# ORIGINAL ARTICLE

# Assessment of left ventricular mechanical dyssynchrony by phase analysis of gated-SPECT myocardial perfusion imaging and tissue Doppler imaging: Comparison between QGS and ECTb software packages

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*Background.* Recently, the phase analysis of gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has become feasible via several software packages for the evaluation of left ventricular mechanical dyssynchrony. We compared two quantitative software packages, quantitative gated SPECT (QGS) and Emory cardiac toolbox (ECTb), with tissue Doppler imaging (TDI) as the conventional method for the evaluation of left ventricular mechanical dyssynchrony.

*Methods and Results.* Thirty-one patients with severe heart failure (ejection fraction  $\leq 35\%$ ) and regular heart rhythm, who referred for gated-SPECT MPI, were enrolled. TDI was performed within 3 days after MPI. Dyssynchrony parameters derived from gated-SPECT MPI were analyzed by QGS and ECTb and were compared with the Yu index and septal-lateral wall delay measured by TDI. QGS and ECTb showed a good correlation for assessment of phase histogram bandwidth (PHB) and phase standard deviation (PSD) (r = 0.664 and r = 0.731, P < .001, respectively). However, the mean value of PHB and PSD by ECTb was significantly higher than that of QGS. No significant correlation was found between ECTb and QGS and the Yu index. Nevertheless, PHB, PSD, and entropy derived from QGS revealed a significant (r = 0.424, r = 0.478, r = 0.543, respectively; P < .02) correlation with septal-lateral wall delay.

*Conclusion.* Despite a good correlation between QGS and ECTb software packages, different normal cut-off values of PSD and PHB should be defined for each software package. There was only a modest correlation between phase analysis of gated-SPECT MPI and TDI data, especially in

Reprint requests: Tahereh Ghaedian, MD, Department of Nuclear Medicine and Molecular Imaging, Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Vali-e-Asr Ave., Niayesh Blvd., Tehran, Iran; *tghaedian@gmail.com*  1071-3581/\$34.00 Copyright © 2014 American Society of Nuclear Cardiology. the population of heart failure patients with both narrow and wide QRS complex. (J Nucl Cardiol 2014;21:1062–71.)

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#### INTRODUCTION

Since heart failure is a relatively common condition with a high rate of morbidity and mortality, the development of more effective treatment strategies is of particular importance. Cardiac resynchronization therapy (CRT) was approved in 2001 by the United States (US) Food and Drug Administration (FDA) and the American College of Cardiology (ACC)/American Heart Association (AHA) Heart Failure Guidelines indicate class I recommendation for CRT in patients with left ventricular ejection fraction (EF)  $\leq$ 35%, sinus rhythm, New York Heart Association (NYHA) functional class III-IV, and cardiac dyssynchrony, defined as QRS duration >120 ms.<sup>1</sup>

Although CRT can improve quality of life, exercise capacity, and left ventricular EF, about one-third of carefully selected heart failure patients do not show significant benefits.<sup>2,3</sup> On the other hand, it seems that current definition of cardiac dyssynchrony on the basis of QRS width may be imperfect and some groups of symptomatic patients with a narrow QRS and evidence of mechanical dyssunchrony identified by imaging modalities might still have potential benefit from CRT.<sup>4-7</sup> More efforts directed at defining more precise criteria for the selection of patients before CRT by different imaging modalities are, therefore, required.<sup>2</sup> Although large randomized trials did not show a clinical benefit for echocardiography to predict response to CRT,<sup>8,9</sup> tissue Doppler imaging (TDI) is the most commonly used imaging tool for the evaluation of mechanical dyssynchrony<sup>10</sup> and is reported to be more accurate than strain rate imaging in the prediction of reverse remodeling after CRT in heart failure patients.<sup>11,12</sup>

