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ORIGINAL ARTICLE

Early clinical outcomes of robot-assisted surgery for anterior mediastinal mass: its superiority over a conventional sternotomy approach evaluated by propensity score matching†

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Abstract

OBJECTIVES: We performed this study to assess early clinical outcomes of robot-assisted surgery for anterior mediastinal mass by comparing results of the robot group with those of the sternotomy group after propensity score matching.

METHODS: Between 2008 and 2012, 145 patients underwent resection of anterior mediastinal mass. Robot-assisted surgery was performed in 37 patients, and conventional surgery by sternotomy in 108 patients. Propensity score matching was done between two groups with variables of age, sex, size of the mass, myasthenia gravis, resection of other organ and pathological diagnosis. Thirty-four patients from the robot group and 34 from the open group were matched, fitting the model. The clinical outcomes of matched groups were compared.

RESULTS: In the robot group, mediastinal cyst consisted of 47.1% (16 of 34), thymoma 32.4% (11 of 34), thymic carcinoma 8.8% (3 of 34), thymic hyperplasia 8.8% (3 of 34) and liposarcoma 2.9% (1 of 34). The mean duration of follow-up was 1.11 ± 0.21 and 1.85 ± 0.19 years for the robot and open groups, respectively. There were no mortality or recurrence in both groups during the follow-up. There were no significant differences in operation time, postoperative white blood cell and C-reactive protein increase, maximum visual analogue scale score for pain as well as postoperative intensive care unit care between the two groups. The robot group revealed a lesser number of drains (1.09 ± 0.1 vs 1.41 ± 0.1) and 24-h tube drainage (189.4 ± 20.5 vs 397.6 ± 52.6 ml), lower haemoglobin loss (0.54 ± 0.4 vs 1.35 ± 0.1 g/dl) and haematocrit decrease (1.92 ± 0.5 vs 3.85 ± 0.4%), shorter chest tube days (1.53 ± 0.2 vs 3.06 ± 0.2) and length of hospital stay (2.65 ± 0.2 vs 5.53 ± 0.8) after operation, which were all statistically significant. Although statistically insignificant, there were no postoperative complications in the robot group, but there were 5 (14.7%) in the open group ($P = 0.063$).

CONCLUSIONS: In carefully selected patients with relatively smaller sized masses, robot-assisted surgery resulted in excellent early clinical outcomes with lesser tube drainage, lower blood loss, shorter tube days and length of hospital stay without any postoperative complications, compared with the matched open group. Further investigation for long-term clinical outcomes and oncological outcomes is required for a robotic approach. Particularly, long-term follow-up for the local recurrence rate according to the pathological diagnoses is required.

Keywords: Sternotomy • Robotics • Thymectomy

INTRODUCTION

Anterior mediastinal masses most commonly increase from the thymus, and in these cases, thymectomy by median sternotomy is the standard surgical treatment. However, minimally invasive surgery for anterior mediastinal masses—including thoracoscopic surgery and robot-assisted surgery—has been introduced. Video-assisted thoracoscopic (VATS) surgery for anterior mediastinal masses has been reported earlier [1, 2]. Robot-assisted surgery for mediastinal mass was later introduced, but it became increasingly popular with its benefits over conventional thoracoscopy including three-dimensional (3D) technology, articulating instruments and others [3–6]. There have been many reports comparing the results of video-assisted thoracoscopic surgery for anterior mediastinal masses with a sternotomy approach, but there are not many reports that compare the outcomes of robotic surgery with those of conventional open surgery by the sternotomy approach [7–10]. This study was performed to evaluate early clinical outcomes of robot-assisted surgery for anterior mediastinal masses by comparing the outcomes of robotic approach with those of the sternotomy approach. To minimize the shortcomings of our nonrandomized and retrospective study, we compared the early outcomes between the matched two groups after performing propensity score analysis.

