Relevance of robotic surgery for thymoma: a narrative review

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Background and Objective: Thymectomy with median sternotomy is the gold standard for thymoma and myasthenia gravis, although minimally invasive procedures such as robot-assisted surgery have recently become more common. However, the superiority of these approaches has not been established, and they are infrequently recommended for localized lesions. The International Thymic Malignancies Interest Group warned that despite the perceived reduction in length of hospital stay and pain, the benefits of these approaches compared to the open approach have not been fully substantiated and that prospective collaborative data collection is critical in defining the value of these techniques. Whether thymectomy is necessary for stage I thymomas in the absence of myasthenia gravis or anti-acetylcholine receptor antibodies is also unclear. This study reviews and discusses the literature on this subject.

Methods: A narrative review was conducted using PubMed and Scopus databases. Original research articles comparing robotic to video-assisted thoracic surgery or to open thymectomy for thymomas were included. A comparison of partial resection and total thymectomy (thymothymectomy) for thymomas was also conducted.

Key Content and Findings: Perioperative outcomes such as blood loss, operative duration, complications, and length of hospital stay were better for robot-assisted resection of early-stage thymomas than for open thymoma surgery. It would be premature to consider partial resection as an appropriate treatment option for thymomas.

Conclusions: Robotic thymothymectomy is safe with effective and promising long-term results and oncological and surgical outcomes in patients with thymoma. Robotic thymectomy can become the standard procedure in patients with early-stage thymomas.

Keywords: Robotic surgery; thymoma; da Vinci; thymectomy

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Introduction

Background

Thymomas are rare neoplasms that exhibit a wide range of behaviors, from indolent to fatal (1). However, several unanswered questions require further research. Thymectomy is the standard procedure for thymoma treatment and an important component of multidisciplinary treatment for myasthenia gravis. Although there are several approaches to thymectomy, including minimally invasive approaches, median sternotomy remains the golden standard (2). However, in recent years, treatment methods have changed significantly with the widespread use of minimally invasive approaches. The advent of robot-assisted surgery has led to several innovations. Since Yoshino *et al.* first performed robotic surgery for thymoma in 2001, various approaches to robotic surgery have been developed (3). Although the use of video-assisted thoracic surgery (VATS) or robot-assisted



Figure 1 Extent of resection. Partial thymectomy removes a portion of the thymus gland with a margin from the tumor (solid line); thymothymectomy removes the same area as a total thymectomy (dotted line).

thoracic surgery (RATS) has increased in recent years, its superiority over conventional open thoracic surgery has not been established, and it is infrequently recommended as an approach for localized lesions (4-6). It is unclear whether thymectomy is necessary for stage I thymomas without symptoms of myasthenia gravis or the presence of antiacetylcholine receptor antibodies. Although the extent of resection is not of considerable concern with sternotomy, the difficulty of complete dissection has led to a debate that should be resolved as minimally invasive approaches become more popular: whether thymectomy is necessary for localized thymomas or localized resection is sufficient (*Figure 1*). No coherent reports on this subject have been reported and no definite conclusions have been drawn. Therefore, we review and discuss the literature on this subject.

The curative treatment for thymic epithelial tumors is surgical resection. If thymic epithelial tumors are suspected on imaging and complete resection is possible, surgical treatment is performed without pathological biopsy. The principal surgical technique is thymectomy through median sternotomy. In particular, patients with myasthenia gravis are indicated for extended thymectomy, wherein the fatty tissue below the thyroid gland in the anterior cervical region is resected.

Rationale and knowledge gap

The thoracoscopic approach to stage I-II thymomas is an

acceptable technique according to the Japanese guidelines, though the level of evidence is low (4-8). The Japanese guidelines have provided the same level of recommendation as for thoracoscopic surgery. However, minimally invasive surgery is not routinely recommended in the National Comprehensive Cancer Network guidelines because of the lack of long-term results and evidence (9-13).

Objective

The use of robotic surgery for thymomas has increased in recent years. We outline the protocol for robotic surgery for thymoma, and review the literature to clarify the suitability of the robotic surgical approach and the extent of resection that should be performed. In addition, we also consider whether thymectomy is necessary or partial resection is sufficient in cases of localized thymoma. We present this article in accordance with the Narrative Review reporting checklist (available at https://med.amegroups.com/article/ view/10.21037/med-23-37/rc).

