

# Prevention and management of pelvic organ prolapse

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## Abstract

Pelvic organ prolapse is a highly prevalent condition in the female population, which impairs the health-related quality of life of affected individuals. Despite the lack of robust evidence, selective modification of obstetric events or other risk factors could play a central role in the prevention of prolapse. While the value of pelvic floor muscle training as a preventive treatment remains uncertain, it has an essential role in the conservative management of prolapse. Surgical trends are currently changing due to the controversial issues surrounding the use of mesh and the increasing demand for uterine preservation. The evolution of laparoscopic and robotic surgery has increased the use of these techniques in pelvic floor surgery.

## Introduction

Pelvic organ prolapse refers to loss of support to the uterus, bladder and bowel leading to their descent from the normal anatomic position towards or through the vaginal opening. Based on pelvic examination, the prevalence of pelvic organ prolapse varies between 30% and 40% [1,2]. In large epidemiological studies, 6% to 8% of women report a sensation of a mass bulging into the vagina [3,4]. Pelvic organ prolapse may seriously influence the physical, psychological and social well-being of affected individuals [5] and is associated with considerable resource implications for the health service.

Modern health care systems are becoming gradually more community focused, with the emphasis being on prevention rather than cure. While there are well established models in other fields of medicine, the attempts at prevention of pelvic floor dysfunction remain in the very early stages. The demand for conservative management increases in an ageing population, especially with women giving birth in older age. The rapid adoption of minimally invasive techniques (laparoscopic and robotic surgery) and the development of synthetic and biological grafts have dramatically transformed pelvic organ prolapse surgery. We shall briefly discuss the evidence regarding prevention

measures, and conservative and surgical management options for pelvic organ prolapse.

## Prevention

### *Pathophysiology and risk factors*

Despite the high prevalence of pelvic organ prolapse, there is limited knowledge about its pathophysiology. A number of cross-sectional epidemiological studies have reported several risk factors for pelvic organ prolapse (see Table 1). As pelvic organ prolapse usually presents many years after childbirth, recent large longitudinal and national cohort studies with long-term follow-up have improved our current knowledge [6,7,8]. Without identifying the risk factors, efforts at prevention are fruitless, and therapy can only be empirical [9].

Over the last few years, there has been increasing interest in the role of levator ani muscle injuries in the development of pelvic organ prolapse. Studies with magnetic resonance imaging (MRI) [10] and three-dimensional pelvic floor ultrasonography [11] have established the association between levator ani defects and pelvic organ prolapse. Women with levator ani defects are at least twice as likely to show clinically significant pelvic organ prolapse (relative risk [RR] 1.9) and experience recurrence after pelvic surgery (RR 2.3-3.3) [12]. Levator ani trauma could

**Table 1. Risk factors and pelvic organ prolapse**

Demographics	Age Postmenopausal status
Obstetric factors	Parity Vaginal delivery Instrumental vaginal delivery
Pelvic surgery	Hysterectomy Pelvic organ prolapse surgery Colposuspension Rectopexy
Bowel dysfunction	Chronic constipation Defecatory straining
Connective tissue disorders	Ehlers-Danlos/Benign joint hypermobility syndrome Marfan syndrome
Lifestyle factors	Obesity Smoking : Chronic Obstructive Pulmonary Disease High-impact exercise Physically strenuous (manual) occupation
Genetics	Family history White Caucasian, Asian race

represent the missing link between childbirth and pelvic organ prolapse and could be used as a surrogate marker in future longitudinal studies, or as an essential co-variable in the selection of treatment options of women with pelvic organ prolapse.