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MATERIALS AND METHODS

Patients

From May 2008 to August 2012, 146 patients underwent resection of anterior mediastinal mass at the Seoul National University Hospital. Thirty-eight underwent resection by robot-assisted attempt, one of whom was converted to sternotomy due to severe pleural adhesion and 108 underwent resection by median sternotomy. Excluding the single-converted case, we retrospectively reviewed 145 patients' characteristics, procedural/pathological data of the lesion and early clinical outcomes. This study was performed after obtaining approval from our institutional review board.

Anaesthesia and postoperative management

Endotracheal intubation with a double-lumen tube was performed in every case. An arterial catheter was placed for monitoring, and a central venous catheter was placed in an internal jugular vein or subclavian vein. In patients with myasthenia gravis (MG), depolarizing muscle relaxants were not used; otherwise, adequate amounts of non-depolarizing relaxants were used. In the robot-assisted surgery group, single-lung ventilation was mandatory. In the median sternotomy group, single-lung ventilation was performed only when visualization of each phrenic nerve during thymectomy was needed. After the surgery, extubation in the operating room was attempted in all patients, also including patients with MG. Every patient with MG was sent to the intensive care unit for immediate post-surgical observation. Chest tubes were removed when 24-h drainage amount was <250 ml or each of two consecutive 8-h drainage amounts was <80 ml.

Robot-assisted surgery

Robot-assisted resection of anterior mediastinal mass was performed by three surgeons. When only a thymic cyst was more likely than a tumour from the preoperative computed tomography scan or magnetic resonance imaging, robotic surgery was not performed and VATS surgery was preferred. Approach to the anterior mediastinum was performed via right, left or bilateral sides, according to the extent and location of the mass. In patients with MG, approach from bilateral sides was performed.

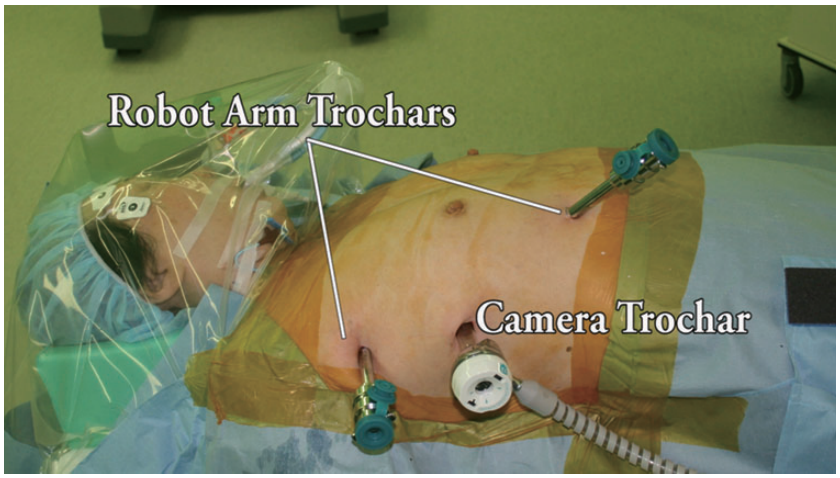

Figure 1: Patient's position and trocar placement in the robotic approach.