Methods

Literature search strategy

Thymectomy-specific publication searches were conducted using PubMed and Scopus databases to find relevant publications for this clinical evaluation (*Table 1*). Publication searches were conducted as listed: (robot[All Fields] OR robot assist[All Fields] OR robotic[All Fields] OR da vinci[All Fields] AND "surgery"[all fields] AND "thymoma"[all fields]).

All citations returned from the above searches were exported into an EndNote library. Duplications were removed and titles and abstracts were reviewed by two authors (M.M., A.W.) for inclusion in the library.

Review

Surgery

For reference, we outline the protocol of thymoma surgery used in our department. Since 2018, we have been performing robotic surgery for thymomas using the da Vinci Xi Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) in our department (14). The patient's position is shown in *Figure 2*. The robotic 8 mm port was placed between the second and eighth intercostal spaces, according to the patient's physique. Four robotic arms were placed

Table 1 The search strategy summary

| Items | Specification |
|---|--|
| Date of search | January 1 st , 2023 and August 31 st , 2023 |
| Databases and other sources searched | PubMed, Scopus |
| Search terms used | MeSH: (robot[All Fields] OR robot assist[All Fields] OR robotic[All Fields] OR da vinci[All Fields] AND "surgery"[all fields] AND "thymoma"[all fields]) |
| Timeframe | From January 2010 to August 2023 |
| Inclusion criteria and exclusion criteria | Inclusion: original articles, review. Exclusion: case report, abstract of meeting |
| Selection process | M.M. and A.W. conducted the selection. Consensus of all authors was obtained |



Figure 2 Port placements. Robotic 8-mm ports were placed in the second, fourth, sixth and seventh intercostal space. Then, an assistant port with a 12-mm air seal port placed in the sixth intercostal space.

(*Figure 2*). Fenestrated bipolar forceps, an 8-mm endoscope, Maryland-type bipolar forceps, and Vessel Sealer Extend (Intuitive Surgical Inc.) were used. The port placed at the sixth intercostal space was used as an assistant port with a 12-mm air-seal port (Medical Leaders Inc., Tokyo, Japan). The intraoperative thoracic carbon dioxide insufflation pressure was set at 8–10 mmHg. The thymus with the thymoma was removed through a 30 mm or larger assistant port or extended port incision. In our department, we performed median sternotomy for tumors larger than 5 cm. However, as we became more proficient with this technique, we expanded its use to include larger tumors.

Comparison of RATS, VATS, and open surgery

Historically, prudence has been required while using minimally invasive approaches to thymic tumors because of the risk of damaging the tumor capsule, which may increase the risk of local recurrence (13,15,16). With the application of minimally invasive surgeries for thymomas, the International Thymic Malignancies Interest Group (ITMIG) proposed several standard policies in 2011. "To ensure an adequate margin of safety, thymomas should be resected with the surrounding normal thymus and fat". Intact thymic tissue and perithymic fat should be used for tumor grasping and traction in a "no touch" technique that avoids the risk of capsular rupture (17). It should be noted that capsular rupture makes analysis by the pathologist difficult, so to avoid the risk of rupture, the utility incision must be adapted so that the capsule does not rupture in the extraction bag when the specimen is removed. ITMIG warned that despite the perceived reduction in length of hospital stay and pain, the benefits of these approaches in comparison to those of the open approach have not been fully substantiated, and that prospective collaborative data collection is critical in defining the value of these techniques.

Recently, the number of reports on robot-assisted surgery has increased. Perioperative outcomes with robotassisted surgery are better than with open or thoracoscopic approaches while comparable outcomes to those with thoracoscopic approaches have been reported (16,18-24) (Tables 2,3). Regarding long-term prognosis, the 5-year overall survival did not differ significantly between thoracoscopic and open approaches, although both groups included stage III or higher cases (21,22). Only Yang et al. found the 5-year overall survival difference in minimally invasive cardiothoracic surgery (MICS) vs. open (90.7 vs. 86.9 months, P=0.04), but this difference was lost after propensity score matching (PSM) (89.4 vs. 81.6 months, P=0.2) (22). However, long-term outcomes beyond 10 years remain unclear. Furthermore, open thoracotomy has been compared with thoracoscopic surgery, including robot-

