Review

Should uterus be removed at pelvic organ prolapse surgery: A reappraisal of the current propensity

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Abstract: Pelvic organs are anatomically supported by ligamentous-fascial attachments of endopelvic fascia and muscular support provided by levator ani muscle complex. Dysfunction or disruption of these components, alterations in tissue tensile forces, which are associated with collagen content and turnover within the tissue, as well as lack of hormonal support emerging as the menopausal transition advances, contribute to the pelvic organ prolapse. Hysterectomy has been the treatment of choice for years, despite the recent trend shifting toward uterus preserving measures. In this article, we intended to review the pros and cons of both hysterectomy and uterus preserving approaches through a critical perspective.

Keywords: Pelvic organ prolapse; Hysterectomy; Uterus preservation.

INTRODUCTION

Pelvic organ prolapse is downward descent of pelvic organs including vagina, uterus, bladder, bowels or post-hysterectomy vault, resulting in the protrusion of these structures or some combinations. Although the prevalence of pelvic organ prolapse is as much as 40% in women aged above 45[1], only 10-20% of those seek evaluation for their condition[2]. The incidence is still rising as a result of aging population and increasing obesity rates[1]. Pelvic organ prolapse typically does not engender morbidity or mortality but can disrupt a woman's quality of life, and is associated with physical, psychological and sexual problems.

Epidemiological studies of the frequency of the condition are rare. The overall prevalence of POP varies significantly depending upon the definition utilized, ranging from 3% to 50%[3]. The reported prevalence is 3-6% if POP is defined and graded on symptoms, whereas it remains at around 50% when the definition is based on examination. The difference in the prevalence rates arises from the fact that mild prolapse is a common finding on examination and frequently asymptomatic[4-6]. The lifetime incidence of surgical intervention for POP is estimated to be 10-20%, with 13% of patients undergoing repeat surgery for POP within 5 years[7,8].

The incidence and prevalence for prolapse surgery increase with age. The peak incidence of such surgery is in women aged 60-69 years (42.1 per 10 000 women). However, almost 58% of procedures are undertaken in people younger than 60 years[9]. The most commonly performed surgical procedure for uterine prolapse is hysterectomy[10-12] and 15% to 18% of all hysterectomies are performed for POP, making POP the third most common reason for hysterectomy overall and the leading indication in postmenopausal population[13,14]. Current studies report more than 430,000 inpatient hysterectomies performed in the United States annually with uterovaginal prolapse cited as the indication for approximately 74,000 cases[15]. However, whether or not the uterus should be removed is debatable since the argument that the uterine descent is result rather than the cause of the problem is still largely accepted. More recently, a trend of preserving uterus remarked by both patients and physicians has arisen for a variety of reasons. This article will critically review the reasons, risks and benefits for hysterectomy and the evidence for its efficacy in modern practice.

ANATOMICAL CONSIDERATIONS

Pelvic organs are anatomically supported by a variety of structures, including ligamentous-fascial attachments of endopelvic fascia and muscular support provided by levator ani muscle complex. Dysfunction or disruption of these components can lead to loss of support and, eventually, pelvic organ prolapse[14]. Levator ani muscle is the essential component of active support with three major components identified: pubococcygeal, iliococcygeal and puborectal[16]. Puborectal bundle, the thick and medial sphincteric region spreading from the pubis to external anal sphincter, plays an essential role in pelvic organ support and urogenital hiatus closure[17]. Levator ani muscle, as well as internal obturator muscle, is covered by a layer of connective tissue, named endopelvic fascia, which is a loose connective tissue network consisting of a variable layer of collagen-elastin, smooth-muscle cells, and neurovascular pedicles[18]. Endopelvic fascia thickens into a true pubourethral ligament in the middle third of the urethra at the pubic symphysis. At the lateral sides of pelvic floor, two collagenous connective condensations are identified as the tendinous and ligamentous condensations of endopelvic fascia, the arcus tendineus levator ani and arcus tendineus fasciae pelvis[19]. Arcus tendineus fasciae pelvis suspends vagina and bladder from their lateral aspects, bonding them to the pelvic wall. Uni- or bilateral detachment from the tendinous arc induces pelvic imbalance that may lead to lateral cystocele.

The uterosacral and cardinal ligaments hold the uterus and upper third of the vagina in the pelvic space above the levator plate[19]. Uterosacral ligaments originate from the presacral fascia at the level of S2-S3-S4 without direct bone insertion and are attached to the postero-lateral aspect of the cervix at the level of the internal os and to the lateral vaginal fornices. The posterior third fans out to attach to the presacral fascia opposite the sacroiliac joint. Given the major supportive effects of uterosacral ligament, there is a substantial concern that the removal of uterus disrupts the uterosacral ligament, which may further weaken the support. However, uterosacral ligament attaches into the distal cervix and proximal vagina and thus the supportive effects of the ligament would continue following hysterectomy. Moreover, support of the vaginal vault after hysterectomy relies on the uterosacral ligaments[20].

