DR NINA KRISTIINA MATTSSON (Orcid ID : 0000-0003-2304-3938)
PROFESSOR ANNA-MAIJA TOLPPANEN (Orcid ID : 0000-0001-9270-9268)

Article type : Original Research Article

Methods of surgery for pelvic organ prolapse in a nationwide Cohort (FINPOP 2015)

Nina Kristiina MATTSSON[1,5], Päivi KARJALAINEN[2,5], Anna-Maija TOLPPANEN[3], Anna-Mari HEIKKINEN[4,5], Jyrki JALKANEN[6,10], Päivi HÄRKKI[7,8], Kari NIEMINEN[9,10]

[1]Department of Obstetrics and Gynecology, Kanta-Häme Central Hospital, Hämeenlinna, Finland
[2]Department of Obstetrics and Gynecology, Central Finland Central Hospital, Jyväskylä, Finland
[3]School of Pharmacy, University of Eastern Finland, Finland
[4] Terveystalo, Finland
[5] Institute of Clinical Medicine, University of Eastern Finland, Finland
[6] Central Finland Hospital District, Finland
[7] Department of Obstetrics and Gynecology, Helsinki University Hospital, Finland
[8] Faculty of Medicine, University of Helsinki, Finland
[9] Department of Obstetrics and Gynecology, Tampere University Hospital, Finland
[10] Faculty of Medicine and Life Sciences, University of Tampere, Finland

Corresponding author:
Nina Kristiina Mattsson
Kanta-Häme Central Hospital, Ahvenistontie 20, 13530 Hämeenlinna, Finland
E-mail: nina.mattsson@fimnet.fi

Conflict of interest statement:

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Funding

The study was funded by Finnish Society of Gynecological Surgery and supported by grants from the Emil Aaltonen's foundation, the Finnish Cultural Foundation, Häme Regional Fund and the Ministry of Health and Social Welfare in Finland via Medical Research Funds of Kanta-Häme Central Hospital.

ABSTRACT

Introduction: The management of pelvic organ prolapse (POP) varies significantly between countries. The objective of this study was to describe the methods used for POP surgery in Finland and to identify the factors that affect clinicians' choice to use either a native tissue repair (NTR) or mesh repair method. **Material and Methods:** This prospective cohort study included 3,535 surgeries covering 83% of all POP operations performed in Finland in 2015. The operative details and patient characteristics, including the Pelvic Floor Distress Inventory (PFDI-20), were compared between three selected surgical methods (NTR, transvaginal mesh (TVM), and abdominal mesh (AM)). The predictive factors for the use of mesh augmentation were also studied with logistic regression analysis. **Results:** The most common method was NTR (N=2855, 81%), followed by TVM (N=429, 12%) and AM (N=251, 7%). Approximately 92% of patients who underwent primary prolapse surgery underwent NTR, and mesh surgery was used mainly for recurrent prolapse. The strongest predictor of mesh surgery was previous POP surgery for the same vaginal compartment (adjusted odds ratio (OR) = 56, 95% confidence interval (CI) = 38-84 for TVM; adjusted OR = 22, 95% CI = 14-34 for AM). Other predictive factors for mesh surgery were previous hysterectomy, healthcare district, severe bulge symptoms and advanced prolapse. TVM was associated with advanced anterior prolapse and older age. AM surgery was associated with advanced apical and/or posterior compartment prolapse. PFDI-20 scores were the highest in the AM group (108 vs 103 in the TVM group and 98 in the NTR group, p=0.012), which indicates more bothersome symptoms than in the other groups. **Conclusions:** The Finnish practices follow international guidelines that advocate NTR as the principal surgical method for POP. Synthetic mesh augmentation was mainly used in patients with recurrent and advanced

prolapse with severe symptoms. The variation in the rates of mesh augmentation for POP surgery in different hospitals implies a lack of sufficient evidence of the most suitable treatment method and indicates a need for national guidelines.

Key Words
prolapse, surgical techniques, urogynecology, laparoscopy, hysterectomy

ABBREVIATIONS
POP, pelvic organ prolapse;
NTR, native tissue repair;
TVM, transvaginal mesh;
AM, abdominal mesh;
PFDI, Pelvic Floor Distress Inventory;
OECD, Organisation for Economic Co-operation and Development

Key message
In Finland, pelvic organ prolapse is repaired vaginally with native tissue in eight out of ten surgeries. Mesh surgery is used mainly for recurrent prolapse and for patients with advanced prolapse and bothersome symptoms.

1. INTRODUCTION

More than one in ten women undergoes pelvic organ prolapse (POP) surgery in their lifetime.[1, 2] In Finland, the lifetime likelihood of POP surgery is 13%, and approximately 4,200 operations are performed annually.[3, 4] There are numerous different methods for POP surgery.[5] Clinicians must choose between vaginal and abdominal surgical approaches, decide whether to use native tissue or a surgical mesh, choose to repair one or multiple sites of prolapse, and decide whether concomitant surgery, such as hysterectomy or incontinence surgery, is necessary. The operative method depends on the nature, site and severity of the prolapse and the symptoms affecting urinary, bowel or sexual function.[6] The patient's general health and individual needs and values should be considered when determining the operative method.[7, 8]

There continues to be a limited level of evidence to guide clinicians in choosing the best surgical technique for a particular patient.[7] Furthermore, a surgeon's own preferences

and capabilities influence the decision. There is significant heterogeneity (>10-fold) in the rates at which individual POP procedures are performed in different countries.[9] Recently, the risks related to mesh augmentation have caused debate regarding the safety of this method for POP surgery.[10] Thus, different surgical techniques and their safety and effectiveness requires further assessment.