Recently, the phase analysis of gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has been introduced as a new method for the evaluation of left ventricular mechanical dyssynchrony.<sup>13</sup> Earlier studies especially with Emory cardiac toolbox (ECTb) from Emory University<sup>14,15</sup> and then quantitative gated SPECT (QGS) from Cedars-Sinai medical center,<sup>16</sup> showed good results in patients undergoing CRT. However, regarding the different sampling systems used in these software packages,<sup>17,18</sup> there seems to be basic differences in the values of dyssynchrony indices measured by the two techniques. Previous studies, separately, reported different cut-off values for phase standard deviation (PSD) and phase histogram bandwidth (PHB) measured by these two most commonly used software packages.<sup>14,16</sup> Given these differences, in addition to the growing acceptance and application of phase analysis in heart failure patients, we sought to study these two different methods in a same population of heart failure patients and compared them with the dyssynchrony parameters of TDI as a conventional method for the evaluation of left ventricular mechanical dyssynchrony.

## **MATERIALS AND METHODS**

## **Patient Selection**

This study includes a prospective cohort of 31 consecutive patients with reduced left ventricular EF ( $\leq$ 35%), who were referred for gated-SPECT MPI due to clinical indications. The inclusion criteria were EF  $\leq$ 35% determined by echocardiography and regular heart rhythm on electrocardiography (ECG) irrespective of the QRS complex width. All patients had NYHA functional class III-IV. Patients with acceptable quality of rest gated-SPECT MPI were referred for TDI in the following 3 days. Patients with previous CRT, implantable cardiac defibrillator (ICD), or pacemaker were excluded.

# **Gated-SPECT Myocardial Perfusion Imaging**

The rest gated-SPECT MPI study was performed 45-60 minutes after intravenous administration of 15-20 mCi (555-740 MBq) of <sup>99m</sup>Tc-sestamibi with a dual-head gamma camera (Symbia T2, Siemens Healthcare). Images were obtained at rest via the step and shoot protocol with 32 projections over 180° arc from the right anterior oblique view to the left posterior oblique view lasting 30 seconds per projection (Matrix size  $64 \times 64$ ; pixel size 6.6 mm). ECGgated data acquisition was done with 16 frames per cardiac cycle and 30% acceptance window for R-R interval length using forward-backward gating method. The projections were then reconstructed with filtered back projection using a Butterworth filter with order 5 and a cut-off frequency of 0.40 to produce short-axis images. No attenuation or scatter correction was done. Next, the phase of the regional count changes in the left ventricle throughout the cardiac cycle was analyzed by two software packages from Cedars-Sinai medical center (quantitative gated SPECT-QGS; version 0.4; May 2009) and Emory University (Emory cardiac toolbox-ECTb; version 1; copyright 2007) to provide the indices of left ventricular mechanical dyssynchrony, including PHB, which represents the degree of the cardiac cycle that corresponds to 95% of the phase distribution, and phase standard deviation (PSD), which is the standard deviation of the phase distribution.<sup>13</sup>

# Phase Analysis with QGS Software

Using a short-axis data set, QGS computes myocardial surfaces coordinated to an ellipsoidal sampling system,<sup>19</sup> along which unidimensional arrays are created for each spatial sampling point that contains the local maximum myocardial count at each interval. The phase angle of the first-harmonic Fourier transform of this array is the basis for all the synchrony measurements. Due to low temporal variations and inaccurate phase measurement, 5% of the samples with lowest amplitudes are removed. The QGS software also provides another index of dyssynchrony, entropy, which is normalized to its maximum value and reported as a percentage.<sup>20</sup>

## **Phase Analysis with ECTb Software**

The same short-axis images used for phase analysis with QGS software were then submitted to the ECTb for phase analysis. The sampling is performed on the short-axis slices using a hybrid cylindrical-spherical coordinate system, the center of which is the left ventricular long axis.<sup>21</sup> Thereafter, the three-dimensional count distributions of each of the 16 left ventricle short-axis data set are extracted and analyzed using first-harmonic fast Fourier transform to calculate the phase array for the entire left ventricle, representing the regional onset of mechanical contraction. Two other parameters of phase histogram skewness and phase histogram kurtosis are also measured by ECTb software; they indicate the symmetry of the histogram and the degree to which the histogram is peaked, respectively.<sup>13</sup>