On the other hand, cardinal ligaments, areolated connective tissue with neuro-vasculature, inserts to the antero-su-

perior cervical neck and pubocervical fascia. A morphological study of the pelvic floor revealed that only the round and uterosacral ligament exist[21]. Other so called ligaments contain adipose tissue, vessels and nerves and together may be confounded as a ligamentous structure when in fact they have no function as ligament, i.e. the cardinal 'ligament'. Even though these septa may be attached to the fascia of levator ani they argue that they are not supportive.

Given the complexity of the regional anatomy and uncertainity of the roles and the mechanical properties of the pelvic floor structures, a set of theories[22-26] sought the pathophysiological mechanisms underlying pelvic organ prolapse. Petros's integral theory explains pelvic organ prolapse by laxity of connective tissue and ligamentous-fascial structures and describes a sagittal ligamentous-fascial support, 'hammock', which extends from the posterior aspect of the pubis to the sacral concavity. This sagittal hammock comprises, from front to back, the urethra, bladder, uterus, and upper rectum between the two uterosacral ligaments[23,25]. Conversely, according to DeLancey, the keystone to the urogenital prolapse pathophysiology was 'paravaginal support' and he described a pelvic support 'hammock' on a transverse plane[24]. This musculofascial hammock is constituted by vaginal wall and endopelvic fascia connected to the arcus tendineus fasciae pelvis and the urethra lies on this hammock and is compressed under abdominopelvic pressure[19].

CONCOMITANT DISEASES

The lifetime risk of a woman's undergoing hysterectomy in the USA has been reported as 45%[27]. As the hysterectomy procedure has been questioned in its role as part of POP surgery more frequently, there has been a renewed interest in uterine conservation among patients. Moreover, recent published data indicated uterine-sparing procedures to be an acceptable option for most patients with uterovaginal prolapse[28]. However, careful patient selection is a crucial step prior to considering uterine conservation in women with pelvic organ prolapse. There exist several reported contraindications for uterine preservation, including fibroids, adenomyosis, abnormal endometrial sampling, abnormal uterine bleeding, endometrial abnormalities, current or recent cervical dysplasia, postmenopausal bleeding, familial cancer syndrome BRCA 1 and 2 due to the increased risk of ovarian cancer and theoretical risk of fallopian tube and serous endometrial cancer, hereditary non-polyposis colonic cancer, which imposes 40-50 % lifetime risk of endometrial cancer, tamoxifen therapy, inability to comply with routine gynecological surveillance[28,29]. Given the high frequency of fibroids, adenomyosis, abnormal uterine bleeding in the similar age group that uterovaginal prolapse also occur, it would be reasonable to think that the women undergoing uterus-preserving surgery would continue to carry the potential risks of having these pathological conditions and the associated sequel. Hence, cons and pros of preserving uterus should be analyzed in detail prior to the surgical correction.

Vaginal bleeding in perimenopausal women may rarely be due to malignancy and distinguishing hormonal-based irregular bleeding from that of cancer is challenging without a thorough evaluation of all women with these complaints in order to avoid overlooking malignant conditions. Four to eleven percent of postmenopausal women experience vaginal bleeding, which constitute 5% of all doctor visits[30,31]. The main reason for focusing on postmenopausal bleeding is the high proportion of malignancy, mainly of the cervix and corpus uteri, which ranges from 8 to 17.5%[32,33]. On the other hand, endometrial carcinoma accounts for approximately 10% of causes of postmenopausal bleeding[31]. Although dilatation & curettage (D&C) and hysteroscopy have been the gold standard for the endometrial diseases and in evaluating women with postmenopausal bleeding, both have significant false negative rates (10% and 3%, respectively)[31]. Moreover, the controversies in the efficacy of biopsies, evaluation and the frequency of follow-up visits and the financial and psychological burden, render postmenopausal bleeding still a challenging task for clinicians. Recent studies revealed the need for hysterectomy in women with postmenopausal bleeding, even with a negative work-up, because of the high risk of unanticipated endometrial cancer or hyperplasia[34].

On the other hand, women at perimenopausal years may not desire the continuation of menses, which possibly occur irregularly or excessively due to the anovulatory cycles, even in the lack of any of the above-mentioned conditions. Uterine preserving procedures would give the chance of maintaining fertility and burden the risk of undesired pregnancies.

