Adhesion Barriers in Cardiac Surgery: A Systematic Review of Safety and Efficacy

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Abstract

BACKGROUND: Postoperative pericardial adhesions have been associated with increased morbidity, mortality, and surgical difficulty. Barriers exist to limit adhesion formation, yet little is known about their use in cardiac surgery. The study presented here provides the first major systematic review of adhesion barriers in cardiac surgery. METHODS: Scopus and PubMed were assessed on November 20, 2020. Inclusion criteria were clinical studies on human subjects, and exclusion criteria were studies not published in English and case reports. Risk of bias was evaluated with the Cochrane Risk of Bias Tool. Barrier safety and efficacy data were assessed with Excel and GraphPad Prism 5. RESULTS: 25 studies were identified with a total of 13 barriers and 2,928 patients. Polytetrafluoroethylene (PTFE) was the most frequently evaluated barrier (13 studies, 67% of patients) with an infection rate of 1.14%, bleeding event rate of 0.75%, mortality rate of 1.22%, adhesion formation rate of 37.31%, and standardized tenacity score of 26.50. Several barriers had improved safety and efficacy. In particular, Cova CARD had an infection rate of 0.00%, a bleeding event rate of 0.00%, and a tenacity score of 15.00. CONCLUSIONS: Overall, the data varied considerably in terms of study design and reporting bias. The amount of data was also limited for the non-PTFE studies. PTFE has historically been effective in preventing adhesions. More recent barriers may be superior, yet the current data is non-confirmatory. No ideal adhesion barrier currently exists, and future barriers must focus on the requirements unique to operating in and around the heart.

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ABSTRACT:

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METHODS:

Scopus and PubMed were assessed on November 20, 2020. Inclusion criteria were clinical studies on human subjects, and exclusion criteria were studies not published in English and case reports. Risk of bias was evaluated with the Cochrane Risk of Bias Tool. Barrier safety and efficacy data were assessed with Excel and GraphPad Prism 5.

RESULTS:

25 studies were identified with a total of 13 barriers and 2,928 patients. Polytetrafluoroethylene (PTFE) was the most frequently evaluated barrier (13 studies, 67% of patients) with an infection rate of 1.14%, bleeding event rate of 0.75%, mortality rate of 1.22%, adhesion formation rate of 37.31%, and standardized tenacity score of 26.50. Several barriers had improved safety and efficacy. In particular, Cova CARD had an infection rate of 0.00%, a bleeding event rate of 0.00%, and a tenacity score of 15.00.

CONCLUSIONS:

Overall, the data varied considerably in terms of study design and reporting bias. The amount of data was also limited for the non-PTFE studies. PTFE has historically been effective in preventing adhesions. More recent barriers may be superior, yet the current data is non-confirmatory. No ideal adhesion barrier currently exists, and future barriers must focus on the requirements unique to operating in and around the heart.

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INTRODUCTION:

Adhesions are fibrotic connections resulting from tissue trauma and subsequent inflammation and ischemia during surgery. While adhesions are germane to many forms of surgery, postoperative pericardial adhesions (PPAs) are an important clinical problem in cardiac surgery. The resulting obliteration of tissue planes puts vital structures at risk for injury during re-operation and sternal re-entry, particularly the aorta, right ventricle, and right atrium. At least 10% of cardiac surgeries require re-operation.[1] The incidence of re-entry injuries in these procedures is relatively low at approximately 3%; however, they are associated with almost three times greater mortality rates.[2] PPAs hinder dissection and visibility too, thereby increasing operative time, cardiopulmonary bypass time, and blood loss. The increased morbidity, mortality, and economic costs

posed by PPAs during re-operation ultimately place the patient at risk and pose an undue burden on the surgical team.

In an effort to improve outcomes, barriers have been developed to limit adhesion formation. These adhesion barriers have now been used in cardiac surgery for over four decades and can be divided into two categories: nonresorbable and bioresorbable.[3]Nonresorbable barriers include both prosthetic and/or xenograft materials while bioresorbable barriers include pharmacologic agents and/or resorbable membranes.[3, 4] Nonresorbable barriers create indefinite physical separation between tissue planes and provide a readily discernable area at re-operation. Nonresorbable barriers were the first type of products developed to prevent PPAs. However, bioresorbable barriers have recently been developed more and have garnered interest among both patients and surgeons. Bioresorbable barriers confer a potential relative benefit by not leaving a foreign body in place for long periods of time and not requiring re-operation for barrier removal. The only licensed adjuncts for PPA prevention at this point in time are either nonresorbable or bioresorbable physical barriers.[5] Pharmacotherapy agents that act at the molecular level have yet to be identified. Although numerous products currently exist, a perfect solution to PPAs has yet to be identified.

