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Experimental Study / Deneysel Çalışma

Combined use of barrier methods to prevent pericardial adhesions: Is it always better?

Perikardiyal adezyonları önlemede bariyer yöntemlerin kombine kullanımı: Her zaman daha iyi midir?

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ABSTRACT

Background: This study aims to investigate the effects of combined and individual use of pericardial closure, expanded polytetrafluoroethylene membrane and resorbable adhesion barrier (REPEL-CV®) on pericardial adhesions on a rabbit model.

Methods: Thirty rabbits were randomly assigned to six groups: control, pericardium, expanded polytetrafluoroethylene, resorbable membrane, expanded polytetrafluoroethylene + resorbable membrane, and pericardium + resorbable membrane. At the postoperative five weeks, the tenacity of the adhesions was evaluated using a qualitative grading system, and histological specimens were examined.

Results: Resorbable membrane group had significantly lower tenacity scores, compared to the control, pericardium, and expanded polytetrafluoroethylene groups ($p<0.01$). The scores of the expanded polytetrafluoroethylene + resorbable membrane and pericardium + resorbable membrane groups were lower than the control group ($p<0.05$ and $p<0.01$ respectively). Combined use of resorbable membrane, compared to the solitary use, did not produce significantly different tenacity scores. Macroscopically, in the resorbable membrane group after sternotomy, there were filmy adhesions over the epicardium which could be easily dissected digitally. In the expanded polytetrafluoroethylene + resorbable membrane and pericardium + resorbable membrane groups, there were also adhesions beneath the sternum.

Conclusion: Resorbable membrane was effective in reducing postoperative pericardial adhesions when used alone or in combination with expanded polytetrafluoroethylene membrane or pericardial closure. Solitary use of resorbable membrane, compared to combined use, can be preferable, since the addition of expanded polytetrafluoroethylene membrane and pericardial closure increase substernal fibrosis.

Keywords: Biocompatible materials; reoperation; surgical adhesions.

ÖZ

Amaç: Bu çalışmada bir tavşan modeli üzerinde perikard kapatılması, genişletilmiş politetrafloroetilen (ePTFE) membran ve rezorbe edilebilen adezyon bariyerinin (REPEL-CV®) kombine ya da ayrı ayrı kullanımının perikardiyal adezyonlar üzerine etkileri araştırıldı.

Çalışma planı: Otuz tavşan altı gruba randomize edildi: kontrol, perikard, genişletilmiş politetrafloroetilen, rezorbe edilebilen membran, genişletilmiş politetrafloroetilen + rezorbe edilebilen membran ve perikard + rezorbe edilebilen membran. Ameliyat sonrası beşinci haftada yapışıklıkların yoğunluğu kalitatif bir derecelendirme sistemi kullanılarak değerlendirildi ve histolojik örnekler incelendi.

Bulgular: Rezorbe edilebilen membran grubunun tenasite skorları kontrol, perikard ve genişletilmiş politetrafloroetilen gruplarına kıyasla, anlamlı düzeyde düşük bulundu ($p<0.01$). Genişletilmiş politetrafloroetilen + rezorbe edilebilen membran ve perikard + rezorbe edilebilen membran gruplarının skorları, kontrol grubuna kıyasla, daha düşük bulundu (sırasıyla $p<0.05$ ve $p<0.01$). Rezorbe edilebilen membranın kombine kullanımında, tek başına kullanımına kıyasla, skorlarda anlamlı farklılık saptanmadı. Makroskopik olarak rezorbe edilebilen membran grubunda sternotomi sonrası perikard üzerinde parmak ile kolayca diseke edilebilir ince yapışıklıklar vardı. Genişletilmiş politetrafloroetilen + rezorbe edilebilen membran ve perikard + rezorbe edilebilen membran gruplarında sternum altında da yapışıklıklar izlendi.

Sonuç: Rezorbe edilebilen membran tek başına ya da genişletilmiş politetrafloroetilen membran veya perikard kapatılması ile kombine olarak kullanıldığında, perikardiyal adezyonları azaltmada etkiliydi. Genişletilmiş politetrafloroetilen membran ve perikardium kapanması substernal fibrozisi artırdığından, rezorbe edilebilen membranın kombine kullanımından ziyade tek başına kullanımı tercih edilebilir.

Anahtar sözcükler: Biyouyumlu malzemeler; tekrar ameliyat; cerrahi adezyonlar.

