Literature Review

Prognosis in Thymoma Patients with Myasthenia Gravis Undergoing Video-Assisted Thoracoscopic Surgery (VATS) Thymectomy: An Evidence-Based Case Report

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Abstract

Background: Thymoma, a tumor in the anterior mediastinum, is common in adults and often linked with myasthenia gravis (MG). Thymectomy is recommended for MG patients with thymoma and traditionally done via median sternotomy, which is invasive. Minimally invasive methods like video-assisted thoracoscopic surgery (VATS) offer benefits like less blood loss and quicker recovery. However, more extensive studies are needed to confirm long-term oncological outcomes.

Methods: A literature search was conducted using PubMed, Cochrane, and Scopus databases focused on terms related to thymoma, myasthenia gravis, VATS thymectomy, and survival. Duplicates were excluded, and studies were selected based on criteria. The selected studies were then critically appraised for validity, importance, and applicability.

Results: Three manuscripts are selected for this case report. He et al showed that the cumulative CSR in the VATS group (26.7%) was significantly higher than the transsternal group (*P*=0.026). Maggi et al reported that the VATS group is significantly correlated with CSR (*P*=0.0349). Meanwhile, Tian et al showed there was no significant difference in the level of CSR (32.7% vs. 36.7%; *P*=0.622) between the VATS and trans-sternal groups. Tian et al also showed that survival results in the VATS group were higher than in the trans-sternal group, but it was not statistically significant (*P*=0.109).

Conclusion: The prognosis of thymoma patients with MG who undergo thymectomy using the VATS method is not significantly different compared with the trans-sternal method.

Keywords: CSR, myasthenia gravis, survival, thymoma, VATS

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INTRODUCTION

Thymoma is a type of tumor in the anterior mediastinum that is more common in adults.[1,2] Thymoma is generally considered a benign tumor, but it can become malignant. Although the cause of the development of this tumor is not yet known with certainty, there is a relationship between this tumor and several conditions, one of which is myasthenia gravis.[3]

Myasthenia gravis (MG) is an autoimmune disorder because IgG autoimmune antibodies target muscle nicotinic acetylcholine receptors (AChR), disrupting postsynaptic neuromuscular transmission. The relationship between thymoma and myasthenia gravis (MG) is quite significant. Approximately 50% of thymoma patients develop MG, while 10–20% of patients with MG also have thymoma. This interconnection occurs because of the relationship between thymus tissue function and the development of myasthenia gravis.[4]

The presence of a thymic tumor is a class I recommendation for thymectomy to be done in patients with myasthenia gravis.[5] Generally, trans-sternal thymectomy using the median sternotomy approach is considered the traditional gold standard. Sternotomy is carried out by splitting the sternum bone, and then fixation will be carried out using wire sutures after the operation is complete. Although median sternotomy allows for a more complete and thorough thymectomy, it is associated with relatively greater surgical trauma.[6–8] Other approaches, such as video-assisted thoracoscopic surgery (VATS), may also be used for thymectomy. Video-assisted thoracoscopic surgery is a minimally invasive surgery that uses a video camera with a keyhole incision. In this method, neither the bones are broken

nor the ribs are stretched.[9]

Research shows that minimally invasive approaches to thymectomy have several advantages over trans-sternal approaches. Minimally invasive is generally associated with less blood loss, shorter duration of chest tube use, less postoperative pain, quicker patient mobilization, shorter hospital stay, and better outcomes in terms of postoperative scars.[6,10] Although short-term results demonstrate the effectiveness of the VATS approach, medium- and long-term oncological data regarding survival rates and complete stable remission (CSR) in larger studies are still very limited.[11]

METHODS

A literature search was performed on April 21st, 2024, using three databases, including PubMed, Cochrane, and Scopus. The keywords were “Thymoma”, ”Myasthenia Gravis”, “Video-assisted thoracoscopic surgery”, “Thymectomy”, “Complete stable remission”, and “Survival” with their synonyms and related terms, which are shown in Table 1.

We found 126 articles based on the keywords. The articles were then filtered to eliminate duplicates. Articles were selected using inclusion criteria such as articles with thymoma patients with myasthenia gravis, articles comparing outcomes between VATS thymectomy and trans-sternal thymectomy, and systematic reviews with/without meta-analysis of prognostic studies or cohort design studies. The search strategy is shown in Figure 1. The selected studies were critically appraised for their validity, importance, and applicability.

