Thymic *en-bloc* resection with veins: case demonstrations and review of the literature

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Abstract: Locally invasive thymic neoplasms are challenging clinical scenarios and typically require a multidisciplinary approach. The involvement of major mediastinal veins such as the superior vena cava (SVC) used to be a contraindication to surgery, but with improved surgical technique and outcomes, this paradigm has shifted. In some situations, complex resections and reconstructions may be indicated and required to improve the long-term outcome of these patients. We report two of our cases along with a current review of literature. We also describe the preoperative workup, operative techniques, postoperative management, complications, and outcomes of patients with invasive thymic neoplasms that involve the mediastinal veins. Our first case describes a patient who was diagnosed with a thymoma extending from the diaphragm to the base of the neck that was also encasing major vascular structures including the SVC and left innominate vein. Our second case describes a patient who was also diagnosed with a large anterior mediastinal mass encasing the great veins and invading the chest wall. We describe the management of these patients and then delve deeper into operative techniques including SVC resection and reconstruction. We describe the types of conduits that can be used and complications to be mindful of when clamping the great veins, such as the SVC. Improvements in conduit materials and neoadjuvant and adjuvant therapies over the years have made it more feasible for patients with invasive thymic neoplasms to undergo surgery.

Keywords: Invasive thymoma; thymic carcinoma; mediastinal vein; superior vena cava resection (SVC resection)

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Introduction

The management of invasive thymic neoplasms has evolved in the last few decades. A major determinant of long-term outcomes in these cases is the completeness of resection (1). The involvement of the major vessels of the mediastinum, in particular the superior vena cava (SVC), was previously a contraindication to resection due to the poor long-term prognosis and lack of suitable replacements. That paradigm has shifted with the advent of adjuvant treatments, new conduit materials, and a growing experience of resection of these vessels *en bloc* with thoracic malignancies (2-4). The Masaoka-Koga classification is used to stage thymic malignancies. Select patients with stage III (macroscopic invasion into neighboring organs such as pericardium and great vessels) and stage IV disease (pleural, pericardial or lymph node metastasis) should be considered for thymectomy with *en-bloc* resection of the involved venous structures (5-7).

Case 1

Patient was a 53-year-old woman with a history of tobacco

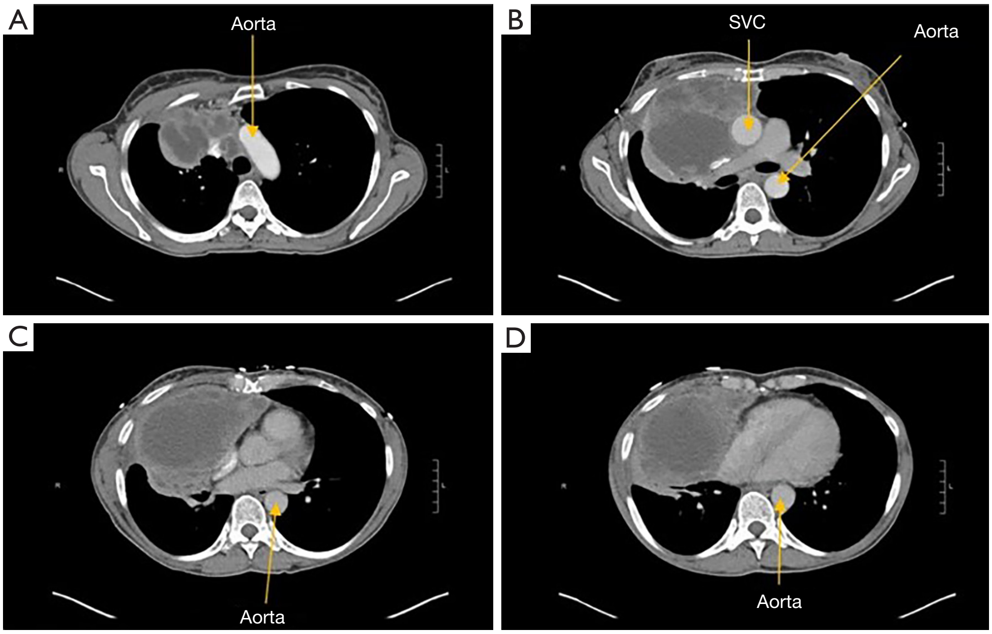

Figure 1 CT with intravenous contrast images after neoadjuvant therapy of a patient with encasement of the SVC and abutment of ascending aorta by an invasive thymoma. SVC, superior vena cava; CT, computed tomography.

