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Myocardial Perfusion, Function, and Dyssynchrony in Heart Failure Patients: Baseline Results from the SPECT Imaging Ancillary Study of the Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION) Trial

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Abstract

Background—There are currently limited data on the relationships between resting perfusion abnormalities, LVEF, New York Heart Association (NYHA) functional class, and exercise capacity as defined by peak VO_2 and six-minute walk test in patients with heart failure and reduced left ventricular ejection fraction. Furthermore, the association between resting perfusion abnormalities and left ventricular dyssynchrony is currently unknown. This manuscript addresses The Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION) gated SPECT imaging (gSPECT) substudy baseline results.

Methods—HF-ACTION was a multi-center, randomized controlled trial of aerobic exercise training vs. usual care in 2331 stable patients with LVEF ≤35% and NYHA class II–IV heart failure symptoms treated with optimal medical therapy. Subjects enrolled in the HF-ACTION sub-

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Conflicts

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study underwent resting Tc 99m tetrofosmin gSPECT at baseline (n=240). Images were evaluated for extent and severity of perfusion abnormalities using a 17-segment and a 5-degree gradation severity score (SRS). LV function and dyssynchrony were assessed using validated available commercial software.

Results—The average age of patients enrolled was 59, 69% were male, 63% were white, and 33% were African-American. Of the 240 participants, 129 (54%) were ischemic and 111 (46%) were non-ischemic in etiology. The median LVEF by gated SPECT for the entire cohort was 26%. Among the nuclear variables, there was a modest correlation between LVEF and SRS (r= − 0.31, $p < 0.0001$) and there were stronger correlations between phase SD and SRS (r= 0.66, $p< 0.0001$) as well as phase SD and LVEF (r= −0.50, $p< 0.0001$). Patients with NYHA class III symptoms had more severe and significant degrees of dyssynchrony, median phase SD 54°, than those with NYHA class II symptoms, median phase SD 39° (p *value=0.001*). Patients with an ischemic etiology had a higher SRS ($p< 0.0001$) and significantly more dyssynchrony ($p< 0.0001$) than those who were nonischemic. However, there was no difference in LVEF or objective measures of exercise capacity between these groups. With respect to peak VO2, there was a weak correlation with LVEF (r = 0.18, p= 0.006) and no correlation with SRS (r = −0.04, $p= 0.59$) or with dyssynchrony (r= −0.13, $p= 0.09$). A weak, but statistically significant correlation between SRS and 6-minute walk was observed (r= −0.15, $p = 0.047$).

Conclusions—Gated SPECT imaging can provide important information in patients with heart failure due to severe LV dysfunction including quantitative measures of global systolic function, perfusion and dyssynchrony. These measurements are modestly but significantly related to symptom severity and objective measures of exercise capacity.

Introduction

Heart failure (HF) currently affects more than 5 million Americans with an estimated 500,000 new diagnoses each year 1. Advances in medical therapy have lead to significant improvements in morbidity and mortality in patients with HF and reduced left ventricular function. In addition to medical therapy, recognition of sudden death due to ventricular dysrhythmias and recent advances in device therapy with implantable cardioverter defibrillators (ICD) have further added to the armamentarium of treatment options for patients with HF 2⁻4. More recently, the emergence of ventricular dyssynchrony and subsequent treatment with cardiac resynchronization therapy (CRT) in appropriately selected HF patients has been shown to provide incremental improvements in morbidity and mortality in addition to standard background medical therapy 5⁻7. Despite these major improvements in treatment, the overall morbidity and mortality of patients diagnosed with HF remains high. HF also continues to be a major contributor to the economic burden of cardiovascular care in the United States with an estimated annual cost of approximately $33 billion 8. Given the increasing number of patients, persistently high morbidity and mortality, and escalating economic costs of HF, improvements in risk stratification and attention to less expensive and potentially beneficial therapies such as exercise training are warranted.

The Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION), an NIH/NHLBI funded study, is the largest randomized study of exercise therapy in HF patients to date. The overall HF-ACTION study design and rationale, including inclusion and exclusion criteria, has been previously published 9. Radionuclide imaging has been evaluated as a technique to noninvasively assess myocardial perfusion patterns to help distinguish between ischemic and nonischemic etiologies for HF and provide additional prognostic information 10⁻15. More recently, evaluation with technetium (Tc) 99m gSPECT imaging allowed for the simultaneous evaluation of perfusion defects, function, and left ventricular volumes that provided a more accurate and reproducible way to noninvasively distinguish between HF of ischemic versus nonischemic etiologies 16, 17.

Additionally, the prognostic significance of perfusion defects as assessed by the summed rest score (SRS) on SPECT myocardial perfusion imaging has been well established [18–20].

Recent developments in gSPECT imaging have led to an automated method to extract amplitude and phase from regional LV count changes during gated SPECT imaging as a way to objectively quantify left ventricular dyssynchrony [21–24]. Preliminary studies utilizing this novel software application have shown it to be a highly reproducible method with good correlation to traditional echocardiographic markers of dyssynchrony [25–28]. However, the relationships of left ventricular dyssynchrony and resting perfusion defects with ischemic etiology, symptom severity, and exercise capacity have not been evaluated. The HF-ACTION gated single-photon emission tomography (gSPECT) substudy provided a valuable opportunity to examine these relationships, and included assessments of resting perfusion abnormalities, left ventricular function, mechanical dyssynchrony, NYHA class, peak VO_2, and six-minute walk distance.

