

# Thymic MIS: state of the art across the world (Russian Federation)

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**Abstract:** First VATS thymectomy was performed 25 years ago (Landreneau *et al.*, 1992). After that, minimally invasive approaches for surgical procedures have rapidly increased in the world. The aim of this paper was study of current problems and the status of surgery for thymus diseases in Russia. This is first global survey of all thoracic centers, which had experience in thymic surgery.

**Keywords:** Surgery of thymus gland; robot-assisted thymectomy; minimally invasive thoracic surgery

Received: 12 April 2017; Accepted: 24 July 2017; Published: 14 September 2017.

doi: 10.21037/jovs.2017.07.14

View this article at: <http://dx.doi.org/10.21037/jovs.2017.07.14>

## Background

Modern management of mediastinal diseases expand the role of surgery greatly. Most thymic masses need the surgical treatment, and total resection of tumors is a general prognostic factor for good results. Any thymic masses may be malignant, so conservative treatment or observation without morphological verification is associated with high risk of tumor invasion into the border organs. In addition, thymectomy, regardless of morphological changes of the thymus considered as a component of comprehensive treatment of myasthenia gravis. Regardless of morphogenesis (malignant or benign), any mass in the anterior mediastinum is a potential threat to the compression of vital organs.

There is more than 70 years history of open approaches for surgical treatment of thymic tumors. Most authors prefer different types of sternotomy than thoracotomy. VATS access became widely introduced only last 20 years, and quickly became popular among thoracic surgeons. First papers, which showed the possibility of using robot-assisted operations in thymic surgery, appeared in 2006–2007 years.

The aim of this paper is to show the current situation of minimally invasive surgery of thymic diseases in the Russian Federation.

## Thymic surgery in Russia: literature review

Analysis of Russian literature with national search system (<http://elibrary.ru>) showed 299 papers, which contain key word: thymectomy. Clinical trials, which were performed during last 10 years, were selected. Articles with the same title and with the same list of authors were excluded. Thereby eight original trials were found, that contain results of 561 thymectomies (*Table 1*). Forty-three percent of patients (244 from 561) were operated by VATS. Most articles are devoted to surgical treatment in patients with myasthenia gravis. Comparison trials showed advantages of VATS versus open approaches (sternotomy and thoracotomy). Rate of postoperative complications was 7.7–17% and 10–30%, mortality was 0–2.6% and 0–3.7% for minimally invasive and open thymectomy, respectively. Also VATS groups of patients are characterized by less pain and early recovery. Also noteworthy, the technical protocol for VATS thymectomy in some clinics provides the absence of chest tube in cases with uneventful surgery.

Unfortunately, existing publications do not reflect all features of thymic surgery. The annual report of the Association of Thoracic Surgeons of Russia contains limited information about the number of surgeries, complications

**Table 1** Results of literature review

Year	First author	Diseases	Number of patients, n	Approach	Complication rate, %	Mortality rate, %
2006	Kondratiev AV	Miastenia gravis	73	VATS (n=36); sternotomy (n=37)	7, 7; 8, 1	–
2008	Yablonskii PK	Timoma, hyperplasia, cyst	47	VATS	17	2
2009	Kul AV	Timoma, hyperplasia	23	VATS	–	–
2012	Skvortsov MB	Miastenia gravis	205	Sternotomy	10	2, 6
2010	Nikishov VN	Timoma, hyperplasia, cyst	130	VATS (n=75); thoracotomy (n=55)	–	0; 3, 7
2014	Terechina OG	Miastenia gravis	20	Sternotomy	20	–
2015	Sigal EI	Miastenia gravis + Timoma	38	VATS	29	2, 6
2015	Benyan AS	Timoma, hyperplasia, cyst	25	VATS	8	4

and mortality. In this context, the survey of all Russian thoracic centers was performed to study the general trend in this field.

