The influence of sarcopenia and cancer cachexia on recovery of gastric and colonic surgery

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1) To investigate what changes are present in skeletal muscle tissue of elderly gastric and colonic cancer patients (>80) compared with younger gastric and colonic cancer patients (

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

Summary

ID

NL-OMON37020

Source
ToetsingOnline

Brief title
Sarcopenia in gastric and colonic surgery

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal therapeutic procedures

Synonym
colorectal cancer, gastric cancer, sarcopenia

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cancer cachexia, colonic cancer, gastric cancer, sarcopenia

Outcome measures

Primary outcome

On frozen sections of muscle biopsies, the next parameters will be investigated: fiber typing, quantity of fibers, mean fiber cross sectional area, the number of satellite cells per fiber. Moreover, apoptosis is studied, which is an important process prior to muscle wasting in cancer patients.

The primary study outcome is the difference in muscle composition between elderly (>80) and younger (<60) cancer patients.

Secondary outcome

Fat tissue: inflammation.

Colonic tissue: collagen composition, proliferation, inflammation, apoptosis, goblet cells, mucins and prostaglandins. These factors have an important function in intestinal healing.

Gastric tissue: collagen composition, proliferation, inflammation, apoptosis and prostaglandins. These factors have an important function in gastric healing.

Plasma: inflammation, markers of intestinal damage.

Study description

Background summary

The Netherlands will encounter a disproportionate increase of an ageing population. The number of elderly cancer patients is concomitantly increasing in the Netherlands, as is the number of the elderly undergoing surgical treatment. Fifty percent of patients with colorectal cancer are above age 70.

While survival of all cancer types is increasing, improvement of cancer outcome has been relatively limited in older patients, which can at least partly be explained by an increased postoperative mortality. Recovery after surgery plays a crucial role in cancer treatment in terms of survival, treatment response and morbidity. *Frail* elderly have a 3-fold increased risk of postoperative mortality, while *non-frail* elderly have just a minimally increased risk. There are many controversial issues surrounding the definition of frailty and on its mechanisms leading to postoperative morbidity and mortality. The syndrome of frailty is a state of increased vulnerability towards stressors in older individuals, leading to an increased risk of developing adverse health outcomes. However, the definitions and biological characteristics of frailty are subject to debate. Weight loss, low muscle strength, reduced physical activity, exhaustion, and slowed walking speed are symptoms of a physical definition of frailty, whereas comorbidity, polypharmacy, physical functioning, nutritional and cognitive status, depression and social support are a more multidimensional tool to assess frailty. Skeletal muscle wasting is an element of frailty in both definitions. Preliminary results of our research group indicated that sarcopenia in elderly cancer patients undergoing colorectal surgery is associated with increased postoperative morbidity. Moreover, results of this study showed increased intestinal damage in several patients undergoing colonic resection. These patients had an increased risk of developing severe postoperative complications. Therefore, we hypothesize that sarcopenia and/or cancer cachexia negatively affect postoperative recovery after surgery for malignancy. To find treatment strategies for these adverse effects, it is necessary to study skeletal muscle changes in these patients and how these changes can affect postoperative recovery.

Study objective

1) To investigate what changes are present in skeletal muscle tissue of elderly gastric and colonic cancer patients (>80) compared with younger gastric and colonic cancer patients (<60) and compared to elderly controls and younger controls.
2) To investigate how these changes affect important elements of gastric and colonic healing.

Study design

The following patients will be enrolled in the current study:
15 patients undergoing gastric surgery for malignancy older than 80 years of age,
15 patients undergoing gastric surgery for malignancy younger than 60 years of age,
15 patients undergoing colonic surgery for malignancy older than 80 years of age,
15 patients undergoing colonic surgery for malignancy younger than 60 years of

age,
15 patients undergoing abdominal wall incisional hernia repair older than 80 years of age,
15 patients undergoing abdominal wall incisional hernia repair younger than 60 years of age.
These study groups give the opportunity to investigate the effects of sarcopenia (caused by age) as the effects of cachexia (caused by cancer). It is hypothesized that cachexia will be most prevalent in patients with gastric cancer, to a lesser extent in patients with colonic cancer and not prevalent in patients with incisional hernia.

Muscle biopsies
In all patients, a biopsy of the rectus abdominis muscle will be taken peroperatively. After skin incision and dissection of subcutanous fat, the anterior rectus sheath will be opened and a muscle biopsy of approximately 1,5 cm^3 will be taken. Surgery time will be extended less than one minute and no extra incisions are needed. Opening the rectus sheath is part of routine care in gastric surgery, colonic surgery and hernia repair. The muscle tissue will be snap frozen immediately in liquid nitrogen cooled isopenthane en stored at -80ºC until batch analysis in the laboratory of the department of general surgery (MUMC).

Fat biopsies
Inflammation of fat tissue and loss of fat tissue are important aspects of cancer cachexia. Therefore in all patients, a biopsy of fat tissue will be taken peroperatively. After skin incision, a subcutaneous fat (SF) biopsy of approximately 1,5 cm^3 will be taken. After opening of the muscle layers and muscle biopsy, a visceral fat (VF) biopsy of approximately 1,5 cm^3 will be taken of the omentum. Fat biopsies can be taken without blood loss. Surgery time will be extended less than one minute and no extra incisions are needed. The fat tissue will be snap frozen immediately in liquid nitrogen cooled isopenthane en stored at -80ºC until batch analysis in the laboratory of the department of general surgery (MUMC).

Colonic tissue
In patients undergoing colonic surgery, a small part of the specimen that is resected will be removed for the current study. In left hemicolectomies and sigmoid resections, the most proximal 2 cm of the specimen will be taken, and the most distal 2 cm of the specimen will be taken in right hemicolectomies. The tissue will be snap frozen and stored at -80ºC until batch analysis in the laboratory of the department of general surgery (MUMC).

Gastric tissue
In patients undergoing colonic surgery, a small part of the specimen that is resected will be removed for the current study. 4 cm^2 of gastric wall will be taken from the proximal part of the specimen. The tissue will be snap frozen and stored at -80ºC until batch analysis in the laboratory of the department of

general surgery (MUMC).

Venous puncture
Venous blood will be collected in EDTA vaccuum tubes (5 milliliter per sample) prior to surgery, one day postoperatively and three days postoperatively. This does not include extra venous puncture for study purposes, as standard care includes venous puncture at the specified timepoints in all patients. Blood samples will be centrifuged and stored at -80ºC until batch analysis in the laboratory of the department of general surgery (MUMC).

Study burden and risks

The rectus abdominis muscle biopsy and fat biopsies are the only burden associated with participation. The rectus abdominis muscle layer is dissected in gastric surgery, colonic surgery and abdominal hernia repair surgery as part of standard care. Access to subcutaneous fat and visceral fat is possible without extra incisions. The biopsies might increase postoperative pain slightly.

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

Patients undergoing gastric or colonic resection of a primary tumor who are older than 80 years or younger than 60 years of age. Surgery types: gastric: BII subtotal gastrectomy, total gastrectomy with Roux and Y reconstruction. Colon: right hemicolectomy, left hemicolectomy, sigmoid resection. Both open resections and laparoscopic resection will be included.
Patients undergoing abdominal wall incisional hernia repair who are older than 80 years or younger than 60 years of age.

Exclusion criteria

Metastasized tumors (TNM stage M1 or higher). To avoid variation of tumorload within patient groups, patients with metastases beyond lymph nodes will be excluded.
Acutely ill patients will be excluded as this influences inflammatory markers. Acutely ill is defined as: pneumonia, urinary tract infection, (intra-abdominal) abscess, etc.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	13-11-2012
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	11-07-2012
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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
CCMO	NL40632.096.12