Omentum preservation versus complete omentectomy in gastrectomy for gastric cancer

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The OMEGA trial will primarily investigate if omentum preservation (partial omentectomy) during gastrectomy for gastric cancer is non-inferior to complete omentectomy in terms of three-year overall survival.

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

Summary

ID

NL-OMON56599

Source
ToetsingOnline

Brief title
OMEGA trial

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal therapeutic procedures

Synonym
gastric adenocarcinoma, Gastric cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: SLMK fonds via de AMC foundation

Intervention

Keyword: Gastrectomy, Gastric cancer, Omentectomy, Survival

Outcome measures

Primary outcome

Overall survival at three-years after the operation, defined as the period of time between operation and death from any cause. Patients alive at last follow-up are censored.

Secondary outcome

• Operating time

• Intraoperative blood loss

• Intraoperative complications

• Postoperative complications, defined according to the Clavien-Dindo classification25 and comprehensive complication index (CCI)

• Late intra-abdominal complications, defined as complications related to the initial operation, occurring between >30 days and five years after surgery

• Distribution of lymph node metastases

• R0 resection rate, defined as the percentage of patients who underwent a microscopically complete (R0) resection

• Rate of malignant cells in cytology

• Serum CRP levels at postoperative days 3, 5 and 7

• Molecular classification of gastric cancer

• ICG fluorescent enhancement of omentum after resection, in omentum preservation group only (in centers that have ICG fluorescence available)

• Protocol compliance to allocated treatment

• Escalation of care

• Hospital stay, defined as time interval between date of surgery and date of hospital discharge

• Intensive care length of stay

• Readmission rate within 30-days after surgery

• Reintervention rate within 30-days after surgery

• Reoperation rate within three years after surgery

• Quality of life at baseline, 3, 6, 9, 12, 18 and 24 months, the following questionnaires will be used: EQ-5D-5L, QLQ-C30, and QLQ-OG25

• 3- & 5-year disease-free survival, defined as the period of time from operation to locoregional recurrence, peritoneal recurrence, distant metastases, second gastric cancer or death from any cause. Patients alive and free of all these events will be censored at the last follow-up

• 5-year overall survival, defined as the period of time from operation to death from any cause. Patients alive and free of all these events will be censored at the last follow-up

• Cost-effectiveness

Study description

Background summary

Gastric cancer is the fifth most prevalent type of cancer worldwide and the third most common cause of cancer-related death. Overall, survival has improved in recent decades with the introduction of perioperative chemotherapy; but as yet, a radical gastrectomy remains the foundation of curative treatment for advanced gastric cancer. An oncological resection involves a radical (R0) gastrectomy with a modified D2 lymphadenectomy. Generally, a complete resection

of the greater omentum is also performed, with the hypothesis that the omentum cold contain micrometastatic disease.

The necessity of complete omentectomy in gastrectomy for locally advanced cancer is still unclear world-wide. This issue is currently also reflected by various clinical practice guidelines. At present, the Japanese gastric cancer guideline recommends a total omentectomy for clinically staged T3-T4 gastric tumors, and partial omentectomy for T1-T2 tumors. Likewise, the National Comprehensive Cancer Network (NCCN) Guidelines advises a total omentectomy during resection with curative intent. Meanwhile, the European Society for Medical Oncology (ESMO) guidelines makes no statement about the necessity of omentectomy in the treatment of gastric cancer and the Dutch gastric cancer guideline advises to perform at least a partial omentectomy.

The omentum contributes to the defense against infections, by functioning as regulator of regional immune responses(6-9). Furthermore, the omentum prevents the occurrence of adhesions that can lead to small bowel obstruction. In (laparoscopic) gastric cancer surgery, omentectomy can be a time-consuming and technically demanding procedure which has been shown to increase the risk of intraoperative injuries to the colon and mesocolon, and additionally is associated with an increased risk of postoperative complications following various types of surgery, including gastric cancer surgery.

Also, there is little evidence supporting a survival benefit of routine complete omentectomy in gastrectomy for cancer. Several non-randomized studies have shown no survival difference between partial and complete omentectomy as part of radical gastrectomy for gastric cancer. A recent systematic review pooled the results of these studies and found that patients who underwent partial omentectomy had a statistically higher 3-year and 5-year overall survival rate than those who underwent total omentectomy. These studies suggest that a total omentectomy can be omitted as part of potential curative surgery. Therefore, preservation of the omentum could reduce early and late morbidity and mortality, reduce operation time and readmissions resulting in improved cost-effectiveness and improved quality of life for patients after gastrectomy for cancer

Currently, two phase III trial are conducted in Japan and China (NCT04843215). The aim of both trials is to confirm the non-inferiority of omentum preservation compared with omentectomy. However, both trials exclude patients receiving neoadjuvant chemotherapy, and patients undergoing minimally invasive gastrectomy are excluded as well in the Japanese trial. Also, most of the retrospective studies were performed in Asian countries, where gastric cancer is more prevalent and more patients are diagnosed with early gastric cancer as a consequence of screening. Hence, the results from Asian studies cannot directly be applied to the Western world.

To date, the influence of omentectomy on survival has not yet been investigated

in a randomized controlled trial in a Western gastric cancer population. Our preliminary study showed that the incidence of metastases in the greater omentum is low, and when present, is associated with advanced disease and a non-radical resection. With a median survival of 7 months, none of these patients survived more than two years (submitted).