### Current status of thymic surgery in Russia: methods of investigation

ESTS Database annual report is one of the most detailed reports containing data on thymic surgery (1). There is no analogue of this database in Russia, unfortunately. Analysis of annual report of Association of Thoracic Surgeons of Russia showed that overall number of surgical procedures for mediastinal diseases remains at the same level last years (1,324–1,405 surgeries per year). Little part of these (14%) performed for diseases of the thymus.

We developed a questionnaire in order to find branches of evolution of minimally invasive surgery of thymic gland in our country. There were different questions about features of preoperative examination, indications for surgery, surgical techniques and postoperative management of patients with thymic diseases (*Table 2*). To make a survey we have sent out a questionnaire to 30 thoracic centers in all regions of the Russian Federation, which had experience in thymic surgery.

### Results of the survey and its discussion

We received responses from 25 (83%) thoracic departments.

This frequency of response matched with data of Association of Thoracic Surgeons of Russia about number of thoracic centers, which had experience in minimally invasive thymic surgery. At least 25 radical operations per year for thymic diseases were performed in each center. Today, the main part surgical procedures are performed by minimally invasive approach, and our survey was planned for study of these. In addition we asked about open approaches in one of the questions. So the most surgeons (19/76%) prefer sternotomy among all open approaches (*Figure 1*).

### Preoperative assessment of patients

Symptoms of the diseases of the thymus gland are divided into four groups: local symptoms of compression or invasion of surrounding organs, general symptoms, thymus-associated syndromes, asymptomatic. The essential feature of the thymic disease is a high rate of thymus-associated syndromes (neuromuscular diseases, hematologic syndromes, diffuse connective tissue diseases and endocrine syndromes). Therefore, a diverse clinical picture necessitates a detailed examination of patients. Current diagnostic algorithm is described in “*Clinical recommendations for the diagnosis and treatment of myasthenia gravis*” by Russian Society of neurologists [2013].

Radiological methods are the most commonly used diagnostic procedures. Routine X-ray examination is

Table 2 Questionnaire

Question	Responses
1. How many radical surgical procedures for thymic diseases are performed in your department per year?	A. 0–5 B. 5–15 C. 15–25 D. More than 25
2. How often did you find the aberrant parts of the thymus?	A. Never B. Up to 30% of cases C. Up to 50% of cases D. More than 50% of cases
3. What is rate of minimally invasive thymectomies (VATS or robot-assisted approach)?	A. 0–30% B. 30–50% C. More than 50%
4. Which open approach for performing thymectomy is used in your department?	A. Sternotomy B. Right side thoracotomy C. Left side thoracotomy D. Open approach not used
5. Which minimally invasive approach for performing thymectomy is used in your department?	A. Singleportal VATS B. Biportal VATS C. Threeportal VATS D. Fourportal VATS E. Subxifoidal VATS F. RATS
6. What approach (left or right side) is preferable to minimally invasive thymectomy for hyperplasia?	A. Right side B. Left side C. Bilateral D. Subxifoidal E. Other ...
7. Does the choice of the left or right side approach depend on the predominant enlargement of the left or right thymic lobes?	A. Yes B. No
8. Do you perform simultaneous operations on the thymus and thyroid glands?	A. Yes B. No
9. What size of the tumor of the thymus is an indication for minimally invasive approach?	A. Up to 3 cm B. Up to 5 cm C. Up to 8 cm D. The size of the tumor does not matter

Table 2 (continued)

Table 2 (continued)

