Accurate Preoperative Diagnosis of Pericardial Constriction Using Cine Computed Tomography

RON M. OREN, MD, MALEAH GROVER-McKAY, MD, FACC,
WILLIAM STANFORD, MD, FACC, ROBERT M. WEISS, MD
Iowa City, Iowa

Objectives. The purpose of this study was to determine the accuracy of cine computed tomography in the diagnosis of constrictive pericarditis.

Background. Constrictive pericarditis is characterized by abnormalities of both cardiac structure and function. Accurate diagnosis requires detection of both a thickened pericardium and abnormal ventricular diastolic filling. At present, no one diagnostic technique has demonstrated sufficient accuracy in this setting. Cine computed tomography is a relatively new cardiac imaging mode with very high time and spatial resolution that has the potential to accurately diagnose constrictive pericarditis.

Methods. Twelve consecutive patients were retrospectively identified who had catheterization findings suggestive of constrictive physiology, had undergone a cine computed tomographic examination and had pathologic data that delineated the status of the pericardium. Group 1 (with constrictive pericarditis; n = 5) had surgical confirmation of thickened pericardium and improved clinically after pericardectomy. Group 2 (no constrictive pericarditis; n = 7) had cardiomyopathy with normal pericardium.

The clinical manifestations of constrictive pericarditis mimic a variety of cardiopulmonary disorders, making the diagnosis of this condition sometimes difficult. A recent surgical series (1) indicated that 12% of patients referred to the operating room for pericardial resection had a normal pericardium at the time of operation. Constrictive pericarditis is characterized anatomiclly by an abnormally thickened and noncompliant pericardium that acts to limit ventricular compliance during mid to late diastole. Consequently, nearly all ventricular filling occurs very rapidly in early diastole. This results in elevated cardiac filling pressures and the characteristic hemodynamic waveforms during which the diastolic pressures of the cardiac chambers equalize (2). The clinical presentation of constrictive pericarditis is not unique, however, because several other conditions can produce similar signs, symptoms and hemodynamic data (3).

The ideal single-imaging technique for the accurate preoperative diagnosis of pericardial constriction would simultaneously provide both anatomic and physiologic data describing the thickened pericardium and physiologic data describing the abnormal diastolic ventricular filling. Several imaging techniques have been reported to have the ability to identify either the abnormal structure or the abnormal function of patients with this disorder. However, none of these techniques have been validated to simultaneously provide an accurate assessment of both the anatomic and the physiologic features of this syndrome.

Cine computed tomography is a relatively new imaging technique that provides very high resolution tomographic cardiac images. It has demonstrated precision in the quantitative assessment of right and left ventricular structure and both systolic and diastolic function (4–8). In addition, cine computed tomographic measurements of pericardial thickness in ex vivo preparations have been shown to correlate well with histologic assessments (9). Thus, cine computed
tomography may allow the simultaneous demonstration of the altered anatomy and physiology seen in constrictive pericarditis. Therefore, the following study was performed to determine the ability of this technique to provide an accurate preoperative assessment of patients with suspected pericardial constriction.

**Methods**

**Study group.** The study group comprised 12 patients and 7 normal subjects. Patients were identified by review of the data base at the University of Iowa and included all patients from November 1985 to October 1990 with the following inclusion criteria: 1) clinical suspicion of pericardial constriction; 2) hemodynamic data on cardiac catheterization consistent with pericardial constriction (2) (including equalization of diastolic pressures and the characteristic pressure waveforms); 3) cine computed tomographic examination; and 4) pathologic data that delineated the status of the pericardium.

Examination of these data revealed 12 patients who were separated into two groups on the basis of the pathologic data. Group 1 (with constrictive pericarditis; mean age 62 ± 7 years) comprised five patients with clinical and surgical evidence of pericardial constriction, including both thickened pericardium at operation and sustained clinical improvement after pericardectomy. Group 2 (no constrictive pericarditis, mean age 66 ± 5 years) comprised seven patients with both a clinical suspicion and a hemodynamic profile suggestive of pericardial constriction but with pathologic evidence of either 1) normal pericardium at autopsy or operation, or 2) myocardial inflammation and fibrosis on endomyocardial biopsy. Group 3 comprised seven normal volunteers (mean age 23 ± 3 years) who underwent cine computed tomographic examination.

