


BMJ Open Non-absorbable versus absorbable sutures for anterior colporrhaphy: study protocol for a randomised controlled trial in South Korea

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ABSTRACT

Introduction The anterior vaginal wall is the segment most commonly affected by prolapse. Traditionally, anterior vaginal wall prolapse is repaired via anterior colporrhaphy, which is known to have a high recurrence rate. Several factors might affect the outcome of anterior colporrhaphy, and the use of absorbable sutures might also be associated with the high recurrence rate because the sutures might not be able to retain adequate strength until the plicated pubocervical fascia remodels and regains maximum tensile strength. Nonetheless, no comparative data exist about the relative efficacy and safety of anterior colporrhaphy using non-absorbable versus absorbable sutures. The objective of this study is to compare the surgical outcomes of anterior colporrhaphy using non-absorbable sutures with those of anterior colporrhaphy using absorbable sutures.

Methods and analysis This is a randomised, multicentre, superiority trial. Anterior colporrhaphy will be performed in a traditional manner with midline plication of the fibromuscular layer using either non-absorbable or absorbable sutures. The primary outcome is composite surgical success 1 year after surgery defined as the absence of all of the following: (1) anterior vaginal descent beyond the hymen, (2) the presence of vaginal bulge symptoms and (3) retreatment for recurrent anterior vaginal wall prolapse with either surgery or pessary. The secondary outcomes include the individual components of the composite primary end point, anatomical outcomes, condition-specific quality of life and adverse events related to anterior colporrhaphy. The planned number of participants is 192.

Ethics and dissemination This study was approved by the Institutional Review Board of Seoul National University Hospital (H-1810-037-977). The results of the study will be published in peer-reviewed journals, and the findings will be presented at scientific meetings.

Trial registration number NCT03736811

INTRODUCTION

The anterior vaginal wall is the segment most commonly affected by prolapse.¹ Traditionally, anterior vaginal wall prolapse is repaired with anterior colporrhaphy, which is known to have a high recurrence rate. When strict

Strengths and limitations of this study

- This is the first study to compare surgical outcomes of anterior colporrhaphy using non-absorbable sutures with those of anterior colporrhaphy using absorbable sutures.
- The findings will be strengthened by the multicentre, randomised design, masking both participants and outcome assessors to randomisation assignment, and the use of validated measures to assess anatomic and symptomatic outcomes.
- Our study participants consist of Korean women, and therefore, the findings may not apply to more racially diverse population.

anatomic criteria are used (pelvic organ prolapse quantification (POPQ) stage ≥ 2), recurrence rates after anterior colporrhaphy are reported up to 70%.² The use of mesh repair may decrease the recurrence rate, but the complication rate is higher compared with anterior colporrhaphy.³ Therefore, anterior colporrhaphy remains the most common procedure performed to correct anterior vaginal wall prolapse.

Anterior colporrhaphy involves the midline plication of fibromuscular layers (pubocervical fascia) of the anterior vaginal wall. Absorbable sutures are most often used.⁴ Several factors, including the preoperative degree of pelvic organ prolapse, might affect the outcome of anterior colporrhaphy,^{5 6} and the use of absorbable sutures might also be associated with the high recurrence rate after anterior colporrhaphy. Wound healing is divided into three phases: inflammation (1–4 days), proliferation (5–20 days) and remodelling (21 days to 2 years).⁷ The wound begins to regain its tensile strength from the proliferative phase (up to 15%–20% of its original tissue strength) and gain maximum strength in the remodelling phase (approximately

70%–80% of its original tissue strength).⁸ Meanwhile, absorbable sutures such as polyglactin 910 or polydioxanone commonly used for anterior colporrhaphy lose at least half of their tensile strength within 1 month and the entire strength within 2–3 months.⁸ This may be sufficient for wounds under little or no tension. However, plicated pubocervical fascia may need more time to remodel and regain maximum tensile strength because the increased abdominal pressure generated from daily activity, coughing, straining, exercise and so forth may act as a factor that impedes wound healing.⁹

