Assessment of women’s sexual quality of life after benign adnexal surgery using vNOTES approach in comparison to conventional laparoscopy: protocol for a randomised controlled trial

Eloise Krull,1,2 Shahzia Lambat Emery,2 Manuela Viviano,2 Leen Aerts,2 Patrick Petignat,1,2 Jean Dubuisson1,2

ABSTRACT

Introduction Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) has already proven its non-inferiority to conventional abdominal laparoscopy (CAL) for hysterectomy without conversion. The results in terms of efficacy and safety are promising. However, we note a lack of medical literature and no specific randomised controlled trial assessing women’s sexual function after vNOTES for benign adnexal surgery. The aim of this RCT is to confirm the non-inferiority of the vNOTES approach for benign adnexal pathology compared with CAL on women’s sexual function. Secondary outcomes will evaluate vNOTES’s efficiency, morbidity and postoperative complications compared with CAL for benign adnexal surgery. The relationship between adnexal mass morcellation and the quality of the histological analysis will also be evaluated as secondary outcome.

Methods and analysis Women aged 18–70 years undergoing a benign adnexal surgery at the Geneva University Hospitals will be eligible and randomised with a 1:1 ratio to the CAL arm or the vNOTES arm, if inclusion criteria are met. Participants will complete the Female Sexual Function Index, the Couple Satisfaction Index-16 and a self-reported questionnaire on dyspareunia within 4 weeks prior to randomisation and at 3+6 months after surgery. General and clinical data will be collected when the patient is enrolled in the study, during hospitalisation and at 1 month postoperative to assess secondary outcomes. An absence of impairment on sexual function will be confirmed with a stability or an improvement of the evaluated scores in each group at 3 and 6 months postoperative compared with the preoperative scores. We expect to have no statistically significant difference in sexuality questionnaires scores between the two groups.

Ethics and dissemination Protocol of this study was validated by the Cantonal Research Ethics Commission of Geneva, Switzerland, on 9 August 2022. We aim to publish the study’s results in peer-reviewed journals within 3 years.

Trial registration number NCT05761275.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a single-centre randomised controlled trial.
⇒ This trial studies sexual quality of life in a multidimensional way and with two valid questionnaires.
⇒ All information collected are accurate and complete.
⇒ This study is unblinded.
⇒ Procedures will be performed by different surgeons.

INTRODUCTION

By the end of the 20th century, conventional abdominal laparoscopy (CAL) became the gold standard for minimally invasive surgery in many gynaecological indications, especially to treat benign adnexal pathologies. Nevertheless, surgical techniques are constantly evolving with the aim of being ever less invasive and improving surgical efficiency. NOTES (natural orifice transluminal endoscopic surgery) is the latest evolution in minimally invasive surgery. This surgical technique uses natural orifices of the human body for surgical approach (for instance oropharynx, rectum or vagina).

Transvaginal NOTES (vNOTES) is a surgical technique in full expansion in Europe. The technique requires a specific NOTES training and learning curve to start compared with CAL. Surgical technique is mastered when it is performed regularly and on a sufficient volume load of procedures.

The first randomised controlled trial (RCT) available in the medical literature compared vNOTES and CAL hysterectomy for a benign pathology.1 This study proved that vNOTES is effective and noninferior to CAL with a shorter procedure duration and length of stay, a lower pain Visual Analogue Scale (VAS) and a lower rate of postoperative complications.
Although vNOTES for adnexal surgery is also considered effective and safe,\(^2\)\(^-\)\(^8\) there is little evidence available. Up to now, there is only one recent RCT comparing vNOTES technique to CAL for benign adnexal surgery (BAS) in the medical literature.\(^9\) The NOTABLE trial demonstrated non-inferiority of vNOTES approach in terms of effectiveness (success of the allocated intervention without the need for conversion to another technique). It also demonstrated shorter procedure time, lower pain VAS and diminished use of pain medication during the first postoperative week with the vNOTES approach. However, the study showed a trend for more adverse effects with vNOTES approach (one case of intraperitoneal spilling, four cases of postoperative bleeding) but without a statistically significant difference between the two approaches for intraoperative and postoperative complications.

vNOTES adnexal surgery is particularly attractive because it does not involve any parietal scarring\(^10\)\(^-\)\(^11\) and thus represents a reduced risk of parietal complications. The transvaginal approach bypasses the intra-abdominal adhesions by using a direct route. vNOTES for adnexal pathology seems to be a promising technique but the consequences of a transvaginal approach on women’s sexual quality of life (QoL), including a vaginal scar, are not well established yet.

