

ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
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ClinicalTrials.gov ID: NCT02630329

Study Identification

Unique Protocol ID: B689201526268

Brief Title: Notes Adnexectomy for Benign Pathology Compared to Laparoscopic Excision
(NOTABLE)

Official Title: Adnexectomy for Benign Gynaecological Pathology by Natural Orifice Transluminal
Endoscopy or Laparoscopy

Secondary IDs:

Study Status

Record Verification: January 2016

Overall Status: Recruiting

Study Start: December 2015

Primary Completion: May 2018 [Anticipated]

Study Completion: May 2018 [Anticipated]

Sponsor/Collaborators

Sponsor: Imelda Hospital, Bonheiden

Responsible Party: Principal Investigator

Investigator: Dr Jan Baekelandt, MD [jbaekelandt]

Official Title: Dr

Affiliation: Imelda Hospital, Bonheiden

Collaborators:

Oversight

FDA Regulated?: No

IND/IDE Protocol?: No

Review Board: Approval Status: Approved

Approval Number: 689/151145

Board Name: Commissie Medische Ethiek

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Data Monitoring?: Yes

Plan to Share Data?: No

Interim analyses of major endpoints will be supplied, in strict confidence, to an independent Data Monitoring and Ethics Committee (DMEC) along with updates on results of other related studies, and any other analyses that the DMEC may request.

Oversight Authorities: Belgium: Federal Agency for Medicines and Health Products, FAMHP

Study Description

Brief Summary: Objective: To compare vNOTES (vaginal Natural Orifice Transluminal Endoscopic Surgery) and established laparoscopic removal of benign adnexal masses Study design: Randomized controlled/single center/single-blinded/parallel-group/non-inferiority/efficacy trial.

Study population: Women aged 18 to 70 years with symptomatic or persistent benign adnexal masses detected by clinical examination and ultrasound.

Randomization: Women will be randomly allocated to undergo one of two techniques for removal of the benign adnexal mass immediately before surgery by using a computer generated randomization list. The investigators will use stratified randomization according to the cyst diameter.

Intervention: Women will be treated by a surgeon who is not blinded to the treatment allocation and who is equally skilled in performing both techniques. In the intervention group a vNOTES technique will be used.

Control: In the control group surgery will be done by a classical laparoscopic technique.

Participants, nursing staff and outcome assessors will be blinded.

Main study parameters/endpoints:

Primary outcomes: successful removal of a benign adnexal mass without spill.

Secondary outcomes: the proportion of women discharged the same day based on their own preference; postoperative pain scores using a VAS (Visual Analogue Scale) measured between day 1 till 7 by the participating women following surgery and the total amount of analgesics used as described in the standardized pain treatment protocol between day 1 till 7; postoperative infection defined by lower abdominal pain with fever > 38°C and positive clinical signs or laboratory findings; per- or postoperative complications according to the Clavien- Dindo classification detected during the first six weeks of surgery; duration of the surgical procedure; incidence and intensity of dyspareunia recorded by the participants at 3 and 6 months by self-reporting using a simple questionnaire and VAS scale; sexual wellbeing recorded by the participants at 3 and 6 months by SSFS (Short Sexual Functioning Scale); direct costs associated up to 6 weeks after the surgical intervention with both procedures.

Detailed Description: 1. Objectives of the NOTABLE Trial

The primary research questions of this IDEAL stage 2b efficacy trial are as follows: is a vNOTES adnexectomy at least as effective compared to the standard transabdominal laparoscopic approach (LSC) for removing a benign adnexal mass without spill? (non-inferiority design)

Secondary research questions are:

- Do more women treated by vNOTES prefer to leave the hospital on the day of surgery compared to LSC?
- Do women treated by vNOTES suffer from less pain compared to women treated by LSC in the first postoperative week?
- Is the removal of a benign adnexal mass by vNOTES faster compared to LSC?
- Does a vNOTES cause more pelvic infection or other complications compared to LSC?
- Does a vNOTES cause more hospital readmissions within 6 weeks following surgery compared to LSC?