Methods

The overall design and rationale for the nuclear substudy of the HF-ACTION trial has been previously published [29]. A total of 240 patients were enrolled from the overall study population, of which baseline SRS data was available on 238 (Figure 1). All subjects enrolled in the substudy underwent resting gated perfusion SPECT imaging with a minimum dose of 25 mCi Tc 99m tetrofosmin at baseline and again at 12 months. All images were obtained with a minimum of 30 seconds per step and a minimum of 60 frames at 8 frames per cycle. A standard 64 by 64 matrix low energy/high-resolution collimator was used. It was recommended that a 180° rotation be acquired from a 45° right anterior oblique to a 45° left posterior oblique position. For gated imaging, the R-R window used was within a 20% window of the average electrocardiogram cycle length. The short axis data sets were generated using Butterworth filtering followed by filtered back projection reconstruction and oblique reorientation. SPECT images were processed using standard commercially available software (Emory Toolbox, Emory University; Atlanta, GA). Each nuclear study was independently interpreted and clinically reviewed by 2 experienced nuclear medicine/ nuclear cardiology physicians centralized at the nuclear core laboratory who were blinded to the patient information, including randomized treatment assignment. Perfusion defects were semi-quantified using 5 gradations and reported using a 17-segment model for resting perfusion defects to calculate a summed rest score (SRS). LV function and volumes were quantified via automated software processing. For the purposes of phase analysis to evaluate left ventricular mechanical dyssynchrony, phase standard deviation (SD) and bandwidth were evaluated. This method for phase analysis has been incorporated into the Emory Cardiac Toolbox (Emory University/Syntermed, Atlanta, GA). A representative phase histogram is shown in Figure 2.

For descriptive summaries of baseline data, counts and percentages for categorical variables were presented. For continuous measures, emphasis was given to medians and interquartile ranges. Hypothesis tests comparing two groups (ischemic versus non-ischemic etiology of HF, or NYHA class II vs. III) were performed using Wilcoxon rank sum tests. P-values for correlations were derived from an approximate t distribution, using n – 2 degrees of freedom. Scatter plots of the data were used to check for nonlinear relationships between the variables. In HF-ACTION, ischemic etiology was defined as having at least 1 of the following: angiographic stenosis of ≥ 75% in at least 1 major epicardial vessel, history of MI, history of revascularization procedure, or evidence of significant perfusion defect in the setting of ischemic symptoms [29].

Results

The baseline demographics and medical history for the patients enrolled in the nuclear substudy of the HF-ACTION trial are shown in Table 1. Data are presented by ischemic and non-ischemic strata since data have shown different characteristics and outcomes for these two groups of HF patients. The average age of patients enrolled was 59, 69% were male, 63% were white, and 33% were African-American. Of the 240 participants, 129 (54%) were ischemic and 111 (46%) were non-ischemic, which reflects a very balanced but unusual distribution given the predominance of ischemic etiology in the United States. Of the total group, 65% of the patients had a medical history significant for hypertension, 67% for hyperlipidemia, 33% for diabetes mellitus, and 16% for atrial fibrillation or atrial flutter. A total of 128 patients (53%) had a previous history of ICD placement and 44 patients (18%) had a history of bi-ventricular pacemaker placement. Background medical therapy at the time of enrollment is listed in Table 2. There was a very high utilization rate of ACE-I or ARB (94%), beta blocker (96%), and aspirin therapy (73%). Also of note, 48% of the total cohort was on an aldosterone antagonist, 40% were on digoxin, and 72% were on a loop diuretic.

The baseline nuclear characteristics are shown in Table 3. The median LVEF by gated SPECT for the entire cohort was 26% and end systolic and end diastolic volumes were markedly enlarged with median values of 165 mL and 226 mL, respectively. Left ventricular mechanical dyssynchrony as assessed by phase analysis was clinically significant for the total cohort with a median phase SD of 41°. There were strong correlations between phase SD with baseline SRS, (r= 0.66, $p< 0.0001$) (Figure 3), and with gated SPECT LVEF (r= −0.50, $p< 0.0001$) (Figure 4). There was a statistically significant, but weaker correlation between gated SPECT LVEF and SRS (r = − 0.31, $p< 0.0001$).

With respect to the ischemic versus the nonischemic HF strata, there was no difference in LVEF with a median of 26% for each group ($p= 0.56$). The median SRS (25^{th}, 75^{th} percentile) was 29 (18, 39) for the ischemic stratum and 6 (2, 17) for the nonischemic stratum ($p< 0.0001$). Also, there was more dyssynchrony in patients with an ischemic etiology compared with those with a nonischemic etiology, median phase SDs of 57° and 29° respectively ($p< 0.0001$). Interestingly, there was no significant difference in peak VO2 ($p=0.35$) and 6 minute walk distance ($p=0.69$) between these groups.

Those with NYHA class III symptoms had significantly more dyssynchrony than those with NYHA class II symptoms as measured by phase SD (median 54° versus 39°, $p= 0.001$) and histogram bandwidth (median 139° versus 104°, $p= 0.025$) (Table 4). Table 5 illustrates the baseline exercise variables for the nuclear substudy participants. The median peak VO_2 was 15.3 mL/kg/min and the mean exercise duration was 10.0 minutes (IQR 7.4–12.5). The median distance in the six-minute walk test for the overall cohort was 381 meters. There was a relatively weak, but statistically significant correlation between peak VO_2 and baseline LVEF, (r=0.178, $p=0.006$) (Figure 5). There was no correlation between peak VO_2 and dyssynchrony (r= −0.13, $p=0.09$) or between peak VO2 and SRS (r = −0.035, $p=0.59$).

Discussion

LVEF, peak VO_2, and six-minute walk distance are well-described and powerful prognostic factors in patients with HF and systolic dysfunction [30–35]. Several prior studies have established that there is a relative lack of correlation between the degree of left ventricular systolic dysfunction and the severity of HF symptoms and decrease in exercise capacity [36, 37]. The present study examined a large group of well-defined patients with systolic LV dysfunction. We assessed radionuclide measures of LV ejection fraction, perfusion, and

dyssynchrony and their relationships with subjective ratings of symptoms and objectively measured exercise capacity and 6 minute walk distance. Our findings demonstrate that more severe dyssynchrony is associated with higher SRS and lower LVEF. Furthermore, those with ischemic HF and worsened NYHA class also had more advanced degrees of dyssynchrony. Among the nuclear variables, only LVEF was significantly associated with objective measures of exercise capacity. This relationship, however, was modest at best and explained only 3% of the variability of peak exercise VO_2 ($r^2 = 0.032$).

The SRS derived from rest or stress nuclear perfusion imaging is also a validated and independent prognostic variable in the care of patients with cardiovascular disease [19, 20, 38, 39]. Given the fact that LVEF, peak VO_2, 6-minute walk distance, and SRS have all been previously demonstrated to be independent clinical predictors that represent very different aspects in the broad spectrum of HF patients, it is not unexpected that weaker correlations between these variables were observed.

