EXPERIMENTAL STUDY

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Role of anti-adhesive barriers following rotator cuff repair surgery: an experimental study

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Objective: This experimental study investigates the effectiveness of expanded polytetrafluoroethylene (Dualmesh®, Gore Medical, Flagstaff, AZ, USA), sodium hyaluronate-carboxymethyl cellulose (Seprafilm®, Genzyme, Cambridge, MA, USA), and polysiloxane (silicone) as anti-adhesive barriers for inhibition of fibrosis in the subacromial area following rotator cuff repair.

Methods: Rabbit rotator cuff tenotomy and repair was conducted on 24 rabbits in 4 groups: control (Group A), Dualmesh® (Group B), Seprafilm® (Group C), and silicone (Group D). Anti-adhesive barrier materials were sutured over the repaired rotator cuff. Macroscopic and histological evaluations were made at the end of the sixth postoperative week.

Results: Macroscopic evaluation revealed that minimal adhesion occurred in the control and silicone groups, while the Seprafilm® and Dualmesh® groups showed evidence of fibrosis. Microscopic evaluation revealed diffuse fibrosis and collagen accumulation in the Dualmesh® and Seprafilm® groups, whereas minimal collagen deposition and inflammatory cell reaction was found among the silicone and control groups. Significant differences were found between the silicone and Dualmesh® ($p=0.001$) and silicone and Seprafilm® groups ($p=0.002$), as well as between the control and Dualmesh® ($p=0.002$) and control and Seprafilm® groups ($p=0.002$).

Conclusion: Expanded polytetrafluoroethylene (ePTFE/Dualmesh®) and sodium hyaluronate carboxymethyl cellulose (SH-CMC/Seprafilm®) did not prevent or attenuate postoperative subacromial fibrosis following cuff tear repair. Nor did silicone prevent or attenuate fibrosis. More detailed research is needed for development of an effective anti-adhesive barrier for use after rotator cuff tear surgery.

Keywords: Antiadhesive barrier; rotator cuff; subacromial fibrosis.

Recovery from rotator cuff tear surgery and regaining of shoulder joint functions are impacted by a number of environmental and biological factors. Successful results depend on effective repair and early rehabilitation to restore motion.[1] Postoperative adhesions and fibrosis of the joint capsule and the subacromial area produce un-

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satisfactory results. Early motion is the standard practice to prevent shoulder stiffness following surgery. Few reports of experimental and clinical results have been published regarding prevention of stiffness and promotion of motion following cuff repair in order to decrease fibrosis in the subacromial area during the tendon healing process.

In this study, we investigated the effectiveness of certain synthetic surface materials for prevention of adhesions in the subacromial region following the repair of rotator cuff tear. In 1971, Hunter introduced a technique using Dacron-reinforced silicone tendon prosthesis for 2-stage flexor tendon reconstruction. This prosthesis, together with early active motion, enabled a proper environment for tendon gliding and nourishment for the second stage of tendon reconstruction.[2] Based on this mechanism, it might theoretically be beneficial to use polysiloxane (silicone) sheet to prevent adhesion and promote gliding in the subacromial space. Another surface agent with anti-adhesive characteristics is expanded polytetrafluoroethylene (ePTFE, commercially Dualmesh® [Gore Medical, Flagstaff, AZ, USA]). This material is a nonabsorbable synthetic sheet with dual surface characteristics, used particularly in abdominal and pelvic laparotomies, and as a defect filler for hernia repairs. One surface of the sheet provides an environment for increased tissue adhesion and proliferation, whereas the other surface prevents adhesion. This synthetic prosthetic material has been reported to produce favorable clinical results in laparoscopic and open ventral and inguinal abdominal wall reconstructions, as well as chest wall reconstructions, and experimentally in the prevention of peridural fibrosis.[3–6] In this study, we hypothesized that ePTFE promotes tendon healing on the repair site as well as prevents adhesion on the subacromial surface. Another material investigated in the study is sodium hyaluronate-carboxymethylcellulose (SH-CMC, commercially Seprafilm® [Genzyme, Cambridge, MA, USA]). This material is a biodegradable membrane used in abdominal surgery as an adhesion inhibitor interface, which is hypothesized to prevent adhesion between the repaired tendon and acromion.[7]

The study aims to evaluate the anti-adhesive function of ePTFE (Dualmesh®), SH-CMC (Seprafilm®), and silicone in a rabbit rotator cuff tenotomy-repair model.

