical decisions were altered intraoperatively due to the application of TEE monitoring (clinical details see Table 2).

All 36 patients completed the whole process of their operations as planned. Complete resection of the tumor was achieved in 32 patients (89%), while the rest 4 patients (11%) underwent incomplete resection, which was determined by CT scan 1 month after the operation. Summary of outcome measurements including anesthetic and operative times, total volume of blood loss, allogeneic transfusion rates, ICU LOS, and hospital LOS were exhibited and compared between group of 1-stage operation and group of 2-stage operations (Table 3). The allogeneic transfusion rates and ICU LOS were not different between the 2 groups (*P* > .05). Autologous blood transfusion with cell-saver was applied in 25 patients (70%), and all of them were eventually transfused with the washed red blood cells. Postoperative complications occurred in patients from both groups, including subhepatic abscess, pelvic hematoma, bowel obstruction, fat liquefaction of incision, and atrial flutter (Table 4). The first surgery of 2-stage operations had no postoperative complications, and all complications were detected after the 2nd surgery of 2-stage operations. Taken together, postoperative complication rates were not significantly different between the 2 groups (*P* = .684). All patients recovered successfully at the discharge from the hospital.

The gross specimen indicated that the tumor was mostly cord-like, rubbery, and with complete envelope (Fig. 3). The classic histopathology showed benign smooth muscle tumor inside venous channel limited by endothelium. There was no abnormal mitotic activity, hypercellularity, or necrosis found in the HE staining of all the 36 specimens (Fig. 4).

Thirty patients (83%) were regularly followed up in the outpatient clinic with scheduled TTE and CT of the chest and abdomen every 6 months. The other 6 patients refused to undergo imaging studies and therefore were lost to follow-up. During the mean follow-up duration of 36.1 months (range: 4–79 months), all the 30 patients survived, but recurrence occurred in 7

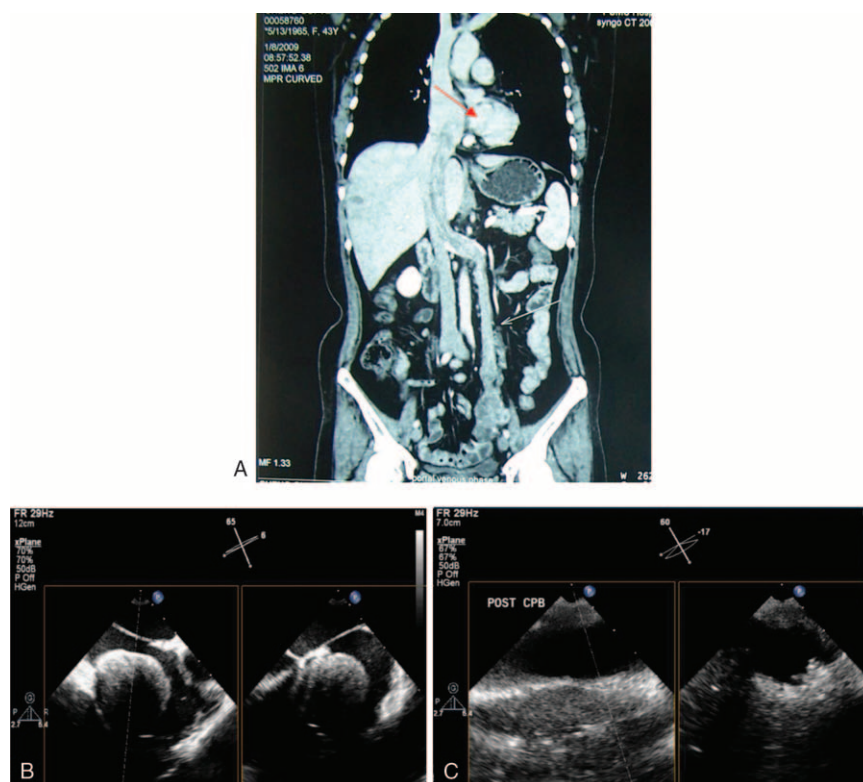


Figure 2. Preoperative and intraoperative imaging. (A) A preoperative enhanced CT scan showed the tumor extending from the inferior vena cava (white arrow) all the way to the right atrium (red arrow). (B) A mid-esophageal aortic valve short-axis view of intraoperative transesophageal echocardiography right before resection showed the tumor nearly occupying the entire right atrium, without any attachment to either the right atrium or the inferior vena cava. (C) After surgical resection, a hepatic vein view of the inferior vena cava showed no residual tumor, indicating a complete resection. CPB= cardiopulmonary bypass, CT= computed tomography.

of them (23%). Among all the recurrence cases, 5 patients had already achieved complete resection of their tumor after surgical treatment (5 out of 32, 15.6%) while the other 2 had experienced incomplete resection (2 out of 11, 18.2%).

