Thallium 201 Imaging and Gated Cardiac Blood Pool Scans in Patients with Ischemic and Idiopathic Congestive Cardiomyopathy

A Clinical and Pathologic Study

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SUMMARY In ischemic cardiomyopathy (CM) fibrosis replaces large segments of myocardium, but in idiopathic congestive CM the myocardium contains only small foci of fibrosis or is morphologically normal. As coronary disease and myocardial infarction may be clinically silent, it is not always possible to distinguish ischemic from idiopathic congestive CM during life without cardiac catheterization. To determine whether noninvasive methods, thallium 201 myocardial (TI) imaging and technetium 99m gated cardiac blood pool scans (GCBPS), could separate the entities, we evaluated radioisotope images of the heart in 13 patients with ischemic, and eight patients with idiopathic congestive CM, and 14 patients with normal hearts. Diagnosis was established by cardiac catheterization and/or autopsy in each of the 35 patients. The 14 normals could be readily distinguished from CM, and ischemic could be distinguished from idiopathic dilated CM in 20 of 21 patients. All patients with myocardiopathy showed hypokinetic and dilated left ventricles, but right ventricular dilatation was evident mainly in those with idiopathic CM. TI images in the ischemic type had defects of greater than 40% of image circumference which corresponded to segmental wall motion abnormalities on GCBPS, whereas those with the idiopathic congestive form were homogeneous or had defects of less than 20% of image circumference. Autopsy studies in 7 of 35 patients correlated TI defects of greater than 20% of circumference with transmural myocardial fibrosis.

ISCHEMIC CARDIOMYOPATHY may produce a clinical picture virtually indistinguishable from idiopathic congestive cardiomyopathy.1,4 In the former, the coronary arteries are severely narrowed by atherosclerosis leading to extensive myocardial damage and dysfunction. In the latter, the coronary arteries are widely patent, the myocardium intact, and morphologically normal, but for unknown reasons functioning poorly.5,6 As myocardial infarcts may be both symptomatically and electrocardiographically silent the absence of historic evidence for ischemic heart disease does not exclude an ischemic etiology for idiopathic congestive heart failure in a given patient. The differentiation between ischemic and idiopathic congestive cardiomyopathy is important since prognosis and therapy of the two conditions differ.

Thallium 201 myocardial perfusion imaging and technetium 99m human serum albumin cardiac blood pool scanning with technetium 99m human serum albumin allow noninvasive evaluation of left ventricular myocardial perfusion and function. Thallium 201 myocardial perfusion imaging has proved useful in evaluation of coronary artery disease.7,8 Thallium 201 uptake reflects not only coronary perfusion but myocardial viability as an agent that is actively taken up and concentrated by the myocardial cell. Areas of myocardium devoid of viable muscle for whatever reason appear as “cold spots” on the thallium 201 image. Technetium 99m human serum albumin gated cardiac blood pool scanning provides a noninvasive evaluation of ventricular function. Left ventricular ejection fraction determined by this technique has correlated well with standard left ventricular contrast angiography.9 The combined use of these techniques had been useful in the detection and localization of myocardial infarction. They have also been found to be useful in the evaluation of primary hypertrophic, and secondary cardiomyopathies.10,11 The purpose of the present study was to determine whether these noninvasive techniques could be used to distinguish ischemic from primary idiopathic congestive cardiomyopathy.

Methods

Patients Studied

Thirty-five patients were evaluated including 13 with ischemic congestive cardiomyopathy, eight with idiopathic congestive cardiomyopathy, and 14 normal control subjects. The diagnosis of congestive cardiomyopathy was made on the basis of a clinical history of severe or intractable left ventricular failure. Patients were subdivided into those with ischemic cardiomyopathy or idiopathic congestive cardiomyopathy on the basis of cardiac catheterization and/or postmortem data.

Ischemic cardiomyopathy was defined as severe left ventricular dysfunction due to myocardial damage resulting from occlusive coronary artery disease. Criteria for selection of patients with this diagnosis included cardiomegaly, severe or intractable left ventricular failure (class III-IV, New York Heart Association); and either 1) a left ventricular ejection fraction of less than 35% established by left ventricular contrast angiography without a discrete left ventricular aneurysm, and greater than 70% narrowing of one or more major coronary arteries as determined by selective coronary arteriography, or 2) a darkly dilated left ventricular chamber with evidence of extensive myocardial scarring (i.e., involving at least 30% of left ventricular wall) and greater

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than 70% lumenal narrowing of at least one vessel demonstrable at postmortem examination.