EVIDENCE OF HARM

For decades, the effects of hysterectomy on pelvic organ function have been controversial. Several studies reported that hysterectomy, irrespective of route or mode of surgery, increased the risk for subsequent uterovaginal prolapse[14,35,36] or stress urinary incontinence surgery[37-39]. The most commonly adopted rationale for this association was the trauma of surgery itself when the uterus is severed from pelvic-floor supportive tissues during hysterectomy[40]. On the other hand, hysterectomy was reported to interfere with the urethral sphincter mechanism by distorting local nerve supply to the urethra from pudendal nerves and inferior hypogastric plexus[41,42]. Moreover, the procedure might cause changes in urethral pressure dynamics by damage to pelvic-organ anatomy, including urethral and bladder neck support[24,43].

The uterosacral and cardinal ligaments maintain the temporospatial anatomy of uterus within the pelvic space[19]. Uterosacral ligaments originate from the presacral fascia at the level of S2-S3-S4 without direct bone insertion and are attached to the postero-lateral aspect of the cervix at the level of the internal os and to the lateral vaginal fornices, thus proximal support of the vaginal vault after hysterectomy is maintained by uterosacral ligaments[20]. Considering that the cervix plays a crucial role in preventing uterovaginal prolapse, it could be reasonable to compare long-term postoperative incontinence and prolapse outcomes between women undergoing total and subtotal hysterectomies, and the results of supracervical hysterectomies could be extrapolated to uterine-sparing surgery. In 2007, Gimbel H[44] published a meta-analysis of 34 randomized controlled trials comparing the effects of subtotal and total abdominal hysterectomies and reported that less women suffered from urinary incontinence and prolapse and cervical stump problems after total than after subtotal hysterectomy. Similarly, Andersen et al.[45] reported that a smaller proportion of women suffered urinary incontinence after total abdominal hysterectomy than after subtotal abdominal hysterectomy 5 years postoperatively. However, subtotal hysterectomy was faster to perform, had less peroperative bleeding, and seemed to have less intra- and postoperative complications. The difference regarding pelvic organ prolapse between total and subtotal hysterectomies was associated to performing a suspension of the vaginal top at total hysterectomy, which might serve as a

minor bladder neck suspension procedure, thus decreasing/removing the problem of incontinence by decreasing the bladder neck mobility[44]. Persson et al[46] reported no difference in pelvic organ prolapse measurements and pelvic floor dysfunction symptoms between patients who underwent total or subtotal hysterectomies in a long-term follow-up study. A recent randomized clinical trial with 14-year questionnaire follow-up revealed that subtotal abdominal hysterectomy was not superior to total abdominal hysterectomy on any outcomes and more women had subjective urinary incontinence 14 years after subtotal than after total abdominal hysterectomy[47].

Another concern that the physicians hesitate to perform a hysterectomy was the sexual life and functioning after hysterectomy due to the belief that hysterectomy may have detrimental effects on orgasm by eliminating the uterine contribution and by possible neuronal damage in the surgery. However, Gimbel[44] reported that sexual functioning did not differ between women undergoing subtotal and total abdominal hysterectomy. On the other hand, recent studies report favorable outcomes with regard to sexual and urinary outcomes following nerve-sparing radical hysterectomies[48-52]. These studies conferred better clinical outcomes with fewer long-term bladder, colorectal and sexual complications. Moreover, post-operative quality of life after nerve-sparing procedures was better as compared to traditional radical hysterectomies.

TOTAL/SUBTOTAL COST

According to the 2014 report of Centers for Disease Control and Prevention (CDC) risk of developing cervix, corpus uteri and ovary malignancy is 0.66%, 2.69% and 1.37%, respectively and risks of dying from these cancers are 0.23%, 0.55% and 0.99%, respectively[53]. Number needed to prevent (NNP) could be assessed in order to help clinicians assess the overall impact of hysterectomy on mortality rates due to associated disease over a one-year period. Given the total percentage of the development of cervix and corpus uteri malignancies would be 3.35%, the number of women needed to be hysterectomized to prevent one woman at any age from developing cervix-corpus uteri carcinoma during the one-year follow-up was calculated as 30. Moreover, based on these rates, 25 hysterectomy plus oophorectomy would prevent the development of 1 cervix-corpus-ovary cancer.

