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### Title

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**Title:**

**Flattening of the interventricular septum (D-shape left ventricle) in addition to high RV tracer uptake and increased RV volume found on gated SPECT studies strongly correlates with right ventricular overload**

**Running Title: Septal flattening on gated SPECT and RV overload**

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**Key words:** right ventricular overload, myocardial perfusion, gated SPECT, Septal flattening, pulmonary hypertension, D-shape left ventricle

**Abstract:**

**Background:** Flattening of the interventricular septum (D-shaped left ventricle) detected during echocardiographic examination is correlated with significant right ventricular (RV) overload. There are no reports of this finding with cardiac gated SPECT imaging. We report an observational study correlating this finding with the presence of RV overload.

**Method:** Retrospectively we compared eight cases with flattening of the interventricular septum on cardiac gated SPECT imaging of which echocardiographic correlations and clinical data were available for the presence of RV overload.

**Results:** All patients but one had pulmonary hypertension ranging from 42 to 52 mmHg measured by echocardiographic doppler studies. Except one all patients had reasons for RV overload (chronic obstructive pulmonary disease in three, history of atrial septal defect in three, pulmonary embolism in one and obstructive sleep apnea in one). Septal flattening present on gated SPECT images was seen in 50% of the cases by echocardiography. Other signs of RV overload (RV enlargement, RV hypertrophy) were observed by echocardiography in five patients and by the gated SPECT in seven patients.

**Conclusion:** The presence of interventricular septal flattening on gated SPECT studies correlates with right ventricular overload and should be routinely assessed during interpretation of gated SPECT studies.

**Background:**

Right ventricular overload can be assessed using echocardiography. Echocardiographic signs of RV overload include RV enlargement, increased pulmonary arterial pressure, right atrial enlargement, paradoxical septal motion and flattening of the septum causing a D-shaped left ventricle.<sup>1-6</sup> Myocardial perfusion imaging is not performed for RV overload assessment and the ACC/AHA guidelines for clinical use of cardiac nuclear imaging do not mention any indication for RV function or overload evaluation.<sup>7</sup> Right ventricular overload on myocardial perfusion imaging usually presents with high tracer uptake in the RV wall or increased peak counting method using right to left ventricular peak count ratio.<sup>8-11</sup> There are no reports in the nuclear cardiac literature describing flattening of the interventricular septum similar to echocardiographic findings of septal flattening in patients with RV overload.

We present eight cases demonstrating flattening of the interventricular septum in the short axis view of gated SPECT imaging similar to echocardiographic findings in patients with documented RV overload in which echocardiographic examinations were available. This is the first observational study reporting this finding with echocardiographic correlation and signs of RV overload and interventricular septal flattening.

**Methods:**

During the interpretation of gated SPECT images at the University of California, Irvine Medical Center, we observed a correlation between interventricular septal flattening seen in the short axis view of myocardial perfusion imaging and right ventricular overload.

This study is a retrospective observational study from a pool data of perfusion images that was done for ischemia evaluation and not for RV assessment. Our finding was incidental from a large number of images. We did not actively look for septal flattening routinely for the purpose of this study and noticed only very obvious cases by coincidence. The pool data were from perfusion studies at our institution in the last 14 months with approximate total of 800 studies. There were approximately 18 cases of septal flattening in our data pool however we had 8 cases of which echocardiographic correlation was available that we used for our study.

All patients underwent dual isotope protocol with injection of Thallium 201 for resting study and  $^{99m}\text{Tc}$  Myoview after stress (exercise in two, adenosine in five and dobutamin in one). All patients waited approximately 30 minutes before the gated SPECT was performed. Two underwent exercise treadmill; one had dobutamine and 5 had adenosine infusion as a route of stress.

Flattening of the septum was defined as a straight interventricular septum or displacement of the septum towards the left ventricular cavity observed by three independent nuclear medicine trained physicians. Right ventricular overload on echocardiographic examination was suspected using known echocardiographic signs of RV overload and clinical data (elevated Doppler estimated PA pressure, RV enlargement,

RV hypertrophy, septal flattening and history of congenital heart disease that could cause RV overload such as atrial septal defect (ASD).

