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Histopathological and mechanical properties of different meshes in a rat model of pelvic prolapse surgery

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ABSTRACT

Different types of mesh materials are used to support pelvic structures in urogynecologic procedures. Our aim was to compare histopathological and mechanical effects of Prolene®, UltraPro®, Vypro II®, and Permacol® meshes used in pelvic organ prolapse.

Thirty Sprague-Dawley rats were randomized into five groups. Group 1 served as a sham-operated control (n=6); Prolene® was used in group 2 (n=6), UltraPro® in group 3 (n=6), Vypro II® in group 4 (n=6), and Permacol® in group 5 (n=6). A 0.5 × 1 cm mesh was placed between the paravaginal tissue and bladder. After 12 weeks, the rats were reoperated and meshes were excised. Histopathological tissue reactions were compared.

The muscle penetration rate was 67% in the Prolene® group, which was significantly higher than that in the other groups (p=0.026). Minimum preserved postoperative surface area was seen with Prolene® at 0.31 cm^2 and maximum with UltraPro® at 0.45 cm^2, which was statistically significant. UltraPro® had the most preserved postoperative surface area and less shrinkage than the other meshes.

The mesh materials cause an inflammatory reaction in surrounding tissue. Prolene® mesh had superior muscle penetration and tensile strength compared to the other materials.

Key Words: Pelvic organ prolapse, polypropylene, surgical mesh, tensile strength

Introduction

An estimated 35-50% of elderly women will have pelvic organ prolapse during their lifetimes (1,2). About 11% of these women will undergo pelvic prolapse surgery and approximately 30% will be reoperated within 4 years of the index surgery (3,4).

Different types of mesh materials are used to support pelvic anatomical structures in urogynecologic procedures (5). There is often difficulty in choosing the optimal mesh material in gynecologic reconstructive vaginal and stress urinary incontinence surgery. Although there are many mesh products, there is no consensus on the optimal choice. Furthermore, the FDA (U.S. Food and Drug Administration) has issued a warning about the use of mesh in surgery for pelvic organ prolapse and stress incontinence after increased complication rates (6).

In recent years, autologous, xenograft, alloplastic, and synthetic materials have been used for pelvic reconstructive surgery. The meshes have different efficacies and complications such as infection and erosion rates. The ideal material is defined as sterile and causing no immunologic reaction, and is noncarcinogenic, with maximal efficacy, and compatible with host tissue with minimal complication rates (7,8).

In this study, we aimed to investigate local histopathological changes in pelvic tissue as well as baseline and postoperative mechanical properties of four different type of mesh in an experimental animal model.

Materials and Methods

Study protocol: This study was performed at our University Experimental Animal Laboratory after approval by the ethics committee of the same

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institution. Thirty Sprague-Dawley rats were obtained from the experimental animal laboratory and randomized to five different groups. The first group (n=6) served as a sham-operated control. Prolene (polypropylene monofilament, pore size 1-2 mm; Ethicon, USA) mesh was used in the second group (n=6), UltraPro (lightweight polypropylene + poliglecaprone monofilament, pore size 3-4 mm; Ethicon) in the third group (n=6), Vypro II (polypropylene + polyglactin multifilament, pore size 4-5 mm, Ethicon) in the fourth group (n=6), and Permacol (acellular porcine dermal collagen, Covidien, USA) in the fifth group (n=6) (Figure 1).

