



Trends in thymus surgery: the turning point for minimally invasive thymectomy?

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Over the last 30 years thoracic surgeons have witnessed the slow adoption of video-assisted thoracic surgery (VATS) in their routine, and this was one of the most important surgical skill shifts for a generation of surgeons. Nevertheless, it took several years to scientifically demonstrate that VATS could represent a cost-effective procedure with few complications, reduced pain, shorter length of stay, and an improvement in the postoperative quality of life of patients (1,2). Despite those advantages, some institutions preferred to stick to conventional approaches, especially to treat oncological thoracic diseases, as they understood that there was no clear benefit of VATS over the long-established open approach.

Surgery of the thymus faces the same paradigms, but with the additional challenge of being much less common than other thoracic procedures such as lung resection (3). This fact impairs the development of larger studies and comparison of different surgical techniques. The implementation of robotic-assisted surgery in the 2000s was considered a significant progress in minimally invasive thoracic surgery and, since then several authors described their experience with robotic (RATS) thymectomy both for nonthymomatous myasthenia gravis (MG) and thymomas. Unfortunately, those reports are frequently restricted to single-center retrospective studies, thus, the present analysis of National Inpatient Sample (NIS) of Seo *et al.* with more than 23,000 subjects is one of the first studies to shed a light of the current panorama in thymus surgery over the last decades (4).

The presented temporal trend shows that the open technique had a gradual decline between 2008 and 2014.

While it was performed in 78% of the patients in 2008, it was adopted in only 53% of the cases in 2014. The same tendency was observed among 16,895 lung resections in US in a recent database analysis (Veteran Affairs Surgical Quality Improvement database) that found that the adoption of thoracotomy for lung resection declined from 78% to nearly 30% between 2008 and 2018 (5). The same authors evaluated this transition for thymectomy and showed that VATS thymectomy increased from 0% to 61% between 2008 and 2019 (6). If the present study had extended their analysis to the second half of 10s, we would probably see the predominance of minimally invasive surgery (MIS) techniques over the open approach, considering the observed pace of growth of VATS/RATS between 2008 and 2014.

It is also noteworthy the steep increase of RATS adoption when compared to VATS. If we consider that the videothoracoscopic approach took 15 years to reach the proportion of nearly 20% among all thymectomies, after the first report of a VATS thymectomy by Sugarbaker in 1993, it is remarkable that the robotic technique increased from 0% to 23% in less than half of the time (2008–2014) (7). The escalation of MIS techniques in the present study was mainly due to an increase of RATS and not to the VATS approach. This broad acceptance may be due to the dexterity that RATS provides for narrow anatomical regions and manipulation of critical structures, such as those located in the mediastinum. Still, some of the reasons for not fully embracing this technology include the lack of tactile feedback, the need of long-term follow-up data, the alleged drawbacks when dealing with bigger and/or complex

lesions, and, finally, the associated costs (8).

The supposed advantages of RATS thymectomy over VATS are related to dexterity, accuracy and consequently the greater potential to resect complex lesions. However, both techniques are not so different concerning its physiological implications and surgical trauma. In this way, it was not expected that significant differences were going to be found on parameters such as mortality. Indeed, among more than 7,200 patients submitted to the MIS procedure no in-hospital deaths occurred, reflecting the similar safety of both techniques.

Two meta-analysis published in 2019 and 2022 compared the results of RATS and VATS thymectomy (9,10). The 2022 study included all papers of the 2019 paper and another 4 studies released between 2019–2020. Curiously, while in the 2019 study no significant differences in length of stay could be found (weighted mean difference -0.81 , 95% CI: -2.22 to 0.59), the 2022 one found a reduced length of stay favoring the RATS approach (weighted mean difference = -1.07 , 95% CI: -1.74 to 0.41). This is an interesting finding since the difference could be possibly related to a higher level experience with RATS in more recent studies. This may be the underlying reason for the fact that a similar difference was observed in the present database analysis, which only covers the period between 2008 and 2014, although it was not statistically significant.

The authors also assessed the occurrence of complications of both techniques and found a similar proportion among both groups (VATS 18% *vs.* RATS 19%). The most recent meta-analysis comparing both approaches evaluated the complications among 598 subjects and found that the RATS approach was associated with few events (odds ratio = 0.53 ; 95% CI: 0.31 to 0.91) (9). One of the hypotheses to explain this discrepancy is the contrasting methodology inherited each study design and their consequences regarding patient selection and real-world representativeness.