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| Author | Study year | Study design | Duration | Study arm | Sample size | Approach | Age (years) ^{\dagger} | Thymoma stage | Follow-up interval [†] |
|--------------|---------------|--------------|-----------|--------------|----------------|----------------------------|---|--|---------------------------------|
| Balduyck | 2011 | PC | 2004–2008 | R | 14 | Rt or Lt multiport | 49 [18–63] | A: 1, B1: 2, B2: 1, AB: 1 | 34 mo |
| (20) | | | | 0 | 22 | Median sternotomy | 56 [23–84] | A: 1, B1: 2, B2: 5, B3: 1, AB: 3 | 50 mo |
| Burt (18) | 2017 | ITMIGDB | 1997–2012 | R | 146 | NA | 56 [15–85] | MICS I: 199, II: 186, III: 27, IV: 12 | NA |
| | | | | VATS | 315 | NA | NA | NA | NA |
| | | | | 0 | 2,053 | Sternotomy/ thoracotomy | 54 [8–88] | I: 669, II: 654, III: 344, IV: 130 | NA |
| Qian (19) | 2017 | RC | 2009–2014 | R | 51 | Rt or Lt, 3-port | 49±13 | I: 19, IIA: 21, IIB: 21 | 421±469 d |
| | | | | VATS | 35 | Rt or Lt, 3-port | 50±13 | I: 10, IIA: 14, IIB: 11 | 701±382 d |
| | | | | 0 | 37 | Median sternotomy | 47±14 | I: 10, IIA: 12, IIB: 15 | 818±592 d |
| Ye (16) | 2013 | RC | 2009–2012 | R | 21 | Rt or Lt, 3-port | 53±8 | l: 21 | 17 [6–48] mo |
| | | | | VATS | 25 | Rt or Lt, 3-port | 53±5 | l: 25 | 25 [6–48] mo |
| Marulli (24) | 2018 | RCC-PSM | 1982–2017 | R | 41 | Rt or Lt, multiport | 58±11 | I: 8, II: 33 | 28 [18–61] mo |
| | | | | 0 | 41 | Mediansternotomy | 58±10 | I: 9, II: 32 | 88 [62–116] mo |
| Yang (22) | 2020 | NCDB | 2010–2014 | R | 176 | NA | 59.6±12.7 | I-IIa: 203: lib:77, III: 37 | 35.9 [24.9–52.2] mo |
| | | | | VATS | 141 | NA | NA | NA | 40.7 [27.3–56.8] mo |
| | | | | 0 | 906 | Sternotomy/ thoracotomy | 57.4±14.1 | I-lia: 432, lib: 196, III: 278 | NA |
| Yang (22) | 2020 | NCDB-PSM | 2010–2014 | MICS | 185 | NA | 61.6±10.4 | I-lia: 110, lib: 49, lll: 26 | 36.4 [25.8–55.4] mo |
| PSM | | | | 0 | 185 | Sternotomy/ thoracotomy | 62.6±11.1 | I-lia: 116: lib: 40, III: 29 | 35.9 [25.4–50.5] mo |
| Kamel (23) | 2019 | NCDB | 2010–2014 | R | 300 | NA | 63 [54–72] | 4.5 (range, 3.1–6.3) cm | NA |
| | | | | VATS | 280 | NA | 62 [53–70] | 5.0 (range, 3.5–7.8) cm | NA |
| Kamel (23) | 2019 | NCDB-PSM | 2010–2014 | R | 197 | NA | 62 | 5.0 cm | NA |
| PSM 1 | | | | VATS | 197 | Sternotomy/ thoracotomy | 62 | 5.3 cm | NA |
| Kamel (23) | 2019 | NCDB-PSM | 2010–2014 | R | 272 | NA | 61 | 5.1 cm | NA |
| PSM 2 | | | | 0 | 272 | NA | 61 | 5.1 cm | NA |

Table 2 Study characteristics of thymothymectomy according to robotic, thoracoscopic and open approaches

[†], data are presented as mean ± standard deviation or mean [range]. Yang matched: age, sex, race, Charlson-Deyo comorbidity score, regional education levels, tumor size, insurance type, histology, stage, year of diagnosis, distance from facility, and facility type. Kamel matched: age, gender, Charlson comorbidity index, induction therapy, tumor size and tumor extension. PC, prospective study; R, robotic; O, open approach; Rt, right; Lt, left; mo, months; ITMIGDB, International Thymic Malignancy Interest Group Database; NA, not applicable (not reported); VATS, video-assisted thoracic surgery; MICS, minimally invasive cardiothoracic surgery; RC, retrospective cohort; d, days; PSM, propensity score matching; RCC-PSM, retrospective case control study using PSM; NCDB, National Cancer Database; NCDB-PSM, NCDB study using PSM.

assisted surgery, using PSM adjusted for confounding factors, but significant differences in short-term prognosis, long-term prognosis, or perioperative outcomes have not been reported, despite significant differences in length of hospital stay (18,21,23).