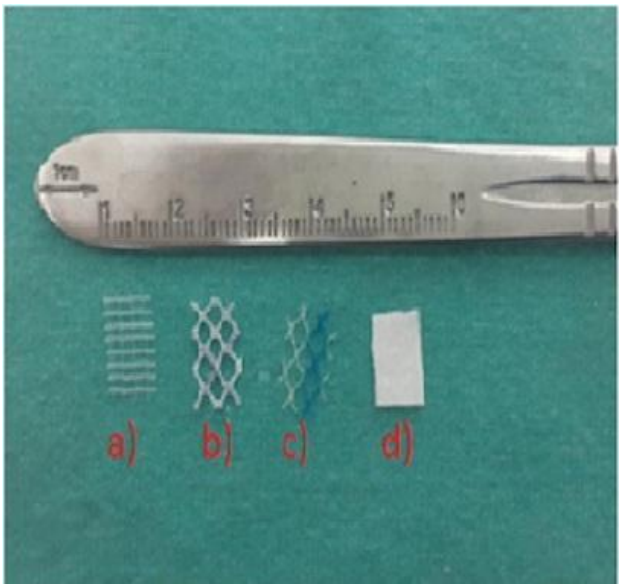

Fig. 1. The mesh materials are shown (0.5×1cm) **a)** Prolene **b)** VyproII **c)** UltraPro **d)** Permacol.

Analysis of Mechanical properties: The 0.5 × 1 cm mesh materials were prepared before the procedures. A previously described tensometer setup was used to evaluate the mechanical properties of the meshes (9). An empty intravenous (IV) bag was fixed to a clamp at the lower part of this setup. A 3.000 cc fluid-filled IV bag was fixed to a clamp at the top of this setup. The two clamps were set facing each other. An IV infusion set was connected between the two IV bags. The meshes were fixed between two facing clamps. Fluid flow was started from the upper to the lower IV bag via a rate-adjustable IV infusion set. The structural changes and break points of the meshes were measured and recorded after initiation of fluid flow. Fluid flow was stopped when the mesh broke (maximum tensile strength). The total collected fluid amount in the lower IV bag was weighed using a sensitive electronic scale and recorded. The measurements were converted from grams to gravity (Newton) by using the formula: F (Newton) = kg × G (Gravity) (G was accepted as 9.8). This procedure was performed preoperatively and 12 weeks postoperatively to compare mechanical properties of the meshes (Figure 2).

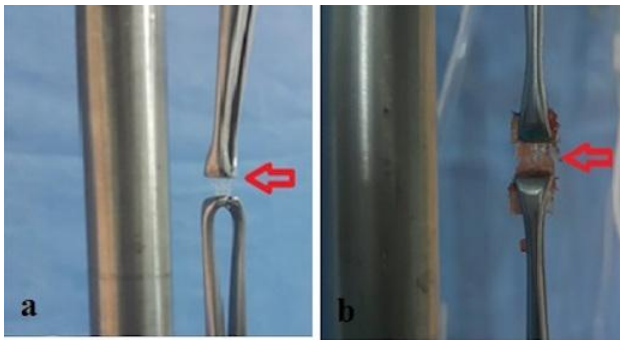

Fig. 2. The picture shows the tensometer setup **a)** The picture shows preoperative basal meshes **b)** The picture shows postoperative meshes.

Surgical procedure: The animals were anesthetized by administering 50 mg/kg 10% ketamine hydrochloride (Ketasol; Richter Pharma) and 5 mg/kg 2% xylazine (Rompun; Bayer Health Care) intramuscularly. Before the operation, the abdominal skin was shaved and disinfected with 10% povidone-iodine solution (Batticon; Adeka Laboratories). A 3-cm midline incision was made, and the bladder and paravaginal tissues were exposed. A 0.5 × 1 cm mesh was fixed with 5/0 Prolene suture in the paravaginal vault distally and bladder vault proximally. In all animals, abdominal incisions were closed by two layers of 4-0 polyglycolic acid suture (Vicryl; Johnson and Johnson Medical, Ethicon) for the peritoneum and 3-0 polyglactin suture for the skin. After the animals recovered from surgery, they were housed separately at a controlled temperature of 22°C and a 14-hour light cycle, with food and water ad libitum. The surgery time was limited to 15 minutes for each rat to prevent tissue drying at room temperature. All surgical procedures were performed by the same researchers. All rats were sacrificed 12 weeks later, as previous studies reported that tissue reactions are thought to develop over this time period; surrounding paravaginal and bladder tissues were excised for histopathological evaluation. The postoperative mesh materials were retained for evaluation of mechanical properties (Figure 3,4).