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Adhesion formation can prove to be problematic in various surgical disciplines. The risk increases, particularly in congenital cardiac surgery where the staged operations and not uncommon recurrent lesions augment the number of patients requiring redo surgery. In addition, cardiac surgery is prominent in the sense of the vitality of the structures under the risk of injury during these operations. This increased risk has been demonstrated on various cohorts of patients. This is the primary rationale of the ongoing research to effectively reduce the formation of pericardial adhesions.

Several methods which have been investigated to manage pericardial adhesions involve fibrinolytic agents to activate intrapericardial fibrosis, control inflammatory response through anti-inflammatory agents, using permanent physical barriers and to prevent early fibrin deposition on pericardial surfaces by resorbable barriers.[1] Among these methods, fibrinolytic agents have caused serious postoperative bleeding in the initial trials[2] and were not, therefore, further studied. Although anti-inflammatory agents have been shown to be effective in the experimental studies,[3,4] their potential for systemic side effects is an important drawback for their widespread use. Permanent physical barriers involve pericardial closure and use of expanded polytetrafluoroethylene (ePTFE) membrane as a pericardial substitute. Although these methods effectively keep the heart apart from the sternum, their main disadvantage is that they are unable to prevent fibrosis formation.[5,6] Among the aforementioned methods, resorbable barriers to prevent early fibrin deposition have been most widely investigated.

Materials used as a resorbable barrier involve polylactic acid,[7,8] sprayable polyethylene glycol,[9] porcine collagen membrane,[10] hyaluronic acid membrane,[11,12] hyaluronic acid/carboxymethyl cellulose solution,[13] and polyethylene glycol/polylactic acid membrane.[14,15] Among these materials, polyethylene glycol/polylactic acid membrane[16] and hyaluronic acid membrane[17] have been shown to decrease pericardial adhesions when used in combination with ePTFE membrane, compared to the isolated use of ePTFE membrane. However, there is no consensus on whether resorbable barriers are more effective when used alone or in combination with an ePTFE membrane.

In the present study, we aimed to investigate whether the solitary use of a resorbable barrier, namely polyethylene glycol/polylactic acid, was more effective in solitary use, compared to the combined use with ePTFE membrane and pericardial closure.

MATERIALS AND METHODS

The ePTFE prosthetic membrane (Gore PRECLUDE Pericardial Membrane; WL Gore & Associates, Inc., Flagstaff, Arizona, USA), a non-resorbable pericardial substitute, had a thickness of 0.1 mm and was cut in 4x4 cm sized squares. The resorbable adhesion barrier (REPEL-CV Adhesion Barrier, SyntheMed, Inc., Iselin, NJ, USA) was composed of polyethylene glycol/polylactic acid ratio of 1.5. It was soaked in saline at room temperature for two min before use and was also used in the form of 4x4 cm squares. This product was designed to provide an inert mechanical barrier between the heart and sternum to limit the adhesion formation. It is mostly absorbed within 1 to 2 days.[18]

This study was conducted between November 2014 and June 2016. The Animal Experiments Local Ethics Committee approved the study protocol with the registration number 2013/63-03. Thirty New Zealand albino male rabbits weighing between 2.2 and 3.8 kg were randomly assigned to six groups of five rabbits in each: control, pericardium, ePTFE, resorbable membrane, ePTFE + resorbable membrane, and pericardium + resorbable membrane. All underwent an abrasion protocol. In the control group, the pericardium was left open after the abrasions. In the pericardium group, the pericardium was closed primarily using 5-0 polypropylene (Prolene, Ethicon Inc., Cincinnati, OH, USA) interrupted sutures. In the ePTFE group, ePTFE membrane was used to repair the pericardial defect by interrupted 5-0 polypropylene sutures. In the resorbable membrane group, polyethylene glycol/polylactic acid membrane was placed on the surface of the heart and attached to the edges of the pericardium by interrupted 5-0 polypropylene sutures. In the ePTFE + resorbable membrane group, polyethylene glycol/polylactic acid membrane was placed on the surface of the heart and attached to the pericardium by interrupted 5-0 polypropylene sutures and ePTFE membrane was placed outer to polyethylene glycol/polylactic acid and attached to pericardium by interrupted 5-0 polypropylene sutures. In the pericardium + resorbable membrane group, polyethylene glycol/polylactic acid membrane was attached to the pericardium in the same manner and the pericardium was closed primarily.