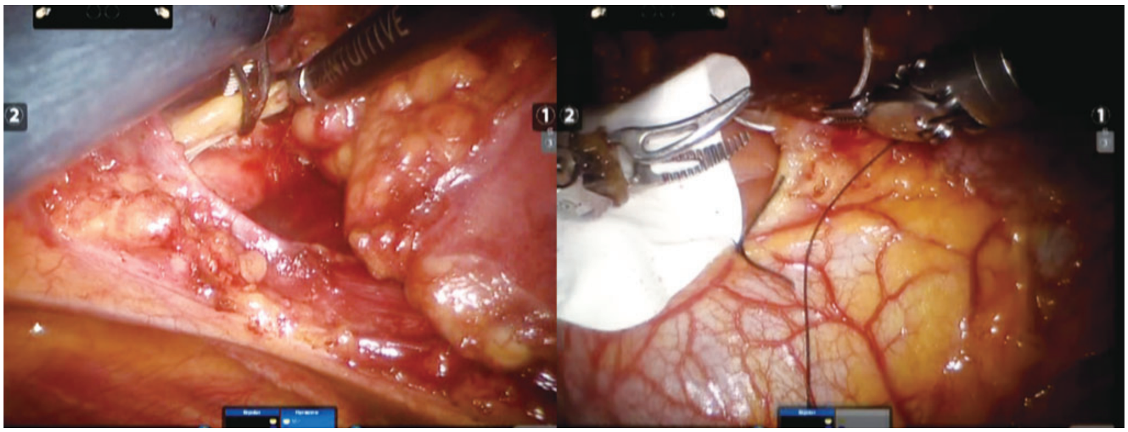

Figure 2: (Left) Resection of the superior pole by utilizing the multiarticulated robot arm movement. (Right) Pericardial reconstruction with a PTFE membrane, utilizing the 3D technology.

A three-arm da Vinci S/Si robotic system (Intuitive Surgical, Inc., USA) was used. Patients were placed in supine position with elevation of the side to be approached using a vacuum-moldable positioning pad (Olympic Vac-Pac®, Natus Medical, San Carlos, USA) with his/her ipsilateral arm adducted and placed low. This adduction and lower positioning of the ipsilateral arm enables the robotic arm and trocar near the axilla to move more freely without injuring the patient by pressing. Three incisions for camera and instruments were made, following pre-emptive intercostal block with 2 ml of 0.5% bupivacaine at each intercostal space (ICS). The camera trocar was first inserted at the fifth ICS, along the anterior axillary line. Then, CO_2 gas was insufflated under single-lung ventilation with 8 mmHg pressure and 10 l/min flow. Another trocar for grasping and dissecting arm (Maryland Bipolar Forceps for *da Vinci S/Si*, Intuitive Surgical, Inc.) was inserted at the third ICS, along the anterior axillary line. Then, the other trocar for an ultrasonic device (Harmonic ACE® Curved Shears for *da Vinci S/Si*, Ethicon, USA) was inserted at the fifth or sixth ICS (Fig. 1). When thymic pathology was suspected, *en bloc* thymectomy was performed with resection beginning lower from diaphragm, proceeding cephalad. Small vessel tributaries were divided using Harmonic ACE®, but larger arterial and venous branches were divided after applying plastic clips (Hem-o-lok® Clip Applier, Teleflex Medical, USA). Total thymectomy was performed from a phrenic to the other phrenic nerve, with maximum removal of superior poles by gradual, gentle pulling down and dissection (Fig. 2, left). When direct invasion to near organ/tissue was suspected, *en bloc* resection was performed, and pericardial reconstruction was performed with a polytetrafluoroethylene (PTFE) membrane (Gore® Medical Membrane, Gore & Associates, Inc., USA) when needed, utilizing the multiarticulated robot arms (Fig. 2, right). After completing the resection, the specimen was put in an endoscopic vinyl bag, and then retrieved through the most anterior port incision. In most of the cases, a single 24-Fr chest tube was placed only in one pleural cavity at the side of approach.

Surgery by median sternotomy

The patients were placed in supine position with both their arms adducted. Median full sternotomy or upper partial sternotomy was used according to the characteristic of the mass, and then standard *en bloc* resection was performed.

Statistical analysis

Statistical analysis of the data was performed by Student's *t*-test and χ^2 test using PASW statistics 18 (SPSS, Inc., USA). Propensity score matching analysis was performed with the help of the medical research collaborating centre (MRCC) in our institution. McNemar's test and paired *t*-test were used for analyses after propensity score matching.

RESULTS

Patients characteristics

Excluding the single sternotomy-converted case, there were 37 patients in the robot group and 108 in the open group. When comparing patient characteristics between two groups, there were significant differences in the size of the mass and resection of additional organ/tissue (Table 1, $P < 0.001$, $P = 0.034$).