Question	Responses
10. Do you use combined approaches for minimally invasive thymectomy?	<ul style="list-style-type: none"> <li>A. No such experience</li> <li>B. Bilateral thymectomy</li> <li>C. Thymectomy in conjunction with cervical access</li> <li>D. Other ...</li> </ul>
11. What is the main tool do you use for mobilization of the thymus gland during minimally invasive thymectomy?	<ul style="list-style-type: none"> <li>A. Ultrasonic tools</li> <li>B. Bipolar tools</li> <li>C. Ligasure</li> <li>D. Monopolar tools</li> <li>E. Shape method with clips</li> </ul>
12. Which method of closure of the Keynes vein is used in your department?	<ul style="list-style-type: none"> <li>A. Closure with metal clips</li> <li>B. Closure with hem-o-lock</li> <li>C. Closure with bipolar/monopole coagulation</li> <li>D. Closure with ultrasonic tools</li> </ul>
13. What is your attitude to the opening of the contralateral mediastinal pleura?	<ul style="list-style-type: none"> <li>A. It is obligatory step of the operation</li> <li>B. It is not an obligatory stage of the operation, it does not require additional interventions</li> <li>C. It is not an obligatory stage of the operation, it requires the drainage of the contralateral pleural cavity</li> </ul>
14. What is the main radiological diagnostic method used in your department in cases thymic diseases?	<ul style="list-style-type: none"> <li>A. CT</li> <li>B. MRI</li> <li>C. PET-CT</li> <li>D. Chest X-ray</li> </ul>
15. Intravenous injection of contrast during computed tomography of chest cavity organs is a routine procedure for diagnostic of pathological changes in the thymus gland, isn't it?	<ul style="list-style-type: none"> <li>A. Obligatory procedure</li> <li>B. Additional procedure</li> <li>C. Never performed</li> </ul>
16. What immunological diagnostic methods used in patients with myasthenia gravis before thymectomy?	<ul style="list-style-type: none"> <li>A. Antibodies to acetylcholine receptors</li> <li>B. Anti-titin antibodies</li> <li>C. Antibodies to muscle-specific tyrosine kinase</li> <li>D. Never performed</li> </ul>
17. Is the thyroid status assessed in all patients with thymic diseases before surgery?	<ul style="list-style-type: none"> <li>A. Yes</li> <li>B. No</li> </ul>
18. Do you always perform thymectomy for patients with signs of hyperplasia of thymus?	<ul style="list-style-type: none"> <li>A. Only in cases with Myasthenia gravis</li> <li>B. No</li> <li>C. In cases with Myasthenia gravis, if neurological treatment was ineffective</li> </ul>

Table 2 (continued)

Table 2 (continued)

Question	Responses
19. Do you perform a thymectomy for thymus hyperplasia in conjunction with the ophthalmic form of myasthenia gravis?	A. Yes, if neurologist found indication for surgery B. No C. Yes, if suspicion of a tumor presence
20. Do you perform an immunohistochemical study for thymic tumors?	A. Yes B. No C. Yes (in another clinic)
21. Which prophylaxis of specific complications is performed in the preoperative period of thymectomy in patients with myasthenia gravis?	A. Extracorporeal methods of blood purification B. Immunoglobulins C. Glucocorticosteroids D. Cytostatics E. Never performed
22. What is the main method of treatment of myasthenic crisis that occurred after thymectomy?	A. Extracorporeal methods of blood purification B. Immunoglobulins C. Glucocorticosteroids D. Individual approach
23. What are the criteria for radiation therapy after thymectomy?	A. Tumor size more than 8 cm B. Cytoreductive surgery C. Extracapsular invasion of tumor D. Tumor invasion into adjacent structures (pericardium, lung, etc.)
24. What difficulties for spreading of minimally invasive operations on the thymus gland in Russia?	A. Inadequate equipment of the clinic B. Insufficient training of the surgical team C. There are no difficulties, this method is the main one in our clinic

associated with a very low diagnostic efficacy. Currently, computed tomography is used in all clinics in the Russian Federation as a gold standard for diagnostic of mediastinal masses. Nevertheless, the computed tomography with intravenous injection of contrast is performed routinely only in 52% (13 centers) of all thoracic departments. MRI is an infrequent examination (5/25% of respondents). We received information that PET-CT used only in one clinic.