The rabbits were anesthetized using 55 mg/kg intramuscular ketamine (Ketalar, Pfizer İlaçları Ltd. Şti., İstanbul, Turkey) and 5 mg/kg xylazine (Alfazyne %2, Ege Vet Hayvancılık San. ve Tic. Ltd. Şti., İzmir, Turkey). Spontaneous breathing was maintained to avoid mechanical ventilation. The fur on the chest was shaved and the surgical site was disinfected using povidone-iodine solution.

Midline sternotomy was performed from the second intercostal space to the xiphoid process using straight surgical scissors taking care not to injure the pleura or the pericardium. The pericardium over the right ventricle was opened longitudinally about 3 cm in length. The epicardium of the right ventricle was abraded 10 times with sterile gauze to create micro-hemorrhages to induce adhesion formation. The pericardium was closed based on the group properties described above. The sternum was closed using 2-0 silk sutures. The skin and subcuticular tissue were closed in continuous fashion using 3-0 polyglactin (Vicryl, Ethicon Inc., Cincinnati, OH, USA) sutures. The rabbits were injected intramuscular sulbactam/ampicillin and paracetamol and taken to the cages after waking up in responsive condition. They were followed on a standard diet.

Five weeks after the operation each rabbit was euthanized by exsanguination under the same anesthetic protocol. The anterior chest wall was removed *en bloc* with the heart. The adhesions of epicardium to pericardium and sternum were macroscopically evaluated by two cardiac surgeons blinded to the process of the experiment and the materials which were used. A qualitative grading system was used to evaluate the tenacity of the adhesions: 0, without adhesions; 1, filmy, light, with a foamy dissection plane without bleeding; 2, required some sharp dissection, but most of them were lyzed by digital manipulation and this process resulted in moderate bleeding; 3, dense, easily bleeding, with marked obliteration of tissue planes and required exclusive sharp dissection.[19]

The *en bloc* specimens were embedded fixed in 10% formaldehyde. Full-thickness gross sections from sternal internal periosteum to right ventricular myocardium were taken from each specimen at the site where the maximum adhesions were observed. These samples were embedded in paraffin and sectioned into 5 μm slices. Hematoxylin-eosin staining was performed for light microscopic evaluation. Additionally, the sections were stained with picrosirius red to identify and quantify the fibrosis formation.

Statistical analysis

Statistical analysis was performed using the PASW Statistics version 17.0 (SPSS Inc., Chicago, IL, USA). The results were expressed in mean ± standard deviation. The Mann-Whitney U test was used to compare data among the groups. A power analysis was conducted using an alpha = 0.05 and beta = 0.80, based on the data from a recent study by Kaushal et al.[16] using similar materials. The projected sample size required for the study was minimum 24 with four rabbits in each group. A p value of less than 0.05 was considered statistically significant.

RESULTS

After five-week follow-up, 30 rabbits were euthanized and the second procedure was performed under direct observation of two independent surgeons. For each rabbit, the mean score of the two evaluating surgeons was recorded and, then, for each group, the mean scores and standard deviations were calculated. Resorbable membrane group had a lower tenacity score (0.2±0.45), compared to the control (2.8±0.45; p=0.005), pericardium (2.5±0.71; p=0.006) and ePTFE groups (2.6±0.71; p=0.006). However, compared to pericardium + resorbable membrane (1.4±0.45) and ePTFE + resorbable membrane groups (1.8±1.06), lower values in the resorbable membrane group did not reach statistical significance (p=0.096 and 0.056 respectively). Although the tenacity scores of the pericardium and ePTFE groups were not significantly different, compared to the control group, the scores of the ePTFE + resorbable membrane and pericardium + resorbable membrane groups were lower ($p<0.05$ and $p<0.01$ respectively) (Table 1).

Macroscopic evaluation

The control group demonstrated marked adhesions of the right ventricle to the pericardium and even to the sternum. Sharp dissection was required to develop a plane of cleavage. In the pericardium group, the right ventricle was not adhered to the sternum directly; however, there were dense adhesions beneath the sternum and between pericardium and

Table 1. Evaluation of tenacity scores

	Control group	Pericardium group	ePTFE group	Resorbable membrane group	ePTFE + resorbable membrane group	Pericardium + resorbable membrane group
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Tenacity score	2.8±0.5	2.5±0.7	2.6±0.6	0.2±0.5	1.8±1.1	1.4±0.5

ePTFE: Expanded polytetrafluoroethylene; SD: Standard deviation.

epicardium. In the ePTFE group, there were dense adhesions between both sternum and the ePTFE membrane; and ePTFE membrane and right ventricular epicardium. The plane of dissection was also dense and required sharp dissection. In the resorbable membrane group, there were virtually no adhesions. There were filmy adhesions over the epicardium following sternotomy, which could be easily dissected digitally. In the groups ePTFE + resorbable membrane and pericardium + resorbable membrane, there were adhesions beneath the sternum. However, once the pericardium or the ePTFE membrane was dissected out, there were little or no adhesions between the ePTFE membrane or the pericardium and the epicardium. The tenacity and visibility were similar to that of the resorbable membrane group (Figure 1).