#### **Two-Dimensional Tissue Doppler Imaging**

Tissue velocity imaging was performed using commercially available equipment (Vivid 7, GE Vingmed) with a standard phased array 2.5 MHz multi-frequency transducer. The images were acquired from the apical four-chamber, twochamber, and three-chamber views, with the patient in the left lateral position, at the end of expiration. All the patients were in sinus rhythm. Cine loops of at least 3 heart beats were acquired with high temporal resolution (maximal frame rate a frame rate range =  $80 \pm 28$  Hz) and stored digitally for subsequent off-line analysis. The stored data, containing gray-scale and color tissue as well as spectral tissue Doppler velocity information, was analyzed off-line. Adjustment of the ECG was done for noise minimization. Subsequently, the timing of left ventricular ejection was determined from the beginning to the end of the pulsed Doppler flow of the left ventricular outflow tract. Next, the region of interest in the basal and mid regions of the opposite left ventricular walls was determined to generate time-velocity curves. The time from the onset of QRS to peak systolic velocity of each region was obtained, and a total of 12 values were determined. Significant left ventricular dyssynchrony on TDI was defined by the two parameters of the standard deviation of time-to-peak systolic velocity in 12 segments (Yu index) and delay in peak systolic velocity between the basal septum and the lateral wall (septallateral wall delay) with cut-off values of  $\geq$ 33 and  $\geq$ 60 ms, respectively.<sup>12,22,23</sup>

## **Statistical Analysis**

Statistical analysis was performed using SPSS software (SPSS Statistics for Windows, version 17.0. Chicago: SPSS Inc.). The quantitative continuous variables are expressed as mean ± standard deviation, and the categorical variables are presented by numbers (percentages). The independent samples t test was employed to compare the synchrony parameters by TDI, QGS, and ECTb between subgroups, and the paired t test was utilized to compare the variables measured by the two software packages. The correlations of the dyssynchrony parameters derived by the two software packages with TDI dyssynchrony indices and with each other were evaluated using the Pearson correlation analysis. Bland-Altman plots for the assessment of the agreement between the two software packages in the measurement of PSD and PHB as well as scatter diagrams with regression lines for the evaluation of the correlation between the dyssynchrony indices by phase analysis and the parameters of mechanical dyssynchrony on TDI were generated by MedCalc software for Windows, version 8.0 (MedCalc Software, Ostend, Belgium). A P value <.05 was considered statistically significant in all the analyses.

#### RESULTS

# **Patient Population**

The study population comprised of 31 patients, of whom 20 patients had ischemic cardiomyopathy and 11 had non-ischemic etiologies. The demographic data and clinical characteristics of the patients are depicted in Table 1.

As presented in Table 2, given the relevant cut-off values for each parameter, only 58% of the patients had significant mechanical dyssynchrony as determined by TDI and ECTb, whereas up to 74% of the patients were found to have mechanical dyssynchrony by QGS, which rose to 86% in a subgroup of patients with QRS duration  $\geq$ 120 ms. A comparison of dyssynchrony parameters derived from ECTb and QGS between subgroups with  $QRS \ge 120 \text{ ms}$  and QRS < 120 ms, revealed statistically significant differences in the mean values of all the dyssynchrony indices measured by QGS as well as PSD and skewness measured by ECTb. However, the difference regarding TDI parameters between the two groups was not significant. A comparison between the patients with ischemic and non-ischemic cardiomyopathy also showed no statistically significant differences in the

Age (years)	57.4 ± 15.9
Male/female	20 (64.5%)/11 (35.5%)
Ischemic cardiomyopathy	20 (64.5%)
QRS width (ms)	124.2 ± 36.3
CAD risk factors	
Diabetes mellitus	10 (32.3%)
Hypertension	11 (35.5%)
Hyperlipidemia	9 (29.0%)
Family history	6 (19.4%)
Smoking	10 (32.3%)
Echocardiographic findings	
EF (%)	21 ± 6
EDV (mL)	198 ± 84
ESV (mL)	155 ± 72
Perfusion findings	
TPD <sup>a</sup>	19.15
Percent of nonviable myocardium (%) <sup>b</sup>	31.38

**Table 1.** Clinical characteristics of the study patients (n = 31)

Data are represented as mean  $\pm$  SD or number (percentage). *CAD*, Coronary artery disease; *EF*, ejection fraction; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *TPD*, total perfusion defect.