#### **Interventions to prevent pelvic organ prolapse**

Despite the presence of modifiable risk factors for pelvic organ prolapse, little is known about the efficacy of relevant interventions for its prevention. Vaginal childbirth is probably the most important factor in the aetiology of pelvic organ prolapse. However, the concept of a planned caesarean section for the prevention of pelvic floor dysfunction is controversial, due to the risks associated with caesarean section [13] and the obvious resource implications for health care systems. While caesarean section cannot be considered as preventative for developing pelvic organ prolapse, it could be offered antenatally to selected women with an increased risk of developing prolapse. Based on the recent epidemiological studies, a scoring system (UR-CHOICE) has been proposed to predict the risk of future pelvic floor dysfunction [14]. This scoring system includes several major risk factors, such as urinary incontinence before pregnancy, ethnicity, age at birth of first child, body mass index, family history (mother and sister) of pelvic floor dysfunction, and baby's weight and maternal height (if baby weighs >4 kg and mother's height <160 cm). In the future, more variables, such as a diagnosis of benign joint hypermobility syndrome [15] or specific genotypes [16], could be included in more sophisticated models that could be used for the prediction of pelvic organ prolapse.

Certain surgical techniques have been linked to the development or recurrence of pelvic organ prolapse. While abdominal subtotal hysterectomy does not prevent the development of prolapse compared to total hysterectomy [17], a McCall culdoplasty at the time of a vaginal hysterectomy could prevent it [18]. Appropriate use of a vaginal apical support procedure at the time of prolapse surgery might reduce the long-term risk of recurrence [19].

Pelvic floor muscle training (PFMT) has been proposed as a measure to prevent pelvic organ prolapse. However, a recently published study [20], comparing a nurse-led intervention (pelvic floor muscle training and bladder training) at 5, 7, and 9 months after delivery to standard care, showed that the prevalence of prolapse symptoms or objectively measured pelvic organ prolapse did not differ between the groups at the 12-year follow-up [20]. A more intense programme of PFMT (individualised physiotherapy appointments, maintenance via Pilates-based classes and annual one-to-one check-ups) is currently being evaluated for pelvic organ prolapse prevention by a trial with a two-year follow-up (NCT01171846).

As pelvic organ prolapse has been associated with urogenital atrophy, it is possible that oestrogens, alone or in conjunction with other measures, may prevent its development by improving the strength of weakened supporting ligaments, muscles and vaginal mucosa [21]. However, there are no studies in the literature to assess this hypothesis. If we generalise findings from studies regarding lower urinary tract symptoms and hormone replacement therapy, local oestrogen treatments appear more promising compared to systemic administration [22]. There is a need for rigorous randomised controlled trials, with long-term follow-up, to assess oestrogen preparations for the prevention of pelvic organ prolapse.

Modification of other risk factors could also reduce the risk of pelvic organ prolapse. Reduction of straining and intra-abdominal pressure could help prevent the development of prolapse. The widely accepted practice of treatment of bowel dysfunction/chronic constipation has not been tested as systematic intervention to prevent pelvic organ prolapse. Weight loss with diet or bariatric surgery has also been suggested as a preventive measure. The few published cohort studies with short-term follow-up have shown that weight reduction is associated with subjective improvement in prolapse symptoms [23] but no objective change was seen in examination using the pelvic organ prolapse quantification (POP-Q) system [24].

## Non-surgical treatment

Conservative interventions include physical interventions to improve the function and support of the pelvic floor muscles (via pelvic floor muscle training) and mechanical interventions (insertion of vaginal pessaries) to support the prolapse. They are often offered for lower grades of prolapse and to women unwilling or unfit to undergo surgery.

### Pessaries

From ancient times, a wide variety of items have been used to manage urogenital prolapse. Currently, a range of vaginal pessaries are available which can be broadly divided into two types: support and space-occupying. A recent Cochrane review has highlighted the lack of robust evidence regarding the effectiveness of vaginal pessaries [25]. Despite this, 77% of the members of the American Urogynecologic Society use pessaries as first-line therapy [26]. As there is no evidence to support the use of a specific type, choice is based on experience and trial and error. When the insertion of the pessary is successful, there is significant improvement in prolapse symptoms, and in bladder, bowel and sexual function [27]. Combining pessary management with PFMT was evaluated in a feasibility study (PEPPY), but conclusions could not be drawn due to the small sample size [28].