The ability to use gated SPECT perfusion imaging as a noninvasive method to distinguish ischemic from nonischemic etiologies of HF has also been described [16, 40]. These data were validated in this study where the ability to distinguish ischemic from nonischemic cardiomyopathy was robust in a blinded core lab interpretation (Table 3 and Figure 6).

CRT is approved for the treatment of HF patients with New York Heart Association class III–IV symptoms, LVEF ≤ 35%, and QRS duration ≥120 milliseconds. Quality of life, NYHA functional class, exercise capacity, ejection fraction, and mortality have all been shown to have significant improvements when CRT is applied to this patient population [5–7, 41]. Despite these improvements, approximately 30% of patients fail to benefit from CRT when the current selection criteria are used [42]. Noninvasive methods to assess mechanical left ventricular dyssynchrony have traditionally involved echocardiographic parameters derived from M-mode and tissue Doppler imaging. However, the recently reported Predictors of Response to Cardiac Resynchronization Therapy trial (PROSPECT) demonstrated that echocardiography did not improve patient selection for CRT and was also susceptible to high interobserver variability and a lack of reproducibility [43]. A novel technique has been developed to quantify mechanical dyssynchrony using phase analysis of gated SPECT myocardial perfusion imaging [21, 25, 28, 44]. Potential advantages of this technique include its automation and reproducibility [27]. Phase SD and histogram bandwidth are indices derived from this application that have been shown to have a good correlation with traditional echocardiographic markers of dyssynchrony [45]. An early study utilizing this technique in patients who met guideline indications for bi-ventricular pacemaker implantation demonstrated that a phase SD ≥ 43° had a reasonable sensitivity and specificity for predicting response to CRT [25].

Patients enrolled in the HF-ACTION nuclear ancillary study had significant degrees of dyssynchrony at baseline. Interestingly, those with an ischemic etiology of HF had significantly more dyssynchrony than those with non-ischemic etiology. This was also demonstrated in the strong correlation between the baseline SRS and phase SD. Not surprisingly, a declining LVEF was also associated with increasing amounts of mechanical dyssynchrony. Weaker correlations between dyssynchrony and peak VO_2 as well as dyssynchrony and distance in the 6-minute walk test were observed. However, there was a significant difference in the degree of dyssynchrony between those with NYHA class III and NYHA class II symptoms. These findings are similar to those recently reported by Ypenburg et al. where an association between severity of HF symptoms and worsening mechanical dyssynchrony was also observed [46]. SPECT imaging offers unique advantages over noninvasive methods to evaluate dyssynchrony that includes the simultaneous assessment of LVEF, LV volumes, and myocardial perfusion. This is an important

consideration as perfusion defects and infarct location have been shown to be independent predictors of response to CRT [47–49].

The assessments of central cardiac function made in the present study had relatively modest relationships with measured peak exercise VO_2. This may be partly due to the fact that exercise capacity in patients with HF involves a complex interplay between reduced cardiac output, maladaptive peripheral hemodynamics, and deranged skeletal muscle function and metabolism [50]. Important peripheral effects of the HF milieu include impaired arterial formation and response to nitric oxide (NO), reduced skeletal muscle capillary density and abnormal fiber type switching, early lactic acid formation in response to exercise owing to altered intrinsic skeletal muscle metabolism and mitochondrial function, and skeletal muscle apoptosis [50].

One major limitation in the assessment of dyssynchrony in this study is that the clinical applicability of gated SPECT phase analysis has yet to be determined. Also, there are limited data with respect to dyssynchrony as defined by nuclear imaging and its relationship with patient outcomes. However, it still remains a promising new technique to assess mechanical left ventricular dyssynchrony and, with further study, may help improve patient selection for CRT. Another limitation is that of possible selection bias in this trial; which is comprised of patients willing to undergo an exercise program. Thus, relationships such as that of peak VO2 to the etiology of HF could be affected by this bias.

Conclusion

Gated SPECT imaging can provide important information in patients with HF due to severe LV dysfunction including quantitative measures of global systolic function, perfusion and dyssynchrony. These measurements are modestly but significantly related to symptom severity and objective measures of exercise capacity. Patients with the greatest degree of dyssynchrony had lower LVEF and greater amount of perfusion defect/scar. Furthermore, the novel measure of dyssynchrony appears to help discriminate ischemic from non-ischemic patients, correlates with NYHA symptom severity, and is modestly related to objective measures of exercise capacity.

