Surgical approach in myasthenia gravis: a systematic review and meta-analysis.

Paola Solis- Pazmino, Joseph B Shrager, Oscar Ponce, Eddy Lincango-Naranjo, Ioana Baiu

Citation

Paola Solis- Pazmino, Joseph B Shrager, Oscar Ponce, Eddy Lincango-Naranjo, Ioana Baiu. Surgical approach in myasthenia gravis: a systematic review and meta-analysis.. PROSPERO 2020 CRD42020166827 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020166827

Review question

Participants: Adults with myasthenia gravis

Interventions: Extended Transcervical thymectomy (TCT) Extended TCT using the cooper thymecomy retractor Extended with thoracoscopy (videoscopic) technology without intercostal incisions Thoracoscopic thymectomy VATS unilateral alone or combined with robotic technology Bilateral VATS or robotic, including VATET Extended Transternal thymectomy Transcervical and transternal maximal Subxiphoid Thymectomy, VATS or robotic

Comparator(s)/control: We will include studies with at least one of the following comparators: 1. Extended Transcervical thymectomy (TCT) 1.1 Extended TCT using the cooper thymectomy retractor 1.2 Extended with thoracoscopy (videoscopic) technology without intercostal incisions 2. Thoracoscopic thymectomy 2.1 VATS unilateral alone or combined with robotic technology 2.2 Bilateral VATS or robotic, including VATET 3. Extended Transternal thymectomy 4. Transcervical and transternal maximal 5. Subxiphoid Thymectomy, VATS or robotic

Outcomes: Complete Stable Remission and Pharmacological remission

Times: mean or median fu must be at least 3 years

Studies: Comparative studies

Searches

A systematic literature search of articles published up to May 2019 will be conducted with the assistance of an experienced librarian in electronic databases (Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily, The Cochrane Library, Ovid EMBASE, and Scopus) without any language restriction.

Types of study to be included

We will include comparative cohort studies. We will exclude letters, editorials, consensus statements, guidelines and review articles.

Condition or domain being studied

Myasthenia gravis (MG) is an autoimmune disease. It has been mainly treated with thymectomy. However, the ideal operative technique for thymectomy in myasthenia gravis remains controversial. The aim of this study is to clarify the effectiveness of the surgical approach for patients with myasthenia gravis focusing on long-term outcomes and complete stable remission.

Participants/population

• Patients older than 18 year with myasthenia gravis with or without thymoma

Exclusion:

• Patient with preoperative evidence of cervical lymph node metastasis or distant metastasis.

• Articles with less than 20 participants.

• In case of studies with overlapping population, we will exclude the study with fewer patients.

Intervention(s), exposure(s)

We will include studies with at least one of the following interventions:

1. Extended Transcervical thymectomy (TCT)

1.1 Extended TCT using the cooper thymectomy retractor

1.2 Extended with thoracoscopy (videoscopic) technology without intercostal incisions

2. Thoracoscopic thymectomy

2.1 VATS unilateral alone or combined with robotic technology

2.2 Bilateral VATS or robotic, including VATET

3. Extended Transternal thymectomy

4. Transcervical and transternal maximal

5. Subxiphoid Thymectomy, VATS or robotic

Comparator(s)/control

We will include studies with at least one of the following comparators:

1. Extended Transcervical thymectomy (TCT)

1.1 Extended TCT using the cooper thymectomy retractor

1.2 Extended with thoracoscopy (videoscopic) technology without intercostal incisions

2. Thoracoscopic thymectomy

2.1 VATS unilateral alone or combined with robotic technology

2.2 Bilateral VATS or robotic, including VATET

3. Extended Transternal thymectomy

4. Transcervical and transternal maximal

5. Subxiphoid Thymectomy, VATS or robotic

Main outcome(s)

• Complete Stable Remission (CSR): defined as asymptomatic without medication for at least 6 months; or we will also accept studies where “complete remission” is defined as asymptomatic and taking only single drug immunosuppression for at least 6 months.

• Pharmacological remission: single drug, asymptomatic for at least 6 months (Must be analyzed by Kaplan Meier analysis where 3 year results are either reported or can be collected from a graph; or crude cumulative “survival” analysis without KM is acceptable if all patients reported have been followed for at least 3 years (collect also 5 years KM and 5 years cumulative for papers that have this data available)).

