Left ventricular mechanical dyssynchrony in patients with coronary artery disease

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Received Jan 14, 2016; accepted Jan 14, 2016
doi:10.1007/s12350-016-0416-4

See related article, pp. 482–490

The use of phase analysis from gated SPECT myocardial perfusion imaging (MPI) for the evaluation of left ventricular mechanical dyssynchrony (LVMD) was introduced by Chen and Garcia¹ in 2005. In patients with coronary artery disease (CAD), the need to assess resynchronization arises in the presence of systolic heart failure when another solution for left ventricular treatment in addition to heart failure medications is needed. Although device-based solutions, such as cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillator (ICD) therapy, has been found to improve symptoms of heart failure and reduce overall mortality, the lack of a beneficial response was reported in a substantial number of patients.² Current indications for CRT are NYHA class 3–4, LVEF $\leq 35\%$, left bundle branch block or QRS width > 120 ms. However, LVMD is not included, although it has been recognized for more than 10 years. A considerable number of studies have shown that high values of phase standard deviation (SD) and/or phase histogram bandwidth (BW) indicate LVMD, and that they can assist clinicians in the selection of patients for CRT. Furthermore, LVMD may serve as a predictive factor of both cardiac outcome and all-cause mortality.^{3–6}

LVMD has been studied in various clinical subsets, including patients with systolic LV dysfunction, such as ischemic and nonischemic cardiomyopathy,^{7–9} and patients with end-stage renal failure and on chemotherapy, in whom LVMD was found to be a useful

prognosticator.^{10–12} Others investigated the yield of LVMD as part of gated SPECT in consecutive unselected patients with suspected CAD or known CAD who were referred for evaluation of ischemia. The findings showed that LVMD has value as an independent predictor of cardiac outcome, in addition to LV ejection fraction (LVEF) and perfusion defects.^{13,14}

The article by Hess et al¹⁵ in this issue of the *Journal of Nuclear Cardiology* reports the study of LVMD in a large group of patients ($n = 1244$) with CAD who underwent gated SPECT MPI in 1993–1999. Phase analysis assessment was done retrospectively in the patients in whom at least one major epicardial CAD was documented. The cohort was followed for all-cause death and cardiac death. At 8 years, LVMD showed a stronger relationship with outcome than electrical dyssynchrony measured by QRS duration. After adjustment for baseline characteristics and continuous measured LVEF, neither mechanical nor electrical dyssynchrony was independently associated with all-cause death or cardiac death. However, among patients with LVEF $> 35\%$, mechanical and electrical dyssynchrony together had a prognostic value above that afforded by LVEF alone ($P = .0181$).

This study has 2 merits. First, it studied the value of LVMD in a large group of patients with CAD and showed that a high histogram BW is more strongly associated with mortality than QRS. Hess et al¹⁵ graphically demonstrated the distribution of phase BWs in the CAD population and analyzed the presence of LV dyssynchrony by BW values of more or less than 100° . They found an incremental association between clinical variables, QRS duration, LBBB, and all-cause or cardiovascular death as indicated by global Chi-square in serial multivariable models ($P > .0001$).

The second merit of the study is the finding that histogram BW may serve as an independent predictor of mortality in patients with CAD and LVEF $> 35\%$. Furthermore, on multivariate analysis, after adjusting for clinical characteristics, sequential models indicated that

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J Nucl Cardiol 2017;24:491–3.

1071-3581/\$34.00

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Table 1. Prognostic studies of LV dyssynchrony by phase SD and histogram BW in different populations with different LVEF values

Study	Population No./indication*	LVEF (%)	SD (°)	BW (°)	Prediction
Aljaroudi et al ⁹	72/ICD	<40	60	185	Death or shock
Uebleis et al ⁸	135/CAD	38	24	63	Death
Goldberg et al ⁷	324/NICMO	35-50	23		Death
Pazhenkottal et al ¹³	202/unselected†	58	24	62	MACE
Zafirir et al ¹⁴	787/unselected†	62-44	40		MACE
Aggarwal et al ¹¹	828/ESRD	55	≥21	>56	Death
Zafirir et al ⁶	143/ICD/CRTD	≤35	60		MACE
Hess et al ¹⁵	1244/CAD	62	52	>100	Death

LV, Left ventricular; SD, standard deviation; BM, bandwidth; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; NICMO, nonischemic cardiomyopathy; ICD, implantable cardioverter-defibrillator; CRTD, cardiac resynchronization therapy device; MACE, major cardiac event.

* Indication for SPECT MPI.

† Unselected patients referred for MPI.

BW was more strongly associated with all-cause death than phase SD (192.8 vs 188.1, global Chi square).

This study has some limitations. (1) The correlation of severity of CAD and LVMD was not demonstrated. It seems from the numerical data that patients with 3 vessel disease had more LVMD of BW ≥ 100 than patients with BW < 100 (43.9% vs 34.6%) compared to patients with 1 or 2 vessel disease ((65.4% vs 67.8%) who had similar LVMD. It is also suggested that most of this population underwent intervention (percutaneous coronary intervention, coronary artery bypass graft) which could influence outcome, but these data were not provided. (2) No data regarding ischemia are presented, as expected from a SPECT MPI study, and as such, they were not included in the univariate analysis. (3) On analysis of the adjusted outcome, the authors included among the clinical variables also history of congestive heart failure but not NYHA classification, which is known to be the most powerful predictor of mortality. Additionally, as concluded in the study, patients with CAD found to have a BW above 100° might have a worse prognosis regardless, owing to other variables such as burden of ischemia and infarct size.

Although both phase SD and BW contribute to the prediction of adverse outcome, the optimal LVMD values correlating with prognosis or therapy are inconsistent, varying in the different studies from 24° to 60° for SD and from 60° to 185° for BW, irrespective of the presence of CAD (Table 1). The reasons are related to selection of the patient population and to different values of LV function (LVEF). As such, it seems that for predictive purposes, different cutoff values for LVMD need to be defined according to normal or abnormal range of LV function.

To summarize, every patient referred for gated SPECT, whether for diagnosis of CAD or with known CAD, may benefit from the comprehensive assessment of perfusion, function, and dyssynchrony in one study. Combination of the LVMD values with a correlation to CAD, as shown by Hess et al,¹⁵ may provide better information regarding prognosis and better assist clinicians in therapeutic decision-making between device-based therapy, in cases of LV dysfunction, or improved medical treatment.

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