Studies looking at women’s perceptions of vNOTES showed that young nulliparous women, although more concerned than older women about vNOTES’s cosmetic benefits, were less likely to accept it because they feared for their future sexual function (including dyspareunia) and fertility.\(^10\)\(^-\)\(^12\) Bucher et al detailed women’s fears and showed that 76% of their participants had concerns regarding postoperative intercourse abstinence after vNOTES.\(^11\)

Assessment of women’s sexual function before and after vNOTES has already been studied for non-gynaecological surgical procedures. Although a 2016 review of the medical literature\(^13\) concluded that there was no risk of sexual dysfunction after vNOTES gynaecological surgeries, we note a lack of data assessing women’s sexual function.

Objectives and hypotheses

The primary objective of this RCT is women’s sexual QoL evaluation after BAS by vNOTES compared with CAL using Female Sexual Function Index (FSFI), Couple Satisfaction Index-16 (CSI-16) questionnaires and a self-reported questionnaire on dyspareunia.

Based on the data available, our hypothesis is that vNOTES does not alter women’s sexual function after BAS, with similar outcomes to CAL.

The secondary objective of this study is to confirm the vNOTES technique’s equivalency in terms of efficiency, morbidity and complications compared with CAL. Evaluation of the relationship between adnexal mass morcellation/aspiration and the quality of histological analysis of the surgical specimen are also secondary outcomes.

METHODS

Study design

This is a single-centre, parallel-group, unblinded, balanced randomisation study (1:1 matching for vNOTES and CAL) conducted in the Department of Paediatrics, Gynaecology and Obstetrics at the Geneva University Hospitals, Switzerland. We will be using a non-inferiority study design to address the primary outcome of vNOTES versus CAL for elective BAS.

Study dates

Recruitment of the first patient in the study is estimated for early September 2023.

Participants

All women aged from 18 to 70 years regardless of parity in whom a BAS (including ovarian cystectomy, paratubal cystectomy, oopherectomy, adnexectomy, salpingectomy and/or tubal sterilisation) is planned in the division of Gynaecology of the Geneva University Hospitals will be proposed this study, if they do not meet exclusion criteria.

The study needs a total number of participants of 62 (31 in each group) to achieve sufficient power. To give visibility to the study, oral presentations will be made and flyers distributed in the consultation rooms/offices.

Inclusion criteria are the following:

1. Women aged from 18 to 70 years.
2. Discernment capacity with oral and written consent signed.
3. Heterosexual intercourse (with vaginal penetration) within 4 weeks prior to inclusion in the study.

Exclusion criteria are the following:

- History of rectal surgery.
- Suspected rectovaginal/retrocervical endometriosis.
- History of brachytherapy or pelvic radiation.
- History of severe pelvic inflammatory disease.
- Active lower genital tract infection.
- Pregnancy.
- Women who do not speak fluent French or English.
- Patients under tutelage (with or without capacity of judgement).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of the research.

Instruments and study procedure

Table 1 shows the data collection plan.

Figure 1 summarises the study procedure.

A medical-logbook containing general and clinical information will follow the patient at each stage of her medical pathway (preoperative, intraoperative, during hospitalisation and at 1 month postoperatively) and will
### Table 1  Data collection plan

<table>
<thead>
<tr>
<th>General information</th>
<th>Preop</th>
<th>Within 4 weeks prior to randomisation</th>
<th>Intraop</th>
<th>During hospital stay</th>
<th>At 1 month postop</th>
<th>At 3 months postop</th>
<th>At 6 months postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity/gestity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of vaginal deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Habits (smoking, alcohol, drugs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infertility: primary or secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-gynaecological comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gynaecological comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active follow-up for sexual function disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of abdominal or pelvic surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis of anxiety-depressive disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of sexual abuse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatments</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Questionnaires

| Female Sexual Function Index               |       |                                      |         |                     |                  |                   |
| Couple Satisfaction Index-16              |       |                                      |         |                     |                  |                   |
| Dyspareunia                                |       |                                      |         |                     |                  |                   |