Materials and methods

This study was conducted with the approval and supervision of the local animal studies ethical board.

The study included 4 groups of rabbits: Dualmesh® (ePTFE), Seprafilm® (SH-CMC), silicone (polysiloxane), and control groups. In order to obtain a statistically significant result, 24 1-month-old (approx. 3000 g) New Zealand rabbits were used.

Following appropriate anesthesia and preparation, the subacromial space was approached through an approximately 4-cm skin incision on the lateral aspect of the left shoulder over the scapulohumeral joint. The deltoid muscle fibers were retracted to reach the subacromial area. Acromioplasty was made with a thin rasp, followed by a full-thickness transverse cut to the supraspinatus tendon 0.5–1 cm proximal to its insertion to the humerus (Figure 1). The iatrogenic tear was primary repaired using 3/0 Ethibond® sutures (Johnson & Johnson, Neenah, WI, USA) (Figure 2). Afterwards, materials to be investigated (Seprafilm®, Dualmesh®, silicone) were sutured on the repaired supraspinatus tendon with fine sutures (Figure 3), taking care not to induce a bulky mass on the repair area. Special care was taken in the Dualmesh® group to suture the sheet correctly, with the adhesive surface against the tendon. Following the suturing of the investigational material, unrestricted range of motion (ROM) was noted intraoperatively. Fascia and

Fig. 1. Surgically induced full thickness supraspinatus tear. [Color figures can be viewed in the online issue, which is available at www.aott.org.tr]

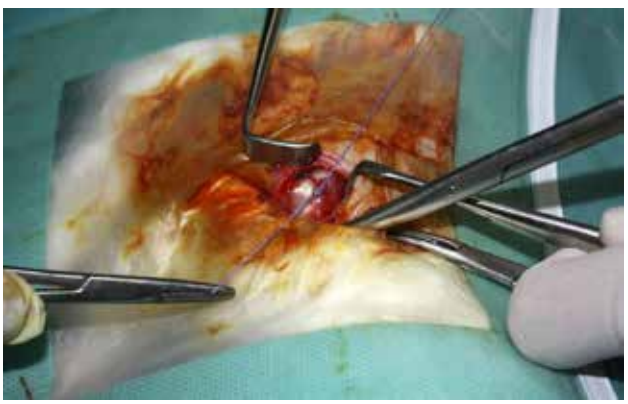

Fig. 2. Primary repair of the tear. [Color figures can be viewed in the online issue, which is available at www.aott.org.tr]