Since cancer is a heterogenous disease, there exist several variables that affect the total cost of the management of a cancer patient, including the stage of the disease, therapeutic options employed and the years of survival. The direct medical care costs associated with cervical cancer were estimated to equal $1.7 billion in 1996 dollars[54]. Chemotherapy typically costs $10,000-$200,000, depending on the chemotherapeutic agents used, how they are administered and the number of treatments required. Twelve-month cost of treating cervical cancer among Medicaid beneficiaries in the USA has been reported to be $46,681 and $83,494 for stage II-IVA and stage IVB cancers, respectively[55]. Another study reported that a common combination of Cisplatin, which is thought to be the most active single agent in periodic diseases, with radiotherapy, typically costs about $41,000 total, while adding Gemcitabine increased the total cost to more than $61,000[56]. Since the 5-year survival rate for patients diagnosed with localized cervical cancer is 92%, patients will need regular follow-up through Pap test, performed every 3 months for the first 2 years, every 6 months for the next 3 years and yearly thereafter, and PET/CT in early local recurrence and metastasis detection, which would increase the total cost.

On the other hand, mean total hospital cost for vaginal hysterectomy was $7903 whereas was $10,069 for LAVH, $11,558 for TLH[57]. The total cost of performing vaginal hysterectomy in order to prevent one corpus-cervix carcinoma would be $237,090 whereas $197,575 to prevent one corpus-cervix-ovary carcinoma.

Moreover, in women undergoing uterine-preserving surgery the necessity of continuation of cervical and ovarian cancer screening, risk for menstrual disorders and associated therapies, and the side-effects of these therapies should be taken into account when considering cost-effectivity of pelvic organ prolapse surgeries.

PROPHYLACTIC HYSTERECTOMY AND OOPHORECTOMY

Tissue collagen content has a key role in the setting of uterovaginal prolapse. Collagen also appears to play a role in maintenance of normal urinary continence by imparting structural stability to the proximal urethra through the paraurethral connective tissue connections to the pelvic floor[58]. In women with pelvic organ prolapse, total collagen content is decreased in the vaginal wall compared with premenopausal controls[59] while the proportion of immature collagen is increased[60]. Also, it has been suggested that collagen metabolism shifts to a degradative state after menopause and in the setting of vaginal prolapse, with increased activity of endogenous matrix proteases[59,61]. These studies suggest the crucial role of estrogen in the maintenance of extracellular matrix and connective tissues for pelvic organ support. Estrogen supplementation increases collagen content of the skin, vasculature, and pelvic tissues in postmenopausal women[62,63]. Animal studies demonstrated increases in collagen mRNA expression after systemic estradiol treatment[64]. Recent studies reported that estrogen treatment increased total and cross-linked collagen content and markedly stimulated collagen mRNA expression and relief of epithelial atrophy in menopausal animal models[65]. These results may have important clinical implications in menopausal women with uterovaginal atrophy, urogenital ageing and associated prolapse symptoms.

As well as urogenital senescence, most menopausal women experience a variety of problems, including bone fractures due to decreased bone mineral density, increased risk for cardiovascular diseases, regression in cognitive functions and depression and vasomotor symptoms often lasting longer than one decade. Since the majority of these problems are considered to derive from estrogen deprivation, hormone therapy (HT) might be recommended to postmenopausal women to overcome these clinical issues[66]. HT, which initially comprised of estrogen monotherapy, is known to improve quality of life, vasomotor symptoms, vulvovaginal symptoms and sexual function whereas decrease the risks of vertebral and hip fractures by increasing bone mineral density, colon cancer, ischemic heart disease and cardiometabolic risk by improving insulin sensitivity[67-69]. However, unopposed systemic estrogen therapy (ET) in postmenopausal women with an intact uterus is associated with increased endometrial cancer risk related to the estrogen dose and duration of use. In order to negate this increased risk, adequate concomitant progestogen is recommended for women with an intact uterus when using systemic ET, however, the addition of a progestogen to the HT regimen has been associated with an increased risk of breast cancer[70]. Several randomized controlled studies revealed an increased risk of breast cancer in women receiving estrogen-progestogen combination than in women using estrogen monotherapy[71-73]. WHI trial indicated that the risk of breast cancer was affected by addition