#### Clinical information

| Pain: mean VAS, location                   |       |                                      |         |                     |                  |                   |
| Pain relief (level)                        |       |                                      |         |                     |                  |                   |
| Uterus size and morphology                |       |                                      |         |                     |                  |                   |
| Ovaries and adnexal mass: size, type (O-RADS and/or IOTA classification) | | | | | | |
| Other findings                            |       |                                      |         |                     |                  |                   |
| Tumorous markers: CA 125, others          |       |                                      |         |                     |                  |                   |
| Urine pregnancy test                      |       |                                      |         |                     |                  |                   |
| Successful removal                        |       |                                      |         |                     |                  |                   |
| Intraop complications: see chapter ‘secondary outcome measures’ | | | | | | |
| Parietal adhesions, need for adhesiolysis |       |                                      |         |                     |                  |                   |
| Visualisation of endometriosis (rAFS score or Enzian classification) | | | | | | |
| Procedure duration                        |       |                                      |         |                     |                  |                   |
| Surgical specimen extraction: transvaginal/ transparietal, use of endoscopic bag, need to enlarge the incision, need for morcellation/aspiration, number of fragments. | | | | | | |
| Postop complications: see chapter ‘secondary outcome measures’ | | | | | | |
| Need for an intervention procedure/reoperation |       |                                      |         |                     |                  |                   |

Continued
be filled in by each medical provider (surgeons, residents, anaesthetists, nurses and the research nurse).

All three questionnaires will be provided in French or English depending on the patient’s preference and self-completed by the patient within 4 weeks prior to randomisation and at 3+6 months postoperative on a secure online platform. If patients do not respond on time, the online response platform will send them up to three reminders. We have deliberately not given a latency period before resuming sexual activity to avoid biasing women according to the surgical technique used. We do not fear more infectious complications when resuming sexual activity based on body’s sensations.

**Study intervention**

Patients arrive at the hospital on the day of surgery (unless they have comorbidities that require additional preoperative monitoring), fasting, and are unaware of their allocation group. They are treated according to the guidelines of the division of Gynaecology at the Geneva University Hospitals. A urine pregnancy test is performed preoperatively in all patients of childbearing age.

**First common steps**

General anaesthesia, prophylactic antibiotic, 0° Trendelenburg position, bladder catheterisation during the whole procedure, pelvic clinical examination.

**vNOTES interventional group**

The operative field is exposed with vaginal retractors. The posterior cervical lip is grasped with a tenaculum and the vaginal posterior fornix mucosa is infiltrated with diluted epinephrine solution according to patient comorbidities. A 2.5–3cm «smile-like» posterior colpotomy is performed with a cold scalpel, 2cm away from the cervix. The pouch of Douglas is accessed after dissection and peritoneal incision with scissors. The Alexis retractor-protector (Applied Medical, Rancho Santa Margarita, California, USA) is then inserted into the created space and connected to the GelPoint access platform. A 7cm vNOTES port is chosen. The optical trocar is laced at 6 o’clock and two accessory trocars at 10 and 2 o’clock. A pneumoperitoneum is created with CO₂ using a low intra-abdominal pressure (8–10mm Hg). The patient is then placed in a 20° Trendelenburg position. A 0° 10mm endoscope and standard laparoscopic instruments are used.

The abdominal cavity is inspected and a peritoneal washing is performed.

Then the specific procedure steps are the same as during CAL.

The vNOTES GelPoint platform and the Alexis retractor are removed at the end of the procedure.

At the end of the procedure, the posterior colpotomy is closed using a running absorbable suture, including vaginal mucosa and peritoneum.

**CAL control group**

A pneumoperitoneum is created for the laparoscopic entry using a Veres needle, either at the Palmer point or in the umbilicus. A 0° 5mm or 10mm endoscope is inserted through the umbilicus (or higher depending on the size of the tumour) and three accessory trocars are used during the procedure with a 12mm Hg pressure for the pneumoperitoneum.

