EVALUATION OF RISK FACTORS AND SURGICAL SAFETY OF VAGINAL PELVIC ORGAN PROLAPSE RECONSTRUCTION WITH IMPLANTS

Ph.D. Thesis Booklet

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1. Introduction

1.1. Overview of the topic

1.1.1. What is the topic?

My research focuses on evaluating the safety and effectiveness of vaginal pelvic organ prolapse (POP) surgeries using implants compared to procedures that utilize the patient's native tissue (NT). We also identified the most frequent, clinically relevant complications and the risk factors that predispose patients to the most common implant-related complication. By characterizing these predictors, surgical technique can be better individualized.

1.1.2. What is the problem to solve?

The central problem is determining whether vaginal implants in POP surgery provide benefits that outweigh their risks, particularly given the high recurrence rates after NT repair and the significant safety concerns associated with implant-related complications. Although implants may offer more durable anatomical support, regulatory warnings, complication reports, and national bans have created uncertainty regarding their appropriate

use. Consequently, there is a critical lack of evidence-based guidance on which patient subgroups may safely and effectively benefit from implant-related POP surgery. Addressing this issue requires clarifying the true risk–benefit profile of vaginal implants and identifying the patients for whom their use is justified.

1.1.3. What is the importance of the topic?

POP is a common condition that significantly affects women's quality of life, with about half of women over 50 affected and 11% undergoing surgery by age 80. Symptoms include anatomical complaints, such as a vaginal bulge or pain, and functional disturbances, including urinary incontinence and voiding difficulties. When conservative management fails or a pessary is declined, surgical intervention may be indicated. NT repairs have high recurrence rates (up to 30%) and involve multiple surgical techniques, highlighting the need for more durable approaches. Vaginal implants can provide improved anatomical support, but their use is complicated by risks such as VWE. Many countries have completely banned the use of vaginal implants due to high

complication rates. Despite evidence of potential benefit, clear guidance on which patients may safely benefit from implant-based POP surgery is lacking. Systematic evaluation of safety and effectiveness across surgical approaches is needed to optimize outcomes and identify patients for whom vaginal implants can be used safely.

1.1.4. What would be the impact of our research results?

The findings could transform clinical practice by supporting individualized, evidence-based use of vaginal implants in POP surgery. We identify high-risk patient subgroups and those most likely to benefit, promoting safer, more effective outcomes. The results can inform guideline updates on patient selection, surgeon experience, and surgical volume, advocate for reconsideration of implant bans, and highlight the need for prospective registries and long-term RCTs. We may also guide the development of safer implant materials, improving patient care and advancing POP management.

2. Objectives

2.1. Study I. – Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients

This study evaluated the complications and effectiveness of female POP surgery with and without vaginal implants. We aimed to determine whether implant-related risks outweigh their potential benefits compared with native tissue repair. To address this, we performed a systematic review and meta-analysis comparing complication rates and clinical outcomes of implant-related versus NT vaginal POP surgery.

2.2. Study II. – Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis

Previous meta-analyses identified vaginal wall erosion (VWE) as the only clinically significant complication of implant-related vaginal POP surgery. Given interindividual variability, this study aimed to identify prognostic factors associated with VWE. We conducted a systematic review and meta-analysis to assess the impact

of patient- and procedure-related risk factors on VWE development.

3. Methods

3.1. Search Strategy

Studies I and II were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). To ensure methodological transparency and reproducibility, both study protocols were prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the identifiers CRD42022369386 and CRD42023364171.

3.2. Eligibility Criteria

3.2.1. Study I

The PICO (Population, Intervention, Comparison, Outcome) framework was used to pose our questions. Studies on females with pelvic organ prolapse (P) who underwent vaginal surgery with implants (I) in comparison to surgery without implants (C) were included. All complication types reported (Outcome 1)

and the effectiveness (Outcome 2) of the two methods were compared. Complications were reported in terms of number of patients with the complication, the rate of reoperation for complications, and the different complication types. To determine the effectiveness, data on anatomical success (based on definitions used by the authors, Pelvic Organ Prolapse Quantification [POP-Q] stage, POPQ points) and the rate of reoperation for recurrence were collected. Clinical recurrence was defined as POP-Q stage ≥2. RCTs and prospective and retrospective cohort studies were eligible. Studies were excluded if they reported on either implant surgeries or on NT surgeries alone, if the data could not be further processed, or if the publication was a conference abstract, review, case series, or case report.

