Role of Pericardial Constraint for Right Ventricular Function in Humans*

Wolfram Burger, MD; Martin Straube; Michael Behne, MD; Koppany Sarai; Friedhelm Beyersdorf, MD; Lothar Eckel, MD; Adrienne Derserer, MD; Peter Satter, MD; and Martin Kaltenbach, MD

Study objective: To analyze the extent of pericardial constraint on right ventricular function in humans.

Patients and methods: Twenty patients, 59 ± 2 (mean ± SEM) years old, undergoing coronary bypass surgery. Right ventricular volumes and pressures were evaluated using a rapid response Swan-Ganz thermodilution catheter.

Interventions: Parameters were determined before and after pericardiectomy, both before and during increased right ventricular systolic pressure by partial compression of the pulmonary artery (before pulmonary compression: 25 ± 1 mm Hg; during: 39 ± 1 mm Hg).

Results: Pericardiectomy alone did not significantly affect right ventricular end-diastolic volume (before: 79 ± 4 mL m⁻²; after: 78 ± 3 mL m⁻³), right ventricular ejection fraction (before: 48 ± 1%; after: 48 ± 2%), and right atrial pressure (before: 4.3 ± 0.8 mm Hg; after: 4.3 ± 0.7 mm Hg). Before pericardiectomy, the increase in right ventricular afterload significantly increased right atrial pressure (to 5.5 ± 0.7 mm Hg, p<0.05) and reduced right ventricular ejection fraction (to 43 ± 2%, p<0.01). Right ventricular end-diastolic volume remained unchanged. After pericardiectomy, the increase in right ventricular afterload significantly increased right ventricular end-diastolic volume (to 85 ± 3 mL m⁻², p<0.01) and also reduced right ventricular ejection fraction (to 42 ± 2%, p<0.01), while right atrial pressure was not significantly changed. During increased right ventricular afterload, the right ventricular diastolic pressure-volume relation was shifted rightward.

Conclusions: At normal levels of right ventricular diastolic filling, the pericardium does not exert constraining effects on right ventricular function. However, with increasing levels of right ventricular preload, pericardial constraint significantly influences right ventricular function in humans.

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Key words: pericardial constraint; pericardium; right ventricular ejection fraction; right ventricular function; thermodilution method

In animal experiments, removal of the pericardium induced considerable downward and/or rightward shifts of left and right ventricular diastolic pressure-volume relations. These pericardial influences were more pronounced in the right ventricle as compared with the left ventricle. Only a few studies have investigated the role of the pericardium in humans. For obvious reasons, these investigations are confined to patients undergoing cardiac surgery, in whom, up to now, only transesophageal echocardiography could be used to yield methodologically limited information on right ventricular volumes. Therefore, previous studies in man were restricted to sole pressure measurements and could provide only indirect information about the effect of pericardiectomy on ventricular pressure-volume relations.

Recently, the long-known thermodilution method for the determination of ventricular volumes was improved by the introduction of a new computer-aided algorithm for the evaluation of thermodilution curves obtained by a fast-response Swan-Ganz thermodilution catheter. This computerized method permits sequential determinations of right ventricular volumes and ejection fraction in intervals shorter than 30 s together with continuous measurement of pulmonary circulatory pressures. The method shows good correlation with contrast angiography and radionuclide methods.

The aim of the present study was to evaluate whether pericardial constraint plays a significant role for right ventricular function at normal and elevated right ventricular filling pressures. This was investigated in patients with stable coronary artery disease undergoing aortocoronary bypass surgery.