**Cine computed tomography. General description of the system.** The cine computed tomographic machine used in these studies is the Imatron C-100 and has been described elsewhere (4-10). In the scanning mode used in the present study, tomographic movies consisting of eight levels and 10 frames are generated. Acquisition time is 58 ms/frame, slice thickness is 8 mm. Nonionic contrast medium injected at a rate of 1.5 to 2.5 ml/s was utilized in all studies to delineate the cardiac chambers. Two dye injection/scanning sequences are required to image the whole heart. This method has been previously demonstrated to exert negligible effects on systolic function, hemodynamic variables and ventricular volumes (6).

**Image analysis.** All cine computed tomographic images were analyzed for right and left ventricular end-diastolic and end-systolic volumes, heart rate, pericardial thickness and early diastolic filling characteristics.

The volumes of the entire right and left ventricles were calculated using methods described and validated previously in animal models that utilize a modified Simpson's rule (6). The timing of the end-diastolic image was computer-triggered on the R wave of the electrocardiogram (ECG), whereas the end-systolic image was identified visually as the image in which the left ventricular volume was the smallest. Early diastolic filling characteristics were determined using frame by frame analysis of ventricular volumes at each frame during diastole. Of the 10 cine frames in each tomographic movie, 6 to 7 occurred during systole, leaving 3 or 4 diastolic images in each movie available for analysis. This truncation of the imaging sequence is necessary owing to the limited image storage capacity of the imaging computer. Although the use of more images per cardiac cycle may be preferable, it would require additional dye injection and X-ray exposure. The cumulative filling fraction (%FF) was calculated for each framing time in the diastolic period by the following formula:

\[
\%FF = \frac{Vol - ESV}{SV} \times 100\% ,
\]

where Vol = ventricular volume (in ml) at the framing time, ESV = end-systolic volume and SV = stroke volume. The result was equal to the fraction of total diastolic filling that had occurred at each cine computed tomographic frame during early diastole.

Pericardial thickness was determined by a computer-assisted edge detection system previously described in animal experiments to determine left ventricular mass (5). In this method, a line was manually drawn from the myocardium, across the pericardium and into the adjacent tissue (usually lung). Image analysis software then generated a graph of computed tomographic density versus distance along this line. Because the pericardium is of a higher computed tomographic number than the surrounding structures, three peaks were produced in this graph: one for the myocardium, one for the pericardium and one for the surrounding tissue. Pericardial thickness was then measured as the width of the pericardial peak at one half of its height (Fig. 1).

In this study the pericardial thickness was assessed at 10° intervals around the circumference of both right and left ventricles at low, mid and high ventricular levels, and an average value for each patient or subject was determined as the mean of these values. The presence of pericardial calcification was assessed visually by its characteristic high radiodensity. In four normal subjects and two patients in Group 2, there were some segments in which the pericardium was not visible, and no plateau could be identified between the myocardial density and its surrounding structure. In this situation, which occurred in <5% of pericardial thickness measurements in these subjects, a pericardial thickness of 0.5 mm was assigned to these areas for statistical purposes.

**Statistical analysis.** Data on clinical characteristics, early ventricular diastolic filling and pericardial thickness in each patient and subject were calculated and reported as mean value ± SD. Intergroup comparisons were performed by
repeated measures analysis of variance. A p value < 0.05 was considered statistically significant.

**Results**

**Clinical characteristics of the patients (Table 1).** The presumed etiology of pericardial thickening in Group 1 included external radiation (n = 1), previous coronary artery bypass grafting (n = 1) and idiopathic origin (n = 3). The etiology of cardiac disease in Group 2 consisted of regurgitant valvular disease (n = 2) and ischemic (n = 2) or idiopathic (n = 3) cardiomyopathy. The normal status of the pericardium in Group 2 was identified by autopsy in three patients. Two patients with cardiomyopathy had "mild inflammation and fibrosis" on endomyocardial biopsy. The remaining two patients had visually normal pericardium at operation. All patients in Groups 1 and 2 had symptoms (including peripheral edema and dyspnea) classified in New York Heart Association functional class III (n = 3 in Group 1, n = 4 in Group 2) or IV (n = 2 in Group 1, n = 3 in Group 2). The hemodynamic profiles of the patients in Groups 1 and 2 were similar and demonstrated diastolic equalization of pressures.