Research efforts analyzing adhesion barriers have historically focused on abdominal and gynecologic surgery.[6, 7, 8, 9]Limited data currently exists with respect to cardiac surgery. Recent systematic review have assessed adhesion and particularly PPA formation and prevention methods.[3, 5] However, none have compared the efficacy and safety of specific adhesion barriers for preventing PPAs in the clinical setting. The study presented here addresses this knowledge gap by providing the first major systematic review of adhesion barriers in cardiac surgery.

MATERIALS AND METHODS:

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.

Literature Search

A literature search for relevant articles was conducted using the two major databases Scopus and PubMed. The Scopus search strategy was as follows:

(cardiac OR cardio OR heart OR pericardial OR pericardiotomy OR intrapericardial) AND adhesion* AND (barrier* OR seprafilm OR gortex OR "gor-tex" OR polytetrafluoroethylene OR tachosil)

The PubMed search strategy was as follows:

("Cardiac Surgical Procedures"[Mesh] OR cardiac[ti] OR cardio[ti] OR "Heart"[Mesh] OR heart[ti] OR pericardial[ti] OR pericardiotomy[ti] OR intrapericardial[ti]) AND ("Tissue Adhesions"[Mesh] OR adhesion*[tw]) AND (barrier*[tw] OR seprafilm[tw] OR gortex[tw] OR "gor-tex"[tw] OR polytetrafluoroethylene[tw] OR tachosil[tw])

Both databases were searched on November 24, 2020 with no limit for article dates. Inclusion criteria were clinical studies on human subjects, and exclusion criteria were case reports and studies published in a language other than English.

Two reviewers separately performed the initial title and abstract screening for all articles followed by the full-text review. Specific reasons were provided for the articles excluded during full-text review. Conflicts at any stage were resolved by a third reviewer. Of the resulting full-text articles, any reference(s) of other adhesion barrier(s) was assessed through a similar title and abstract screening with subsequent full-text review. The Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used as the primary screening and evaluation tool for all reviewers. Risk of bias in the studies was evaluated by a single reviewer using the Cochrane Risk of Bias Tool.[10]

Data Extraction and Analysis

A single reviewer performed all data extraction to ensure consistency across each study. The results were broadly divided into two categories: safety and efficacy. After performing a full-text review, the most frequently discussed variables pertaining to safety (i.e. rates of infection, bleeding events, and mortality) and efficacy (i.e. adhesion formation rate and standardized tenacity scores) served as the major focus for analysis. "Infection" corresponded to any mention of infectious processes related to superficial site infection, sternal wound infection, mediastinitis, or sepsis after insertion of the adhesion barrier. "Bleeding event" corresponded to any mention of blood loss events intra- or post-operatively. "Mortality" corresponded to any mention of death in patients receiving a barrier. "Adhesion formation" corresponded to any mention of post-operative adhesions identified either at re-operation or through imaging. "Standardized tenacity score" (TSS) corresponded to any mention of a scaled-method for reporting adhesion severity.[11, 12] No universal grading scale exists, and the studies assessed ranged from 0-3 to 0-21 point scales. All scales included a value for no adhesions (largely "0"), and they then varied along a spectrum from mild to severe adhesions requiring blunt to sharp dissection. A TSS equation that standardized the reported tenacity score values was developed and is presented in Figure 1.

A separate reviewer performed all data analysis using Excel. The rates of infection, bleeding events, and mortality, were determined by calculating the mean number of events in the patients receiving adhesion barriers and the available control groups via Excel. The adhesion formation was determined by calculating the mean number of events in patients the patients with adhesion barriers that received re-operation(s) and the available control group patients that received re-operation(s) via Excel. The TSS was determined by using the equation described previously (see Figure 1) via Excel. Issues during either data extraction and/or analysis were resolved by a third reviewer.