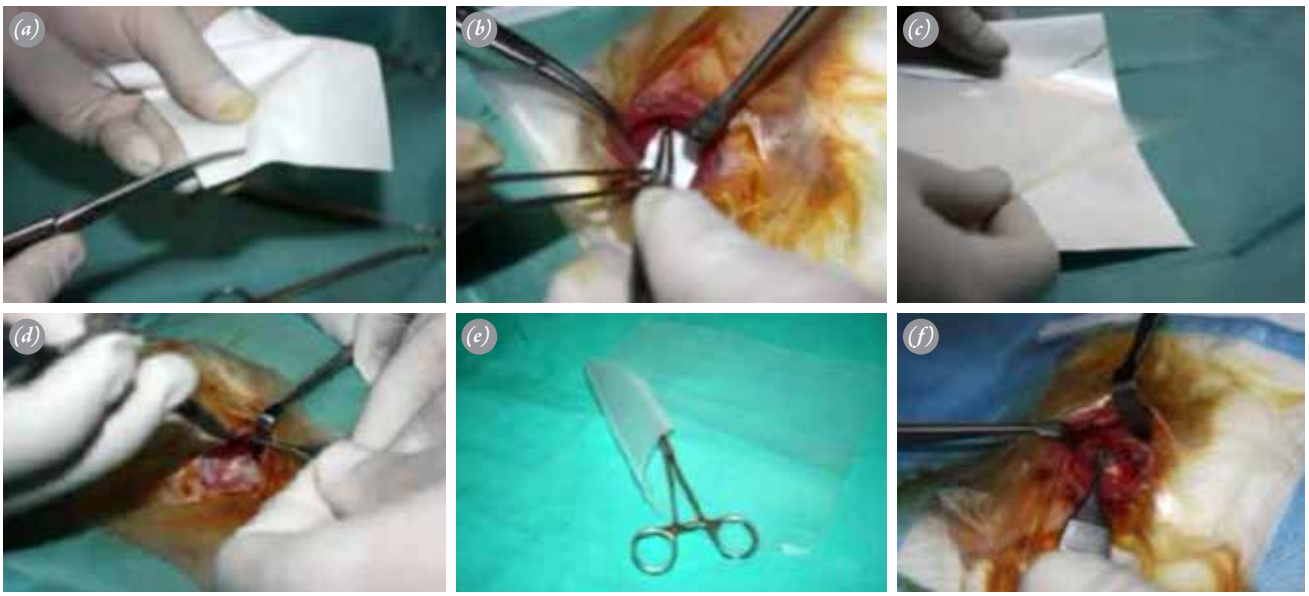

Fig. 3. Anti-adhesive barrier sheets and their application; Dualmesh® **(a, b)**, Seprafilm® **(c, d)**, silicone **(e, f)**. [Color figures can be viewed in the online issue, which is available at www.aott.org.tr]

skin were closed appropriately, and the subjects were returned to their cages without any method of activity restriction or immobilization. All rabbits were taken under routine care with appropriate care until the end of the experimental period.

The animals were sacrificed at the end of the sixth postoperative week. At necropsy, the subacromial area was approached through the previous incision, and the space was macroscopically investigated. Macroscopic assessment was made using the adhesion scale developed by Garrard et. al.[8] (Table 1). Specimens 5x5 mm in size were collected from the subacromial area for routine assessment and histological analysis. The collected tissues were stained with hematoxylin-eosin and Masson's trichrome to evaluate the inflammatory cell reaction and collagen deposition. Histopathological evaluations of the specimens were made based on the criteria defined by Ozog et. al.[9] (Table 2). The highest score was accepted as the score of the subject. Statistical analyses of the data were performed using the Kruskal-Wallis nonparametric test and the Bonferroni correction. A p value <0.05 was set as the level of significance. Results were given as median and min–max.

Table 1. Garrard et al. adhesion scale.[8]

Type of adhesion	Score
No adhesions	1
Filmy adhesions, easily broken manually	2
Dense adhesions, requiring blunt dissection	3
Very dense adhesions requiring sharp dissection	4

Results

None of the specimens were lost during surgery or postoperatively, and no adverse reaction such as infection or functional limitation was observed.

Results of the macroscopic inspection are detailed in Table 3. Minimal adhesion was observed in the control group and the silicone group (median scores:

Table 2. Ozog et al. histological scoring system for collagen deposition and inflammatory cell reaction.[9]

	Score			
	None (0)	Minimal (1)	Mild (2)	Extensive (3)
Collagen deposition	0	1	2	3
Inflammatory cell reaction*				
Eosinophils/neutrophils	0	1–5	6–10	>10
Macrophages/foreign body giant cells	0	1–5	6–10	>10
Mononuclear cells	0	1–5	6–10	>10

*Number of cells per high-power field (400x magnification).

Table 3. Results of macroscopic evaluation of subacromial space.

Macroscopic adhesion	Score	
	Median	Min–max
Control	1	1–2
Dualmesh®	3	3–4
Seprafilm®	4	3–4
Silicone	1	1–3

Table 4. Results of histopathological evaluation.