In this randomized controlled trial, we test our hypothesis that omentum preservation during gastrectomy in patients with locally advanced gastric cancer is non-inferior to complete omentectomy in terms of three-year overall survival. The OMEGA trial will be the first Western randomized controlled trial that will determine if complete omentectomy during gastrectomy for cancer can be omitted in the future, potentially reducing overtreatment and thereby increasing quality of life and decreasing medical costs.

Study objective

The OMEGA trial will primarily investigate if omentum preservation (partial omentectomy) during gastrectomy for gastric cancer is non-inferior to complete omentectomy in terms of three-year overall survival.

Study design

OMEGA is a randomized controlled, open, parallel, non-inferiority, multicenter trial. Eligible patients have to be operable (ASA <4) with resectable (*cT4aN3bM0) gastric cancer. Patients will be randomized in a 1:1 ratio between radical (sub)total gastrectomy with omentum preservation or complete omentectomy. Patients will be stratified according to center, neoadjuvant therapy and type of surgery (total or subtotal gastrectomy). The primary endpoint is overall survival at three-years after the operation. In total, 654 patients will be randomized.

The study will be conducted in five Dutch university hospitals, nine Dutch teaching hospital and multiple international university hospitals, all performing more than 20 gastrectomies annually.

Intervention

In this study, preservation of the omentum distal to the gastroepiploic vessels will be compared with complete omentectomy during gastrectomy for cancer.

Study burden and risks

Theoratically, by not performing an omentectomy tumor cells could remain in the body. However, previous studies have never concluded that omentectomy contributes to a survival benefit. In addition, at six different times patients are asked to complete a questionnaire about quality of life. These will all be

taken during the check-up appointments at the outpatient clinic so that the burden on the patient remains minimal. Furthermore, blood samples will be taken on days 3, 5 and 7 postoperatively. In almost all cases, in practice, blood is already drawn from patients postoperatively on days 3, 5 and 7. As a result, the burden here will be very small.

As a rule, the entire omentum is also removed during a gastric resection. The idea behind this is that metastases are removed. However, there are also disadvantages to performing a complete omentectomie. It is a technically challenging part of the surgery that is time consuming and can lead to complications such as damage to the colon and its blood supply, especially in today's widely used minimally invasive surgeries. The average duration of a complete omentum removal is over one hour. In addition, the omentum plays an important role in fighting bacterial infections in the abdominal cavity and preventing adhesions in the abdomen. Studies have shown that complete omentum removal is an important risk factor for the development of adhesions and associated complications, such as ileus (small bowel obstruction). Smaller retrospective studies suggest that complete omentum removal during gastric resection does not improve survival. A recently published systematic review even suggests that patients may have a survival advantage with an omentum-sparing gastrectomy (2). However, most of these studies have been conducted in Asian countries, where gastric cancer is more common and more patients are diagnosed with early gastric cancer as a result of screening.

It is expected that partial omentum removal during gastric resection is non-inferior to surgery with complete omentum removal; that is, sparing the omentum will not negatively affect 3-year survival. In addition, partial omentectomy is expected to lead to better outcomes in terms of operative time, complications (short and long term), quality of life and cost-effectiveness.

This means that it is reasonably plausible that the interest to be served with the research is in proportion to the objections and the risk for the study participants, and the conduct of the research is therefore justified in the assessment of the OMEGA trial study group.

2.Zizzo, M., Zanelli, M., Sanguedolce, F., Palicelli, A., Ascani, S., Morini, A., Tumiati, D., Mereu, F., Zuliani, A. L., Nardecchia, M., Gatto, F., Zanni, M., and Giunta, A. (2022) Gastrectomy with or without Complete Omentectomy for Advanced Gastric Cancer: A Meta-Analysis. Medicina 58, 1241

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Primary resectable gastric adenocarcinoma, clinical stage T1-4aN0-3M0
- ASA 1-3 (able to undergo surgery)
- Scheduled for open or minimally invasive (sub)total gastrectomy with modified D2-lymphadenectomy, with or without perioperative chemotherapy
- Age above 18 year
- Able to complete questionnaires in Dutch, English or Italian
- Written informed consent
- Esophageal invasion < 2 cm defined from the upper margin of the gastric rugae as determined by endoscopy

Exclusion criteria

- Gastric cancer clinically staged as T1N0
- Locally advanced gastric cancer requiring multi-visceral resection
- Pregnancy
- Previous malignancy (excluding non-melanoma skin cancer, pancreatic neuroendocrine tumor (pNET) <2cm, and gastrointestinal stromal tumor (GIST)

<2cm), unless no evidence of disease and diagnosed more than three years before diagnosis of gastric cancer, or with a life expectancy of more than five years from date of inclusion
- Serious concomitant systemic disorders that would compromise the safety of the patient or his/her ability to complete the study, at the discretion of the investigator
- Previous gastric or omental surgery, with the exclusion of a gastric perforation
- Indication for thoracotomy/thoracoscopy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-03-2024
Enrollment:	554
Type:	Actual

Ethics review

Approved WMO

Date:	13-10-2023
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	NCT05180864
CCMO	NL80328.029.22