<sup>a</sup>Estimated by Quantitative Perfusion SPECT (QPS) software. <sup>b</sup>Estimated by Emory cardiac toolbox (ECTb) software as the percentage of the myocardial mass that contains less than 50% of the maximal uptake value in myocardium. values of the dyssynchrony parameters by TDI, ECTb, and QGS, except for phase histogram kurtosis (P < .05) (Table 3).

A comparison of the PHB and PSD values, as were measured by the two software packages, demonstrated that the values derived by ECTb were significantly higher than those measured by QGS ( $P \le .001$ ) (Table 4). However, the Pearson correlation analysis revealed a significant correlation between the two software packages with respect to PHB and PSD measurement (Table 5). The Bland-Altman plots of the two software packages also showed mean differences of 38.0 and 19.7 for PHB and PSD, respectively (Figure 1).

In comparison to the Yu index on TDI, no significant correlation was found for the dyssynchrony parameters derived by the two software packages, except for entropy which showed a significant but low correlation with the Yu index (r = 0.383; P < .05). However, in comparison to septal-lateral wall delay, a moderate but significant positive correlation was seen for QGS-derived PHB, PSD, and entropy with Pearson correlation coefficients of 0.424 (P = .017), 0.478 (P = .006), and 0.543 (P = .002), respectively (Table 6).

Our regression analysis also revealed a significant correlation between QGS-derived dyssynchrony parameters and septal-lateral wall delay, as shown in Figure 2.

**Table 2.** Left ventricular mechanical dyssynchrony parameters by different methods in the study population

		Number signific	(%) of patien ant dyssynch		
Parameters	Mean ± SD	$\begin{array}{l} QRS \geq 120 \\ (n = 21) \end{array}$	$b \ge 120$ QRS < 120 = 21) (n = 10)		Cut-off values for significant dyssynchrony
TDI					
Septal-lateral wall delay (ms)	60.6 ± 39.5	12 (57%)	5 (50%)	17 (55%)	60
Yu index (ms)	37.4 ± 12.5	14 (67%)	4 (40%)	18 (58%)	33
ECTb					
PHB (°)	150.2 ± 74.8	15 (71%)	3 (30%)	18 (58%)	135 <sup>14</sup>
PSD (°)	48.3 ± 23.5	15 (71%)	2 (20%)	17 (55%)	43 <sup>14</sup>
Skewness	2.5 ± 0.8	-	-	-	-
Kurtosis	8.6 ± 6.1	-	-	-	-
QGS					
PHB (°)	112.2 ± 49.2	18 (86%)	5 (50%)	23 (74%)	72.5 <sup>16</sup>
PSD (°)	28.7 ± 13.1	17 (81%)	4 (40%)	21 (68%)	19.6 <sup>16</sup>
Entropy (%)	63.6 ± 9.3	-	-	-	-

*TDI*, Tissue Doppler imaging; *PHB*, phase histogram bandwidth; *PSD*, phase standard deviation; *ECTb*, Emory cardiac toolbox; *QGS*, quantitative gated SPECT.

