Relation Between Heart Rate and Left Ventricular Mechanical Dyssynchrony in Patients With End-Stage Renal Disease

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The effect of heart rate (HR) on left ventricular (LV) mechanical dyssynchrony has not been studied by phase analysis of myocardial perfusion imaging and has yielded conflicting results by echocardiography. We measured indexes of LV dyssynchrony by automated analysis of gated single-photon emission computed tomography in 140 patients with end-stage renal disease (ESRD) and 133 subjects with normal renal function (control group). Patients with abnormal perfusion pattern or QRS duration >120 ms were excluded. HR at time of acquisition of gated images was recorded. LV ejection fraction (EF), volumes, mass, and 2 indexes of dyssynchrony, phase SD and bandwidth, were derived. Almost 50% of patients in each group had an abnormal LVEF (<50%). HR at rest ranged from 48 to 113 beats/min (75 ± 13). Patients with abnormal LVEF had a higher phase SD (30 ± 13° vs 22 ± 11° and 28 ± 16° vs 15 ± 6° for the ESRD and control groups, respectively, p <0.001 each) and higher histographic bandwidth (88 ± 44° vs 62 ± 33° and 80 ± 49° vs 43 ± 14° for the ESRD and control groups, p <0.001 each). Patients with ESRD and normal LVEF had higher SD and bandwidth than the control group (22 ± 11° vs 15 ± 6° and 62 ± 33° vs 43 ± 14°, respectively, p <0.001 each). The control and ESRD groups were divided into tertiles based on HR. The phase SD and bandwidth were similar in the first (slowest HR) and third (highest HR) tertiles in every group (p = NS). There were no significant correlations between phase SD or bandwidth and HR in either group. In conclusion, within the HR range examined in this cross-sectional study, there was no relation between HR at rest and LV dyssynchrony. **(Am J Cardiol 2011;107:1235–1240)**

The impact of heart rate (HR) on dyssynchrony is not known because almost all studies, regardless of imaging method, are performed at rest. It is conceivable that the degree of dyssynchrony at faster HR might be different from dyssynchrony at lower HR because of changes in left ventricular (LV) volumes and ischemia. This cross-sectional study was designed to examine the relation between dyssynchrony and HR.

Methods

The study population consisted of patients referred for stress myocardial perfusion imaging (MPI) for clinical indications from August 2008 through May 2009. Inclusion criteria were (1) age >18 years, (2) normal QRS duration on 12-lead surface electrocardiogram at time of study, (3) normal MPI finding at rest or during stress (exercise or pharmacologic), and (4) end-stage renal disease (ESRD) on dialysis. Pregnant women, patients with hypertrophic cardiomyopathy or other congenital heart disease, left or right bundle branch blocking, ventricular pacing, atrial fibrillation, and any perfusion abnormality (fixed or reversible) were excluded. We also identified consecutive patients with a glomerular filtration rate >60 ml/min/m^2 within the same time frame and who otherwise met the same inclusion criteria and served as a control group. Demographics and other pertinent data were extracted through chart reviews.

Gated single-photon emission computed tomography MPI was obtained at stress (exercise or pharmacologic) and rest with technetium-99m sestamibi according to American Society of Nuclear Cardiology guidelines[1] as previously described.[2–4] LV ejection fraction (EF), volumes, and mass were measured from gated studies at rest (because it was performed using a higher tracer dose of 30 to 45 vs 10 to 15 mCi for the stress study) based on a method described by Germano et al.[5] HR was recorded at the time of gated single-photon emission computed tomographic acquisition at rest. Most studies were with 8 frames/cycle.

Phase SD and histographic bandwidth were measured as previously described and briefly summarized in this report.[3,4,6] Three-dimensional count distributions were extracted from each LV short-axis dataset and subjected to Fourier phase analysis, thus generating a 3-dimensional phase distribution (0° to 360°) spanning the entire RR interval. The latter was displaced on a polar map and on a histogram. Two dyssynchrony indexes were derived: (1) phase SD, which represents the SD of the phase distribution, and (2) histographic bandwidth, which represents duration of the cardiac cycle during which 95% of the myocardium initiated contraction. These parameters are related to onset of mechanical contraction or systole and thus reflect systolic dyssynchrony.