### **Results:**

The clinical data, echocardiographic and gated SPECT results are summarized in **Table 1**. The patient's ages ranged from 41 to 82 years old. All gated SPECT imaging were performed for risk stratification of cardiac ischemia. Symptoms at the time of the SPECT study included dyspnea in five patients, chest-pain in two, and arrhythmia in one. Except one, all had a normal ejection fraction. Septal flattening was seen in all patients on the gated SPECT images but was seen in 50% of the cases echocardiographically. All patients but one had pulmonary hypertension ranging from 42 to 52 mmHg measured by doppler of tricuspid regurgitation jets. Except for one patient, all had risk factors for RV overload (chronic obstructive pulmonary disease in three, history of atrial septal defect in three, pulmonary embolism in one and obstructive sleep apnea in one). In five patients there were other signs of RV overload on the echocardiographic examination. In seven patients there were additional signs of RV overload on the gated SPECT study. The details of other RV overload signs are as follows (see Table 1): RV dilatation in 7 of 8 patients, right ventricular hypertrophy (RVH) in 2 of 8 patients, high RV tracer uptake in 7 of 8 patients, The combination of all three signs (RVH, RV dilatation and high RV tracer uptake) was found in 2 of 8 patients and combined RV dilatation with high tracer uptake in 6 of 8 patients.

Two examples of interventricular septal flattening seen in both echocardiographic

and gated SPECT images are shown in **figure 1** through **4**. Two examples of septal flattening seen only in the Gated SPECT examinations are shown in **figure 5** through **8**.

### **Discussion:**

Assessment of right ventricular function using gated SPECT is not considered an indication for myocardial perfusion studies. Guidelines on the diagnosis and treatment of pulmonary arterial hypertension do not mention gated SPECT examination for right ventricular assessment. There are findings, however, on gated SPECT that correlate with RV overload. These signs are described mostly in the pediatric population with congenital heart disease as a cause of right ventricular overload, and in adults with pulmonary hypertension. Increased right ventricular uptake and a peak count ratio of right to left ventricular counts over 0.45 have been advocated for RV overload.<sup>8-12</sup>

There are reports about nonspecific perfusion abnormalities in the RV seen on gated SPECT studies in patients with arrhythmogenic RV dysplasia without RV overload.<sup>13</sup> Paradoxical septal motion is commonly described in patients with pulmonary hypertension and RV pressure overload during echocardiographic examinations<sup>14,15</sup> but rarely reported during myocardial perfusion studies.<sup>16</sup> Interventricular septal flattening is described and reported commonly during echocardiographic examinations of patients with significant RV overload<sup>3-6</sup> but not reported on gated SPECT perfusion studies.

There are a few case reports which mention the displacement of the interventricular septum toward the left ventricular cavity in patients with RV pressure overload.<sup>17</sup> However, the term interventricular septal flattening has not been described in the literature despite similar anatomical appearance and pathophysiological cause of this phenomenon between echocardiography and myocardial perfusion imaging. The increase

in metabolic uptake in the interventricular septum in FDG-PET scans has been observed in patients with atrial septal defect but again there is no report about occurrence of septal flattening.<sup>18</sup>

We present the first observational study of eight patients who showed flattening of the interventricular septum during gated SPECT imaging with echocardiographic confirmation of pulmonary hypertension or right ventricular overload. Interestingly, despite significant pulmonary hypertension in the majority of the patients with flattening of the septum seen on gated SPECT imaging, only 50% had septal flattening documented by echocardiography. These observations suggest that flattening of the interventricular septum may be more sensitive using the Gated stress SPECT study than echocardiography. Furthermore, all patients had other signs of RV overload. Wackers et al.<sup>19</sup> describe the mechanism of high tracer uptake in RV wall which is related to high RV work load and not just right ventricular hypertrophy (RVH). This explains our observation that septal flattening and high tracer uptake in the RV did not occur only in patients with RVH but in patients with RV overload regardless of the cause.

The question remains why the septal flattening is seen only in 50% of echocardiogram. We don't have any obvious explanation. It is possible that exercise causes more stress toward already overloaded RV inducing more dilatation. However, gated SPECT studies are performed approximately 30 minutes after tracer injection, and therefore, RV stress should not be present at the time of gating. Another plausible explanation could be the possibility that gated SPECT is more sensitive for RV overload detection. This theory is consistent with the Aepfelbacher et al. study<sup>20</sup> which showed that 52 patients with RV dilatation that were seen on gated SPECT study, only 9



patients (17%) had RV dilatation by echocardiography. The authors had no convincing explanation about their finding.

Based on our observations, we suggest that physicians should give more attention to the shape of the interventricular septum which could help detect pulmonary arterial hypertension or right ventricular overload. The discovery of *interventricular septal flattening (D-shaped left ventricle)* should be a part of myocardial perfusion report similar to the echocardiographic report of RV overload.