Histopathological analysis: The excised tissues were fixed in 10% buffered formalin solution for 24 hours. After fixation, a routine tissue-

processing procedure was performed, and the samples were embedded in paraffin. Paraffin wax blocks were cut into 4-mm-thick sections with the use of a microtome (Leica RM2125RTS, Leica Biosystems Nussloch GmbH) and stained with hematoxylin-eosin and Masson trichrome. Inflammation, granulocyte, macrophage, lymphocyte, fibroblast, collagen density, and vascularity parameters were scored as reported in a previous study (10). The score was 0 if there was no reaction around the tissue, 1 if there was a less than 25% involvement, 2 if 25%-50%, 3 if 50%-75%, and 4 if more than 75%. The bladder muscle was evaluated for penetration of the mesh materials, and the presence of a foreign body reaction and necrosis were also evaluated. The histopathological analysis was performed by the same expert pathologist (Figure 5, 6).

Statistical analysis: SPSS for Windows 11.5, USA) was used for statistical analysis. The Kruskal-Wallis test was used to analyze independent continuous variables for histopathological scoring and mechanical properties. The Bonferroni correction of the

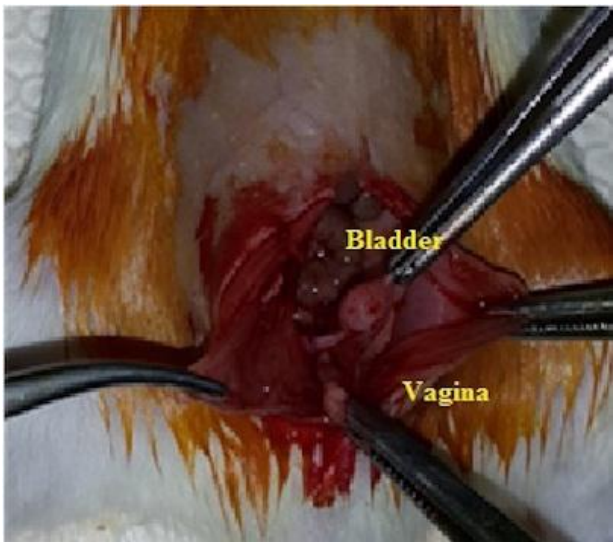

Fig. 3. The picture shows exposed bladder and vaginal tissue of the rat.

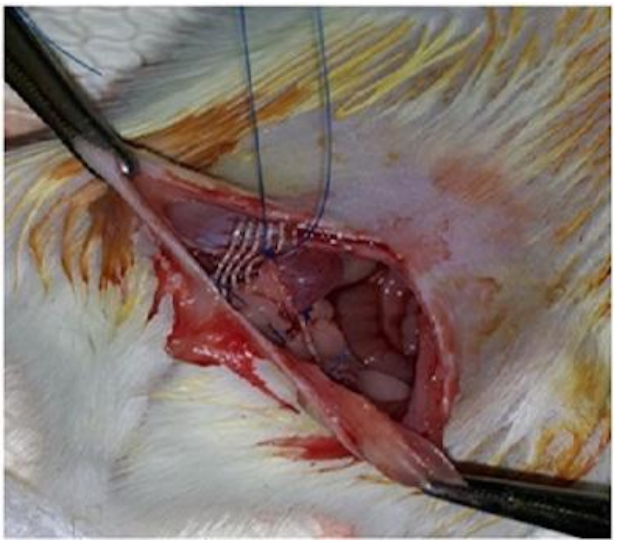

Fig. 4. The picture shows insertion of a 0.5 × 1 cm mesh material between bladder and paravaginal tissue.