use disorder and no other significant medical history who presented with a cough, intermittent fevers, and unintentional weight loss and was found on computed tomography (CT) chest to have a 10.5 cm × 10.5 cm × 15.8 cm heterogenous anterior mediastinal mass that was compressing the right upper lobe bronchus. The mass extended from the diaphragm to the base of the neck. Mediastinal lymphadenopathy, pleural and pericardial effusions, and multiple hepatic lesions were also noted. She underwent a biopsy via Chamberlain procedure and was diagnosed with thymoma. Given the extent of her disease, the patient underwent four cycles of neoadjuvant chemotherapy with cyclophosphamide, adriamycin, and cisplatin. She had a poor response with restaging CT scan demonstrating a minimally decreased tumor size with no change in mass effect (*Figure 1*). The patient then underwent a right thoraco-sternotomy (hemi-clamshell) through the 6th intercostal space (*Figure 2*). The mass was encasing the SVC and the left innominate vein, and an *en-bloc* resection was performed of the mass, right lung parenchyma, SVC, left innominate vein, proximal right innominate vein, and azygous vein. The SVC and the two innominate veins were repaired with 14-mm Gore-Tex bifurcating limbs that were sewn to a 20-mm graft. The azygous was sewn to the posterior aspect of the 20-mm graft (*Figure 3*).

Case 2

A 50-year-old woman presented with chest pain and on workup was found to have a large anterior mediastinal mass encasing the great veins (*Figure 4*). At the time of surgery, upon palpation of the lower table of the sternum, it was clear the tumor was invading the chest wall. She underwent *en-bloc* resection of the chest wall with the brachiocephalic veins and SVC. During the dissection, a shunt was placed from the right internal jugular vein to the right atrium. The reconstruction was performed with tailored bovine pericardium. We initially placed a conduit from the right internal jugular to the proximal SVC. Then, the remainder of the vessels were reconstructed and anastomosed to the SVC replacement (*Figure 5*).

Preoperative workup

An appropriate preoperative workup is essential in the management of patients with invasive thymic malignancies undergoing potential mediastinal venous resection and reconstruction. Appropriate pre-operative pulmonary and cardiac testing should be done. The most common imaging

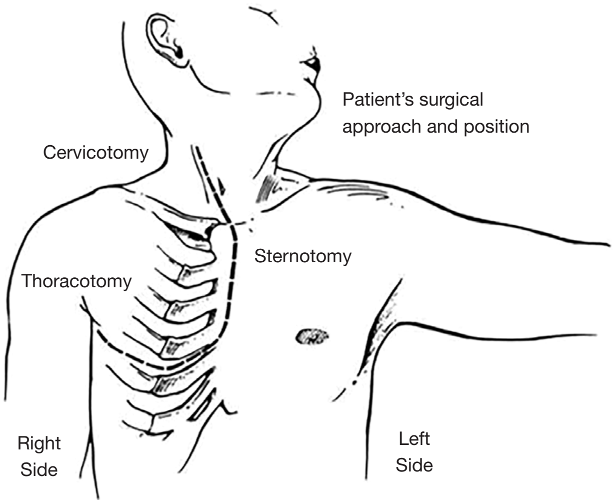

Figure 2 Right thoraco-sternotomy while patient is supine with slight neck extension [Mugabure *et al.* (8)].