### Pelvic floor muscle training

A robust evidence base has recently emerged regarding the role of PFMT in the treatment of pelvic organ prolapse. A number of single-centre [29,30] and multi-centre (POPPY) [31] randomised controlled trials (RCTs) have assessed the value of several individualised PFMT programs, compared to lifestyle advice, for women with a symptomatic stage I-III prolapse. Based on their findings, one-to-one PFMT for 16 weeks to 6 months is effective for the improvement of prolapse symptoms. A greater proportion of women had an improvement in their prolapse stage (POP-Q) in the PFMT group (19–27%) compared to the control group (8–20%), with the difference being statistically significant in the study by Braekken *et al.* ( $P = 0.035$ ) [29] and not significant in the POPPY trial ( $P = 0.10$ ) [31].

The combination of PFMT with surgery or insertion of vaginal pessary has recently gained the attention of some researchers. A pilot study has shown the benefit of perioperative PFMT in the post-surgery reduction of symptoms and pelvic organ prolapse recurrence [32]. However, perioperative behavioural therapy with pelvic floor muscle training did not improve prolapse

symptoms or anatomical success in a large multi-centre RCT (OPTIMAL) comparing transvaginal surgical procedures used to correct apical prolapse [33].

## Surgical treatment

Despite the availability of conservative options, the lifetime risk for women undergoing pelvic organ prolapse surgery is 10 to 20% [34,35]. A recent systematic review and meta-analysis of RCTs showed that surgical interventions can improve the quality of life of women with pelvic organ prolapse [36]. Over the last few years, prolapse surgery has been changing constantly, with emerging trends gradually gaining or losing their popularity.

### Native tissue repairs versus vaginal mesh for anterior and posterior vaginal wall prolapse

Historically, surgeons have relied on patients' native tissue for surgical correction of pelvic organ prolapse. Due to the reported high rates of recurrence [37] and the known weakness of the tissue associated with prolapse, a number of synthetic and biological grafts have been introduced to improve surgical outcomes. The success of the synthetic midurethral slings [38], and data showing dramatic improvement of the outcomes with the use of mesh for repair of femoral and inguinal hernias [39], supported the introduction of grafts in vaginal surgery. There was a sudden increase in vaginal mesh use with cases performed in the US almost doubling between 2005 and 2007. These then plateaued between 2008 and 2010 [40]. However, in view of the reported high risk of complications (e.g. erosion, pain) the US Food and Drug Administration issued two warnings, in 2008 and 2011 [41]. Following these, a dramatic decrease of mesh-augmented vaginal repairs has been reported [42] and many commercial transvaginal mesh kits have been withdrawn from the market. National and international professional bodies have published consensus documents on informed consent process and patient selection [43,44,45].

Standard anterior native tissue repair is associated with lower objective (47 versus 82%,  $P < 0.001$ ) and subjective (62 versus 75%,  $P = 0.008$ ) success compared to transobturator polypropylene (permanent) mesh repair [46]. However, these outcomes do not translate into improved functional outcomes when validated questionnaires have been used. Mesh repairs are also linked with higher rates of surgical complications and post-operative adverse events (e.g. vaginal exposure rate over 10%). A decision-analytic Markov model, examining the cost-utility of anterior repair augmented with synthetic mesh, compared with non-mesh repair, suggests that the

use of mesh is not cost-effective [47]. Despite its theoretical potential in reducing complications, a recent RCT showed that collagen-coated polypropylene mesh causes vaginal exposure in 13% of women with anterior vaginal wall prolapse [48].