3.2.2. Study II.

The PFO (Population, Factors, Outcome) framework was used to construct our question. Eligible studies involved adult females who had undergone pelvic organ prolapse vaginal surgery with alloplastic implants (P), and patients with and without risk factors (F) for the odds of VWE (O)

were compared. Eligible studies reported the event numbers in groups of risk factors or as ORs. Randomized controlled trials and prospective and retrospective cohort studies were eligible. No studies were excluded based on language criteria. Conference abstracts, reviews, case series, and case reports were also excluded.

3.3. Study selection and data extraction

In both studies, two independent reviewers performed study selection using EndNote X20.2 (V.7) and conducted data extraction with a standardized data collection form. Discrepancies were resolved through discussion; if consensus was not achieved, a third reviewer was consulted or the study authors were contacted for clarification.

3.4. Quality Assessment

Two independent authors assessed study quality, with disagreements resolved through discussion, review of study details, or consultation with a third reviewer. Risk of bias was evaluated using the ROBINS-I tool for nonrandomized studies and the ROB 2 tool for

randomized controlled trials, in accordance with the Cochrane Handbook. The GRADE system was applied to assess the quality of evidence for each outcome.

3.5. Data synthesis and analysis

3.5.1. Study I

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated as effect size measures. For intraoperative complications, total reoperations, and reoperations for recurrence or other complications, effect sizes were pooled using a random-effects Mantel-Haenszel model with Hartung-Knapp adjustments (Harrer, 2021). Heterogeneity was assessed with Higgins & Thompson's I^2 statistic. For functional complications, nonfunctional complications, and anatomical success outcomes, a multivariate model was used to account for intra- and inter-study correlations and to test moderator effects. Sandwich-type cluster-robust variance-covariance estimates were applied for model coefficients and CIs. Small-study publication bias was evaluated via funnel plots, and outliers were identified using Baujat plots and leave-one-out analyses (Harrer, 2021).

3.5.2. Study II

Considerable between-study heterogeneity was assumed; therefore, a random-effects model was used to pool effect sizes. Odds ratios (ORs) with 95% confidence intervals (CIs) were used as effect size measures. When available, raw data (total patients and events per group) were extracted to calculate study and pooled ORs. If only ORs were reported, these and their 95% CIs (assuming Wald-type intervals if not provided) were used. All analyses were performed in R (v4.4.1) using the meta package (v7.0.0) for basic meta-analysis calculations and plots, and dmetar (v0.1.0) for additional influence analyses. Results were considered statistically significant if the pooled CI excluded the null value. Findings were summarized in forest plots, and, where appropriate, prediction intervals were reported. Between-study heterogeneity was quantified using Higgins & Thompson's I^2 statistic. Small-study publication bias was assessed via funnel plots and the Harbord (modified Egger's) test for ORs, with $p < 0.10$ indicating possible bias, acknowledging limited reliability for fewer than ~10

studies. Potential outlier studies were explored using influence measures and plots following Harrer et al. (2021).

4. Results

4.1. Study I.

Following full-text selection, we collected data from 50 articles, of which 19 were RCTs and 31 were observational studies. Regarding postoperative nonfunctional complications, vaginal bleeding (OR 1.67, CI 1.15–2.40) and erosion (OR 14.05, CI 7.96–24.80) were significantly more frequent in the implant group, whereas buttock pain was more common in the NT group (OR 0.34, CI 0.17–0.70). There were no clinically relevant or statistically significant differences between the implant and NT groups in the odds of groin pain, haematoma, pelvic abscess formation, pelvic pain, postoperative fever, thrombosis, urinary tract infection, vaginal adhesion or stenosis, or vaginal discharge. Among postoperative functional complications, the odds for de novo SUI development were significantly higher (OR 1.44, CI 1.189–1.75) in the implant group. The difference

in odds for the remaining functional complications (de novo dyspareunia, de novo overactive bladder, de novo urgency, defecation difficulties, micturition difficulties, and urinary retention) were not statistically significant. However, the odds of reoperation for complications were significantly higher in the implant group among randomised trials (OR 2.15, CI 1.20–3.87). The odds of achieving an anatomically successful reconstruction were 3.22 times higher (CI 2.06–5.01) in the vaginal implant group, while the probability of presenting with POPQ stage 3 at the end of follow-up was 69% higher (OR 0.31, CI 0.16–0.62) in the NT group. Furthermore, among RCTs the reoperation rate for recurrence was higher in the NT group (OR 0.55, CI 0.36–0.85).