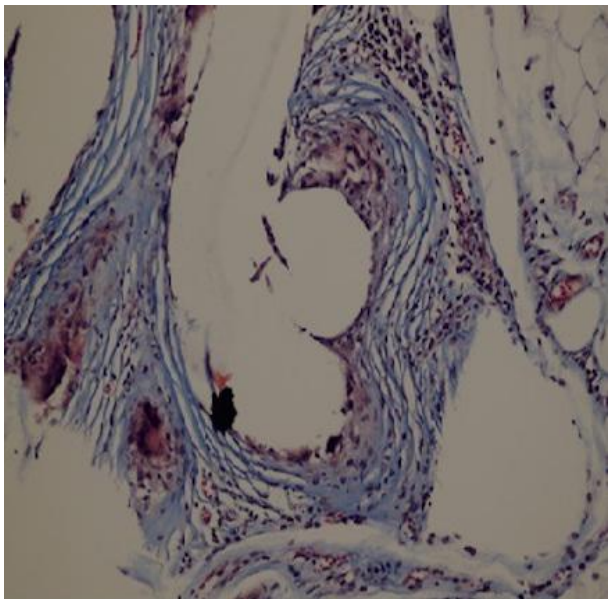

Fig. 5. The picture shows increased fibrosis areas-Prolene mesh (Masson- trichrome x200)

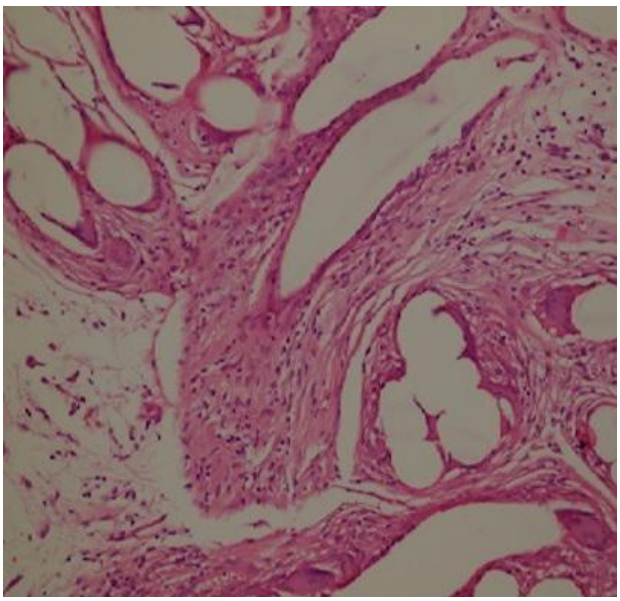

Fig. 6. The picture shows minimal inflammatory cells and increased giant cell formations-VyproII (Hematoxylin-eosin x100).

Mann-Whitney U test was used for post hoc evaluation. The chi-square and goodness-of-fit tests were used to analyze noncontinous variables. A p value <0.05 was considered as statistically significant.

Results

Histopathological results of the study groups are shown in Table 1. There were significant differences between the sham group and the four

Table 1. Comparison of histopathological results of the study groups

	Control	Prolene®	Ultrapro®	VyproII®	Permacol®	*p* value
Inflammation, median (IQR)	0	2 (1)	1(1)	2(0)	2(2)	.002¥ .002µ .004≠ .002Ω .004€
Granulocyte, median (IQR)	0	1(1)	1(1)	2 (1)	1(1)	.002¥ .002µ .004≠ .002Ω .004€
Macrophage, median (IQR)	0	1(1)	1(1)	3 (0)	2(2)	<.001¥ .002µ .004≠ .002Ω .004€ .002α .004β
Lymphocyte, median (IQR)	0	1(1)	1(1)	2 (0)	1(0)	<.001¥ .002µ .004≠ .002Ω
Fibroblast, median (IQR)	0	1(1)	1(1)	1 (0)	1(0)	.001¥ .002µ .004≠ .002Ω .004€
Collagen density, median (IQR)	0	2(1)	2(1)	1.5 (1)	1(1)	.002¥ .002µ .004≠ .002Ω .004€
Vascularity, median (IQR)	0	2(1)	2(1)	1 (1)	1(1)	.002¥ .002µ .004≠ .002Ω .004€
Muscular penetration %	0	67	20	17	0	.026¥
Foreign body reaction %	0	100	100	100	100	<.001¥

