SURGICAL TREATMENT OF MYASTHENIA GRAVIS USING A ROBOTIC SYSTEM – A LITERATURE REVIEW AND A DESCRIPTION OF THE FIRST SURGERY IN POLAND

Chirurgiczne leczenie miastenii – przegląd literatury i opis pierwszego zabiegu z zastosowaniem systemu robotycznego w Polsce

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Abstract

Introduction and objective: Surgical treatment of myasthenia gravis with a use of the robotic system has been applied worldwide over past 20 years. On February 22, 2022, for the first time in Poland, extended thymectomy using robot-assisted thoracoscopic surgery approach was performed at the Military Institute of Medicine – National Research Institute in Warsaw. **Material and methods:** Three port, left-sided approach with CO_2 insufflation was performed. The left phrenic nerve was located and left lower pole of the thymus with fat of the left diaphragmatic angle was dissected. Further dissection of the thymus from the pericardial sac and along the left phrenic nerve with visualisation of the left brachiocephalic vein up to the level of the thyroid lobes was performed. Thymic veins were managed and the upper poles of the thymus were dissected. Right pleural cavity was opened and thymus was removed along right phrenic nerve with right lower pole of the thymus and surrounding fat tissue of right diaphragmatic angle. Specimen was removed and both pleural cavities were drained using single 24 Fr drain. **Results:** The operative time was 162 minutes, postoperative course was uneventful. The total postoperative drainage measured 50 ml and chest tube was removed on the first postoperative day. The amount of pain the patient suffered was moderate. The patient was discharged from the hospital on the second postoperative day. On the pathological study an atrophic thymus with mediastinal lymph nodes and fatty tissue were found. **Conclusions:** Robot-assisted thoracoscopic surgery extended thymectomy allowed for safe and radical resection of the thymus and surrounding fat tissue with a reduction in the time of hospitalization.

Streszczenie

Wprowadzenie i cel: Na świecie leczenie miastenii z użyciem systemów robotycznych jest stosowane w chirurgii klatki piersiowej od 20 lat. W Polsce po raz pierwszy operację torakochirurgiczną z zastosowaniem takiego systemu przeprowadzono 22 lutego 2022 r. w Wojskowym Instytucie Medycznym – Państwowym Instytucie Badawczym w Warszawie. Wykonano wtedy tymektomię rozszerzoną metodą torakoskopii z użyciem systemu robotycznego da Vinci Xi. **Materiał i metody:** Zastosowano dostęp lewostronny z użyciem trzech trokarów roboczych i insuflacją CO_2. Po uwidocznieniu lewego nerwu przeponowego uwolniono lewy dolny róg grasicy wraz z tłuszczem lewego kąta przeponowo-żebrowego. Następnie odpreparowano grasicę wzdłuż lewego nerwu przeponowego od worka osierdziowego, uwidoczniono lewą żyłę ramienno-głowową, zaopatrzono gałęzie żylne do grasicy i wypreparowano rogi górne grasicy do poziomu dolnych biegunów tarczycy. Szeroko otwarto prawą jamę opłucnej i wypreparowano grasicę wzdłuż prawego nerwu przeponowego wraz z otaczającą tkanką tłuszczową oraz tłuszczem prawego kąta przeponowo-żebrowego. Preparat usunięto z pola operacyjnego i do obu jam opłucnej założono pojedynczy dren 24 Fr, wprowadzony przez jeden z portów torakoskopowych. **Wyniki:** Operacja trwała 162 minuty. W okresie pooperacyjnym nie stwierdzono powikłań, drenaż całkowity wyniósł 50 ml, dren usunięto w 1. dobie po zabiegu. Nasilenie bólu pooperacyjnego było na średnim poziomie, co pozwoliło na wypisanie pacjentki w 2. dobie po operacji. W badaniu histopatologicznym preparatu pooperacyjnego wykazano obecność zanikowej grasicy wraz z otaczającym tłuszczem i węzłami chłonnymi. Wnioski: Zastosowanie systemu robotycznego w rozszerzonej resekcji grasicy u pacjentki z miastenią pozwoliło na przeprowadzenie bezpiecznego i radykalnego zabiegu, a przez to zmniejszenie nasilenia bólu pooperacyjnego i skrócenie hospitalizacji.