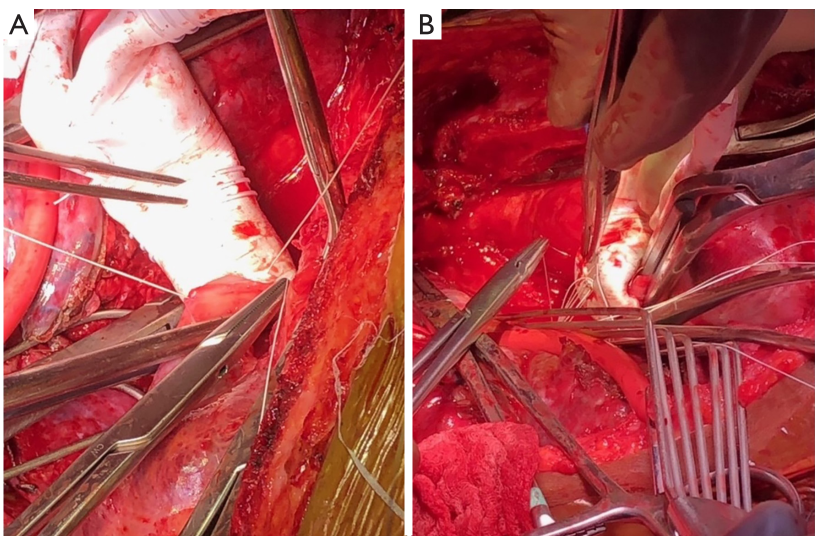

Figure 3 Venous reconstruction using a Gore-Tex Y-graft. (A) Gore-Tex anastomosis to the SVC; (B) reimplantation of the azygous vein to the graft. SVC, superior vena cava.

modality included in the workup is a contrast CT scan. This can give an idea of the extent of tumor involvement and aid in determining a surgical plan. Usually with regards to the surgical anatomy, a contrast CT scan is sufficient, and other tests such as a magnetic resonance imaging (MRI) or angiography are not necessary but can be helpful (3). In some cases, a biopsy may also be indicated, particularly when differentiating the histology of thymoma from thymic carcinoma.

For thymic neoplasms requiring resection of the SVC or innominate veins, determining the stage of the disease is crucial. This typically includes a positron emission tomography-CT (PET-CT) scan. Because phrenic nerve involvement typically requires resection of the nerve, bilateral phrenic nerve involvement would require careful pulmonary assessment prior to surgery and plans for bilateral diaphragm plication. Given the complexity of these cases, a multidisciplinary approach is often needed to individualize the treatment plan and determine the appropriate neoadjuvant or adjuvant therapy (2).