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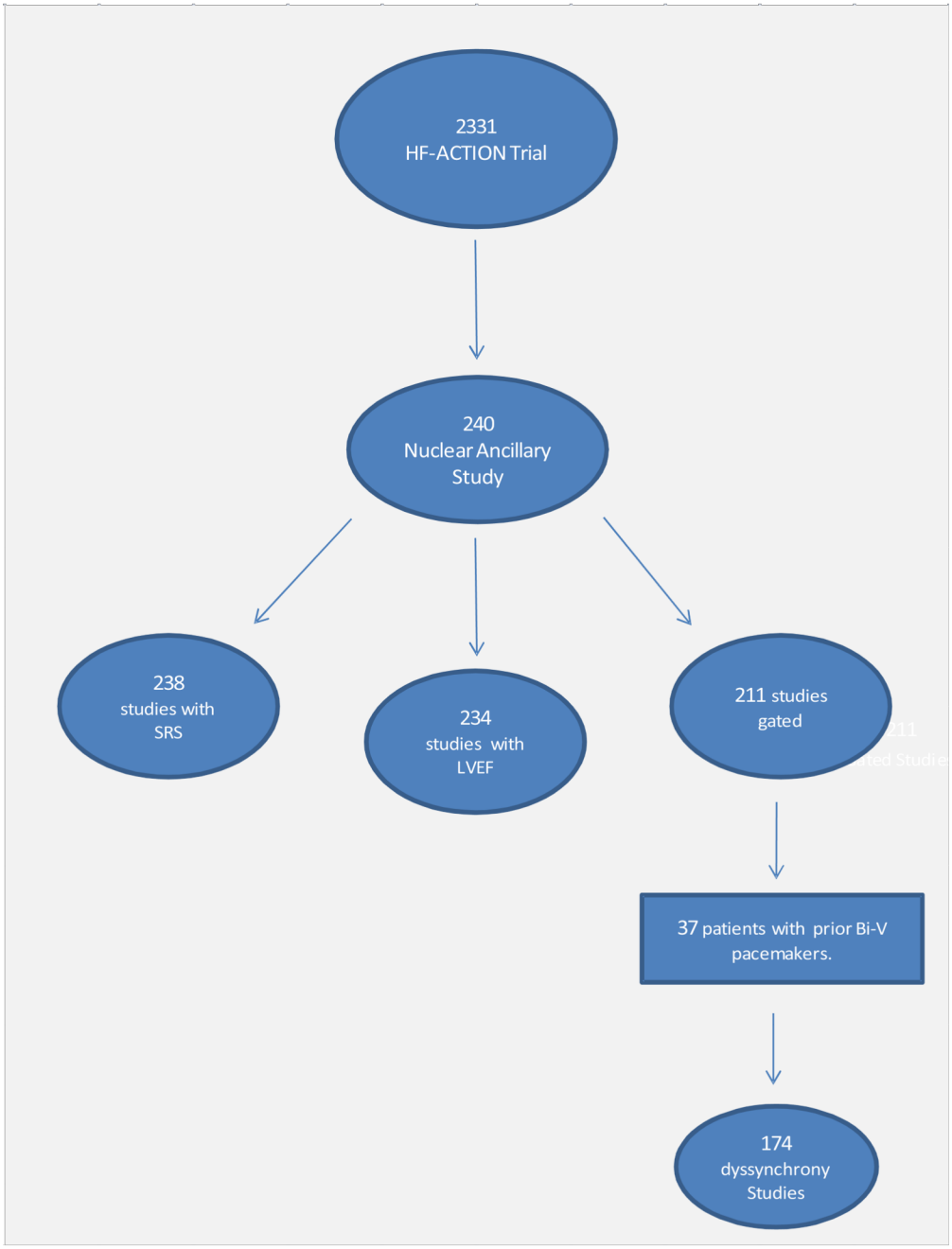
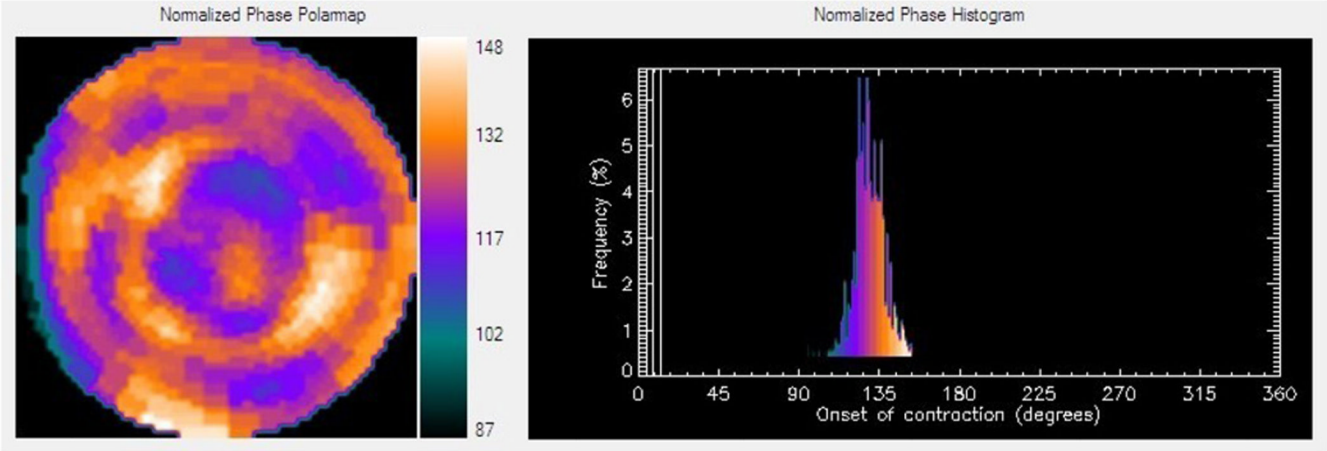


Figure 1.
240 patients from the overall HF-ACTION trial were enrolled in the nuclear substudy. 238 studies were included for the SRS analysis (2 studies not interpretable). LVEF and volumes were unavailable in 6 studies. There were 29 non-gated studies (i.e. multigated acquisition, MUGA) where LVEF and ventricular volumes were reported, but dyssynchrony analysis could not be performed. An additional 37 patients with bi-ventricular pacemakers were excluded from the dyssynchrony analysis.

A.



B.

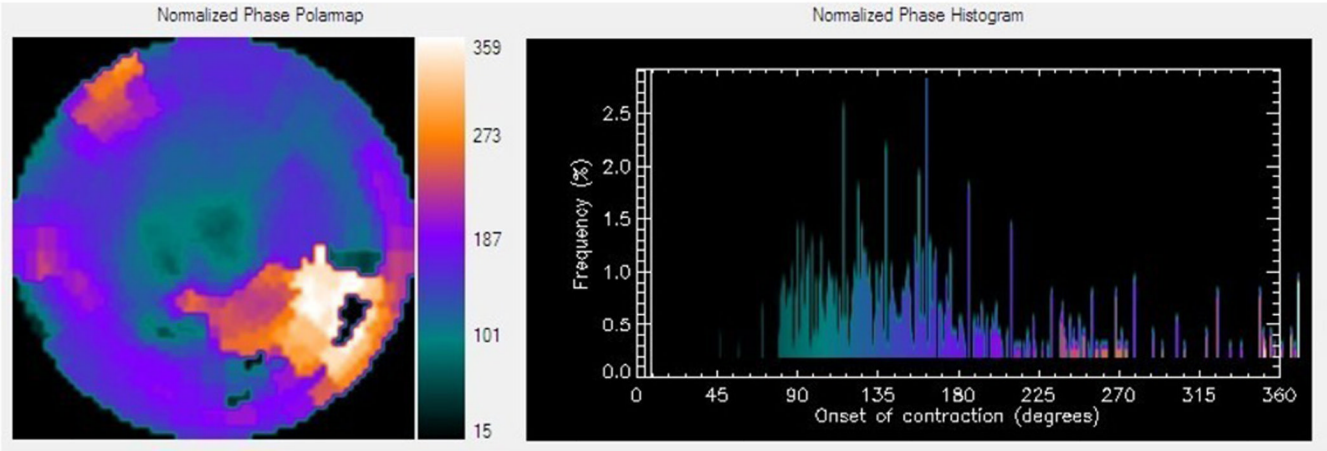


Figure 2.