	QRS < 120 (n = 10) Mean ± SD	QRS ≥ 120 (n = 21) Mean ± SD	<i>P</i> value	ICMP (n = 20) Mean ± SD	NICMP (n = 11) Mean ± SD	<i>P</i> value
TDI						
Septal-lateral wall delay (ms)	45.0 ± 31.3	68.0 ± 41.5	NS	57.0 ± 40.1	67.2 ± 39.5	NS
Yu index (ms)	32.2 ± 10.5	40.0 ± 12.9	NS	35.9 ± 11.2	40.3 ± 14.8	NS
ECTb						
PHB (°)	110.6 ± 84.8	169.1 ± 63.2	NS	162.3 ± 69.8	128.3 ± 81.9	NS
PSD (°)	37.2 ± 20.8	55.0 ± 22.1	.019 <sup>a</sup>	51.3 ± 20.5	42.9 ± 28.4	NS
Skewness	3.1 ± 0.8	$2.3 \pm 0.7$	.017 <sup>a</sup>	2.3 ± 0.7	2.9 ± 1.0	NS
Kurtosis	12.2 ± 7.5	6.9 ± 4.7	NS	6.6 ± 4.2	12.1 ± 7.7	.047 <sup>a</sup>
QGS						
PHB (°)	78.6 ± 24.2	128.2 ± 50.39	.001 <sup>a</sup>	108.9 ± 45.1	118.3 ± 57.8	NS
PSD (°)	20.9 ± 6.9	32.4 ± 13.8	.005 <sup>a</sup>	28.1 ± 12.8	29.6 ± 14.1	NS
Entropy (%)	57.5 ± 5.2	66.5 ± 9.5	.002 <sup>a</sup>	63.4 ± 9.0	64.0 ± 10.3	NS

Table 3.	Comparison	of left	ventricular	mechanical	dyssynchrony	parameters	between	subgroups
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ICMP, Ischemic cardiomyopathy; NICMP, non-ischemic cardiomyopathy; TDI, tissue Doppler imaging; PHB, phase histogram bandwidth; PSD, phase standard deviation; ECTb, Emory cardiac toolbox; QGS, quantitative gated SPECT; NS, non-significant. <sup>a</sup>A *P* value <.05 is significant.

**Table 4.** Comparison of the mean value for PHB
 and PSD between ECTb and QGS software

	ECTb Mean ± SD	QGS Mean ± SD	P value
PHB (°)	150.2 ± 74.8	112.2 ± 49.2	.001 <sup>a</sup>
PSD (°)	48.3 ± 23.5	28.7 ± 13.1	<.001 <sup>a</sup>

PHB, Phase histogram bandwidth; PSD, phase standard deviation; ECTb, Emory cardiac toolbox; QGS, quantitative gated SPECT. "A *P* value <.05 is significant.

#### DISCUSSION

#### **Comparison of Two Software Packages**

This study shows a significant and good correlation between two software of Cedars-Sinai medical center and Emory University for the measurement of the mechanical dyssynchrony parameters of PSD and PHB (r = 0.731 and r = 0.664, respectively; P < .001).However, the mean values of PSD and PHB by QGS software were significantly lower than those estimated by ECTb. Previously, Boogers et al<sup>16</sup> reported lower cut-off values for PSD and PHB by QGS software for prediction of response to CRT as compared to cut-off values reported by other studies using ECTb<sup>13,14</sup> and suggested that such differences could be due to differences in patient populations or differences in sampling systems used by the two software. Nevertheless, our

Table 5. Correlation coefficient of PHB and PSD between ECTb and QGS software

	Correlation coefficient	P value	
РНВ	0.664	<.001 <sup>a</sup>	
PSD	0.731	<.001 <sup>a</sup>	

PHB, Phase histogram bandwidth; PSD, phase standard deviation; ECTb, Emory cardiac toolbox; QGS, quantitative gated SPECT. <sup>a</sup>A *P* value <.05 is significant.

study, comparing the two software packages in a same population of patients, also showed significantly different values by these software packages in spite of a good correlation. It can, therefore, be argued that these results are more likely related to differences in the quantification technique of the two software packages and more probably in the sampling system, as was suggested by Boogers et al.<sup>16</sup> These findings indicate the importance of application of relevant normal limits and cut-off values for the use of each software package in research and clinical settings and especially in the follow-up of patients by serial studies to avoid the over or underestimation of mechanical dyssynchrony.