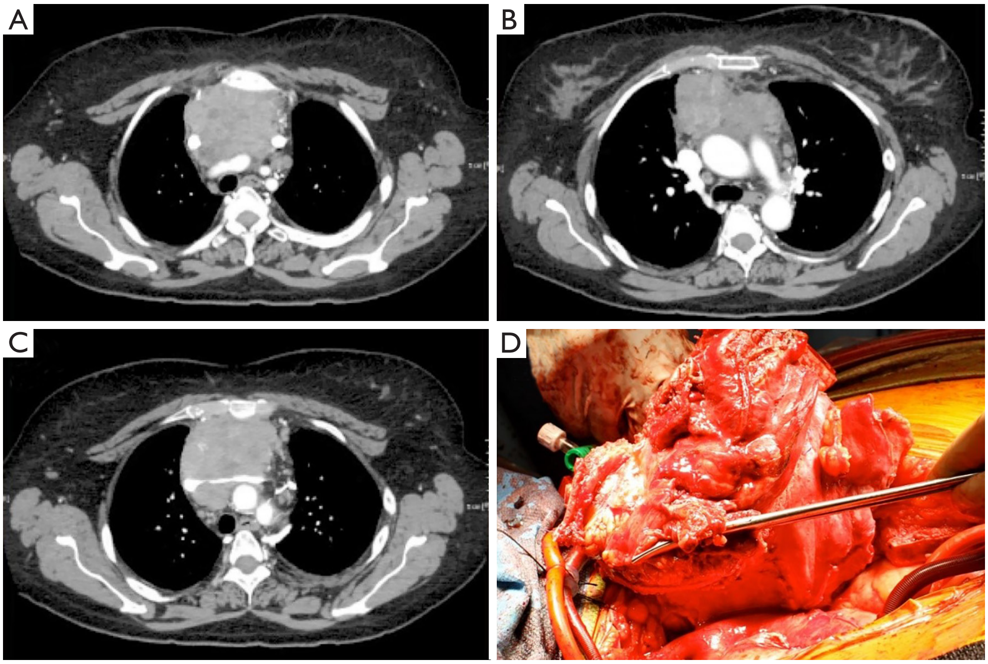

Figure 4 Invasive thymoma involving mediastinal veins. (A-C) CT with intravenous contrast images; (D) thymic resection with *en-bloc* superior vena cava and brachiocephalic veins. CT, computed tomography.

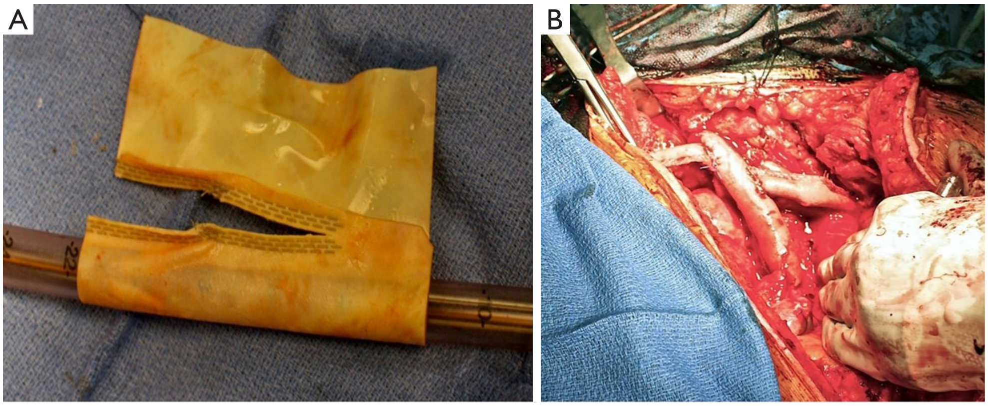

Figure 5 Venous reconstruction using a bovine pericardium. (A) Creation of conduit from bovine pericardium sized over a chest tube with vascular load staplers; (B) reconstruction *in situ*.

Operative approach

The operative approach used should be individualized, should maximize exposure of the critical structures, and should be familiar to the surgeon. The vast majority of these cases are done via a sternotomy, although a hemi-clamshell or a cervico-sternotomy are reasonable options (2,3,5-7).

Prior to selecting the optimal operative approach, it's important to understand the limitations. For example, when a thoraco-sternotomy is used, there is limited access to the contralateral chest. Therefore, if the tumor is large and bulky, the inability to get access to both sides of the mediastinum may be an important limiting factor to attaining an R0 resection.

Others have reported minimally invasive approaches utilizing video-assisted thoracoscopy, although long-term follow-up has been limited in these reports (9-11). For the two aforementioned cases, a minimally invasive approach would not be feasible given the bulky nature of the tumors.

Lower extremity large bore intravenous access is necessary, and we frequently use a femoral vein central line as this provides reliable intravenous access throughout the case. A double lumen endotracheal tube may also be required for single lung ventilation.

After the initial dissection of the tumor, involvement of the SVC and surrounding structures should be assessed. This can be done by mobilizing the tumor and delivering it away from the mediastinum. The thoracotomy extension of the hemi-clamshell allows for lateral exposure to the heart and great vessels to aid in determination of resectability of the tumor. The SVC, the azygous vein, and the innominate veins should be dissected and encircled with vessel loops when possible. It may be necessary to get venous control distally. Additionally, the phrenic nerve should be mobilized and preserved if possible; however, it is often involved and is therefore sacrificed. There is some debate regarding the maximum involvement of the SVC that will permit a partial resection. Some surgeons advocate for no more than 30% involvement, stating increased risk of kinking, thrombosis and occlusion (5-7), while other surgeons advocate for less than 50% (2-4). When performing a partial resection, a partial occlusion clamp can be utilized and the SVC can be resected *en bloc* with the tumor. The SVC can then be repaired either primarily if a small resection was performed or with autologous pericardium, autologous vein, or prosthesis if a larger resection was done (2,11,12).