METHODS

Twenty patients (5 women, 15 men) at a mean age of 59 (range, 45 to 72) years were investigated after informed and written consent had been obtained. The study protocol was approved by the institutional committee on human research of our hospital. The patients were investigated during aortocoronary bypass sur-

EDV=end-diastolic volume; EF=ejection fraction; ESV=end-systolic volume; RF=residual fraction

*From the Departments of Cardiology (Drs. Burger and Kaltenbach and Mr. Straube), Anesthesiology (Drs. Behne and Deroser), and Cardiac Surgery (Drs. Sarai, Beyersdorf, Eckel, and Satter), University Hospital Frankfurt, Theodor-Stern-Uai 7, Frankfurt, Germany. Manuscript received January 25, 1994; revision accepted May 19. Reprint requests: Dr. Burger, Department of Cardiology, University Hospital, Theodor-Stern-Uai 7, 60590 Frankfurt, Germany.
surgery. Three-/two-/one-vessel disease, defined as an inner diameter reduction of at least 70%, was present in 9, 10, and 1 patient, respectively. With the same definition for a diseased vessel, the right coronary artery was involved in 15 patients. Previous myocardial infarction had occurred in seven patients. Angiographically determined left ventricular ejection fraction was 70 ± 2% (mean ± SEM; range: 53 to 86%). All patients were in regular sinus rhythm; patients with frequent premature beats were excluded from the study to obtain technically correct thermal washout curves. Patients with angina class 4 according to the Canadian Heart Classifications, patients with unstable angina, and patients showing intraoperative ST-segment changes in the surface ECG suggestive of myocardial ischemia were excluded from the study.

Routine cardiac premedication consisted of an oral nitrate, a calcium channel blocker, and 300 mg of spironolactone. The latter was given during the preceding 2 preoperative days. General anesthesia was induced by pancuronium (1 mg), fentanyl (0.2 mg), etomidate (0.2 mg/kg), and succinylcholine (1 mg/kg) and was maintained with fentanyl, midazolam, and pancuronium during controlled ventilation with an oxygen-nitrous oxide mixture (ratio 1:1). To support renal circulation, intravenous dopamine (200 μg/min, "renal dose") was administered. During the 15-min period of investigation, medication was not changed and surgical manipulations were interrupted.

All measurements were taken with the chest kept open by a sternal retractor. After determination of control values, measurements during increased right ventricular afterload were performed. This was accomplished by compression of the proximal pulmonary artery by a finger of the surgeon through a 2-cm pericardial incision. Thereby right ventricular systolic pressure was increased to approximately 40 mm Hg. Then the pericardium was completely opened and measurements were repeated before and during compression of the pulmonary artery.

Arterial blood pressure was determined via cannulation of the radial artery. Right atrial pressure was measured using the atrial lumen of the Swan-Ganz thermomodulation catheter (model 93A-431 7.5 F G, American Edwards Laboratories, Santa Ana, Calif) that was also used for determinations of right ventricular volumes. The thermomodulation method is described in detail elsewhere. 

Briefly, after intraatrial injection of ice-cold saline solution, a computer-aided algorithm determines right ventricular residual fraction (RF) from the logarithmic temperature decay recorded via a fast-response thermistor in the pulmonary artery (REF-1 ejection fraction cardiac output computer, American Edwards Laboratories, Santa Ana, Calif). Right ventricular ejection fraction (EF) is then calculated by the computer as EF=1-RF. Thereafter right ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) are calculated as follows: EDV=cardiac output/(EF×heart rate); ESV=EDV-stroke volume. Heart rate is determined via a surface ECG interfaced with the computer (REF-1). Volumetric data represent averages of fourfold thermodilutional measurements. Right ventricular pressure was obtained by direct puncture of the right ventricle by a 12-gauge steel needle.

Data are given as mean and standard error of the mean. A nonparametric analysis of variance (Friedman test) was used to evaluate significant differences among the four investigated stages of the study protocol. In case of significance, multiple paired two-tailed nonparametric tests were performed according to Wilcoxon and Wilcoxon.

### RESULTS

Table 1 summarizes hemodynamic and right ventricular volumetric results. Before pericardiotomy, compression of the pulmonary artery significantly decreased mean arterial blood pressure and right ventricular EF. Right atrial pressure, right ventricular systolic pressure, and right ventricular ESV were increased, while the other parameters remained unchanged. Pericardiotomy without compression of the pulmonary artery did not change the control values (Table 1). After pericardiotomy, compression of the pulmonary artery increased both right ventricular EDV and ESV, while right ventricular EF was reduced. Mean arterial blood pressure, right atrial pressure, and the remaining parameters were not significantly influenced by pulmonary artery compression after pericardiotomy. Substituting right atrial pressure as an estimate for right ventricular diastolic pressure, Figure 1 shows a rightward shift of the diastolic right ventricular pressure-volume relation after pericardiotomy during increased right ventricular afterload.