	Score	
	Median	Min–max
Control	0	0–1
Dualmesh®	2	2–3
Seprafilm®	3	2–3
Silicone	0	0–1

1 and 1, respectively). No fibrosis was observed with silicone film, and ROM was similar to that of the uninvolved shoulder. No difference was observed between the control group and the silicone group. Adversely, the Dualmesh® and Seprafilm® groups displayed substantial fibrosis (median scores: 3 and 4, respectively). The sheets were embedded on a fibrous envelope, and ROM was severely restricted compared to the uninvolved shoulder. Intergroup analyses indicated significant differences between the Dualmesh® and control groups, as well as between the Seprafilm® and control groups (p=0.002 and p=0.002, respectively). Similarly, significant difference were observed between both the Dualmesh® and Seprafilm® groups and the silicone group (p=0.001 and p=0.002, respectively). There was no difference noted between the Dualmesh® and Seprafilm® groups.

Microscopic evaluation results are listed in Table 4 and shown in Figure 4. Similar to the macroscopic evaluation results, low collagen accumulation and inflammatory cell reaction were observed in the silicone and control groups (Figures 4a, b, g, h). In the Dualmesh® and Seprafilm® groups, increased inflammatory cell infiltration areas accompanied by multinuclear giant cells and increased collagen deposition with muscle fibrosis and increased synovial proliferation were seen (Figures 4c-f). Specifically, the fibrotic surface of Dualmesh® specimens showed intense fibrosis, and bands of fibrosis were also noted on the nonfibrotic surface. Analyses of microscopic evaluation scores showed outcomes similar to those of the macroscopic assessments. The Dualmesh® and Seprafilm® groups had higher scores than the control and silicone groups (Table 4). Significant differences were observed between the Dualmesh® and control groups, and also the Seprafilm® and control groups (p=0.002 and p=0.002, respectively). Similarly significant differences were observed between the Dualmesh® and silicone groups, and also the Seprafilm® and silicone groups (p=0.002 and p=0.002, respectively). Similar to the macroscopic results, the differences between the silicone-control groups and Dualmesh®-Seprafilm® groups were not significant.

Discussion

Adhesion following tendon repair is a problem which causes loss of ROM and the necessitation of further treatment. Prevention of adhesions directly impacts the treatment process, patient satisfaction, and return to normal daily life. Although arthroscopic surgery is currently widely preferred, adhesions following these procedures still occur. Additionally, prolonged postoperative immobilization may accentuate arthrofibrosis. Rehabilitation, manipulation under anesthesia, and arthroscopic or open release may be required for further treatment.[10,11]

Use of ePTFE (Dualmesh®) has provided successful results as a defect restorer and adhesion inhibitor, especially on abdominal surgery. No adhesion was reported in 91% of cases reoperated following laparoscopic ventral incisional hernia repair using synthetic meshes,[12] which have been shown to induce good structural support as well as reduce fibrosis.[13] ePTFE was used as a tendon prosthesis for massive irreparable supraspinatus tears. Although good results have been anecdotally reported in case series, the exact mechanism of tendon healing, incorporations, and function have yet to be determined.[14] Theoretically, it is beneficial to induce fibrous tissue proliferation while avoiding fibrosis on the opposite surface, which is desirable on cuff repair surgery. In our study, Dualmesh® was sutured over the repaired tendon in the subacromial interval, aiming to protect the repair area as well as decrease adhesion, thus preserving mobility. Reviewing the macroscopic results, it was noted that the adhesive surface of the material showed fibrous tissue penetration, and the anti-adhesive surface of the material formed uniform fibrotic bands. However, microscopic inspection revealed foreign material reaction, muscle tissue-related fibrosis, necrosis of muscle tissue, fibrosis, and the thickening of the synovial membrane, all of which negatively impact the repair. These results may be explained by the foreign body reaction which took place in the subacromial space, which is a highly reactive synovial environment, especially during a cuff repair setting. Further studies are necessary for use of ePTFE as a motion-preserving repair area protector.

