A novel adhesion barrier facilitates reoperations in complex congenital cardiac surgery

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Objective: Reoperations are associated with an increased surgical risk due to adhesions. We prospectively evaluated a bioresorbable membrane after surgery for congenital heart defects over a 3.5-year period.

Methods: The surgical membrane (CV Seprafilm, Genzyme, Cambridge, Mass) was applied in 350 of 1024 patients; 30 of them underwent reoperation and were evaluated in comparison to 10 random reoperated patients. Adhesions were evaluated using a subjective scoring system [1 (lowest tenacity) to 5 (highest tenacity)] and extent in percent at different regions of the heart.

Results: Patients were operated for atrioventricular septal defect (69), tetralogy of Fallot (65), functional single ventricle (75), valve surgery (48), ventricular septal defect (20), subaortic stenosis (17), hypoplastic left heart syndrome (17), and other diagnoses (39). Application of the surgical membrane was safe in all patients, without any infections. At reoperation patients received Glenn (14), total cavopulmonary connection (6), and others (10). Overall mortality was 2/350 (0.57%). There was a remarkable reduction in tenacity score (3.3 vs 4.3) and in the extent of adhesions (77.7% vs 86%). Duration of reoperation was significantly reduced.

Conclusions: A bioresorbable surgical membrane leads to a significant reduction in the tenacity and amount of adhesions. It is recommended for general use whenever repeat operation is anticipated in congenital as well as in adult cardiac surgery.

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Congenital cardiac surgery is characterized by an increasing number of patients receiving early complete corrections. Others can be safely operated on by staged approaches. In both groups reoperations may be required. Patients with univentricular physiology receive several surgical procedures during the first years of life. Others, for example patients after surgical correction for tetralogy of Fallot (TOF), may require reoperation of the right ventricular outflow tract (RVOT) later in life.

Any reoperation in congenital or adult cardiac surgery imposes an increased surgical risk onto the individual patient. This increased risk is mostly caused by the occurrence of surgical adhesions. Adhesions lead to more difficult sternal reentry and cardiac dissection, to blunted visibility of distinct cardiac structures, to potential injury of cardiac structures (including the atria, ventricles, and coronary arteries), as well as to an increased risk of surgical bleeding, all associated with an increase in morbidity and mortality. Furthermore, reoperations due to adhesions are more

TABLE 1. Number of pediatric cardiac operations for individual patients as well as use of the adhesion barrier and mortality during the 3.5-year period in a tertiary care center

Pediatric cardiac operation for the individual patient	n	Mortality, n (%)	Use of adhesion barrier (n)	Mortality, n (%)
Primary	744	8 (1.1%)	190	1 (0.5%)
First reoperation	198	4 (2%)	108	1 (0.9%)
Second reoperation	66	1 (1.5%)	39	—
Third reoperation	13	—	10	—
Fourth reoperation	3	—	3	—
Total	1024	13 (1.3%)	350	2 (0.57%)

TABLE 2. Palliative pediatric cardiac operations for the individual patients as well as use of the adhesion barrier during the 3.5-year period in a tertiary care center

Palliative pediatric cardiac operation	n	Use of adhesion barrier (n)
Primary	95	49
Secondary	49	34
Tertiary	7	2
Total	161	85

time-consuming, and because of the increased difficulty they are associated with a greater level of stress for the individual surgeon.

No effective means to prevent such adverse adhesions are available at present. Direct closure of the autologous pericardium is possible in a small number of young patients only. This is due to the fact that in the majority of patients autologous pericardium is excised to be used for surgical corrections (eg, ventricular septal defect closure, atrioventricular septal defect [AVSD] repair, or RVOT patch enlargement procedures). Use of surgical membranes (eg, polytetrafluoroethylene [PTFE]; Gore-Tex, W. L. Gore & Associates, Inc, Flagstaff, Ariz) has clearly led to facilitated sternal reentry. However, intrapericardial adhesions still are substantive in most patients. A bioresorbable material would theoretically allow safe sternal closure with the later development of a free dissection plane for any reoperation. Restoring a plane by applying a film between the heart and surrounding tissues may improve cardiac function and simplify access on a future occasion.