4. Discussion

The present study shows that patients undergoing 1-stage operation experience more blood loss, yet shorter operation

and anesthesia times, as well as shorter hospital LOS, compared with patients receiving 2-stage operations. More importantly, intraoperative TEE monitoring is capable of optimizing the surgical plan and sparing the patient from unnecessary sternotomy, CPB, and DHCA.

ICLM occurs in more than 10% of patients with IVL.^[9] This ratio is slightly higher in our institution. According to the previously published data from 2002 to 2015, among 76 patients who were treated for IVL at Peking Union Medical College

Table 2

Clinical data of 5 patients whose surgical decisions were changed intraoperatively due to TEE examination.

Patients	Location	Planned operation	Differences revealed by pre-resection TEE	Actual operation	Any CPB or DHCA
1	IVC to RA, RV, PA	Sternolaparotomy, CPB, and DHCA	Valve apparatus actually intact, mild TVR	Laparotomy, venotomy, and tumor extraction from IVC	Neither
2	IVC to RA	Laparotomy, CPB and DHCA, open heart surgery standby	Tumor is mobile and smaller than expected	Laparotomy, venotomy, and tumor extraction from IVC	Neither
3	IVC to RA, RV	Sternolaparotomy, CPB, and DHCA	Valve apparatus actually intact, mild TVR	Laparotomy, venotomy, and tumor extraction from IVC	Neither
4	IVC to RA, RV	Sternolaparotomy, CPB, and DHCA	Tumor only located in RA, IVC not completely occluded	Sternolaparotomy, tumor extraction from RA	CPB without cardiac arrest
5	IVC to RA, RV	Laparotomy, CPB and DHCA, open heart surgery standby	Tumor is mobile, no adhesion to IVC, valve apparatus intact	Sternolaparotomy, venotomy, and tumor extraction from IVC	Neither

CPB= cardiopulmonary bypass, DHCA= deep hypothermic circulatory arrest, IVC= inferior vena cava, PA= pulmonary artery, RA= right atrium, RV= right ventricle, TEE= transesophageal echocardiography, TVR= tricuspid valve regurgitation.

Table 3

Comparison of outcome measures between groups of 1- and 2-stage operations (data shown as mean ± SD).

	One-stage operation (n=19)	Two-stage operations (n=17)	P
Blood loss, mL	5487 ± 3028	3064 ± 2179	<.05
Operation time, min	501 ± 178	634 ± 275	<.05
Anesthesia time, min	590 ± 180	729 ± 288	<.05
Allogeneic transfusion rates, %	57.9	47.1	>.05
ICU length of stay, h	102.4 ± 76.4	55.8 ± 32.3	>.05
Hospital length of stay, d	22.5 ± 7.1	41.9 ± 16.0	<.05

ICU=intensive care unit, SD=standard deviation.

Hospital, 28 (37%) had cardiac extension.^[10] Since the gross pathology of IVL is quite different from that of malignant tumors, in that it is mostly cord-like, rubbery, with complete envelope, and unanimously growing within the venous channels, complete surgical resection is the treatment of choice.^[11] Currently, the widely accepted surgical approach for the resection of ICLM is either 1-stage approach or 2-stage approach.^[12] In our study, more patients underwent 1-stage operation, indicating that it may be more beneficial to the patients because they experienced shorter operation time, anesthesia time and managed to recover faster with shorter hospital LOS. Although 1-stage operation resulted in more blood loss, the allogenic transfusion rates and postoperative complication rates did not differ between the 2 groups. Therefore, we presume that unless the patient's general condition is poor, or they have serious abdominal and pelvic adhesion, complete resection should be performed in 1-stage fashion to reduce the risk of increased bleeding during subsequent surgeries caused by tissue adhesion.

The intraoperative bleeding of 1-stage approach could be primarily attributable to the dissection of the adhesive tumor tissue from the involved IVC wall during intraabdominal procedures rather than open heart surgeries and CPB, which means that surgical difficulties predominantly depend on the degree of adhesion of the mass as opposed to purely its length of involvement in the venous lumen.^[13] Careful selection of candidates receiving 1-stage approach should be considered. However, the literature to date barely provides any evidence for the selection criteria of whether the patient should receive 1-stage approach or 2-stage approach. Gan et al^[14] described a quaternary classification system to choose the best surgical strategy but failed to take into account the general condition of the patients. Since we have in possession a relatively larger institutional case series, we herein propose that such criteria should involve both the anatomy of the tumor and the ability of the patient to tolerate the planned procedure. On one hand,

Table 4

Number of patients with postoperative complications in groups of 1- and 2-stage operations.