Perioperative outcomes such as blood loss, operative

duration, respiratory complications, and postoperative length of hospital stay were better for thoracoscopy-assisted resection of stage I–II thymic epithelial tumors than for open thoracic surgery (4,5,9). However, there was no significant difference in the R0 resection rate, which was approximately 80% with both techniques (7,8).

| Fable 3 Ou | tcomes of | f robotic t | hymectomy by | other app | roaches | | | | | | | | | | | |
|--|------------------------|------------------------|--------------------------------------|------------------------|---------------------------------|-----------------------|---|-----------|------------------------|-------------|--------------------------------|------------|---|-----------|---------------------|------------|
| uthor | Study arm | Sample size | Operative time (min) [†] | P value | Blood loss (mL) [†] | P value | In-hospital duration (days) [†] | P value | Conversion rate (%) | P value | 5-year overall survival (%) | P value | Mortality (in- hospital or 30-day, %) | P value | R0 resectior (%) | P value |
| alduyck | ы | 14 | 224.2±66.5 | NS | NA | I | 9.6±3.9 | NS | 7.1 | I | NA | I | 0 | NS | NA | I |
| 50) | 0 | 22 | 243.8±55.5 | I | NA | I | 11.8±5.7 | I | NA | I | NA | I | 0 | I | NA | I |
| 3urt (18) | 0 | 146 | NA | I | NA | I | NA | I | 0 | I | NA | I | 0 | NS | 92 | 0.2 |
| | VATS | 315 | NA | I | NA | I | NA | I | NA | I | NA | I | 0 | I | 86 | I |
| | | 2,053 | NA | I | NA | I | NA | I | NA | I | NA | I | I | I | NA | I |
| Qian (19) | 0 | 51 | 71.2±39.8 | I | 77.5±69.5 | I | 4.3±1.1 | <0.001 | 0 | I | NA | I | 0 | NS | NA | I |
| | VATS | 35 | 88.5±37.6 | I | 246±316.5 | > | 6.6±1.4 | I | NA | I | NA | I | 0 | I | NA | I |
| | | 37 | NA | I | NA | I | NA | I | NA | I | NA | I | I | I | NA | I |
| Ye (16) | œ | 21 | 97±38 | I | 61.3±21.9 | <0.01 | 3.7±1.1 | <0.01 | 0 | I | NA | I | NA | I | NA | I |
| | 0 | 25 | 214.5±35.4 | I | 466.1±91.4 | I | 11.6±10.4 | I | NA | I | NA | I | NA | I | NA | I |
| Marulli (24) | £ | 41 | 132.5 [115–170] | <0.001 | AN | I | 3 [3-4] | <0.01 | 3.5 | I | NA | I | 0 | SN | 100 | SN |
| | 0 | 41 | 115 [90–137] | I | AN | I | 6 [5–7] | I | NA | I | NA | I | 0 | I | 100 | I |
| Yang (22) | MICS | 317 | NA | I | NA | I | NA | I | NA | I | 90.7 | 0.04 | NA | I | NA | I |
| | 0 | 906 | NA | I | NA | I | NA | I | NA | I | 86.9 | I | NA | I | NA | I |
| Yang (22) | MICS | 185 | NA | I | NA | I | 3 [2-4] | <0.001 | 19 | I | 89.4 | 0.2 | <10 | NS | 76.2 | 0.84 |
| PSM | 0 | 185 | NA | I | NA | I | 4 [3–5] | I | NA | I | 81.6 | I | <10 | I | 69.7 | I |
| Kamel (23) | œ | 197 | NA | I | NA | I | 4±5 | 0.76 | 23 | 0.031 | 93 | 0.571 | - | NS | 50 | 0.47 |
| PSM 1 | VATS | 197 | NA | I | NA | I | 4±5 | I | . + | I | 94 | I | N | I | 57 | I |
| Kamel (23) | œ | 272 | NA | I | NA | I | 4±8 | 0.057 | NA | I | 91 | 0.094 | - | NS | 32 | 0.13 |
| N MSL | 0 | 272 | NA | I | NA | I | 5±7 | I | NA | I | 80 | I | N | I | 47 | I |
| [†] , data are MICS, minir | presente nally invɛ | d as mea asive carc | an ± standard diothoracic sur | deviation gery; PSN | or mean [rar A, propensity | nge]. R, r score m | obotic; O, open a atching. | approach; | NS, not sign | ificant; N/ | A, not applicabl | e (not rep | orted); VATS, | video-ass | isted thoracic | : surgery; |