This nationwide prospective annual cohort study reports the methods used for POP surgery in Finland in 2015. The patient characteristics and symptoms were compared between women who were treated with native tissue repair (NTR), a vaginal mesh or an abdominal mesh (AM) augmentation to identify the factors that affect clinicians' choice to use a mesh instead of NTR for POP surgery.

2. MATERIAL AND METHODS

All Finnish hospitals that performed POP surgery in 2015 were invited to participate in this nationwide prospective multicenter study. The study was organized by the Finnish Society for Gynecological Surgery, and the study protocol of a national multicenter study with local doctors in charge was similar to a previous study of hysterectomies (FINHYST 2006).[11] The study period was between 1.1.2015 and 31.12.2015. We retrieved the actual total number of POP operations performed in Finland during this period from the Finnish Hospital Discharge Register of the National Institute for Health and Welfare.[4] The inclusion criteria for the patients were age older than 18 years old and ability to communicate in written and oral Finnish or Swedish. Written informed consent was obtained from each patient.

The surgical treatment and patient characteristics were derived from questionnaires filled out by both doctors and patients. The usefulness and reliability of the questionnaires (paper and electronic forms) and the study protocol were tested in a pilot study performed in 2014 at Tampere University Hospital, Central Finland Central Hospital and Kanta-Häme Central Hospital. The data from the pilot study are not included in this analysis.

The surgeons completed an electronic study questionnaire. The degree of prolapse was assessed using a simplified Pelvic Organ Prolapse Quantification (POPQ) system.[6] The surgeons recorded the single most distal Pelvic Organ Prolapse Quantification point of all three compartments of the vagina (anterior, posterior or apical) in centimeters from the hymen. They also documented the operative method with a description and a code from the Nordic Classification of Surgical Procedures (NCSP).

The participants completed a questionnaire either as an electronic or paper form based on their own preferences. They reported their worst symptoms related to pelvic floor dysfunction, such as an awareness of a bulge or a feeling of pelvic pressure, urinary or defecation problems, pain, or other symptoms. They also reported their height (cm), weight (kg), chronic diseases, medication, parity, mode of delivery, and smoking status. We administered validated health-related quality of life questionnaires either in Finnish[12] or Swedish[13] and the short version of the Pelvic Floor Distress Inventory (PFDI-20),[14] which measures the severity of POP symptoms. The questionnaires were collected separately by the investigators and were not available to the surgeons. The surgical method was determined by the individual surgeon's preference based on clinical judgment.

2.1. Statistical analyses

The operations were categorized into three groups: NTR, transvaginal mesh augmentation (TVM), and abdominal mesh (AM) augmentation. Patient characteristics and surgical details were analyzed in the whole study population and in each surgical method group. The statistical significance was set at $P<0.05$. The differences in categorical variables between the surgery groups were tested with the χ^2 test. Q-Q-plots were used to assess the distribution of continuous variables, and Levene's test was used to assess the equality of variances in the different groups. When the variances were equal, the differences among continuous variables between the groups were tested with an analysis of the variance, and the Bonferroni method was applied to assess pairwise comparisons. For variables with unequal variance, the Brown-Forsythe test was used to assess the differences between the groups, and Dunnett's T3 was used to assess pairwise differences. Binary logistic regression was used to identify the predictors for the use of a vaginal mesh or an AM. The results were adjusted for age, sexual activity, previous hysterectomy or POP surgery, degree of bulge symptoms, health care district and type of hospital. There were no indications for collinearity between the factors included in the model (all correlation coefficients<0.4). All statistical calculations were performed with SPSS 24.0 (IBM Corp., Armonk, NY, USA).

2.2. Ethical approval

The Research Ethics Committee of the Northern Savo Hospital District approved the protocol (Reference number 5//2014). Approval was also obtained from the Finnish Ministry of Social Affairs and Health and from the institutional review boards of each participating hospital. The study was included in the ClinicalTrials.gov protocol registration system

(NCT02716506) and followed the ethical standards for human experimentation established by the Declaration of Helsinki of 1964, revised in 2013.[15]

3. RESULTS

Forty-one of the 45 (91%) hospitals performing POP surgeries in Finland participated: all five Finnish university hospitals, 17/18 secondary hospitals, 15/17 primary hospitals and 4/5 private clinics. Of the 3,535 operations included in the study, 1,169 (33%) were performed in tertiary, 1,562 (44%) in secondary, and 745 (21%) in primary hospitals, and 44 (1.3%) in private clinics. The participation rate varied between centers and was 42–100% (Supporting Information Appendix S1). The flow chart of participant enrollment and the data availability are presented in Figure 1. In 2015, altogether 4,240 POP operations were performed in Finland, corresponding to a rate of 1.52 per 1,000 women. The study population (N=3515 patients, 3535 operations) covered 83% of all women that underwent surgery for POP in Finland in the 2015. Approximately 83% (N=2903) of the participants completed all the preoperative questionnaires including the PFDI-20 questionnaire.

