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Up to 16 years follow-up of aortic valve reconstruction with pericardium: a stentless readily available cheap valve?☆

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Abstract

Objective: There is lack of information regarding the long-term behavior of aortic valve reconstruction with pericardium (AoR). A 16-year follow-up is reported here. **Methods**: Between 1988 and 1995, 92 consecutive patients had AoR with bovine (Group I, $n=27$) or glutaraldehyde-treated autologous pericardium (Group II, $n=65$). The mean age was 30 years (range 12–68). There were 65% males, 92% in sinus rhythm, 84% had rheumatic etiology and 36% had 'other valve' surgery. Mitral valve replacement with a mechanical prosthesis is a contraindication to the operation. **Results**: Hospital mortality was 2%. The reconstructed aortic valve performed well with excellent hemodynamics. The mean follow-up interval was 10.5±4 years, range 9–16 years (longer for group I,12 versus 10 years) with 4% late deaths and seven patients lost to follow-up. Survival rate was 85±4%. There were no episodes of thromboembolism. Freedom from reoperation for the whole group was 68±5% at 10 years and 47±6% at 16 years. For group I, it was 68±9% at 10 years and 48±10% at 16 years, while for group II it was 72±6 and 45±8% at 10 and 15 years, respectively. Excluding endocarditis (one in group I and seven in group II) and 'other' reasons for reoperation (two in group I and three in group II), the freedom from structural valve degeneration (SVD) at 10 and 16 years was 78±1 and 55±10% for group I. For group II, it was 80±5% at 10 years and 58±9% at 15 years. The mean interval at which the valve degenerated was 8.8 years±3.6 and did not differ between the two groups. **Conclusions**: AoR is feasible with good hemodynamics, low mortality and thromboembolic rate. Its behavior at 10 years is comparable to that of stentless aortic valve bioprosthesis. It can be performed with either xenopericardium or glutaraldehyde-treated autologous pericardium, but the latter has the advantage of being inexpensive and readily available.

Keywords: Aortic valve; Pericardium; Valve reconstruction

1. Introduction

Most surgeons treat aortic valve lesions with a replacement which offers a satisfactory solution to the problem. The awareness of long-term problems of the available prosthesis and the standardization and universal acceptance of the repair techniques on the atrioventricular valves have awakened interest in aortic valve repair. The most important consideration in determining the feasibility of aortic valve repair is the quality of aortic valve leaflets. When deficient, a leaflet can be extended or replaced by bovine or autologous pericardium or other material. Single cusp extension is demanding and does not yield consistent results. It is our contention that cusp extension or replacement of the three aortic cusps with a single strip of pericardium is technically more reliable [1–3]. This report describes up to 16 years follow-up in 92 consecutive patients who underwent aortic valve reconstruction utilizing this technique [4–7].

2. Materials and methods

2.1. Patients

Between 1988 and 1995, 1114 patients underwent aortic valve procedures at our institution with 393 (35%) being repairs. Out of the 393 repairs, 92 consecutive patients had aortic valve reconstruction utilizing pericardium. Initially, commercially available bovine pericardium was used. This constituted group I ($n=27$ patients). However, it was thought that glutaraldehyde-treated autologous pericardium would be a better material. Therefore, this material was utilized in most of the patients. This constituted group II ($n=65$ patients). The autologous pericardium was treated with 0.5% buffered glutaraldehyde solution for 10 min and rinsed for 10 min prior to use.

All patients' diagnoses were established by color Doppler transthoracic echocardiography. Cardiac catheterization was only done to rule out coronary artery disease in older patients (men > 40 years, women > 45 years), or if there was

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Table 1
Patients' clinical profile: aortic valve reconstruction with pericardium

Variable	Group I 27	Group II 65	*P*-value	Total 92
Age (years)				
Mean	21.2	33.3	0.68	30
Range	12–36	12–68		12–68
Median	21	29		26
Male:female	18:9	47:18	0.59	65:27
Sinus rhythm	25	61	0.83	86
Mean NYHA-FC	3	2.5	0.92	2.6
Diagnosis				
Regurgitation	14	35	0.2	49
Stenosis	2	13	0.2	15
Mixed	11	17	0.2	28
Cause				
Rheumatic	27	49		76
Degenerative	0	12	0.005	12
Congenital	0	2		2
Infective	0	2		2
Surgery				
Isolated	15	44		59
+Mitral	9	18		27
+Mitral+tricuspid	3	3		6

a discrepancy between clinical data and echocardiography findings. The mean age for the whole group was 30 years with a range from 12 to 68. The clinical profile of the patients is represented in Table 1. The left ventricular function was normal or mildly impaired in most of the patients. Other valve surgery was performed in 36% of the cases.