- Does a vNOTES approach result in more women reporting dyspareunia or less sexual wellbeing at 3 or 6 months after surgery when compared to women treated by LSC?
- What are the direct costs up to 6 weeks of a vNOTES compared to LSC?

TRIAL DESIGN 2.1. Design A single center, single-blinded, parallel group randomized, non-inferiority efficacy trial.

2.2. Simple pilot randomized trial: minimal extra workload 2.3. Time schedule Based upon the mean number of laparoscopic adnexectomies performed annually at the department of Obstetrics and Gynecology of the participating center (36) the investigators estimate that the duration of recruitment will be 21 months. Based upon the follow up (6 months) and the period of analysis/reporting (3 months) the total study period will be 2.5 years.

2.4. Participating center Department of Obstetrics and Gynecology Imeldahospital Imeldalaan 9 2820 Bonheiden Belgium

- ELIGIBILITY, CONSENT AND RANDOMIZATION 3.1. Screening and consent prior to surgery All women aged 18 to 70 years regardless of parity presenting with a symptomatic or asymptomatic persistent benign adnexal mass on clinical examination confirmed by ultrasound are eligible for inclusion. The diagnosis of benign adnexal mass will be based upon the prospectively validated IOTA classification(International Ovarian Tumour Analysis Group) simple ultrasound rules to distinguish between benign and malignant adnexal masses.

3.2. Determining eligibility All women aged 18 to 70 years regardless of parity presenting with a symptomatic or asymptomatic persistent benign adnexal mass on clinical examination who provide consent to participation are eligible in the NOTABLE trial based on the findings of the ultrasound findings and will be randomized before the procedure.

3.3. Randomization If the woman is eligible for the NOTABLE trial, the trial secretary will obtain a randomized allocation the day before surgery. This will be done using a randomization list generated by a free computer software program offered by Research Randomizer (<https://www.randomizer.org>). The random sequence generation will be concealed using sequentially numbered opaque sealed envelopes. The envelope will be opened by the nurse assistant on the day before the surgical intervention for logistic reasons. The investigators will use stratified randomization in this small pilot RCT (randomized controlled trial) according to the cyst diameter.

3.4. Patients with strong preference for treatment A minority of women will express a clear preference for one of both treatments (e.g. strong desire to have no scar) and for this reason will not wish to be randomized between surgical treatments. To investigate how outcomes vary by choice, these women could be followed up in exactly the same way as for those women randomized into the NOTABLE trial. A formal non-randomized follow-up of these women will not be done for simple logistical reasons.

3.5. Stratification of randomization A blocked randomization procedure will be used to avoid chance imbalances for the parameter 'cyst diameter'.

To avoid any possibility of foreknowledge, the randomized allocation will not be given until all eligibility and stratification data have been given.

- TREATMENT ALLOCATIONS 4.1. Surgical procedures The principal investigator, who has training and experience in both laparoscopy and NOTES, will perform all surgical procedures. He is therefore not blinded. All vNOTES participants will be blinded by three superficial "mock" skin incisions similar to those routinely done with the laparoscopic technique.

4.1.1 vNOTES adnexectomy This is the surgical procedure done in the intervention arm of the NOTABLE trial.

4.1.2 LSC adnexectomy This is the surgical procedure done in the control arm of the NOTABLE trial.

- FOLLOW-UP AND OUTCOME MEASURES 5.1. Clinical assessments 5.1.1
Format PROMs will be collected using a postal questionnaire, which will include a combination of disease specific and generic measurement instruments.

The postal questionnaires will be sent from the NOTABLE Trial Office with postage paid envelopes two weeks before the due date. Reminders will be sent to the participants if the questionnaire is not returned within one week of the due date and attempts will be made to contact the women by phone if the questionnaire is not returned by two weeks after the due date.

