Short- and long-term effects of robot-assisted plication in diaphragmatic paralysis – the prospective RAPIDLY-study

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Andreas Palm, MD, PhD
Department of Medical Sciences
Lung-, allergy-, and sleep research
Uppsala University
SE-781 85, Uppsala
Sweden

andreas.palm@medsci.uu.se

Participating centers/ co-workers

Uppsala
Össur Emilsson, ossur.emilsson@medsci.uu.se
Karin Ersson, karin.ersson@medsci.uu.se
Tomas Hansen, tomas.hansen@uu.se
Per Landelius, per.johan.landelius@akademiska.se
Andrei Malinovschi, andrei.malinovschi@medsci.uu.se
Emma Thorén, emma.thoren@akademiska.se
Andreas Palm, andreas.palm@medsci.uu.se

Linköping
Miklos Boros, miklos.boros@regionostergotland.se
Kricka Ozren, kricka.ozren@regionostergotland.se

Lund
Jesper Andreasson, jesper.andreasson@skane.se
Jonas Einarsson, jonas.einarsson@med.lu.se
Magnus Ekström, pmekstrom@gmail.com

Umeå
Anders Blomberg, anders.blomberg@umu.se
Mattias Karlsson, mattias.karlsson@regionvasterbotten.se
Ala Muala, ala.muala@umu.se

Göteborg
Anders Andersson, anders.andersson@lungall.gu.se
Maya Landenhed-Smith, maya.landenhed.smith@vgregion.se
Martin Silverborn, martin.silverborn@vgregion.se

Introduction
Diaphragmatic paralysis is a rare condition caused by damage to the phrenic nerve and can be either idiopathic or originate from, for example, an infection or previous surgery. This condition often causes significant suffering through breathlessness, accentuated when lying down and during exertion. Over the years, selected patients have found relief from their symptoms through diaphragmatic plication. This operative procedure tightens and lowers the elevated diaphragmatic dome. Furthermore it recruits lung volume and reduces paradoxical diaphragmatic movement (1). Traditionally, these operations have been performed with open thoracotomy, but in recent years, minimally invasive techniques, video-assisted thoracoscopic surgery (VATS) (2, 3) have been developed. Compared to traditional open surgical techniques, VATS can provide faster recovery, reduced need for postoperative pain medication, and shorter hospital stays, with equally good surgical outcomes (1, 4). In several single-center cohorts, post-operative improvement in forced expiratory volume in 1 second (FEV1) and vital capacity (VC) with

12-21% and 12-25%, respectively, have been reported. Dyspnea quantified by the Medical Research Council (MRC) scale improved by up to 2 steps (5) and 6-minutes walking distance improved by 51 meters (6). However, a new technique, robot-assisted diaphragmatic plication, is spreading and increasingly replacing VATS. (7). One small retrospective study of 43 patients found comparable results between these techniques with a 7% increase in FEV_1 in both groups. In this study, symptom improvement was not analysed. Other published studies on robot-assisted thoracic surgery are also single-center studies on small cohorts consisting of 11-46 patients (8-12), often focusing on surgical safety and complications. Lung function and radiological changes have also sometimes been measured along with retrospective evaluation of symptoms before and after the operation, a design with major methodological weakness. However, no significant complications have been reported, and patients seem to improve their lung function and their symptom burden (8-12). Prospective studies evaluating RATS diaphragmatic plication are lacking.
This prospective cohort study, the **R**obot-**a**ssisted **p**lication **i**n **d**iaphragmatic para**ly**sis study (The RAPIDLY-study) aims to evaluate the short- and long-term effect of robot-assisted diaphragmatic plication on physical performance, subjective breathlessness, lung function, blood gases, and radiology at five Swedish university hospitals, Gothenburg, Linköping, Lund, Umeå, and Uppsala.

Method

Study design and population

This multicenter observational cohort study will include patients with symptomatic unilateral diaphragmatic paralysis persisting for ≥1 year (6), scheduled for RATS at thoracic surgery clinics in five Swedish university hospitals (Gothenburg, Linköping, Lund, Umeå, and Uppsala). The expected number of patients per center is estimated to 3-5 annually.
Exclusion criteria are inability to complete forms in Swedish, neuromuscular disease as the cause of diaphragmatic paralysis, and other significant causes of dyspnea and impaired physical capacity than diaphragmatic paralysis.
Patients will be assessed preoperatively and postoperatively after one to three months and after one and three years.

Assessments

Patient characteristics

Age, sex, height, and weight will be recorded. Body mass index (BMI) is calculated by dividing a person's weight by their height in meters squared.
Aetiology of diaphragmatic paralysis, relevant co-morbidities and use of long-term oxygen therapy and/or mechanical ventilation will be recorded.
The date for symptom debut, if known, is recorded.
Smoking history is defined as current smoker, ex-smoker (smoking history of ≥100 cigarettes and having quit smoking ≥6 months ago), and never smoker (smoking history of <100 cigarettes) (13). Smoking is quantified by pack-years (the number of packs of

cigarettes a person has smoked daily, multiplied by the number of years they have smoked) (14).