The patient is placed in a 20–25° Trendelenburg position during the procedure.

The abdominal cavity is inspected and a peritoneal washing is performed.

The parietal incision of the accessory trocar is potentially enlarged to remove the specimen, depending on its size and the need for morcellation and/or aspiration.

**Common final steps**

An endoscopic bag is inserted to remove the specimen and avoid any cell spillage, depending on the specimen’s size and the need for morcellation and/or aspiration.

No vaginal packing and no Foley catheter are needed in the postoperative period following the principles of FAST TRACK surgery.

The patients will know their allocated group in the postoperative period. The surgeon fills in the intraoperative part of the medical logbook.
Figure 1  Study protocol. CAL, conventional abdominal laparoscopy; Postop, postoperative; Preop, preoperative; vNOTES, transvaginal natural orifice transluminal endoscopic surgery.
The postoperative instructions correspond to the usual and standard protocol used in the division of Gynaecology of the Geneva University Hospitals. There are no authorisations or limitations specific to the study.

**Primary outcome measure**

Sexual function is a complex and multidimensional issue. It interacts closely with emotional well-being. QoL, relationship with partner and health status. In our study, emotional well-being is assessed by verifying the presence of anxiety or a depressive disorder during the medical preoperative consultation. Information about the patient’s health status will also be collected during the preoperative medical consultation. We added a self-developed questionnaire on superficial and/or deep dyspareunia.

**Female Sexual Function Index**

FSFI, created in 2000 by Raymond Rosen, is a reliable and complete multidimensional self-reported instrument for the measurement of female sexual function. It is validated in English and French. It assesses 19 items divided in six domains of the sexual function. Each item focuses on the situation during the last 4 weeks.

The total score is the sum of answers provided for each of the six domains. The lower the score, the worse the patient’s sexual function. A total score below 26 defines impaired sexual function.

**Couple Satisfaction Index-16**

CSI is a precise, consistent and validated scale that evaluates the quality of a couple’s relationship satisfaction. We chose the 16-items version because it provides enough information for the assessment of relationship satisfaction and reduces the number of questions to be answered. The total score can range from 0 to 81. Higher is the total score, better is the relationship satisfaction. A relationship dissatisfaction is suggested when the total score is below 51.5.

The absence of impairment on sexual function, after elective BAS by vNOTES in comparison with CAL, refers to the stability or improvement of FSFI total scores in each group at 3 and 6 months after surgery compared with the preoperative score and the absence of a statistically significant difference in FSFI total postoperative scores between the two groups.

The results of preoperative CSI-16 and self-reported questionnaire on dyspareunia provide an indication of the patient’s baseline status. Results and evolution of these questionnaire scores at 3 and 6 months postoperatively allow us to specify, in the case of a de novo postoperative sexual dysfunction, whether it is solely related to the surgical technique used, in which case CSI-16 and self-reported questionnaire on superficial dyspareunia scores are the same as baseline values or below the diagnostic cut-off point, or whether it is associated with a relationship issue or superficial dyspareunia, in which case such scores are statistically increased in comparison with baseline values.

**Secondary outcomes measure**

The secondary outcomes are as follow:

1. Evaluation of the success rate (removal of the specimen without the need of conversion to laparoscopy or open-surgery), the procedure duration including the need for adhesiolysis, recovery (length of stay, pain scores) and perioperative complications up to 30 days postoperatively.
   **Intraoperative complications:**
   - Failure to enter the peritoneal cavity (need for adhesiolysis).
   - Need for conversion/hybrid surgical approach.
   - Intraoperative complication during peritoneal cavity access.
   - Intraoperative blood loss (mL), vessel injury and the need for blood transfusion.
   - Bowel injury.
   - Other.