Keywords: thoracic surgery, myasthenia gravis, surgical treatment, RATS, da Vinci robotic system

Słowa kluczowe: chirurgia klatki piersiowej, miastenia, leczenie operacyjne, RATS, system robotyczny da Vinci

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Introdution

Myasthenia gravis (MG) is a rare autoimmune disorder in which autoantibodies directed against acetylcholine receptors (AChRs) cause impaired neuromuscular transmission, which manifests as fatigable muscle weakness [1]. The incidence rate of myasthenia gravis is between 0.25 and 2 cases/100,000 people/year, and the prevalence is between 4.5 and 14.2 cases/100,000 people/year [2, 3].

The diagnosis of MG is based on the characteristic clinical presentation and positivity for anti-AChR antibodies, electrostimulation tests (repetitive nerve stimulation and single fibre electromyography) and a positive Tensilon test [4]. A chest CT or MRI scan should be also performed to exclude a thymic tumour (approximately 10–30% of MG cases are associated with thymomas) [5, 6].

Pharmacological treatment of MG involves the use of pyridostigmine, an acetylcholinesterase inhibitor, as the initial treatment. Some patients additionally receive immunosuppressants and corticosteroids. Intravenous immunoglobulin infusions and plasmapheresis are used in the most severe cases.

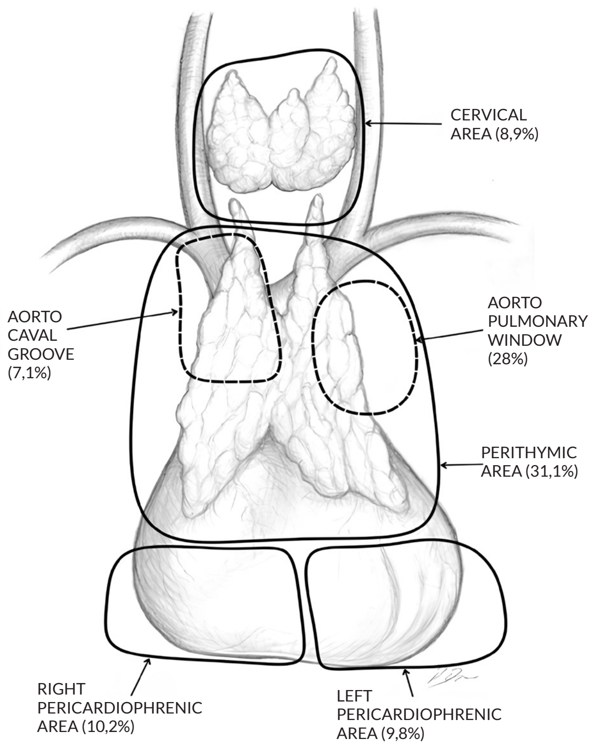

Figure 1. Foci of ectopic thymic tissue in the neck and mediastinal fat in the samples from the Hospital for Lung Diseases in Zakopane [9]

Surgical treatment

Surgical treatment is necessary in cases of thymoma-associated MG (TAMG) and as a therapeutic option to limit or discontinue immunosuppressants in patients who do not improve despite pharmacological treatment or do not tolerate such treatment.

Surgical treatment of MG involves thymectomy, optimally using an extended technique, the goal of which is to remove the entire thymus, including the perithymic fatty tissue that may contain ectopic thymic foci [7, 8]. The extent of adipose tissue resection includes the neck region from the level of the lower thyroid poles, through the adipose tissue around the right and left brachiocephalic veins, the superior vena cava, the brachiocephalic trunk and the aortic arch, to the bilaterally localised fat of the costophrenic angles contained between the right and left diaphragmatic nerve, representing the border of resection (fig. 1).

Types of access for thymectomy and surgical outcomes

To date, the literature has proposed a number of surgical accesses for thymectomy, which can be somewhat simplified into two main groups:

- open surgery – cervical access, sternotomy and thoracotomy;
- minimally invasive surgery – video-assisted thoracoscopic surgery (VATS) and robot-assisted thoracoscopic surgery (RATS).

The first thymectomy for MG was performed by Ernst Ferdinand Sauerbruch in 1911 in a patient with coexisting hyperthyroidism. It involved partial removal of the thymus gland and partial resection of the thyroid gland from a cervical access and resulted in a reduced severity of MG symptoms [10]. Alfred Blalock was the first surgeon to perform elective surgery for MG and he described a series of thymectomies through median sternotomy in 1939 [11].

In the 1960s, due to the high risk of extensive procedures with sternotomy access, there was a return to the much safer interventions with cervical access. In 1987, Papatestas et al. presented the outcomes of 1,100 subtotal thymectomies from cervical access [12].

A significant number of MG recurrences have been observed in subtotal thymectomies from cervical access, with thymic remnants left in the anterior mediastinum [13, 14].