**Ventricular volumetric data (Table 2).** No significant differences were noted in end-diastolic volume of either the right or the left ventricle between any of the groups. Right ventricular ejection fraction was not significantly different between the groups. Left ventricular ejection fraction was significantly higher in Group 3 than in Group 1 and tended to

**Figure 1.** Example of computer-assisted measurement of pericardial thickness. Left panel, Tomogram taken at the midventricular level from a patient with constrictive pericarditis and a thickened, noncalcified pericardium. A manually drawn line (A) extends from the myocardium, across the thickened pericardium and into the surrounding lung tissue. Right panel, Computer-generated graph of computed tomographic density (vertical axis) versus the length of line A (horizontal axis). Proceeding from left to right: A small "dip" is followed by a pericardial "peak" of approximately 180 computed tomographic (CT) units. This is followed by the pericardium/lung transition. Pericardial thickness is measured as the width of the pericardial peak at one half of its height, using both leading and trailing edges. This particular pericardial segment was measured at 7 mm. LV = left ventricle; RV = right ventricle.

**Table 1.** Hemodynamic Profile of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressures (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean RAP</td>
<td>17 ± 2</td>
<td>18 ± 2</td>
<td>NA</td>
</tr>
<tr>
<td>RVP systolic</td>
<td>48 ± 5</td>
<td>50 ± 4</td>
<td>NA</td>
</tr>
<tr>
<td>RVP diastolic</td>
<td>18 ± 3</td>
<td>17 ± 4</td>
<td>NA</td>
</tr>
<tr>
<td>PAP systolic</td>
<td>46 ± 4</td>
<td>49 ± 5</td>
<td>NA</td>
</tr>
<tr>
<td>PAP diastolic</td>
<td>21 ± 4</td>
<td>22 ± 2</td>
<td>NA</td>
</tr>
<tr>
<td>PWP</td>
<td>20 ± 3</td>
<td>20 ± 3</td>
<td>NA</td>
</tr>
<tr>
<td>CI (liters/min per m²)</td>
<td>2.5 ± 0.7</td>
<td>2.3 ± 0.5</td>
<td>NA</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>83 ± 4</td>
<td>82 ± 5</td>
<td>68 ± 3*</td>
</tr>
</tbody>
</table>

*p < 0.05, Group 3 versus Group 1 or 2. All p = NS for Group 1 versus 2. Values presented are mean value ± SD. CI = cardiac index; Group 1 = patients with surgical evidence for constrictive pericarditis; Group 2 = patients with suspected pericardial constriction but normal pericardium; Group 3 = normal volunteers; NA = not available; PAP = pulmonary artery pressure; PWP = pulmonary wedge pressure; RAP = right atrial pressure; RVP = right ventricular pressure.

**Table 2.** Ventricular Volumetric Data

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV EDV (ml)</td>
<td>176 ± 17</td>
<td>183 ± 14</td>
<td>146 ± 7</td>
</tr>
<tr>
<td>RV EDV1 (ml/m²)</td>
<td>93 ± 15</td>
<td>94 ± 13</td>
<td>75 ± 8</td>
</tr>
<tr>
<td>LV EDV (ml)</td>
<td>164 ± 15</td>
<td>171 ± 18</td>
<td>135 ± 8</td>
</tr>
<tr>
<td>LV EDV1 (ml/m²)</td>
<td>84 ± 13</td>
<td>88 ± 15</td>
<td>68 ± 7</td>
</tr>
<tr>
<td>RV ESV (ml)</td>
<td>101 ± 14</td>
<td>97 ± 13</td>
<td>65 ± 5</td>
</tr>
<tr>
<td>RV ESV1 (ml/m²)</td>
<td>53 ± 9</td>
<td>50 ± 12</td>
<td>33 ± 5*</td>
</tr>
<tr>
<td>LV ESV (ml)</td>
<td>84 ± 16</td>
<td>86 ± 18</td>
<td>49 ± 8</td>
</tr>
<tr>
<td>LV ESV1 (ml/m²)</td>
<td>44 ± 15</td>
<td>44 ± 17</td>
<td>25 ± 9</td>
</tr>
<tr>
<td>EF (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV</td>
<td>42 ± 8</td>
<td>47 ± 11</td>
<td>54 ± 4</td>
</tr>
<tr>
<td>LV</td>
<td>49 ± 9</td>
<td>51 ± 13</td>
<td>64 ± 5*</td>
</tr>
</tbody>
</table>