RESULT

Following the search strategy, three original articles were eligible for this evidence-based case report (EBCR), which discusses VATS and trans-sternal thymectomy in thymoma patients with myasthenia gravis who meet our inclusion and exclusion criteria.[12–14] The design and summary of results are available in Table 2. The critical appraisal is shown in Table 3. All articles were cohort studies with a level of evidence of 2.

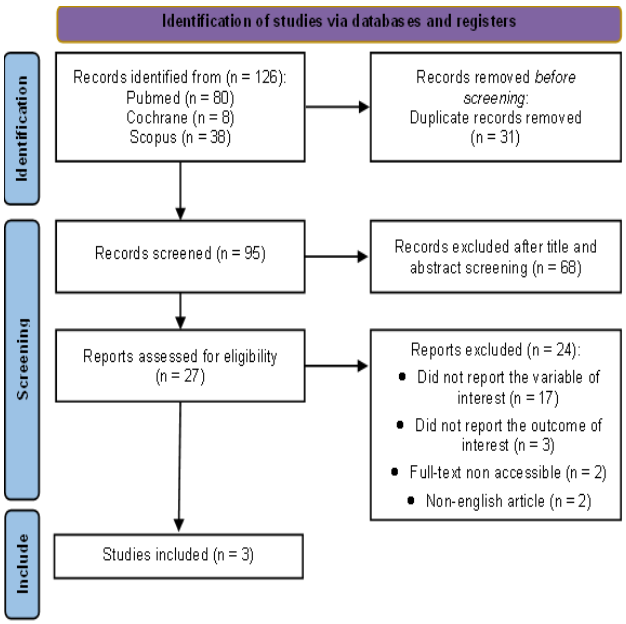

Figure 1. Flow-chart of search strategy

He et al performed a retrospective cohort study on 33 MG patients with homogeneously distributed thymoma undergoing VATS thymectomy (n=15) or trans-sternal thymectomy (n=18) from April 2006 to September 2011.[12]

Table 1. Terminology used in three databases

Database	Terminology	Hits	Selection
Pubmed	((((((Thymoma[MeSH Terms]) OR (Myasthenia gravis[MeSH Terms])) OR (Thymoma[Title/Abstract])) OR (myasthenia gravis[Title/Abstract])) OR (MG[Title/Abstract])) AND ((((VATS Thymectomy[Title/Abstract]) OR (video-assisted thoracoscopic surgery thymectomy[Title/Abstract])) OR (video-assisted thoracoscopic surgery thymectomy[MeSH Terms])) OR (VATS thymectomy[MeSH Terms]))) AND ((Survival[Title/Abstract]) OR (survival[MeSH Terms]) OR (CSR[Title/Abstract]) OR (Complete stable remission[Title/Abstract]))	80	3
Cochrane	((("Myasthenia gravis"):ti,ab,kw OR ("MG"):ti,ab,kw OR ("thymoma"):ti,ab,kw) OR (MeSH descriptor: [Myasthenia Gravis] explode all trees) OR (MeSH descriptor: [Thymoma] explode all trees)) AND (((VATS Thymectomy):ti,ab,kw OR (video-assisted thoracoscopic surgery thymectomy):ti,ab,kw OR (thymectomy):ti,ab,kw) OR (MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees)) AND (((survival):ti,ab,kw) OR (MeSH descriptor: [Survival] explode all trees) OR (complete stable remission):ti,ab,kw))	8	0
Scopus	TITLE-ABS-KEY ("Thymoma" OR "Myasthenia Gravis" OR "MG") AND TITLE-ABS-KEY ("VATS Thymectomy" OR "video-assisted thoracoscopic surgery thymectomy") AND TITLE-ABS-KEY ("survival" OR "complete stable remission" OR "CSR")	38	0

