

POSTER SESSION IV
Saturday, September 13, 2008, 9:30 a.m. – 11:00 a.m.
Coronary Artery Disease and Congestive Heart Failure

24.01

IMPACT OF 123I-BMIPP ON PROGNOSIS OF NONOBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY: FROM 10 YEARS FOLLOW-UP DATA

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Background: Hypertrophic cardiomyopathy (HCM) is characterized by disproportionate left ventricular (LV) hypertrophy. Its histopathologic characteristics include myocyte hypertrophy, interstitial fibrosis, and the presence of abnormal intramural coronary arteries with thickened walls and narrowed lumens. Although it has been reported that beta-methyl-iodophenylpentadecanoic acid (BMIPP) scintigraphic abnormalities associated with myocardial ischemia are present in patients with HCM, few data exist regarding the relationship between these abnormalities and the long-term prognosis in patients with HCM. Therefore, we evaluated the relationship between myocardial scintigraphic abnormalities based on BMIPP uptake and the long-term prognosis in patients with HCM.

Methods: The study consisted of 18 consecutive patients with nonobstructive HCM (13 men and 5 women; baseline ages: 26-68 years; mean age: 53.7). The diagnosis of HCM was based on the echocardiographic demonstration of a hypertrophied left ventricle in the absence of other cardiac or systemic causes for LV hypertrophy. Six of them were diagnosed genetically (1 had beta-myosin heavy chain gene mutation, 4 had cardiac troponin I gene mutation, and 1 had myosin-binding protein C gene mutation). The patients were studied at rest with BMIPP. An intravenous injection of 111MBq of 123I-BMIPP was given, and the first and second single photon emission computed tomography (SPECT) studies were started about 20 min thereafter. The BMIPP score was defined as follows: 0 = no defect; 1 = defect of 1-25% of the LV myocardium; 2 = defect of 26-50%; 3 = defect of 51-75%; 4 = defect of > 75%. We divided the patients into two groups based on the BMIPP scintigraphic findings: group A had no or mild abnormalities (BMIPP score: 0-2), and group B had moderate to severe abnormalities (BMIPP score: 3-4). Follow-up data were obtained over an average period of 10 years (range: 1-18 years). The primary end point for the study was the occurrence of cardiac event (persistent atrial fibrillation, sustained ventricular tachycardia or fibrillation, congestive heart failure requiring hospitalization, or cardiac death).

Results: Group A consisted of 11 patients (BMIPP defect score of 0 for 6 patients, 1 for 4 patients, and 2 for 1 patient) and group B included 7 patients (defect score of 3 for 2 patients, and 4 for 5 patients). During follow-up period, 8 patients suffered at least one cardiac event: 1 had atrial fibrillation, 1 had sustained ventricular tachycardia, 3 required hospitalization for congestive heart failure, and 3 died of congestive heart failure. Interestingly, 7 of 8 events occurred in group B, while only one event occurred in group A ($P < 0.05$).

Conclusions: Patients with nonobstructive HCM and moderate to severe BMIPP myocardial scintigraphic defects representing impaired free fatty acid metabolism associated with myocardial ischemia had a poorer prognosis.

24.02

PROGNOSTIC VALUE OF MYOCARDIAL PERFUSION IMAGING AS COMPARED WITH CORONARY ANGIOGRAPHY AFTER CARDIAC TRANSPLANTATION

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Background: Cardiac allograft vasculopathy (CAV) is the most common cause of late complications and chronic rejection in heart transplant recipients. At the moment annual coronary angiography is used to monitor the heart transplant recipients for the development of this condition. Recently it has been shown that myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) is a cost-effective

and non-invasive method for detecting CAV in heart transplant recipients. In this study we compared the prognostic value of MPI with the coronary angiography in terms of prediction of CAV-related cardiac events.

Methods: We studied 27 post heart transplant patients (23 males and 4 females) (Mean age 47 ± 13 years). All patients underwent MPI and coronary angiography within 6 months of each other. The reversible or fixed perfusion defects on MPI were labeled as abnormal. CAV by coronary angiography was diagnosed if coronary luminal stenosis was $\geq 50\%$. End points of the study were cardiac death, non-fatal myocardial infarction, percutaneous coronary intervention (PCI), coronary artery bypass grafting and re-transplantation. Patients were followed for a mean of 9 ± 3 years and CAV-related cardiac events were recorded. The predictive value of MPI and coronary angiography was compared using Cox proportional-hazards model, hazard ratios were calculated, and p-value of < 0.05 was used to identify the significance.

Results: Out of 27 patients, 12 had no myocardial perfusion defect and 15 had either a reversible or fixed perfusion defect. On coronary angiography, 5 were CAV (-) and 22 were CAV (+). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MPI to detect CAV diagnosed by coronary angiography were found to be 64%, 80%, 93%, 33% and 67% respectively. On univariate Cox proportional-hazard analysis abnormal MPI was found to be a significant predictor of CAV related cardiac events with a hazard ratio of 22.73 as compared with abnormal coronary angiography with a hazard ratio of 0.33 (Table 1).

Table 1. Proportional-hazard model comparing MPI and coronary angiography

Variable	Exp (\hat{a})	Sig. (p-value)	95% CI (\hat{a})
Coronary angiography	0.33	0.42	(0.021 - 5.107)
MPI *	22.73	0.02	(1.521 - 339.915)

*p ≤ 0.05 .

Conclusions: From the results of our study we conclude that MPI after heart transplantation as compared with coronary angiography is a significant predictor of CAV-related cardiac events after a long-term follow up. It is a potential alternative to invasive coronary angiography for monitoring heart transplant recipients that needs to be explored further.

24.03

COMPARISON OF EXERCISE AND ADENOSINE MPI FOR DIAGNOSIS OF TRANSPLANT CORONARY ARTERIOPATHY IN ORTHOTOPIC HEART TRANSPLANT PATIENTS

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Background: Transplant coronary arteriopathy is a delayed complication of orthotopic heart transplant causing death. Coronary angiography has been used at most centers to diagnose this condition. The objective of this study was to evaluate the role of exercise vs adenosine myocardial perfusion imaging (MPI) in diagnosing transplant coronary arteriopathy.