The patient characteristics are depicted in Table 1. The patients who underwent TVM were significantly older, less sexually active, and more likely to have cardiovascular diseases or be treated with medication for chronic disease than patients in the other groups. There was no significant difference in the proportion of obese patients between the groups. The participants' smoking habits and parity did not differ between groups. Altogether, 1,701 (48%) patients had a history of previous pelvic surgery. The total previous hysterectomy rate was 79% for the TVM, 76% for the AM and 23% for the NTR groups (P<0.001). A total of 891 (25%) patients had undergone previous surgery for POP, and all these patients were symptomatic. Prolapse of the anterior compartment of the vagina was the most common form of prolapse. More than one compartment of the vagina was reconstructed in 1,460 (41%) of the operations.

Awareness of a bulge that was reported by 93% of the patients (PFDI-20 question number 3). The patients' assessment of the worst symptom related to their pelvic floor dysfunction was as follows: feeling of a bulge or pressure (2,003, 69%), urinary symptoms (468, 16%), defecation symptoms (297, 10%) and feeling of pain (60, 2%). The total PFDI-20 scores and subscales in the three surgical groups are shown in Table 2. The highest total PFDI-20 scores were observed in the mesh groups, indicating greater distress due to symptoms; in the AM group, the average score was ten points (95% confidence interval (CI)

= 0.3-20, P=0.041) higher than that in the NTR group. The prolapse symptom (Pelvic Organ; Prolapse Distress Inventory (POPDI-6)) scores were also higher in the mesh groups. Urinary symptoms were significantly more common in the TVM group than in the other groups. Colorectal symptom scores (Colorectal-Anal Distress Inventory (CRADI-8)) were similar between the groups.

The types of operations performed are summarized in Figure 2. The most common method of surgery – vaginal hysterectomy and colporrhaphy – was performed in 1,153 (33%) operations. Colporrhaphy without hysterectomy was performed in 1,308 (37%) operations, and isolated posterior colporrhaphy was the most common technique (n=600). Isolated anterior colporrhaphy was performed in 484 operations, and both anterior and posterior colporrhaphy were performed in 224 operations. Isolated vaginal vault repair with native tissue was rare (N=157, 4%), and 118 operations included hysterectomy alone. The Manchester operation was performed for 37 patients, and obliterative surgery (such as colpocleisis and vaginal closure) was performed for 29 (0.8%) patients. More detailed figures of the native tissue surgical procedures are available in Supporting Information Appendix S2. The mesh surgeries were performed in 30 out of 41 hospitals, and the number of mesh surgeries that were included in the study varied from 4 to 107 per center (Appendix S1). A transvaginal mesh was used in 429 operations, which corresponds to 0.15 per 1,000 women, and the most common method was anterior/apical mesh augmentation (n=361, 84%). The TVM kits used during surgery are summarized in Supporting Information Appendix S3. An AM augmentation – sacrocolpopexy – was performed in 251 operations, and 91% of those were performed laparoscopically.

The factors affecting the use of a mesh are described in Table 3. The strongest predictor for the use of a mesh was a previous POP surgery of the same vaginal compartment (OR 56 for TVM and 22 for AM). Other predictive factors were previous hysterectomy and severe bulge symptoms. TVM was associated with advanced anterior prolapse, whereas AM augmentation was associated with advanced apical and posterior prolapse. Regional differences in practices were found. The patient's healthcare district was a strong predictor of the use of mesh surgery; there was almost a 10-fold difference between the highest and lowest odds ratio (OR) for the use of a transvaginal mesh. The hospital level did not explain the variation in the use of a mesh.

A total of 2,644 (75%) operations were performed for patients without prior prolapse surgery, and 92% of these were performed using native tissue. A total of 206 (8%) participants received a mesh for primary prolapse, 103 received TVM, and 103 received AM.

The type of hospital did not affect the risk of primary TVM, but there was significant variation in the practices between hospitals (Supporting Information Appendix S1). Risk factors for TVM as the primary surgery were advanced anterior or apical prolapse, bothersome bulge symptoms, and healthcare district (Table 3). An AM augmentation was used as the primary surgery more often for patients with rectal intussusception (OR = 20.1, 95% CI = 12.9–31.6), and other predictive factors were advanced apical or posterior compartment prolapse. Previous hysterectomy was a risk factor for both transvaginal mesh and AM use during the primary surgeries.

4. DISCUSSION

This nationwide prospective cohort study of 3,535 operations showed that 81% of all patients and 92% of patients without prior prolapse surgery underwent vaginal native tissue reconstruction. The strongest predictors for the use of a mesh were recurrent POP, previous hysterectomy, healthcare district and severe bulge symptoms. TVM was associated with advanced anterior prolapse and older age. AM augmentation surgery was associated with advanced apical and/or posterior compartment prolapse and the highest total PFDI-20 scores indicating more bothersome symptoms than in the other groups. The median preoperative symptom scores were at the same level as in studies with selected patient groups, suggesting that the indications for POP surgery in Finland are comparable to those discussed in other reports.[15, 16]