Microscopic evaluation

In all the specimens, neo-tissue formation was observed lining the myocardium and the adipose tissue as a mesothelium-like cell layer (Figure 2). In the control and pericardium groups, there was a thick fibrous tissue infiltrated with small vessels. In the ePTFE group, fibrosis formation was notable on both sides (epicardial and sternal) of the ePTFE membrane. In the resorbable membrane group and pericardium +

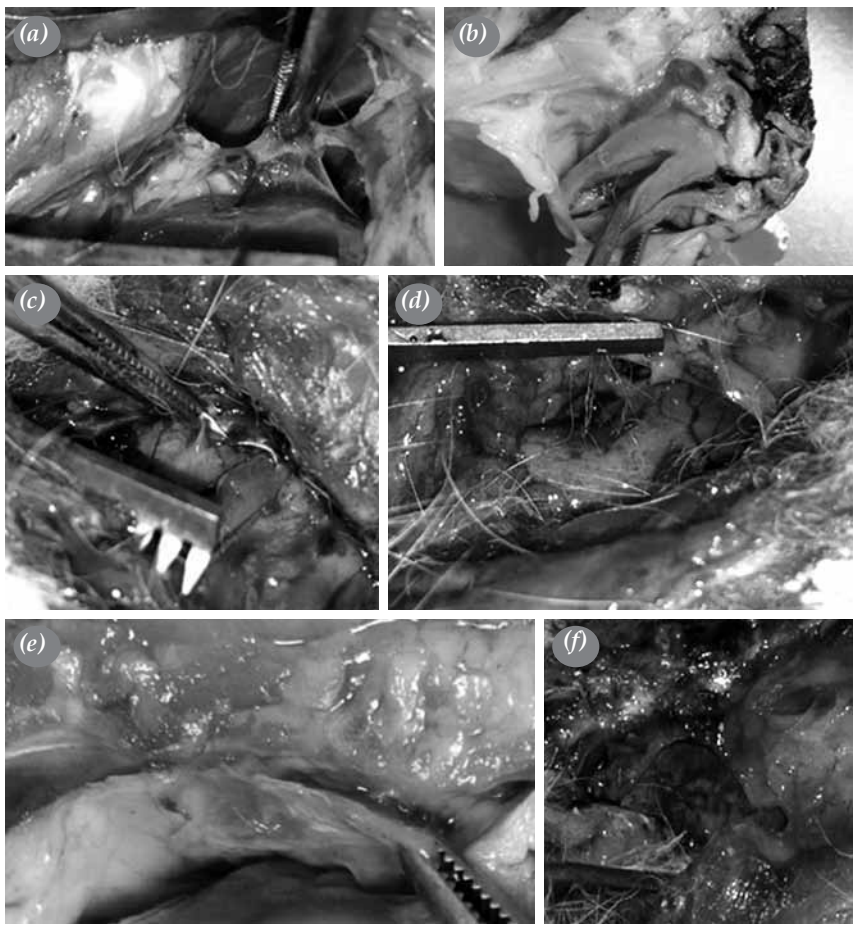

Figure 1. Macroscopic evaluation photographs five weeks after the initial surgery **(a)** High tenacity adhesions through retrosternal region were visible in the control group. **(b)** A pathology specimen from the pericardium group demonstrates adhesions of ventricular epicardium to surrounding pericardium. **(c)** In the ePTFE group dense adhesions of the ePTFE membrane to the sternum and epicardium was visible. **(d)** Resorbable membrane group was almost free of adhesions. Coronary anatomy is clearly visible over the ventricle. **(e)** In the ePTFE + resorbable membrane group adhesion of the ePTFE membrane to the sternum is visible. Adhesions between the ePTFE membrane and the epicardium were minimal. **(f)** Pericardium + resorbable membrane group had dense retrosternal fibrosis. Adhesions between pericardium and myocardium were minimal.
ePTFE: Expanded polytetrafluoroethylene.