Table 2. Characteristics of selected studies

Author (Year)	Title	Sample Size	Study Design	Effect Size	LoE
He, et al. (2013)	Surgical approaches for stage I and II thymoma-associated myasthenia gravis: feasibility of complete video-assisted thoracoscopic surgery (VATS) thymectomy in comparison with trans-sternal resection	33	Retrospective cohort	Cumulative CSR in the VATS thymectomy group (26.7%) was significantly higher than the trans-sternal thymectomy group (*P*=0.026)	2
Maggi, et al. (2008)	Thymoma-associated myasthenia gravis: Outcome, clinical and pathological correlations in 197 patients on a 20-year experience	197	Prospective cohort	• Univariate analysis: VATS thymectomy was significantly correlated with CSR (*P*=0.0349) • Multivariate analysis: Odds of CSR by surgical approach (VATS vs. trans-sternal) 8/71 (11.3%) vs. 11/126 (8.7%) (OR=2.274; 95% CI=0.83-6.21; *P*=0.1090)	2
Tian, et al. (2020)	Surgical effect and prognostic factors of myasthenia gravis with thymomas	194	Retrospective cohort	• Univariate analysis: There was no significant difference in CSR rate between the VATS and trans-sternal groups (32.7% vs. 36.7%, *P*=0.622) • Multivariate analysis: Survival analysis of VATS vs. trans-sternal surgical procedures on CSR was obtained HR=1.228 (95% CI=0.694-2.833; *P*=0.422) • Multivariate analysis of VATS and trans-sternal surgical procedure variables on survival obtained HR=1.502 (95% CI=0.348-6.493; *P*=0.586)	2

Table 3. Critical appraisal of the three studies based on the criteria by the Center for Evidence-Based Medicine, University of Oxford

Parameter	He et al.[12]	Maggi et al.[13]	Tian et al.[14]
Validity			
Was the defined representative sample of patients assembled at a common (usually early) point in the course of their disease?	Yes	Yes	Yes
Was patient follow-up sufficiently long and complete?			
Sufficiently long	Yes	Yes	Yes
Complete	Yes (DO 0%)	Yes (DO 0%)	Yes (DO 12.4%)
Were outcome criteria either objective or applied in a 'blind' fashion?	No	No	No
If subgroups with different prognoses are identified, did adjustment for important prognostic factors take place?	No	Yes	Yes
Importance			
How likely are the outcomes over time?	CSR in VATS is higher compared to trans-sternal (4/15, 26,7%)	CSR in VATS is higher compared to trans-sternal: 8/71 (11.3%) vs. 11/126 (8.7%)	• Out of a total of 162 patients, there were a total of 55 patients who achieved CSR. • There was no significant difference in CSR rate (32.7% vs. 36.7%, *P*=0.622). • OS rate at five years in VATS was higher than trans-sternal (81.9%).
How precise is this prognostic estimate?	CSR (95% CI=0.043–0.491)	CSR (95% CI=0.83–6.21)	CSR (95% CI=0.694–2.388) Overall survival (95% CI=0.348–6.493)
Applicability			
Is my patient so different to those in the study that the results cannot apply?	No	No	No
Will this evidence make a clinically important impact on my conclusions about what to offer to tell my patients?	Yes	Yes	Yes

Note: DO=Drop Out; CSR=Complete Stable Remission; OS=Overall Survival

The follow-up time range was approximately 12–61 months, and no patients dropped out of this study. The cumulative probability of achieving CSR was 26.7% (4 out of 15; 95% CI=0.043–0.491; *P*=0.026) in the VATS group.[12]

Maggi et al conducted a prospective study on 197 patients with thymoma and MG undergoing VATS thymectomy (n=71) or trans-sternal thymectomy (n=126) with a follow-up period of 20 years, starting in 1986 and ending in December 2006. No mortality was observed during the postoperative follow-up period or due to surgery-related complications. The mean patient follow-up period was 7.69±6.0 years, and there were no patient dropouts in this study.

Univariate analysis showed that VATS surgical procedures were significantly (*P*=0.0349) correlated with CSR rates compared with trans-sternal procedures. When the chance of achieving CSR, using the Kaplan-Meier curve analysis, showed that patients who underwent the VATS technique were better in the 5th, 10th, and 15th years, but were not different from the trans-sternal technique at the 20th year after thymectomy (*P*=0.029).[13]

Meanwhile, based on multivariate analysis of several variables, including age, clinical stage of MG, tumor stage, and surgical approach, the probability of CSR occurring in the VATS procedure obtained an OR value of 2.274 (95% CI=0.83-6.21; *P*=0.1090). This study also showed that the VATS procedure was not associated with an increased risk of thymoma recurrence (*P*=0.1523).[13]

Tian et al performed a retrospective cohort study on 194 MG patients with thymoma who underwent VATS thymectomy (n=137) or trans-sternal thymectomy (n=57) from January 2010 to December 2018. The median patient follow-up period was 45 months (range=2–114 months), and there were 24 patients who dropped out, so the number of patients who completed this study was 170 samples (87.6%).