A descriptive analysis was performed examining pertinent variables in the 4 cohorts of patients (ESRD and control with normal [≥50%] and abnormal [<50%] EFs). Furthermore,

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Table 1
Baseline characteristics

Variable	ESRD, EF ≥50% (n = 69)	ESRD, EF <50% (n = 71)	Control, EF ≥50% (n = 68)	Control, EF <50% (n = 65)
Demographics				
Age (years)	50 ± 11[§]	50 ± 12[§]	58 ± 12[§]	57 ± 13[§]
Women	30 (43%)	22 (31%)	39 (57%)[†]	14 (22%)[†]
African-American	41 (59%)[§]	50 (70%)	16 (24%)[†§]	35 (54%)[†]
Co-morbidities				
Diabetes mellitus	31 (45%)[‡]	36 (51%)[‡]	19 (28%)[‡]	22 (34%)[‡]
Hypertension	63 (91%)	66 (93%)	55 (81%)	53 (82%)
Cerebrovascular accident	12 (17%)	7 (10%)	7 (10%)*[‡]	17 (26%)*[‡]
Previous myocardial infarction	0 (0%)	1 (1%)	0 (0%)	4 (6%)
Coronary artery disease	2 (3%)	5 (7%)[§]	0 (0%)[†]	20 (31%)[†§]
Smoker	33 (48%)	34 (48%)[‡]	26 (38%)[†]	47 (72%)[†‡]
Medications				
Aspirin	12 (17%)	18 (25%)[‡]	16 (24%)*	28 (43%)*[‡]
β Blockers	35 (51%)*[‡]	51 (72%)*	25 (37%)*[‡]	41 (63%)*
Angiotensin-converting enzyme inhibitor/receptor blocker	21 (30%)[‡]	33 (46%)	35 (51%)[‡]	39 (60%)
Calcium channel blocker	36 (52%)	30 (42%)[‡]	31 (46%)*	15 (23%)*[‡]
Statins	20 (29%)	23 (32%)	24 (35%)	26 (40%)

Values are expressed as mean ± SD (tertile range) or number of patients (percentage).
* $p < 0.05$; [†] $p < 0.001$ in-group comparison (end-stage renal disease and ejection fraction ≥50% vs <50% and control and ejection fraction ≥50% vs <50%).
[‡] $p < 0.05$; [§] $p < 0.001$ between control and end-stage renal disease (ejection fractions <50% and ≥50%).

each group was divided into tertiles based on HR, and mean values in the first (slowest HR) and third (highest HR) tertiles were compared. Correlations between dyssynchrony indexes and HR were also performed. Student's *t* test was used for continuous variables and Pearson chi-square test for categorical variables. Data are presented as mean ± SD for continuous variables and as percentage for categorical variables. Spearman correlation coefficient was used to evaluate bivariate relations. All p values were 2-tailed with a p value <0.05 set a priori and used as the level of statistical significance. All statistical analyses were performed using SPSS 11.5 for Windows (SPSS, Inc., Chicago, Illinois).

This study was approved by the institutional review board at the University of Alabama at Birmingham.

Results

Baseline characteristics are presented in Table 1. There were 140 patients in the ESRD group and 133 patients in the control group. Patients with ESRD were younger, more likely to be African-Americans, and to have diabetes mellitus. Most patients had hypertension and 2% had previous myocardial infarction, although the perfusion pattern was normal. Mean LVEFs were 62 ± 8% versus 69 ± 9% in the ESRD and control groups with normal EF ($p < 0.001$) and 41 ± 8% versus 43 ± 7% in patients with abnormal EF, respectively (p = NS). LV volumes, mass, and dyssynchrony indexes are presented in Table 2. HR at rest was 75 ± 13 beats/min (range 48 to 113) for all patients. Patients with abnormal LVEF had higher phase SD (30 ± 13° vs 22 ± 11° and 28 ± 16° vs 15 ± 6° for the ESRD and control groups, respectively, $p < 0.001$ each) and greater histographic bandwidth (88 ± 44° vs 62 ± 33° and 80 ± 49° vs 43 ± 14° for ESRD and control groups, $p < 0.001$ each). Patients with ESRD and normal LVEF had higher SD and bandwidth than control patients with normal EF (22 ± 11° vs 15 ± 6° and 62 ± 33° vs 43 ± 14°, respectively, $p < 0.001$ for the 2 comparisons).

Each group was divided based on tertiles of HR, and mean values for LV volumes, mass, EF, and QRS duration for the first and third tertiles are presented in Table 2. LVEF was lower in the ESRD subgroup with EF ≥50% (59 ± 10% vs 69 ± 6% for third vs first tertile, respectively, $p < 0.001$); otherwise, no statistically significant differences were noted in the other subgroups. QRS duration was similar in each group (p = NS). Dyssynchrony indexes were not significantly different in the first and third tertiles (Figure 1). Furthermore, there was no correlation between SD and HR ($r = -0.014$ and 0.14 for ESRD group with normal and abnormal EFs, respectively; $r = 0.15$ and 0.057 for control group with normal and abnormal EFs, respectively, p = NS each) or between bandwidth and HR ($r = -0.014$ and 0.05 for ESRD group with normal and abnormal EFs, respectively; $r = 0.16$ and 0.036 for control group with normal and abnormal EFs, respectively, p = NS each; Figure 2).

Discussion

This is the first study that examined the relation between HR and mechanical LV dyssynchrony by phase analysis. In this cross-sectional analysis there was no relation between HR at rest and phase-derived mechanical systolic dyssynchrony indexes, even in patients with decreased LVEF and significant dyssynchrony.