2.2. Methods

Surgery was performed utilizing cardiopulmonary bypass with single or bicaval venous cannulation and a body temperature of 30–32 °C. Myocardial protection was achieved initially with cold crystalloid cardioplegia, but since 1991 it has been achieved with antegrade and retrograde cold blood cardioplegia. The heart was vented in every case. If there was involvement of other valves, they were first exposed and treated appropriately. Mitral valve replacement with a mechanical prosthesis is considered a contraindication to this operation. Transesophageal echocardiograph (TEE) was used in all patients to assess the valves preoperatively and the result of surgery postoperatively. The idea was to end up with a competent aortic valve with a large surface of coaptation and with a minimal gradient (Fig. 1). The details of the surgical technique are described in detail in previous publications [4–7].

The mean cardiopulmonary bypass time for group I patients was 150 min ± 33, and for group II 129 min ± 25. The mean aortic cross-clamp time for group I was 100 min ± 20 and for group II was 95 min ± 20.

2.3. Statistical analysis

Patient characteristics were summarized as frequencies and percentages for categorical variables and values were expressed as mean ± SD. The survival and event-free values were calculated using the Kaplan–Meier survival analysis. Survival data were compared using the *z*-score. The two-sided *t*-test was used for the computation of the mean

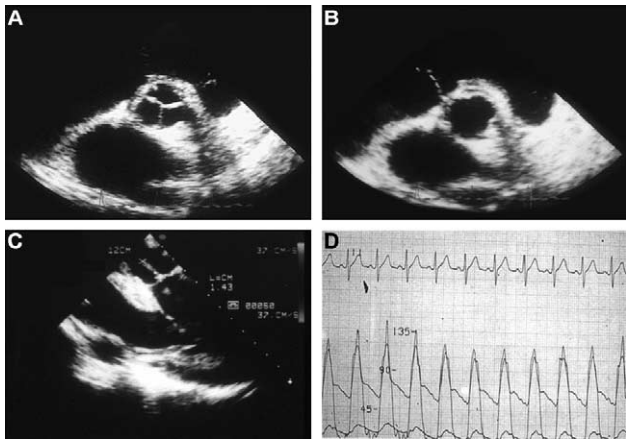

Fig. 1. TEE appearance of aortic valve reconstruction postoperatively. (A) Valve closure, (B) valve opening, (C) no AR—note large surface of coaptation, (D) simultaneous pressure in left ventricle and aorta—no gradient.

interval between surgeries and degenerations. The Chi-square test was used appropriately to make between group comparisons. Statistical analysis was carried out using SPSS 13.0 program. A *P*-value of <0.05 was considered to be statistically significant.

3. Results

3.1. Immediate results

In the operating room, immediate TEE demonstrated a satisfactory result in all patients. However, in four patients done early in the series and not included in this analysis, the result of the reconstruction was not satisfactory and a replacement with prosthesis was performed without mortality. In another patient also not included whose aortic valve reconstruction was good, an emergency aortic valve replacement had to be performed on the same day as the patient developed ischemic changes in the left coronary artery territory. An echocardiography revealed the possibility of left coronary ostial obstruction in diastole by a redundant left coronary leaflet. All technical pitfalls were worked out and subsequently the reconstruction was always successful.

3.2. Mortality and morbidity

There was no operative mortality in group I patients, and two mortalities in group II patients for a 2% total hospital mortality. One patient died of myocardial failure and low cardiac output and the other from hemorrhage due to coronary sinus rupture. There were no major morbidities.

3.3. Anticoagulation

Patients were routinely placed on Aspirin 100 mg once per day. Nine patients were anticoagulated with Coumadin because of atrial fibrillation.