IQR: interquartile range, **¥** Comparison of five different study groups, **µ** Comparison of Control and Prolene groups, **≠** Comparison of Control and Ultrapro groups, **Ω** Comparison of Control and VyproII groups, **€** Comparison of Control and Permacol groups, **α** Comparison of Prolene and VyproII groups, **β** Comparison of Ultrapro and VyproII groups.

mesh groups for inflammation, granulocyte, lymphocyte, fibroblast, macrophage, collagen density, and vascularity scores. However, there was no statistical difference between the four different mesh groups for these parameters. There was a significant difference between Vypro II, Prolene, and UltraPro groups for macrophage scores (p:0.02, p:0.04). There were higher scores in the Vypro II group compared to the other groups for macrophage scores.

There was a significant difference between the groups for muscular penetration (p=0.026). The greatest penetration was seen in the Prolene group with a 67% rate. However, there was no muscle penetration in the sham and Permacol groups. There was a significant difference between the study groups for foreign body reactions (p<0.001). There was a foreign body reaction in all mesh groups but not the control group. Postoperative mesh surface area, shrinkage rate, maximum tensile strength, length at break point, and final elongation percentage against force are shown in Table 2.

Maximum tensile strength was significantly greater for Prolene mesh at 17.6 N compared with the other three mesh types (p:0.009, p:0.002, p:0.002). Maximum tensile strength was also significantly different between UltraPro and Vypro II, and UltraPro and Permacol (p:0.009, p:0.008). There was no statistical difference between Vypro and Permacol for postoperative mesh surface area, shrinkage rate, maximum tensile strength, length at break point, and elongation rate against force.

Preoperative basal and postoperative mesh surface area, collapse rate, maximum tensile strength, length at break point, and elongation rate against force were also compared and are shown in Table 3. The UltraPro mesh was the best preserved material after implantation. The postoperative mesh surface area and postoperative length at break point was less in the UltraPro group compared with Prolene mesh, and this was statistically significant (p:0.04, p:0.04). There was no significant difference between UltraPro and Vypro, or UltraPro and Permacol, for mesh surface area, collapse rate, length at break point, and elongation rate against force.

The figure 7 shows elongation of the meshes against force in preoperative basal and postoperative conditions. This demonstrates that UltraPro, Vypro II, and Permacol mesh have lower break points, and that elongation begins at lower force in contrast to Prolene mesh.

Table 2. Postoperative mesh surface area, shrinkage rate, maximum tensile strength, length at break point, and final elongation percentage against force are shown

	Prolene®	Ultrapro®	VyproII®	Permacol®	*p* value
Mesh surface area, cm^2, median (IQR)	.31(.06)	.45(.07)	.37(.1)	.4(.14)	.013¥ .004≠
Shrinkage, median (IQR)	38(12)	10(15)	25(21)	20(28)	.013¥ .004≠
Maximum tensile strength, Newton, median (IQR)	17.6(3.1)	14.1(3.1)	9.8(3.1)	7.8(1.7)	<.001¥ .009≠ .002€ .002α .009β .008μ
length at break point, mm, median (IQR)	.8(.3)	.8(.2)	.7(.13)	.7(.1)	.14¥
Final elongation percentage against force, median (IQR)	60(65)	60(50)	40(25)	40(20)	.14¥

IQR: interquartile range, **¥** Comparison of four different mesh types, **≠** Comparison of Prolene and Ultrapro (Mesh surface area, Shrinkage, Maximum tensile strength *p*<0,05), **€** Comparison of Prolene and VyproII (Maximum tensile strength *p*<0,05), **α** Comparison of Prolene and Permacol (Maximum tensile strength *p*<0,05), **β** Comparison of Ultrapro and VyproII (Maximum tensile strength *p*<0,05), **μ** Comparison of Ultrapro and Permacol (Maximum tensile strength *p*<0,05).