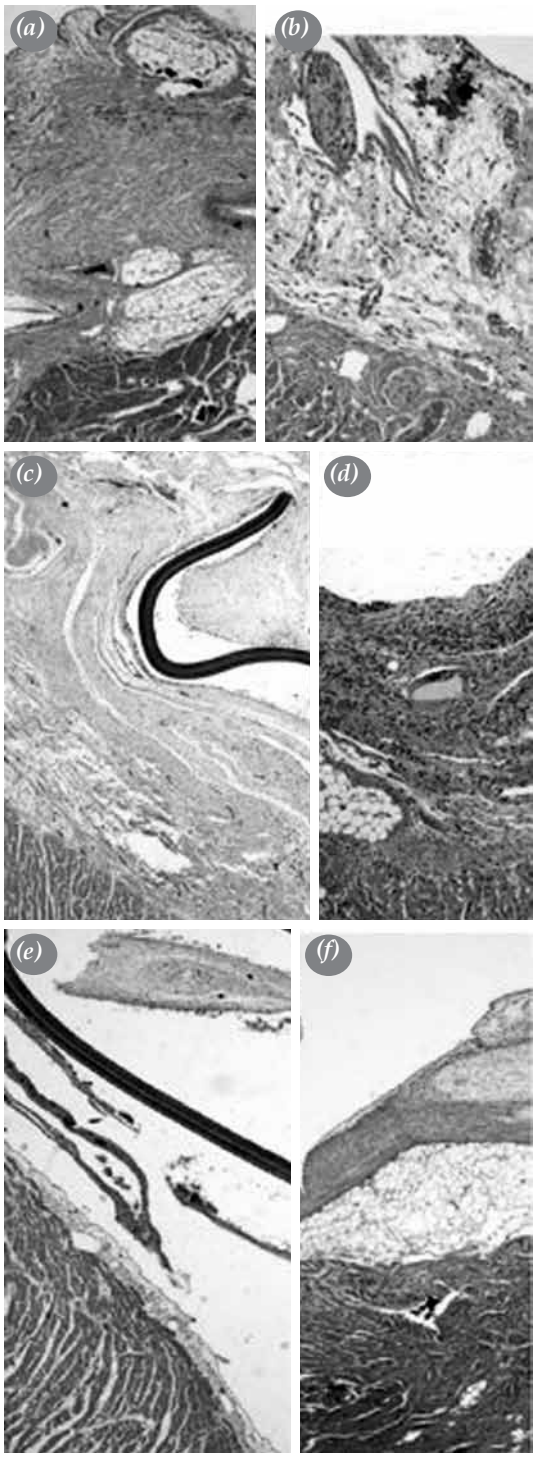

Figure 2. Microscopic evaluations at five weeks postoperatively. **(a)** Control group and **(b)** Pericardium group show thick layers of fibrosis over the myocardium. **(c)** ePTFE group dense fibrosis around the ePTFE membrane. **(d)** In the resorbable membrane group, **(e)** ePTFE + resorbable membrane group and **(f)** Pericardium + resorbable membrane group the layer of fibrosis over the myocardium was relatively thinner (H-E x 40).
ePTFE: Expanded polytetrafluoroethylene.

resorbable membrane group, the fibrous tissue covering the myocardium was thinner, compared to the other groups. In the ePTFE + resorbable membrane group, there was little neo-tissue formation between the epicardium and the membrane. These findings were similar to the macroscopic observations. In addition, in some of the samples in the resorbable membrane group, there were foreign bodies encapsulated in giant cells (Figure 3). These were thought to be remnants of the bio-absorbable membrane. Although the clinical findings for resorbable membrane were favorable, there was a notable inflammatory reaction in some sections.

DISCUSSION

This study demonstrated the efficacy of a resorbable barrier made of polyethylene glycol/polylactic acid membrane in reducing postoperative mediastinal adhesions. Although the solitary use of permanent barrier methods, namely ePTFE membrane and pericardial closure, did not decrease adhesions, compared to control group; their combination with the resorbable barrier yielded favorable results. Solitary use of the resorbable barrier was not statistically superior, compared to its combination with the permanent barriers. However, in combined use, there was more retrosternal fibrosis, compared to solitary use of resorbable barrier, suggesting a conflicting result to the previous reports favoring combined use of ePTFE membrane and resorbable membranes.[16,17]

Pericardial adhesions are the main reason for the increased risk of repeated sternotomy. Although the increased risk of fatal cardiac trauma can be counterbalanced using a meticulous surgical technique, increased operation times and transfusion requirements increase the costs. In a review examining burden caused by repeated sternotomy, Morales et al.[20] reported that the published evidence suggested using certain safety measures in specific clinical scenarios might assist in optimizing clinical outcomes and cost-effectiveness.