5.1.2 Timing of assessments The primary outcome will be measured clinically at the end of the surgical procedure. In addition PROMs will take place the evening of the surgical intervention (return home), during the first postoperative week (pain by VAS scores and analgetic drugs) and at 3 and 6 months (dyspareunia). Clinical physician assessment will take place the evening of the surgical intervention (return home) and during the first six weeks following surgery (pelvic infection, surgical complications, hospital readmission rate).

5.2. Primary clinical outcome measure The proportion of women successfully treated by removing the adnexal mass without spill, using a dichotomous outcome measure, will be used as a measure of efficacy.

5.3. Secondary clinical outcome measures

The following secondary outcomes will be measured:

- The proportion of women discharged the same day based on their own preference, as a dichotomous outcome.
- Postoperative pain scores, as an ordinal outcome, measured using a VAS scale twice daily from day 1 till 7 self-reported by the participating women.
- Postoperative pain defined by the total amount of analgesics used as described in the standardized pain treatment protocol, as a continuous outcome.
- Postoperative infection as a dichotomous outcome.
- Per- or postoperative complications according to the Clavien- Dindo classification detected during the first six weeks of surgery, as a dichotomous outcome.
- Hospital readmission within 6 weeks following surgery, as a dichotomous outcome.
- Incidence and intensity of dyspareunia recorded by the participants at 3 and 6 months by self-reporting using a simple questionnaire and VAS scale, as a dichotomous and ordinal outcome. .
- Sexual wellbeing at baseline, at 3 and 6 months by self-reporting the SSFS.
- Duration of surgery measured as the time in minutes from the insertion of the bladder catheter to the end of vaginal/abdominal wound closure, as a continuous outcome.

5.4. Health economic outcomes The direct costs of both techniques up to 6 weeks after the surgical intervention will be calculated.

- ACCRUAL AND ANALYSIS 6.1. Sample size The sample size for this trial has been chosen to give good statistical power to preclude any clinically important inferiority of vNOTES compared to laparoscopy and is based on evidence retrieved from a systematic review of the literature and a RCT comparing the excision of mature teratoma using culdotomy with and without laparoscopy. Based on the power calculations for the primary outcome and two secondary outcomes and assuming a loss-to-follow-up rate of 10% the investigators decided to include 66 study participants in the NOTABLE trial.

6.2. Projected accrual and attrition rates It is anticipated that recruitment of participants will take two years. Based upon the mean number of laparoscopic adnexectomies performed annually at the department of Obstetrics and Gynecology of the participating center (36) the investigators estimate that the duration of recruitment will be 21 months. Based upon the follow up (6 months) and the period of analysis/reporting (3 months) the total study period will be 2.5 years. First publication will be possible within four years of trial commencement.

Conditions

Conditions: Natural Orifice Endoscopic Surgery
Disease, Adnexal
Laparoscopic Surgery

Keywords: NOTES
Benign adnexal disease
Laparoscopy

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 2

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Double Blind (Subject, Outcomes Assessor)

Allocation: Randomized

Endpoint Classification: Efficacy Study

Enrollment: 66 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: vNOTES adnexectomy Vaginal Natural Orifice Transluminal Endoscopic Surgery	Procedure/Surgery: vNOTES adnexectomy Surgical removal of one or both adnexa by a natural orifice transluminal endoscopic surgical technique using a colpotomy (transvaginal incision)
Active Comparator: LSC adnexectomy Laparoscopic adnexectomy	Procedure/Surgery: Laparoscopic adnexectomy Surgical removal of one or both adnexa by transabdominal laparoscopy

Outcome Measures

Primary Outcome Measure:

1. Successful removal of adnexal mass without spill
[Time Frame: Intraoperative] [Safety Issue: Yes]
The proportion of women successfully treated by removing the adnexal mass without spill, using a dichotomous outcome measure, will be used as a measure of efficacy.

Secondary Outcome Measure:

2. Discharge from the hospital the day of the surgical intervention

[Time Frame: Dichotomous outcome measured on the day of the surgical intervention] [Safety Issue: Yes]
The proportion of women discharged the same day based on their own preference, as a dichotomous outcome. The decision to discharge or to admit to hospital for the night will be based solely on the choice of the woman to return home the same day or stay overnight.