The overall rate of POP surgery in Finland in 2015 was 1.5 per 1,000 women, which is comparable to the results a study of 15 other Organisation for Economic Co-operation and Development (OECD) countries in 2012.[9] The data from other Nordic countries showed that the rate of POP surgery per 1,000 women was 2.0 in Sweden and 1.8 in Denmark in 2012.[9] The rate of TVM was 0.19, and that of AM augmentation was 0.048 per 1,000 women in OECD countries,[9] while in the present study, the rates were 0.15 and 0.090 per 1,000 women, respectively. This finding indicates that transvaginal mesh augmentation was used moderately in Finland during the study period. In comparison, in 2012, the rate of TVM per 1,000 women was 0.37 in Sweden and 0.07 in Denmark, which was reasonably higher in Sweden and lower in Denmark than the rate in the present study. Furthermore, the rate of sacral colpopexy per 1,000 women was 0.015 in Sweden and 0.006 in Denmark, which were both much lower figures than in Finland.[9] Unlike in Denmark, mesh augmentations are not centralized in Finland and Sweden, which may partly explain the higher mesh surgery rates

than in Denmark. However, regional differences in POP surgical methods in Nordic countries have not been reported previously. We observed significant regional variation in the use of mesh augmentation. For transvaginal mesh surgery, this variation was almost 10-fold. This finding may be partly due to differences in the population, but it does imply different practices between hospitals. According to recent European recommendations, mesh augmentations should be restricted to those surgeons with appropriate training who are working in multidisciplinary referral centers.[17]

Recurrence of prolapse is common. Over one to three years of follow-up after NTR, 38% of the patients had a recurrent prolapse on examination, and 19% were aware of this prolapse.[18] In the present study, 25% of the patients had underwent previous surgery for POP, and 17% of the patients had a recurrence in the same vaginal compartment. This finding suggests a moderate recurrence rate after POP surgery in Finland. Relatively few Manchester and obliterative procedures compared to vaginal hysterectomies were performed. In a Danish cohort study, vaginal hysterectomy was associated with a higher recurrence rate than the Manchester procedure, and this method of apical prolapse surgery should be considered if there is no indication for hysterectomy.[19]

The indications for the use of a mesh during POP surgery have been widely debated after the Food and Drug Administration (FDA) of the United States provided second warning on the adverse effects of TVM surgery in 2011.[10] The rate of TVM surgery has diminished dramatically,[20,21] and in some countries, transvaginal mesh use has been abandoned.[22] After the 2015 study period, most commercial transvaginal mesh kits were withdrawn from the market, and the rate of TVM surgery diminished in Finland.[4] Nevertheless, after critical evaluation and based on patient information, transvaginal mesh augmentation remains an option for patients with a high risk of prolapse recurrence.[8, 18] In randomized studies, vaginal mesh augmentation has provided anatomic benefits and decreased prolapse awareness and is associated with higher rates of de novo stress urinary incontinence, bladder injury and reoperations than NTR.[18, 23] Eight percent of patients require repeat surgery due to transvaginal mesh exposure.[18] Abdominal sacrocolpopexy is associated with lower risks of prolapse awareness and recurrence, postoperative stress urinary incontinence and dyspareunia than a variety of other vaginal interventions for apical prolapse.[7]

In the present study, a recurrent POP in the same vaginal compartment was the strongest predictive factor for the use of a mesh. This finding is in line with recent recommendations.[8, 17] For primary prolapse, the use of a synthetic mesh is controversial, and studies do not support using TVM in anterior or posterior compartment repair.[24] In a Scottish

retrospective cohort study of 18,986 women, 7% of the primary operations were mesh surgeries.[25] In our study, a similar number of primary POP operations were mesh operations. Posterior compartment prolapse was a protective factor for TVM, and this finding is in line with recommendations to avoid the use of a mesh with these patients.[8] Advanced anterior prolapse is more prevalent and more prone to failure after repairs; thus, synthetic mesh may be beneficial.[8] In the present study, advanced anterior prolapse was a predictive factor for TVM. Advanced apical and posterior compartment prolapse and rectal intussusception were predictive factors for AM augmentation, also in accordance with the recommendations.[7] Previous hysterectomy was a strong predictive factor for mesh augmentation. This finding is in line with those of previous studies supporting the assumption that hysterectomy increases the risk of later POP surgery, especially posterior compartment prolapse repair.[26, 27]

Our study has some limitations. The participation rate varied between hospitals, which may bias the comparison of treatment practices between hospitals. We did not record the socioeconomic or menopausal statuses of the patients. The surgical method was based on an individual surgeon's assessment and preferences, and the surgeons were not aware of the symptom scores reported on the forms completed by the patients, which may be a limitation but, on the other hand, reflects normal practice. Notably, 3% of patients underwent vaginal hysterectomy alone. This finding may be due to a coding error or a practice pattern, but because of the nature of the study, we could not make any further conclusions on how vaginal cuff suspension was performed in these cases.

The strength of our study is that this nationwide prospective cohort covered the majority of all POP operations performed in Finland, offering a holistic picture of practices within a country. The study protocol also included clinicians' assessments of the preoperative situation and validated health-related quality of life questionnaires. The previous large cohort studies were mainly based on retrospective databases with no symptom questionnaires used.[25, 28]

5. CONCLUSION

The practices reported here follow international recommendations that consider NTR to be the principal surgical method for POP surgery.[17, 18] A synthetic mesh was mainly used in complex cases with recurrent prolapse in the same compartment. However, there was regional variation between the rates of mesh augmentation for POP surgery. In our opinion,

this implies a general lack of sufficient evidence regarding the most suitable treatment methods for POP and indicates a need for national guidelines.