We prospectively evaluated a resorbable membrane over a 3.5-year period. Results on 350 patients as well as 30 reoperations are presented and discussed.

Materials and Methods

Patients

From September 2000 until February 2004 a total of 1024 patients underwent correction for congenital cardiac malformations at our

hospital; 350 of those, all potential candidates for repeat surgical intervention, received artificial pericardial closure during this time interval. This included patients with planned staged procedures, with potential reoperations on the RVOT, with valve reconstructions (eg, AVSD correction), or with other complex cardiac malformations. Thirty of these patients underwent reoperations with repeat cardiac dissection during the study period, most of them for planned staged procedures. Patients with primary total correction in whom no repeat intervention was anticipated were not included in the study. The patient subset is depicted in Table 1, which shows the type of operation as well as mortality. Palliative operations are depicted in Table 2. This is a prospective evaluation study, performed under institutional review board protocol. Repeat sternotomy was performed with an oscillating saw in all patients.

Adhesion Barrier

A sterile and bioresorbable translucent membrane (CV Septrafilm, Genzyme, Cambridge, Mass) composed of US Pharmacopeia glycerol and 2 chemically modified anionic polysaccharides, sodium hyaluronate and carboxymethylcellulose, was used. The size of the membrane was approximately 12 × 12 cm. The CV Septrafilm was packed in a Tyvek holder (DuPont, Wilmington, Del). This allowed cutting or other manipulations of the membrane without disruption due to sticking to unintended places. The membrane was handled in a dry fashion, with dry gloves, a dry gauze, or clean forceps. Application was performed just before sternal closure to the dry mediastinum. The membrane was taken off the holder and applied to the intended tissue. If the membrane stuck to unintended places, it could eventually be removed after careful rinsing with a standard irrigating solution. Depending on patient size, 1 (sufficient in most pediatric operations) or 2 membranes were applied. The CV Septrafilm has been approved for clinical use.

Measurements

Application of the CV Septrafilm surgical membrane as well as eventual sternal reentry were evaluated according to a subjective rating scale filled out by the surgeon: Application was judged as easy handling without complications covering the whole heart, moderately easy handling covering the anterior aspect of the heart only, difficult handling due to unintended adhesion of the membrane, and difficult handling necessitating use of another package of the membrane.

Each adhesion was judged according to its tenacity and its extension and according to the percentage of the specific cardiac region covered. For both the evaluation of tenacity and extension of adhesions during sternal reentry and cardiac redissection, the following different regions were evaluated: The anterior or retrosternal region (A), the inferior or diaphragmatic region (B), the right lateral or atrial region (C), the region around the great vessels (D), and the left lateral or ventricular region (E); furthermore, an overall evaluation was performed (F).

In these different areas the tenacity of adhesions was judged as none (1), filmy requiring blunt dissection (2), moderate requiring blunt and sharp dissection (3), dense requiring sharp dissection (4), or very dense requiring extensive sharp dissection (5). This evaluation was performed according to a previous study with slightly modified rating.¹ Two surgeons took part in this study in a non-blinded fashion.

Patient Evaluation

Follow-up of all patients is routinely performed at the outpatient clinic. This guarantees that all candidates for repeat surgical intervention will be followed up and repeat interventions performed at our hospital. Results of the patients receiving repeat operations after using the adhesion barrier were compared to 10 random patients receiving repeat interventions without use of a specific adhesion barrier. These patients received Glenn (5), total cavopulmonary connection (2), corrections for RVOT obstructions (2), and repeat intervention for AVSD (1).

All data are expressed as mean ± standard deviation. Statistical analysis between groups was performed by the Wilcoxon test for unmatched pairs when appropriate.

Results

Of the total of 350 patients receiving the CV Seprafilm, 30 patients required reoperation throughout the study period and were evaluated.