Propensity score matching analysis

The type of surgical approach (open or robot) defined as a dependent variable, logistic regression model was set and propensity score was calculated by the logistic regression model according to age, size of the mass, gender, presence of MG, resection of additional organ/tissue and pathology as an independent variable. Hosmer and Lemeshow goodness-of-fit test revealed a *P*-value of 0.927, fitting this model. We made propensity score matched pairs between the robot and sternotomy groups, using the Greedy 8 → 1 digit matching method—which makes 1:1 pairs with identical propensity scores beginning from identical 8 digits to 1 digit until no more matching pairs could be made. Statistical analysis between the matched two groups was performed by McNemar's test for categorical variables and the paired *t*-test for continuous variables. A two-sided *P*-value of < 0.05 was considered statistically significant.

A total of 68 patients, 34 in the robot group and 34 in the open group, were matched, and there were no difference in patient characteristics between the two groups after this analysis (Table 2).

However, when overall patient group ($n = 145$) and matched group ($n = 68$) were compared, the matched group revealed a

Table 1: Patient characteristics in each group before propensity score matching

	Robot group ($n = 37$)	Open group ($n = 108$)	*P*-value
Age[a] (year)	52.2 ± 13.9	52.5 ± 11.9	0.895
Mass size[a] (mm)	29.3 ± 17.2	44.0 ± 26.1	<0.001
Male sex,[b] *n* (%)	17 (45.9%)	55 (50.9%)	0.601
Myasthenia gravis,[b] *n* (%)	2 (5.4%)	1 (0.9%)	0.356
Additional resection,[b] *n* (%)	3 (8.1%)	27 (25%)	0.034
Pathology,[b] *n* (%)			
Thymic tumours/hyperplasia	18 (48.6%)	72 (66.7%)	0.108
Cysts	17 (45.9%)	30 (27.7%)	
Others	2 (5.5%)	6 (5.6%)	

[a]Student's *t*-test.
[b]χ^2 test.

Table 2: Patient characteristics after propensity score matching

	Robot group (*n* = 34)	Open group (*n* = 34)	*P*-value
Age[a] (year)	53.7 ± 2.2	52.4 ± 1.8	0.673
Mass size[a] (mm)	28.8 ± 2.9	31.0 ± 3.4	0.594
Height[a] (cm)	160.6 ± 8.9	163.9 ± 8.4	0.145
Body weight[a] (kg)	65.4 ± 11.5	65.1 ± 9.9	0.909
Male sex,[b] *n* (%)	15 (44%)	18 (52%)	0.607
Myasthenia gravis,[b] *n* (%)	2 (5.9%)	1 (2.9%)	1.000
Additional resection,[b] *n* (%)	3 (8.8%)	3 (8.8%)	1.000
Pathology,[b] *n* (%)			
Thymic tumours/hyperplasia	17 (50%)	15 (44%)	0.787
Cysts	16 (47%)	17 (50%)	
Others	1 (2.9%)	2 (5.9%)	

[a]Paired *t*-test.
[b]McNemar test.