Complete SVC resection and reconstruction

If greater than 30–50% of the circumference of the SVC is involved, a complete resection and reconstruction is necessary. This requires clamping of the SVC, which should ideally be done above the azygous vein to preserve flow. We typically administer 5,000 units of heparin intravenously prior to clamping. Although the azygous vein can be ligated (2,3), we typically re-implant the azygous as the increase in flow through the conduit may aid long-term patency.

Clamping of the SVC may result in hemodynamic instability, which can be managed with pressors and intravenous fluid. It may also lead to cerebral edema and thrombosis, which can partly be alleviated with the reverse Trendelenburg position. It is therefore critical to maintain close communication with anesthesia colleagues to closely monitor for any changes in intracranial pressure. More frequently, however, flow through the SVC is chronically impaired due to the tumor, and thus clamping may be well tolerated. Tolerance can be determined using cerebral near infrared spectroscopy (i.e., cerebral oximetry), a non-invasive device that measures the absorption of infrared light through the tissue to determine venous oxygen saturation. This serves as a marker for brain oxygenation. Additionally, we monitor for development of plethora, which is an indication that clamping is not tolerated. The ideal clamp time is unclear, but we try to limit the time to less than 30 minutes. Some authors have safely clamped for 44 minutes, whereas animal models have safely tolerated times up to 60 minutes (13,14).

Since we cannot predict the time needed to successfully perform the resection and reconstruction, we routinely opt for a venous shunt for larger tumors. Options for venous shunting include a caval shunt, internal jugular vein to femoral vein shunt, and a shunt between the right innominate vein and the right atrium (15). In our experience, one must frequently go distally on the veins for the location of the inflow for the shunt. Our preference is to put the outflow into the right atrium, although the femoral vein can be used when that is not accessible. More advanced support such as cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO) are typically not necessary for most cases but can be helpful especially when the tumor is invading the atrium or aorta.

The involvement of the SVC will also determine the anatomy of the reconstruction. In cases where the innominate veins are not involved, a graft can be placed from the proximal SVC to the distal SVC. If the innominate confluence is involved, a number of options are available. A graft can be placed between the left innominate vein and the right atrium to establish venous drainage after which the SVC and innominate confluence can then be resected (2). A benefit of this technique is the early establishment of superior venous drainage while the SVC is resected, but the graft is more likely to kink given the steeper angle to the right atrium (3). Alternatively, we ligate the left innominate vein and place the graft from the right innominate vein to the SVC or the right atrium. Some authors routinely conduct bilateral reconstruction (7,14), citing improved drainage with decreased risk of brain edema. This is also our preferred method. Ligation of one of the innominate veins may lead to upper extremity swelling and development of neurologic symptoms although these are often temporary and managed conservatively as collateral flow from the azygous, hemiazygous and internal mammary veins develop (16).

A variety of conduit materials have been described to replace the SVC and the innominate veins: spiral saphenous vein, tubularized autologous pericardium, bovine or porcine pericardium, polytetrafluoroethylene (PTFE), and even aortic homografts (2,3,5,12,14). The optimal conduit is debated. Jiang and colleagues recently reported on their series of six patients who had SVC replacement with autologous pericardium. Five patients survived, two of whom developed severe SVC syndrome. None of the patients developed graft thrombosis in a 55-month average follow-up period (17).