of a progestin and that women receiving conjugated equine estrogens (CEE) only for a mean of 7.1 years had a 0.77 relative risk of invasive breast cancer as compared to the placebo group[73]. A recent analysis of estrogen only arm of the WHI reported that after 11.8 years of observation, women who had used estrogen treatment for a median of 5.9 years had a lower incidence of breast cancer (RR 0.77, CI 0.62-0.95) compared to placebo[74]. On the other hand, women receiving estrogen – progestin therapy for a median of 5.6 years had a 1.28 (CI 1.11-1.48) relative risk of breast cancer compared to placebo[75]. Similarly, in the EPIC study, women receiving estrogen only therapy had 1.42 relative risk of breast cancer as compared to 1,77 of women on estrogen – progesterone therapy[71]. Now that the addition of a progestogen to estrogen in postmenopausal hormone therapy increases the risk of breast cancer, it is now recommended that hysterectomized women seeking relief of menopausal symptoms with estrogen monotherapy be reassured concerning the long term effects of ET on breast cancer incidence[66]. Moreover, estrogen as a single systemic agent is indicated as appropriate in women after hysterectomy but additional progestogen is required in the presence of a uterus[76]. In the light of the data from these studies, it appears to be plausible to remove the uterus as part of pelvic organ prolapsus surgery to avoid the necessity of addition of a progestogen and, hereby, to prevent the increase in the risk of breast cancer. The limitations of an estrogen monotherapy arising from the increased risk of endometrial cancer could be eliminated and postmenopausal women would not deprive of the multiple beneficial effects of estrogen. More importantly, urogenital tissues could be supported by promoting collagen synthesis, which result in decrease in urogenital ageing, vaginal dryness, dysuria, urethral discomfort, stress urinary incontinance and dyspareneu.

PATIENT PERCEPTION

Pelvic organ prolapse negatively affect a woman's perception of body image, physical and sexual attractiveness, and femininity[77,78], which significantly improve after the surgical correction of prolapse[79]. However, the role of uterus as well as hysterectomy, as part of the surgical treatment of pelvic organ prolapse, in a woman's sexual function and perceived femininity is an issue of debate.

A common concern among women who are candidate for hysterectomy is the possible impacts of the surgery on their sexual function. Hysterectomy is considered to improve the quality of life in the way that alleviation of pain, decrease of anxiety due to elimination of unwanted pregnancies and risk of cancer, positive psychological factors and disease relief[80]. Older studies reported decreased sexual function after hysterectomy-oophorectomy, based on physiological rather that psychological factors[81]. The rationale to assume that removal of the uterus might have detrimental impacts on female sexual functioning was the impairment of the anatomical relations and neuronal innervation in the pelvis and eliminating the uterine contribution to orgasm. However, symptom relief of the primary disease may lead to increased sexual enjoyment and increased orgasm frequency and may outweigh any loss of sensation due to removal of the cervix[82]. Nevertheless, the pathology for which the hysterectomy was performed may differentially affect sexual response[83].

On the other hand, solid evidence is lacking for sexual dysfunction caused by the disruption of local nerve and blood supply, or by changing anatomical relationships[84]. Increased understanding of patients' attitudes and expectations appears to change the perception of body image, sexuality and femininity. Removal of the ovaries at hysterectomy was reported to associate with no change or even an improvement in sexual function, particularly in women on hormone replacement therapy, regardless of surgical method or removal of the cervix. This was attributed to the amelioration of the symptoms that have previously had a negative effect on sexual function[84]. A study by Good et al.[85], investigating the attitudes toward the uterus in women with pelvic organ prolapse, revealed that majority of women did not believe the uterus was important for body image or sexuality and did not believe that hysterectomy would negatively affect their sex lives. In this study, 47.4% of women strongly disagreed that uterus was important for sex while 63.9% and 66.7% strongly disagreed the comments 'hysterectomy will make me less feminine' and 'hysterectomy will make me less whole', respectively. Jeng et al.[86] examined the changes after vaginal hysterectomy or sacrospinous hysteropexy for uterine prolapse correction and reported a decrease in the frequency of orgasm in the both groups. However, they found no significant differences between groups in terms of orgasm frequency, sexual function and sexual interest. Sexual functioning scores also were not different between before and after the surgery in either groups. Komisaruk et al.[83] reviewed the results of studies investigating the relationship between hysterectomy and sexual function, between 1977 and 2007, and accentuated that most of the studies indicated a 'decrease' in dyspareunia while a majority reported 'no change' after hysterectomy in sexual activity, orgasm frequency, orgasm intensity, vaginal lubrication and libido. They also stressed that effects of hysterectomy on sexual response may not always be deleterious but may depend on whether the surgery desensitizes a woman's preferred genital site of stimulation.