Representative phase histograms. A) Normal phase histogram: The X-axis represents the timing of one cardiac cycle (R-R interval) normalized in degrees. The Y-axis represents the percent of myocardium demonstrating the onset of mechanical contraction during any particular phase of the cardiac cycle. The color maps have 256 levels with the minimum level corresponding to black and the maximum level corresponding to white. B) Abnormal phase histogram showing a wide bandwidth indicating a delayed onset of myocardial contraction representing significant left ventricular mechanical dyssynchrony.

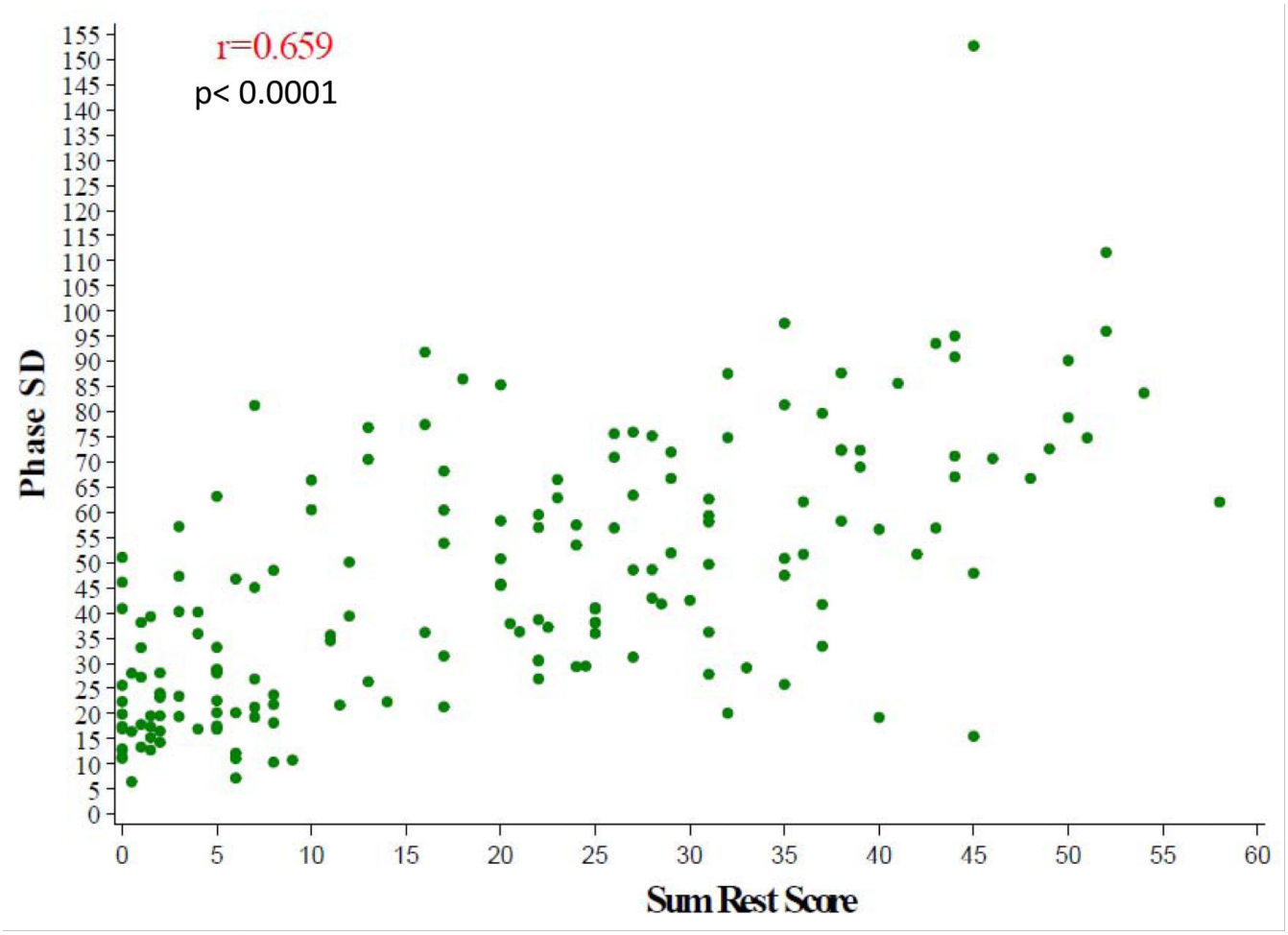


Figure 3.
SPECT Dyssynchrony Phase SD versus Sum Rest Score

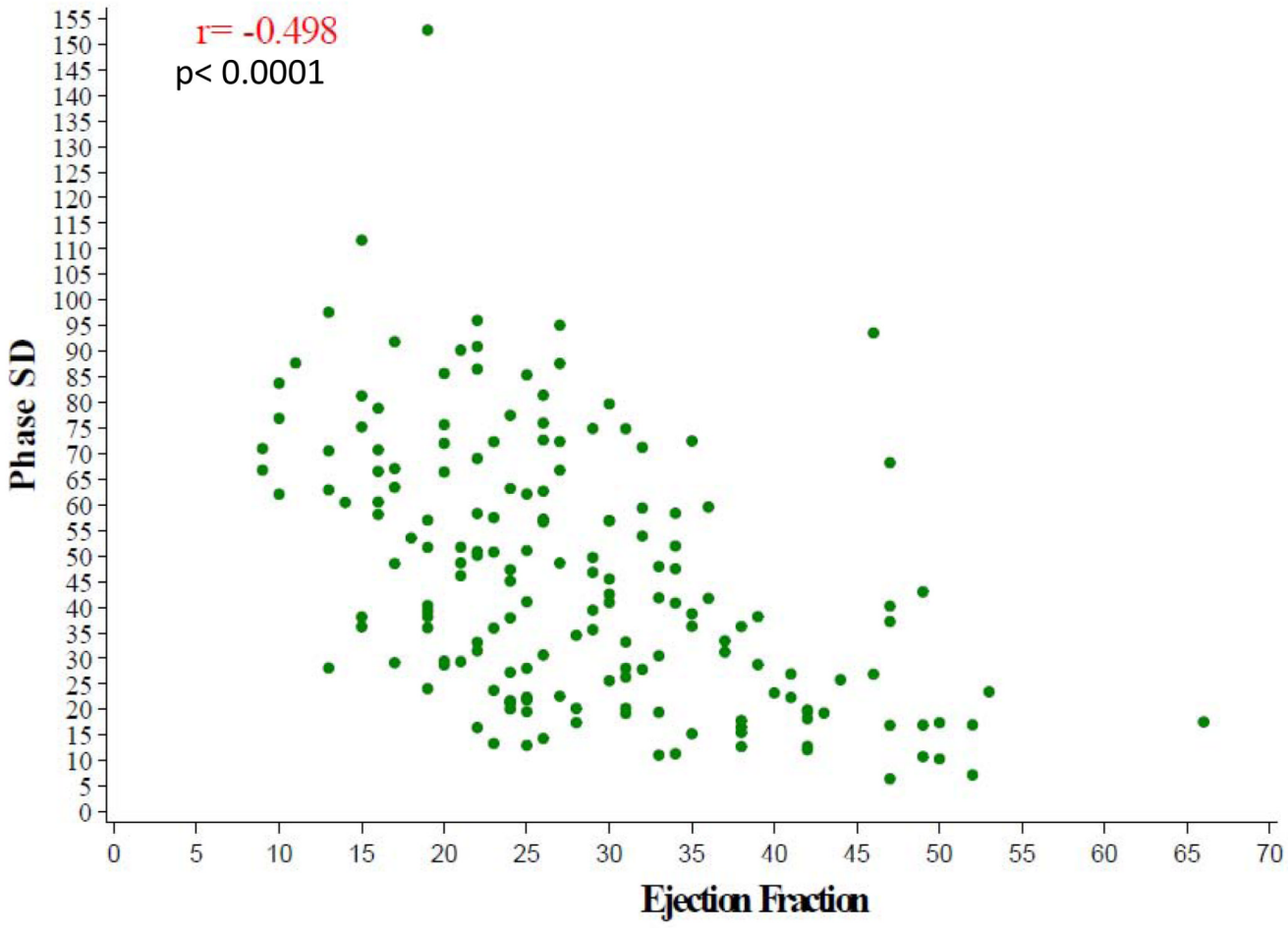


Figure 4.
SPECT Dyssynchrony Phase SD versus EF by SPECT

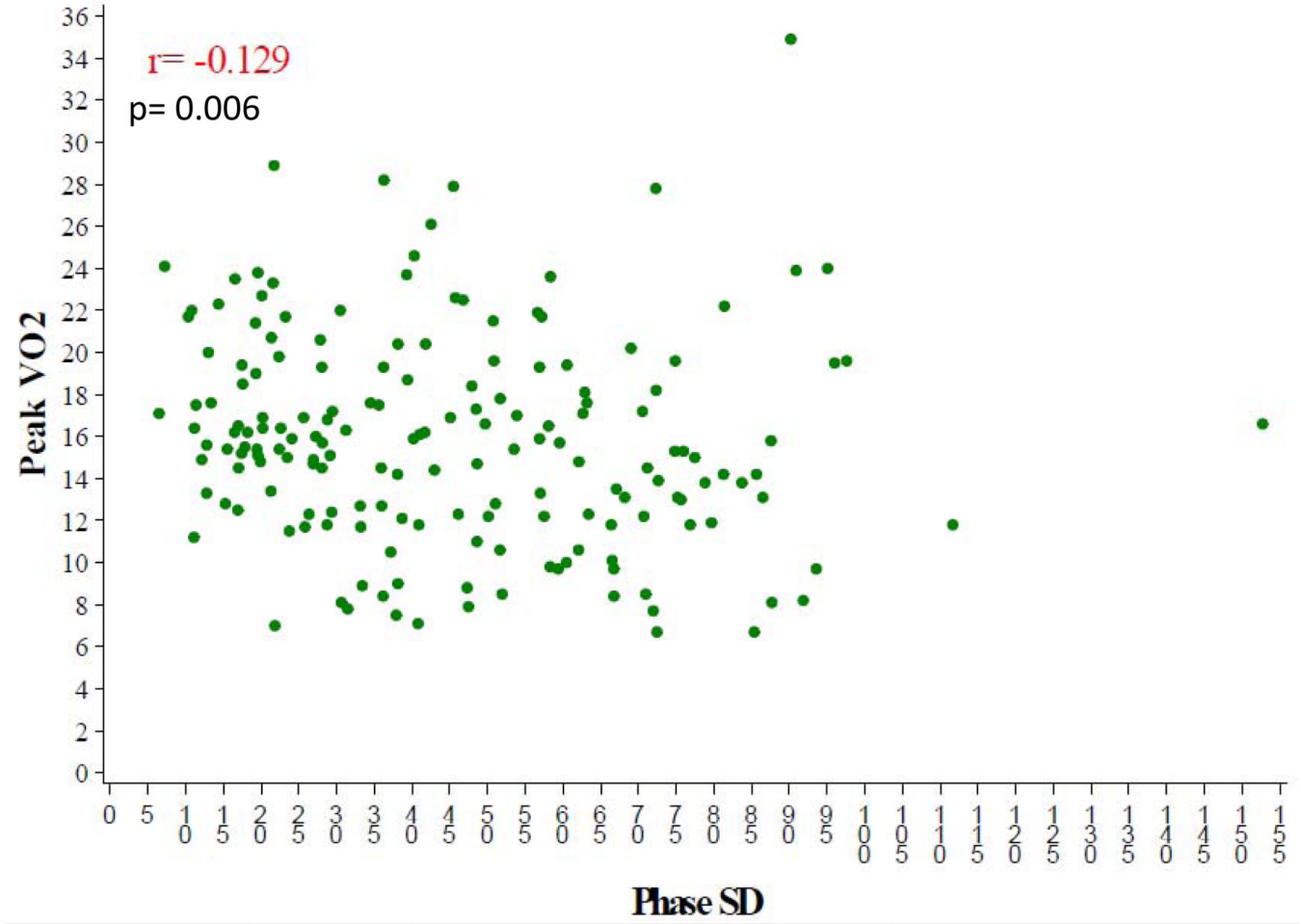


Figure 5.
Peak VO_2 versus SPECT Dyssynchrony Phase SD

A. B.