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**Table 1—Effects of Pericardiotomy and Increase of Right Ventricular Afterload (During Transient Compression of Pulmonary Artery) on Central Hemodynamics and Right Ventricular Volumes in 20 Patients During Cardiac Surgery for Aortocoronary Bypass Grafting**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PA Compression</th>
<th>After Pericardiotomy</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean arterial blood pressure, mm Hg</td>
<td>77 ± 3</td>
<td>71 ± 3</td>
<td>81 ± 3</td>
<td>0.000025</td>
</tr>
<tr>
<td>Heart rate, min⁻¹</td>
<td>80 ± 4</td>
<td>81 ± 4</td>
<td>79 ± 4</td>
<td>0.21</td>
</tr>
<tr>
<td>Cardiac index, L · min⁻¹ · m⁻²</td>
<td>2.9 ± 0.2</td>
<td>2.8 ± 0.1</td>
<td>2.9 ± 0.2</td>
<td>0.083</td>
</tr>
<tr>
<td>Right atrial pressure, mm Hg</td>
<td>4.3 ± 0.8</td>
<td>5.5 ± 0.7</td>
<td>4.3 ± 0.7</td>
<td>0.0036</td>
</tr>
<tr>
<td>RV systolic pressure, mm Hg</td>
<td>25 ± 1</td>
<td>30 ± 1†</td>
<td>25 ± 1</td>
<td>0.000001</td>
</tr>
<tr>
<td>Stroke volume index, mL · m⁻²</td>
<td>38 ± 2</td>
<td>35 ± 2</td>
<td>38 ± 2</td>
<td>0.090</td>
</tr>
<tr>
<td>RV ejection fraction, %</td>
<td>48 ± 1</td>
<td>43 ± 2†</td>
<td>48 ± 2</td>
<td>0.000001</td>
</tr>
<tr>
<td>RV end-diastolic volume index, mL · m⁻²</td>
<td>79 ± 4</td>
<td>83 ± 3</td>
<td>78 ± 3</td>
<td>0.0068</td>
</tr>
<tr>
<td>RV end-systolic volume index, mL · m⁻²</td>
<td>41 ± 2</td>
<td>47 ± 2‡</td>
<td>40 ± 2</td>
<td>0.000027</td>
</tr>
</tbody>
</table>

*Data are given as mean and standard error of the mean. RV=right ventricular; PA=pulmonary artery; p=p value of Friedman test.*

*p≤0.01, †p≤0.05 vs control according to multiple nonparametric paired tests (according to Wilcoxon and Wilcoxon). There were no significant differences between control data before and after pericardiotomy.
**DISCUSSION**

**Methodologic Considerations**

Due to the complex shape of the right ventricular cavity, imaging technique renders difficulties for the quantification of right ventricular volumes. Certain geometric assumptions have to be made, thus making determinations of right ventricular volumes less accurate than determinations of left ventricular volumes.\(^{20}\) Nuclear imaging techniques require additional cardiac catheterization for the evaluation of intracavitary pressures. Furthermore, overlap among the right ventricle and other cardiac chambers may limit the accuracy of radionuclide measurements.\(^{20}\)

Thermodilutional determinations of right ventricular volumes correlated well with angiographic and radionuclide measurements.\(^{12,15-19}\) The coefficient of variation for thermodilutional determination of right ventricular EF was reported as ranging between 7 and 13%.\(^{14,15,18,19,21}\) Similar as the above-mentioned methods, the thermodilution technique is certainly not the “gold standard” for the evaluation of right ventricular volumes. However, independent from space-consuming radionuclide or angiographic equipment, thermodilution can easily be applied at the bedside or, as in the present study, in the setting of the cardiothoracic operating room. Furthermore, the method does not depend on complex geometric assumptions as the above-mentioned imaging techniques.