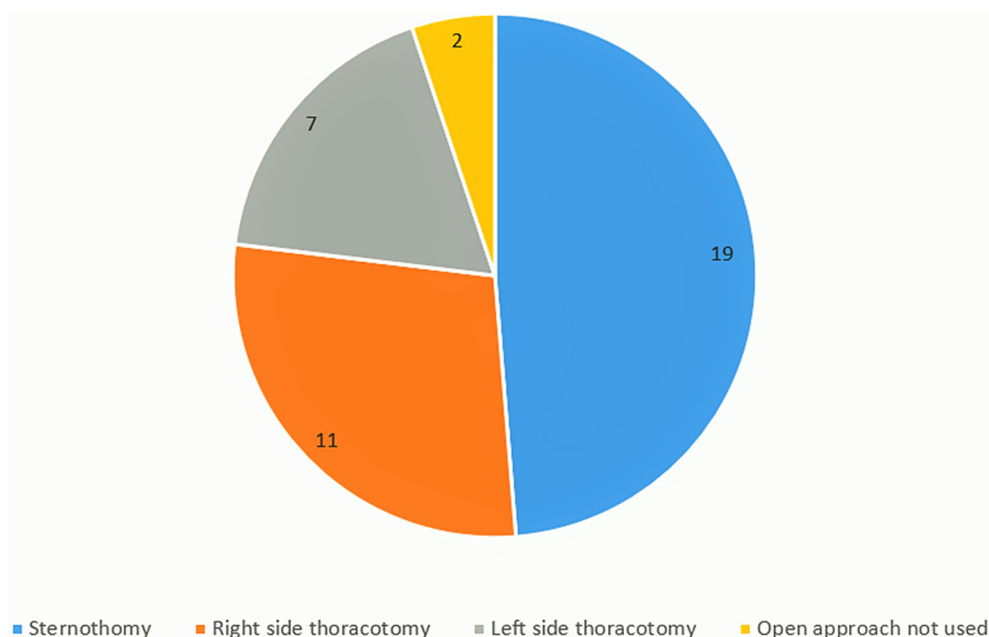
The prevalence of myasthenia gravis and myasthenic syndromes among all thymus-associated syndrome influenced to the plan of preoperative examination. Routine diagnostic algorithm included neuro myography and the level measurement of antibodies to acetylcholine receptors in all centers. Such patients are often transmitted to the thoracic clinic from neurological department (15/60% of respondents) after full examination and course of

preoperative treatment, if required. Other patients come to surgical center (mainly with tumors) after screening radiological examination. Additionally, antibodies to muscle-specific tyrosine kinase are determined in three departments (12%), anti-titin antibodies are determined in five departments (20%).

Widespread belief, that autoimmune diseases of the thyroid gland and myasthenia gravis is frequent combination (2,3). However, the experience of simultaneous operations on the thyroid and thymus glands showed in work only of five thoracic centers (20%). In this context, the assessment of thyroid status performed by nine respondents (36%) before surgery.

#### *Indication and volume for surgery*

All mediastinal masses are an absolute indication for



**Figure 1** Open approaches for thymectomy.

surgery, and also an indication for thymectomy, now well known (4,5). Currently, the most authors consider that the adequate volume of surgery for patients with myasthenia gravis is extended thymectomy with the total remove of the fat tissue in anterior mediastinum and infrathyroid area (6). Frequent opinion is that total remove of fat associated with the possible presence of aberrant thymic tissue in majority of cases. However, 12 respondents (48%) said they had never met aberrant thymus lobes in their practice. Experience of 11 (44%) centers showed presence of aberrant thymic tissue in up to 30% cases.

Surgery for hyperplasia of the thymus gland is marked by heterogeneous views. Sixteen respondents (64%) performed thymectomy in all patients with a combination of hyperplasia and myasthenia gravis. In eight centers (32%), surgical treatment was performed in such cases only if the neurological therapy was ineffective.

### **Perioperative period**

One of the points of the perioperative period is the prevention of specific complications in patients with myasthenia gravis. Extracorporeal methods of blood purification (for crisis) (15 respondents/60%) and glucocorticosteroids (18 respondents/72%) are used in the most of the clinics.