Efforts to limit pericardial adhesions have focused on mechanisms of formation of adhesions. The formation of adhesions is induced by a surgical injury which causes bleeding and inflammation. These are the main triggers of fibrin formation. Surgical injury also leads to loss of pericardial mesothelial cells which produce the ground for accumulation of fibrin within seven days postoperatively; this fibrin accumulation is followed by neo-connective tissue formation which generates adhesions in up to 30 days. Subsequently, normal pericardial mesothelial cell growth is observed on the surfaces free of adhesions.[1] Therefore, the basic methods studied to prevent adhesions include

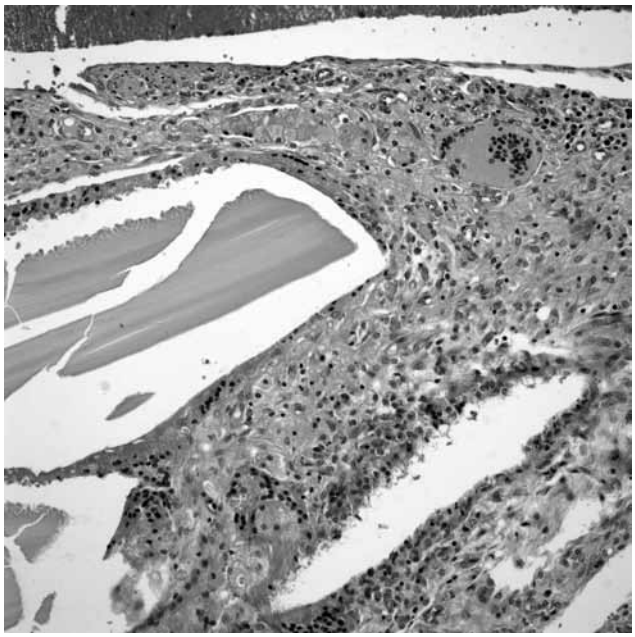

Figure 3. Tissue sample from resorbable membrane group demonstrating foreign body encapsulation and a giant cell (H-E x 200).

fibrinolytic agents,[2] anti-inflammatory agents,[3,4] permanent physical barriers which involve pericardial closure either directly or using an ePTFE membrane as a substitute[5,6] and resorbable barriers to prevent early fibrin deposition[7-17] N-acetyl cysteine have been also shown to reduce adhesions probably through fibroblast inhibition, since it is in liquid form the ideal method of application is still undetermined.[21]

The closure of pericardium has been used as a barrier method to decrease the adhesions.[22] It forms natural physical barrier between the heart and the sternum. However, routine use autogenous pericardium in various congenital cardiac operations and the risk of hemodynamic compromise induced the search for other substitutes. Expanded PTFE has been demonstrated being safe and effective in preventing pericardial adhesions in a retrospective observational study by Jacobs et al.[23] In this multi-center study including 1,085 operations of congenital heart defects, 105 of which were reoperated, injury during resternotomy occurred in one patient only (1%). However, in a more recent animal study by Kuschel et al.,[24] no significant difference of pericardial adhesions was found between the group left uncovered (control) and the group where the pericardial defect was repaired with ePTFE membrane. The authors, therefore, concluded that the macroscopic adhesions observed in this group of patients were the worst of all three groups of the study.

The search for barrier agents which do not induce fibrosis in the long-term has led a branch of research on resorbable barriers. These include polylactic acid,[7,8] sprayable polyethylene glycol,[9] porcine collagen membrane,[10] hyaluronic acid membrane,[11,12] hyaluronic acid/carboxymethyl cellulose solution[13] and polyethylene glycol/polylactic acid membrane.[14,15] These materials act as barriers to reduce fibrin accumulation in the early postoperative phase; and are resorbed after a period approximately one month. Walther et al.[25] also demonstrated the efficacy of hyaluronic acid membrane on a population of congenital heart defects. The study demonstrated a reduction in tenacity score, the extent of the adhesions and duration of the operation. More recently, Kaneko et al.[26] demonstrated similar results. However, in the aforementioned study, some of the patients in hyaluronic acid membrane group had the pericardium left open, some closed and some augmented with ePTFE membrane. The use of ePTFE membrane was associated with higher tenacity scores, compared to the patients where only a resorbable membrane was used. Polyethylene glycol/polylactic acid membrane was studied in another study by Okuyama et al.[27] and was demonstrated to be effective, compared to the control group.