Methods: We evaluated 60 subjects: 26 in exercise MPI group (18 males, mean age 47 ± 12 yrs) and 34 in adenosine MPI group (27 males; mean age 52 ± 10 yrs). In the exercise group, patients underwent exercise treadmill testing with the standard Bruce protocol. In the adenosine group, patients underwent a standard 6 minute adenosine infusion. All subjects underwent coronary angiography within 6 months of stress MPI. Significant CAD was defined as coronary artery narrowing of $\geq 70\%$. There was no significant difference in time post heart transplant between both groups (exercise group 7 ± 3 vs adenosine group was 8 ± 3).

Results: In the exercise group, 15 of 26 (57%) subjects had abnormal MPI and significant CAD by cardiac catheterization. Of the 11 of 26 (43%) who had normal MPI, 7 had significant CAD by cardiac catheterization. In the adenosine group, 24 of 34 (70%) subjects had abnormal MPI and significant CAD by cardiac catheterization. Of the 10 of 34 (29%) who had normal MPI, 6 had significant CAD by cardiac catheterization. The sensitivity of

exercise treadmill MPI was 68% and the sensitivity of adenosine MPI was 80%, $p < 0.01$.

Conclusions: Our study shows that adenosine MPI is superior to exercise MPI for the diagnosis of transplant coronary arteriopathy. The likely explanation is abnormal response to exercise in patients with heart transplant.

24.04

A COMPARISON OF THE 12-LEAD ECG AND THE BODY SURFACE MAP WITH VERIFICATION BY EARLY REST MYOCARDIAL PERFUSION IMAGING IN THE DIAGNOSIS OF ACUTE POSTERIOR MYOCARDIAL INFARCTION

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Background: Two thirds of admissions to coronary care units (CCU) are for non ST elevation (STE) myocardial infarction. Posterior myocardial infarction (MI) is difficult to diagnose by 12-lead electrocardiogram (ECG) since STE originating from the posterior myocardium is not always reciprocated in the anterior chest leads as ST depression. Early identification of posterior MI is important as patients benefit from early revascularisation. The 80-lead body surface map (BSM) samples more of the chest wall inclusive of the posterior thorax than the 12-lead ECG. Myocardial perfusion imaging (MPI) has proven sensitive in identifying the presence and territory of MI. We aimed to compare the findings of the initial ECG and BSM with the results of early MPI.

Methods: All patients presenting with ischaemic type chest pain at rest > 20 minutes to our CCU (pre-hospital and in-hospital) between October 2004 and October 2006 had an initial ECG and BSM recorded. Those who had either ST depression > 0.1mV in leads I, aVL or V1-V6 on 12 lead ECG or posterior STE > 0.05mV on the BSM were recruited. ECGs and BSMs were independently interpreted. All patients had a rest MPI < 24 hours from chest pain interpreted by a physician blinded to the ECG and BSM. Scans were coded using a 17-segment polar plot and posterior wall perfusion defects (PWPD) were recorded. MI was diagnosed when cTroponin T at 12 hours was > 0.09ng/ml.

Results: Seventy-two patients were recruited. STE on the 12-lead ECG was recorded in only 30 patients (42%, 30/72). The predominant STE on the BSM identified 7 inferior (10%, 7/72), 41 posterior (57% 41/72) and 10 right ventricular MIs (14%, 10/72). Fourteen patients had no STE on BSM (19%, 14/72). Sixty-eight (94%, 68/72) had a cTroponin T > 0.09ng/ml. The BSM had a sensitivity of 81% (55/68) (95% CI 70-89%) for identification of MI compared with 44% (30/68) (95% CI 32-57%) sensitivity for the 12-lead ECG (McNemar's $p < 0.001$). Sixty-nine patients had interpretable scans: 60 (87%, 60/69) had a PWPD. Patients with PWPD had a mean percentage of left ventricular involvement of 45% SD 15 with the initial 12-lead ECG showing STE inferiorly in 21 (35%, 21/60) and 39 with non-specific changes (65%, 39/60). The predominant STE on the BSM identified STE in inferior leads in 7 (12%, 7/60), 32 had posterior STE (53%, 32/60), and 9 had right ventricular STE (15%, 9/60). Twelve had no STE (20%, 12/60). The 12-lead ECG did not identify any posterior territory MI (sensitivity 0%). Fifty-one percent (20/39) of patients with PWPD with non diagnostic 12 lead ECG were classified as posterior MI by the BSM. Correlating PWPD with posterior STE (BSM) - sensitivity was 53% (32/60) (95% CI 40-66%).

Conclusions: Sixty-five percent (39/60) of patients with PWPD had non-specific ECG changes. Posterior MIs involved 45% SD 15 of the left ventricle. The BSM identified more (53%, 32/60) of these patients than the 12-lead ECG (0/60) and thus indicates patients who would benefit from early reperfusion strategies.

24.05

IMPAIRED CONTRACTILE RESERVE IN OBESE SUBJECTS: A RUBIDIUM PET STUDY

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Background: Obesity is associated with myriad effects on the cardiovascular system, including left ventricular (LV) hypertrophy and diastolic dysfunction. As the obesity epidemic grows, further elucidation of these

derangements is becoming increasingly important. The effect of obesity on stress-induced augmentation of LV systolic function in an otherwise normal heart (resting ejection fraction [EF] $\geq 50\%$, normal perfusion) is not well known.

Methods: We studied 215 sequential patients without a prior history of coronary artery disease (CAD) or infarction and normal myocardial perfusion and resting EF ($\geq 50\%$) by dipyridamole rubidium-82 positron emission tomography (RPET). RPET was used because of its high sensitivity and specificity for detecting CAD and capturing of LV systolic function at peak stress. EF assessment using RPET correlates well with cardiac magnetic resonance imaging and equilibrium radionuclide angiography measurements, and changes in EF (Δ EF) with pharmacologic stress has been shown to be a strong prognostic tool. We divided patients into two groups based on their body mass index (BMI): Ob: BMI ≥ 30 (125) and NoOb: BMI < 30 (n = 90).