   **Postoperative complications:**
   - Delayed vaginal or parietal healing secondary to:
     - Abscess: a fluid-like collection seen on ultrasound or CT scan with clinical signs (pain, leucorrhoea, fever) and/or biological markers (leucocytosis, increased C-Reactive Protein) infectious signs ± presence of a germ on culture.
     - Haematoma: a haematic collection seen on ultrasound or CT scan with clinical signs.
   - Trocar-site/vaginal scar dehiscence, incisional parietal hernia.
   - Trocar-site nerve injury: iliohypogastric or ilioinguinal nerve injury during fascial closure of the trocar incisions or introduction of the trocars. It is characterised by a persistent pain at 4 weeks postoperative or appearing after surgery such as an electric discharge/burning or a painful cold sensation, respecting the territory of the nerve affected (with irradiation towards the pubis for the iliohypogastric nerve and towards the labia majora with or without presence of dyspareunia for the ilioinguinal nerve) and which may be associated with dyesthesia (tingling, pricking, itching, numbing).  
   - Other.

In order to reduce as much as possible the risk of measurement bias, we will include in our database the diagnoses and management of perioperative complications carried out by the gynaecological emergency service at the Geneva University Hospitals or at other external hospital centres.

2. Evaluation of the relationship between adnexal mass morcellation/aspiration and the quality of histological analysis of the surgical specimen.
The risk of unexpected malignancy needs to be taken into consideration during the extraction of each surgical specimen in order to avoid any tumorous cell spillage. Morcellation or aspiration of an adnexal mass is not recommended. However, it is occasionally performed in an endoscopic bag to provide its extraction in order to limit the cosmetic sequelae and possible consequences of enlarging the incision.

To our knowledge, there is currently no data in the medical literature that investigates such a relationship. In fact, histological analysis is always possible even on a fragmented specimen. However, the ability to obtain an accurate malignancy diagnosis seems to be compromised as the tumour, node, metastases classification of malignant tumours requires macroscopic information such as ovary’s surface invasion for instance.

Table 1 contains all the data required to analyse these secondary outcomes.

**ANALYSIS**

Figure 1 summarises the sequence design. Figure 2 shows the CONSORT (Consolidated Standards of Reporting Trials) 2010 flowchart of our study.

**Figure 2** CONSORT (Consolidated Standards of Reporting Trials) 2010 flowchart. CAL, conventional abdominal laparoscopy; vNOTES, transvaginal natural orifice transluminal endoscopic surgery.
Sample size

Sample size was calculated considering the mean difference in the preoperative and postoperative FSFI score, and comparing such difference between women treated with CAL and with a vNOTES approach (www.sealedenvelope.com). If there is truly no difference between CAL and vNOTES in terms of FSFI score, then a sample size of 56 patients (28 women per group) is needed to be 80% sure that the lower limit of a one-sided 95% CI will be above Δ −2, with a significance level of 5%.

We considered an SD of 3. We selected the non-inferiority margin based on previously published literature according to which a mean difference of FSFI score by as much as 2 was not statistically significant between the abdominal laparoscopic and vaginal approach for hysterectomy.20 Similarly, a study evaluating the FSFI after surgery for endometriosis found a statistically significant difference between the preoperative score of 19.1 and the postoperative score of 22.7. 21

We expect a dropout rate of 10% over the study period, which makes it reasonable to increase the total sample size to 62 patients (31 patients per group).

Sensitivity analyses will be conducted to verify whether the exclusion of participants who no longer conform to the protocol may alter the study’s final results in order to show non-inferiority in both the intention-to-treat and the per-protocol populations.22 Reasons for non-conformity may include, among others, the patient’s preference for one of the two surgical techniques, the patient’s personal decision to dropout of the study after initial inclusion and surgical complications affecting the woman’s intraoperative and postoperative course.

The division of Gynaecology of the Geneva University Hospitals surgically treats an average of 100 BAS per year. Expecting a recruitment rate of 31%, we believe that our study will take 2 years to be completed. A 6-month pilot phase will be conducted to test our recruitment rate and extend the study duration if necessary.

Randomisation

Randomisation of included patients will be computer-generated with a 1:1 ratio, in randomly alternating blocks of 4, 6 and 8. After having signed the study and intervention informed consent form, patients will be allocated to one of the two treatment arms (vNOTES vs CAL) by means of consecutive, numbered, sealed and opaque envelopes. Randomisation will be performed using an automatically-generated computer program (www.randomization.com).