INCIDENTAL CANCER

The recent trend towards uterine preservation in the management of pelvic organ prolapse has necessitated an important issue, the risk of failure to detect an occult malignancy, to be addressed[87]. Besides, in contrast to women with fibroids or menorrhagia, patients seeking treatment for POP rarely exhibit signs or symptoms that raise suspicion for uterine cancer and typically do not have indications to prompt evaluations of the endometrium[88]. The number of studies reporting the incidence of malignancy in specimens obtained from hysterectomies performed with the diagnosis of uterovaginal prolapse are low[87,89-92]. These studies reported low rates of unanticipated uterine malignancies. Renganathan et al.[93] reported an unanticipated endometrial malignancy rate of 0.8% among 517 women undergoing pelvic organ prolapse surgery. Ramm et al.[88] determined 5 endometrial cancer cases (0.6%), 4 of which had had a normal preoperative screening, among 708 women and concluded that endometrial assessment prior to prolapse surgery in asymptomatic women was unreliable at detecting malignancy. Similarly, Wan et al.[94] reported that the frequencies of malignancy and premalignant lesions were 0.47% and 0.78%, respectively, in their cohort of 640 women with uterovaginal prolapse. On the other hand, there has been an effort as to whether asymptomatic women could be detected prior to POP correction surgery. Ramm et al.[88] assessed preoperative screening trends and final pathologic diagnoses of women undergoing uteropelvic prolapse surgery and concluded that endometrial assessment via endometrial biopsy or transvaginal sonography prior to POP/UI surgery in asymptomatic women was unreliable at detecting malignancy. Although an intraoperative dilatation and curettage (with or without hys-

teroscopy) was recommended in women undergoing uterine preservation, the fact that the diagnosis would only be made after the surgery had been completed rendered this approach implausible[93]. Frick et al.[89] reported that premenopausal women with uterovaginal prolapse and normal bleeding patterns or with negative evaluation for abnormal uterine bleeding still had a minimal risk of abnormal gynecologic pathology. In postmenopausal women without bleeding, the risk of unanticipated uterine pathology was 2.6% but may be reduced by preoperative endometrial evaluation. However, in women with a history of postmenopausal bleeding, even with a negative endometrial evaluation, they did not recommend uterine preservation at the time of prolapse surgery. Consequently, the possibility of uterine pathology should be considered when deciding the therapeutic strategy to recommend in women with pelvic organ prolapse and it should be kept in mind that conserving a prolapsed uterus without further investigations runs the risk of missing women with endometrial malignancy[93].

IMPACT OF PRIMARY DISEASE ON INCONTINENCE OR PROLAPSUS

Although the current hysterectomy trend has shifted from abdominal to laparoscopic and robotic approaches through the last decade, the commonest indications for which hysterectomy was performed have not changed, the vast majority being for benign conditions, including fibroids, abnormal uterine bleeding (AUB), pelvic organ prolapse, endometriosis, benign ovary tumors, pain, fibroma, and polyps. Since all these conditions have quite different nature, pathogenesis and clinical consequences, risk of subsequent pelvic organ prolapse in women undergoing hysterectomy for different indications may naturally vary. However, the number of studies investigating the risk of POP surgery after hysterectomy, as the indication for the surgery was considered a risk factor, has remained limited. Two studies by Dallenbach et al.[95,96] demonstrated no difference among the hysterectomy indications in the risk for subsequent POP. They reported that the incidence of pelvic organ prolapse that required surgical correction after hysterectomy was 1.3 per 1,000 women-years. The risk of prolapse repair was 4.7 times higher in women whose initial hysterectomy was indicated by prolapse than indicated by myoma and 8.0 times higher if preoperative prolapse grade 2 or more was present[95]. In their following study, vaginal vault prolapse repair after hysterectomy was reported to be an infrequent event and was due to preexisting weakness of pelvic tissues[96]. Similarly, Blandon et al.[97] reported that, compared with women without prolapse, women who had a hysterectomy for prolapse were at increased risk for subsequent pelvic floor repair. Lykke et al.[98] followed up 154,882 women from hysterectomy to POP surgery and reported that the indications POP, AUB, pain, endometriosis were associated with higher risks of subsequent POP surgery after hysterectomy than the indication fibroids/polyps. Also POP as an indication for hysterectomy was associated with the highest cumulative incidence of subsequent POP surgery. Another large cohort study, comparing vaginal hysterectomy for POP and vaginal hysterectomy for other indications showed that vaginal hysterectomy for POP has a higher hazard ratio (HR) than vaginal hysterectomy for other indications[99]. The increased risk of subsequent pelvic organ prolapse in women undergoing hysterectomy with POP indication could be attributed to underlying risk factors and damage to pelvic floor that they already have. Thus, they become more likely to undergo subsequent POP repair surgery[98]. Based on the results of these studies, it might be reasonable to perform a hysterectomy in a woman presenting with POP, to prevent a subsequent prolapse and POP correction surgery.

EFFECTS OF OPERATIVE COMPLICATIONS

Although the short- and long-term risks of hysterectomy are well described in the literature, morbidities of neither preserving uterus and nor the addition of hysterectomy to a prolapse repair have not been described. There are several complications described in the literature related to surgical correction of uterovaginal prolapse, including buttock pain, blood loss, vaginal or incisional hematoma, ureteral obstruction, urinary tract infection, dyspareunia, vaginal adhesion and rectal injuries[100,101]. Gutman & Maher[29] reviewed the studies reporting the results of surgical correction procedures and reported that vaginal hysterectomy was associated with higher success rates, but also with higher complication rates.