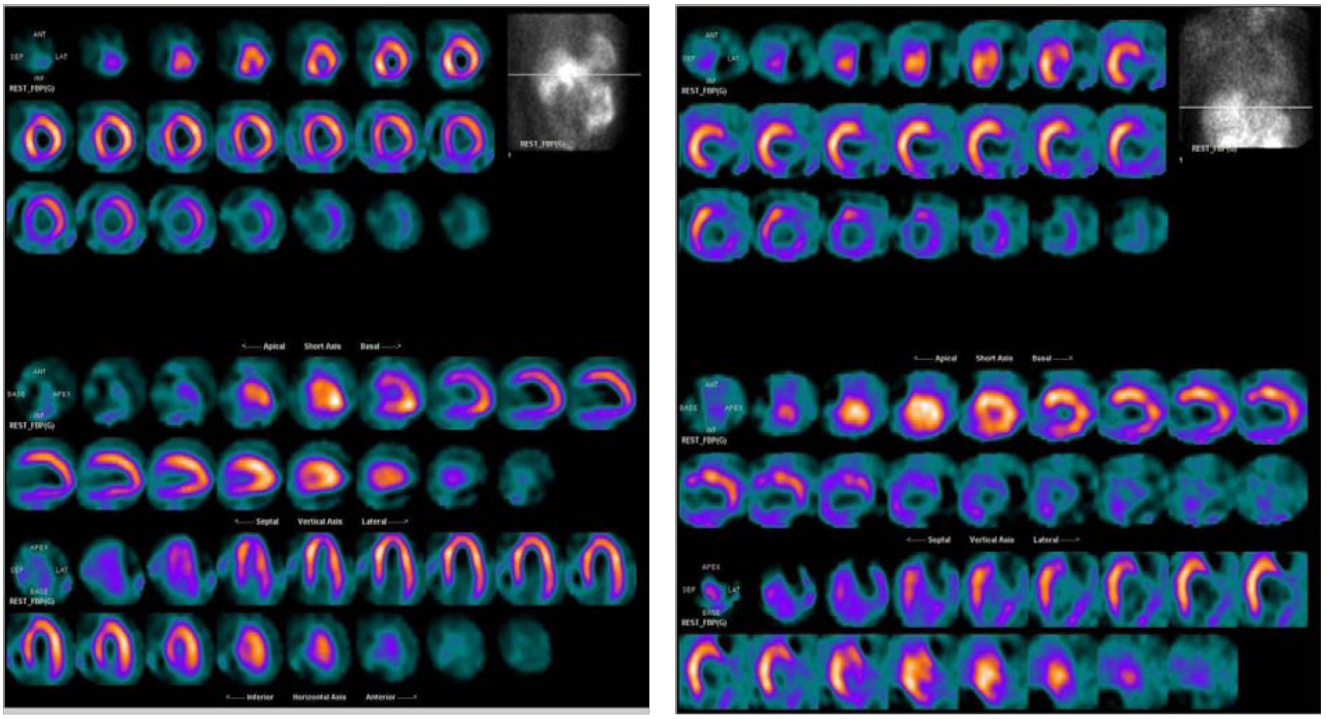


Figure 6.
Perfusion tomographs from the HF-ACTION nuclear substudy demonstrating A) a patient with nonischemic cardiomyopathy and a LVEF of 30%. Note that there is only mild decreased tracer activity in the basal inferior segment secondary to attenuation artifact and B) a patient with an ischemic cardiomyopathy and a LVEF of 28%. Note the severe perfusion defects and infarct in the anterolateral, inferolateral, inferior, and inferoapical segments.

Table 1

Demographics and Medical History by Stratum

Medical history	Ischemic (N=129)	Non-ischemic (N=111)	Total (N=240)
Age			
Median (25th, 75th)	63 (55, 70)	56 (47, 64)	59 (51, 68)
Mean (S.D.)	63 (11)	55 (13)	59 (12)
Sex			
Female	22 (17%)	52 (47%)	74 (31%)
Male	107 (83%)	59 (53%)	166 (69%)
Race			
Black or African American	27 (21%)	51 (46%)	78 (33%)
White	93 (72%)	57 (51%)	150 (63%)
Other	9 (7%)	3 (3%)	12 (5%)
BMI			