The idea that the combination of a permanent barrier with a resorbable barrier can reduce the fibrosis caused by the permanent barrier inspired a number of authors. In a rabbit model, Kaushal et al.[16] demonstrated that, although solitary use of an ePTFE membrane did not significantly reduce adhesions compared to the control group, solitary use of polyethylene glycol/polylactic acid membrane and its combination with an ePTFE membrane were equally effective. In another study, Naito et al.[17] reported similar findings using the combination hyaluronic acid membrane with ePTFE membrane. These two reports, despite being unable to demonstrate any superiority of the combined use, both concluded that the combined use was advantageous, as an additional layer of physical barrier was retained. The results of the present study are consistent with these two studies in the sense that resorbable membrane effectively reduced adhesions both in solitary use and in combination with an ePTFE membrane or pericardial closure. Additionally, no significant difference was demonstrated between solitary or combined use of the resorbable membrane. On the other hand, the finding that combined use could lead to retrosternal fibrosis is contradictory to the findings of the previous studies.

Clinical use of the findings from this study can be limited by the fact that the adhesion induction

was limited, effect of cardiopulmonary bypass was not included, and there was no major bleeding in the pericardial cavity. In addition, reoperation at five weeks postoperatively might be insufficient to reproduce the adhesions formation after the periods encountered in the clinical practice. The five-week-period for reoperation was selected on the basis that previously pericardial adhesion formation was demonstrated in rabbit models after periods of less than 32 days.[18,27] However, periods used in clinical studies were measured in months to years,[23,28] as expected in the real clinical setting. Longer periods of follow-up can produce clearer data. Also, although the population size generated adequate power to detect the efficacy of solitary or combined use of the resorbable membrane, compared to the control group, some smaller differences among other groups might have required a larger population size to be detected.

In conclusion, polyethylene glycol/polylactic acid membrane was effective in reducing postoperative pericardial adhesions when used alone or in combination with expanded polytetrafluoroethylene membrane or pericardial closure. The combination of resorbable membrane with expanded polytetrafluoroethylene membrane or pericardial closure was not found to be advantageous in this study. Based on these findings, solitary use of a resorbable membrane is advisable, particularly in staged operations, to decrease adhesion formation. Nonetheless, further studies are required to compare the efficacy of various resorbable barriers.

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REFERENCES

1. Cannata A, Petrella D, Russo CF, Bruschi G, Fratto P, Gambacorta M, et al. Postsurgical intrapericardial adhesions: mechanisms of formation and prevention. Ann Thorac Surg 2013;95:1818-26.
2. Wiseman DM, Kamp L, Linsky CB, Jochen RF, Pang RH, Scholz PM. Fibrinolytic drugs prevent pericardial adhesions in the rabbit. J Surg Res 1992;53:362-8.
3. Iskesen I, Aksoy O, Cerrahoglu M, Sirin H. The effect of piroxicam on the prevention of postoperative retrosternal and pericardial adhesions. Acta Cardiol 2007;62:559-64.
4. Alizzi AM, Summers P, Boon VH, Tantiongco JP, Thompson T, Leslie BJ, et al. Reduction of post-surgical pericardial adhesions using a pig model. Heart Lung Circ 2012;21:22-9.
5. Meus PJ, Wernly JA, Campbell CD, Takanashi Y, Pick RL, Zhao-Kun Q, et al. Long-term evaluation of pericardial substitutes. J Thorac Cardiovasc Surg 1983;85:54-8.
6. Bunton RW, Xabregas AA, Miller AP. Pericardial closure after cardiac operations. An animal study to assess currently available materials with particular reference to their suitability for use after coronary artery bypass grafting. J Thorac Cardiovasc Surg 1990;100:99-107.
7. Iliopoulos J, Cornwall GB, Evans RO, Manganas C, Thomas KA, Newman DC, et al. Evaluation of a bioabsorable polylactide film in a large animal model for the reduction of retrosternal adhesions. J Surg Res 2004;118:144-53.
8. Gürbüz O, Ercan A, Biçer M, Kumtepe G, Bayram S, Şenkaya I, Saba D. Evaluation of polylactide film for prevention of pericardial adhesion in a rabbit model. Turk Gogus Kalp Dama 2015;23:98-104.
9. Cannata A, Taglieri C, Russo CF, Bruschi G, Martinelli L. Use of CoSeal in a patient with a left ventricular assist device. Ann Thorac Surg 2009;87:1956-8.
10. Bel A, Kachatryan L, Bruneval P, Peyrard S, Gagnieu C, Fabiani JN, et al. A new absorbable collagen membrane to reduce adhesions in cardiac surgery. Interact Cardiovasc Thorac Surg 2010;10:213-6.
11. Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, Wolff BG. 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.
12. Lefort B, El Arid JM, Bouquiaux AL, Soulé N, Chantreuil J, Tavernier E, et al. Is Seprafilm valuable in infant cardiac redo procedures? J Cardiothorac Surg 2015;10:47.
13. Hong JH, Choe JW, Kwon GY, Cho DY, Sohn DS, Kim SW, et al. The effects of barrier materials on reduction of pericardial adhesion formation in rabbits: a comparative study of a hyaluronan-based solution and a temperature sensitive poloxamer solution/gel material. J Surg Res 2011;166:206-13.
14. Lodge AJ, Wells WJ, Backer CL, O'Brien JE Jr, Austin EH, Bacha EA, et al. A novel bioresorbable film reduces postoperative adhesions after infant cardiac surgery. Ann Thorac Surg 2008;86:614-21.
15. Haensig M, Mohr FW, Rastan AJ. Bioresorbable adhesion barrier for reducing the severity of postoperative cardiac adhesions: Focus on REPEL-CV(®). Med Devices (Auckl) 2011;4:17-25.
16. Kaushal S, Patel SK, Goh SK, Sood A, Walker BL, Backer CL. A novel combination of bioresorbable polymeric film and expanded polytetrafluoroethylene provides a protective barrier and reduces adhesions. J Thorac Cardiovasc Surg 2011;141:789-95.
17. Naito Y, Shin'oka T, Hibino N, Matsumura G, Kurosawa H. A novel method to reduce pericardial adhesion: a combination technique with hyaluronic acid biocompatible membrane. J Thorac Cardiovasc Surg 2008;135:850-6.
18. Rodgers K, Cohn D, Hotovely A, Pines E, Diamond MP,