Idiopathic congestive cardiomyopathy was defined as severe or intractable idiopathic left ventricular failure (class III-IV, New York Heart Association), and cardiomegaly, 1) a left ventricular ejection fraction less than 35% established by contrast left ventricular angiography and patent coronary arteries by coronary cineangiography, or 2) a dilated left ventricular cavity with normal or minimally narrowed coronary arteries at postmortem examination.

Of the 13 patients with ischemic cardiomyopathy, 11 had an unequivocal history of previous transmural myocardial infarction, and ten had diagnostic electrocardiograms for previous infarction. In two patients with ischemic cardiomyopathy, past histories of previous angina pectoris or myocardial infarction were uncertain, and in three the electrocardiograms showed no pathological Q waves. Of the eight patients with idiopathic congestive cardiomyopathy, four had a history of some type of chest pain and two had histories of questionable remote myocardial infarctions.

**Thallium 201 Images and Gated Cardiac Blood Pool Scans**

After intravenous injection of 1.5-2.0 mCi of ionic thallium 201, myocardial images were recorded with a high resolution scintillation camera (Ohio Nuclear Series 100) with a high resolution, low energy parallel hole collimator. Fifty thousand counts were recorded over the region of the myocardium with a 20% window set symmetrically around the X-ray peak. Images were obtained in the anterior, 45° and 60° left anterior oblique projections. The gamma camera was then peaked for technetium 99m, and a gated cardiac blood pool scan performed immediately after the intravenous administration of technetium 99m electrolytically labeled human serum albumin in a dose of 20 mCi as previously described. In addition to the gated cardiac blood pool scan, static images of the blood pool of 300,000 counts were obtained with a 10 cm × 1 cm lead marker to calibrate the scans for size.

A group of patients who had normal hearts clinically and at cardiac catheterization and/or autopsy served as controls. Indication for cardiac catheterization in the normals included atypical chest pain despite a negative or equivocal electrocardiographic stress test.

**Autopsy Studies**

The gross hearts of patients in this study who died and came to autopsy were reviewed after postmortem angiography and fixation of the heart with formaldehyde distending the cavities at pressures of 40 to 50 mm Hg. Multiple blocks of myocardium showing defects by thallium scans were additionally sectioned. Microangiograms were performed on each of the injected hearts to assess the patency of the intramural vascular architecture in areas with radionuclide image defects.

Correlations between autopsy findings and scan data were performed with specific attention to morphologic manifestations of wall motion abnormalities and defects in myocardial uptake of tracer.

**Evaluation of Thallium 201 Myocardial Perfusion Scans and Gated Cardiac Blood Pool Scans**

Thallium 201 myocardial perfusion scans and gated cardiac blood pool scans were recalled on a computer and reviewed by three independent observers.

The outline of the left ventricular circumference was traced from the computer display using 30% contrast enhancement. The location of transmural perfusion defects in the left ventricular image was determined and their extent outlined on the traced left ventricular outline. Defects were expressed as a percentage of the outer left ventricular myocardial perimeter, excluding the valve planes. Estimates of defect size among three independent observers in no instance varied by more than 10% of image circumference and duplicate readings for the same observer, by more than 5%. Initially the scans were reviewed with knowledge of the diagnosis and the clinical, catheterization, and autopsy data. At a later date, thallium 201 myocardial perfusion scans and gated cardiac blood pool scans were randomly and blindly recalled on a computer and reviewed by three independent observers. Using criteria established from the initial reviews and autopsy data, patients were separated into one of the three clinical groups.

**Results**

**Evaluation of Thallium 201 and Gated Cardiac Blood Pool Scans**

The results of the evaluation of the cardiac scans in the 35 patients are summarized in table 1.

**Normals (fig. 1)**

The 14 normals showed 1) homogeneous thallium 201 uptake (10 patients), or perfusion defects of less than 10% at the apex of the left ventricle in at least one projection (4 patients); 2) normal-sized left ventricular cavities by gated cardiac blood pool scan without any areas of akinesia or dyskinesia.