Studies conducted mainly in Japan (Masaoka) and the United States (Jaretzki) found that the increase in full MG remissions is related to the extent of resection not only of the thymus itself, but also of the perithymic fatty tissue containing ectopic thymic foci.

The distant surgical outcomes, as measured by the rates of complete remissions achieved using various extended thymectomy techniques, are up to 47% up to 5 years after resection [15–18].

In 1988, Jaretzki et al. presented the technique and outcomes of a 'maximal' thymectomy performed by sternotomy and cervical incision, allowing for extensive resection of the thymus itself along with the surrounding perithymic adipose tissue located in the neck, large mediastinal vessels and bilaterally in the vicinity of costophrenic angles [19]. In parallel, techniques for extended thymectomy with resection of surrounding adipose tissue from cervical access with sternal elevation, proposed in 1988 by Cooper et al. [20], have evolved. The development of thymic surgery in the form of minimally invasive videothoracoscopic surgery continued in the 1990s. The first report was presented in 1994 by Novellino et al., who combined cervical incision with sternal elevation and bilateral 3-port VATS [21]. Zielinski (2000) and Takeo et al. (2001) described a technique for minimally invasive maximal thymectomy from cervical and subxiphoid access with sternal elevation and bilateral, single-port videothoracoscopy [22, 23].

Minimally invasive surgery has achieved a resection extent comparable to that of sternotomy and, most importantly, equally good clinical outcomes in terms of complete remissions [24].

RATS thymectomy for thymoma (Masaoka grade I), performed in 2000 by Yoshino, was the first thoracoscopic thymectomy performed using a robotic system [25]. Ashton et al. performed the first extended RATS thymectomy using the bilateral approach for MG in 2003 [26]. In 2015, Rueckert presented the largest series of 449 RATS thymectomies performed between 2003 and 2014, which included 397 patients with MG, 64 patients with thymoma, 53 patients with TAMG, seven patients with parathyroid adenoma and 29 other patients [27].

The analysis of the largest series of robot-assisted thymectomies demonstrated a high safety profile for RATS procedures and lower complication rates (1.6–7.2%, with lymphadenopathy, bleeding and myasthenic breakthrough being the most common ones), less intraoperative blood loss and shorter hospital stay compared to open surgery. Additionally, RATS and VATS thymectomies are comparable in terms of completeness, number of complications, length of hospital stay and the rates of conversion to sternotomy [28].

In 2016, Wolfe et al. published their prospective randomised study showing that performing maximal thymectomy using sternotomy access in patients with AChR MG improves treatment outcomes and allows for reduced doses of immunosuppressants compared to patients who did not undergo surgery. This study has delivered the most important evidence supporting the efficacy of thymectomy in non-thymomatous MG (NTMG) [29].

The first use of a robotic system in surgical treatment of myasthenia gravis in Poland

In February 2022, the da Vinci Xi robotic system was used for the first time in Poland for a thoracic surgery at the Military Institute of Medicine – National Research Institute in Warsaw. An extended thymectomy was performed in a 22-year-old female patient with EMG-confirmed AChR MG. Left-sided access was used by sequentially inserting three thoracoscopic ports: two 8 mm working ports (in the 3rd and 7th intercostal spaces) and one 12 mm camera port (in the 5th intercostal space). A CO_2-induced pneumothorax was created in the left pleural cavity to 7 mm Hg (fig. 2). The left phrenic nerve was located and, along its course, the left diaphragmatic angle fat and the left lower pole of the thymus were dissected. Further dissection of the thymus from the pericardial sac cranially, along the left phrenic nerve with visualisation of the left brachiocephalic vein was performed. In the neck, the upper poles of the thymus were dissected along with the perithymic fat up to the level of the thyroid lobes (fig. 3). The two thymic veins arising from the left brachiocephalic

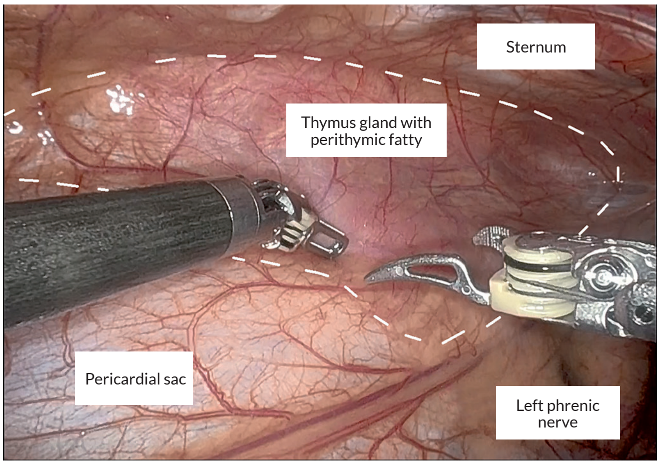

Figure 2. Access through the left pleural cavity – in the marked area, the planned extent of thymectomy including pericardial fat, CO_2 insufflation to 7 mm Hg