Data from several clinical trials support this theory. First, most cases of recurrence after anterior colporrhaphy are detected within the first postoperative year.^{2 10} Second, the short-term follow-up study of uterosacral ligament suspension for apical vaginal prolapse has reported that the use of non-absorbable sutures is associated with a lower failure rate than the use of absorbable sutures, even though no failure has been detected until 6 months after surgery.¹¹ Nonetheless, no comparative data exist about the relative efficacy and safety of anterior colporrhaphy using non-absorbable versus absorbable sutures. The objective of this study is to compare the surgical outcomes of anterior colporrhaphy using non-absorbable sutures with those of anterior colporrhaphy using absorbable sutures.

METHODS AND ANALYSIS

Study design

This trial is a multicentre, prospective, randomised trial conducted with the aim of determining the superiority of anterior colporrhaphy using non-absorbable sutures over absorbable sutures with regard to the primary outcome. The study will be a single-blind study, as it is impossible to blind the study surgeon for the surgical procedure to which the subject is assigned. However, all outcome assessors and the subjects will be blinded to the treatment assignment. Postoperative follow-up will take place after 5 weeks, 6 months and 12 months. Patients will undergo a standard gynaecological examination that includes the POPQ and will fill in questionnaires. The design is presented in [figure 1](#). This study protocol was approved on 8 November 2018 and this manuscript details the protocol on the latest version (V.1.5) approved on 02 April 2020, which adheres to the Standard Protocol Items: Recommendations for Clinical Interventional Trials guidelines (online supplementary file 1).

Study setting

This study will be conducted in nine tertiary hospitals in South Korea. Enrolment, treatment and data collection will be standardised by all sites according to the approved study protocol and this manuscript.

Participants and recruitment

The study population will consist of women aged 30 years or older who have symptomatic anterior vaginal

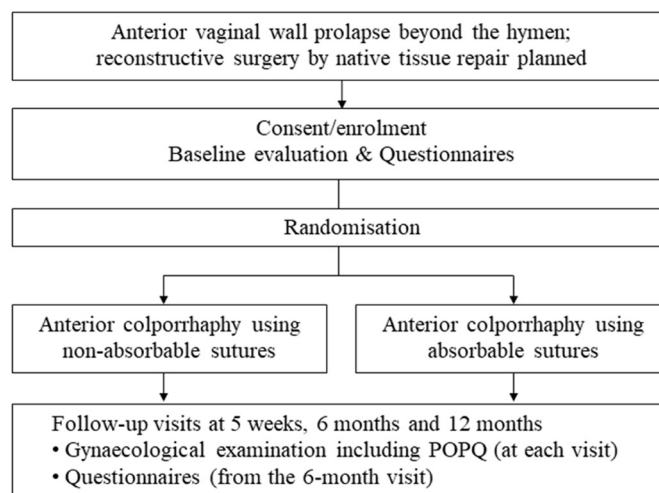


Figure 1 Study flow chart. POPQ, pelvic organ prolapse quantification.

wall prolapse and have opted for reconstructive surgery with native tissue repair. After screening for eligibility, information regarding the study will be provided and written informed consent will be obtained by the research staff (online supplementary file 2). The inclusion and exclusion criteria are presented in [box 1](#). Recruitment commenced on 8 November 2018.

Randomisation

Randomisation will be performed through a website using a computer-generated randomisation table in the operating room by the study surgeon. The subjects will be assigned in a 1:1 ratio to receive anterior colporrhaphy using either non-absorbable sutures or absorbable sutures. The randomisation will be stratified according to the preoperative stage of anterior vaginal wall prolapse, and all subjects will receive a unique study number.

To prevent unmasking the actual procedures, the medical records will indicate the actual surgical procedure without stating the suture materials used for anterior colporrhaphy. Intraoperative data collection will be conducted by the study surgeon rather than by other research staff.