### **Limitations:**

Our study is an observational study with a small number of patients and needs to be confirmed by a larger trial. However, the correlation of septal flattening on the gated SPECT imaging with echocardiographic findings of significant pulmonary hypertension is striking in our study. Pulmonary hypertension was documented during echocardiographic studies and not by right heart catheterization. However, it is well known that pulmonary artery pressure measurements using Doppler studies of tricuspid valve regurgitation jet highly correlate with right heart catheterization findings and most of our patients had other signs as well as a history of right ventricular overload. We had no gold standard for accurate RV overload estimation which limits our study. This study was a retrospective observational study from a pool of perfusion images that was done for ischemia evaluation and not for RV assessment. Our finding was incidental from a large number of images. Therefore, it is impossible to give a prevalence number. Most patients for ischemia evaluation do not have abnormal RV function or RV pathology. Therefore, the number of patients that had myocardial perfusion study for ischemia evaluation can

not be extrapolated to prevalence of patients with septal flattening if RV overload was the reason for study. Any prevalence calculation would be very misleading. Furthermore, we did not actively look for septal flattening routinely and noticed only very obvious cases by incident. Therefore we must have underestimated this finding and the true prevalence of this finding in the population with RV overload which is not known at this time

**Conclusion:**

Flattening of the interventricular septum on the gated SPECT imaging is associated with RV overload and correlate with echocardiographic finding of septal flattening. We suggest that more attention should be given to the shape of the interventricular septum during interpretation of gated SPECT studies and the term of septal flattening (D-shape left ventricle), if present, should be routinely used and reported similar to echocardiographic descriptions of the septum in patients with suspected RV overload.

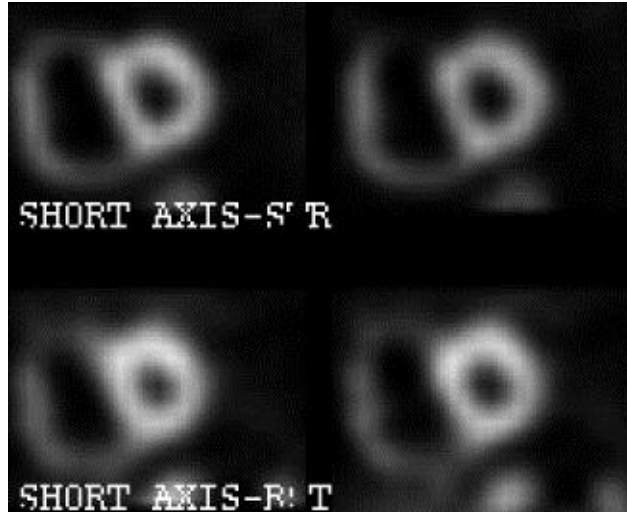


Fig.1: Flattening of the septum seen in short axis view with right ventricular enlargement on the gated SPECT imaging in a patient with systolic pulmonary arterial pressure of 52 mm Hg and history of COPD and atrial septal defect

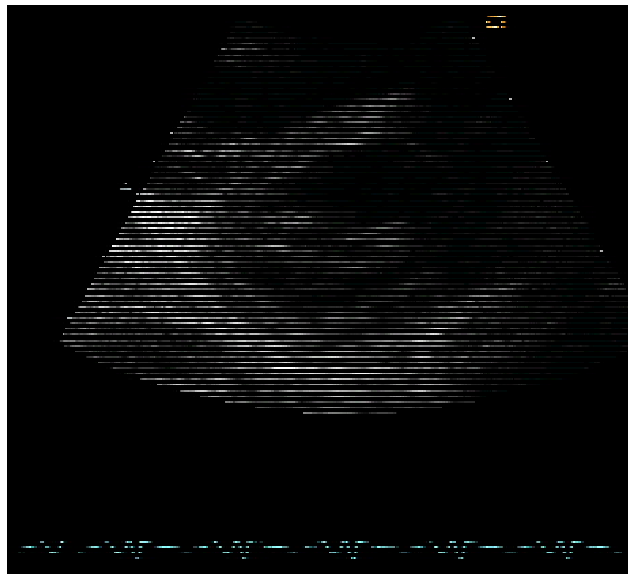


Fig.2: The same patient as in figure 1 with flattening of the septum seen in short axis view of echocardiographic image