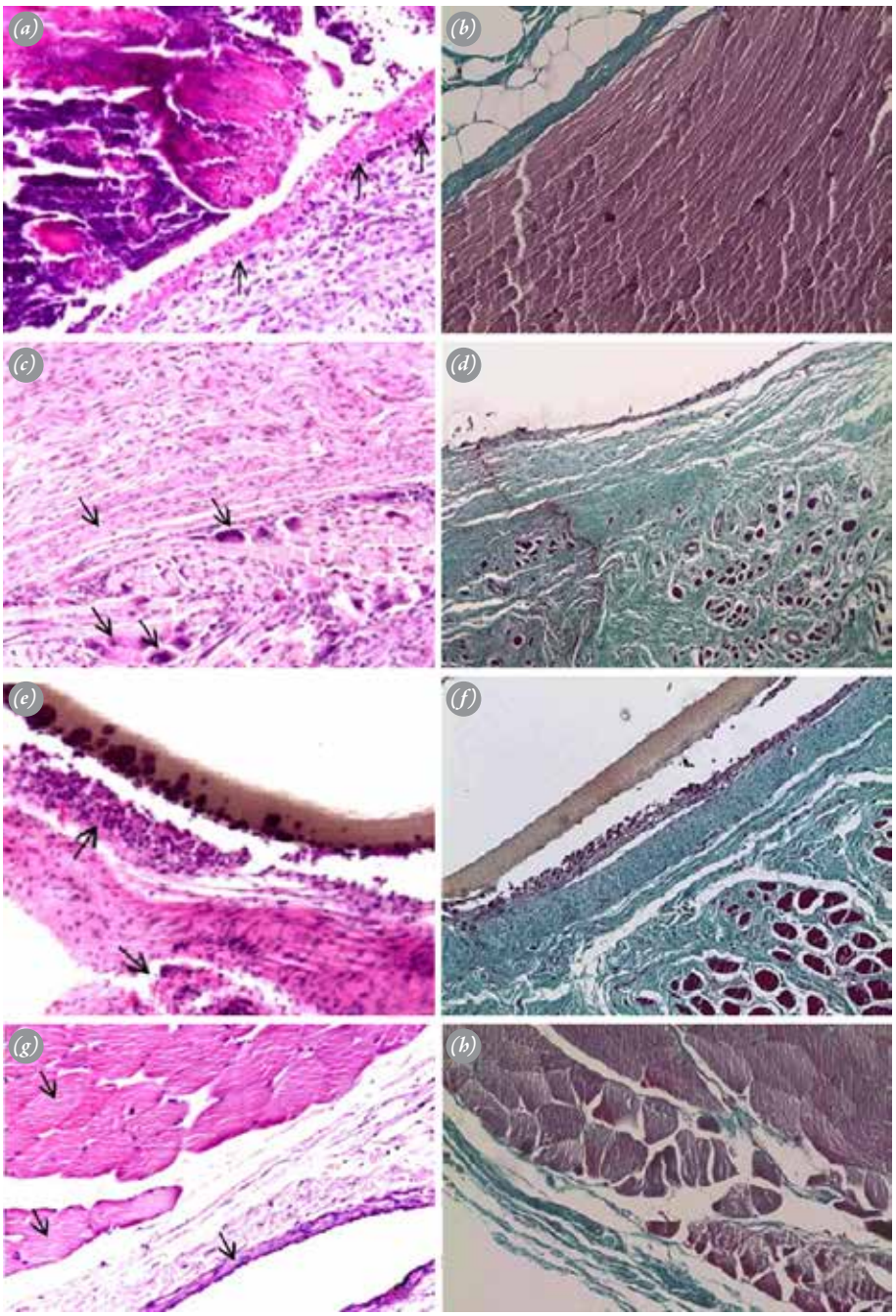

Fig. 4. Photographs of the specimens with hematoxylin-eosin **(a, c, e, g)** and Masson's trichrome **(b, d, f, h)** staining. While the control **(a, b)** and silicone groups **(g, h)** showed minimal inflammatory cell infiltration and growth of connective tissue, the Dualmesh® **(c, d)** and Seprafilm® groups **(e, f)** showed increased areas of inflammatory cell infiltration accompanied by multinuclear giant cells and apparent collagen deposition. [Color figures can be viewed in the online issue, which is available at www.aott.org.tr]