Table 3: Early clinical outcomes of surgery after propensity score matching

	Robot group (*n* = 34)	Open group (*n* = 34)	*P*-value
Mortalities[a] (no.)	0	0	1.000
Recurrence during follow-up[a] (no.)	0	0	1.000
Operation time[b] (min)	157.2 ± 12.6	139.3 ± 8.86	0.268
WBC increase[b] ($\times10^3$/μl)	5.78 ± 0.57	7.37 ± 0.64	0.064
CRP increase[b] (mg/dl)	7.36 ± 0.83	8.85 ± 0.97	0.283
Maximum VAS[b] (day)	5.47 ± 0.34	5.53 ± 0.29	0.881
Postoperative ICU care,[a] *n* (%)	2 (5.9%)	2 (5.9%)	1.000
Number of drains[b] (no.)	1.09 ± 0.05	1.41 ± 0.13	0.032
24-h tube drainage[b] (ml)	189.4 ± 20.5	397.6 ± 52.6	0.002
Haemoglobin loss[b] (g/dl)	0.54 ± 0.37	1.35 ± 0.12	0.023
Haematocrit decrease[b] (%)	1.92 ± 0.45	3.85 ± 0.42	<0.001
Chest tube days[b] (day)	1.53 ± 0.15	3.06 ± 0.21	<0.001
Length of hospital stay (day)	2.65 ± 0.18	5.53 ± 0.75	0.001
Complications,[a] *n* (%)	0 (0.0%)	5 (14.7%)	0.063

[a]McNemar test.
[b]Paired *t*-test.
CRP: C-reactive protein; WBC: white blood cell.

smaller size of the mass (40.3 ± 24.9 vs 29.9 ± 18.3, $P < 0.001$) and more additional resections of other organs ($P = 0.032$).

Thymic cyst was the most common pathology consisting of 16 (47.1%) in the robot group and 17 (50%) in the open group. The next common pathology was thymoma, consisting of 11 (32.4%) in the robot group and 13 (38.2%) in the open group. There were 3 (8.8%) and 1 (2.9%) of thymic carcinoma in the robot and open groups, respectively. Three additional resections in the robot group were: (i) *en bloc* wedge resection of right upper lobe and resection of pericardium, (ii) mediastinal cyst excision which was a pericardial cyst and (iii) *en bloc* medial segmentectomy of right middle lobe and pericardial resection and reconstruction. Three additional resections in the open group were: (i) *en bloc* wedge resection of left upper lobe and pericardial resection and reconstruction, (ii) *en bloc* resection of pericardium and (iii) thoracoscopic excision of posterior mediastinal mass. One (2.9%) case in the robot group turned out to be well-differentiated liposarcoma, and 2 (5.9%) in the open group turned out to be malignant lymphoma and intermediate-grade neuroendocrine tumour. In the open group, 16 (47.1%) underwent full sternotomy, and 18 (52.9%) underwent upper partial sternotomy. Upper partial sternotomy was performed when the mass was more likely to be a cyst.

The single-converted case taken into account, the success rate of our robot-assisted anterior mediastinal mass surgery was 97.4% (37 of 38). In the robot group, 21 (61.8%) were approached from the right side, which was the most common, 9 (26.5%) from the left side and 4 (11.8%) from bilateral sides. There were no early/late mortalities or recurrence during the follow-up period in both the robot and open groups. The mean duration of follow-up was 1.11 ± 0.21 and 1.85 ± 0.19 years for robot and open groups, respectively. The total number of inserted drains (1.09 ± 0.05), 24-h tube drainage amount (189.4 ± 20.5 ml), haemoglobin loss (0.54 ± 0.37 g/dl), haematocrit decrease (1.92 ± 0.45%), days on

Table 4: Comparison between earlier and later robotic surgery

	Robot group (N = 34)		P-value
	Earlier group (n = 17)	Later group (n = 17)	
Operation time[a] (min)	180.6 ± 74.9	133.9 ± 65.7	0.062
WBC increase[a] (×10^3/μl)	5.95 ± 3.0	5.61 ± 3.6	0.776
CRP increase[a] (mg/dl)	7.96 ± 4.4	6.76 ± 5.2	0.477
Maximum VAS[a] (day)	5.18 ± 2.4	5.76 ± 1.6	0.400
Number of drains[a] (no.)	1.12 ± 0.3	1.06 ± 0.2	0.559
24-h tube drainage[a] (ml)	193.5 ± 129.2	185.3 ± 113.4	0.845
Haemoglobin loss[a] (g/dl)	0.35 ± 2.6	0.74 ± 0.9	0.573
Chest tube days[a] (day)	1.71 ± 0.9	1.35 ± 0.8	0.257
Length of hospital stay (day)	2.94 ± 1.0	2.35 ± 1.1	0.110