Intervention

Participants will undergo reconstructive surgery for prolapse, including anterior colporrhaphy using the assigned suture materials under general or spinal anaesthesia. Anterior colporrhaphy will be performed in a traditional manner with midline plication of the fibromuscular layer using either non-absorbable (polyester (Ethibond Excel) or polypropylene (Prolene); Ethicon, Somerville, New Jersey, USA) or absorbable (polyglactin 910 (Vicryl) or polydioxanone (PDS II); Ethicon) sutures.⁴

Concomitant procedures will be performed as intended prior to surgery. Women with a uterus in situ will undergo hysterectomy, and all women will receive an apical suspension procedure, including uterosacral ligament

Box 1 Inclusion and exclusion criteria

Inclusion criteria

- ▶ Anterior vaginal wall prolapse beyond the hymen (POPQ point Ba >0).
- ▶ Vaginal bulge symptoms as indicated by an affirmative response to the following question from the PFDI-20: Do you usually have a bulge or something falling out that you can see or feel in your vaginal area?
- ▶ Reconstructive surgery via native tissue repair is planned.

Exclusion criteria

- ▶ Recurrent anterior vaginal wall prolapse.
- ▶ Reconstructive surgery using mesh or obliterative surgery is planned.
- ▶ Known pelvic malignancy.
- ▶ Current systemic glucocorticoid or immunosuppressant treatment.
- ▶ Subject wishes to retain her uterus.
- ▶ Subject is unable or unwilling to participate.

PFDI, Pelvic Floor Distress Inventory; POPQ, pelvic organ prolapse quantification

suspension, sacrospinous ligament fixation and iliococcygeal suspension with both delayed absorbable and permanent sutures, according to the preference of the surgeon because the loss of apical support is usually present when anterior vaginal wall prolapse extends beyond the hymen, and surgical correction of the anterior wall may fail unless the apex is adequately supported.^{12 13} Posterior colporrhaphy and incontinence surgery will also be performed, if indicated (ie, women with Bp \geq -1 or documented urodynamic stress incontinence). Participating surgeons will be required to have performed a minimum of 20 of each procedure prior to beginning subject enrolment to eliminate a learning curve effect.

All women will receive perioperative antibiotics. Postoperatively a vaginal pack will be placed and removed within 24 hours. A voiding trial will take place on postoperative day 2. A postvoid residual volume of 150 mL or greater will be considered abnormal. Patients with elevated postvoid residual volumes will continue mechanical bladder drainage either via a continuous transurethral Foley catheter or intermittent self-catheterisation until the postvoid residual volumes are consistently less than 150 mL. Patients will receive analgesics in accordance with the local hospital protocol. All patients will be advised to abstain from heavy physical work for a minimal period of 6 weeks.

Data collection

At baseline, the following data will be collected: demographics and medical history data (age, body mass index, parity, menopausal and hormone therapy status, current smoking, previous hysterectomy and previous anti-incontinence surgery, and medical comorbidities (diabetes mellitus, connective tissue disorders)), and data from the standardised POPQ examination in a 45° upright sitting position during maximal Valsalva.¹⁴ Patients will be asked to complete the validated questionnaires regarding condition-specific quality of life (the Korean version of

Pelvic Floor Distress Inventory short form questionnaire (PFDI-20)).¹⁵

Scheduled in-person follow-ups will occur at 5 weeks, 6 months and 12 months. Each check-up will include a clinical examination including POPQ and written questionnaires identical to those at baseline (from the 6-month visit). In addition, an update of current medications, an assessment of new or continuing pelvic floor disorders and adverse events that occurred since the previous evaluation will be obtained by the study coordinator at each visit. All data will be anonymised and collected using case report forms by examiners or trained research coordinators at each participating centre who are blinded to the treatment assignment. Quality checks will be performed by all centres and reviewed every 3 months by an independent data monitoring committee.