diZerega G. Evaluation of polyethylene glycol/polylactic acid films in the prevention of adhesions in the rabbit adhesion formation and reformation sidewall models. Fertil Steril 1998;69:403-8.

19. Lopes JB, Dallan LA, Moreira LF, Carreiro MC, Rodrigues FL, Mendes Pde C, et al. New quantitative variables to measure postoperative pericardial adhesions. Useful tools in experimental research. Acta Cir Bras 2009;24:82-6.
20. Morales D, Williams E, John R. Is resternotomy in cardiac surgery still a problem? Interact Cardiovasc Thorac Surg 2010;11:277-86.
21. Colak N, Nazli Y, Alpay MF, Aksoy ON, Akkaya IO, Bayrak R, et al. Effect of topical N-acetylcysteine in the prevention of postoperative pericardial adhesion formation in a rabbit model. Cardiovasc Pathol 2013;22:368-72.
22. Rao V, Komeda M, Weisel RD, Cohen G, Borger MA, David TE. Should the pericardium be closed routinely after heart operations? Ann Thorac Surg 1999;67:484-8.
23. Jacobs JP, Iyer RS, Weston JS, Amato JJ, Elliott MJ, de Leval MR, et al. Expanded PTFE membrane to prevent cardiac injury during resternotomy for congenital heart disease. Ann Thorac Surg 1996;62:1778-82.
24. Kuschel TJ, Gruszka A, Hermanns-Sachweh B, Elyakoubi J, Sachweh JS, Vázquez-Jiménez JF, et al. Prevention of postoperative pericardial adhesions with TachoSil. Ann Thorac Surg 2013;95:183-8.
25. Walther T, Rastan A, Dähnert I, Falk V, Jacobs S, Mohr FW, et al. A novel adhesion barrier facilitates reoperations in complex congenital cardiac surgery. J Thorac Cardiovasc Surg 2005;129:359-63.
26. Kaneko Y, Hirata Y, Achiwa I, Morishita H, Soto H, Kobayahsi J. Adhesion barrier reduces postoperative adhesions after cardiac surgery. Asian Cardiovasc Thorac Ann 2012;20:257-62.
27. Okuyama N, Rodgers KE, Wang CY, Girgis W, Oz M, St Amand K, et al. Prevention of retrosternal adhesion formation in a rabbit model using bioresorbable films of polyethylene glycol and polylactic acid. J Surg Res 1998;78:118-22.
28. Schreiber C, Boening A, Kostolny M, Pines E, Cremer J, Lange R, et al. European clinical experience with REPEL-CV. Expert Rev Med Devices 2007;4:291-5.