Median (25th, 75th)	29 (26, 33)	31 (27, 39)	30 (26, 35)
Mean (S.D.)	30 (6)	33 (8)	31 (7)
CAD	107 (83%)	0	107 (45%)
Atrial fibrillation/flutter	23 (18%)	15 (14%)	38 (16%)
Hypertension	84 (66%)	70 (63%)	154 (65%)
Hyperlipidemia	107 (83%)	53 (48%)	160 (67%)
Smoking status			
Never	38 (30%)	47 (42%)	85 (36%)
Current	24 (19%)	20 (18%)	44 (18%)
Past	66 (52%)	44 (40%)	110 (46%)
Stroke	16 (12%)	11 (10%)	27 (11%)
Diabetes	55 (43%)	23 (21%)	78 (33%)
COPD	27 (21%)	12 (11%)	39 (17%)
PVD	12 (9%)	3 (3%)	15 (6%)
Anemia	23 (21%)	14 (17%)	37 (20%)
Mild	19 (18%)	12 (15%)	31 (16%)
Moderate to severe	4 (4%)	2 (2%)	6 (3%)
CABG	61 (47%)	0	61 (25%)
PCI	63 (49%)	0	63 (26%)
CABG or PCI	98 (76%)	0	98 (41%)
Pacemaker	24 (19%)	17 (15%)	41 (17%)
AICD	83 (64%)	45 (41%)	128 (53%)
Bi-ventricular pacemaker	23 (18%)	21 (19%)	44 (18%)
AICD or Bi-ventricular pacemaker	87 (67%)	49 (44%)	136 (57%)
AICD and Bi-ventricular pacemaker	19 (15%)	17 (15%)	36 (15%)