[a]χ^2 test.
CRP: C-reactive protein; WBC: white blood cell.

chest tube (1.53 ± 0.15 days) and postoperative length of hospital stay (2.65 ± 0.18 days) were all significantly less than those of the open group. There were no difference in operation time and maximum pain score measured by visual analogue scale (VAS). Although statistically insignificant, there were no complications (0%) in the robot group, but there were 5 (14.7%) complications in the open group—3 of which were postoperative bleeding, 1 was atrial fibrillation and the other was pleural effusion (Table 3). There were no cases of iatrogenic phrenic nerve injury in both groups.

DISCUSSION

Berman *et al.* [4] reported their first robotic surgery of an anterior mediastinal mass with the Zeus robotic surgical system (Computer Motion, Inc., USA), which lacked 3D technology, and Bacchetta *et al.* [3] reported their resection of a pericardial cyst using the *da Vinci*™ system. Since then, the role of robotic surgery in the treatment of mediastinal masses has been growing. There has been concern over video-assisted thoracoscopic resection of malignant mediastinal tumours [1, 2, 11], but with the latest robotic technology, 3D vision with multiarticulated arm movement which reduces surgeons' tremor enables better visualization and safe, meticulous dissection of the mediastinal structures—which is a great advantage over thoracoscopic surgery in anterior mediastinal masses. Robotic thymectomy is thus anticipated to be equivalent to standard total thymectomy by median full sternotomy, which affords complete removal of the thymic tissue from phrenic to phrenic. There have been some reports comparing the robotic with the open approach, but there are not many. Cakar *et al.* [12] reported longer operation time and shorter hospital stay with good neurological outcomes from robotic thymectomies in non-thymomatous MG. Weksler *et al.* [13] reported results similar to ours with less blood loss, shorter hospital stay and less complications in the robot group, but this study was an unmatched, retrospective study with 15 robotic cases. Ruckert *et al.* [14] reported improved outcomes for MG after robotic thymectomy compared with thoracoscopic thymectomy with a cumulative complete remission rate of 39.25 and 20.3%, respectively. Balduyck *et al.* [15] reported that decreased quality-of-life scores after surgery in the robotic group approximated baseline preoperative values faster than in the sternotomy group and that the high burden of decreased physical functioning reported after sternotomy is not seen after a da Vinci robotic-assisted resection. In our series, sometimes we had technical difficulties identifying the contralateral phrenic nerve when performing robotic surgery by the unilateral approach. Wagner *et al.* [16] reported a novel technique of identifying the contralateral phrenic nerve by injecting indocyanine green via peripheral venous catheter and by using intraoperative near-infrared fluorescence imaging.

Our study reveals better early clinical outcomes of the robot group in the aspect of these variables—number of drains, 24-h drainage amount, haemoglobin loss, days on chest tube and length of postoperative hospital stay. We expected less pain in the robot group, but there was no significant difference in the maximum postoperative pain score by VAS (maximum VAS) between the two groups. Although this immediate postoperative pain showed no difference, we expect a faster decrease during follow-up in the robot group. We are planning to perform further evaluation with longer periods. The single most evident variable that may have affected all the other variables seems to be the lower haemoglobin loss in the robot group. We measured intraoperative bleeding by using a collecting bottle in earlier robotic cases, but soon we stopped it because the amount of bleeding was so small that it was almost uncountable in most of the cases. The absence of bone bleeding from sternotomy sites in the robot group might be a reason for lower blood loss in the robot group. Although a lesser haemoglobin loss of 0.7 g/dl in the robot group seems to be small, this was statistically significant, and we think that this haemoglobin difference resulted in a lesser drainage amount difference of 200 ml. Very low blood loss enabled us to put only a single small-bore (24 Fr) chest tube which also could be removed earlier, which resulted in earlier discharge of the patients in the robot group. In the aspect of the operation time, we are still investing effort to decrease the time needed for docking. Since our first case in May 2008, when comparing earlier 17 cases and later 17 cases of robotic surgery, there was no statistical difference in the variables shown above (Table 4). Only the operation time in the later group decreased to 133.9 ± 65.7 min (P = 0.062), showing some tendency to decrease over gained experience. This result reveals that robot-assisted surgery for anterior mediastinal mass is easily adaptable and does not require many cases for the learning curve.