In the entire group, the overall five-year survival rate was 81.9%. The probability of survival in each procedure group, using Kaplan-Meier curve analysis, showed that survival with the VATS technique was better until the 5th year but did not differ from the trans-sternal technique in subsequent years (*P*=0.109). Multivariate analysis of VATS and trans-sternal surgical procedure variables on survival found HR=1.502 (95% CI=0.348–6.493; *P*=0.586).[14]

In the study by Tian et al, after undergoing the procedure, 162 patients had their MG status evaluated, and it was found that 55 patients achieved CSR. The cumulative CSR rate was 19.3% at the end of the second postoperative year and increased to 44.1% at the end of the fifth year. There was no significant difference in the CSR rate (32.7% vs. 36.7%; *P*=0.622) between the VATS and trans-sternal groups. The probability of achieving CSR in each procedure group, using Kaplan-Meier curve analysis, showed that CSR in the VATS technique is better until the 3rd year but is not different from the trans-sternal technique in the following years (*P*=0.751). Multivariate analysis of VATS and trans-sternal surgical procedure variables on CSR obtained HR=1.228 (95% CI=0.694–2.833; *P*=0.586).[14]

DISCUSSION

Based on the validity components, all three studies were adequately valid. These were cohort studies with a sufficient follow-up period. Tian et al. had only successfully followed 87.6% of patients, which is still tolerable. The others successfully followed all the participants. All the studies had equal participants in both groups, who were patients who had both thymoma and MG. All these studies couldn't be done in a “blind” fashion because before the procedure, the surgeons had to explain the procedure with its risks and complications. Besides that, the surgical scars were significantly different between VATS and trans-sternal thymectomy.[12–14]

For importance, two out of three studies showed a significant difference in CSR rate between VATS and trans-sternal thymectomy. He et al. and Maggi et al. reported that VATS has a protective effect, which is shown as a higher CSR rate than trans-sternal.[12,13] Maggi et al. showed that the chance of achieving CSR in patients who underwent the VATS technique was better in the 5th, 10th, and

15th years but was not different from the trans-sternal technique at the 20th year after thymectomy.[13]

However, Tian et al. reported that there was no significant difference in CSR rate between VATS and trans-sternal groups. When looking at the chances of achieving CSR in each procedure group, the VATS technique was only better until the 3rd year, but was no different from the trans-sternal technique in subsequent years. Tian et al. also reported the survival outcome, but the results were not significant. The probability of survival in the VATS technique was better until the 5th year, but did not differ from the trans-sternal technique in the following years.[14]

For the application in our case, surgery for thymoma must refer to national and international guidelines. International guidelines state that surgeons must be experienced in treating thymomas and carcinomas. Minimally invasive surgical skills require sufficient case accumulation for an optimal learning curve. The more cases handled, the better the skills a surgeon will acquire. Hospitals with high VATS volumes (high-volume centers) will certainly produce different outcomes than those with low VATS volumes (low-volume centers).[15]

Regardless of the approach used, whether VATS or transsternal, the oncological principle of performing complete tumor resection cannot be compromised. This aims to achieve complete remission to achieve the best prognosis. Although minimally invasive approaches are still not routinely used due to a lack of long-term data. Minimally invasive treatment can still be done if the oncological goals are achieved. If you want to do it, do it at a central hospital and with an experienced surgeon.[15]

Across the three studies, although there were variations in the results, overall, the VATS approach showed better potential for achieving CSR in thymoma patients with MG and showed a higher survival rate compared with trans-sternal thymectomy until a certain period of time, and after that, the results were equal between VATS and open surgery. These findings indicate that the thymectomy procedure using the VATS approach in thymoma patients with MG is a safe and more desirable option to achieve optimal results.[15]

However, it should be remembered that these studies were conducted in hospitals with a fairly high volume of VATS procedures (high-volume centers). Therefore, apart from considering the patient's condition when deciding on VATS procedures, it is also necessary to consider the hospital where the procedure is performed and the surgeon's clinical skills.[15]

CONCLUSION

There is no evidence to suggest that thymectomy procedures using the VATS method have higher risks or are less safe compared to trans-sternal procedures. This is true both in achieving CSR and in terms of survival of thymoma patients with MG. Thus, the prognosis of thymoma patients with MG who undergo thymectomy using the VATS method is not significantly different compared with the trans-sternal method.

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CONFLICT OF INTEREST

None.

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