Table 2
Results of aortic reconstruction with bovine (Group I) and autologous pericardium (Group II)

Event	Group I, $n=27$		Group II, $N=65$		Total, $n=92$	
Deaths						
In hospital	0		2		2%	
Late	1		3		4%	
At reoperation	2		1		3%	
Embolism	0		0		0	
Anticoagulation (Coumodin)	4		5		9	
Reoperation						
Total	14		27		41	
SVD[a]	11		17		28	
Endocarditis	1		7		8	
Other/miscellaneous	2		3		5	
	10 years	16 years	10 years	15 years	10 years	16 years
Freedom from						
Reoperation	68±9	48±10	72±6	45±8	68±5	47±6
SVD[a]	78±1	55±10	80±5	58±9	81±4	57±6

[a] SVD, structural valve degeneration.

3.4. Follow-up

The patients were followed up in a dedicated valve clinic with clinical evaluation and transthoracic echocardiography at 3 months and 6 months then thereafter every 1–2 years or more frequently if indicated. The mean follow-up was 10.5±5 years with a range from 9 to 16 years. Seven patients were lost to follow-up, three from group I and four from group II. The mean follow-up was longer for group I patients (12 versus 10 years).

Four patients died late, three cardiac (one from group I and two from group II) and one from a car accident (group II). In addition, three patients died at reoperation, two in group I and one in group II for a reoperation hospital mortality of 7%. The survival rate for the whole group at 16 years was 85±4%. No thromboembolic events were detected in any patient (Table 2). Excluding patients who needed reoperation 90% of the survivors are asymptomatic in NYHA-FC I-II.

Four of 19 female patients in childbearing age had six pregnancies and delivered normally two from each group. Both patients from group I had reoperation, one at 14 years (one pregnancy) and one at 10 years (three pregnancies).

In group I, at 16 years, only seven patients remain with no reoperation and we continue to follow up. Five of those had good aortic valve function with minimal AR and mild echocardiographic gradients, though one aortic valve shows thickening and calcification. The remaining two patients have developed considerable thickening, calcification, and stenosis with mean gradients of 42 and 52 mmHg, respectively. Additionally, one of them has considerable mitral and tricuspid valve disease. These two patients, though mildly symptomatic at present, will likely require reoperation (Table 3).

Table 3
Valve status of the remaining patients

	Good valve	Mild disease	Moderate disease	Severe disease
Group I, $n=7$	2	3	2	0
Group II, $N=28$	13[a]	8	6	1

[a] One patient with considerable MV disease.

In group II, at 16 years, 28 patients remain with no reoperation and we continue to follow up. Thirteen patients have a perfectly functional aortic valve with some thickening, but not more than trace AR and very minimal gradients. However, one of those with mitral valve (MV) repair at the time of AoR now has considerable MV disease. Eight patients have mild disease, six patients have moderate dysfunction (in addition, two have considerable MV disease) and one patient has considerable aortic valve stenosis (peak/mean gradient = 62/42—valve area 0.7 cm^2) with thickened heavily calcified valve 11 years after surgery. Hence, four patients will probably require reoperation soon, three for the aortic and one for the mitral valve (Table 3).

3.5. Reoperation

Over the follow-up period of 16 years, 41 patients needed reoperation, 14 from group I and 27 from group II. For the whole group, the overall freedom from all events was 63±5% at 10 years and 40±6% at 16 years (Fig. 2), while the reoperation-free survival was 68±5% at 10 years and 47±6%

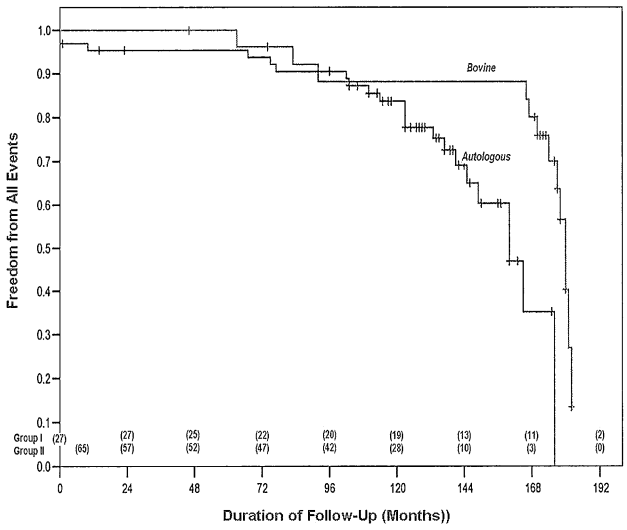

Fig. 2. Freedom from all events. Bovine versus autologous pericardium.