Our previous study revealed that RATS offers the advantage of improved postoperative quality of life according to nursing care systems compared with VATS (14). We found no significant differences in pain between patients with either of the two techniques, at the first and second follow-up visits, although RATS involved the use of more ports and intercostal space access than VATS (14). Şehitogullari *et al.* reported no significant differences in postoperative pain between patients with RATS and VATS (25). Kamel *et al.* found the differences in conversion rates in VATS and RATS (23% *vs.* 11%, P=0.031) (23).

However, many other references report no or little difference. This may be due to differences in facility criteria for conversion.

In recent years, the RATS approach has been used in patients with large thymomas. However, data are scarce. In the existing literature, most investigators warn against the routine use of RATS for thymomas larger than 4 cm (26). How far can the surgeons push the limits of robot-assisted surgery?

Kneuertz *et al.* performed the single institution retrospective study to compare the safety and feasibility of RATS (n=20) and open approach (n=34) for thymoma larger than 4 cm using the PSM (27). They demonstrated that robotic assisted thymectomy is a safe and effective approach even for patients with large thymomas, which can be performed in similar radical fashion and with a high rate of complete resection compared with the traditional open procedure (complication rate: 15% vs. 24%, P=0.45; R0: 90% vs. 85%, P=0.62).

Bongiolatti *et al.* retrospectively reviewed 106 thymectomies from 2010 to 2020, creating two groups based on the surgical approach (open or RATS) and size (28). Kaplan-Meier and Cox regression were used to estimate and identify risk factors of oncological outcomes. To perform a well-balanced analysis, a PSM analysis was conducted for large thymomas. They performed 54 RATS thymectomies and 46.3% (n=24) were large thymomas (larger than 5 cm). All patients had a complete resection. The median and the overall survival rate for larger tumor were similar between RATS and open (109 *vs.* 67 months, 92% *vs.* 83%, P=0.95).

Extent of resection for thymoma surgery

Because of the need for complete resection and the high incidence of myasthenia gravis, thymoma treatment is usually total thymectomy or complete tumor resection. However, in recent years, improvements in minimally invasive thoracic surgery (video- or robot-assisted) have encouraged thoracic surgeons to treat smaller thymomas by performing partial resections rather than resecting the entire thymus gland and thymoma (29-33) (*Tables 4-6*).

In 2016, three articles based on a large national thymus database reported the results of a comparative analysis between partial thymectomy and thymothymectomy. Narm *et al.* used data from the Korean Association for Research on the Thymus Registry. They did not report a significant difference in the recurrence rate of thymoma (29). PSM analysis was performed on data pertaining to 141 patients selected from each group. The 5- and 10-year recurrence-free rates in the partial thymectomy group were 96.3% and 89.7%, respectively, whereas those in the thymothymectomy group were 97.0% and 85.0%, respectively (P=0.86).

In contrast, an analysis of The Japanese Association for Research on the Thymus (JART) database, a prospective study conducted by the Japanese Thymus Study Group (30), and the Chinese Alliance for Research in Thymoma reported a higher recurrence rate in the partial resection group (31). In the JART study, 276 pairs of patients with stage I (T1N0M0) thymomas were compared using PSM. The 5-year overall survival rate was 97.3% in the partial thymectomy group and 96.9% in the thymothymectomy group (P=0.487); hence, local recurrence in the partial thymectomy group was more frequent than in the thymothymectomy group (2.2% vs. 0.4%, P=0.0613). The Chinese Alliance for Research in Thymomas enrolled patients with stage I and II thymomas. They reported similar 10-year overall survival between the two groups (90.9% after thymothymectomy and 89.4% after partial thymectomy, P=0.732). Overall, the recurrence rates were 3.1% after thymothymectomy and 5.4% after partial thymectomy, with no significant difference between the two groups (P=0.149). However, this study had some limitations. In the case of partial thymectomy, the possibility of incomplete resection was high, particularly in patients with stage II disease (2.9% vs. 14.5%) (31).