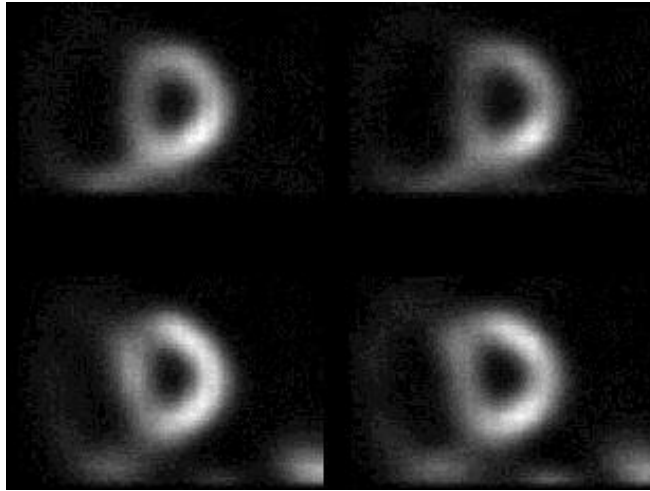


Fig.3: Flattening of the septum seen in short axis view with right ventricular enlargement on the gated SPECT imaging in a patient with systolic pulmonary arterial pressure of 54 mmHg and history of pulmonary embolism

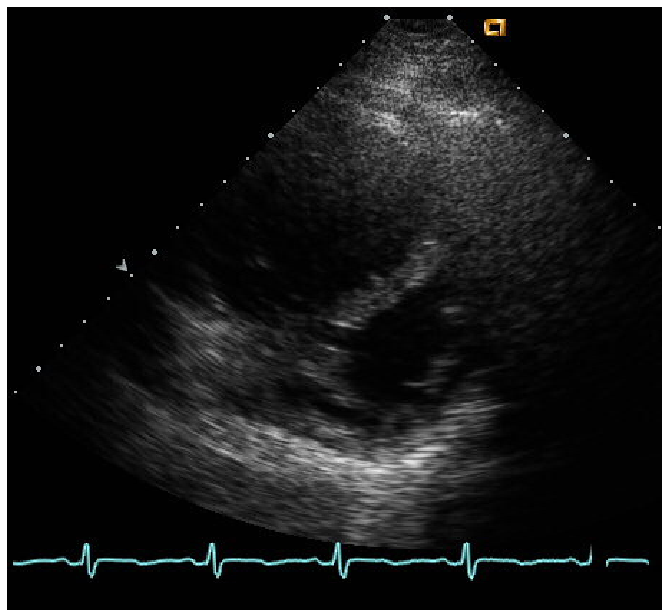


Fig.4: The same patient as in figure 3 with flattening of the septum seen in short axis view of echocardiographic image

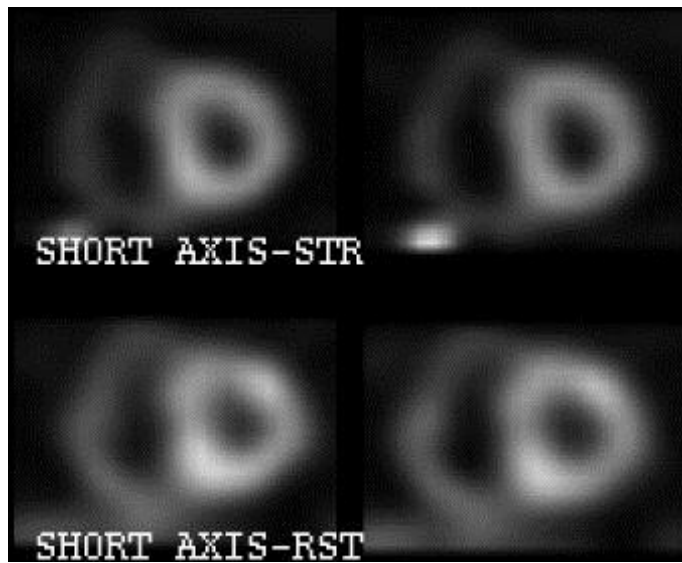


Fig.5: Flattening of the septum seen in short axis view with prominent right ventricle on gated SPECT imaging in a patient with systolic pulmonary arterial pressure of 46 mmHg and history of obstructive sleep apnea

