Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus minimally invasive esophagectomy for resectable esophageal cancer, a randomized controlled trial (ROBOT-2 trial).

Published: 05-04-2023
Last updated: 24-08-2024

The objective is to evaluate the extent of lymph node dissection, efficacy, risks, quality of life and cost-effectiveness of RAMIE as an alternative to MIE as treatment for esophageal cancer.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON51500

Source
ToetsingOnline

Brief title
ROBOT-2

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal therapeutic procedures

Synonym
esophageal cancer

Research involving

Human

Sponsors and support

Primary sponsor: University Medical Center Mainz
Source(s) of monetary or material Support: Het is een investigated initiated onderzoek zonder externe financiering.

Intervention

Keyword: - Esophageal cancer, - Esophagectomy, - Minimally Invasive Surgical Procedures, - Robotic surgical procedures

Outcome measures

Primary outcome

Our hypothesis is that RAMIE has superior lymph node dissection compared to MIE. Therefore, the primary outcome of this study is the number of dissected lymph nodes. The resected specimen will be marked by the surgical team for the position of lymph node dissection. Evaluation will be performed by an experienced pathologist using standard protocols. Stage grouping will take place according to the Union Internationale Contre le Cancer (UICC) protocol using the TNM-8 classification. The exact localization of the lymph nodes is an essential part of the pathologic examination.

Secondary outcome

Secondary outcomes include:

- Overall postoperative complications according to the modified Clavien Dindo classification (MCDC grade I-V) and definitions stated by the Esophagectomy Complications Consensus Group (ECCG). Postoperative complications include: anastomotic leakage, mediastinitis, gastric conduit necrosis, chylothorax and recurrent laryngeal nerve injury, delayed gastric emptying, pulmonary

complications (pneumonia, pneumothorax, pulmonary embolus, acute respiratory distress syndrome (ARDS)), cardiac complications (atrial fibrillation, cardiac asthma, myocardial infarction) and postoperative bleeding. The incidence of incisional hernias and diaphragmatic hernias will be recorded.

- Length of ICU-MCU stay (days), length of hospital stay (days)
- In hospital mortality (IHM) and mortality within 30, 60 and 90 days postoperatively will be reported. For all patients, the cause of death will be noted.
- Pathology results: The pathology report contains the following parameters: site of tumor, type and gradation, extension in the esophageal wall, margins of the resection, extent of resection (R0, R1 or R2), lymph node status with the number of lymph nodes (primary endpoint) (TNM 8)21. Quality control of the pathologic analysis of the resection specimen will be provided by a specialized gastrointestinal pathologist.
- Overall and disease-free survival (2, 3 and 5 years). Overall survival (OS) was calculated from the date of surgery to the date of death or last follow-up. Disease free survival was calculated from the date of surgery to recurrence or death related to disease and/or treatment or last date of follow-up.
- Operation time is defined as time from incision until closure (minutes) for both the thoracic and the abdominal phase of the procedure. Unexpected events and complications occurring during the operation will be recorded (e.g. hemorrhage requiring transfusion, perforation of other organs) as well as blood loss during operation (ml, per phase). In case of conversion to thoracotomy or laparotomy the reason for conversion has to be explained (absolute

numbers/percentage).

- Visual Analogue Scale (VAS) for pain will be noted at following times:

pre-operatively and the first 14 days after surgery and a fixed periods during

follow up (6 weeks, 6 months and yearly post-operatively up to 5 years).

- Quality of life questionnaires will be required at following times: SF-36,

EORTC QLQ-C30 (Dutch), EORTC OES18 (Dutch) and EQ-5D (Appendix 1 & 2)

pre-operative < 5 days and 6 weeks, 6 months and yearly up to 5 years

post-operatively.

- Postoperative functional recovery was defined as: removal of thoracic tubes,

no requirement of intravenous fluid resuscitation, tolerance for solid oral

intake, the ability to mobilize independently and adequate pain control with

oral analgesics. All items will be assessed daily.

- Cost analysis: The approach for the cost-analysis is comparing actual direct

medical costs incurred with both strategies up until 5 years after the

operation. Costs estimates will be based on the recorded volumes and unit costs

associated with both procedures. This includes the costs of operation rooms,

hospital and ICU stay, costs associated with complications and re-operations.

- Surgeons fatigue assessed by Psychomotor Vigilance tests (PVT) before and

after esophagectomy.

Study description

Background summary

For patients with esophageal cancer, radical esophagectomy with 2-field lymphadenectomy is the cornerstone of the multimodality treatment with curative

intent. Both, conventional minimally invasive esophagectomy (MIE) and robot assisted minimally invasive esophagectomy (RAMIE) were shown to be superior compared to open transthoracic esophagectomy considering postoperative complications. However, no randomized comparison was made until now to compare MIE to RAMIE.

Study objective

The objective is to evaluate the extent of lymph node dissection, efficacy, risks, quality of life and cost-effectiveness of RAMIE as an alternative to MIE as treatment for esophageal cancer.

Study design

This is a multicenter investigator-initiated and investigator-driven randomized controlled parallel-group, superiority trial comparing RAMIE to MIE. This study is conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice Guidelines. Written informed consent will be obtained from all participating patients. All centers participating in the ROBOT-2 trial have extensive experience in minimally invasive esophageal surgery and have an experience with at least 50 MIE an 50 RAMIE procedures performed.

Intervention

The RAMIE consists of a technique is using the 4 arm daVinci Xi system (daVinci Xi system, Intuitive Surgical Inc., Sunnyvale, CA, USA).

Study burden and risks

Risks are estimated to be low, the participating surgeons have performed more than the requiered amount of robot assisted surgeries to pass the learning curve. The only burden would be the questionnaires on quality of life.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Histologically proven squamous cell carcinoma, adenocarcinoma or undifferentiated carcinoma of the intrathoracic esophagus (including Siewert I and II)
- Surgically resectable (T1-4a, N0-3, M0)
- Age >= 18 and <= 90 years
- European Clinical Oncology Group (ECOG) performance status 0,1 or 2
- Written informed consent

Exclusion criteria

- Carcinoma of the cervical esophagus
- Carcinoma of the gastro-esophageal junction (GEJ) with the main part of the tumor in the gastric cardia (Siewert type III)
- Prior thoracic surgery at the right hemithorax or thoracic trauma

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-04-2023
Enrollment:	109
Type:	Actual

Ethics review

Approved WMO

Date:	05-04-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04306458
CCMO	NL80509.029.22