In 1991, Dartevelle and his colleagues published their results of 22 patients who had SVC involvement from lung cancer or a mediastinal tumor and subsequently underwent a concomitant resection and reconstruction of the SVC with a PTFE graft. Everyone received anticoagulation therapy for at least 6 months. One patient died postoperatively and another developed mediastinitis that was treated with an omentopexy. The overall actuarial survival rate was 48% at 5 years with a 60% survival rate in those with mediastinal tumors. One graft occlusion occurred in the postoperative period and another 14 months later (4).

A more recent study by Oizumi and coauthors describes the outcomes of 12 patients who also had a combined resection and reconstruction of the SVC with a PTFE graft. Four patients had SVC syndrome preoperatively. Bilateral reconstruction was performed for nine patients, a single right-sided bypass for one patient, and a Y-shaped bypass for another. Anticoagulants were not administered postoperatively. There were no postoperative deaths. Of the 22 grafts, 3 (14%) became occluded (14).

Our current preference is to use autologous vein for simple reconstructions to minimize the risk of thrombosis. An autologous saphenous vein can be fashioned into a patch or a luminal conduit; however, this can be time consuming and the availability of the saphenous vein is a limitation. It is best to have another surgeon harvest the vein and fashion the conduit while the operative resection is being performed. In general, for more complex scenarios requiring significant reconstruction, we use ringed PTFE grafts because it is easy to manipulate, resists external compression, and is associated with a low incidence of complications. From the preoperative contrast imaging, we can estimate the size of the graft needed. Despite this, we typically size the grafts intraoperatively for more accurate measurements.

After vascular clamps are placed for proximal and distal control, and resection of the SVC and possibly the right innominate vein is done, we first perform the proximal anastomosis with a running 5-0 prolene suture. The distal anastomosis is then performed also with a 5-0 prolene suture. Prior to tying down the suture, the graft is de-aired by opening the proximal clamp. Once the anastomosis is complete, the distal clamp is then released.

Postoperative management, complications, and long-term outcomes

Depending on the extent of the venous resection, our patients are either transferred to our stepdown unit or to our intensive care unit (ICU) to monitor for major immediate postoperative complications. Antibiotics are continued for 24 hours. If a prosthetic SVC replacement is placed, we routinely administer anticoagulation for at least 3 months. Because there is always a concern for thrombosis when a non-endothelialized graft is used, we continue some form of low dose anticoagulation or antiplatelet medication, such as aspirin, indefinitely.

Complete R0 resection ranges from 80% to 100% (5,7,18). The postoperative morbidity rate has been reported between 31% and 52% (5-7) and a mortality rate around 8%, although these studies have been more focused on thymic resection with SVC resection (5,6). For patients undergoing thymectomy with mediastinal venous resection, the complications have included pulmonary infection, hemothorax, chylothorax, atelectasis, acute respiratory distress syndrome, and need for blood transfusions (5-7). Respiratory failure is also a common complication (2,12), and aggressive pulmonary toileting is therefore crucial. Graft infection can also occur but is typically secondary to an infectious pulmonary process (2). Reports on long-term 5-year survival range from 44–59% (5-7).

Many factors contribute to complications and long-term survival. There is little doubt that an R0 resection is associated with a better long-term survival than an incomplete resection (6,18). Lung invasion has also been linked with poor outcomes (18). While induction treatment is less often indicated and should be a multidisciplinary decision, we favor its use as one cannot predict the response to treatment. Other areas are more controversial, such as the need for a complete SVC replacement. Some have shown that complete SVC replacement with a prosthetic is associated with an increased risk of death (19) while others have reported that it is equally as safe as partial SVC resection and repair (12). We opt to conduct a partial resection when feasible but acknowledge the utility of a complete resection when necessary.

Conclusions

The management of thymic neoplasms involving the SVC and innominate veins has changed drastically in the last few decades. Where these were once strong contraindications to surgical resection, extirpative surgery is now a reasonable option in select patients who are fit to undergo major cardiothoracic surgery and who have Masaoka stage IIIB and IV thymic neoplasms. Given the improvements in adjuvant therapies and conduit materials, the safety and durability of SVC resection and repair or reconstruction should be considered in a multidisciplinary approach.

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