RESULTS:

695 articles were identified through the initial database searches (Scopus: 558; PubMed 137) (see Figure 2). After removing duplicates, 632 articles were screened. 603 were excluded, and the remaining 29 full-text articles were assessed for eligibility. Four studies were then excluded (three for wrong study design and one for wrong language) with a remaining total of 25 for review (see Table 1). The risk of bias is presented in Figures 3 and 4. 21 out of 25 studies had high bias in blinding of paricipants and personnel, as well as in outcome assessment. 21 out of 25 studies also had high bias in allocation concealment (Figure 3). About 80% of the studies had low bias in selective reporting (Figure 4).

Adhesion Barriers

A total of 13 adhesion barriers and 2,928 patients were identified (2,928 received barrier; 522 received barrier and re-operation). The names and composition of these barriers as well as their study data are outlined in Table 2. The adhesion barriers assessed were Polytetrafluoroethylene (PTFE) (n=13 studies, 67% of patients), Seprafilm (n=3, 14%), COSEAL (n=2, 3%), REPEL-CV (n=2, 3%), Glutaraldehyde-Preserved Equine Patch (n=1, 7%), Silicone Rubber (n=1, 3%), Cova CARD (n=1, 1%), Polyglycolic Acid Mesh (n=1, 1%), SprayGel (n=1, 0.3%), Polyisoprene Blue Band Strips (n=1, 0.3%), and Porcine and Polyester Gelatin Sheet (n=1, 0.2%). Two barrier combinations were also identified: PTFE + SprayGel (n=1, 0.3%) and PTFE + Seprafilm (n=1, 0.1%). The mean number of studies per barrier was 2.2 with a mean of 225 barrier patients and 23 barrier patients with re-operation. Excluding PTFE, the mean number of studies per barrier was 1.3 with a mean of 81 barrier patients and 24 barrier patients with re-operation. The mean study year was 2003 with a range from 1981 (Silicone Rubber) to 2015 (Seprafilm).

Safety

The safety variables discussed most frequently across all studies were infection, bleeding events, and mortality (see Table 3).

Infection:

The mean infection rate for all barriers with reported data was 1.17% (control 0.94%). COSEAL had the highest infection rate (6.58%) followed by REPEL-CV (4.55%; control 1.45%), PTFE (1.14%; control

4.88%), and Glutaraldehyde-Preserved Equine Patch (1.00%). An infection rate of 0.00% was identified for the majority of barriers, including Seprafilm (control 0.00%), Silicone Rubber, Cova CARD, Polyglycolic Acid Mesh, Polyisoprene Blue Band Strips, Porcine and Polyester Gelatin Sheet, and PTFE + Seprafilm (control 0.00%). SprayGel and PTFE + SprayGel were the only barriers to not have reported infection data.

Bleeding event:

The mean bleeding event rate for all barriers with reported data was 1.40% (control 0.75%). COSEAL had the highest bleeding event rate (10.53%), followed by Silicone Rubber (6.86%) and PTFE (0.75%; control 1.22%). Seprafilm (control 0.00%), Cova CARD (control 0.00%), and PTFE + Seprafilm (control 0.00%) had bleeding event rates of 0.00%. The majority of barriers did not have reported bleeding event data.

Mortality:

The mean mortality rate for all barriers with reported data was 4.56% (control 2.43%). REPEL-CV had the highest mortality rate (17.05%; control 13.04%) followed by PTFE (4.89%; control 1.22%), COSEAL (3.26%), Silicone Rubber (0.98%), and Seprafilm (0.57%; control 1.63%). A mortality rate of 0.00% was only demonstrated by the Porcine and Polyester Gelatin Sheet. The majority of barriers did not have reported mortality data.

Efficacy

The efficacy variables discussed most frequently across all studies were the formation of adhesions noted on re-operation and adhesion tenacity scores (see Table 4). TSS was calculated to provide a standardized assessment of adhesion tenacity scores across all relevant studies.

Adhesion Formation:

The mean adhesion formation rate for all barriers with reported data was 77.87% (control 98.31%). An adhesion formation rate of 100.00% was demonstrated with COSEAL, REPEL-CV (control 100.00%), Silicone Rubber, Polyglycolic Acid Mesh (control 100.00%), and Porcine and Polyester Gelation Sheet. Seprafilm had an adhesion formation rate of 95.83% (control 94.12%) followed by Cova CARD (78.95%) and PTFE (37.31%; control 100.00%). Polyisoprene Blue Band Strips was the only barrier to have no adhesion formation (0.00%). The remaining four barriers did not have data regarding the adhesion formation rate.