Results: There were 115 females and average age was 63. There was no significant difference in the resting EF between the two groups: Ob 62.3 ± 7.9 vs. NoOb 63.2 ± 7.3 , $p = 0.42$. We found a significant negative correlation between BMI and stress induced Δ EF $r = -0.20$, $p = 0.003$. In Ob patients a significantly lower Δ EF was noted; $5.8 \pm 4.8\%$ vs. $7.3 \pm 4.5\%$, $p = 0.02$. No patient in the NoOb group showed a decrease in EF with stress and two patients showed no Δ EF (2.2%), as compared to 13 (10.2%) Ob patients showing either no change or decrease in EF, $p < 0.0001$. On multiple regression analysis after adjusting for age, sex, diabetes, hypertension, rest EF, use of beta blockers, ACE inhibitors, angiotensin receptor blockers, calcium channel blocker, and coronary calcium score, BMI was the most significant predictor of stress induced Δ EF, $p = 0.0006$.

Conclusions: Despite normal baseline LV function, normal wall motion, and normal perfusion, obese patients have impaired LV contractile reserve in response to pharmacologic stress (significantly lower augmentation of systolic function with stress) as compared to non-obese patients.

24.06

SPECTRUM OF GATED SPECT MYOCARDIAL PERFUSION IMAGING (MPI) ABNORMALITIES IN PATIENTS WITH LEFT MAIN CORONARY ARTERY DISEASE: A TERTIARY MEDICAL CENTER EXPERIENCE

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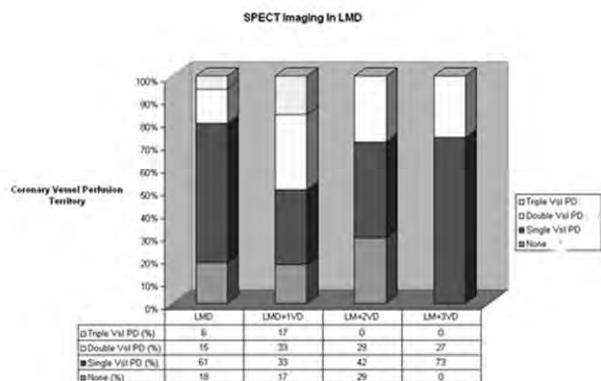
Background: Left main disease (LMD), defined as > 50% lesion stenosis occurs in upto 6% of all patients undergoing catheterization and portends a poor prognosis. Limited data on the value of single-photon emission computed tomography (SPECT) imaging for the diagnosis of LMD exists. We sought to characterize the spectrum of SPECT myocardial perfusion imaging (MPI) findings in patients with LMD.

Methods: Seventy-four consecutive patients with significant angiographic LMD, identified from our cath lab database (over a period of 10 years) and gated exercise (15) or adenosine (59), thallium²⁰¹ or technetium ^{99m} sestamibi SPECT MPI imaging within 1 year of index angiography were included. Group I (Gp I) comprised 33 patients with isolated LMD. Group II (Gp II) consisted of 41 patients with LMD and 1-vessel disease (6), LMD and 2-vessel disease (24) and LMD and 3-vessel disease (11).

Results: The pattern and extent of qualitatively assessed reversible perfusion deficits (PD) on SPECT MPI are depicted in Figure 1. Absence of any reversible PD was observed in 6 (18%) of Gp I and 8 (20%) of Gp II patients. Among Gp I patients, PD in single vessel, double vessel, and triple vessel distribution were seen in 20 (61%), 5 (15%), and 2 (6%) patients, respectively. In comparison, PD in single vessel, double vessel, and triple vessel distribution were observed in 20 (49%), 12 (29%), and 1 (2%) of Gp II patients, respectively. Left Main (LM) scintigraphic pattern was noted in 6 patients (Gp I-2, Gp II-4). Transient ischemic dilatation (TID) was encountered in 44 patients (Gp I-21, Gp II-23) and in 4 patients (29%) with normal perfusion scans. Significant ST-segment depressions on electrocardiogram (≥ 2 mm) in 2 or more contiguous leads were seen in only 7 (9%) patients.

Conclusions: These data represent the largest analysis of patients with 'isolated' LMD. Our findings demonstrate that approximately 19% of patients with significant LMD have no discernible perfusion deficits on SPECT MPI. While LM pattern is rare, single vessel distribution PD and TID represent the most frequently encountered SPECT abnormalities in the setting of LMD.

Figure 1.



24.07
POTENTIAL UTILITY OF CORONARY CALCIUM SCORING IN PATIENTS REFERRED FOR THE EVALUATION OF MYOCARDIAL ISCHEMIA

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Background: Among patients referred for suspected myocardial ischemia, the utility of using coronary calcium score (CCS) to select patients for stress myocardial perfusion imaging (MPI) has not been previously explored.

Methods: Ninety patients referred for assessment of myocardial ischemia underwent stress single-photon emission computed tomography (SPECT) imaging using a standard rest thallium-201/stress Tc-99m sestamibi protocol and quantitative attenuation correction using a line source of Gadolinium-153. Images were scored using a standard 5-point semi-quantitative perfusion score (0 = normal to 4 = absent) and categorized as normal or abnormal. CCS was acquired with a 16-slice multi-detector CT scanner using parameters of 3mm thickness, 120 kV, and 50-100 mA. CCS was categorized as 0, 1-10, 11-100, 101-400, and >400 Agatston units.

Results:

CCS	n	% Normal MPI	Likelihood of CAD		
			Low	Intermediate	High/ Known CAD
Normal (0)	36	100%	61.1%	38.9%	0%
Minimal (1-10)	8	100%	50.0%	50.0%	0%
Mild (11-100)	12	100%	41.7%	50.0%	8.3%
Moderate (101-400)	15	86.7%	6.7%	73.3%	20.0%
Severe (>400)	19	36.8%	0%	47.4%	52.6%

The mean ± SD (median) CCS in patients with normal and abnormal SPECT was 176 ± 609 (2) and 980 ± 731.87 (721) respectively, p=0.00003. The mean ± SD (median) CCS in patients with low (n=32), intermediate (n=44), and high (n=14) likelihood of CAD was 12.48 ± 32.88 (0), 340.44 ± 809.91 (42.50), and 837.64 ± 757.53 (613.50), p=0.0005. The positive predictive value of CCS > 400 was 63% and the negative predictive value of CCS ≤ 100 was 100%.

Conclusion: Patients with absent and low CCS (≤100) have normal myocardial perfusion, irrespective of their pre-test probability of CAD. Increasing CCS is associated with a greater pre-test probability of CAD and with greater incidence of abnormal myocardial perfusion. Among patients referred for evaluation of ischemia, an initial CCS is useful for selecting patients for MPI and may increase the efficiency of SPECT utilization. The cost-effectiveness of this strategy needs to be tested.