*p < 0.05, Group 3 versus Group 1; all others, p = NS. Values are presented as mean value ± SD. EDV and EDV1 = end-diastolic volume and end-diastolic volume index, respectively; EF = ejection fraction; ESV and ESV1 = end-systolic volume and end-systolic volume index, respectively; Groups 1 to 3 as in Table 1. LV = left ventricle; RV = right ventricular.
Figure 2. Early diastolic filling characteristics of the three study groups. By the third cine computed tomographic frame after end-systole, the patients with pathologically confirmed constrictive pericarditis (CP) (Group 1) had achieved a significantly greater degree of left ventricular (LV) filling (A) than had either the patients without pericardial constriction (No CP) (Group 2) or the normal subjects (NI) (Group 3). The results are similar but more marked for the early right ventricular (RV) diastolic filling data (B). *p < 0.05, Group 1 vs. Group 2. tp < 0.05, Group 2 vs. Group 3. The heart rate, a determinant of diastolic function, during the cine computed tomographic examination was not significantly different between the patient groups (Group 1, 83 ± 4 beats/min; Group 2, 82 ± 5 beats/min, p = NS) but was significantly lower in the normal subjects (68 ± 3 beats/min, p < 0.05). The third cine computed tomographic frame after end-systole occurred between one third and one half of total diastolic filling in all groups. The percent of total diastolic filling time at which the third frame occurred ranged from 37% to 46% in Group 1, from 35% to 49% in Group 2 and from 30% to 39% in Group 3 (all p = NS).

Pericardial thickness data. In Group 1 two of five patients had an irregularly calcified pericardium that ranged from 3 to 18 mm in thickness, whereas the remaining three patients had a homogeneously thickened noncalcified pericardium (range 8 to 14 mm). In all patients in Group 2 and all subjects in Group 3, the pericardium was homogeneous, noncalcified and <3 mm thick.

The mean pericardial thickness for each patient and subject is shown in Figure 3. The mean pericardial thickness in Group 1 was 10 ± 2 mm, which was significantly greater than that in Group 2 (2 ± 1 mm, p < 0.05) or Group 3 (1 ± 1 mm, p < 0.05). No overlap existed between the pericardial thickness measurements for patients in Groups 1 and 2. Examples of cine computed tomographic images from
two patients with surgical evidence of pericardial constriction and one patient with suspected pericardial constriction are shown in Figure 4.

**Discussion**

The most important finding is that cine computed tomography provides the necessary anatomic and physiologic data required to reliably differentiate between patients with and without constrictive pericarditis. Second, these studies provide the first volumetric assessment of the abnormal diastolic filling of the right ventricle that occurs in clinical constrictive pericarditis.

Although other imaging techniques have been described that assist in the evaluation of patients with suspected pericardial constriction, none has been validated to simultaneously describe the altered anatomy and physiology seen in this pathologic state. Visualization of the thickened pericardium in patients with constrictive pericarditis has been reported using conventional computed tomography (11-13) and magnetic resonance imaging (14,15); however, a recent clinical study reported that conventional computed tomography failed to detect the abnormal pericardium in 6 (21%) of 29 patients with surgically documented constriction (16). Soulen et al. (14) demonstrated the ability of magnetic resonance imaging to detect pericardial thickening, but surgical or pathologic data corroborating the status of the pericardium in their series were absent. In the report of their experience with magnetic resonance imaging, Sechtem et al. (15) reported that the signal characteristics of pericardial fluid, fat and fibrosis were similar. They relied on "other abnormalities" in the image that allowed identification of pericardial thickening in five or six patients with surgically confirmed pericardial thickening. The potential usefulness of echocardiography has been evaluated in both experimental and clinical constrictive pericarditis (17-22). Tyberg et al. (23) examined the diastolic filling characteristics of seven patients with constrictive pericarditis using digitized contrast ventriculography and demonstrated that diastolic ventricular filling was nearly complete by mid-diastole. This abnormal physiology has also been demonstrated by radionuclide ventriculography (24,25). None of these imaging modalities has been shown to provide both anatomic and physiologic information necessary to confirm a diagnosis of pericardial constriction. The potential utility of cine computed tomography is highlighted by the seven patients in...
Group 2 who had an erroneous diagnosis of pericardial constriction based on a complete conventional evaluation, including invasive hemodynamic study.