Nevertheless, when complication events are scrutinized two interesting findings stand out. The oddly six times higher occurrence of cardiac events among VATS patients is intriguing, since it has already been shown in some series of lung resections a lower occurrence of those events when compared to the RATS technique (11). As stated by the authors, the NIS database does not focus on evaluating specific causes of the complications and, thus, any assumptions concerning this data should be made cautiously. Further research could focus on investigating the postoperative complications of those patients and, thus, those mechanisms could be better understood.

During thymectomy, hemorrhage due to accidental lesion of the several surrounding vessels is one of the major concerns. On that sense, the lower rate of this complication among the RATS group may be a consequence of the mentioned advantage of this approach regarding the capability of manipulation in narrow spaces like the mediastinum. It would be interesting if the authors had evaluated the conversion rates of each MIS approach as well, as this may be considered a general indicative of the difficulties associated with a specific technique. A recent comparison of RATS *vs.* VATS with more than 857 patients evaluated the perioperative outcomes of each procedure. There were no differences regarding 30- or 90-day mortality, but RATS had significantly ($P < 0.001$) better results considering the conversion to the open approach (4.95% *vs.* 14.7%; OR = 0.33), adverse composite outcome (36.7% *vs.* 51.3%; OR = 0.44), and lower rate of positive pathologic margins (24.3% *vs.* 31.6%; OR = 0.59) (12).

Historically, some factors were considered as indicatives for the preference of the conventional approach such as a lesion located in the middle/posterior mediastinum, absence of a clear plane between the tumor and surrounding structures, bilateral tumors, and size. Kneuert *et al.* compared the outcomes of the resection of large thymomas between VATS and conventional techniques (13). The proportion of each Masaoka stage, median tumor size and WHO histologic classification were the same for both groups. There were no differences in most evaluated parameters such as complications, margin status, etc. The only differences that were found, favored the RATS resection, and were related to estimated blood loss (150 *vs.* 25 mL), number of chest tubes (single tube: RATS 85% *vs.* open 56%) and length of hospitalization (3 *vs.* 4 days). Those findings show that old paradigms of the limitations of MIS are gradually being overcome as the experience with the robotic systems increases.

Costs remain of the main limiting factors for a broader adoption of RATS by healthcare providers in several surgical specialties, including thoracic surgery. The abovementioned database analysis shows that VATS is associated with a lower cost, followed by open and RATS. The difference between VATS and RATS was statistically significant, with the latter being 18% more expensive (US\$14,903 *vs.* US\$17,672). Unfortunately, eight years have passed since the last year evaluated on the database and, so, considering that costs are dynamic, this analysis may be outdated.

While the costs of open and VATS approaches may have stabilized over the years considering that they did not have any substantial change in their technology, the same

rationale is not true for robotic surgery. The launch of other robotic systems other than Da Vinci is about to see the light of the day, after two decades of intuitive hegemony. This will probably be a breakthrough in robotic surgery because for the first-time there will be a real competition in the market and not only a reduction in the costs is expected but an expansion in the use of those systems (14).

Over the last years, some authors published their long-term follow-up data after thymectomy considering neurologic and oncological outcomes for myasthenia and for thymoma isolated, respectively (9). Still, one of the major obstacles for a broader adoption of MIS thymectomy is the lack of high-quality evidence of the long-term results of those techniques. Thymectomy for myasthenic patients is a good example of this scarcity, considering that the first large trial [Thymectomy Trial in Non-Thymomatous Myasthenia Gravis Patients Receiving Prednisone Therapy (MGTX)] to demonstrate the benefits of thymus resection for myasthenia gravis was only released in 2016, despite being performed for the first time for this disease in 1936 by Alfred Blalock (15,16). The same happens to thymomas which are usually indolent tumors, and a long lapse of time is required to evaluate the actual benefits of any technique. The proportion of adoption of each technique indicated in the present study, suggests that larger trials with a considerable number of patients are now feasible. The development of such studies could be milestones on the shift from the conventional to MIS thymectomy.

For every surgical procedure, there is a continuous search for faster recoveries, better cosmetics, and safety. Currently, MIS thymectomy can fulfill the expectations of patients and surgeons regarding those variables, except for long-term outcomes for which there is still a gap in the literature. RATS significantly increased its popularity over the last few years and is possibly going to lead the definitive transition from the open approach to MIS thymectomy. The ongoing worldwide implementation of robotic surgical systems, which could be stimulated by a reduction on its cost, will allow surgeons to go even further in the possibilities of resection of thymus lesions.

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