24.08
ISCHEMIC ELECTROCARDIOGRAPHIC RESPONSE TO EXERCISE IS MORE STRONGLY ASSOCIATED WITH THE SEVERITY RATHER THAN THE EXTENT OF SPECT ISCHEMIA

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Background: In patients with exercise-induced ischemia on myocardial perfusion imaging (MPI), it is unknown whether the occurrence of an ischemic electrocardiographic (ECG) response is related to the extent and/or severity of myocardial ischemia.

Methods: We evaluated patients who had ischemia on exercise-stress MPI between January 2004 and May 2007. Single-photon emission computed tomography (SPECT) MPI was performed using a rest thallium-201/exercise Tc-99m sestamibi protocol, and read using a standard 5-point perfusion score (0=normal to 4= absent) and a 17-segment left ventricular model. Summed stress score (SSS) and summed rest score (SRS) were derived as the sum of individual segmental scores at stress and rest, respectively. Myocardial ischemia was diagnosed if the summed difference score (SDS=SSS-SRS) was ≥ 2, and the likelihood ischemia was scored high. Extent of ischemia was determined by the number of segments with difference score ≥ 1, greatest severity of ischemia by the largest difference score among all segments, while the SDS was the composite of extent and severity. An ischemic ECG response was defined as ≥ 1 mm ST-segment depression 80 ms after the J point in 2 contiguous leads.

Results: A total of 3,294 patients underwent exercise MPI, of whom 395 patients had ischemia on MPI. Of these, 231 (58%) had an ischemic ECG response. Patients with ischemic ECG were older (62.6 ± 10.3 vs. 58.5 ± 10.7 years, p < 0.001), had a lower prevalence of smoking (46% vs. 77%, p = 0.04), and a similar prevalence of male gender, diabetes mellitus, hypertension and hyperlipidemia. The SDS (9.8 ± 1.9 vs. 6.5 ± 1.9, p < 0.001), extent (4.9 ± 2.6 vs. 3.7 ± 2.0, p < 0.001), and severity (3.1 ± 0.8 vs. 2.7 ± 0.8, p < 0.001) of ischemia were all significantly greater among patients with ischemic ECG changes. In a multivariable analysis of 9 clinically significant variables, only age (each quartile more predictive compared to lower quartiles) and SDS (OR 2.56, 95% CI 1.84-3.56) were associated with ischemic ECG response. When analyzed separately, the severity of ischemia (OR 1.45, 95% CI 1.07-1.97) was more strongly associated with ischemic ECG response than extent of ischemia (OR 1.19, 95% CI 1.07-1.34).

Conclusions: Among patients with exercise-induced myocardial ischemia by MPI, age and magnitude of ischemia were associated with ischemic ECG response. The severity of ischemia has a stronger association than extent.

24.09
DIFFERENCES IN ELECTRICAL AND MECHANICAL DYSSYNCHRONY AS QUANTIFIED BY PHASE ANALYSIS OF GATED SPECT IMAGING IN PATIENTS WITH MILD TO MODERATE LEFT VENTRICULAR DYSFUNCTION

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Background: Cardiac resynchronization therapy (CRT) is approved for patients with significant heart failure, prolonged quantitative QRS duration, and ejection fraction ≤ 35%. Mechanical dyssynchrony, rather than QRS duration, may better predict which of these patients will benefit from CRT. Limited data suggest that some patients with mild to moderate left ventricular (LV) dysfunction have significant dyssynchrony and may also benefit from CRT. The relationship between QRS duration and mechanical dyssynchrony in patients with mild to moderate LV dysfunction is not known.

Methods: A novel method to quantify dyssynchrony using phase analysis of gated single-photon emission computed tomography (SPECT) imaging has been developed. The technique utilizes a Fourier analysis method to convert the regional LV myocardial counts from the discrete frames per cardiac cycle into a continuous thickening function which allows fine temporal resolution of the phase of the onset of myocardial thickening. The standard deviation of the LV phases (phase SD) and histogram bandwidth are quantitative indices which describe mechanical dyssynchrony. We utilized phase analysis of gated SPECT myocardial perfusion imaging to compare the degree of dyssynchrony in patients with mild to moderate LV dysfunction (ejection fraction 35-50%) and normal QRS duration (n=73) with those with prolonged QRS duration (n=20), to describe the relationship between QRS duration and mechanical dyssynchrony and to determine the prevalence of significant dyssynchrony in these cohorts of patients.

Results: Patients with mild to moderate LV dysfunction who have prolonged QRS duration have higher degrees of dyssynchrony as quantified by phase SD ($49^\circ \pm 18^\circ$ vs. $35^\circ \pm 15^\circ$, $p = 0.002$) and histogram bandwidth ($138^\circ \pm 42^\circ$ vs. $107^\circ \pm 54^\circ$, $p = 0.014$) than those patients with normal QRS duration. However there are weak correlations between QRS duration and phase SD ($r=0.28$) as well as with histogram bandwidth ($r = 0.20$). The prevalence of significant dyssynchrony (phase SD $\geq 43^\circ$) was 65% in patients with prolonged QRS duration as compared to 29% in patients with normal QRS duration.

Conclusions: This is the only study reported to date on the relationship between electrical and mechanical dyssynchrony in patients with mild to moderate LV dysfunction. Although those patients with prolonged QRS duration have higher degrees of dyssynchrony than patients with normal QRS durations, there are weak relationships between electrical dyssynchrony as determined by QRS duration and SPECT derived indices of mechanical dyssynchrony in this cohort of patients.

24.10

VIABILITY OF INFARCTED MYOCARDIUM ASSESSED BY GATED MULTI-PINHOLE (MP)-SPECT PERFORMED DURING DOBUTAMINE STRESS

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Background: Distinguishing the viability of an area of myocardial infarction (MI) has important clinical implications. Acquisition of gated myocardial perfusion images (GMPI) during dobutamine stress provides the ability to assess viability associated with the region of an MI. The enhanced sensitivity of Multi-Pinhole-single-photon emission computed tomography (MP-SPECT) is well suited for the acquisition of such data which is then analyzed in terms of quantified blood flow differences.