Primary outcome
The patients' exercise capacity will be evaluated using the 6-minute walking distance (6MWD). The patients are asked to walk as far as possible on a flat, straight surface for six minutes, and the total distance walked is measured (15-17).

Secondary outcomes
Questionnaires
The **modified Borg Scale** is a tool with a range from 0 to 10 used to measure an individual's perceived level of breathlessness or muscle fatigue during physical activity, where 0 represents no breathlessness, and 10 represents maximal breathlessness (15).
The **modified Medical Research Council** (mMRC) dyspnea scale is used to assess the severity of breathlessness. The scale ranges from 0 to 4, with higher scores indicating more significant breathlessness (18).
The **Dyspnea-12** is a questionnaire used to measure the severity and quality of breathlessness in individuals with respiratory or cardiovascular conditions. It assesses dyspnea's physical and emotional aspects, providing a comprehensive picture of how breathlessness affects a person's life. It consists of 12 items, each with a scale range between 0 (no dyspnea) and 3 (severe dyspnea) (19-21).
The **EQ-5D** is one of the most widely used tools for assessing health-related quality of life. It includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. These dimensions create a descriptive profile that can be converted into a single summary index, where a score of 1.0 indicates perfect health. Additionally, the tool includes a Visual Analog Scale (VAS), ranging from 0 (worst imaginable health) to 100 (best imaginable health), for self-assessment of overall health status (22).

Spirometry
Spirometry will be conducted 15 minutes after bronchodilation (inhalation of 200 µg salbutamol) in both supine and upright positions. Body plethysmography and single-breath DLCO measurement will be performed. Predicted values will be determined using reference equations from the Global Lung Function Initiative (GLI) (23).

One-minute sit-to-stand test (1-MSTST)
This test assesses a person's functional exercise capacity by recording the number of full sit-to-stand repetitions completed in 60 seconds (24).

The **Maximal Inspiratory Pressure (MIP)** test is a respiratory test that measures the strength of the inspiratory muscles, particularly the diaphragm. By inhaling as forcefully as possible in a handheld device, the maximum negative pressure generated is recorded (25).

Blood gas analysis

A capillary or arterial blood gas analysis obtains the partial pressure of Oxýgen and Carbon dioxide (PaCO2) and Base excess (BE). Pulse oximetry obtains oxygen saturation.

Chest X-ray
Chest X-rays are acquired in full inspiration and expiration in frontal and lateral views. The distance from the most cranial part of the lung to the highest part of the diaphragm in both frontal and side views are measured separately.

Computerised tomography (CT) of Thorax
A CT with a standard protocol to identify and quantify lower lobe atelectasis.

Adverse events
Operating time, chest-drain duration, length of hospitalisation, per- and postoperative complications such as pain, bleeding and infections, 30-day readmission and 30-days mortality are recorded.

Statistics
Descriptive statistics summarise the data, and inferential statistics compare group differences.
Associations with the outcomes will be analysed using multivariable regression models, including linear regression (for continuous outcome variables) and logistic regression (for categorical outcomes). Repeated measurements within individuals will be managed through multilevel, random-effects models.

Power calculation: Based on a standard deviation of 90 meters in the 6-minute walk test (6MWT) among the general population (16), and considering that the minimal clinically important difference (MCID) is 53 meters (17), a total of 45 patients is required.

Table of study assessments

	Baseline	1-3 months post-operatively	12 months post-operatively	3 years post-operatively?
Demographics	X			
Height	X			
Weight	X	X	X	X
BMI	X	X	X	X
Waist-hip ratio	X	X	X	X
Co-morbidities	X			
Smoking/PY	X			
Indication for op	X			
Questionnaires (The modified Borg-scale, mMRC, Dyspnea-12, EQ-D5)	X	X	X	X
6MWT	X	X	X	X

Body plethysmography, dynamic spirometry in seated and supine position, and DLCO	X	X	X	X
MIP	X	X	X	X
1 minute Sit-to-stand test	X	X	X	X
Chest X-ray	X	X	X	X
CT-scan	X	X		
Saturation	X	X	X	X
Arterial/capillary blood gas	X	X	X	X
Questionnaire pain/adverse effects		X	X	X

Ethical considerations
Robot-assisted diaphragm plication is performed at several university hospitals in Sweden and abroad. The patients in this study have been clinically approved for this surgery. They are not exposed to any additional risks in this study beyond being examined more thoroughly with surveys and questionnaires, lung function and performance tests, and chest X-rays before and after the surgical procedure. An application will be submitted to the Ethics Review Authority.

Relevance of research
Robot-assisted plication in diaphragmatic paralysis is a new operative method performed at many thoracic centres worldwide without being scientifically evaluated in prospective studies. This national multicenter study, with a large cohort by international standards and with validated, highly relevant outcome variables, is expected to gain significant attention among thoracic surgeons and pulmonary physicians worldwide. The study has been approved by the Swedish Ethical Review Authority, Dnr 2025-01028-01and, and is registered on ClinicalTrials.gov, Dnr 2025-01028-01.

Preliminary results
None.

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