**Ischemic Cardiomyopathy (figs. 2, 3)**

All 13 patients with angiographically and/or autopsy proven ischemic cardiomyopathy had 1) a perfusion defect...
Table 1. Data in 35 Patients

<table>
<thead>
<tr>
<th></th>
<th>Ischemic Myocardial Pathy</th>
<th>Primary Congestive Myocardial Pathy</th>
<th>Normals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>13</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Age (Range, Avg. Yrs.)</td>
<td>38-81 (54)</td>
<td>20-58 (42)</td>
<td>29-59 (41)</td>
</tr>
<tr>
<td>Sex (Female:Male)</td>
<td>4:9</td>
<td>5:3</td>
<td>7:7</td>
</tr>
</tbody>
</table>

**Thallium 201 Images**

<table>
<thead>
<tr>
<th>% defect in circumference</th>
<th>% in Ischemic</th>
<th>% in Normal</th>
<th>% in Primary Congestive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 20%</td>
<td>0</td>
<td>7 (88%)</td>
<td>14 (100%)</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>0-10%</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>10-20%</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>&gt;40%</td>
<td>13 (100%)</td>
<td>1 (12%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Technetium 99m Gated Cardiac Scans**

<table>
<thead>
<tr>
<th>Differences in LV Segmental Wall Motion</th>
<th>% in Ischemic</th>
<th>% in Normal</th>
<th>% in Primary Congestive</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV Dilatation</td>
<td>11 (84%)</td>
<td>2 (20%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Of the eight patients with idiopathic congestive cardiomyopathy 1) all but one showed normal thallium 201 myocardial perfusion with homogeneous uptake, or a perfusion defect of less than 20% of left ventricular circumference in any one projection; 2) all showed a large dilated left ventricle with diffuse hypokinesis, which in two patients appeared to be more marked in the anteroapical region; 3) right ventricular dilatation was present in six (75%) of the eight patients.

**Autopsy-scan Correlations**

Seven of the 35 patients studied here died and came to autopsy, including two with normal hearts, three with ischemic cardiomyopathy, and two with idiopathic congestive cardiomyopathy.

**Normal Hearts**

Two patients with normal hearts who had radioisotope images performed during life died of noncardiac disease. Both were women, ages 29 and 50. Their hearts weighed 340 and 365 g respectively and had normal cavity sizes and wall thicknesses. The cardiac valves were normal and the extra-
mural coronary arteries widely patent. Histologic examination revealed normal myocardium without areas of fibrosis or necrosis, and microangiograms showed widely patent intramural coronary arteries. The thallium 201 images performed in the two patients were similar: homogeneous uptake of tracer by left ventricular myocardium with some diminished uptake (comprising less than 10% of the image circumference) toward the apex of left ventricle in the anteroposterior projection (fig. 1). In both patients, neither the right ventricle nor either atria were visualized by thallium 201 imaging. The gated cardiac blood pool scan showed good contractility in all projections without segmental wall motion abnormalities.

Ischemic Cardiomyopathy (fig. 7)

Three patients with ischemic cardiomyopathy died of their heart disease and were autopsied. The patients were 52, 56, and 60 years of age and two were men. Each had a history of at least one myocardial infarct followed by intractable heart failure. Their hearts weighed from 450 to 480 grams, showed left ventricular hypertrophy, dilatation, and narrowing of two or more major coronary arteries by greater than 75%. The myocardium was extensively replaced by fibrous scars involving 25 to 40% of left ventricular mass. In one patient the area of infarction included septum and anterolateral wall, in one, anterior and inferior wall and in one, septum

Figure 3. Ischemic cardiomyopathy. Thallium scan in AP (A) and LAO (B) projection showing a large defect (arrows) in the inferior and diaphragmatic surface of left ventricle (LV). Although the defect in the AP projection involves >40% of the image circumference, in the LAO, only a defect of <20% is evident, and the LAO view alone would not be sufficient to distinguish the ischemic from idiopathic type of cardiomyopathy. This patient did not have a clear-cut history of myocardial infarction, had no Q waves on ECG, but at cardiac catheterization had severe three vessel disease with a near total occlusion of his right coronary artery.

Figure 4. Idiopathic dilated cardiomyopathy in a 20-year-old man. Thallium 201 images in AP (A) and LAO (B) projection show homogeneous uptake of tracer in both projections. Left ventricle is dilated but right ventricle is not imaged. Gated cardiac blood pool scan in the LAO projection is shown in systole (C) and diastole (D).
and anteroapical left ventricular wall. The cardiac valves were normal. Microangiograms showed normal intramural vasculature in the areas devoid of fibrosis.

Thallium 201 images performed in these patients showed dilated left ventricular cavities and focally thickened left ventricular walls. In two patients, right ventricular activity was seen and appeared to have homogeneous uptake of tracer. Large focal defects in tracer uptake were present in left ventricular wall directly corresponding to the infarcts found at autopsy as listed above. Transmural infarcts were correctly localized, and all transmural lesions (i.e., involving two-thirds or more of left ventricular wall thickness) at autopsy were evident by scan. Gated cardiac blood pool scans showed diffuse left ventricular hypokinesis, which in each heart was most marked in the segments with thallium defects and corresponding infarction at autopsy. The right ventricle or cavities delineated by gated blood pool scans were normal sized in two patients and dilated in one. In the latter case a small portion of right ventricle was involved by infarct, but this was not suggested by the thallium perfusion image.