Table 3. Preoperative basal and postoperative mesh surface area, collapse rate, maximum tensile strength, length at break point, and elongation rate against force are shown

	Prolene®	Ultrapro®	VyproII®	Permacol®	*p* value
Mesh surface area, cm^2, median (IQR)	-.19(.07)	-.05(.08)	-.13(.1)	-.1(.14)	.015¥ .004ǂ
Shrinkage, median (IQR)	38(12)	10(15)	25(21)	20(28)	.013¥ .004ǂ
Maximum tensile strength, Newton, median (IQR)	1.9(3.1)	-2.6(3.1)	-4.2(3.1)	-3.2(1.7)	.003¥ .004ǂ .002€ .004α
Length at break point, mm, median (IQR)	.00(.33)	.1(.25)	.00(.13)	.00(.1)	.245¥
Final elongation percentage against force, median (IQR)	.00(65)	20(50)	.00(25)	.00(20)	.245¥

IQR: interquartile range, ¥ Comparison of preoperative basal and postoperative values of the four different mesh types, ǂ Comparison of Prolen and Ultrapro (Mesh surface area and Length at break point $p<0,05$), € Comparison of Prolen and VyproII (Length at break point $p<0,05$), α Comparison of Prolen and Permacol (Length at break point $p<0,05$).

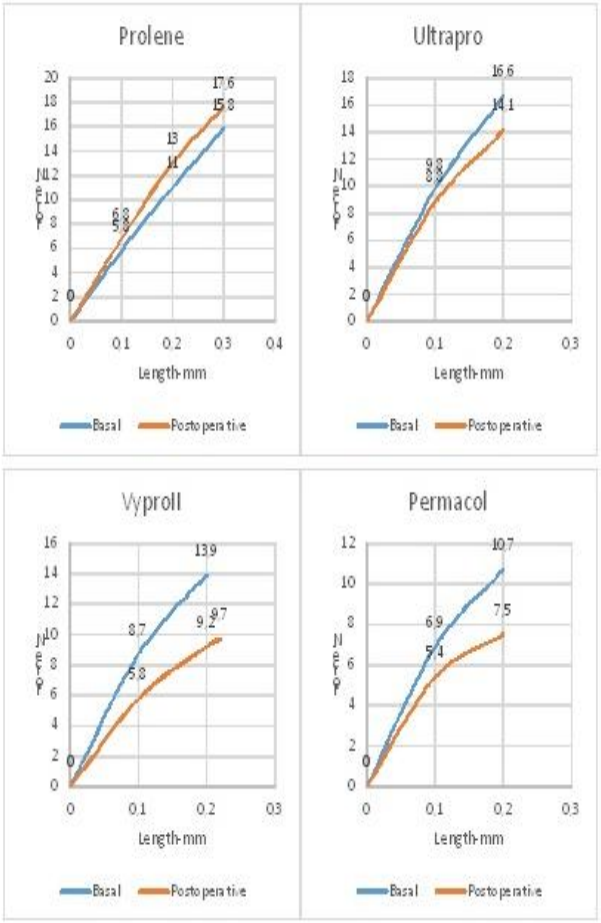

Fig. 7. Elongation of the meshes against force in preoperative basal and postoperative conditions.

Discussion

Mesh materials are commonly used abdominally or vaginally for pelvic reconstructive surgeries and for stress urinary incontinence in daily gynecology practice. The materials first used were autologous fascia lata or rectus fascia grefts. Although the materials had a reportedly high success rate, long recovery periods, long operative duration, and increased morbidity rates were major undesirable features of these materials (11).