Absorbable meshes appear to be attractive options of surgical augmentation, offering strength during the early healing phase without the long-term problems of permanent mesh. Polyglactin mesh underlay improves the anatomical outcome, compared to native tissue repair of anterior pelvic organ prolapse [49]. A number of biological grafts have been evaluated in RCTs. Anterior repair with porcine dermis graft is superior to native tissue repair [50], but inferior to polypropylene mesh augmentation [51] regarding anatomic outcomes. The evidence on the use of porcine small intestine submucosa mesh is conflicting [52,53].

Regarding the posterior compartment, vaginal wall repair may be better than transanal repair in the management of rectocele in terms of recurrence of prolapse. The evidence from a recent Cochrane review does not support mesh overlay or augmentation of a native tissue repair for posterior vaginal wall prolapse [54].

#### **Uterine preservation**

Traditionally, repair of uterovaginal prolapse includes concomitant hysterectomy. However, women increasingly desire uterine preservation and uterine-sparing procedures for apical prolapse are gaining in popularity. A study in the US describing patient preferences showed that, assuming outcomes were equal with hysterectomy and uterine preservation, 36% of the women preferred uterine preservation, 20% preferred hysterectomy, and 44% had no strong preference [55]. If hysterectomy was superior, 21% still preferred uterine preservation, despite inferior efficacy. Education level and the belief that the uterus is important for a sense of self were predictors of preference for uterine preservation, while the doctor's opinion, risk of surgical complications, and risk of malignancy were the most important factors in surgical decision-making [56].

A number of uterine-preserving procedures have been described for apical prolapse, but there are a limited number of prospective RCTs comparing these techniques to vaginal hysterectomy. The benefit of the avoidance of hysterectomy-specific complications should be balanced against the risk of future uterine abnormalities and uncertainty about future pregnancies. Surgeons must provide adequate counselling and preoperative evaluation before proceeding with uterine preservation [57]. Dietz *et al.* reported similar functional outcomes and

quality of life, but a higher rate of apical recurrences (21 *versus* 3%) after sacrospinous hysteropexy compared to vaginal hysterectomy [58]. The findings of this study were challenged by a more recent large RCT, which showed no difference in recurrence of apical prolapse after sacrospinous hysteropexy or vaginal hysterectomy [59]. Another uterine-sparing alternative is the laparoscopic sacrohysteropexy. A study comparing laparoscopic sacrohysteropexy (with the use of polypropylene mesh) to vaginal hysterectomy showed similar subjective and functional outcomes for the two groups with better apical anatomical outcomes after laparoscopic sacrohysteropexy [60].

#### **Post-hysterectomy vaginal vault prolapse**

Apical support procedures can be divided into those performed transvaginally and those performed abdominally. The most common vaginal procedures are the sacrospinous ligament fixation (SSLF) and the uterosacral ligament suspension (USLS). A recent RCT by Barber *et al.* comparing these procedures, showed that two years after surgery neither USLS nor SSLF was significantly superior for anatomic, functional, or adverse event outcomes [33]. However, the use of total vaginal polypropylene mesh kits for apical prolapse should be restricted, due to the high reported exposure rates (16–21%) and similar functional outcomes when compared to USLS [61] and SSLF [62].

Compared to SSLF and USLS, abdominal sacrocolpopexy with a polypropylene mesh has a higher success rate, with less post-operative dyspareunia but with longer operating and recovery times [54]. In an attempt to reduce mesh complications, some surgeons have considered the use of biological grafts. However, fascia lata had inferior anatomic outcomes, compared to polypropylene mesh [63].