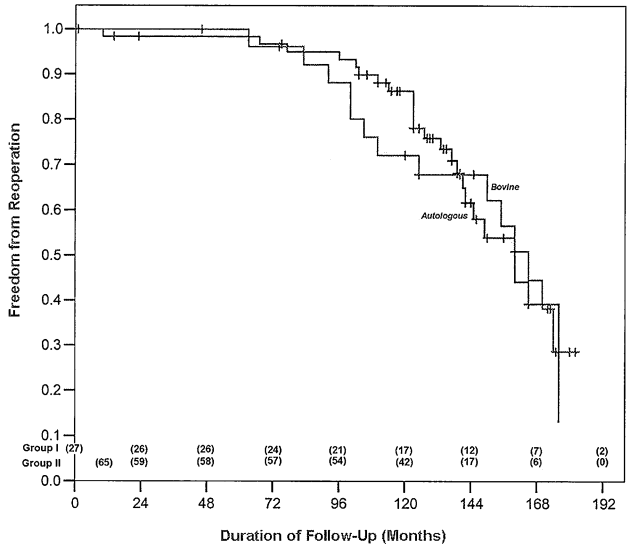

Fig. 3. Freedom from reoperation. Bovine versus autologous pericardium.

at 16 years. The freedom from reoperation was not statistically different between groups I and II (68±9 versus 72±6% at 10 years and 48±10 versus 45±8% at 15 years) (Fig. 3). The mean interval between surgeries was 8.8 years±3.6 with a range from 5 days to 16 years again with no significant difference between groups I and II.

Of the reoperations in group I, one was due to endocarditis, two were due to MV disease and the other 11 reoperations were classified as structural valve degeneration (Table 2). One patient required two reoperations. In the first, the mitral and tricuspid valves were repaired at which time the reconstructed aortic valve was not touched. In the second reoperation, the aortic valve was replaced after 6.3 years. In another patient, at the time of reoperation for MV disease a redundant leaflet of the reconstructed aortic valve was resuspended and that valve remains good 14 years later.

In group II, there were seven reoperations because of endocarditis; two for mitral/tricuspid valve disease, and

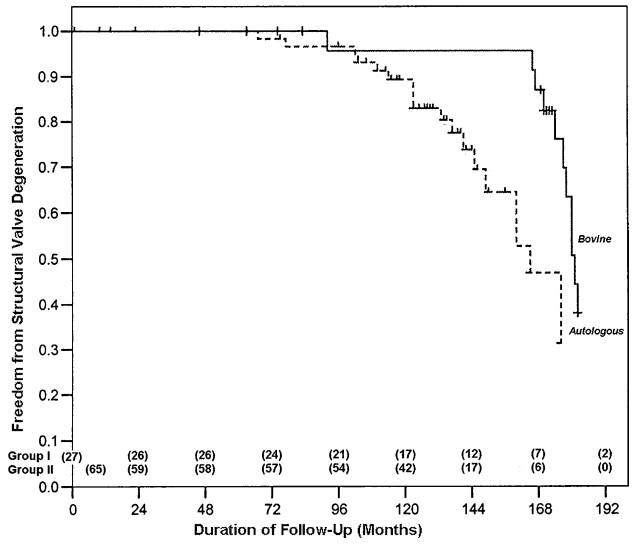

Fig. 4. Freedom from structural valve degeneration. Bovine versus autologous pericardium.

17 due to SVD (Table 2). One patient had the reconstructed aortic valve replaced at 5 days because of AR. The mechanism of failure was not clear, but it was felt that it was related to a dilated aortic annulus.

The freedom from SVD for the 92 patients was 81±4% at 10 years, and 57±6% at 16 years. The freedom from SVD for group I was 78±1% at 10 years, and 55±10% at 16 years. For group II, it was 80±5% at 10 years, and 58±9% at 15 years. There was no difference in SVD between the two groups (Fig. 4).

Three patients died at reoperation (hospital mortality 7%)—one with extensive endocarditis and aortic root abscess.