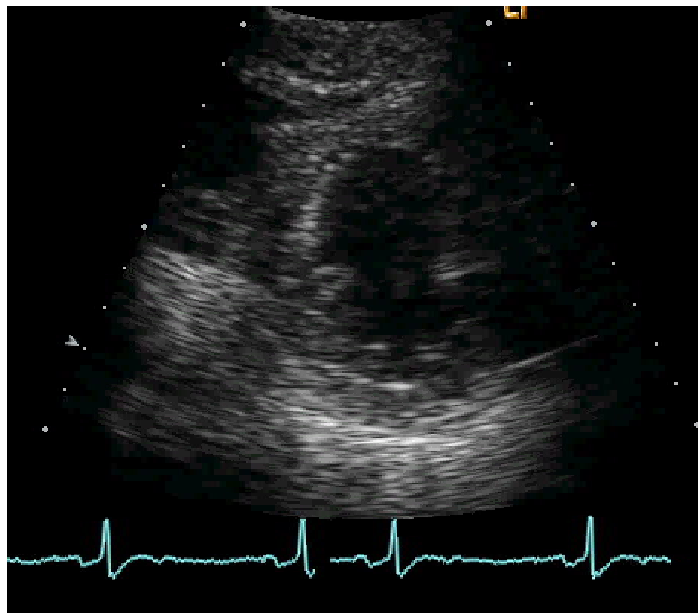


Fig.6: The same patient as in figure 5 showing no flattening of the septum in short axis view of echocardiographic image

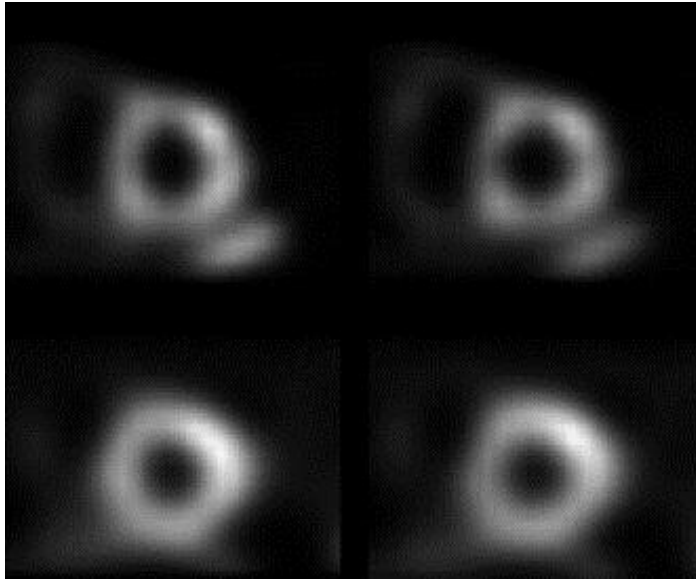


Fig.7: Flattening of the septum seen in short axis view with prominent right ventricle on the gated SPECT imaging in a patient with systolic pulmonary arterial pressure of 51 mmHg and history of COPD

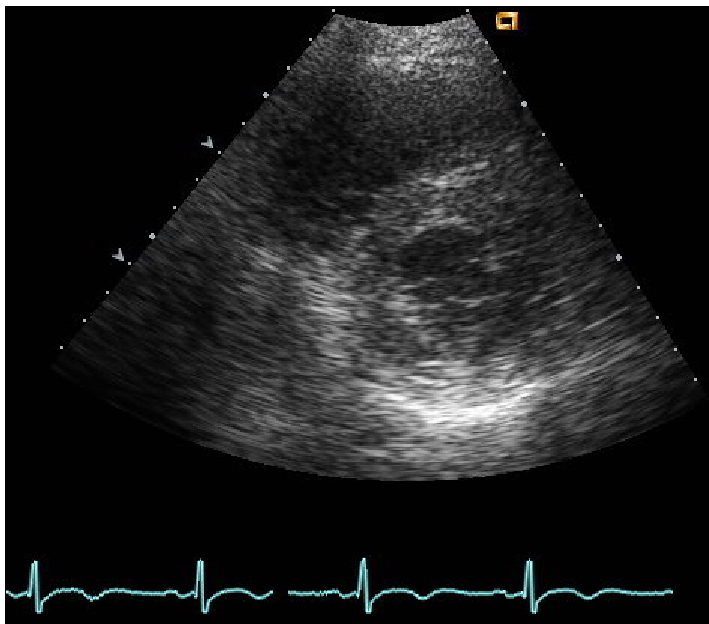


Fig.8: The same patient as in figure 7 showing no flattening of the septum in short axis view of echocardiographic image

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