Technological development has facilitated the adoption of minimally-invasive techniques (laparoscopic and robotic) for sacrocolpopexy. A US population-based study showed a dramatic increase (6 times) in the number of minimally-invasive sacrocolpopexies from 2005 to 2010, while the number of abdominal sacrocolpopexies remained stable [40]. An RCT comparing abdominal sacrocolpopexy to laparoscopic sacrocolpopexy revealed similar anatomic and subjective outcomes, but a shorter hospital stay and reduced blood loss in the laparoscopic group [64]. Comparison of porcine dermis and polypropylene mesh for laparoscopic sacrocolpopexy has shown no difference in subjective and objective results [65]. Robotic sacrocolpopexy is also a safe and effective option in the treatment of apical prolapse [66]. It is associated with similar anatomic and functional outcomes, but with a longer

operating time, and increased pain and cost, compared with the conventional laparoscopic approach [67,68].

### Concomitant stress continence surgery

Further controversy surrounds the role of prophylactic concomitant stress incontinence surgery for patients with symptomatic prolapse, not complaining of stress urinary incontinence (SUI). A number of well-designed RCTs have shown that concomitant continence surgery reduces the risk of postoperative *de novo* SUI in women previously without SUI who are undergoing pelvic organ prolapse surgery, through the abdominal [69] or vaginal route [70]. However, combination surgery is associated with an increased rate of adverse events (such as major bleeding complications, bladder perforation, prolonged catheterisation, urinary tract infections) [71]. As the benefits of combined surgery should outweigh its risks, careful patient selection is of paramount importance. The meta-analysis by van der Ploeg *et al.* showed that, while the number needed to treat to prevent one woman developing *de novo* SUI is nine in all continent women, it is only three in continent women with occult SUI [71]. Therefore, pre-operative evaluation of occult SUI with reduction of prolapse, or the use of a clinical prediction model [72], could be used as a decision-making tool to determine the need for a concomitant continence operation.

### Future directions

Identifying women with an increased risk of developing pelvic organ prolapse could become easier with the implementation of clinical prediction models or the introduction of relevant genetic tests. The identification of a high-risk population could allow a focused modification of risk factors, such as obstetric events, by recommending delivery by caesarean section. A similar screening process, including recognition of levator ani defects [73], could be followed pre-operatively to assess the risk of pelvic organ prolapse recurrence and mesh complications. This information could help tailor surgery to individual needs. It might also help patients accurately assess the risks and benefits of different surgical procedures and facilitate optimal pre-operative counselling directed towards appropriate patients' expectations [74].

Attempts to develop the ideal graft will continue, due to the high recurrence rate of pelvic organ prolapse after native tissue repairs. Modifications of current mesh materials could alter the host response and reduce potential complications [75]. Cell-based tissue engineering strategies could potentially provide attractive alternatives to native tissue repairs or the use of synthetic or biological grafts. Human oral fibroblasts and human adipose-derived stem cells appear to be suitable cell

types, to combine with biodegradable scaffolds, in the development of a tissue engineered repair material [76]. Porcine small intestinal submucosa and thermoannealed poly(L) lactic acid are good candidate scaffolds for development for an *in vivo* tissue-engineering approach [77]. However, the vagina is a complex organ with great demands of functionality, and the perfect match of scaffold, cell, and trophic factor has yet to be found in preclinical studies [78]. It is of paramount importance to establish a robust approval process for new products before they are introduced to the market. The minimum requirements should be: accurate product description; data on the biological properties from animal studies; anatomical cadaveric studies; and prospective clinical studies, followed by a compulsory registry on the first 1,000 patients implanted [79]. With a strict regulatory framework, scientific progress could be secured without compromising patient safety.

### Abbreviations

PFMT, pelvic floor muscle training; POP-Q, pelvic organ prolapse quantification; RCT, randomised controlled trial; RR, relative risk; SSLF, sacrospinous ligament fixation; SUI, stress urinary incontinence; USLS, uter-osacral ligament suspension.

### Disclosures

Ilias Giarenis has received travel expenses from Astellas, Ethicon and Pfizer. Dudley Robinson has consulted for Allergan, Astellas, Ferring and Pfizer and received speaker honoraria from Allergan, Astellas and Pfizer. He has also had involvement in trial participation for Allergan, Astellas and Pfizer.

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