Methods: A group of 19 patients with prior MI (stable for at least one year) underwent dobutamine stress GMPI. Following resting injection of 9.0 mCi of Tc-99m MIBI, sequential measurements of left ventricular ejection fraction (LVEF), segmental motion, and segmental thickening were performed during each stage of dobutamine stress by MP-SPECT technique. At max dobutamine stress, 4.0 mCi of Tl-201 was injected followed by simultaneous stress/rest GMPI. Echo measurement of LVEF, segmental motion, and segmental thickening was also performed at the completion of each dobutamine stress stage.

Results: In this group, 14 of the 19 patients had viable MI, which was demonstrated as abnormal resting segmental motion and segmental thickening which improved during dobutamine stress. Flow differences were seen in 13 of these 14 patients. Flow differences demonstrated in an area of MI predict viability. It is not necessary to quantify the flow differences. In the 5 patients which did not have viable MI, none showed flow differences in the region of the MI as was confirmed by echo. GMPI of combined Tc-99m and Tl-201 during recovery mirrored the changes seen during the progressive stages during induction of dobutamine stress.

Conclusions: Sequential measurements of LVEF, segmental motion, and segmental thickening were provided by MP-SPECT during dobutamine stress. The presence of flow differences in regions of MI is an indicator of segmental viability. Because simultaneous GMPI of Tc-99m and Tl-201 accurately mirrors the stages of dobutamine stress, this method should also be applicable to GMPI performed by MP-SPECT following exercise stress as well.

24.11

IMPACT OF GENDER ON THE PREVALENCE OF CORONARY ARTERY DISEASE IN PATIENTS WITH ABSENT OR LOW CORONARY CALCIUM

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Background: Gender-related differences in the prevalence of obstructive coronary artery disease (CAD) in patients with absent or low coronary calcium (CC) have not been described.

Methods: We used our hospital database to identify patients with absent or low CC who had contrast-enhanced 64-slice multidetector computed tomography (MDCT) for evaluation of suspected CAD. A low CC was defined as an Agatston score of ≤ 100 and obstructive CAD as luminal stenosis of \geq

50%. Stastical analysis was done with commercial software (SPSS v.16) and p value of < 0.05 was considered significant.

Results: Out of 495 patients with low to intermediate likelihood of CAD, we identified 335 patients (men = 151) with absent or low CC. Mean age of men was lower than that of women (51.01 ± 10.33 yrs vs. 57.65 ± 10.75 yrs, $p < 0.05$). Prevalence of obstructive CAD paralleled with increasing CC (28.8% with low CC vs. 4.8% with absent CC, $p < 0.0001$). As a group, higher percentage of men had obstructive CAD as compared to women (22.5% vs. 12.5%, $p = 0.01$). When analyzed separately, 6.3% of men and 4% of women with absent CC had obstructive CAD ($p = 0.7$). However with low CC, higher prevalence of obstructive CAD was found in men (34.5% vs. 22.9%, $p = 0.04$).

Coronary stenosis on MDCT	Absent CC (165)		Low CC (170)	
	Males (64)	Females (101)	Male (87)	Females (83)
No/Non obstructive	60 (93.7%)	97 (96%)	57 (65.5%)	64 (77.1%)
Obstructive	4 (6.3%)	4 (4%)	30 (34.5%)	19 (22.9%)

Conclusions: Absence of CC can reliably exclude significant CAD in both genders. However, at clinically considered low CC, men are more likely to have obstructive CAD, despite their younger age.

24.12

UPGRADING TO BIVENTRICULAR FROM RIGHT VENTRICULAR PACING AND CARDIAC REMODELING

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Background: Chronic right ventricular (RV) pacing may lead to deterioration in cardiac function and upgrading to biventricular (BIV) pacing may be advised. The purpose of this study was to describe the effects of upgrading to BIV from chronic RV pacing on RV and left ventricular (LV) remodeling.

Methods: Eighteen patients with heart failure and chronic RV pacing (duration 4.8 ± 6.4 years, $96 \pm 8\%$ RV pacing) who were upgraded to BIV pacing were studied ($98 \pm 3\%$ BIV pacing 3 months after upgrade). Patients underwent tomographic equilibrium radionuclide angiocardiology during chronic RV pacing immediately before and 3 months after upgrading to BIV pacing. RV and LV ejection fraction (EF), end-systolic volumes (ESV, ml) and end-diastolic (EDV, ml) volumes were measured.

Results: On upgrading from RV to BIV pacing the following significant findings occurred; LVEF increased (0.35 ± 0.11 to 0.40 ± 0.10 , $p = 0.02$), LVESV decreased (126 ± 55 to 100 ± 36 , $p = 0.006$), LVEDV decreased (189 ± 68 to 164 ± 43 , $p = 0.04$), and RVESV decreased (138 ± 66 to 114 ± 44 , $p = 0.03$). There were non-significant tendencies for RVEF to increase (0.43 ± 0.16 to 0.48 ± 0.13 , $p = 0.14$) and RVEDV to decrease (236 ± 76 to 217 ± 58 , $p = 0.14$).

Conclusions: Considerable RV and LV remodeling occurred 3 months after upgrading to BIV from chronic RV pacing. Significant reductions occurred in both RV and LV ESV and LV EDV with little change in RV EDV. Remodeling led to an increase in both RV and LV EF. Upgrading to BIV from chronic RV pacing is an important option to improve RV and LV function in the presence of heart failure.

24.13

THE SIGNIFICANCE OF THE METHOD OF MEASUREMENT OF LEFT VENTRICULAR EJECTION FRACTION WHEN CONSIDERING CARDIAC RESYNCHRONIZATION

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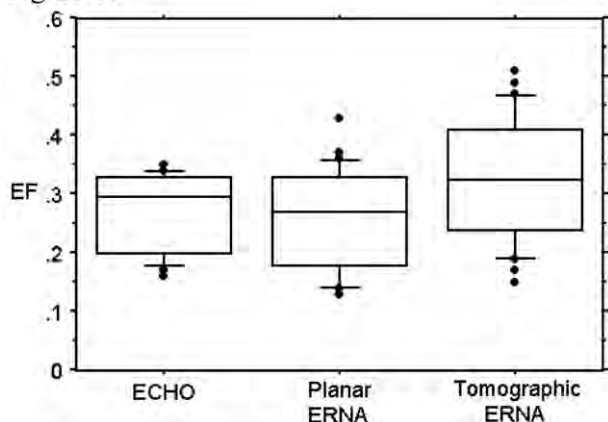
Background: Patients with heart failure, prolonged QRS, and a left ventricular (LV) ejection fraction (EF) of less than or equal to 0.35 may be considered for cardiac resynchronization therapy (CRT). Current guidelines do not designate a specific method of LVEF measurement. This study was undertaken to determine if differences existed amongst methods of LVEF measurement and to determine if these differences could be clinically relevant.