BMI= body mass index, CAD= history of myocardial infarction, mild anemia: Hgb not less than 10 g/dL but less than 12 g/dL, moderate-severe anemia: Hgb < 10 g/dL, COPD= chronic obstructive pulmonary disease, PVD= peripheral vascular disease, CABG= coronary artery bypass grafting, PCI= percutaneous coronary intervention, AICD= automated internal cardioverter-defibrillator

Table 2

Medications by Stratum

Medications	Ischemic (N=129)	Non-ischemic (N=111)	Total (N=240)
ACE-I	86 (67%)	82 (74%)	168 (70%)
contraindicated/intolerance	24 (19%)	20 (18%)	44 (18%)
ARB	36 (28%)	27 (24%)	63 (26%)
ACE-I or ARB	119 (92%)	106 (95%)	225 (94%)
ACE-I + ARB	3 (2%)	3 (3%)	6 (3%)
Beta blocker	123 (95%)	107 (96%)	230 (96%)
contraindicated/intolerance	4 (3%)	3 (3%)	7 (3%)
Digoxin	46 (36%)	50 (45%)	96 (40%)
Spironolactone	59 (46%)	49 (44%)	108 (45%)
Eplerenone	4 (3%)	2 (2%)	6 (3%)
Aspirin	106 (82%)	69 (63%)	175 (73%)
Loop diuretic	92 (71%)	80 (72%)	172 (72%)
Non-loop diuretic	9 (7%)	8 (7%)	17 (7%)
Antiarrhythmic			
Amiodarone	18 (14%)	12 (11%)	30 (13%)
Other antiarrhythmic	1 (1%)	2 (2%)	3 (1%)
Lipid-lowering agent	108 (84%)	49 (44%)	157 (65%)
HMG-CoA reductase inhibitor	86 (67%)	39 (35%)	125 (52%)
Other lipid-lowering agent	11 (9%)	10 (9%)	21 (9%)
Clopidogrel	35 (27 %)	1 (1%)	36 (15%)
Coumadin	39 (30%)	28 (25%)	67 (28%)
Nitrate	38 (29%)	15 (14%)	53 (22%)
Calcium channel blocker	3 (2%)	4 (4%)	7 (3%)
Insulin	23 (18%)	7 (6%)	30 (13%)
Glitazone	5 (4%)	2 (2%)	7 (3%)
SSRI	20 (16%)	20 (18%)	40 (17%)

ACE-I= angiotensin converting enzyme- inhibitor, ARB= angiotensin II receptor blocker, SSRI= selective serotonin reuptake inhibitor

Table 3

Nuclear Characteristics by Stratum

	Ischemic	Non-ischemic	Total	p-value
Sum Rest Score, Composite				
n, Median (25th, 75th)	128, 29 (18, 39)	110, 6 (2, 17)	238, 20 (5, 31)	<0.0001
Mean (S.D.)	28 (14)	10 (11)	20 (15)	
Ejection Fraction				
n, Median (25th, 75th)	127, 26 (21, 33)	107, 26 (20, 38)	234, 26 (21, 34)	0.56
Mean (S.D.)	28 (10)	29 (12)	28 (11)	
ESV (ml)				
n, Median (25th, 75th)	127, 167 (121, 244)	107, 162 (102, 225)	234, 165 (117, 238)	0.27
Mean (S.D.)	187 (88)	178 (101)	183 (94)	
EDV (ml)				
n, Median (25th, 75th)	127, 229 (178, 305)	107, 224 (152, 287)	234, 226 (168, 297)	0.16
Mean (S.D.)	249 (93)	236 (106)	243 (99)	
Dyssynchrony Phase SD				
n, Median (25th, 75th)	91, 57 (36, 72)	83, 29 (19, 47)	174, 41 (23, 63)	<0.0001
Mean (S.D.)	55 (25)	35 (21)	46 (25)	
Dyssynchrony Bandwidth				
n, Median (25th, 75th)	91, 160 (102, 228)	83, 82 (60, 137)	174, 111 (71, 207)	<0.0001
Mean (S.D.)	164 (81)	107 (67)	137 (80)	

ESV= end systolic volume, EDV= end diastolic volume

Table 4

Comparison of SPECT Dyssynchrony Indices by NYHA Functional Class

	NYHA Class II	Class III	P-value
Phase SD			
n, Median (25^{th}, 75^{th})	116, 39 (20, 57)	58, 54 (31, 75)	0.0012
Mean (S.D.)	41 (23)	55 (28)	
Bandwidth			
n, Median (25^{th}, 75^{th})	116, 104 (62, 187)	58, 139 (84, 217)	0.0246
Mean (S.D.)	128 (78)	155 (81)	

Table 5

Exercise Variables by Stratum

Exercise test variables	Ischemic	Non-ischemic	Total	p value
Peak VO_2 (ml/kg/min)				
Median (25th, 75th)	14.8 (12.1, 18.2)	15.6 (12.7, 19.2)	15.3 (12.3, 18.5)	0.35
Mean (S.D.)	15.5 (4.9)	15.8 (4.5)	15.6 (4.7)	
Exercise duration (minutes)				
Median (25th, 75th)	9.2 (7.4, 12.6)	10.2 (7.5, 12.4)	10.0 (7.4, 12.5)	0.57
Mean (S.D.)	10.1 (4.4)	10.1 (3.6)	10.1 (4.0)	
Six-minute walk test				
Able to walk	127 (98%)	108 (97%)	235 (98%)	0.69
Distance walked, meters (25^{th}, 75^{th})	378 (305, 454)	390 (301, 454)	381 (305, 454)	
HR at peak exercise (bpm)				
Median (25th, 75th)	117 (102, 132)	127 (110, 141)	120 (105, 137)	0.003
Mean (S.D.)	118 (21)	126 (22)	122 (22)	
Heart rate reserve (bpm)				
Median (25th, 75th)	47 (35, 64)	54 (39, 70)	48 (36, 67)	0.05
Mean (S.D.)	49 (20)	54 (21)	51 (21)	