4. Discussion

Valve replacement is a well-established modality for treatment of aortic valve disease. However, in young patients including women of childbearing age, valve replacement still presents a problem because of the limited durability of bioprostheses and because of the difficulties associated with the long-term anticoagulation with Coumadin required for mechanical prostheses. Under these circumstances, valve repair may offer a better solution. Conservative operations on the aortic valve have a long history dating back to the early days of cardiac surgery and went through phases of enthusiasm and discouragement [8]. In general, the repair can be done utilizing native aortic valve leaflets by various techniques that include commissurotomy, subcommissural annuloplasty, free edge unrolling, cusp resuspension, supraaortic crest enhancement, free edge reinforcement, wedge resection, etc. [9]. Such techniques of repair are not always possible and carry a significant rate of reoperations, particularly in a young rheumatic population [3].

In the presence of cusp retraction, these maneuvers cannot be used and cusp extension is an option. Aortic cusp extension or replacement of a single leaflet was proposed by several investigators in the 1960s, but results were variable and mostly negative [10]. Al-Fagih et al. reintroduced the principle of aortic valve repair using bovine pericardium for cusp extension [2]. Individually tailored bovine pericardial extensions to the native cusps were done. We felt the technique was demanding and did not give consistent results. We therefore used an extension of all three cusps with a single strip of pericardium (bovine or glutaraldehyde-treated autologous pericardium), and this technique we refer to as aortic valve reconstruction (AoR) [5–7].

We started the series in 1988 and up to 1995, 92 consecutive patients underwent aortic valve reconstruction: 27 patients (group I) utilizing bovine pericardium and 65 patients (group II) utilizing glutaraldehyde-treated autologous pericardium. Both groups were followed up closely and early results of up to 8 years were reported [11]. We now have up to 16-year follow-up (mean 10.5 years) with complete data in 85 patients; seven patients were lost to follow-up.

The technique is reproducible and can be carried out with minimal mortality and morbidity. The hemodynamic

performance is excellent. Immediate echocardiographic data were optimal not only in terms of valve competence, but also with regard to gradients even in the presence of a small aortic annulus. This encouraged us to use this procedure in older patients with stenotic and calcified aortic valves with small annulus. There were no thromboembolic episodes and anticoagulation was only required for patients in atrial fibrillation (10%).

After 16 years, 35 patients (38%) remain with no reoperations and of those, 30 patients (32%) have good aortic valve function. The 10-year freedom from reoperation was 68±5% and from SVD was 81±4%. Taking into consideration our very young population, this compares favorably with other aortic valve replacements including stentless xenografts and homografts which are mostly used in older age groups, usually >60 years [12–15].

Initially, we thought that autologous pericardium would behave better than bovine pericardium. Our earlier follow-up seemed to confirm this trend [11]. However, at 16 years there was no statistically significant difference between the two materials. As a matter of fact, the mean interval at which the valve degenerated was almost exactly the same in the two groups at 8.8 years±3.6.

There were 14 reoperations in group I and 27 reoperations in group II. Seven patients in group II developed endocarditis, a surprisingly high incidence and is a matter of concern. This is a higher incidence than what we see with other valve prosthetic endocarditis in our hospital. In close to 4000 valve procedures performed over a 15-year period, 131 cases of endocarditis were recorded with 57% being in prosthetic valves, but no particular valve prosthesis stood out as being more prone to endocarditis than others. Interestingly, in the series of Senning and Rothlin [16] of single and triple cusp extension and total valve replacement with fresh autologous fascia lata, infective endocarditis was present in 14% of the patients. Whether this potential problem is inherent in the use of autologous tissue is unknown. From our data it appears that this risk is a continuous hazard since these patients developed endocarditis both early and late (1.4, 5, 8.2, 48, 61, 99 and 163 months after operation). This hazard was not present in the bovine pericardial group where only one patient developed endocarditis 62 months after operation. Whether the continuous leaching of glutaraldehyde in the fully treated bovine tissue plays a defensive role is not known. On the other hand, while histology showed in both tissues an acellular core, the autologous pericardium had a continuous epithelium-like layer that should theoretically protect it.