In 2021, Guerrera *et al.* published a study comparing short- and long-term outcomes of partial thymectomy and thymothymectomy in patients with non-myasthenia gravis stage I thymoma using the European Society of Thoracic Surgeons Thymic Database. The 5-year overall survival (55% vs. 89%) and 5-year disease-free survival (79% vs. 96%) of patients who underwent partial thymectomies were worse than those of patients who underwent thymothymectomies (32). This result suggests that we cannot perform partial resection for thymoma with

Table 4 Study characteristics of partial thymectomy and thymothymectomy for thymoma

| Author | Study | Study | Duration | Study | Sample | Age (years), | Diagnosis | Thymoma stage | Follow-up interval |
|-----------|-------|--------|-----------|---------|------------|--------------|--------------|---------------------------|--------------------|
| Addition | year | design | (year) | arm | size, open | mean ± SD | Diagnosis | mymorna stage | [range], mo |
| Narm (29) | 2016 | RC | 2000–2013 | Limited | 295 | 49±13 | Masaoka-Koga | I: 161, IIA: 70, IIB: 64 | 48 [0.3–189] |
| | | | | Total | 467 | 52±12 | Masaoka-Koga | I: 241, IIA: 147, IIB: 79 | 50 [0.2–178] |
| Narm (29) | 2016 | RCC- | 2000–2013 | Limited | 141 | 50±14 | Masaoka-Koga | I: 80, IIA: 34, IIB: 27 | 48 [0.3–189] |
| PSM | | PSM | | Total | 141 | 50±12 | Masaoka-Koga | I: 88, IIA: 28, IIB: 25 | 50 [0.2–178] |
| Nakagawa | 2016 | RC | 1991–2010 | Limited | 289 | 61.1±13.2 | Masaoka | I: 174, II: 115 | NA |
| (30) | | | | Total | 997 | 57.0±13.2 | Masaoka | I: 479, II: 518 | NA |
| Nakagawa | 2016 | RCC- | 1991–2010 | Limited | 276 | 60.6±13.2 | Masaoka | l: 161, ll: 115 | 48 |
| (30) PSM | | PSM | | Total | 276 | 61.0±11.9 | Masaoka | I: 158, II: 118 | 59 |
| Gu (31) | 2016 | RC | 1994–2012 | Limited | 251 | 52.3±11.9 | Masaoka | I: 178, II: 73 | 38 |
| | | | | Total | 796 | 50.9±12.2 | Masaoka | I: 523, II: 273 | 38 |
| Guerrera | 2021 | RC | 1994–2012 | Limited | 30 | 65.9±10.8 | Masaoka | T1a: 26, T1b: 4 | 37 [17–72] |
| (32) | | | | Total | 441 | 60.9±13.0 | Masaoka | T1a: 388, T1b: 53 | 37 [17–72] |
| Guerrera | 2021 | RCC- | 1994–2012 | Limited | 30 | 65.9±10.8 | Masaoka | T1a: 26, T1b: 4 | 37 [17–72] |
| (32) PSM | | PSM | | Total | 90 | 65.0±11.3 | Masaoka | T1a: 79, T1b: 11 | NA |
| Yano (33) | 2017 | PC | 2007–2011 | Limited | 36 | 61±12 | Masaoka | l: 22, ll: 14 | 63.1 |

Narm matched: age, sex, surgical approach, tumor size, WHO histology type, Masaoka-Koga stage, and adjuvant radiotherapy. Nakagawa matched: age, sex, tumor size, WHO histologic subtype, Masaoka stage, and adjuvant radiotherapy. Guerrera matched: age, gender, cardiac comorbidity, other comorbidities, thymoma size, surgical approach, WHO histology and pathological TNM. SD, standard deviation; mo, months; RC, retrospective cohort; PSM, propensity score matching; RCC-PSM, retrospective case control study using PSM; NA, not applicable (not reported); PC, prospective cohort; WHO, World Health Organization.

impunity. Future prospective randomized studies are needed to evaluate the extent of resection in early-stage thymoma surgery.