	One-stage operation (n=19)	Two-stage operations (n=17)	P
Subhepatic abscess	1	0	
Pelvic hematoma	1	0	
Bowel obstruction	1	2	
Fat liquefaction of incision	0	1	
Atrial flutter	0	1	
Postoperative complication rates, %	15.8	23.5%	.684



Figure 3. Gross specimen of the tumor after complete removal. The upper enlarged part was its cardiac end.

patient should consider undergoing 1-stage approach if the size of the intracardiac portion of the tumor is limited, tricuspid valve regurgitation is mild or absent, blood flow inside the lumen of IVC is visible, and tumor adhesion to intracardiac structures is absent. On the other hand, the functional status of the patients should be no worse than NYHA II for them to tolerate the 1-stage operation.

Increasing evidence has proved that intraoperative TEE monitoring can provide valuable information for the surgical team that preoperative TTE fails to supply.^[15] The predominant advantage of it is the ability to assist the cardiac surgeons to identify the potential cases in which direct extraction of the entire tumor through single incision is viable, either through the right atrium or IVC. As a result, patients can be completely spared from the CPB, DHCA, or even sternotomy. Currently, there have been 4 cases of ICLM in which the authors reported successful removal of the intravascular tumor via laparotomy without the need for entering the chest surgically, due to the assistance of TEE monitoring.^[7,8,16,17] Among them, 3 patients underwent the surgery without CPB and DHCA. Moreover, intraoperative TEE imaging managed to reveal a thin sliver of residual tumor entangled in the tricuspid valve during rewarming phase and thereby modified the surgical management in another case.^[18] In our study, 4 out of 36 patients adopted the surgical technique of

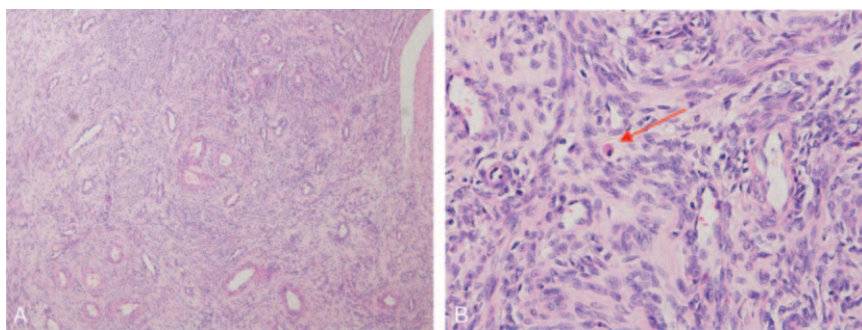


Figure 4. HE staining of tumor specimen. The classic histopathology showed hypocellularity of the tumor with abundant blood vessels (A, $\times 60$). Tumor cells presented mild atypia without abnormal mitotic activity and necrosis, and there was a mast cell in the central area (B, indicated by arrow, $\times 150$).

direct tumor extraction from abdominal approach with complete avoidance of CPB and DHCA due to TEE monitoring. Additionally, another patient in our study was able to avoid cardiac arrest and experienced complete tumor extraction directly through the right atrium with the guidance of TEE. Like the 4 cases previously reported, our 5 cases also demonstrate that intraoperative TEE imaging guidance makes 1-stage excision of ICLM through the abdominal approach or the right atrium possible. Therefore, we recommend that TEE imaging should be utilized in 3 phases of the surgery: before, during, and after resection.^[18]

The echocardiographic features of ICLM are quite different from that of other intracardiac neoplasm in that the tumor is oval (mostly) or serpentine in appearance, with well-demarcated borders and homo- or hetero-echogenic texture, and is always located in the right heart having extended from the IVC.^[19,20] Therefore, we also propose that it may be possible for the tumor of ICLM to be extracted through the abdominal approach only if it has the following features shown by intraoperative TEE: tumor is mobile and free from attachment to the intracardiac structures and IVC; blood flow inside the lumen of IVC is visible; and tricuspid valve apparatus is intact with only mild regurgitation.

Our study has its limitations. Since it is a retrospective study in nature, some confounding factors between groups of 1-stage and 2-stage operations cannot be entirely eliminated. For instance, the extent of cardiac extension of the tumor and its impact on patients' clinical symptoms and performance status may be different between the 2 groups. The volume of blood loss could also be influenced by the duration of CPB due to its effect on coagulation. Furthermore, we will record more details about surgical manipulations in future prospective studies, such as incision of the IVC or hepatic mobilization, since these may also influence patients' outcomes.

5. Conclusion

ICLM usually occurs in middle aged women with common presenting symptoms of shortness of breath, chest pain, palpitation, edema of the lower extremities, syncope, and pelvic mass. Precise and full-scale preoperative evaluation of both the anatomy of the tumor and the patient's tolerability to the surgery should be performed. TEE plays a crucial role in guidance of surgical decision making and 1-stage extraction of tumor through either the abdominal approach or the right atrium may be possible.

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