Acknowledgments

We want to express our appreciation to all the Finnish colleagues who participated in patient recruitment. In particular, we want to acknowledge the work done by contact persons in participating hospitals: Tomi Mikkola, Pontus Molander, Maritta Pöyhönen-Alho, Tuuli Soini, Tapio Väyrynen, Esa Räty, Susanna Naukkarinen, Pia Heinonen, Elina Kuikka, Liisa Tikkala, Mari Vehviläinen, Kirsi Nissinen, Reijo Hiltunen, Seppo Varpuluoma, Marja-Liisa Eloranta, Marja Vainio, Pekka Staven, Timo Tiilikainen, Anu Hänninen, Pentti Kiilholma, Minna Kauko, Jari Sjöberg, Sari Koivurova, Leena Häivä, Satu Laurila, Marko Niemimaa, Eila Knuuti, Pia Vittaniemi, Päivi Malmström, Johanna Haikonen, Katja Murtoniemi, Päivi Selänne, Anna Sorvaniemi, Helena Hieta-Heikurainen, Benyamin Ashraf, Signe Linkolm, Hannele Torkkeli, Pirkko Juvonen, Kari Österberg, Eija Lampela, Marja Tiihonen, Pauliina Aukee and Riikka Aaltonen.

REFERENCES

1. Wu JM, Matthews CA, Conover MM, Pate V, Funk MJ. Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery. *Obstet Gynecol*. 2014;123:1201-1206.
2. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol*. 1997;89:501-506.
3. Kurkijarvi K, Aaltonen R, Gissler M, Makinen J. Pelvic organ prolapse surgery in Finland from 1987 to 2009: A national register based study. *Eur J Obstet Gynecol Reprod Biol* 2017;214:71-77.
4. Finnish National Institute for Health and Welfare. Somatic special health care in Finland 2014-2015. Available online at: http://www.julkari.fi/bitstream/handle/10024/132354/Tr10_17.pdf?sequence=1. (Accessed April 20, 2017)
5. Cundiff GW, Azziz R, Bristow RE. Te linde's atlas of gynecologic surgery. New York: Lippincott Williams & Wilkins, 2013.
6. Haylen BT, Maher CF, Barber MD, et al. An international urogynecological association (IUGA)/international continence society (ICS) joint report on the terminology for female pelvic organ prolapse (POP). *Int Urogynecol J*. 2016;27:655-684.
7. Maher C, Feiner B, Baessler K, Schmid C. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013:Cd004014.
8. Davila GW, Baessler K, Cosson M, Cardozo L. Selection of patients in whom vaginal graft use may be appropriate. consensus of the 2nd iuga grafts roundtable: optimizing safety and appropriateness of graft use in transvaginal pelvic reconstructive surgery. *Int Urogynecol J*. 2012;23 Suppl 1:S7-S14.

9. Haya N, Baessler K, Christmann-Schmid C, et al. Prolapse and continence surgery in countries of the organization for economic cooperation and development in 2012. *Am Obstet Gynecol*. 2015;212:755.e751-755.e727.
10. Food and Drug Administration (FDA). Urogynecologic surgical mesh: Update on the safety and effectiveness of transvaginal placement for pelvic organ prolapse. Available online at: https://www.fda.gov/downloads/medicaldevices/safety/alertsandnotices/ucm262760.pdf. (Accessed July, 2011)
11. Brummer TH, Jalkanen J, Fraser J, et al. FINHYST 2006--national prospective 1-year survey of 5,279 hysterectomies. *Hum Reprod (Oxford, England)*. 2009;24:2515-2522.
12. Mattsson NK, Nieminen K, Heikkinen AM, et al. Validation of the short forms of the pelvic floor distress inventory (PFDI-20), pelvic floor impact questionnaire (PFIQ-7), and pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12) in Finnish. *Health Qual Life Outcomes*. 2017;15:88.
13. Teleman P, Stenzelius K, Iorizzo L, Jakobsson U. Validation of the Swedish short forms of the pelvic floor impact questionnaire (PFIQ-7), pelvic floor distress inventory (PFDI-20) and pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12). *Acta Obstet Gynecol Scand*. 2011;90:483-487.
14. Barber MD, Walters MD, Bump RC. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). *Am J Obstet Gynecol*. 2005;193:103-113.
15. World Medical Association. World medical association declaration of helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310:2191-2194.
16. Gelhorn HL, Coyne KS, Sikirica V, Gauld J, Murphy M. Psychometric evaluation of health-related quality-of-life measures after pelvic organ prolapse surgery. *Female Pelvic Med Reconstr Surg*. 2012;18:221-226.
17. Chapple CR, Cruz F, Deffieux X, et al. Consensus statement of the european urology association and the european urogynaecological association on the use of implanted materials for treating pelvic organ prolapse and stress urinary incontinence. *Eur Urol*. 2017;72:424-431.
18. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. *Cochrane Database Syst Rev*. 2016;2:CD012079.
19. Tolstrup CK, Husby KR, Lose G, Kopp TI, Viborg PH, Kesmodel US, et al. The Manchester-Fothergill procedure versus vaginal hysterectomy with uterosacral ligament suspension: a matched historical cohort study. *International urogynecology journal*. 2018;29:431-40.
20. Iyer S, Botros SM. Transvaginal mesh: a historical review and update of the current state of affairs in the United States. *Int Urogynecol J*. 2017;28:527-535.
21. Ghoniem G, Hammett J. Female pelvic medicine and reconstructive surgery practice patterns: IUGA member survey. *Int Urogynecol J*. 2015;26:1489-1494.
22. Therapeutic Goods Administration (TGA). Australian government, department of health. Tga actions after review into urogynaecological surgical mesh implants. Available online at:

https://www.tga.gov.au/alert/tga-actions-after-review-urogynaecological-surgical-mesh-implants. (Accessed December 22, 2017)

