Perspective

Video-assisted thoracoscopic surgery versus sternotomy in thymectomy for thymoma and myasthenia gravis

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Thymectomy involves the removal of all the soft tissue in the pre-vascular plane of the anterior mediastinum between the two phrenic nerves. Surgical success in controlling myasthenia and the most important factor influencing survival in patients with thymoma depends on complete clearance of thymic tissue. Currently there is a perception that the open (median sternotomy) approach offers better visualisation of the thymic tissue. This perceived advantage is thought to justify the invasive nature of the procedure associated with increased morbidity. Video-assisted thoracoscopic surgery (VATS) for thymectomy has evolved significantly over the last decade, including bilateral and unilateral VATS (either left or right) approaches. The laterality of the approach remains largely on surgeon preferences, with the decision influenced by their experience and training. VATS offers superior illumination and magnification, particularly with the availability of advanced cameras with variable angles that provide better exposure and lighting of the operative field. The use of three-dimensional operating imaging has also revolutionised the VATS technique. VATS thymectomy is a superior and radical technique in minimising access trauma and removing all thymic tissue that may be scattered in the anterior mediastinum and cervical fat. Other advantages of VATS include less intraoperative blood loss, early removal of chest drains, less requirement for blood products, decreased inflammatory cytokine response, shorter hospital stay and superior cosmesis. There is also a decreased risk of respiratory and cardiac related complications compared to the open (sternotomy) technique. Furthermore, no significant difference has been found in long-term complications and survival rate between VATS and open approaches. Subsequently, the VATS approach should be encouraged as more surgeons are adopting the minimally invasive practice as routine.

Keywords: Video-assisted thoracoscopic surgery (VATS); thymectomy; thymoma; myasthenia gravis; thoracic surgery

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Introduction

Thoracoscopy was first performed in 1910 by Hans Christian Jacobaeus, Professor of Medicine. He used a modified cystoscope for lysis of pleural adhesions to obtain therapeutic pneumothorax in a patient with pulmonary tuberculosis (1). With the arrival of drug treatment of tuberculosis and the end of the era of pneumothorax therapy, the use of thoracoscopy declined. However, its use was retained by respiratory physicians in a number of European centres as a diagnostic tool. Resurgence of interest in the field of thoracoscopy ensued after two international symposiums on thoracoscopy; Marseille in 1980, then Berlin in 1987 (2).

In the late 80s and early 90s, the success of laparoscopic cholecystectomy and other abdominal surgeries encouraged thoracic surgeons to adopt the technology. Dedicated thoracoscopic surgical instruments were developed. With the advent and advancement of endoscopic video systems, fibreoptic light transmission and endoscopic surgical staplers, the term video-assisted thoracoscopic surgery (VATS) became popular. During its pioneering days, VATS was primarily used for diagnostic procedures such as

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drainage of pleural effusion, pulmonary wedge resections, pleural biopsy and pleurodesis.

With better experience and advancements in the instruments utilised, all major thoracic resections are now performed by VATS as they confer lower conversion rates and better outcomes (3,4). In the modern era, VATS has become the default approach for many thoracic surgeons.

VATS thymectomy was introduced in 1992 as a minimally invasive alternative to sternotomy for patients with myasthenia gravis requiring thymectomy. VATS thymectomy has gradually gained popularity; however, there are controversies and concerns in the literature regarding incomplete resections (5,6).

Thymoma and myasthenia grevis

Thymomas are generally slow growing tumors, commonly diagnosed in the third decade of life. The exact aetiology of thymoma is unknown but has been linked to autoimmune diseases such as myasthenia gravis, cytopenias, hypogammaglobulinemia, systemic lupus erythematosus (SLE), rheumatoid arthritis, thyroiditis, Sjogren's syndrome and ulcerative colitis. Most patients with thymomas are asymptomatic but can present with systemic symptoms of cough, tiredness and autoimmune disease. Thymomas may cause local symptoms associated with compression of surrounding structures. About 30% of patients with thymomas have myasthenia gravis (7), but only 21% of patients with myasthenia have thymomas (8). Thymomas are primary tumors of thymic epithelial cells. They are generally considered cytologically benign whereas thymic carcinomas have malignant cytological features. Thymic carcinoma carries a significantly worse prognosis (9-11).