Idiopathic Congestive Cardiomyopathy (fig. 8)

Two patients (ages 38 and 56) were studied at autopsy. Both died of intractable heart failure. Their hearts weighed 545 and 620 grams, had dilatation of all four chambers, and hypertrophy of their left ventricular walls. There were no areas of necrosis or fibrosis by gross examination, and by light microscopy only small foci of interstitial fibrosis were evident. Both hearts contained organizing right and left ventricular mural thrombi. Their extramural coronary arteries were widely patent, intramural vessels normal by microangiography, and their cardiac valves were normal.

Thallium 201 myocardial images in these patients showed dilatation of both right and left ventricles. In one patient, tracer uptake was homogeneous in all four projections without any focal defects. In the other patient, tracer uptake was homogeneous in 30, 45 and 60° left anterior obliquity but in the anterior projection a focal defect of approximately 20% of the left ventricular circumference was present at the apex. Correlation with the heart at autopsy failed to show...
necrosis or fibrosis in the apex of the heart, but apically the myocardial wall was thinnest, as it normally is, and was layered with organized thrombus which encircled the trabecular muscle of the subendocardium (fig. 9). Microangiograms from the apex of the heart in the vicinity of the thallium defect failed to show abnormalities of the intramural coronary arteries. Gated cardiac blood pool scans in the two autopsied patients showed biventricular dilatation and diffusely decreased contractility of the left ventricles. The patient with the apical perfusion defect showed a small segmental wall apical motion abnormality as well.

**Blind Evaluation of Tracer Studies**

Using the above results, the 35 scans were randomly recalled for review and blindly separated into three patient groups. All of the 14 normal images were correctly identified as being normal and were readily distinguished from the 21 patients with congestive cardiomyopathy by both thallium 201 and gated cardiac blood pool scan. Gated cardiac blood pool scans alone, showing dilated hypokinetic left ventricles, were sufficient to separate normals and the cardiomyopathy groups. Of the 21 patients identified as cardiomyopathy it was not possible to separate the ischemic from idiopathic type by blood pool scans alone as all showed diffuse hypokinesis and differences in motion of different myocardial segments were not marked. Using the thallium 201 images in addition to the blood pool scans, however, all 13 patients with angiographically and/or autopsy proven ischemic cardiomyopathy were correctly identified as having ischemic cardiomyopathy because of the large perfusion defects, exceeding 40% of the left ventricular image (fig. 2). Although myocardial images in every view did not show perfusion defects (fig. 3), in each patient a defect of at least 40% of the left ventricular image was present in at least one view. Of the eight patients with angiographically and/or autopsy proven idiopathic congestive cardiomyopathy, seven were correctly identified (figs. 4, 5). The one patient with angiographically normal coronary arteries but a focal thallium defect of greater than 40% in the anterior wall, with a corresponding regional myocardial wall motion abnormality on gated cardiac blood pool scans, was miscalled as ischemic myocardial disease (fig. 6). A similar abnormality of regional myocardial wall motion was present on left ventricular contrast angiography in this patient. There were no interobserver disagreements in these blind readings.

**Discussion**

The results of this study suggest that myocardial imaging with radioactive tracers may be of value in the noninvasive investigation of patients with congestive cardiomyopathy. The combined use of thallium 201 myocardial perfusion imaging and gated cardiac blood pool scanning with technetium 99m human serum albumin allowed separation of patients with congestive cardiomyopathy from normal, and a
differentiation into those with idiopathic congestive cardiomyopathy and ischemic cardiomyopathy. The gated cardiac blood pool scans were useful in distinguishing the normal from the cardiomyopathies. Diffuse hypokinesis was associated with both forms of cardiomyopathies. Segmental wall motion abnormalities most marked in the regions of the perfusion defect were not sufficiently different from areas without perfusion defects to allow for differentiation between the two forms of cardiomyopathy by gated pool scan alone (fig. 2). Right ventricular dilatation was, however, more striking in the patients with idiopathic congestive cardiomyopathy, compared to those with ischemic cardiomyopathy but this was not consistent. Thallium 201 myocardial perfusion images were the most reliable for distinguishing those with primary from secondary cardiomyopathy. All of the patients with ischemic cardiomyopathy could be recognized by a large perfusion defect on their thallium 201 images. A false positive image for ischemic cardiomyopathy was present in only one of the eight patients with congestive cardiomyopathy.

