An alternative method to examine the predictive value of mechanical dyssynchrony

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Myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) has traditionally been used to assess the presence or absence of epicardial coronary artery disease.[1,2] The prognostic significance of perfusion defects measured by SPECT MPI is well-validated.[3,4] With the advent of software developments, electrocardiographically gated SPECT MPI (GSPECT MPI) can also measure left ventricular (LV) mechanical dyssynchrony.[5] The degree of heterogeneity in the onset of mechanical contraction (phase standard deviation (SD)) and the range of time during which 95% of the LV is initiating contraction (phase bandwidth (BW)) are key measures of dyssynchrony. The prognostic value of these measures of mechanical dyssynchrony is not adequately studied. A central question is whether there is a threshold below which adverse events are unlikely to occur.[6]

For the current analysis, data sources were the Duke Nuclear Cardiology Databank and the Duke Databank for Cardiovascular (CV) Disease. The latter enrolls patients with angiographically significant coronary heart disease. Patients presenting for GSPECT MPI between June of 1993 and May of 1999 with concurrent electrocardiographic results and assessment of LV function were included in this study. Dyssynchrony data were obtained by post-processing using commercially available software (Emory Toolbox, Emory University, Atlanta, GA). Baseline clinical characteristics were examined using medians (25th and 75th percentiles) for continuous variables and percentages for categorical and ordinal variables. Time to CV and all-cause deaths stratified by QRS duration and phase BW were examined using the Kaplan-Meier methods. Associations between phase BW and CV and all-cause deaths were examined using Cox-proportional hazards modeling. The linear relationship between BW and outcomes was examined using cubic spline testing, and transformations were implemented if necessary to satisfy this assumption. For adjustment, standard clinical covariates were used.

In a sensitivity analysis, the same models were assessed using phase SD in lieu of phase BW. Tests were two-sided, and significance was present if $p < 0.05$. Analyses were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC). The Duke University Health System institutional review board approved the study and granted a waiver of consent.

Baseline patient characteristics are shown in Table 1. The median age of the study population was 64 (interquartile range 55-72) years. Patients were predominantly men and whites. A majority had

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Table 1. Baseline characteristics

Characteristics	Study population (n = 1244)
Age, years	64 (55–72)
Male	68.7
Race	
White	72.8
Black	23.3
Native American	2.3
Other	1.6
Body mass index, kg/m^2	28.7 (25.2–33.0)
Medical history	
Hypertension	77.1
History of congestive heart failure	24.7
New York Heart Association Class	
None	83.1
I	1.3
II	6.3
III	6.5
IV	2.8
Cerebrovascular disease	12.5
Chronic obstructive pulmonary disease	6.4
Diabetes	37.0
Hyperlipidemia	69.5
Myocardial infarction	32.3
Peripheral vascular disease	10.8
Renal disease	4.8
Smoking	48.6
Laboratory data	
Left ventricular ejection fraction	62 (51–70)
QRS duration, ms	93 (85–105)
Left bundle branch block	2.7
Nuclear dyssynchrony, °	
Phase bandwidth	60 (42–104)
Phase standard deviation	25 (15–41)

Values are presented as % or median (IQR)

hypertension and diabetes; a minority had heart failure or peripheral vascular disease.

Figure 1 shows unadjusted, predicted 4-year rates of all-cause death and CV death according to phase SD and phase BW. Irrespective of dyssynchrony measure or cause of death, there was no clear threshold below which events were unlikely to occur.

Table 2 shows dyssynchrony measures stratified according to the predicted event rate in both unadjusted and adjusted analyses. The values of dyssynchrony varied according to the event rate assessed.

Several prior studies of dyssynchrony measured by GSPECT MPI have used discrete threshold values of normality.[5,7-10] By contrast, the current analysis, which, to our knowledge, has the largest sample size as well as the longest follow-up period to date, suggests that such a threshold does not exist among patients with coronary artery disease. Rather, the likelihood of events is related in a continuous fashion to the degree of dyssynchrony. Consequently, for statistical modeling purposes, we support the use of continuously valued dyssynchrony if available. We nonetheless acknowledge the importance of cut-off values in clinical medicine. If predictive tools using mechanical dyssynchrony are developed and implemented, discrete cut-off values may be selected based on the expected event rate and time horizon. Future studies should assess whether there are significant thresholds in other patient populations.