Sequence design

The surgeon will give eligible women who agree to participate in the study all the information specific to the two surgery approaches in order to have the surgical consent form signed in a free and informed manner during the medical preoperative consultation. Any qualified surgeon practicing in the division of Gynaecology of the Geneva University Hospitals can include patients in the study. Then, the research nurse will complete general information and will get the study informed consent form signed. The research nurse will give the patient a study number and will send it to the research assistant. To avoid selection bias, the research assistant will not be allowed to see the patient’s file and will not be involved in the data collection. The research assistant will send allocation to the research nurse. The research nurse will insert the randomised pairing choice into a sequentially numbered opaque envelope. To avoid the risk of switching the allocation sequence, the participant’s name and date of birth will be written on the envelope in addition to the allocated number. The surgeon will find out the patient’s allocation to one of the two treatment arms on the day before surgery or on the day of surgery and inform the patient about her allocation after the surgery.

Blinding

This is an unblinded study where neither the surgeon, nor the patient is blinded to treatment arm assignment.

Statistical analysis

As recommended by the CONSORT statement, analysis will be performed in an intention-to-treat principle. Continuous variables will be reported as means with the relative SD. Non-normally distributed continuous variables will be reported as medians with the relative IQR. Categorical variables will be reported as absolute numbers and percentages. Student’s t-test will be used to compare continuous variables when reported as means, whereas the χ² test will be used to compare categorical variables. The alpha value will be set at 5%, with a probability (p) less than 0.05 to be considered as statistically significant.

Monitoring

The sponsor-principal investigator will regularly fulfill the monitoring duties in the division of Gynaecology of the Geneva University Hospitals with the research nurse and the main co-investigators. An employee of the Geneva University Hospitals clinical research platform, other than the research nurse and independent from the sponsor, will be responsible for external monitoring the study (pre-visit, study initiation visit, intermediate visits, closing visit). The sponsor-principal investigator will be informed of any reports of these visits. The decision to terminate the study will depend on these internal and external reports and the competent authorities. All adverse events reported by the patients themselves and any medical provider will be recorded and declared to the competent authorities in accordance with the rules in force.

ETHICS AND DISSEMINATION

The protocol of this study (V.8.3 dated 24 July 2022) was realised in accordance with The Code of Ethics of the Declaration of Helsinki and validated by the Cantonal Research Ethics Commission of Geneva, Switzerland.
on 9 August 2022 (registration no: 2022–00407). Major changes to the protocol will have to be submitted to the same authority. We aim to publish the results of our study in peer-reviewed journals within 3 years of recruiting the first patient. This study is also part of an MD thesis.

Participation is voluntary and withdrawal from the study can be made at any time without justification. The free and informed signature of the consent form, after having received all the necessary information and having benefited from a period of reflection if needed, is mandatory.

To ensure patient confidentiality, all patient data will be anonymised. Patients included in the study will immediately receive a study number on a first-come, first-served basis, which will follow them on all study documents (care maps and logbooks) according to the ‘main courante’ principle. For instance, the third participant included in the study will be known under patient 3 and she will keep this number throughout the study, regardless of the allocation.

Clinical data management will be carried out with the help of the Geneva University Hospitals Clinical Research Center in accordance with all laws and regulations relating to Good Clinical Trial Practice. We have chosen the REDCap (Research Electronic Data Capture) platform as our data collection and online questionnaire response platform. This platform provides secure and anonymous data collection, analysis and storage. Patients will receive an invitation to complete the questionnaires by email. They will register to the online questionnaire platform using their study number.

Only the investigators and the research nurse will have access to the patient’s names assigned to the study numbers. All study documents will be locked in the Gynaecology division of the Geneva University Hospitals. The person responsible for data analysis will only have access to the study numbers and data will be collected in a computerised file.

Study numbers will be randomised to one of the two interventional arms using an automatically-generated computer program. The allocation of the study number to the intervention arm will be inserted in an opaque envelope and placed in the patient’s file by the research nurse. This envelope will also include the patient’s name to avoid any risk of exchange.