Standardized Tenacity Score:

The mean TSS for all barriers with reported data was 43.06 (control 73.55). Polyglycolic Acid Mesh had the highest TSS (78.33 (control 84.33)), followed by Spraygel (66.67; control 73.33), PTFE + SprayGel (63.33; control 73.33), REPEL-CV (58.42; control 77.67), Seprafilm (50.32; control 70.01), COSEAL (36.12; control 75.00), Porcine and Polyester Gelatin Sheet (33.33), Glutaraldehyde-Preserved Equine Patch (32.00; control 64.00), PTFE (26.50; control 80.26), and Cova CARD (15.00). Similar to the adhesion formation rate, Polyisoprene Blue Band Strips was the only barrier to have a TSS of 0.00. Silicone Rubber and PTFE + Seprafilm did not have reported data for TSS.

CONCLUSIONS:

Barriers to prevent the formation of PPAs are heterogeneous with respect to composition and effectiveness. The present systematic review of the literature identified a total of 13 barriers, including two barrier product combinations. These models were analyzed with respect to their safety and efficacy in the clinical setting for the cardiac surgery patient.

The safety of adhesion barriers varies considerably with respect to rates of infection, bleeding events, and mortality. No barrier had reported rates of 0.00% for all three variables; however, Seprafilm demonstrated the lowest combined rates (infection 0.00% vs control 0.00%; bleeding event 0.00% vs control 0.00%; mortality 0.57% vs control 1.22%). Cova CARD, Porcine and Polyester Gelatin Sheet, and PTFE + Seprafilm also demonstrated rates of 0.00% for at least two categories with no reported data on the third. The heterogeneity in reporting was found to be prevalent, as few barriers had reported control data. Only four of the 13 barriers

had reported data for all three safety variables. PTFE and COSEAL were two of these barriers, and they also demonstrated relevant safety concerns. PTFE had the second greatest mortality rate (4.89% vs control 1.22%), third greatest infection rate (1.14% vs control 4.88%), and third greatest bleeding event rate (0.75% vs control 1.22%). Although less than the control population, PTFE may influence infection and bleeding because it requires both sutures for placement as well as re-operation for removal. Another explanation for these findings is that PTFE was assessed in the greatest number of studies with some dating back to over three decades ago; general surgical techniques have likely improved considerably since that point in time. Silcone rubber had the second greatest bleeding event rate (6.86%); however, it also was assessed in the earliest study identified (1981).[13]

COSEAL had the greatest infection rate (6.58%) and bleeding event rate (10.53%). COSEAL is a sprayable synthetic polymeric hydrogel that is bioresorbable. No possible reasons for the infection or bleeding event rates have been proposed; however, infection and bleeding were also among the greatest adverse events in a randomized control trial of COSEAL in vascular surgery.[14] REPEL-CV also demonstrated significant safety concerns with not only the greatest mortality rate (17.05%; control 13.04%) but also the second greatest infection rate (4.55%; control 1.45%). The primary study of REPEL-CV was in infants undergoing initial sternotomy for eventual staged palliative cardiac operations with no significant difference identified in mortality rates between the barrier and control group (p=0.6405).[15] The immune system function of these infants was likely limited as well and may have influenced the response to a foreign body, resulting in increased infection rates relative to the control group. Overall, the ability to draw comparisons between the safety of the adhesion barriers is limited due to the heterogeneity with respect to study design and reporting bias. As noted, many studies did not provide control groups for comparion. The varied procedures performed in differing patient populations suggest further limit the ability to draw definitive conclusions between the groups. No major studies have also identified the overall rates of infection, bleeding event, and mortality in cardiac surgery without adhesion barriers. A detalied understanding of these topics would be of great value for those attempting to weigh the risks and benefits of adhesion barrier use in cardiac surgery.