The World Health Organisation (WHO) has developed the most widely adopted classification system for thymic epithelial tumor by taking into account both histological and morphological features (12).

There are two staging systems for thymic epithelial tumors (13). The most widely used staging system was first described by Masaoka and colleagues in 1981, and is a clinical system describing thymomas in terms of local extension of the tumor (14). The TNM staging follows the pattern of T for tumor descriptor, N for nodal spread and M for distance metastasis, and is primarily used as a research tool.

VATS thymectomy approaches

Radical thymectomy involves the removal of all the soft tissue in the pre-vascular plane between the two phrenic nerves. For patients with myasthenia, ectopic thymic tissue may be found anywhere in the pre-vascular space. Surgical success in controlling myasthenia and post-operative survival outcomes in patients with thymomas depends on the completeness of thymic tissue resection and clearance (15). VATS approaches include bilateral and unilateral VATS (either left or right). There is controversy over the exact technique and, in particular, whether the thymus should be approached from the left, right or bilaterally. Mineo *et al*. suggested that dissection manoeuvres are safer from left side because the superior vena cava lies outside the surgical field. Thus the authors suggested that dissection of the peri-thymic fatty tissue around the left peri-cardiophrenic angle can be more readily carried out from the left side (16).

Alternatively, surgeons who are using the right-sided approach have advocated that the superior vena cava can be clearly identified from the right and used as a landmark to dissect around the innominate veins. It is also comfortable for the right handed surgeon to start at the inferior pole by allowing greater manoeuvrability of instruments in a wider right pleural cavity, especially in patients with cardiomegaly (17).

Surgeons who use the bilateral VATS approach advocate that it allows better visualisation of key anatomical structures and therefore facilitates complete excision. The laterality of approach remains largely on surgeon preferences, which are influenced by their experience and training (18).

Overall, individual case series have reported data that support the validity and success of all the approaches; however, there are insufficient large prospective studies to show whether one VATS thymectomy technique is superior to another (19-21). Irrespective of the VATS approach used to access the mediastinum, VATS thymectomy carries the benefit of minimizing trauma and removing all thymic tissue including ectopic thymic tissue, which may be scattered in the anterior mediastinum and cervical fat.

Limitations of VATS

Theater charges represent 30% of the cost of treating a surgical patient. There is a steep learning curve associated with VATS procedures, leading to increases in theatre operative time and cost. However, operative time improves with experience. Another concern has been raised over the possibility of capsular rupture and risk of pleural spread with the VATS approach. This concern is not substantiated by published evidence. Lucchi *et al*. have

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reported pleural recurrence after VATS thymectomy as well as sternotomy (22). In Kimura's series, three (6.7%) cases with VATS approach had disease recurrence with pleural dissemination (23). Of the three, two had capsular injury during VATS resection and the tumor size in all the three patients was more than 5 cm. Both these studies were retrospective and non-randomised with relatively small sample size. However, in reviewing the rates of recurrence and other complications, there is no convincing evidence that sternotomy is a better approach than VATS for thymectomy.

Discussion

In spite of controversies, VATS thymectomy is gaining popularity and several studies have demonstrated the superiority of the VATS approach over sternotomy. The potential benefits include a smaller incision away from the midline leading to better cosmesis, less trauma to the chest wall, faster healing, earlier return to normal activities and work, decreased post-operative length of stay, decreased cytokines, complete remission and no difference in outcome as compared to the open approach. Less trauma and faster healing times also permit earlier administration of adjuvant chemo-radiation treatment in advanced cases (24-27).

There is perception that the open (median sternotomy) approach offers better visualisation but it is more invasive and confers greater morbidity. The trans-cervical approach through a small horizontal incision across the lower part of the neck is less invasive. Shorter recovery period has been advocated by Cooper *et al*. in their review of long term clinical outcome after trans-cervical thymectomy (28). The limited follow up data in the review made interpretations difficult. There are technical issues with the trans cervical approach such as limited neck extension in the elderly and access to rare thymic extensions behind the left brachiocephalic vein. This novel approach undoubtedly has its advantages but may be difficult to be mastered.