Primary and secondary outcome measures

Initially the primary outcome was surgical success assessed at 1 and 5 years after surgery. As our sample size calculation could not reflect the 5-year outcome, we changed to assess the primary outcome only for 1 year after surgery during the revision of this manuscript. Surgical success is defined as the absence of all of the following: (1) anterior vaginal descent beyond the hymen, (2) presence of vaginal bulge symptoms and (3) retreatment for recurrent anterior vaginal wall prolapse by either surgery or pessary. The secondary outcomes include the individual components of the composite primary end point, anatomical outcomes (the rate of suboptimal anatomical outcome in each compartment (POPQ point Ba, C or Bp \geq -1), change in POPQ values from baseline (POPQ Ba, C, Bp and total vaginal length)), condition-specific quality of life (change in PFDI-20 scores from baseline), and the rate of adverse events related to anterior colporrhaphy that occurred since baseline (both intraoperative (bladder injury, ureteral obstruction, massive bleeding] and postoperative (haematoma, vesico-vaginal fistula, ureteral obstruction, urinary tract infection, incomplete bladder emptying, overactive bladder or stress incontinence symptoms, suture erosion, vaginal wound dehiscence, infection or granulation tissue, etc)).

Sample size and power considerations

The statistical power calculation is based on a comparison of a binary primary outcome. Previous studies using similar definitions to ours demonstrated that the 1-year surgical success rates after anterior colporrhaphy were 97% with non-absorbable sutures and 85% with absorbable sutures.^{11 16} Based on this information, we estimate that at least 86 patients are needed in each treatment group for 80% power to detect a 12% difference in the primary outcome measure, with a two-tailed type I error of 5%, at 1 year after surgery. Considering a 10% drop-out rate, we will recruit and randomise 192 subjects in this protocol.

Data analysis

The baseline characteristics between the two groups will be compared using a two sample t-test or Mann-Whitney U test for continuous variables and a χ^2 test or Fisher's exact test for categorical variables.

The analyses for all outcome measures will be performed on both an intention-to-treat and as-treated basis, but the principal analysis will be the intention-to-treat analysis for the effectiveness (all outcomes except adverse events) and the as-treated analysis for the safety (adverse events).

The primary outcome will be analysed using a χ^2 test based on the intention-to-treat principle after missing values for it are imputed with multiple imputation. In addition, as a sensitivity analysis, the group difference in the primary outcome will be compared using a generalised linear mixed-effect model (mixed-effects logistic regression) with group as a fixed effect and hospital as a random effect to account for correlation of results within each hospital. If the baseline variables are found to be significantly different between groups, they will be included as covariates in the mixed-effects model.

Secondary outcomes will be analysed as follows: The individual components of the composite primary end point and the rate of suboptimal anatomical outcomes in each compartment will be analysed similar to the primary outcome. Changes in POPQ values and PFDI-20 scores will be analysed using the linear mixed models including hospital as a random effect, with adjustment for baselines. The rate of adverse events related to anterior colporrhaphy will be compared with a χ^2 test or Fisher's exact test

Patient and public involvement

Neither the patients nor the public were involved in the design, conduct, reporting or dissemination of this study.

Data monitoring

Data monitoring will be performed every 3 months by an independent data monitoring committee. The committee will monitor protocol deviations, violations, data quality and serious adverse events. No interim analysis is planned during this trial.

Ethics approval and dissemination

The study will be conducted in accordance with the principles of the Declaration of Helsinki and 'good clinical practice' guidelines. This trial was approved by the Institutional Review Board (SNUH 1810-037-977). Prior to randomisation informed consent will be obtained. All participant-identifiable data, such as consent forms, screening and identification logs, will be stored in the investigator site files, accessible only to delegated members of the study team. Any personal information will be neither recorded in case report forms nor shared with others. The datasets used and/or analysed after completing the study will be available from the corresponding author on reasonable requests. The results of the study will be published in peer-reviewed journals, and the findings will be presented

at scientific meetings. Authorship will be determined by the guidelines set out by the International Committee of Medical Journal Editors.

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