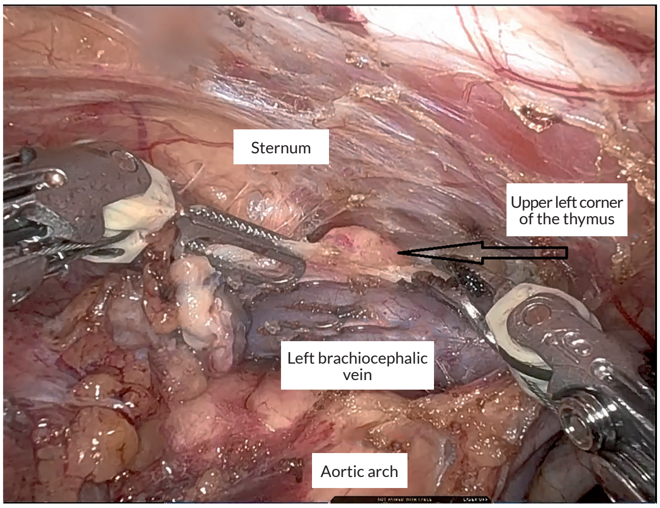

Figure 3. In the foreground, the dissected aortic arch and left brachiocephalic vein; view during dissection of the left superior thymic horn up to the level of the lower pole of the thyroid gland

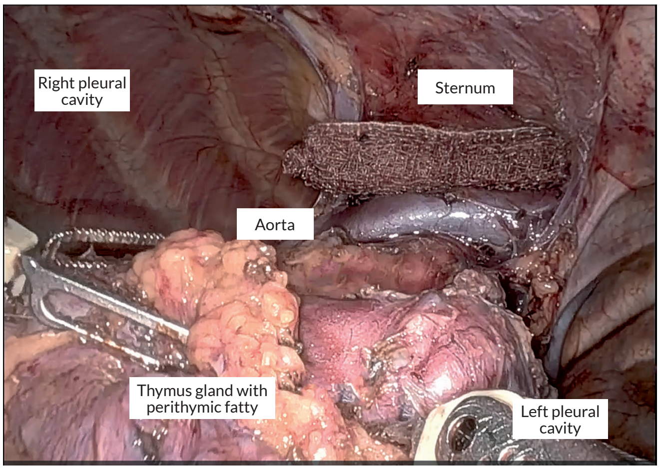

Figure 4. Wide-open both pleural cavities. The patient was intraoperatively ventilated using a double-lumen endotracheal tube for selective lung ventilation

vein were closed using bipolar coagulation. The right pleural cavity was opened and the thymus along with the surrounding fat was successively dissected from the aortic arch, superior vena cava, pericardial sac and right phrenic nerve, removing the right costophrenic angle fat along with the specimen (fig. 4). At the next stage, lymph nodes were removed from the area of the aortic arch and the left pulmonary artery, as well as the right brachiocephalic vein and the superior vena cava. The specimen was removed in a retrieval bag through a 12 mm camera port and a single 24 Fr drain was inserted through the left pleural cavity, with its end located in the right pleural cavity.

The operative time was 162 minutes and intraoperative blood loss was approximately 20 mL. The postoperative period was uneventful, the drain was removed on day 1 and the total postoperative drainage was 50 mL. The use of the minimally invasive RATS technique allowed for early patient mobilisation and discharge on day 2 postoperatively. The postoperative pain was moderate, requiring paracetamol and metamizol, with no need for morphine. Histopathological examination of the postoperative specimen showed atrophic thymus with surrounding fat and lymph nodes.

At 12 months postoperatively, the dose of the reversible acetylcholinesterase inhibitor was reduced by 67% compared to preoperatively.

Conclusions

The benefits of using the Vinci Xi robotic system in thoracic surgery include the minimally invasive nature of the surgical access due to the use of 8 and 12 mm thoracoscopic ports. Rapid postoperative patient mobilisation reduces the risk of complications. Magnified three-dimensional visualization of operative filed combined with a considerable range of instrument motion allows for precise tissue dissection in small space and makes it possible to achieve the full radicality of the procedure.

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