* Measures of effect

Must be analyzed by Kaplan Meier analysis (KM) where 3-year results are either reported or can be collected from a graph; or crude cumulative “survival” analysis without KM is acceptable if all patients reported have been followed for at least 3 years (collect also 5 years KM and 5 years cumulative for papers that have this data available).

Additional outcome(s)

None

* Measures of effect

None

Data extraction (selection and coding)

Before initiating study selection and data extraction phase, we will conduct a pilot with 5 articles to assess clarity of the eligibility criteria and extraction form. Also, two reviewers independently will screen each study and extract data from the ones that were selected. Selection of studies: First, titles and abstract will be screened and a study will follow to full-text screening if at least one reviewer considered the study eligible. Second, in full-text screening, only studies included by both reviewers will be considered included for this systematic review. Any disagreement during this phase will be solved by an expert in thymectomy. Reasons of exclusions will be recorded as either not meeting the population, intervention, comparator, outcomes or study design criteria. Kappa statistics is to be calculated for full-text screening. Data extraction: The following data from each included study will be extracted by using standardized forms: (i) study author, date of publication, country, study design, period, setting, area, inclusion criteria and sample size), (ii) participant characteristics (such as age and sex, pre- and post- operative Osserman and MGFA class, MGFA thymectomy classification) and (iii) information on the reported outcome (complete Stable remission or pharmacological remission, analyzed by Kaplan Meier analysis (KM) or crude cumulative “survival” analysis)

Risk of bias (quality) assessment

Study quality will be assessed by two independent reviewers based on CLARITY tool for cohort studies.

Strategy for data synthesis

For time-to-event outcomes, we will follow the recommendations given by Tierney et al. First, we will convert all reported hazard ratios (HRs) into their log forms and calculate the variance (Vs) of the logHR from the reported confidence intervals and then combine them in a random effects meta-analysis. When this data is not published, we will use the observed (O) and logrank expected events (E) to calculate the corresponding hazard ratios and variances. Lastly, if only Kaplan-Meier curves are reported, we will estimate HRs and Vs of each trial by using the template published by Tierney et al. Additionally, we will calculate relative risks and their confidence intervals of each trial by using specific follow-ups. We will combine this data by using random-effects meta-analysis. The I^2 statistic will be used to explore heterogeneity among the included studies. Subgroup analysis will be performed for the following groups. Significance tests will be perform and reported with their corresponding p values.

Analysis of subgroups or subsets

In terms of subgroups analyses, predefined comparisons based on age, MGFA score, Osserman score, and

duration of disease prior to thymectomy and anti-acetylcholine-receptor antibodies.

Contact details for further information
Paola Solis- Pazmino
paosolis@stanford.edu

Organisational affiliation of the review
Division of Thoracic Surgery, Department of Cardiothoracic Surgery, Stanford School of Medicine, Stanford University, Stanford, California
Knowledge and Evaluation Research Unit, Mayo Clinic, Rochester, Minnesota, USA

Review team members and their organisational affiliations
Dr Paola Solis- Pazmino. Department of Otolaryngology–Head and Neck Surgery, School of Medicine, Stanford University, Stanford, California, USA
Assistant/Associate Professor Joseph B Shrager. Division of Thoracic Surgery, Department of Cardiothoracic Surgery, Stanford School of Medicine, Stanford University, Stanford, California.
Dr Oscar Ponce. Unidad de Conocimiento y Evidencia, Universidad Peruana Cayetano Heredia, Lima, Perú
Eddy Lincango-Naranjo. Knowledge and Evaluation Research Unit, Mayo Clinic, Rochester, Minnesota, USA
Dr Ioana Baiu. Division of Thoracic Surgery, Department of Cardiothoracic Surgery, Stanford School of Medicine, Stanford University, Stanford, California

Type and method of review
Meta-analysis, Systematic review

Anticipated or actual start date
20 May 2020

Anticipated completion date
20 May 2021

Funding sources/sponsors
None

Conflicts of interest

Language
English

Country
United States of America

Stage of review
Review Ongoing

Details of final report/publication(s) or preprints if available

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
MeSH headings have not been applied to this record

Date of registration in PROSPERO
28 April 2020

Date of first submission

26 January 2020

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

28 April 2020