The efficacy of adhesion barriers in preventing PPA formation and limiting tenacity scores varied as well. Unlike the safety data, most barriers did have reported data for both efficacy variables. Only one barrier had an adhesion formation rate of 0.00% with a TSS of 0.00: Polyisoprene Blue Band Strips. The study regarding Polyisoprene Blue Band Strips did not identify a control group for comparison though and only had nine patients in the barrier group with a mean placement time of 31 days.[16] The strips were applied to the major vessels surrounding the heart and were not used to cover the heart itself. Excluding Polyisoprene Blude Band Strips, PTFE demonstrated the lowest adhesion formation rate (37.31% vs control 100.00%) and the third-lowest TSS (26.50 vs control 80.26%). PTFE was the most frequently used barrier among all studies (67% of patients) with the widest range of years (1988-2012). PTFE has historically been effective because it is physiologically inert, has low adhesiveness with cells/tissues, separates damaged surfaces without degradation, and is biocompatible.[3] PTFE is commonly used in cardiac surgery today due to its demonstrated effectiveness in reducing adhesions; however, the safety concerns discussed previously should be considered. Applying PTFE in combination with other barriers is a particular area of interest that may address these concerns, as PTFE + Seprafilm resulted in limited infections and bleeding events.[17]

Cova CARD was also among the most effective barriers with the third lowest adhesion formation rate (78.95%) and the second lowest TSS (15.00). Cova CARD is a relatively new barrier that acts as a resorbable, malleable porcine collagen membrane, promoting tissue regeneration.[3, 18] While the human data is limited, collagen sheets have been shown to resemble native pericardial membranes at 24 weeks after operation in animal models.[3, 19] The adhesion formation rate may be greater relative to PTFE; however, the improved TSS suggests that this barrier may provide easier dissection than PTFE. Easier dissection may also explain the improved safety identified regarding infection and bleeding events relative to PTFE. Adhesion formation occurred with almost every patient when using Seprafilm (95.83% vs control 94.12%), COSEAL (100.00%), REPEL-CV (100.00%; control 100.00%), Silicone Rubber (100.00%), Polyglycolic Acid Mesh (100.00% vs control 100.00%), and Porcine and Polyester Gelatin Sheet (100.00%). The study assessing Polyglycolic Acid Mesh should be discussed though, as it used computerized tomography (CT) imaging instead of re-operation

to identify adhesion formation.[20] Polyglycolic Acid Mesh was compared against PTFE and a no barrier control group that both had adhesion formation rates of 100.00% as well. The increased rate of adhesions for PTFE in this study relative to its overall adhesion formation rate (37.31%) suggests that CT imaging may allow for more detailed identification of adhesions that may not necessarily be clinically relevant in the re-operation setting. Nevertheless, the study did note that PTFE was a more effective substitute than Polyglycolic Acid Mesh with respect to the reported "total adhesion scores" ($p < 0.001$). While the adhesion formation rate was high for nearly all barriers, the TSS demonstrated noteworthy variance. The similar TSS scores in the control groups also suggest that comparison may be appropriate among the barriers' TSS scores. Nevertheless, the wide variance in reported values for safety and efficacy likely relates to the subjective approach used to report these variables and suggests a need for standardization moving forward.

This study has limitations given its study design as a systematic review. These limitations relate to the evidence included in the review as well as the review process itself. With respect to the evidence included, not all studies reported the same safety and efficacy variables. Some of the relevant variables discussed in this review were not mentioned in some studies; furthermore, other variables included in a few studies were not assessed here to ensure appropriate comparisons. Statistical analyses comparing the barriers was also limited due to the heterogeneity of data reported. A major contributor was the variance in study design and presence of control groups, which contributed to the risk of bias in the studies. Future adhesion barrier studies should address these limitations by providing detailed safety and efficacy data that includes the variables discussed here for both the intervention and comparison cohorts. Other potentially valuable variables include structural injuries, visibility, dissection duration, and ease of use. With respect to the review process, the search strategies were unable to assess all publications to date on adhesion barriers in the clinical setting of cardiac surgery. Although the search strategies used were broad and included two separate databases, other relevant articles may have not been identified. Publication bias likely influenced the results as well in that only published studies were used in this systematic review. Future systematic reviews should be mindful of these limitations and pursue a more inclusive approach as additional PPA barrier studies are published.