## **Comparison with Tissue Doppler Imaging**

Despite some previous studies reporting a good correlation between the dyssynchrony indices of the phase analysis and relevant parameters by TDI, the



**Figure 1.** Scatter diagrams with regression lines as well as Bland-Altman plots for PSD and PHB measured by QGS and ECTb software. Regression equation for (A) is y = 1.00x + 37.01 and for (B) is y = 1.30x + 10.78. *ECTb*, Emory cardiac toolbox; *QGS*, quantitative gated SPECT; *PHB*, phase histogram bandwidth; *PSD*, phase standard deviation.

Table 6.	Correlation analysis of left ventricular mechanical dyssynchrony parameters derived by phase
analysis a	nd tissue Doppler imaging

	Septal-lateral wall d	lelay	Yu index		
	Correlation coefficient	P value	Correlation coefficient	P value	
ECTb					
РНВ	0.173	NS	0.141	NS	
PSD	0.192	NS	0.079	NS	
Skewness	-0.240	NS	-0.219	NS	
Kurtosis	-0.245	NS	-0.255	NS	
QGS					
РНВ	0.424	.017 <sup>a</sup>	0.273	NS	
PSD	0.478	.006 <sup>a</sup>	0.327	NS	
Entropy	0.543	.002 <sup>a</sup>	0.383	.033 <sup>a</sup>	

*PHB*, Phase histogram bandwidth; *PSD*, phase standard deviation; *ECTb*, Emory cardiac toolbox; *QGS*, quantitative gated SPECT; *NS*, non-significant.

<sup>a</sup>A *P* value <.05 is significant.

results of the present study do not support such good correlations with either QGS or ECTb. Henneman et al<sup>24</sup> reported that PHB and PSD, using ECTb, had good and

significant correlations with delay in peak velocity between the earliest and latest activated segments by TDI (r = 0.89 and r = 0.80, respectively) in 75 heart



**Figure 2.** Scatter diagrams with regression lines for dyssynchrony parameters derived by TDI and QGS software. Regression equations are as follows: (A) y = 0.34x + 22.38, (B) y = 1.44x + 19.26, (C) y = 2.35x - 89.57, and (D) y = 0.52x + 3.79. QGS, quantitative gated SPECT; *PHB*, phase histogram bandwidth; *PSD*, phase standard deviation; *TDI*, tissue doppler imaging.

failure patients eligible for CRT. Another study by Marsan et al<sup>25</sup> on 40 heart failure patients with EF <35% and wide QRS complex, also showed a significant correlation between ECTb-derived dyssynchrony parameters and the standard deviation of time-to-peak velocities of the 12 myocardial segments by tri-plane TDI (r > 0.7). Since our study population included heart failure patients regardless of the ORS complex width, such different results could be partly related to the different characteristics of the study populations. Our study also found no significant correlations between TDI and phase analysis in the subgroups of patients with narrow or wide QRS complex; nonetheless, significant differences were found between patients with narrow and wide QRS complex in the mean dyssynchrony parameters of the phase analysis in contrast to TDI parameters. Accordingly, the inclusion of patients with both narrow and wide QRS complex might be responsible for this controversy. On the other hand, it indicates the need for further focused investigation regarding the

evaluation of mechanical dyssynchrony in these patients via different methods.

Despite the lack of a significant correlation between ECTb and TDI in our study, QGS-derived parameters of PSD and PHB showed significant but moderate correlation with septal-lateral wall delay (r = 0.478 and r = 0.424, respectively; P < 0.05). This is relatively concordant with the results of the study by Boogers et al<sup>16</sup> who also reported a significant but higher correlation between these parameters (r = 0.69 and r = 0.65 for PHB and PSD, respectively). The authors also performed their study in a population of patients with wide QRS complex, but they did not report the Yu index, which showed no significant correlation with PHB and PSD measured by QGS in our study.