In 2017, Yano et al. evaluated the efficacy of partial or subtotal thymectomy for early-stage thymoma in the prospective study (33). Thirty-three out of 36 patients underwent partial resection of the thymus and all patients remained recurrence-free with the mean follow-up of 63 months. According to the authors, preserving the thymus could benefit the rest of one's life as an immunological supplement against future diseases. Some surgeons believe that thymomas behave docilely and complete resection is not required. Choe et al. performed a retrospective study of 72 patients who underwent resection of thymic epithelial tumors with de novo metastasis to the pleura or pericardium (34). Patients with negative or microscopically positive R0 or R1 resection margins were compared with those with grossly positive margins (R2). The overall survival was 11.8 vs. 5.5 years, respectively. In the present study, incomplete resection was identified as a major

negative predictive factor for overall survival. Therefore, it would be premature to consider partial thymectomy as an appropriate treatment for thymoma.

Drawbacks of robotic surgery

Robotic surgery has several limitations including the high cost, lack of tactile sensation, annual maintenance costs, and expensive disposable robotic equipment. However, some of these limitations can be countered by the interdisciplinary use of robots (35). The interference of surgical instruments in the narrow mediastinum, which was a problem with VATS, has been eliminated with RATS, coupled with the expansion of the surgical field by CO_2 insufflation. Furthermore, in recent years, robots with tactile senses have been developed and proven to be effective, yet robots currently in widespread use do not have antennae (36). It should also be noted that it can take time to respond to unexpected injuries or bleeding from the innominate vein.

| Author | Study arm | Sample size | Operative time (min), mean [range] | P value | Blood loss (mL), mean [range] | P value | Complication rate (%) | P value | In-hospital duration (days) | P value | MICS rate (%) | P value |
|------------------|--------------|----------------|--|---------|-------------------------------------|---------|--------------------------|---------|-----------------------------------|---------|--|---------|
| Narm (29) | Limited | 295 | NA | - | NA | - | NA | - | NA | - | VATS: 71.9; sternotomy: 17.3; *others: 10.8 | <0.01 |
| | Total | 467 | NA | - | NA | - | NA | - | NA | - | VATS: 18.2; sternotomy: 73.2; *others 8.6 | - |
| Narm (29) PSM | Limited | 141 | 110 [72–136] | <0.01 | 50 [0–200] | <0.01 | 7 | 0.55 | 5 | 0.95 | VATS: 51.1; sternotomy: 34.0; *others: 14.9 | 0.44 |
| | Total | 141 | 133 [112–165] | - | 150 [35–300] | - | 5 | - | 5 | - | VATS: 53.9; sternotomy: 33.3; *others: 12.8 | - |
| Nakagawa | Limited | 276 | NA | - | NA | - | 12 | 0.0397 | NA | - | NA | - |
| (30) PSM | Total | 276 | NA | - | NA | - | 23 | - | NA | - | NA | - |
| Gu (31) | Limited | 251 | NA | - | NA | - | NA | - | NA | - | VATS: 22.8; thoracotomy: 68; sternotomy: 9.2 | <0.001 |
| | Total | 796 | NA | - | NA | - | NA | - | NA | - | VATS: 27.6; thoracotomy: 9.8; sternotomy: 62.6 | - |
| Guerrera | Limited | 30 | NA | - | NA | - | 62 | 0.079 | NA | - | MICS: 70 | <0.001 |
| (32) | Total | 441 | NA | - | NA | - | 4 | - | NA | - | MICS: 25.4 | - |
| Guerrera | Limited | 30 | NA | - | NA | - | NA | - | NA | - | MICS: 70 | 0.91 |
| (32) PSM | Total | 90 | NA | - | NA | - | NA | - | NA | - | MICS: 71 | - |
| Yano (33) | Limited | 36 | NA | - | NA | - | NA | - | NA | - | VATS: 29, sternotomy: 5, thoracotomy: 2 | - |

Table 5 Outcomes of partial thymectomy and thymothymectomy for thymoma

*others = missing data. MICS, minimally invasive cardiothoracic surgery; NA, not applicable (not reported); VATS, video-assisted thoracic surgery; PSM, propensity score matching.