Moreover, allograft and xenograft mesh materials have decreased success rates due to the difficulty in sterilization (7,11). In the early 1990s, polyester, nylon and Gore-Tex were evaluated and felt to be inappropriate due to increased infection and erosion rates (12). Polypropylene mesh materials were very popular, with high success and decreased complication rates; they were easy to use in surgery and are still commonly used in daily gynecology practice (13,14). However, there was reportedly an increased rate of adhesions in tissue after use of polypropylene mesh materials (15,16). Utiyama et al. (10) reported that polypropylene (high density) and UltraPro (low density) showed the same results for inflammatory reactions, shrinkage rate, adhesions, and complication rates in a rat hernia repair model. Yildirim et al. (17) reported that use of tension-free vaginal tape (TVT, polypropylene monoflament, 75 um), intravaginal slingplasty (IVS, polypropylene

multifilament, 0.1 mm), and the suprapubic arch sling (SPARC, polypropylene monofilament, 1 mm) materials showed the same histopathological changes 30 days after implantation. Krause et al. (18) evaluated TVT, SPARC, Prolene IVS, and Vypro II meshes and concluded that IVS and Vypro II meshes had greater inflammatory and tissue reactions three months after implantation (19). In our study, we found that Prolene (heavy polypropylene monofilament, 1.2 mm), UltraPro (light polypropylene/poliglecaprone monofilament, 3 mm), Vypro II (light polypropylene/polyglactin multifilament, 3 mm), and Permacol (acellular porcine dermis) showed no histopathological differences (inflammation, granulocyte, lymphocyte, fibroblast, collagen density, and vascularity) three months after implantation. However, there was a difference in the macrophage count between Vypro II, Prolene, and UltraPro meshes. We speculate that Vypro II has more long-term tissue reactions due to the high macrophage score.

Atis et al. (20) reported no statistical difference between IVS, TVT, and Vypro for muscle penetration. In our study, there was a statistical difference between mesh types for muscle penetration, at 67% for Prolene, 20% for UltraPro, and 17% for Vypro II, but there was no penetration in the Permacol group.

Pierce et al. (21) compared porcine dermis and light polypropylene for prolapse and incontinence surgeries and concluded that porcine meshes were weaker and more homogeneous, with minimal tissue reactions compared to light polypropylene meshes. In our study, Permacol mesh showed no muscle penetration and had less tensile strength.

It is known that mesh materials tend to collapse after surgery. This also occurs with tissue retraction around the mesh material. It is reported that 60% tissue shrinkage occurs after mesh insertion (22). Dora et al. (5) reported 50% shrinkage reduction with autologous fascia and 41% with small intestinal submocosa (SIS). However, they reported no reduction with porcine dermis and polypropylene (SPARC) when compared with other mesh materials. Utiyama et al. (10) reported similar collapse rates for polypropylene (high density) and UltraPro (low density) in a rat hernia repair model. In our study, we observed no statistical reduction in postoperative shrinkage rates for all mesh groups when compared with preoperative baseline rates. However, the most shrinkage was seen in the Prolene group and the least was in the UltraPro mesh group, and the result was statistically significant.

Other preferred mesh features are mechanical strength and long life. In a meta-analysis the strongest materials were reportedly Prolene, UltraPro, and Vypro (8). Dora et al. (5) reported that porcine dermis and SIS had less tensile strength compared with baseline values. However, this reduction was less with propylene and autologous fascia meshes. In our study, preoperative baseline and postoperative tensile strength rates were compared; they showed a decrease in UltraPro, Vypro II, and porcine groups, but there was less reduction in the Prolene group, and the difference was statistically significant.

In conclusion, the mesh materials cause inflammatory reactions in surrounding tissue. Prolene mesh is superior, with higher muscle penetration and tensile strength than other materials. UltraPro mesh is the most preserved material compared with baseline. Permacol mesh seems to be weaker than other meshes, with no muscle penetration.