Although echocardiographic-based studies report relatively high prevalence of left ventricular mechanical dyssynchrony in patients with narrow QRS complex with a range of 27%-56%,<sup>26-28</sup> large randomized trials have demonstrated no beneficial effect of CRT in patients with narrow QRS complex.<sup>8</sup> Our study also showed a relatively high prevalence rate of mechanical dyssynchrony in patients with narrow QRS complex by the two methods. However, the prevalence of significant mechanical dyssynchrony in the patients with wide QRS complex was higher with the phase analysis (71%-86%) as compared to TDI.

Finally, it should be noted that although some degree of discordant results could be due to different sample sizes and characteristics, it seems that TDI and phase analysis could have different results in the evaluation of mechanical dyssynchrony which could be related to inherent technical differences and limitations of the two methods. Nevertheless, the present study could not precisely evaluate these controversial results due to a lack of gold standard method for comparison.

We also found that entropy, another dyssynchrony parameter provided only by QGS software, not only had highest correlation coefficient with septal-lateral wall delay on TDI, but also was the single dyssynchrony parameter in our study that exhibited a significant correlation with the Yu index, although the correlation coefficient was only equal to 0.38. Entropy is an indicator of variability which is related to the number of the phase angle on the phase histogram and ranges from 0 to the maximum value of 1 or 100% with an increase in the degree of mechanical dyssynchrony.<sup>29</sup> Assessment of left ventricular mechanical dyssynchrony with gated-SPECT blood pool studies shows good reproducibility and accuracy for entropy derived from the phase analysis.<sup>29-31</sup> Van Kriekinge et al reported that entropy can accurately differentiate patients with left bundle branch block from those with a low likelihood of conduction abnormality. They also indicated that entropy is less dependent to the shape of the phase histogram.<sup>20</sup> A recent study by Leva et al<sup>32</sup> reported good reproducibility for entropy in gated-SPECT MPI and suggested that entropy is better than PSD for the individual assessment and separation of heart failure and non-heart failure patients. Our results also indicated better performance of entropy as compared to PSD and PHB for prediction of left ventricular mechanical dyssynchrony on TDI. However, further studies are needed to evaluate the potential capability of this parameter for the clinical application and prediction of response to CRT.

As a limitation, it must be noted that the importance of dyssynchrony evaluation is mainly linked to the prediction of response to CRT and not necessarily the presence of mechanical dyssynchrony on TDI. Consequently, the present study succeeded in evaluating the phase analysis for the measurement of mechanical dyssynchrony indirectly. Studies in patients undergoing CRT will provide more clinically useful results. The relatively small sample size of our study is another limitation, and since our study was comprised of only 10 patients with narrow QRS complex, larger studies recruiting more patients with both narrow and wide QRS complex are needed for a more accurate evaluation of phase analysis performance in different groups of patients who might obtain potential benefits from CRT.

# **NEW KNOWLEDGE GAINED**

Since PSD and PHB values derived by QGS software were significantly lower than those measured by ECTb, it can be stated that these parameters measured by the two software packages are not interchangeable. In contrast to TDI-derived dyssynchrony parameters, the phase analysis by the two software packages showed significant differences between subgroups of patients with wide and narrow QRS complex, which indicates better performance of phase analysis to differentiate these patient groups. Although our study found only a modest overall correlation between phase analysis and TDI, entropy showed better correlation with TDI as compared to other dyssynchrony parameters measured by the two software packages.

## CONCLUSION

We conclude that despite a good correlation between QGS and ECTb software packages for the measurement of PHB and PSD, different normal cut-off values for these parameters should be used by each software package. We also found that although TDI and phase analysis have not a good correlation in the evaluation of mechanical dyssynchrony, entropy derived by QGS software, seems to be more correlated with TDI for the assessment of left ventricular mechanical dyssynchrony, especially in the population of heart failure patients with both narrow and wide QRS complex. Further investigation is needed.

# **Conflict of interest**

The authors declare that they have no financial conflicts of interest.

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