Drawbacks of partial thymectomy

Some studies claim that partial thymectomy has a lower complication rate, less operative time and less blood loss. However, consideration should be given to the increased likelihood of incomplete resection with limited resection of the thymus, especially in stage II, as shown in a study by the ChaRT study (2.9% vs. 14.5%) (31). In addition, partial resection of the thymus could not secure the safe anatomic margins and eventually could lead to leave behind multifocal thymic epithelial tumors (37,38). The final stage is established on the pathological examination of the specimen, sometimes the diagnosis is corrected compared to preoperative imaging. We should keep in mind these drawbacks when considering the partial thymectomy for thymoma. Furthermore, it is important to note that performing partial resection does not allow node removal following the 2015 ITMIG recommendations (39).

Limitations

Our narrative review has some limitations. First, considering the advances in RATS technology, we basically excluded an article published before 2010. This may have resulted in selection bias. Furthermore, there is still a lack of sufficient long-term outcome data to analyze the survival rates of RATS and Open approaches for early-stage thymoma.

Conclusions

Robotic thymectomy is a proven procedure performed

| lable o Lo. | ng-term out | comes of | partial thyi | nectomy a | nd thymot | hymecton | iy tor thyn | loma | | | | | | | |
|-------------|--------------|---------------|--------------|----------------|------------|--------------|-------------|---------------|-----------|------------------|------------|-------------|---------|---------------------------------|-----------------|
| Author | Study arm | 5-year DFS | P value | 10-year DFS | P value | 5-year OS | P value | 10-year OS | P value | Mortality (%) | P value | R0 (%) | P value | Recurrence rate (%) | P value |
| Narm (29) | Limited | NA | I | NA | I | NA | I | NA | I | NA | I | ΝA | I | 11 | 0.1 |
| | Total | NA | I | NA | I | NA | I | NA | I | NA | I | ΝA | I | 19 | I |
| Narm (29) | Limited | 96.3% | 0.86 | 89.7% | 0.86 | 94.1% | 0.82 | 86.8% | 0.82 | 17 | 0.65 | 96.5 | 0.76 | 7 | >0.99 |
| PSM | Total | 97% | I | 85% | I | 96.9% | I | 86.0% | I | 23 | I | 95.7 | I | 5 | I |
| Nakagawa | Limited | 93.8% | 0.588 | NA | I | 97.3% | 0.487 | NA | I | ٣ | SN | 97.8 | 0.142 | 11 | 0.102 |
| (30) PSM | Total | 94.9% | I | NA | I | 96.9% | I | NA | I | ÷ | I | 99.3 | I | 5 | I |
| Gu (31) | Limited | NA | I | NA | I | NA | I | 89.4% | 0.732 | Ŧ | SN | 98.4 | 0.267 | Stage I: 1.4; stage II: 14.5 | Stage I: 0.259 |
| | Total | NA | I | NA | I | NA | I | 90.9% | I | ÷ | I | 98.7 | I | Stage I: 3.1; stage II; 2.9 | Stage II: 0.001 |
| Guerrera | Limited | %62 | <0.001 | NA | I | 55% | 0.002 | NA | I | 0 | 0.23 | 94.6 | 0.83 | NA | I |
| (32) | Total | 96% | I | NA | I | 89% | I | NA | I | 12 | I | 93.7 | I | NA | I |
| Guerrera | Limited | %62 | 0.025 | NA | I | 49% | 0.144 | NA | I | NA | I | AN | I | NA | I |
| (32) PSM | Total | 98% | I | NA | I | 80% | I | AA | I | NA | I | AN | I | NA | I |
| Yano (33) | Limited | 94.1% | I | NA | I | 94.1% | I | NA | I | 2 | I | NA | I | 0 | I |
| DFS, disea | se free surv | ival; OS, | overall sur | vival; NA, | not applic | able (not | reported); | PSM, pro | pensity s | core match | ing; NS, n | ot signific | ant. | | |

of partial thymectomy and thymothymectomy for thymoma Table 6 Long-

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at many centers. Current data indicate that it is safe with effective and promising long-term results and oncological and surgical outcomes in patients with thymoma. Future prospective randomized studies are needed to evaluate its superiority over the standard thoracoscopic techniques. Robotic thymectomy can become the standard procedure in patients with early-stage thymomas. Furthermore, it is premature to consider partial thymectomy as an appropriate treatment for thymomas.

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