Buttock pain is a prevalent complication POP surgery that lasts no longer than 6 weeks. Several studies reporting the results of correction surgery, with or without hysterectomy, indicated buttock pain as a complication of the procedures, with a rate up to 18% of the patients[86,100,102-104]. However, the comparison of this complication's rate between uterine preserving procedures and hysterectomy remains sparse in the literature. Hefni et al[103] compared the outcomes of sacrospinous hysteropexy with vaginal hysterectomy and reported the rates of buttock pain to be 3% vs. 4%, respectively. Another prospective study comparing sacrospinous hysteropexy with vaginal hysterectomy reported transient buttock pain with comparable rates between the groups[86].

Some studies comparing vaginal hysterectomy with sacrospinous hysteropexy reported an increase in overactive bladder and urge incontinence symptoms in vaginal hysterectomy groups[101,103,105]. Another complication of pelvic organ prolapse surgeries is mesh erosion, which was reported with varying rates and the evidence in the literature regarding the mesh exposure is conflicting. Although Collinet et al.[106] reported a 5-fold increase in the rates of mesh exposure in vaginal hysterectomy group, other studies reported comparable mesh erosion rates between groups with and without hysterectomy[107,108]. Gutman & Maher[29] indicated that the risk of mesh erosion was approximately 4 times greater if a hysterectomy was performed at the time of sacral colpopexy compared to no-hysterectomy or subtotal hysterectomy. They extrapolated that introducing synthetic mesh transvaginally or laparoscopically after vaginal hysterectomy, or through a posterior vaginal excision appears to significantly increase the risk of mesh erosion after sacral colpopexy, probably due to exposure of the synthetic mesh to vaginal microbiota.

In the current literature, uterine-preserving procedures have been reported to associate with shorter operating time and lesser intraoperative blood loss as compared to vaginal hysterectomy[103,105,107,109]. A RCT comparing sacrospinous hysteropexy with vaginal hysterectomy and uterosacral ligament suspension reported that hysteropexy was associated with shorter hospitalisation, quicker recovery with more rapid return to work and longer vaginal length[110]. Another study comparing uterine-preserving surgery with vaginal hysterectomy reported that uterus-preservation at time of POP-surgery was associated with significantly shorter operation time[109]. Similarly, Chu et al.[107] compared women undergoing hysterectomy with uterine preservation and hysteropexy group had a shorter operating time and

less blood loss. Results of the studies investigating the operative complications reveal more favorable outcomes in women undergoing uterine preserving procedures.

LONG TERM OUTCOME AND RECURRENCE WITH OR WITHOUT HYSTERECTOMY

Success rates of uterine preserving procedures and hysterectomy were compared in several studies. A RCT by Dietz et al[110] reported the success rates of sacrospinous hysteropexy and vaginal hysterectomy as 79% vs 97%, respectively, without statistical significance. Van Brummen et al[101] demonstrated the success rates of these two procedures to be 89% and 93% respectively. Hefni & El-Toukhy[104] compared these two surgeries and the success rate of vaginal hysterectomy was 97% as compared to sacrospinous hysteropexy was 92%. Chu et al[107] compared hysterectomy plus mesh with uterine preservation plus mesh and demonstrated that hysterectomy was superior with a success rate of 100% as compared to sacrospinous hysteropexy with a 96% success. Similarly Neumann & Levy[108] reported a success rate of 95% in hysterectomy group compared to 91% in hysteropexy group. A meta-analysis by Gutman & Maher[29] revealed no difference in the mean objective success rate of 87% in the sacrospinous hysteropexy vs 93% in the hysterectomy group.