4.2. Study II

We compared 25 studies in our meta-analysis. Data were available for a total of 7,567 patients, of which 642 (8.5%) women experienced VWE during the study period. The risk factors primarily investigated in the articles were age (n: 10) and concomitant hysterectomy (n: 9); other factors investigated included body mass index (BMI), smoking

habits, sexual activity, comorbidities, HRT, previous vaginal surgeries, menopausal status, implant type, vaginal compartment operated on, and postoperative hematomas. A total of three studies, covering 504 patients, were selected for the analysis of age as a risk factor. The mean age of the women with and without erosion was 59.1 ± 10.6 vs. 60.6 ± 10.1. Therefore, there was neither a clinically relevant nor a statistically significant difference between the groups (OR: 1.13, CI: 0.46–2.80). Moreover, the OR for elderly patients (age over 65 years) was 0.40 (CI: 0.04–4.07), indicating that age over 65 was not a risk factor, as there was no statistically significant or clinically relevant difference between the groups over and under 65 years. The occurrence of VWE was higher in patients with diabetes mellitus (DM) than in patients without DM, which was clinically relevant, but the difference was not statistically significant (OR: 2.91, CI: 0.67–12.71). In terms of VWE in patients with or without hypertension (OR: 2.27, CI: 0.31–13.78) and women with or without menopause (OR:0.88, CI:0.11–8.53), there were no statistically significant differences. There were no statistically

significant differences between OR for BMI (OR: 0.96, CI: 0.69–1.33) and sexual activity (OR: 3.07, CI: 0.72–13.19). In addition, VWE was significantly more common in smokers than non-smokers (OR: 3.65, CI: 2.56–5.20). Concomitant hysterectomy significantly increased the risk of erosion (OR: 3.33, CI: 1.71–6.48); however, previous hysterectomy did not predispose to VWE (OR: 1.45, CI: 0.54–3.88). Previous prolapse surgery and HRT had no statistically significant effect on the risk of VWE (OR: 1.74, CI: 0.72–4.19 and OR: 1.29, CI: 0.13–12.63). The risk of VWE was associated with a significantly higher occurance of postoperative hematomas (OR: 2.52, CI: 1.98–3.20).

5. Conclusions

5.1. Study I.

Vaginal surgery for POP with implants appears more effective than non-implant procedures, with complication rates generally within acceptable limits. Vaginal wall erosion remains the main clinical concern but may be reduced through better patient selection, improved implant materials, refined surgical techniques, and higher

surgical volume. These findings suggest that the current ban on vaginal implants for POP repair may warrant reconsideration.

5.2. Study II.

Our findings suggest that smoking and concomitant hysterectomy increase the risk of VWE in POP surgeries with implants. Postoperative hematoma may also contribute, though evidence is limited. Larger studies are needed to clarify these and other risk factors. These results underscore the importance of careful patient selection, addressing modifiable risks (e.g., smoking cessation), and ongoing refinement of implant materials and surgical techniques.

6. Bibliography

6.1. Publications related to the thesis:

1. Ács J, Szabó A, Fehérvári P, Skribek B, Cavalcante BGN, Váncsa S, Romics M, Szarvas T, Nyirády P, Ács N, Hegyi P, Majoros A. Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic

review and meta-analysis. Sci Rep. 2025 Nov 19;15(1):40780. doi: 10.1038/s41598-025-24569-5.

IF: 3,9

2. Ács J, Szabó A, Fehérvári P, Harnos A, Skribek B, Tenke M, Szarvas T, Nyirády P, Ács N, Hegyi P, Majoros A. Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients. Eur Urol Focus. 2024 Jul;10(4):525-534. doi: 10.1016/j.euf.2023.11.001.

   IF: 5,6

6.2. Publications not related to the thesis:

1. Ács Júlia, Sonkodi Balázs, Soós Zita, Nyirády Péter, Kopa Zsolt: Az orgazmus nem kívánt hatása: "Orgazmust követő betegség" tünetcsoport (POIS) - új adatok, MAGYAR UROLÓGIA 35: 1 pp. 8-10. (2023)