In conclusion, this is the first systematic review of adhesion barrier safety and efficacy in cardiac surgery. The findings suggest that no ideal adhesion barrier currently exists for preventing PPAs. While the barriers assessed in this study are commonly used in other forms of surgery, future barrier development must focus on the requirements unique to operating in and around the heart during cardiac surgery. PTFE has historically been used, but the relevant safety and efficacy concerns identified here suggest areas for improvement. Recent adhesion barriers have been developed that demonstrate improvements in infection rates, bleeding event rates, mortality, adhesion formation, and tenacity scores. In particular, Cova CARD may provide better outcomes. Combinations of adhesion barriers, such as PTFE + SprayGel and PTFE + Seprafilm, may also provide synergistic improvements in safety and efficacy. However, further validation is required before drawing any conclusions. PPAs ultimately pose a major burden to patients and providers in terms of morbidity, mortality, and surgical ease. Reducing their formation is vital to improving outcomes for all cardiac surgery candidates.

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William T Head BA: Concept/design, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article, Statistics, Data collection

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TABLES:

Table 1: Studies included in the Systematic Review

Author, year	Adhesion Barrier	Comparison	Sample size
Amato et al, 1989[21]	PTFE	No barrier	96/60
Armoiry et al, 2013[18]	Cova CARD	No barrier	36/13
Bhatnager et al, 1998[22]	PTFE	No barrier	138/164
Copeland et al, 2001[23]	PTFE	No barrier	14/36
Harada et al, 1988[24]	PTFE	-	61/-
Holman et al, 1993[25]	PTFE	-	7/-
Jacobs et al, 1996[26]	PTFE	-	1085/-
Jaroszewski et al, 2009[16]	Polyisoprene Blue Band Strips	-	9/-
Kaneko et al, 2012[17]	PTFE + Seprafilm	Mixed (No barrier or PTFE)	4/23
Kaneko et al, 2012[17]	Sepraflim	Mixed (No barrier or PTFE)	21/23
Konertz et al, 2003[11]	Adhibit*	No barrier	16/5
Lahtinen et al, 1998[20]	PTFE	No barrier	18/17
Lahtinen et al, 1998[20]	Polyglycolic Acid Mesh	No barrier	17/17
Laks et al, 1981[13]	Silicone Rubber	-	102/0
Lefort et al, 2015[27]	Seprafilm	No barrier	29/42
Leprince et al, 2001[28]	PTFE	No barrier	23/-
Lodge et al, 2008[15]	REPEL-CV	No barrier	73/69
Loebe et al, 1993[29]	PTFE	-	321/-
Matsumura et al, 2008[30]	Porcine and Polyester Gelatin Sheet	-	5/-
Minale et al, 1988[31]	PTFE	-	110/-
Ozeren et al, 2002[32]	PTFE	-	56/-
Pace Napoleone et al, 2009[33]	COSEAL	-	76/-
Salminen et al, 2011[34]	PTFE	No barrier	8/10

Author, year	Adhesion Barrier	Comparison	Sample size
Salminen et al, 2011[34]	PTFE + SprayGel	No barrier	8/10
Salminen et al, 2011[34]	SprayGel	No barrier	10/10
Schreiber et al, 2007[35]	REPEL-CV	-	15/-
Vitali et al, 2000[36]	PTFE	-	20/-
Von Segesser et al, 1987[37]	Glutaraldehyde-Preserved Equine Patch	No barrier	200/13
Walther et al, 2005[12]	Seprafilm	No barrier	350/674

PTFE = Polytetrafluoroethylene *Adhibit is identical to COSEAL and is referenced to in the systematic review as COSEAL. "-" denotes lack of comparison group and/or lack of primary outcomes discussed by the authors.

Table 2: Adhesion Barrier Study Information

Adhesion Barrier	Chemical Composition	Bioresorbable	Number of Studies	Range of Study Years	Number of Patients Receiving Barrier	Number of Reoperations with Barrier
PTFE (aka Gore-Tex, Preclude)	Polytetrafluoroethylene	no	13	1988 - 2012	1957	238
Seprafilm	Sodium hyaluronate/ carboxymethylcellulose	yes	3	2005 - 2015	400	80
COSEAL (aka Adhibit)	Two synthetic polyethylene glycol polymers	yes	2	2003 - 2009	92	47
REPEL-CV	Polylactic acid/ polyethylene glycol	yes	2	2007 - 2008	88	69
Glutaraldehyde-Preserved Equine Patch		no	1	1987	200	9
Silicone Rubber	-	no	1	1981	102	7
Cova CARD	Porcine type 1 collagen	yes	1	2013	36	19
Polyglycolic Acid Mesh	-	yes	1	1998	17	17
SprayGel	Two synthetic polyethylene glycol polymers	yes	1	2011	10	10