Methods: Twenty-six patients with heart failure and right ventricular pacing who underwent CRT were studied. In all patients, echocardiographic (ECHO) determination of LVEF was performed and utilized to decide on the need for CRT: LVEF by ECHO was less than or equal to 0.35 in all patients. These patients also underwent both planar and tomographic

equilibrium radionuclide angiography (ERNA) prior to CRT to measure LVEF; tomographic ERNA had been previously successfully validated against computed tomographic angiography for LVEF assessment. **Results:** LVEF measured by ECHO was 0.27 ± 0.06 , range 0.16 to 0.35 and was similar to that measured by planar ERNA (0.26 ± 0.08 , 0.13 to 0.43); both ECHO and planar ERNA LVEF were significantly ($p = 0.01$ and $p = <0.0001$ respectively) less than that measured by tomographic ERNA (0.33 ± 0.10 , 0.15 to 0.51). Box plots (Figure 1) illustrate the markedly different ranges of LVEF seen among the three methods. Of note, 3 of the 26 patients (12%) with planar ERNA and 10 of the 26 patients (38%) with tomographic ERNA had LVEF > 0.35 .

Conclusions: There was considerable variation between LVEF measured by ECHO and planar and tomographic ERNA. LVEF in over one-tenth of patients following planar and LVEF in over one-third following tomographic ERNA exceeded ECHO LVEF criterion for CRT. Thus, when considering CRT, the method of LVEF determination may have an impact on patient selection for CRT and should be considered when planning clinical trials to assess CRT.

Figure 1.



24.14

ASSOCIATION OF MORTALITY AND LEFT VENTRICULAR DYSSYNCHRONY MEASURED BY SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY IMAGING IN ISCHEMIC SYSTOLIC HEART FAILURE PATIENTS WITH CORONARY ARTERY DISEASE

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Background: Patients with severe left ventricular (LV) dysfunction due to coronary artery disease (CAD) have high morbidity and mortality rates. Many of these patients demonstrate LV dyssynchrony on 2D echo imaging. Identifying which patients will benefit from targeted device therapies, such as cardiac resynchronization therapy, has been challenging. A novel method to quantify dyssynchrony using phase analysis of gated single-photon emission computed tomography (SPECT) imaging was used in our study. We examined the relationship between the degree of LV dyssynchrony and mortality.

Methods: We performed a retrospective analysis of systolic heart failure patients with known CAD and ischemic cardiomyopathy. Patients with ischemia defined by a sum difference score > 3 on SPECT imaging or with acute coronary syndrome were excluded. Dyssynchrony analysis was completed using the phase analysis tool from Emory Cardiac Toolbox. This tool utilizes Fourier analysis to convert the regional LV myocardial counts from discrete frames per cardiac cycle into a continuous thickening function. Previously validated histogram dyssynchrony characteristics of LV dysfunction, phase standard deviation (phase SD) and bandwidth, were measured. T-tests comparing patients with and without mortality based on the social security database were performed.

Results: From January 2004 to July 2007, 92 consecutive patients were identified and stratified regarding presence or absence of mortality. Greater than 93% of patients were on beta-blockers, angiotensin converting enzyme inhibitors, and statins. All patients had an implanted cardioverter defibril-

ator. Our population had a mean ejection fraction of $30 \pm 11\%$ and a mean end diastolic volume of $221 \pm 82\text{ml}$. During a mean follow-up of 20 ± 11 months, 12 patients (13%) died. Predictors of mortality with univariate analysis included age ($p = 0.02$), ejection fraction ($p = 0.005$), and QRS duration ($p = 0.001$). More than 90% of patients had a phase SD and bandwidth > 1 standard deviation above mean values demonstrated by patients in a validated normal cohort. Histogram dyssynchrony characteristics by phase analysis are shown in Figure 1.

Figure 1. Histogram dyssynchrony characteristics by phase analysis

	No mortality	Mortality	p-value
Phase standard deviation (degrees) Normal value: 15.7 ± 11.8 degrees	52 ± 18	67 ± 9	< 0.001
Bandwidth (degrees) Normal value: 42 ± 28 degrees	171 ± 70	227 ± 43	0.002

Conclusion: In patients with LV systolic dysfunction secondary to CAD, nuclear assessment of mechanical dyssynchrony using SPECT imaging may identify patients at higher risk in this already high-risk population.

24.15

INTEGRATION OF QUANTITATIVE CARDIAC PET-CT AND CT ANGIOGRAPHY IN THE CHARACTERIZATION OF CORONARY ARTERY DISEASE

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Objective: Integration of perfusion positron emission tomography (PET) with computed tomography angiography (CTA) allows for assessment of microvascular reactivity, atherosclerotic plaque burden, and regional ischemia in a single study. We sought to characterize different disease patterns in an intermediate risk population referred for workup of coronary artery disease (CAD).

Methods: Rest/dipyridamole Rb-82 PET-CT with CTA was performed in 35 consecutive patients (pts) on a 64-row GE Discovery Rx VCT PET-CT scanner. Rb-82 images were qualitatively evaluated for regional perfusion defects, and coronary flow reserve (CFR) was quantified using a previously validated retention model. CTA was visually analyzed to obtain a plaque burden score from vascular remodeling/noncalcified/calcified plaque in 17 coronary segments.