The availability of a noninvasive technique to distinguish primary idiopathic congestive cardiomyopathy from ischemic cardiomyopathy is of clinical importance. While in most instances the clinical history and course allow differentiation, there are a number of patients who present with a history and physical signs of congestive cardiomyopathy in whom the etiology of heart failure is not evident on clinical grounds alone. Coronary artery disease and myocardial infarction may be symptomatically and electrocardiographically silent. Myocardial infarction particularly with posterior involvement may not be evident on electrocardiogram, or may be masked by a pre-existing intraventricular conduction defect. Clinical and pathologic studies have shown anatomic evidence of myocardial infarction to be present in anywhere from 10 to 60% of patients without accompanying historical or electrocardiographic evidence. Conversely patients with proven idiopathic congestive cardiomyopathy may have electrocardiograms suggestive of myocardial infarction without accompanying pathologic evidence of infarction.

Although the patients with primary congestive cardiomyopathy in the present study could be differentiated from those with ischemic cardiomyopathy, on the basis of their thallium 201 myocardial perfusion images, three of the eight patients with idiopathic cardiomyopathy had small focal areas of reduced tracer uptake which were greater than those present in any of the normals. One of the patients with idiopathic congestive cardiomyopathy and a focal thallium 201...
defect was studied at autopsy and did not have a corresponding area of myocardial scarring. There was, however, an apical organized thrombus which encircled the endocardium. It is possible that the thrombus impaired segmental myocardial wall motion and, therefore, reduced local myocardial oxygen demands, myocardial blood flow, and hence thallium 201 uptake. A primary membrane defect resulting in focal defects of thallium 201 uptake cannot be excluded. Morphologic studies indicate that in primary myocardial disease small foci of interstitial and at times replacement fibrosis may occur and in the other two patients with focal defects in tracer uptake, the possibility of focal myocardial scarring also must be considered.

While the criteria used for the separation of patients with ischemic cardiomyopathy from primary congestive cardiomyopathy on the basis of myocardial imaging with radioactive tracers were adequate to separate the majority of patients, there was one patient in the present series in whom an error in diagnosis was made. This patient with normal coronary arteries demonstrable by contrast angiography had a large segmental defect on the thallium 201 myocardial perfusion image, and a corresponding akinetic area on the gated blood pool scan (and also one with left ventricular contrast angiography) and her scan suggested the diagnosis of ischemic cardiomyopathy (fig. 6). The explanation for the focal defect in thallium 201 uptake and the regional myocardial wall motion abnormality in this patient is unclear. One possibility is an embolic episode resulting in an undiagnosed myocardial infarction. This patient also might be an example of the obscure group of patients with myocardial infarction and normal coronary arteries. Whatever the cause in our patient, some form of myocardial damage, as evidenced by the area of akinesia on both the gated cardiac blood pool scan and left ventricular contrast angiography, was reflected in the defect in the thallium image and it is likely that this damage related to her heart failure.

Echocardiography has been used to differentiate ischemic cardiomyopathy from primary congestive cardiomyopathy by detection of segmental areas of abnormal myocardial wall motion in the former. Although echocardiographic correlations were not performed in the present study, it is highly likely that the patient misdiagnosed by the radioactive tracer techniques would also have been misdiagnosed by echocardiography, since this regional myocardial wall motion abnormality, as defined by left ventricular contrast angiography, would have led to an error in diagnosis by echocardiography using present criteria. Although in most patients the information derived from echocardiography would be similar to that obtained from a gated cardiac blood pool scan, standard echo techniques employ a limited window which primarily assesses basal segmental wall motion. The combined radioactive tracer procedure used in this study provides two-dimensional images in multiple views that reflect myocardial perfusion and myocardial integrity, as well as corresponding regional myocardial wall motion. Thus, the information provided by thallium images should also increase the accuracy of diagnosis, as regional wall motion abnormalities that might be present by echo or blood pool scan do not always correspond to irreversibly damaged myocardium.

With the information provided by these several non-invasive techniques it appears likely that ischemic and idiopathic congestive cardiomyopathy can be differentiated from each other in the majority of instances without cardiac catheterization, and that cardiac catheterization, which is particularly hazardous in such patients, can be reserved for those with ischemic cardiomyopathy who appear to be potential surgical candidates. Most importantly the non-invasive myocardial imaging techniques may provide a safe means for long-term follow-up and evaluation of natural history and effect of therapeutic interventions in these seriously ill patients.

References

Thallium 201 imaging and gated cardiac blood pool scans in patients with ischemic and idiopathic congestive cardiomyopathy. A clinical and pathologic study.
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