The data in the current study demonstrate that, by analyzing the degree of total diastolic filling that occurs in the first one-third to one-half of diastole, the abnormally rapid early diastolic filling of the left ventricle in patients with pericardial constriction can be identified with cine computed tomography and differentiated from findings in patients without constrictive pericarditis. In addition, the study data indicate that the rapid early diastolic filling also occurs in the right ventricle and suggest that this abnormality is more pronounced in the right than in the left ventricle. Finally, the study demonstrates that the spatial resolution of the cine computed tomographic image is able to clearly separate the thickened pericardium of clinical constrictive pericarditis from the normal pericardium that was noted in the control group. This separation was clear both when the thickened pericardium was irregular and densely calcified and when it was homogeneously thickened and noncalcified.

Study limitations. Several aspects of the current study deserve comment. 1) Because of the rare nature of this condition, these studies were necessarily retrospective and included a small number of patients. 2) No clinically unstable patients were studied; however, the rapid image acquisition time of cine computed tomography lends itself to the study of critically ill patients. Although it is likely that early diastolic images and accurate assessments of pericardial thickness could be obtained in patients with tachycardia or tachypnea, this remains to be critically evaluated. 3) The accurate definition of diastolic ventricular filling depends on an accurate definition of end-systole. One potential concern of an imaging procedure with a relatively slow framing rate such as cine computed tomography is that the end-systolic frame may not represent true end-systole. Rumberger et al. (7) addressed these concerns in studies describing the utility of cine computed tomography in assessing diastolic function. They concluded that a framing rate of 17 frames/s (as was used in the current study) adequately defines end-systole. 4) The classic definition of patients with constrictive pericarditis describes normal left ventricular systolic function, whereas the patients in the current study demonstrated a mild decrease in left ventricular ejection fraction and a statistically insignificant trend toward an increase in left ventricular end-diastolic volume compared with values in normal subjects. This decrease has been described in previous studies as well (25) and may be related to epicardial fibrosis or atrophy (26,27) and seems to indicate a worse postoperative prognosis (28). The increase in ventricular volume may also be due in part to the elevated filling pressures. 5) Group 2 is a pathophysiologically heterogeneous group. We do not intend the data to support any conclusions with regard to cardiac structure or performance in this group other than to state that they can be clearly distinguished from patients with pericardial constriction. 6) The accuracy of pericardial thickness measurements may be improved by use of the newer “high resolution” scanning mode (3-mm slices, 0.7-mm in-plane resolution); however, this requires additional scanning sequences and does not yield dynamic global to volumetric data. 7) The patients were significantly older than the normal subjects. It is not likely that this difference accounts for the difference in diastolic filling. Bonow et al. (29) have shown that diastolic filling rate tends to decrease with age, whereas our patients demonstrated a pronounced increase. 8) Two patients in Group 2 had biopsy evidence of cardiomyopathy. Although this finding does not absolutely exclude the possibility of pericardial constriction, it does provide an explanation for their clinical presentation. Reanalysis of our data excluding these two patients does not alter any of the conclusions of this study.

Conclusions. These studies provide validation that, in contrast to other imaging modalities, cine computed tomography can define both the thickened pericardium and abnormal rapid diastolic filling that characterize patients with constrictive pericarditis. Thus, cine computed tomography can simultaneously obtain both the anatomic and physiologic data necessary for the accurate preoperative diagnosis of pericardial constriction.

References