Another point is the detailed examination of removed specimens with determination of the type of thymoma

and degree of tumor's invasion. Pathological examination includes an immunochemistry tests in all centers.

Postoperative treatment has to be performed under supervision of neurologist, if required. The reasons for radiation therapy are tumor invasion into surrounding organs (18 respondents/72%), extracapsular tumor invasion (9 respondents/36%) and cytoreductive surgery (13 respondents/52%).

### ***Surgical approach for thymectomy: features of VATS thymectomy***

Today VATS is the most usable approach for surgical procedures for thymic diseases (more than 50% surgeries per year in 17 from 25 clinics). Nevertheless, different surgical schools showed various techniques.

The feasibility of uniportal thoracic surgery is proved on the example of lobectomies. However, uni- and biportal VATS were performed only in three centers (12%), according to the results of the survey. Most common approach is three portal VATS (23 centers/92%). We did not get results about the use of subxyfoidal access in any clinic (*Figure 2*).

The preferred side of the approach is the right (*Figure 3*) (7). However, five respondents (20%) used left-side (*Figure 4*) (8), and one used bilateral approach (4%). Sixty-eight percent of the respondents (17 respondents) planned operation in conformity with enlarged right or left lobes of thymus gland,



in the most thoracic centers were resections of mediastinal masses and thymectomy. Generally, spread of robotic thoracic surgery in the Russian Federation associated with difficulties due to the high cost. Today, we have information about initial experience of robotic thymectomy in three centers in Russia.

Features of operation and preoperative preparation are the same as for VATS thymectomy. Additional step is the docking of robotic system under 15–20 degree of patient head. We use VATS-based approach for robot-assisted operation with three robotic ports (one port for camera and two ports for tools) and one assistant port. Suction/irrigation, retraction and removal of specimen

are performed from assistant port. Precise preparation and improved visualization during robotic surgery make it possible to refuse of the additional cervical approach for to remove infrathyroid fat. The side of surgery also depends on localization of thymoma or the most enlarged lobe of thymus gland. However, left-side approach for thymectomy is more comfortable versus VATS, due to technical features of robotic surgical system.

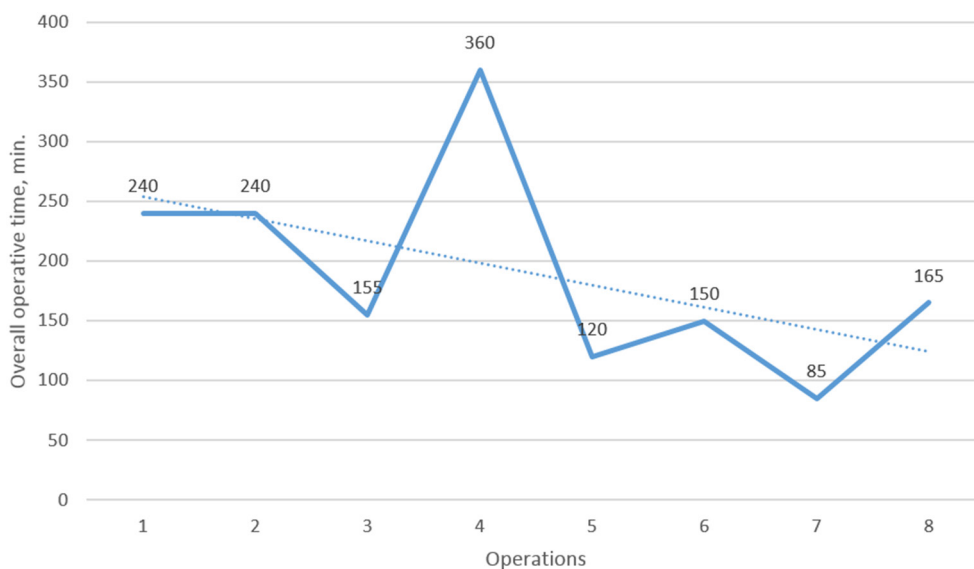
**Single-center experience in robot-assisted thymectomy (Saint-Petersburg Research Institute Phthisiopulmonology)**

During period from January 2014 to March 2017, 14 patients with different disease of thymus gland underwent thymectomy with using of surgical robotic system (da Vinci Si Robotic System). There were 11 patients with thymomas and 3 patients with thymic cysts. Three cases were associated with myasthenia gravis and were underwent preoperative treatment in neurological department.