SH-CMC is a biodegradable membrane which has been shown to be effective in abdominal and pelvic surgeries, as well as on tendon and nerve repairs as an adhesion inhibitor. Beck et al. observed more than 1791 patients who received abdominopelvic surgery and concluded that Seprafilm® created a safe barrier preventing adhesion.[15] Other studies have reported favorable results with Seprafilm® application following tendon repair.[16] Studies evaluating the use of injectable SH-CMC following rotator cuff repair have reported good clinical outcomes.[17] SH-CMC membrane is used on subacromial space to provide a uniform surface with

enhanced gliding characteristics, thus favoring motion. The only noted issue with SH-CMC membrane in our study was the difficulty of implantation due to the fragility of the material. Although good results were reported in previous clinical and experimental studies, the results obtained in the current study were unfavorable. This may be attributable to the foreign body reaction which took place (similar to ePTFE) and difference of tissue that had been investigated anatomically (supraspinatus vs leg flexor). Therefore, further studies on the anti-adhesive effect of SH-CMC membrane in rotator cuff tear surgery are needed.

Polysiloxane (silicone) was selected as the Group D experimental material based on the Hunter's tendon prosthesis.[2] It was theorized in our study that application of silicone film over the subacromial area would prevent fibrosis by acting as a barrier. Macroscopic results were similar to those of the control group, and there was no significant difference. The implant was easily extracted from the area of application at necropsy, and when inspected microscopically, it was noted that the implant had no negative impact on adhesion to the material and healing of the muscle tissue. This effect is due to the inert nature of the material and surface characteristics, which neither induced nor inhibited fibrosis.

There are some limitations of the present study. One of the controversial aspects of this study is the rabbit supraspinatus tenotomy and repair model that was used. This model was used previously to evaluate intrinsic tendon healing properties.[18] It was also shown that the bursa and underlying bone contribute to the repair tissue, not the tendon itself.[19] Therefore, covering of the repair area with a fibrosis inhibitor interface to avoid excessive fibrous reaction and a generalized fibrotic process appeared to be an appropriate procedure. However, the results obtained did not support this hypothesis. Although no healing problems were encountered in the current study, inserting a foreign material between the repair area and subacromial space appeared to have a negative impact on tissue healing. Another drawback of this study is the animal model that was used. The rabbit supraspinatus repair model is a preferred method for evaluation of repair technique, healing quality, and muscle function.[20] Since the rabbit shoulder has only partial similarities to the human rotator cuff, findings obtained in these studies can rarely be adapted to the clinical setting. However, we believe that the clearly unfavorable results obtained with some techniques in the current study are significant in terms of their application to human rotator cuff surgery.

Anti-adhesion barrier sheets produced from ePTFE, SH-CMC, and silicone did not produce better results than the non-treatment control in terms of reduction of subacromial fibrosis after supraspinatus repair in a rabbit model. Future studies are necessary to develop a safe and effective nonreactive anti-adhesive biomaterial to avoid fibrosis following cuff tear surgery.

Conflicts of Interest: No conflicts declared.