23. Nieminen K, Hiltunen R, Takala T, et al. Outcomes after anterior vaginal wall repair with mesh: a randomized, controlled trial with a 3 year follow-up. *Am J Obstets Gynecol*. 2010;203:235.e231-e238.
24. Glazener CM, Breeman S, Elders A, et al. Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT). *Lancet (London, England)*. 2017;389:381-392.
25. Morling JR, McAllister DA, Agur W, et al. Adverse events after first, single, mesh and non-mesh surgical procedures for stress urinary incontinence and pelvic organ prolapse in Scotland, 1997-2016: a population-based cohort study. *Lancet (London, England)*. 2017;389:629-640.
26. Altman D, Falconer C, Cnattingius S, Granath F. Pelvic organ prolapse surgery following hysterectomy on benign indications. *Am J Obstet Gynecol*. 2008;198:572.e571-e576.
27. Lykke R, Blaakaer J, Ottesen B, Gimbel H. The indication for hysterectomy as a risk factor for subsequent pelvic organ prolapse repair. *Int Urogynecol J*. 2015;26:1661-1665.
28. Dandolu V, Akiyama M, Allenback G, Pathak P. Mesh complications and failure rates after transvaginal mesh repair compared with abdominal or laparoscopic sacrocolpopexy and to native tissue repair in treating apical prolapse. *Int Urogynecol J*. 2017;28:215-222.

Supporting Information legends:

Appendix S1. Participating hospitals and number of POP surgeries that were included in the study.

Appendix S2. Surgical methods of 2855 operations performed by native tissue reconstruction.

Appendix S3. Name, number and type of vaginal suspension of the used transvaginal mesh kits.

Table and figure legends

Table 1. Patient characteristics

Table 2. Preoperative symptom scores from Pelvic Floor Distress Inventory (PFDI-20) with 20 questions. Higher scores indicate greater symptom distress.

Table 3. Factors affecting the use of mesh, compared to native tissue repair group. Adjusted for the confounding factors including age, sexual activity, previous hysterectomy, previous POP surgery, bulge symptom degree, health distinct area and type of hospital.

Figure 1. Flow diagram of enrollment and analysis of the study participants.

Figure 2. Surgical methods of operations for POP included in the study. *Native tissue repair methods are described in Supporting Information Appendix S2.

Table 1. Patient characteristics

Characteristic	All (N = 3515)	NTR (N = 2850)	TVM (N = 421)	AM (N = 244)	P*	Data available, N (%)
Age at operation (years) (mean ± SD)	64.0 ± 10.7	63.3 ± 11.0	68.5 ± 7.7	63.9 ± 10.0	< 0.001	3512 (100)
Min - max (years)	26.1 - 91.7	26.1 - 91.7	48.1 - 89.3	34.4 - 85.7		
< 50 y, n (%)	361 (10.3)	340 (11.9)	2 (0.5)	169 (6.9)	<0.001	
50 - 64 y, n (%)	1403 (39.9)	1169 (41.0)	131 (31.1)	103 (42.2)	<0.001	
65 - 79 y, (%)	1556 (44.3)	976 (41.4)	257 (61.0)	111 (45.5)	<0.001	
≥ 80 y, n (%)	192 (5.5)	150 (5.3)	31 (7.4)	11 (4.5)	0.076	
BMI (kg/m^2) (mean ± SD)	26.9 ± 4.1	26.9 ± 4.1	27.0 ± 3.8	26.1 ± 3.7	0.022	2825 (80.4)
Min - max (kg/m^2)	16.0 - 59.5	16.0 - 59.5	18.3 - 42.5	16.9 - 36.9		
BMI <25, n (%)	1010 (35.7)	813 (35.7)	112 (32.1)	85 (40.7)	0.121	
BMI 25-29.9, n (%)	1252 (44.3)	994 (43.7)	167 (47.9)	91 (43.5)	0.336	
BMI ≥ 30, n (%)	572 (20.2)	469 (20.1)	70 (20.1)	33 (15.8)	0.251	
Current smokers, n (%)	252 (8.7)	206 (8.7)	28 (7.9)	21 (9.9)	0.626	2913 (82.9)
Parity (mean ± SD)	2.55 ± 1.4	2.60 ± 1.5	2.30 ± 1.1	2.45 ± 1.4	0.122	2924 (83.2)
Min – max	0 - 16	0 - 16	0 - 8	0 - 11		
Vaginal deliveries, median (min – max)	2 (0 - 14)	2 (0 - 14)	2 (0 - 6)	2 (0 - 10)	0.666	
Caesarean sections, median (min – max)	0 (0 - 4)	0 (0 - 4)	0 (0 - 4)	0 (0 - 3)	0.830	
No deliveries, n (%)	13 (0.4)	11 (0.5)	0 (0)	2 (0.9)	0.566	
Medical history						2924 (83.2)
Cardiovascular disease, n (%)	1257 (43.0)	995 (42.3)	181 (50.7)	81 (37.2)	0.004	
Diabetes mellitus, n (%)	286 (9.8)	226 (9.6)	35 (9.8)	25 (11.8)	0.589	
Respiratory disease, n (%)	321 (11.0)	256 (10.9)	46 (12.9)	19 (9.0)	0.327	