The types of operations for the 350 patients are given in Table 3. Overall mortality was 2 (0.57%) of 350 throughout the study period. One neonate with complex cardiac anatomy died after primary operation, receiving a modified Blalock-Taussig shunt and pulmonary artery banding; the other died after Norwood II procedure with additional ligation of major aortopulmonary collateral arteries after reoperation. All other patients were discharged from the hospital and there was no mortality during follow-up.

There were no mediastinal infections throughout the study period. Even at delayed sternal closure (n = 17 patients in this study), the surgical membrane was safely applied without any further problems.

At repeat sternotomy landmarks and epicardial coronary vessels were not as indistinct as when using a PTFE membrane. However, visibility was different from primary operations. Adhesions were reduced wherever the absorbable membrane had been placed. In this study there was no relation between elapsed time since initial operation and the ease of reoperation. We did not see any impact on bleeding and transfusion requirement.

Application of the membrane was feasible in all patients. It was judged as easy without complications covering the whole heart in 63.7%, moderately easy covering the anterior aspect of the heart only in 29.7%, difficult due to unintended adhesion of the membrane in 5.1%, and difficult necessitating use of another package of the membrane in 1.4% of the patients, respectively. After initial experience had been gained, it was more easily accomplished throughout the study. Initially the membrane was positioned anteriorly only; after some experience with reoperations, it was also positioned around the heart. This led to a lesser degree of tenacity of the adhesions in most lateral and inferior parts and to easier repeat thoracotomy.

In the 30 patients with reoperations, the time between initial operation and repeat intervention was 12.7 ± 12.2

Table 3. Primary operations for the 350 patients receiving the adhesion barrier

Primary operation	n
Atrial and atrioventricular septal defect repair	69
Tetralogy of Fallot and pulmonary atresia repair	65
Functional single ventricle procedures	
Shunt	28
Glenn	27
TCPC	16
Pulmonary artery banding	4
Valve surgery (aortic, mitral, pulmonary)	48
Switch operation	5
VSD, closure	20
Subaortic stenosis resection	17
Norwood I	17
Persistent truncus arteriosus repair	6
Rastelli	5
Other	23

TCPC, Total cavopulmonary connection; VSD, ventricular septal defect.

Table 4. Reoperations performed in 30 patients (mean interval between primary and secondary operation was 12.7 + 12.2 months)

Reoperations	n
Glenn	14
TCPC	6
Multiple VSD closure	2
Correction for AVSD plus tetralogy of Fallot	2
Correction for RVOT stenoses	2
Rastelli repair	1
Switch	1
Other	2

TCPC, Total cavopulmonary connection; VSD, ventricular septal defect; AVSD, atrioventricular septal defect; RVOT, right ventricular outflow tract.

months (range 1-41 months). Reoperations are listed in Table 4. The adhesion barrier led to a subjective but remarkable facilitation of surgical repeat intervention due to a decrease in tenacity and extent of adhesions and thus an easier repeat thoracotomy. Results on the subjective tenacity scoring are given in Figure 1. Results on the extent of surgical adhesions in the different areas as well as on the duration between incision and start of extracorporeal circulation are given in Figure 2. Overall, the surgeons felt much more comfortable performing a reoperation in the presence of the adhesion barrier. They judged its presence as a clinically relevant benefit, rendering the reoperation easier and leading to an increased safety for the patient.

Discussion

Adhesions after cardiac operations lead to an increased risk and difficulty of surgical repeat intervention. Optimal mea-

Figure 1. Intensity of adhesions according to the subjective tenacity scoring for 30 study patients (CV Seprafilm) in comparison with 10 random control patients. Adhesions are evaluated according to different areas during repeat cardiac dissection. See text for further definition of the score.

Figure 2. Extent of adhesions as judged by the percentage of the different areas covered as well as duration between skin incision and start of extracorporeal circulation for 30 study patients (CV Seprafilm) in comparison with 10 random control patients. * $P < .05$.

sures to prevent adhesions are not available at present. Direct closure of the patient's own pericardium may lead to a lesser extent of adhesions and to easier sternal reentry. However, it is not feasible in most patients undergoing congenital cardiac surgery, because the autologous pericardium is partially being used for surgical correction.