Results: Normal CTA was found in 11 pts, while 18 pts had atherosclerosis without regional perfusion defects and 7 pts had atherosclerosis with regional perfusion defects. Global CFR was significantly higher in normal CTA vs nonobstructive atherosclerosis and regional ischemia (2.5 ± 0.4 vs 1.8 ± 0.5 vs 1.5 ± 0.2 ; $p < .05$). In pts with nonobstructive atherosclerosis, there was a nonsignificant trend towards lower CFR with higher plaque burden ($r = -0.35$; $p = 0.09$). Regionally, there was no significant difference of flow reserve between plaque-laden and plaque-free vascular territories in the same patient (1.9 ± 0.5 vs 1.8 ± 0.5 ; $p = .12$). No difference in CFR was observed in predominantly calcified vs noncalcified atherosclerosis (1.9 ± 0.5 vs 1.8 ± 0.5 ; $p = 0.68$).

Conclusions: Nonobstructive atherosclerosis is associated with decreased flow reserve even in morphologically plaque-free vascular territories, suggesting presence of global endothelial dysfunction. Integration of quantitative flow and coronary atherosclerosis allows for bio-morphologic characterization of early manifestations of CAD by hybrid PET-CT.

24.16

NUCLEAR INDICES OF MYOCARDIAL INFARCTION ARE SIGNIFICANTLY ASSOCIATED WITH TROPONIN LEVELS: A COMMUNITY-BASED STUDY

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Background: The 2007 Universal Definition of myocardial infarction (MI) recommends the use of troponin (c-TnT) as the biomarker of choice for diagnosis of MI. Data relating c-TnT to single-photon emission computed tomography (SPECT) infarct size in patients (pts) with MI are limited.

Objectives: To evaluate the relationship between c-TnT levels with infarct size and left ventricular ejection fraction (LVEF) quantitated by gated SPECT sestamibi in pts with MI.

Methods: A subset of pts with first MI participating in a community-based cohort of MI in Olmsted County, MN, was prospectively enrolled in this study. All cases were validated using standardized guideline criteria. Serial c-TnT levels were obtained at presentation, 12 hours, day 1, day 2, day 3, and day 4 after onset of pain. Peak c-TnT was the maximum c-TnT value. The third generation cardiac c-TNT assay was used to quantitate c-TNT values.

Results: One hundred twenty-one pts (age 61 ± 13 ; 31% women) with MI underwent gated SPECT sestamibi imaging at a median (25%; 75%) of 10 (5; 15) days post-MI. Fifty-nine pts (49% of the population) had no measurable infarction by SPECT, which can sometimes fail to detect infarcts smaller than 3% of the left ventricle. Median infarct size was 1% (0%; 1%) and median first pass LVEF was 54% (47%; 60%). In logistic analysis, adjusting for age, gender, MI type, and MI location, independent predictors for measurable MI included c-TnT at days 1, 2, 3, 4 and peak c-TnT. In receiver operator characteristics (ROC) analysis, the area under the curve (AUC) increased with later measurements of c-TnT (day 1 = 0.67; day 2 = 0.70; day 3 = 0.77, day 4 = 0.86). The AUC for peak c-TnT was 0.72. The best cut-off to differentiate between measurable and non-measurable infarction was a c-TnT value of 1.0 ng/ml at day 4. For the pts with measurable MI, there was a positive correlation between c-TnT values at days 1, 2, 3, and 4 with MI size and the r value increased with later measurements (Table 1). There was a significant negative correlation between c-TnT values at 12 hours, day 3, day 4 and peak with LVEF.

Table 1.

Time	Infarct size		LVEF	
	R (Spearman)	p value	R (Spearman)	p value
Admission	0.07	0.64	-0.05	0.78
12 hours	0.22	0.18	-0.48	0.006
Day 1	0.33	0.02	-0.21	0.21
Day 2	0.34	0.04	-0.33	0.09
Day 3	0.48	0.02	-0.59	0.005
Day 4	0.58	0.006	-0.48	0.007
Peak	0.24	0.07	-0.34	0.01

Conclusions: In a community-based cohort of pts with MI defined by contemporary criteria, independent predictors for measurable MI included c-TnT at days 1, 2, 3, 4 and peak c-TnT. c-TnT measurements at days 3 and 4 correlated best with MI size and first pass LVEF. The best cutoff to differentiate between measurable and non-measurable MIs was a c-TnT of 1.0 ng/ml at day 4.

24.17

MEASURING LEFT-VENTRICULAR CONTRACTION AND RELAXATION EFFICIENCY BY PHASE ANALYSIS OF ECG-GATED MYOCARDIAL PERFUSION SPECT STUDIES

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Background: Phase analysis has been developed and validated to automatically measure left ventricular (LV) dyssynchrony from conventional gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) studies. The purpose of this study is to use it to measure LV contraction efficiency (LVCE) and LV relaxation efficiency (LVRE).

Methods: Amplitudes and phases of LV regional contraction and relaxation were calculated for more than 600 LV regions using 2-harmonic phase analysis. A weighting factor (WF), varied between 1 and -1, was then calculated for each region based on its contraction phase difference from the mean contraction phase of the entire ventricle. WF=1 when the phase difference was 0°, whereas WF=-1 when the phase difference was 180°. All regional contraction amplitudes were weighted by the corresponding WFs and then summed to represent the net contribution of wall thickening to the LV contraction. LVCE was calculated as the ratio of the net contribution to the sum of the all contraction amplitudes. Conceptually, if all regions exhibit the exact contraction phase, LVCE would be 100%. Similarly, the net contribution of wall thinning to the LV relaxation was calculated, and LVRE was obtained. Twenty-nine normal controls (Group A) and 88 consecutive patients with congestive heart failure (CHF) were enrolled. Forty-five CHF patients had LV ejection fraction (LVEF) greater than 50% (Group B), and 43 had LVEF lower than 50% (Group C). LVCE and LVRE

were calculated for all subjects and compared between groups using student t test.

Results: Five and 8 subjects in Groups B and C were excluded after processing because of significant gating errors identified by the automatic quality control tool of the Emory Cardiac Toolbox. There were significant differences between Groups A and B in LVCE ($90.1 \pm 3.1\%$ vs. $87.3 \pm 5.6\%$, $p = 0.0108$) and LVRE ($89.0 \pm 4.1\%$ vs. $85.1 \pm 6.5\%$, $p = 0.0031$), but not in LVEF ($67.6 \pm 8.5\%$ vs. $66.2 \pm 10.3\%$, $p = 0.5191$). Thirteen patients in Group B had LVCE and/or LVRE lower than Group A by greater than 2 standard deviations. Groups A vs. C showed greater significant differences than Groups A vs. B for both LVCE ($90.1 \pm 3.1\%$ vs. $62.5 \pm 18.7\%$, $p < 0.0001$) and LVRE ($89.0 \pm 4.1\%$ vs. $58.9 \pm 22.8\%$, $p < 0.0001$). All patients in Group C had LVCE and/or LVRE lower than Group A by greater than 2 standard deviations.