The study is designed to be as fair as possible. The target population for this study is chosen to correspond to the population most commonly affected by benign adnexal disease that may require surgical management. The exclusion criteria for this study correspond mainly to the exclusion criteria for the vNOTES surgical technique. The limitation of this study including only French or English speaking women, excluding a major part of the Geneva’s foreign population, is explained by the limited availability of the questionnaires in a validated translated version. Indeed, the validity of an RCT study depends on the validity of its measurement instruments. The validity of the study also relies on the review of non-affiliated parties.

By using two types of surgery techniques already used routinely and considered safe and valid for the indication of benign adnexal disease, this study represents potential benefits to society that outweigh the risks involved. As the study progresses, patients will be informed of new findings, which may influence their decision to participate or not. A patient who presents more risks than benefits from such a randomised allocation will be withdrawn from the study for safety reasons. Adverse effects will be managed by following the standard protocols of the Geneva University Hospitals. In the event that significant side effects are observed and attributed to the study, the study will be stopped. The results will be shared with the patients at the end of the study.

By providing new knowledge, this study contributes to clinical research. Improving the QoL of women in gynaecological surgery, while ensuring safety of care, is our priority. The rigorous methodology of this study, and the resulting valid clinical and scientific evidence, could lead to a change in recommendations for a better surgical experience for the patient.

To meet legal requirements, this protocol is recorded in the open access database ClinicalTrials.gov.

**WHO trial registration data set**

- **Primary registry and trial identifying number:** ClinicalTrials.gov ID: NCT05761275.
- **Date of registration in primary registry:** May 2023.
- **Secondary identifying numbers:** Study number 2022–00407.
- **Source(s) of monetary or material support:** Department of Gynaecology of Geneva University Hospitals.
- **Primary sponsor:** Dr Jean Dubuisson, MD. Division of Gynaecology, Department of Paediatrics, Gynaecology and Obstetrics, Geneva University Hospitals and University of Geneva, Bd de la Cluse 30, 1205 Geneva, Switzerland.
- **Secondary sponsor(s):** none.
- **Contact for public queries:** Dr J. Dubuisson.
- **Contact for scientific queries:** Dr J. Dubuisson.

**Public title:** Assessment of women’s sexual quality of life after benign adnexal surgery using vNOTES approach in comparison to conventional laparoscopy.

**Scientific title:** Assessment of women’s sexual quality of life after benign adnexal surgery using vNOTES approach in comparison to conventional laparoscopy: protocol for a randomised controlled trial.

**Countries of recruitment:** Switzerland.

**Health condition(s) of problem(s) studied:** Sexual QoL, surgical morbidity.

**Intervention(s):**

- Study intervention: BAS using vNOTES.
- Control intervention: BAS using CAL.
- Key inclusion and exclusion criteria:
  - Inclusion criteria: Women aged from 18 to 70 years; discernment capacity with oral and written consent signed; heterosexual intercourse (with
vaginal penetration) within 4 weeks prior to inclusion in the study.

- Exclusion criteria: History of rectal surgery; suspected rectovaginal/retrouterine endometriosis; history of brachytherapy or pelvic radiation; suspected ovarian malignancy; history of severe pelvic inflammatory disease; active lower genital tract infection; pregnancy; women who do not speak fluent French or English (language of surveys); patients under tutelage.

- Study type: Interventional; randomised (1:1 ratio); unblinded; parallel groups.
- Date of first enrolment: 01 September 2023.
- Target sample size: 62.
- Recruitment status: Pending.
- Primary outcome(s): Women’s quality of sexual life evaluation after BAS using FSFI, CSI-16 questionnaires and a self-reported questionnaire on dyspareunia.

Key secondary outcomes: Comparison on effectiveness, morbidity, complications rate, morcellation/aspiration and histological analysis of the surgical specimen.

Contributors
JD is the sponsor of the trial. EK and JD are principal investigators of the trial. This study is part of EK’s MD thesis. JD is the thesis director. EK wrote and histological analysis of the surgical specimen.

Funding
This work is supported by the private foundation of the medical direction of the university hospitals of Geneva.

Competing interests
None declared.

Patient and public involvement
Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication
Not applicable.

Provenance and peer review
Not commissioned; externally peer reviewed.

Open access
This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID ID
Eloïse Krull http://orcid.org/0009-0000-8210-0125

REFERENCES