Mesh Complications Following POP Repair with or without Vaginal Hysterectomy

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Controversial issues in medicine have immerged throughout history and involve all medical fields, including surgery. These controversies exist due to differences in treatment approaches. These disputes often arise from the emergence of new technologies that change the face of medicine, developments in surgical techniques, and accumulation of data over time and from different populations. These medical or surgical controversies are also rooted in differences in approaches between innovation on the one hand and conservatism on the other. Many controversies exist in the field of urogynecology and pelvic floor medicine as well [1]. Two of these controversies in pelvic floor medicine that appear time and again in pelvic floor clinical practice as well as in the academic world are the use of vaginal mesh in pelvic organ prolapse (POP) reconstructive surgery and the need for hysterectomy during POP reconstructive surgery versus uterine preservation.

In the current edition of the *Israel Medical Association Journal* (*IMAJ*), Ganer Herman and colleagues [2] evaluated the risk of mesh erosion following mesh augmented POP repair, with or without concomitant vaginal hysterectomy (VH). In this retrospective cohort study of 70 patients who underwent vaginal mesh-augmented POP repair between 2007 and 2010, approximately half (51.4%) had a concomitant VH while the remainder underwent mesh repair without VH. In their study, the authors found a generally low mesh complication rate and they found no significant differences between the groups (with and without VH). They concluded that vaginal mesh augmentation concomitant with VH for POP repair does not carry an increased risk for mesh erosion.

This study is important because of its reassuring findings regarding safety both of mesh augmentation repair and of uterine preservation surgery, although a longer follow-up would be needed to evaluate differences in sustained efficacy. However, the authors addressed two of the most widespread controversies in urogynecology and pelvic floor medicine: the use of vaginal mesh in POP reconstructive surgery and the role of hysterectomy during POP reconstructive surgery versus uterine preservation.

VAGINAL MESH IN POP RECONSTRUCTIVE SURGERY

POP is common with a prevalence currently estimated to be approximately 40% in women aged 45 to 85 years. As many as 30% of these women are symptomatic [3]. Symptoms include complains of urinary, bowel, or sexual dysfunction as well as symptoms of vaginal pressure, heaviness, or pain [4]. They may greatly impact patient well-being and quality of life [5].

The efficacy of conservative treatment such as pelvic floor exercise or a pessary is limited. It is estimated that about 11% of all women will undergo surgery for POP repair during their lifetime, and 30% of these will need reoperation because of prolapse recurrence within 4 years after the initial surgery [6].

A transvaginal mesh kit is considered a newer technique that differs from the traditional native tissue repair (anterior or posterior colporrhaphy). In vaginal mesh procedures, instead of individual sutures used to plicate the endopelvic connective tissue, trocars are used to insert and fasten a standardized mesh to augment support to the pelvic structures and overlay the vaginal wall and central defect. These mesh kits represent a more standardized approach. The mesh used is usually a permanent one as opposed to the delayed absorbable sutures used during native tissue repair [7].

Recently, the use of synthetic materials in general and specifically mesh for the repair of POP has been controversial. Warnings about increased complication rates and fear of litigation have steered the industry as well as surgeons away from preforming mesh repairs, ignoring the advantages that these techniques may carry. While in some countries the use of vaginal mesh has been totally banned due to concerns regarding safety and complications, in others, that focus is on their advantages, and these procedures are still performed with certain limitations on selected patients (i.e., high risk for recurrence) by trained specialists. In April 2019 the U.S. Food and Drug Administration (FDA) halted sales of pelvic mesh in the United States, citing safety concerns for women. As with many other clinical issues, professional opinions have a pendular tendency of swaying between extremes, until a wide consensus is reached [8].

The main complication of mesh augmentation surgery is mesh exposure. In

a recent meta-analysis of 14 randomized-controlled trials, the rate of mesh exposure was shown to be higher than 10%. Of these, only 7.7% had an additional surgery for mesh exposure [9]. It should be noted that a small mesh exposure may be asymptomatic and does not necessarily require additional surgery for excision of the mesh [10]. Postoperative pain (pelvic pain, groin pain, leg pain, and dyspareunia) is another complication that is associated with mesh repair. Rates of pain after mesh repair are variable. According to a recent Cochrane report, the rate was relatively low, with only 0.5% of women requiring mesh removal for this reason [11]. Nevertheless, 38.6% of complaints to the FDA included vaginal pain and/or dyspareunia [11]. Other less frequent complications of mesh repair include de-novo urinary incontinence, intraoperative bladder injury, neuromuscular problems, vaginal scarring or shrinkage, and urethral injuries [12].

Lack of methodological unity in different trials, use of different surgical kits, varying experience of surgeons, alternative research protocols, diverse patient selection, and varying methods for assessing success limit the accuracy of existing data [8]. It has been shown that with highly skilled medical professionals and by using new and innovative mesh with unique structure and properties, low rates of adverse outcomes may be achieved [13].