On the contrary, VATS offers superior illumination and magnification, especially with the availability of advanced cameras with variable angles that provide better exposure and lighting of the operative field (7,29). The lack of three-dimensional (3D) vision during early days of VATS has been addressed with 3D-operating imaging (30). In the initial phase of the surgeon's "learning curve", operative time may be prolonged with VATS but improves with experience.

Published data has demonstrated comparable mortality results in thymectomy by VATS and sternotomy, and no significant differences in mid- to long-term complications rates or survival (31,32). However, the VATS approach is more advantageous in the immediate post-operative period and short-term outcomes.

Other factors that make VATS a superior approach include less intra-operative blood loss, early removal of chest drains and reduced requirement for blood products (20). With the VATS approach, there is reduced risk of respiratory and cardiac related complications (e.g., pneumonia, pleural effusion or arrhythmias) as compared to the open (sternotomy) technique. These complications require specific treatment that leads to slower recoveries and prolonged hospital stays (21,31). Furthermore, decreased post-operative length of stay with VATS approach benefits both the patient and the hospital. It is beneficial for the patient as it enables rapid return to normal activities (7) and reduced length of stay permits the organisation to treat more patients. In the current era of significant economic pressure, VATS approach is more cost-effective than sternotomy. Although there is initial investment required in a VATS setup, this has become standard equipment in the operating theatre. In the long term, VATS wins the economic argument through benefits of reduced hospital stay, less post-operative complications and improved patient turnover (33,34).

VATS has shown promise as a superior oncological technique as a result of its effect on the immune system. Surgical trauma has long been recognised to cause a systemic inflammatory cytokine response, resulting in increased circulating levels of interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α). Although there are no studies comparing the systemic inflammatory response in patients undergoing thymectomy with various surgical approaches, several studies have compared the open and minimally invasive thoracic procedure techniques and demonstrated attenuated immune-chemokine disturbance with VATS procedures (35).

Surgical tissue trauma is rapidly followed by a complex cascade of inflammatory signalling and activation of epithelial, endothelial and inflammatory cells, platelets and fibroblasts. Recent research has identified that many of the growth factors, chemokines, and cytokines released in the wound healing process may promote local and distant tumor progression (36). There is also circumstantial evidence that in some patients, cancer surgery may actually provoke growth of distant metastases (37). Studies comparing open and minimal access techniques have demonstrated that reduced trauma following minimal access compared with

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conventional open thoracic surgery results in reduced postoperative C-reactive protein, IL-6, and IL-8 responses (38,39). Collectively, all these factors promote rapid recovery and healing and facilitate early post-operative multi-modality intervention.

Disadvantages of sternotomy

Thymectomy for thymomas has traditionally been performed through a trans-sternal approach. Complications of deep sternal wound infection with reported incidences range from 0.4% to 5% (40), leading to prolonged morbidity and long-term mortality. The incidence of this increases with advanced age, obesity, diabetes, smoking, COPD and steroid therapy. Many patients with myasthenia gravis are on steroids, further increasing the risk of sternal wound infection or wound dehiscence.

Sternotomy can cause significant post-operative pain and increased risk of respiratory complications that require dedicated post-operative care, prolong hospital stay and delayed return to normal life and work.

Sympathetic stimulation that occurs with sternotomy may result in arrhythmias and can lead to hemodynamic instability requiring close cardiac monitoring and management. Other significant complications of sternotomy include brachial plexus injury from sternal retraction, pseudoarthrosis, long-term neuropathic pain and large scars with the risk of keloid formation and hypertrophy that may affect cosmesis. All these complications can lead to significant morbidity, distress for patient and delayed recovery.

Conclusions

VATS thymectomy is a safe and sound technique for thymectomy. It has the advantages of fewer complications, being minimally invasive and facilitating faster recovery. The VATS approach should be encouraged, as more surgeons are adopting minimally invasive practice as routine.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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