One patient in group II required reoperation within 5 days due to the development of severe aortic regurgitation which was felt to be related to significant aortic root dilation. Five other patients underwent reoperation because of mitral/tricuspid valve dysfunction. In these patients, the aortic valve was still functioning well and was not touched except in one patient in group I where the aortic valve was re-repaired and continues to function well to date.

Excluding these patients, a total of 11 patients in group I and 17 patients in group II required reoperation because of SVD [17]. Freedom from SVD was 78±1% at 10 years and 55±10% at 16 years for group I. For group II, it was 80±5% at 10 years and 58±9% at 15 years. In our opinion, these results are very satisfactory considering that our patients had a mean age of 30 years and 83% of them had a rheumatic etiology justifying the continued utilization of the technique. Either bovine or autologous pericardium can be used, as our analysis did not demonstrate any statistically significant difference in their performance at 15 years.

The mode of valve degeneration differed between the bovine pericardium and the autologous pericardium. The failed bovine pericardial valves tended to show heavy calcification and extensive fibrosis that made the reoperation technically more difficult than with the autologous pericardium which showed still pliability with less fibrosis and calcification. It is worth mentioning that despite the absence of pericardium in group II, sternal reentry was not difficult. As a matter of fact there was no catastrophic reentry in any of the redo patients. At reoperation and in patients with heavy calcification extending to the aortic root a full aortic root replacement with coronary transfer was required in almost half of the redo patients. Progressive dilatation in the aortic root with severe AR was the cause for two reoperations in group II.

According to the patient's characteristics, the dysfunctional valves were replaced using a mechanical prosthesis, a bioprosthesis (stented or stentless), autograft, or a homograft.

5. Summary

In summary, we present here a series of aortic valve reconstructions in a relatively young patient cohort with mostly rheumatic etiology. Bovine pericardium and glutaraldehyde-treated autologous pericardium were utilized.

After 16 years of close follow-up, we conclude that (1) the hemodynamic performance is excellent, (2) the long-term results are acceptable and comparable at least to stentless aortic valve replacement (if not better) considering the longer follow-up and the younger patients, (3) either bovine or autologous pericardium can be utilized in the technique. Autologous pericardium, however, is readily available and inexpensive, but if not available we should not hesitate to use bovine pericardium.

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Appendix A. Conference discussion

Dr A. Kappetein (*Rotterdam, The Netherlands*): What worries me a little bit is that you say that your valve compares favorable with a stentless valve, I think you compared them with a stentless valve which is on the market and I've never heard of a structural valve deterioration of 58% for these valves. I think this is a rather poor figure. A reoperation mortality of 10% also needs some explanation.

Dr Al-Halees: The 58% freedom for SVD is for the bovine pericardium, and that's why I said initially we are not using the bovine pericardium anymore, and the 76% is for the autologous pericardium, which I think at 15 years is comparable to any stentless aortic valve on the market currently taking into consideration that the mean age for our patients is 30 years.

Dr M. Antunes (*Coimbra, Portugal*): People must realize that the population you're talking about is a very difficult one, where all types of prostheses have a different behavior. So, I agree that it probably compares favorably with others' experiences. I know that you were also using the Ross operation in this population. Do you now have any data comparing these methods with the Ross operation in the medium and the long-term?

Dr Al-Halees: For the Ross operation, we have two distinct groups, the group that is rheumatic and the nonrheumatic. In the group that is rheumatic, at about 10 years the freedom from reoperation is almost similar. However, for those patients with congenital aortic valve disease and the Ross procedure, the freedom from reoperation is much better, and actually those with congenital aortic valve stenosis have done extremely well with the Ross procedure with a very low reoperation rate. That's why we look at the Ross operation now as being the procedure of choice for patients with congenital aortic valve stenosis.

Dr J. Melo (*Carnaxide, Portugal*): Can you give us some details for how long you keep those valves cross-linked with glutaraldehyde? And with your device, what kind of pressure does this put on the pericardium? Is this high-pressure fixation or is it low-pressure? Do you have any idea on that?

Dr Al-Halees: The glutaraldehyde is 0.5% and we keep the pericardium for 10 min, and then the pericardium is washed in three cycles, 5 min each, prior to being implanted. In terms of the pressure, this is a very light pressure. It is just the sheet of pericardium and the plastic mold goes on top of that, so it hardly produces any pressure.