Our study has some limitations. Even though this study used propensity score matching, it is a retrospective study with a small number of patients during a relatively short period of follow-up. As mentioned earlier, overall matched patients showed smaller size of the mass and more additional resections of other organs. In conclusion, robot-assisted surgery for mediastinal mass resulted in excellent early clinical outcomes with lesser tube drainage, lower blood loss, shorter tube days and length of hospital stay without any postoperative complications in carefully selected patients with relatively smaller masses. There are many reports of robotic thymectomy in patients with MG, but whether robotic thymectomy can be performed in thymic malignancy with oncological radicality is still unclear [17–21]. Further investigation for long-term clinical outcomes and oncological outcomes is required for the robotic approach. Particularly, long-term follow-up for the local recurrence rate according to the pathological diagnoses is required.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

Dr S. Cassivi *(Rochester, MN, USA)*: I am going to start with asking you about the operative times. The issue with robots, the daunting thing about robots, is all of the preparation time. Clearly we know it gets better, if you have a dedicated team, over time. My question relates to the times that you report in this presentation. Are those incision to closure times, or are they entry into the operating room to exit out of the operating room times?

Dr Seong: From the docking to the finishing of the operation.

Dr Cassivi: I would encourage you, in order to have complete truth in accounting when we are talking about the robot, is to include the times of the patient entering the room to the patient leaving the room, because that is often what is very daunting about this extra addition.

Dr F. Detterbeck *(New Haven, CT, USA)*: I think your follow-up is a little bit too short to really comment on how useful this is. There is no problem with doing things minimally invasively. I think we need to make sure that we are doing the same operation and we are not cutting some corners. You didn't really get into that, whether there were positive margins or any issues with that with thymomas. We have to be a little bit cautious that we are not focused on the technique, that we are focused on what we are really doing for the patient. So do the same operation.

Lastly, I would say that the differences were relatively minor, so while I am very much a proponent of minimally invasive approaches and new techniques, I think that we also can take away from this that the differences were really relatively minor. So for people who are not doing a lot of thymoma surgery, it may not really be worth the learning curve to avoid the sternotomy.

Dr K. Athanassiadi *(Athens, Greece):* I have two questions. The first thing is, how long must the incision be in order to pull out the thymoma plus pericardium for a collapsed lung? Is it worth the expense? And secondly, do you really need a patch to the pericardium after you excise it?

Dr Seong: For your first question, as I showed in my slide, the patient's position, the port for the right arm was placed most anteriorly where the intercostal space is the widest, and through that intercostal space, yes, we had to elongate the incision a bit. But if we felt it to be very short, then we tried to elongate it more and more and, with about a 2.5 cm incision, many of the masses came out without much difficulty.

And for your second question, there are some cases where we reconstructed the pericardium in my series. There is also a case without reconstruction of the pericardium. In this video, we thought the defect was somewhat large, so we reconstructed with Gore-Tex membrane.

Dr J. Kuzdzal *(Krakow, Poland)*: My question is whether in your series you encountered any case with disruption of the thymoma tumour capsule during the preparation?

Dr Seong: I beg your pardon?

Dr Kuzdzal: Did you have any case with a disruption of the thymoma capsule during the dissection?

Dr Seong: Not yet. As Dr. Detterbeck commented, an important message to me is that my colleagues and I until now never hesitate to do a sternotomy when a tough procedure is anticipated.

THORACIC