Based on an understanding of the advantages of mesh repair, almost all of the expert opinions and clinical statements of professional organizations worldwide suggest and recommend improving the clinical practice regarding these procedures, such as meticulous patient selection and improved surgical training. Therefore, it is of great importance to develop strategies for decreasing complications and allowing transvaginal mesh repair to be an acceptable option of treatment. With improved research, increased attention to surgical technique, and meticulous patient selection, there might still be hope for mesh repair, with its greater efficacy and expectable rates of adverse effects [8].

HYSTERECTOMY DURING POP RECONSTRUCTIVE SURGERY VERSUS UTERINE PRESERVATION

Hysterectomy is often performed at the time of POP repair. This practice is dependent on the surgical technique used for pelvic reconstruction and other potential benefits. In contrast, there is concern that concomitant hysterectomy may increase the risk of some perioperative complications (e.g., mesh erosion, pelvic neuropathy, and disruption of natural support structures such as the uterosacral-cardinal ligament complex) and, in addition, women are increasingly choosing apical POP surgeries that preserve the uterus [14]. A third of women will choose uterine-preserving POP surgery as an important component of their body image (provided outcomes are similar). In addition, patients may enjoy some safety benefits with hysteropexy as opposed to POP surgery with hysterectomy [15].

Uterine sparing procedures correct apical prolapse by attaching the lower uterus or cervix to a supportive structure (uterosacral-cardinal ligament complex). During POP repair, surgeons have traditionally performed hysterectomy rather than uterine-sparing procedures for several reasons. First, apical prolapse is often present in symptomatic women, and the most commonly performed techniques for apical prolapse repair require hysterectomy. Second, it is believed that retaining the uterus increases the risk of recurrent prolapse, although there are limited data to support this [16]. Last, hysterectomy removes current or risk of future cervical or intrauterine pathology. However, today, these benefits are less relevant with advances in minimally invasive treatments of abnormal uterine bleeding and in cervical cancer screening.

Uterine-sparing techniques offer the advantages of a shorter operative time, reduced blood loss, and decreased impact on sexual function. They provide the potential for preserving fertility. However, their efficacy is controversial [17,18]. Prolapse recurrence was found to be higher in women who underwent uterine-sparing techniques in two randomized trials. However, statistical significance was reached only in one trial [18]. Complication rates were similar for the two groups in both studies [17,18]. A multicenter, prospective parallel cohort study from eight institutions reported similar one-year cure rates as well as improvement in pelvic floor symptoms, sexual function, and satisfaction rates [19]. The advantage of decreased impact on sexual function proposed for uterine sparing surgery is uncertain [20]. Data is lacking regarding the risk of intrapartum complications and postpartum recurrence of prolapse following uterine sparing POP repair [16].

The study by Ganer Herman et al. [2] has provided us with reassuring findings regarding the safety of both mesh augmentation repair and uterine preservation surgery. Even though much was published about mesh augmentation surgery, a lack of unity regarding the optimal surgical technique and mesh kits used, identifying the finest implanted materials and tools for assessing success hinder accurate estimations of the true benefits and actual rates of adverse effects of these procedures. Further research, using unified techniques and outcome measures as well as improved mesh materials, is urgently needed to preserve this option in our surgical arsenal. Until then, careful patient selection and surgical education as well as meticulous surgical protocols are required for increasing efficacy and reducing complications. While uterine sparing techniques may offer benefits of decreased operative time and reduced blood loss, their efficacy and decreased risk for complications have yet to be proven and warrant farther investigations into long term safety and efficacy issues.

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Capsule

Stress and the immune system

Psychological stress affects cognitive performance, and severe stress can contribute to chronic disease. **Kertser** and co-authors tested responses in mice to a stressful event involving electrical shocks. Central nervous system immunosurveillance plays a role in the ability to cope with mental stress. However, severe stress interfered with this process. Severe stress led to reduced trafficking of white blood cells along the choroid plexus, a major interface between the brain and the immune system. Blocking corticosteroid and glucocorticoid signaling locally restored choroid plexus functioning, mitigating the impact of stress on immune function.

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Capsule

Tempering dendritic cell activation

Checkpoint blockade targeting cytotoxic T lymphocyte associated protein 4 (CTLA-4) and programed cell death 1 (PD-1) have changed the landscape of cancer therapeutics. However, much remains to be learned about the biology of these molecules. CTLA-4 expressed on T cells captures costimulatory molecules CD80 and CD86 from antigen-presenting cells by transendocytosis to inhibit CD28-mediated costimulation of T cell activation. **Ovcinnikovs** et al. report that regulatory T cells (T_{regs}) outperform conventional T cells in their ability to transendocytose CD80 and CD86 and that migratory dendritic cells are the main population targeted by Treg-expressed CTLA-4 in vivo. These findings elucidate why CTLA-4 expressed on Tregs is so central in maintaining immune homeostasis.

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"A true and worthy ideal frees and uplifts a people; a false ideal imprisons and lowers"

W.E.B. Du Bois (1868–1963), American sociologist, historian, civil rights activist, and author