Medication						2924 (83.2)
Medication for chronic disease, n (%)	2022 (69.1)	1600 (67.9)	273 (76.5)	149 (70.3)	0.004	
Anticoagulative medication, n (%)	309 (10.6)	246 (10.5)	43 (12.0)	20 (9.4)	0.564	
Hormone replacement therapy, n (%)	535 (18.3)	405 (17.2)	84 (23.5)	46 (21.7)	0.007	
Local estrogen therapy, n (%)	605 (20.7)	480 (20.4)	80 (22.4)	45 (21.2)	0.668	
Sexually active, n (%)	1054 (39.1)	877 (40.2)	93 (28.8)	82 (42.2)	<0.001	2698 (76.7)
Previous surgery						3515 (100)
POP surgery, n (%)	872 (24.8)	412 (14.4)	318 (77.2)	142 (58.2)	<0.001	
Same compartment operated previously, n (%)	604 (17.2)	200 (7.0)	287 (68.2)	117 (48.0)	< 0.001	
Different compartment operated previously, n (%)	268 (7.6)	212 (7.4)	31 (7.4)	25 (10.2)	0.245	
Urinary incontinence surgery, n (%)	199 (5.7)	142 (5.0)	35 (8.3)	22 (9.0)	0.001	
Hysterectomy, n (%)	1170 (33.3)	654 (22.9)	332 (78.9)	184 (75.4)	<0.001	
Prolapse beyond the hymen						
Anterior vaginal wall (POPQ Aa or Ba>0), n (%)	1731 (50.6)	1312 (47.7)	315 (73.8)	104 (42.2)	< 0.001	3420 (97.3)
Posterior vaginal wall (POPQ Ap or Bp >0), n (%)	985 (28.9)	791 (28.9)	83 (19.6)	111 (44.8)	< 0.001	3409 (97.0)
Apex of the vagina (POPQ C>0), n (%)	843 (25.9)	627 (32.2)	80 (18.8)	136 (54.4)	< 0.001	3374 (96.0)
At least one of these > 0, n (%)	2717 (79.0)	2121 (76.7)	376 (88.3)	220 (88.4)	< 0.001	3441 (98.0)
Vaginal compartment of current surgery						3515 (100)
Anterior only, n (%)	655 (18.5)	554 (19.4)	101 (23.5)	0 (0)	< 0.001	

Apical only, n (%)	242 (6.8)	154 (5.4)	12 (2.8)	76 (30.4)	< 0.001
Posterior only, n (%)	728 (20.6)	686 (24.0)	27 (6.3)	15 (6.0)	< 0.001
Anterior and posterior, n (%)	282 (8.0)	268 (9.4)	12 (2.8)	2 (0.8)	< 0.001
Apical and anterior, n (%)	778 (22.0)	574 (20.1)	170 (39.6)	34 (13.6)	< 0.001
Apical and posterior, n (%)	175 (5.0)	97 (3.4)	30 (7.0)	48 (19.2)	< 0.001
All three compartments, n (%)	673 (19.0)	521 (18.3)	77 (17.9)	75 (30.0)	< 0.001

*P-value was calculated for the difference between the surgical method groups (NTR, TVM, AM).

NTR, native tissue repair; TVM, transvaginal mesh; AM, abdominal mesh; BMI, body mass index.
POPQ, Pelvic Organ Prolapse Quantification System; Aa, Anterior point of vaginal wall 3 cm proximal to the external urethral meatus; Ba, most distal point of any part of the anterior vaginal wall from vaginal cuff to point Aa; Ap, a point located in the midline of the posterior vaginal wall 3 cm proximal to the hymen; Bp, a point that represents the most distal part of posterior vaginal wall from vaginal cuff to point Ap.

Table 2. Preoperative symptom scores from Pelvic Floor Distress Inventory (PFDI-20) with 20 questions. Higher scores indicate greater symptom distress.

SYMPTOM Scores	All (N = 2903)	NTR (N = 2335)	TVM (N = 359)	AM (N = 209)	P*
POPDI-6, mean (95%CI)	40.9 (40.1 – 41.6)	40.2 (39.4 – 41.0)	42.7 (40.6 – 44.7)	45.5 (42.5 – 48.5)	< 0.001
CRADI-8, mean (95%CI)	26.4 (25.7 – 27.1)	26.4 (25.6 – 27.2)	24.5 (22.7 – 26.4)	29.8 (26.8 – 32.9)	0.054
UDI-6, mean (95%CI)	32.4 (31.6 – 33.2)	31.8 (31.0 – 32.7)	35.9 (33.8 – 38.0)	33.1 (30.0 – 36.1)	0.003
Total PFDI-20 Scores, mean (95%CI)	99.7 (97.9 – 101.5)	98.4 (96.4 – 100.3)	103.1 (98.3 – 108.0)	108.4 (100.7 – 116.1)	0.012

* Data was derived from questionnaires filled in for analysis of PFDI-20 scores (n=2903).
† P-value was for the difference between the three different surgical modalities (NTR, native tissue repair; TVM, transvaginal mesh; AM, abdominal mesh).
POPDI-6, Pelvic Organ Prolapse Distress Inventory of six questions about the inconvenience of the prolapse; CRADI-8, Colorectal-Anal Distress Inventory with eight questions concerning difficulties of defecation; UDI-6, Urinary Distress Inventory with six questions about difficulties in urination

Table 3. Factors affecting the use of mesh, compared to native tissue repair group.
Adjusted for the confounding factors including age, sexual activity, previous hysterectomy, previous POP surgery, bulge symptom degree, health distinct area and type of hospital.