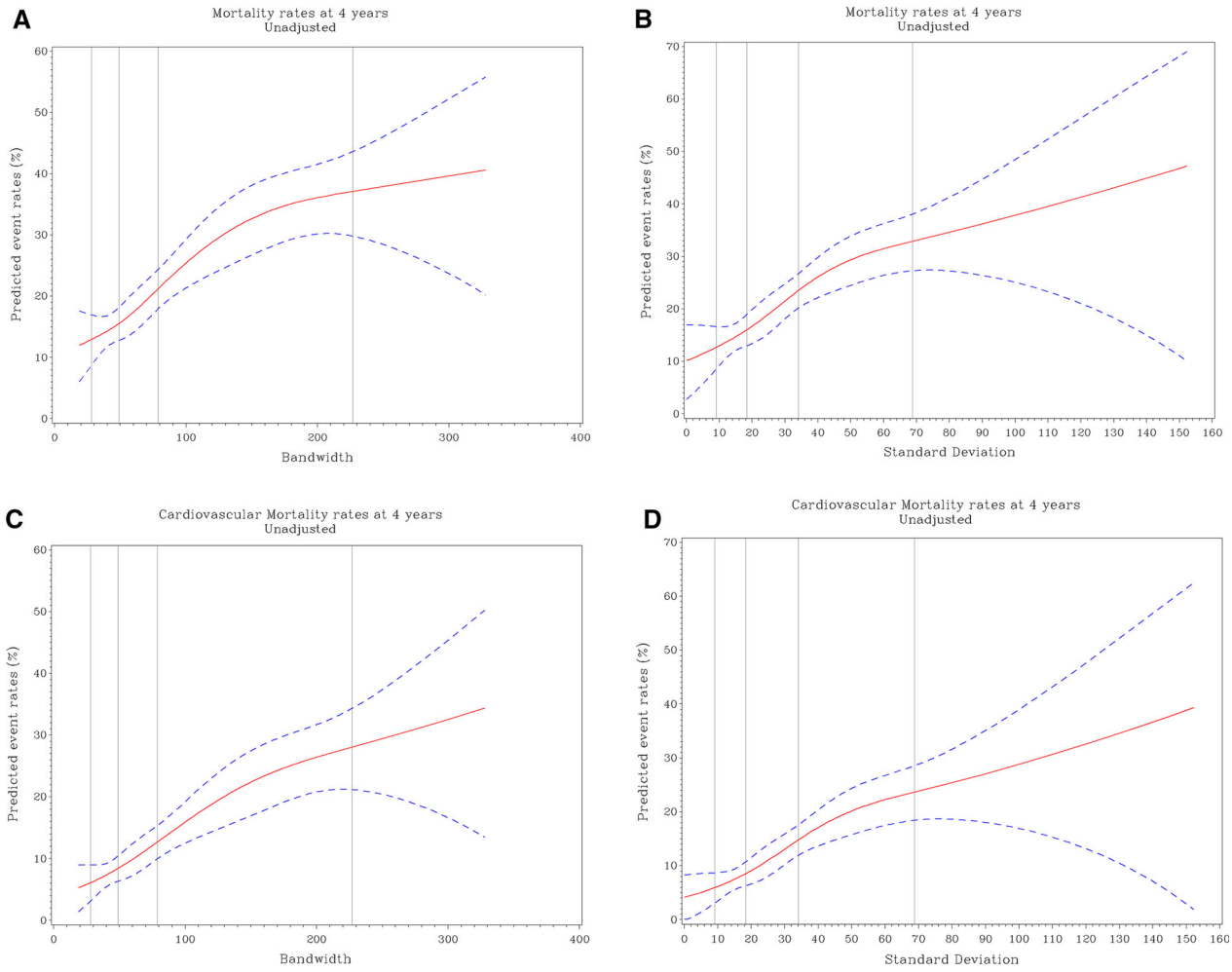

Figure 1. (**A**)-(**D**) outcome probability at 4 years across dyssynchrony measures. (**A**) Mortality and bandwidth, (**B**) mortality and standard deviation, (**C**) cardiovascular mortality and bandwidth, (**D**) cardiovascular mortality and standard deviation.

Table 2. Four-year event rates, unadjusted and adjusted across dyssynchrony measures

Event	4 Years probability (unadj)	Standard deviation*	Bandwidth*
Mortality	15%	16	46
	20%	27	73
	25%	37	97
CV Mortality	15%	35	94
	20%	49	129
	25%	77	179

*Adjusted for age, sex, race, body mass index, hypertension, congestive heart failure, New York Heart Association class, cerebrovascular disease, chronic obstructive pulmonary disease, diabetes, hyperlipidemia, prior myocardial infarction, peripheral vascular disease, renal disease, smoking, ejection fraction, QRS duration, and left bundle branch block

Disclosures

Authors have no relevant conflicts of interest.

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