Conflicts of interest statement: None

References

1. MacLennan AH, Taylor AW, Wilson DH, Wilson D. The prevalence of pelvic floor disorders and their relationship to gender, age, parity and mode of delivery. BJOG 2000; 107: 1460-1470.
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. Natale F, La Penna C, Padoa A, et al. A prospective, randomized, controlled study comparing Gynemesh, a synthetic mesh, and Pelvicol, a biologic graft, in the surgical treatment of recurrent cystocele. Int Urogynecol J Pelvic Floor Dysfunct 2009; 20: 75-81.
4. Şentürk MB, Güraslan H, Çakmak Y, Ekin M. Bilateral sacrospinous fixation without hysterectomy: 18-month follow-up. J Turk Ger Gynecol Assoc 2015; 16: 102-106.
5. Dora CD, Dimarco DS, Zobitz ME, Elliott DS. Time dependent variations in biomechanical properties of cadaveric fascia, porcine dermis, porcine small intestine submucosa, polypropylene mesh and autologous fascia in the rabbit model: implications for sling surgery. J Urol 2004; 171: 1970-1973.
6. FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for

Pelvic Organ Prolapse. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm262435.htm. (Accessed on November 29, 2012).

7. Roth CC, Holley TD, Winters JC. Synthetic slings: which material, which approach. Curr Opin Urol 2006; 16: 234-239.
8. Konstantinovic ML, Lagae P, Zheng F, et al. Comparison of host response to polypropylene and non-cross-linked porcine small intestine serosal-derived collagen implants in a rat model. BJOG 2005; 112: 1554-1560.
9. Aksoy E, Çakmak A, Orazakunov E, Gürel M. Evaluation of mesh fixation strength after placement. Journal of Ankara University Faculty of Medicine 2009; 62: 9-43.
10. Utiyama EM, Rosa MB, Andres Mde P, et al. Polypropylene and polypropylene/polyglecaprone (Ultrapro) meshes in the repair of incisional hernia in rats. Acta Cir Bras 2015; 30: 376-381.
11. Rodríguez LV, Blander DS, Raz S. New millennium, new slings. Curr Urol Rep 2001; 2: 399-406.
12. Ghoniem GM, Kapoor DS. Nonautologous sling materials. Curr Urol Rep 2001; 2: 357-363.
13. Ulmsten U, Henriksson L, Johnson P, Varhos G. An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1996; 7: 81-86.
14. Atherton MJ, Stanton SL. The tension-free vaginal tape reviewed: an evidence-based review from inception to current status. BJOG 2005; 112: 534-546.
15. Burger JW, Halm JA, Wijsmuller AR, ten Raa S, Jeekel J. Evaluation of new prosthetic meshes for ventral hernia repair. Surg Endosc 2006; 20: 1320-1325.
16. Primus FE, Harris HW. A critical review of biologic mesh use in ventral hernia repairs under contaminated conditions. Hernia 2013; 17: 21-30.
17. Yildirim A, Basok EK, Gulpinar T, et al. Tissue reactions of 5 sling materials and tissue material detachment strength of 4 synthetic mesh materials in a rabbit model. J Urol 2005; 174: 2037-2040.
18. Krause HG, Galloway SJ, Khoo SK, Lourie R, Goh JT. Biocompatible properties of surgical mesh using an animal model. Aust N Z J Obstet Gynaecol 2006; 46: 42-45.
19. Klosterhalfen B, Junge K, Klinge U. The lightweight and large porous mesh concept for hernia repair. Expert Rev Med Devices 2005; 2: 103-117.
20. Atis G, Arisan S, Ozagari A, et al. Tissue reaction of the rat urinary bladder to synthetic mesh materials. Scientific World Journal 2009; 9: 1046-1051.
21. Pierce LM, Rao A, Baumann SS, et al. Long-term histologic response to synthetic and biologic graft materials implanted in the vagina and abdomen of a rabbit model. Am J Obstet Gynecol 2009; 200: 546.e1-8.
22. Brown CN, Finch JG. Which mesh for hernia repair? Ann R Coll Surg Engl 2010; 92: 272-278.