As in all volumetric methods, extrasystoles and atrial fibrillation enhance beat-to-beat variation of ventricular volumes. Therefore, the present study included only patients with regular sinus rhythm. According to Spinale et al.,\(^{20}\) tricuspid regurgitation causes underestimation of right ventricular EF. Since the mean right atrial pressure was within normal range, relevant tricuspid regurgitation can be excluded in the patients of this study.

**Comparison With Previous Determinations of Right Ventricular Volumes**

The reported values of right ventricular EF are considerably lower as compared with data obtained with the identical thermodilution method by Danchin et al\(^{14}\) in awake patients without previous myocardial infarction undergoing percutaneous transluminal coronary angioplasty for single-vessel coronary artery disease. However, the values are in line with data obtained in patients similarly characterized as ours during coronary bypass surgery.\(^{23}\)

**Pericardial Effects on the Right Ventricle**

This investigation confirms earlier intraoperative studies in humans showing that normal right atrial or right ventricular diastolic pressure is not influenced by pericardiomyotomy.\(^{5,7}\) However, our data are in contrast to the study by Mathru et al\(^{8}\) previously reported in this journal. This group, using also thermodilution for intraoperative determinations of right ventricular volumes, observed a significant reduction of right atrial pressure with pericardiomyotomy.\(^{8}\) Additionally and in contrast to our patients, the patients of Mathru et al\(^{8}\) showed a significant increase of right ventricular EDV with opening of the pericardium. The differences between these and our observations might be caused by the preoperative treatment of our patients with high doses of an aldosterone antagonist, as compared with the patients of Mathru et al, lower right atrial pressure. Mathru et al did not vary right ventricular load as it was performed in the present investigation.

Animal experiments showed enhanced pericardial influence on diastolic right ventricular function with increased right ventricular filling.\(^{1-3}\) To obtain different levels of right ventricular preload, the present study varied right ventricular afterload. This was accomplished by partial obstruction of right ventricular outflow. During this intervention, a significant increase in right atrial pressure was achieved only with the intact, but not with the opened, pericardium (Table 1, Fig 1), suggesting a constraining effect of the pericardium. In addition to pressure measurements, the current investigation determined right ventricular volumes to construct right ventricular end-diastolic pressure-volume relations (Fig 1). By this, a pericardium-dependent shift of the diastolic right ventricular pressure-volume relation could be demonstrated (Fig 1). However, these influences did not occur at low levels of right ventricular preload. Only with increased

![Figure 1: Right ventricular (RV) diastolic pressure-volume relation before (filled circles) and after (open circles) pericardiomyotomy. Mean ± SEM, N=20. Only during increased right atrial pressure (caused by increased right ventricular afterload during pulmonary artery [PA] compression), pericardiomyotomy induced a significant rightward shift of the right ventricular diastolic pressure-volume relation.](image-url)
right ventricular preload, pericardial constraint significantly influenced right ventricular function.

The data imply that right ventricular diastolic performance does not depend solely on myocardial but also on pericardial properties. This also implies, that at a given right ventricular preload, the length of cardiac muscle-fiber is modulated by pericardial influences. Therefore, the Frank-Starling mechanism may be modified for the right ventricle by pericardial constraint. This may even exert effects on the systemic circulation, as can be seen from the decrease of mean arterial blood pressure before pericardiectomy in pulmonary artery compression (Table 1).

As LeWinter and Pavelč24 could demonstrate in animal experiments, pericardial influences diminish during long-term increase of ventricular preload. Therefore, our data cannot be applied to situations with chronically increased right ventricular preload in the chronically failing heart. Also, transferring these data to normal persons without coronary heart disease may be limited, although there was no evidence in the present study for intraoperative ischemia as concluded from intraoperative ST-segment analysis.

CONCLUSION

In contrast to earlier investigations—in comparison to our patients—at slightly higher right ventricular diastolic pressures,8 we could not observe significant changes in right ventricular pressures and volumes following pericardiectomy. Therefore, at normal right ventricular filling, pericardial constraint does not play a relevant role for right ventricular function. However, with acutely increased right ventricular diastolic pressures, pericardial influences become significant, with effects even on the systemic circulation.

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