Adhesion Barrier	Chemical Composition	Bioresorbable	Number of Studies	Range of Study Years	Number of Patients Receiving Barrier	Number of Reoperations with Barrier
Polyisoprene Blue Band Strips	-	no	1	2009	9	9
PTFE + SprayGel	Polytetrafluoroethylene + Two synthetic polyethylene glycol polymers	hydrand yes	1	2011	8	8
Porcine and Polyester Gelatin Sheet	Gelatin composed of pathogen-free porcine skin and a bioabsorbable polyester mesh	yes	1	2008	5	5
PTFE + Seprafilm	Polytetrafluoroethylene + Sodium hyaluronate/ carboxymethylcellulose	hydrand yes	1	2012	4	4

"-" denotes that the chemical composition is not discussed in detail.

Table 3: Safety Data for Adhesion Barriers in Cardiac Surgery

Adhesion Barrier (barrier patients/control patients)	Infection (barrier)	Infection (control)	Bleeding Ev
PTFE (1957/238)	1.14%	4.88%	0.75%
Seprafilm (400/80)	0.00%	0.00%	0.00%
COSEAL (92/47)	6.58%	-	10.53%
REPEL-CV (88/69)	4.55%	1.45%	-
Glutaraldehyde-Preserved Equine Patch (200/13)	1.00%	-	-
Silicone Rubber (102/0)	0.00%	-	6.86%
Cova CARD (36/13)	0.00%	-	0.00%
Polyglycolic Acid Mesh (17/17)	0.00%	-	-
SprayGel (10/10)	-	-	-
Polyisoprene Blue Band Strips (9/0)	0.00%	-	-
***PTFE + SprayGel (8/10)**	-	-	-
Porcine and Polyester Gelatin Sheet (5/0)	0.00%	-	-
***PTFE + Seprafilm (4/23)**	0.00%	0.00%	0.00%

*Studies looked at two barriers combined. "-" denotes that the study did not discuss the variable in the relevant group.

Table 4: Efficacy Data for Adhesion Barriers in Cardiac Surgery

Adhesion Barrier (barrier re-operation patients/control re-operation patients)	Adhesion Formation (barri
PTFE (220/28)	37.31%
Seprafilm (80/75)	95.83%
COSEAL (47/5)	100.00%
REPEL-CV (69/49)	100.00%
Glutaraldehyde-Preserved Equine Patch (9/13)	-
Silicone Rubber (7/0)	100.00%
Cova CARD (19/13)	78.95%
Polyglycolic Acid Mesh (17/17)	100.00%
SprayGel (10/10)	-
Polyisoprene Blue Band Strips (9/0)	0.00%
***PTFE + SprayGel (8/10)**	-
Porcine and Polyester Gelatin Sheet (5/0)	100.00%
***PTFE + Seprafilm (4/23)**	-

TSS = Standardized Tenacity Score. *Studies looked at two barriers combined. "-" denotes that the study did not discuss the variable in the relevant group. Standardized Tenacity Score is on a 100-point scale.

FIGURE LEGENDS:

Figure 1: Standardized Tenacity Score Equation

TSS = Standardized Tenacity Score. TSR = Reported mean tenacity score. m = Reported tenacity score scale size. n = Sample size. Subscripts denote study number.

Figure 2: PRISMA Diagram of Study Extraction and Inclusion

Full-text articles excluded for wrong study design.[4, 38, 39]

Full-text articles excluded for wrong language.[40]

Figure 3: Individual Study Risk of Bias

Figure 4: Conglomerate Risk of Bias

$$\boldsymbol{TSS = 100 \times \frac{\left(\frac{TSR_1}{m_1}\right)(n_1) + \left(\frac{TSR_2}{m_2}\right)(n_2) + \ldots + \left(\frac{TSR_k}{m_k}\right)(n_k)}{n_1 + n_2 + \ldots + n_k}}$$