Conclusion: This study indicated that CHF with normal LVEF does not necessarily have preserved systolic function and diastolic dysfunction. LVCE and LVRE, more comprehensive measures of LV functional status than LVEF, are promising classifiers for CHF. The next step is to enroll a large number of CHF patients to establish an objective and quantitative classification for CHF based on LVCE and LVRE and to validate their clinical values in CHF prognosis.

24.18

RIGHT AND LEFT VENTRICULAR TRACER UPTAKE RATIO WITH DIPYRIDAMOLE RB-82 PET MYOCARDIAL PERFUSION IMAGING IN IDENTIFYING PATIENTS WITH LEFT MAIN OR 3-VESSEL CAD

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Background: Myocardial perfusion imaging plays an important role in the diagnosis and risk stratification of patients with coronary artery disease. However, its dependence on relative differences in myocardial blood flow between coronary territories means that in some cases of 3-vessel disease, where myocardial blood flow is similarly decreased between coronary territories, a false negative test may result. Although this can be addressed by absolute flow quantification with positron emission tomography (PET), it is not routinely performed at most centers. Ratios of tracer uptake in the right ventricle (RV) and left ventricle (LV) at stress and rest have been used to identify high-risk individuals with single-photon emission computed tomography (SPECT) imaging. However, these results are yet to be reported with PET.

Methods: Rb-82 PET perfusion studies of 22 normal volunteers and 169 consecutive patients (who also underwent coronary angiography) were included in the study. Based on the presence of $\geq 50\%$ left main stenosis or $\geq 70\%$ stenosis of other coronary arteries on angiography, patients were categorized as having no significant coronary stenosis ($n = 60$), 1- or 2-vessel disease ($n = 81$) and left main disease/3-vessel disease ($n = 28$). The maximum RV and LV myocardial Rb-82 uptake was measured (MBq/cc) during stress and rest. The difference between RV and LV stress and rest uptake ratios (RV:LVdif) was computed for each subject as below.

$$RV:LVdif = RV_{stress}/LV_{stress} - RV_{rest}/LV_{rest}$$

Results: RV:LVdif is a statistically significant predictor of coronary artery stenosis ($F = 9.58$ $p = 0.0001$). Patients with left main or 3-vessel disease had a significantly higher RV:LVdif compared to those with single or double vessel disease or no significant coronary stenosis (Table 1).

Table 1.

			RV:LVdif		
	N	%	Mean	Standard deviation	p value versus left main / 3 vessel Disease
No significant CAD	60	36	0.006	0.073	0.0003
Single or Double vessel disease	81	48	0.006	0.077	0.0002
Left Main or 3 Vessel Disease	28	17	0.079	0.104	NA

RV:LVdif has an area under the receiver operator characteristic curve of 0.71 (95% confidence interval 0.59-0.83). An RV:LVdif of ≥ 0.1 yields a specificity of 93% and a sensitivity of 47% for prediction of left main or 3-vessel disease. The upper 95%

confidence limit cut off value for the normal volunteers was 0.08, which yields a 91% specificity and 47% sensitivity for prediction of left main or 3-vessel disease.

Conclusion: Quantifying rest and stress RV and LV uptake ratios with PET myocardial perfusion imaging may be useful for identifying patients with the highest risk anatomy. An RV:LVdif of ≥ 0.1 is 93% specific and 47% sensitive for the presence of left main or 3-vessel disease.

24.19

BENIDIPINE AMELIORATES MYOCARDIAL DYSFUNCTION INDUCED BY OXIDATIVE STRESS IN DAHL SALT-SENSITIVE HYPERTENSIVE RATS

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Background: Mitochondrial dysfunction subsequent to increased oxidative stress and alterations in energy metabolism is considered to play a role in the development of cardiac hypertrophy and its progression to failure. We previously reported that increased myocardial Tc-99m sestamibi (MIBI) clearance reflected myocardial mitochondrial dysfunction induced by oxidative stress in Dahl salt-sensitive (DS) hypertensive rats. A long-acting calcium channel blocker, benidipine, which is widely used in the clinical setting, has been shown to prevent oxidative stress, as indicated by some clinical and experimental reports. The aim of the present study was to

examine whether benidipine ameliorated myocardial mitochondrial dysfunction in DS hypertensive rats by evaluating myocardial MIBI clearance.

Methods: DS hypertensive rats were divided into 3 groups, which were respectively treated with 1) only vehicle [DS-HT], 2) benidipine (1mg/kg/day) [DS-LB], and 3) benidipine (3mg/kg/day) [DS-HB]. And those fed a low-salt diet through the experiment [control]. DS hypertensive rats and the age-matched control DS rats were used in the study. To investigate systemic and myocardial oxidative stress, we measured serum NOx, 24-hour urine 8OH-dG as an index of systemic oxidative stress and myocardial 3-nitrotyrosine (3NT) as a biomarker of peroxynitrite in the myocardium. After 74 MBq of MIBI was administered to 6 rats in each group, planar imaging data was acquired at the early (10 min) and delayed (180 min) phases. Myocardial washout rate (WR) was calculated from the couple of the data.

Results: In the urinary 8OH-dG and myocardial 3NT, those in DS-HT and DS-LB rats were higher than those in control and DS-HB rats, respectively. The calculated MIBI-WR was significant higher in DS-HT and DS-LB rats (20.8 ± 6.6 , 22.7 ± 4.0 %, respectively) than in control and DS-HB rats (7.4 ± 3.5 , 12.5 ± 2.1 %, respectively).

Conclusions: These data suggested that high-dose benidipine suppressed systemic and myocardial oxidative stress and ameliorated myocardial mitochondrial dysfunction. These results were direct evidence that the phenomenon of increased myocardial MIBI clearance was based on myocardial mitochondrial abnormalities induced by systemic and myocardial oxidative stress in DS hypertensive rats. Myocardial MIBI-WR is a useful parameter to evaluate myocardial mitochondrial dysfunction in hypertensive heart disease.