Long-term outcomes of surgical correction of POP and the subsequent risk of pelvic organ prolapse after hysterectomy have been controversial[101,103,105]. Dietz et al[110] reported that women who underwent a vaginal hysterectomy for uterine descent stage 2 or more had considerably fewer recurrences (3%) of the apical compartment compared to women after a sacrospinous hysteropexy (27%). Moreover, of women with stage IV prolapse who underwent hysteropexy, all recurred within a year. Symptomatic recurrent prolapses were 4-times higher in the uterine-preservation group than in vaginal hysterectomy group (23.8% vs. 6.7%; p = 0.023). Dallenbach et al. stressed that vaginal hysterectomy was not a risk factor when preoperative prolapse was taken into account[95,96]. An 8-year follow-up study after vaginal hysterectomy revealed a 10% rate of vaginal vault prolapse, which correlated with severity of preoperative rectocele, not with severity of uterine descent[111]. In a 10-year follow-up study of 456 women who underwent a primary operation for pelvic organ prolapse, predominantly vaginal hysterectomy with colporraphy, the rate of reoperation for POP was reported to be 2.9%[112]. Contrarily, Forsgren et al.[99] compared women having vaginal hysterectomy due to or with concurrent prolapse repair and those having vaginal or total abdominal hysterectomy for other gynecological indications in their large population-based cohort study. They reported that the greatest risks of POP (HR 4.9, 95% CI 3.4-6.9) or SUI surgery (HR 6.3, 95% CI 4.4-9.1) were observed subsequent to vaginal hysterectomy for pelvic organ prolapse and consequently suggested that hysterectomy in general, in particular vaginal hysterectomy, was associated with an increased risk for subsequent POP and SUI surgery. Gutman & Maher[29] stressed that women with severe advanced prolapse desiring uterine conservation were at a high risk of recurrence and should consider alternative approaches to hysteropexy.

In previous population-based studies, hysterectomy, in particular vaginal hysterectomy, has been blamed to excess the risk of subsequent pelvic floor disorders[36,37,113,114]. Even though this notion has wide acceptance, prospective studies are few, small in size, and hampered by limited inference to the general population[35,115]. Vaginal hysterectomy is predominantly performed in women with uterovaginal prolapse[116]. Large cohort studies report that vaginal hysterectomies comprises 30% of all hysterectomies, whereas 95.5% of vaginal hysterectomies are performed for pelvic organ prolapse indications[117]. In other words, women undergoing vaginal hysterectomy already possess the risk factors for pelvic organ prolapse and have damage to pelvic floor, which would continue to exist after the surgery, rendering them more prone to develop subsequent prolapse. Hence, it is difficult to distinguish the effects of underlying pathophysiologic pathway of the primary disease from those attributable to the harm of surgical procedure itself, which appears to be the source of bias. Nevertheless, the authors reporting the association between vaginal hysterectomy and subsequent prolapse admit that they could not fully adjust for selection bias caused by surgeons selecting patients with particular characteristics for vaginal hysterectomy which, in turn, could contribute to an overestimation of prolapse and urinary incontinence subsequent to vaginal hysterectomy[99]. Additionally, many studies lack data on confounders such as body mass index, smoking and obstetrical history.

FUTURE RESEARCH TARGETS

Prolapse surgery must consider the cost–benefit analysis, success, complication rate and morbidity of the procedure, both immediately and over the long-term. Long-term data on uterine preserving procedures are limited and the subsequent need for hysterectomy in the surgical correction of POP is not known (Grade C). Uterine preserving techniques appear to be a promising option in women with POP, particularly in those with future desire of fertility. However, long-term follow up studies with appropriate control groups are still lacking.

Randomized control trials with close long-term follow-up and quality-of-life assessment are still lacking and would be necessary to determine the benefit of such preventive techniques. Sacrospinous hysteropexy is as effective as vaginal hysterectomy and has reduced the operation time, blood loss and hospital stay as compared to vaginal hysterectomy. However, the advantage of the procedure is hampered by the higher recurrent prolapse rates than that of vaginal hysterectomy (single RCT). Moreover, the more severe the prolapsus is, the more common the subsequent prolapsus is. Thus, women with stage IV uterovaginal prolapse or cervical elongation should have a concurrent hysterectomy as part of their surgery. Vaginal hysterectomy plus uterosacral ligament suspension is superior to sacral hysteropexy in terms of reoperation rates (Level 1). Moreover, hysterectomy lowers the risks of uterine or cervical malignancy and postmenopausal bleeding, and thus, the surveillance or therapeutic costs for these situations. Careful patient selection is a crucial step prior to considering uterine conservation in women with pelvic organ prolapse and women with abovementioned diseases should not be candidates for uterine preserving procedures.

Mesh use in anterior compartment has similar outcomes between sacrospinous hysteropexy and hysterectomy, however, performing a vaginal hysterectomy at the time of sacral colpopexy increases the risk of mesh exposure four- to five times compared to uterine preservation (Grade B).

Based on the data available, decision of the kind of the uterovaginal prolapse surgery should be tailored to the patient with careful consideration and uterine preserving procedures should be reserved for patients with early stage prolapse, who desire future fertility. Vaginal hysterectomy with uterosacral ligament suspension, and thus, removing

the 'weight' and tightening the 'hammock', still appears to be rational to uterosacral hysteropexy or laparoscopic hysterectomy alone. Reattaching uterosacral and cardinal ligaments at the time of hysterectomy may help strengthen these fibers and thus minimize the risk of post-hysterectomy prolapse.

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