Characteristic	Transvaginal mesh OR (95%CI) adjusted, p		Abdominal mesh OR (95%CI) adjusted, p	
	All operations	**Primary operations**	**All operations**	**Primary operations**
Age at operation (years)				
< 50 y, n (%)	0.07 (0.02-0.29)	0.11 (0.03-0.46)	1.10 (0.57-2.13)	0.66 (0.28-1.41)
50 - 64 y, n (%)	0.70 (0.49-0.99)	0.68 (0.50-0.93)	1.16 (0.78-1.71)	0.67 (0.29-1.59)
65 - 79 y, (%)	1.00 (reference), <0.001	1.00 (reference), 0.002	1.00 (reference), 0.484	1.00 (reference), 0.708
≥ 80 y, n (%)	0.35 (0.16-0.77)	0.60 (0.30-1.20)	0.54 (0.20-1.41)	0.86 (0.17-4.42)
Sexual activity				
No	1.00 (reference), 0.175	1.00 (reference), 0.519	1.00 (reference), 0.249	1.00 (reference), 0.065
Yes	0.78 (0.54-1.12)	0.90 (0.66-1.23)	1.25 (0.86-1.81)	1.64 (0.97-2.77)
Previous surgery				
No previous POP surgery	1.00 (reference), <0.001		1.00 (reference), <0.001	
Previous POP surgery				
- same compartment	56.31 (37.86-83.74)		22.19 (14.48-34.02)	
- different compartment	2.60 (1.53-4.43)		3.05 (1.76-5.28)	
- both same and different compartment	18.82 (9.60-36.90)		14.75 (7.30-29.79)	
No hysterectomy	1.00 (reference), <0.001	1.00 (reference), <0.001	1.00 (reference), <0.001	1.00 (reference), <0.001
Previous hysterectomy	12.97 (9.47-17.75)	12.93 (9.44-17.70)	14.61 (9.67-20.74)	6.22 (3.71-10.44)
Prolapse beyond the hymen				
Anterior vaginal wall (POPQ Aa or Ba>0)	2.89 (2.09-4.25), <0.001	3.75 (2.72-5.16), <0.001	0.78 (0.54-1.12), 0.173	0.87 (0.52-1.46), 0.600
Posterior vaginal wall (POPQ Ap or Bp >0)	0.56 (0.38-0.84), 0.004	0.42 (0.30-0.59), <0.001	1.97 (1.38-2.82), <0.001	1.74 (1.06-2.87), 0.030
Apex of the vagina (POPQ C>0)	1.03 (0.68-1.56), 0.884	1.58 (1.07-2.31), 0.020	4.19 (2.90-6.05), <0.001	4.32 (2.48-7.53), <0.001
At least one of these > 0	2.52 (1.58-4.01), <0.001	2.37 (1.58-3.56), <0.001	2.52 (1.49-4.26), 0.001	1.60 (0.80-3.20), 0.182
Prolapse symptom (bulge)				
No	1.00 (reference), 0.007	1.00 (reference), 0.017	1.00 (reference), 0.001	1.00 (reference), 0.013

Figure 1. Flow diagram of enrollment and analysis of the study participants.

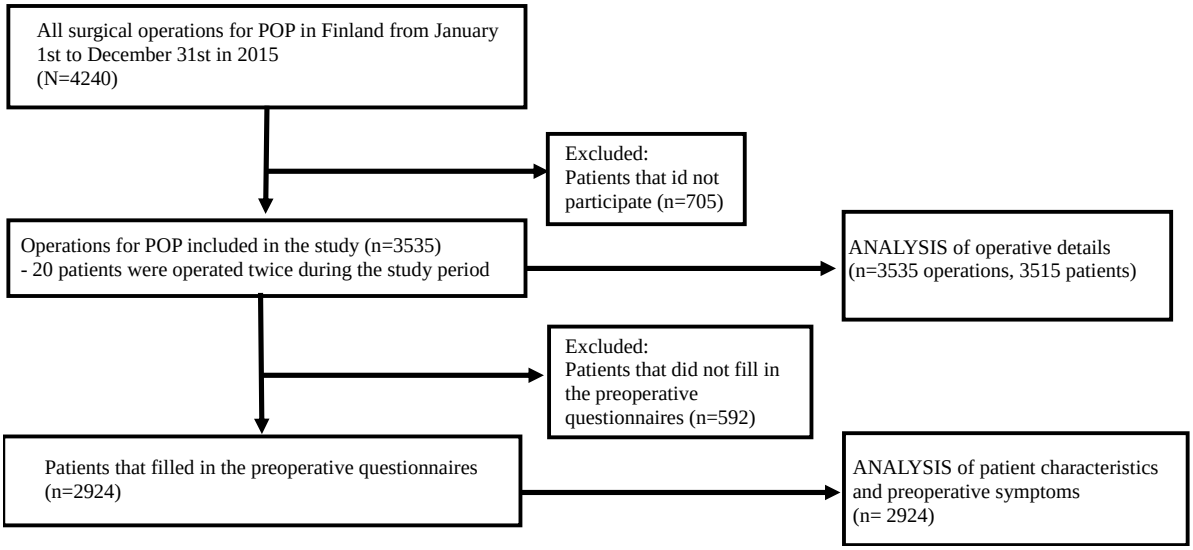

Figure 2. Surgical methods of operations for POP included in the study.
*Native tissue repair methods are described in Appendix 2.