The most operations were performed with right-side approach (10 patients/77%) (Figure 5) (9). Learning curve of surgery showed on Figure 6. In these cases average operative time was 202+81 min (console operative time was 87+29 min). Intraoperative blood loss was 30–200 mL. In two cases of thymoma robot-assisted thymectomies were combined with: (I) robot-assisted right upper lobectomy (for peripheral NSCLC); (II) right-side hemi-thyroidectomy thyroid goiter (transcervical approach).



**Figure 5** RATS thymectomy (right-side approach) (9). Available online: <http://www.asvide.com/articles/1665>



**Figure 6** Learning curve of right-side robot-assisted thymectomy.





**Figure 7** RATS thymectomy (left-side approach) (10). Available online: <http://www.asvide.com/articles/1666>

Left-side approach was used in four cases (average and console operative time were  $252 \pm 17$  and  $210 \pm 10$  min respectively) (Figure 7) (10). Intraoperative blood loss was 30–100 mL.

There was one case (7%) with conversion to thoracotomy due to large size of tumor and dense adhesions in the area of apex of tumor, and it was the case with previous strumectomy (for thyroid goiter).

There were no postoperative morbidity and mortality in this initial series of patients.

## Conclusions

The question of the validity of minimally invasive surgery in diseases of the thymus gland has been widely discussed in the medical literature in the last 20 years.

Current status of thymic surgery in Russia is presented by VATS as a standard access for all thymic diseases (in 19 thoracic centers/6%).

Robotic surgery today is a developing technology today, in this way the first results showed the possibility of robotic procedures as a future alternative for VATS approach in the thymic surgery.

Nevertheless, inadequate equipment (3 centers/12%) and insufficient training (5 centers/20%) of surgical team are factors, which brake the development of minimally invasive surgery in some thoracic centers.

## Acknowledgements

We thank our colleagues: Ablitsov AY (Moscow), Avzalethdinov AM (Ufa), Akopov AL and Dvoreckii CY (St. Petersburg), Atjukov MA (St. Petersburg), Bagirov MA

(Moscow), Bazarov DV (Moscow), Benyan AS (Samara), Broder IA and Sekhniadze DD (Tyumen), Gumerov II (Ulyanovsk), Kochenogov AV (Vologda), Kotrunov V.V. (Volgograd), Korobeinikov FV (Novosibirsk), Kozak AR (St. Petersburg), Nechay VS (Tula), Pikin OV (Moscow), Pechetov AA (Moscow), Pischik VG (St. Petersburg), Popov MI (Moscow), Porkhanov VA and Danilov VV (Krasnodar), Pushkin SY (Samara), Ratnov SA (Lipetsk), Razumovsky AY (Moscow), Sigal AM (Kazan), Skriabin SA (Murmansk), Sulimanov RA (Novgorod), Topolnitsky EB (Tomsk), Voronchikhin AE (Izhevsk), who provided the insight and expertise that was greatly assisted in the research, although they may not agree with all of the interpretations and conclusions of this paper. We thank Vadim Pischik and Evgenii Shepichev for provision of video of VATS thymectomy that much improved the manuscript. We also thank Igor Vasilev for help in concept and design of this paper and Nina Koneva for improving the use of English in the manuscript.

## Footnote

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

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doi: 10.21037/jovs.2017.07.14

**Cite this article as:** Yablonskii P, Kudriashov G, Pischik V, Sigal E, Nuraliev S. Thymic MIS: state of the art across the world (Russian Federation). *J Vis Surg* 2017;3:119.