3. Postoperative pain scores
[Time Frame: The first week after the surgical intervention] [Safety Issue: No]
Postoperative pain scores, as an ordinal outcome, measured using a VAS scale twice daily from day 1 till 7 self-reported by the participating women
4. The use of analgesics for postoperative pain
[Time Frame: The first week after the surgical intervention] [Safety Issue: No]
Postoperative pain defined by the total amount of analgesics used as described in the standardized pain treatment protocol, as a continuous outcome.
5. Postoperative infection
[Time Frame: The first six weeks after the surgical intervention] [Safety Issue: Yes]
Postoperative infection defined by lower abdominal pain with fever > 38°C and positive clinical signs or laboratory findings, detected during the first six weeks of surgery, as a dichotomous outcome.
6. Complications
[Time Frame: The first six weeks after the surgical intervention] [Safety Issue: Yes]
Per- or postoperative complications according to the Clavien- Dindo classification detected during the first six weeks of surgery, as a dichotomous outcome
7. Hospital readmission
[Time Frame: The first six weeks after the surgical intervention] [Safety Issue: Yes]
The proportion of women readmitted to hospital within six weeks of surgery, as a dichotomous outcome
8. Pain during sexual intercourse
[Time Frame: At baseline, 3 months and 6 months after the surgical intervention] [Safety Issue: No]
Incidence and intensity of dyspareunia recorded by the participants at 3 and 6 months by self-reporting using a simple questionnaire and VAS scale, as a dichotomous and ordinal outcome
9. Sexual well being
[Time Frame: At baseline, 3 months and 6 months after the surgical intervention] [Safety Issue: No]
Sexual wellbeing at baseline, at 3 and 6 months by self-reporting using the SSFS (Short Sexual Function Scale).
10. Duration of the surgical intervention
[Time Frame: Intraoperative] [Safety Issue: No]
Duration of surgery measured as the time in minutes from the insertion of the bladder catheter to the end of vaginal/ abdominal wound closure, as a continuous outcome
11. Direct costs
[Time Frame: Up to 6 weeks postoperative] [Safety Issue: No]
Calculating the comparative direct costs of both techniques up to 6 weeks after the surgical intervention

Eligibility

Minimum Age: 18 Years

Maximum Age: 70 Years

Gender: Female

Accepts Healthy Volunteers?: Yes

Criteria: Inclusion Criteria:

- All women aged 18 to 70 years regardless of parity with a symptomatic adnexal mass presumed to be benign based on ultrasound examination by applying the IOTA simple rules

- All women aged 18 to 70 years regardless of parity with an asymptomatic persistent adnexal mass presumed to be benign based on ultrasound examination by applying the IOTA simple rules
- Written informed consent obtained prior to surgery

Exclusion Criteria:

- History of hysterectomy by any technique
- History of rectal surgery
- Suspected rectovaginal endometriosis
- Suspected endometriotic cyst
- Solid adnexal mass
- High suspicion of adnexal malignancy based on clinical, ultrasound or biochemical findings
- History of pelvic inflammatory disease, especially prior tubo-ovarian or pouch of Douglas abscess
- Active lower genital tract infection e.g. Chlamydia, N. gonorrhoeae
- Virgo
- Pregnancy
- Need for other uterine surgical intervention (i.e. endometrial ablation, resection, myomectomy or hysterectomy)
- Additional pathology necessitating hysterectomy
- Failure to provide written informed consent prior to surgery

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References

Citations: [Study Results] Baekelandt J. Poor man's NOTES: can it be a good approach for adhesiolysis? A first case report with video demonstration. J Minim Invasive Gynecol. 2015 Mar-Apr;22(3):319. doi: 10.1016/j.jmig.2014.11.001. Epub 2014 Nov 10. PubMed 25460516

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Links:

Study Data/Documents: