Laparoscopic advanced Imaging Techniques in Endometriosis therapy: the LITE study. A pilot trial.

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To determine which advanced image enhanced modality is the most feasible for the detection of endometriosis lesions, with respect to the specificity and sensitivity of the investigated modalities. To determine which imaging modality reveals more...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peritoneal and retroperitoneal conditions
Study type	Observational invasive

Summary

ID

NL-OMON43974

Source
ToetsingOnline

Brief title
LITE study

Condition

- Peritoneal and retroperitoneal conditions
- Menstrual cycle and uterine bleeding disorders
- Obstetric and gynaecological therapeutic procedures

Synonym
Appearance of endometrial tissue outside the womb, Endometriosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Endometriosis, Imaging, Laparoscopy

Outcome measures

Primary outcome

To evaluate the sensitivity and specificity of Narrow Band Imaging,

near-infrared imaging with ICG and 3D-laparoscopy compared to conventional

white light laparoscopic imaging.

To evaluate if more endometriosis lesions are found with 3D, NBI and ICG

compared to conventional white light laparoscopy.

Secondary outcome

-Descriptive analysis of the by endometriosis affected ovaries and intestines

-Use of hormonal therapy

-Use of pain medication

-Operating time

-Blood loss

-(Serious) adverse events

Study description

Background summary

Endometriosis is a benign, chronic, estrogen-dependent gynaecological disorder. It is defined as the presence of endometrial glands and stroma outside the uterine cavity, which induces a chronic, inflammatory reaction. It*s an established cause of infertility and causes dysmenorrhea, dyspareunia and pelvic pain. The prevalence in the general population is not known and difficult to determine because of the variety in symptoms. Estimates range from

2 to 10% of women in reproductive age, and up to 50% in subfertile women and symptomatic patients. Despite it*s proven efficacy, recurrence after surgery remains a major challenge and a crucial issue in the long-term management of endometriosis. Evers et al. argue that 10% of patients redeveloped signs and symptoms of endometriosis after a 1-year follow-up period, 25% after 3 years, and 45% after 5 years. Guo et al calculated that the disease relapse rate is >20% at 2 years and 40 to 50% at 5 years. Even in young women <=21 years of age, the 5-year recurrence rate was as high as 56%, irrespectively of site and stage of endometriosis. The need for hospital admission for endometriosis within four years after surgery for additional surgical treatment is 27% and reoperation occurs in more than 50% of the patients with endometriosis, where about 27% needs three or more surgeries. As repeated surgery is associated with an increase in health care costs, morbidity and damage to ovarian reserve, the need for radical resection during primary surgery is underlined.

During laparoscopy, peritoneal endometriosis micro lesions can be hard to distinguish from normal tissue and not all endometriosis lesions are macroscopically identified, resulting in incomplete relief of pain after surgery. Macroscopic identification of endometriosis lesions is currently poor, with histological examination having a positive predictive value of 66% for suspected lesions in laparoscopy. Because of the polymorphic appearance of endometriosis lesions, they can be mistaken easily for other structures such as adhesions and (post)inflammatory and changes. The American Society for Reproductive Medicine classification distinguishes among red, white, and black superficial implant types. In particular, the appearance of red and white superficial implant types can vary widely. In the literature, red and white endometriosis lesions frequently are subsumed as *nonpigmented* as opposed to black *pigmented* lesions. Previous reports have shown that nonpigmented areas of endometriosis represent the active form of the disease.

To improve the detection of peritoneal lesions of endometriosis by laparoscopy and accomplice a more complete resection. We will conduct this trial to investigate which advanced imaging technique, narrow-band imaging (NBI), three-dimensional laparoscopy (3D) or near-infrared imaging with fluorescent Indocyanin Green (ICG) is the most accurate to visualize endometriosis lesions and which technique shows more endometriosis lesions.

Secondarily we will also investigate operating time, blood loss, usability, direct costs and safety of the different modalities.

Study objective

To determine which advanced image enhanced modality is the most feasible for the detection of endometriosis lesions, with respect to the specificity and sensitivity of the investigated modalities. To determine which imaging modality reveals more endometriosis lesions compared to white light laparoscopy.

-3D: Drie-dimensionele imaging
-NBI: Narrow-band imaging
-NIR-ICG: Near-infrared imaging with Indocyanin Green

Study design

Prospective, phase-1 pilot (feasibility) trial.
We include 20 patients (see study population). In each of these patietns we will, after introduction of the laparoscope and two assisting trocars, inspect the pelvis with the following modalities: conventional white-light laparoscopy, 3D, NBI and NIR-ICG. Each region of the pelvis is inspected with every modality in a systematically rotating different order. Images of suspected endometriosis lesions are taken for each modality. After all lesions are photographed for each modality, biopsies are taken of suspected endometriosis lesions. Biopsies of healthy tissue will also be taken for negative control. After the procedure the images are compared to the pathology results of the biopsies, thus determining the sensitivity and specificity for each modality. Biopsies of apparent endometriosis lesions is standard care for endometriosis therapy by protocol.

The best imaging modality with best detection of endometriosis (higher sensitivity when compared to white light laparoscopy, with comparable specificity) will be investigated in a phase-3 randomised trial.

Study burden and risks

Participation in this study adds three extra proceedings:
1) the use of different imaging modalities may increase operating time and time under narcosis.
2) possible adverse reaction to ICG, possible decrease in kidney and liver function.
3) extra biopsies of unhealthy and healthy tissue will be taken.

Frequency/damage
The chance for damage as a result of this study is estimated at low risk. This is because we have anticipated for the potential risks by excluding the patients with kidney and/or liver function insufficiency and because patients are intraoperatively monitored by the anaesthesiologist for possible adverse effects.

Known risk
1) Extra operating time results in extra time under narcosis.
- The damage caused by this is negligible for our study population (young relatively healthy females, ASA < 3)

2) In 1 out of every 10.000 patients and anaphylactic or urticarial reaction

can occur as a result of intravenous ICG injection.
- The damage caused by this adverse event is moderate and reversible.
- If an anaphylactic reaction occurs, the anaesthesiologist can anticipate by following a checklist in the SPC.
- Patients with an Iodine allergy (who are more susciptable for anaphylactic reaction) are excluded.

3) Bleeding can occur as a result of biopsies.
- The damage caused by this advert event is light and reversible.
- Any bleedings can be coagulated by the operating physician.
- No biopsies will be taken from regions with increased risk of bleeding or perforation of the organ (e.g. intestines and ovaries)

No additional physical, psychological or social burdening is caused by this study for the study subjects.

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

-Oral and written informed consent
-Age 18 years and older
-Premenopausal women
-Elective laparoscopic treatment of endometriosis lesions by CO 2 laser/ bipolar diathermy or surgical excision.
-Presence of endometriosis (ASRM III-V) confirmed by previous laparoscopy or likely to be present based on TVUS or MRI, including uni- or bilateral ovarian endometrioma.
-Regular preoperative work-up

Exclusion criteria

-Women who are legally or mentally incapable or unable to give informed consent
-Age younger than 18 years
-ASA (American Society of Anaesthesiologists) score higher than 3
-Woman who have had major open abdominal surgery
-Pregnancy
-Malignancy
-Iodine allergy
-Hypersensitivity reaction to prior indocyanine green injection
-Hyperthyoidism or autonomous thyroid adenoma
-Chronic kidney failure (eGFR<55)
-Chronic liver failure (ASAT, ALAT, AF and yGT > two times the max normal value)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ICG-Pulsion
Generic name:	Indocyanin Green
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2016
Application type:	Amendment
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

ID: 25841
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2015-000644-42-NL
CCMO	NL52456.029.15
OMON	NL-OMON25841

Study results

Date completed:	09-05-2017
Actual enrolment:	20