Different techniques to replace the pericardium as well as to potentially decrease the tenacity and the amount of adhesions have been applied as documented in the literature. However, no definitive method has yet evolved. Different techniques such as PTFE membranes,²⁻⁴ sprayable polymeric matrices,^{1,5} hydrophilic polymeric solutions,⁶ hyaluronic acid films or cellulose,⁷⁻⁹ bioresorbable membranes,¹⁰ hydrogel derivatives,¹¹ polymer films,¹² and medical anti-inflammatory therapy¹³ have been published. However, none of these approaches has proven optimal effectiveness. Thus, there is still need for a universal, safe, effective, and easy-to-use material to significantly reduce surgical adhesions. This would be extremely helpful in cardiac as well as general surgery repeat procedures.

Use of a hyaluronic acid carboxymethylcellulose bioresorbable membrane (Seprafilm) has been shown to be effective in abdominal surgery.¹⁴

Application of the resorbable membrane was feasible throughout our study. However, the membrane should be handled with dry hands only and disruption may occur after unforeseen contact with parts of the open chest. After some experience application as such is easy. However, a sprayable substance would probably be even easier to handle.

According to our results the CV Seprafilm resorbable membrane has proven effectiveness in reducing the tenacity as well as the extent of surgical adhesions. This leads to a relevant facilitation of any reoperation as documented by a significantly shorter duration between incision and start of extracorporeal circulation. The membrane is applicable for both pediatric and adult cardiac surgical patients; in the latter, a slightly larger package would be favorable. In all instances use of such a membrane leads to a relevant reduction in the risk of repeat surgical thoracotomy and thus is of clinical benefit for the individual patient.

We did not perform a blinded randomized trial, which would be superior in demonstrating the clinical benefit of a new bioresorbable membrane. However, diagnoses as well as the potential amount, tenacity, and formation of adhesions differ between individual patients. Thus, a randomized trial would only partially offer more reliable clinical results. Due to the variability in diagnoses as well as to the fact that we initially evaluated the usefulness of the new product, we did not perform a randomized trial.

A combination of using a resorbable membrane together with a PTFE membrane would eventually be of additional benefit. However, with the resorbable membrane a sufficient plane for safe sternal reentry is usually present as seen in our study. Additional PTFE, therefore, is not required. Whenever sufficiently available, we would close the autologous pericardium and place parts of the resorbable membrane below as well as above.

As shown in Table 3 we see an indication for using such an adhesion barrier in all patients receiving planned staged approaches (functional single ventricle palliation or Norwood procedures) as well as in those eventually requiring repeat intervention. This includes all patients receiving valve reconstructions (AVSD repair, single or combined valve surgery) as well as TOF repair. Few patients receiving total corrections (eg, switch operation) are candidates for using an adhesion barrier.

Is there an indication to use such a membrane in all patients receiving cardiac surgery? In terms of facilitated repeat thoracotomy there would be a clear benefit. Patients in whom any repeat intervention may be required in due course, approximately within the following 1 to 5 years, will clearly benefit. At present, we cannot foresee whether it would be advantageous for all patients, even for pediatric

patients who may require coronary or valve surgery much later in life. As there was no increased risk and especially no incidence of mediastinitis from using the membrane, there is no disadvantage when using it in every patient.

The cost-effectiveness has to be considered as well. Ease and reduced duration of repeat surgical procedures will always justify the use of the membrane. Sometimes it will be difficult to exactly foresee which patient will require reoperation. However, general use of a bioresorbable membrane may be restricted due to financial issues.

In summary, excellent intermediate-term results were demonstrated after using a bioresorbable surgical membrane in selected patients receiving congenital cardiac surgical operations. A clinically relevant reduction in the tenacity as well as the overall extent of adhesions was proven. This results in a significant reduction of reoperative risk and a benefit for the individual patient.

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