References

1. Ross D, Maerz T, Lynch J, Norris S, Baker K, Anderson K. Rehabilitation following arthroscopic rotator cuff repair: a review of current literature. J Am Acad Orthop Surg 2014;22:1–9. CrossRef
2. Hunter JM, Salisbury RE. Flexor-tendon reconstruction in severely damaged hands. A two-stage procedure using a silicone-dacron reinforced gliding prosthesis prior to tendon grafting. J Bone Joint Surg Am 1971;53:829–58.
3. Akiba T, Marushima H, Nogi H, Kamiya N, Kinoshita S, Takeyama H, et al. Chest wall reconstruction using Gore-Tex® dual mesh. Ann Thorac Cardiovasc Surg 2012;18:166–9. CrossRef
4. Aura T, Habib E, Mekkaoui M, Brassier D, Elhadad A. Laparoscopic tension-free repair of anterior abdominal wall incisional and ventral hernias with an intraperitoneal Gore-Tex mesh: prospective study and review of the literature. J Laparoendosc Adv Surg Tech A 2002;12:263–7.
5. DiFazio FA, Nichols JB, Pope MH, Frymoyer JW. The use of expanded polytetrafluoroethylene as an interpositional membrane after lumbar laminectomy. Spine (Phila Pa 1976) 1995;20:986–91. CrossRef
6. Treviño JM, Franklin ME Jr, Berghoff KR, Glass JL, Jaramillo EJ. Preliminary results of a two-layered prosthetic repair for recurrent inguinal and ventral hernias combining open and laparoscopic techniques. Hernia 2006;10:253–7.
7. Beck DE. The role of Seprafilm bioresorbable membrane in adhesion prevention. Eur J Surg Suppl 1997;577:49–55.
8. Garrard CL, Clements RH, Nanney L, Davidson JM, Richards WO. Adhesion formation is reduced after laparoscopic surgery. Surg Endosc 1999;13:10–3. CrossRef
9. Ozog Y, Konstantinovic ML, Verschueren S, Spelzini F, De Ridder D, Deprest J. Experimental comparison of abdominal wall repair using different methods of enhancement by small intestinal submucosa graft. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:435–41. CrossRef
10. Elhassan B, Ozbaydar M, Massimini D, Higgins L, Warner JJ. Arthroscopic capsular release for refractory shoulder stiffness: a critical analysis of effectiveness in specific etiologies. J Shoulder Elbow Surg 2010;19:580–7. CrossRef
11. Vezeridis PS, Goel DP, Shah AA, Sung SY, Warner JJ. Postarthroscopic arthrofibrosis of the shoulder. Sports Med Arthrosc 2010;18:198–206. CrossRef

12. Koehler RH, Begos D, Berger D, Carey S, LeBlanc K, Park A, et al. Minimal adhesions to ePTFE mesh after laparoscopic ventral incisional hernia repair: reoperative findings in 65 cases. JSLS 2003;7:335–40.
13. Deeken CR, Abdo MS, Frisella MM, Matthews BD. Physicomechanical evaluation of absorbable and nonabsorbable barrier composite meshes for laparoscopic ventral hernia repair. Surg Endosc 2011;25:1541–52. CrossRef
14. Arora M, Khedekar RG, Shetty SH, Parikh M. Polytetrafluoroethylene patches for massive rotator cuff tears: An update of current concepts. J Arthrosc Joint Surg 2015;2:12–5. CrossRef
15. Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, Wolff BG; Adhesion Study Group Steering Committee. A prospective, randomized, multicenter, controlled study of the safety of Seprafilm adhesion barrier in abdominopelvic surgery of the intestine. Dis Colon Rectum 2003;46:1310–9. CrossRef
16. Yilmaz E, Avci M, Bulut M, Kelestimur H, Karakurt L, Ozercan I. The effect of seprafilm on adhesion formation and tendon healing after flexor tendon repair in chicken. Orthopedics 2010;33:164–70. CrossRef
17. Oh CH, Oh JH, Kim SH, Cho JH, Yoon JP, Kim JY. Effectiveness of subacromial anti-adhesive agent injection after arthroscopic rotator cuff repair: prospective randomized comparison study. Clin Orthop Surg 2011;3:55–61. CrossRef
18. Choi HR, Kondo S, Hirose K, Ishiguro N, Hasegawa Y, Iwata H. Expression and enzymatic activity of MMP-2 during healing process of the acute supraspinatus tendon tear in rabbits. J Orthop Res 2002;20:927–33. CrossRef
19. Uhthoff HK, Sano H, Trudel G, Ishii H. Early reactions after reimplantation of the tendon of supraspinatus into bone. A study in rabbits. J Bone Joint Surg Br 2000;82:1072–6. CrossRef
20. Gupta R, Lee TQ. Contributions of the different rabbit models to our understanding of rotator cuff pathology. J Shoulder Elbow Surg 2007;16(5 Suppl):149–57. CrossRef