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Diagnosis of exercise-induced left bundle branch block at rest by scintigraphic phase analysis

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Abstract. Accurate diagnosis of diseases of the ventricular conducting system is essential for their appropriate therapy. Some conduction abnormalities, such as exercise-induced left bundle branch block (EX-LBBB), are not apparent on resting electrocardiograms. Phase analysis of rest and exercise radionuclide ventriculograms (RVG's) was used to compare four EX-LBBB patients with six normal controls. All patients had normal resting electrocardiograms, ejection fractions, and visually normal wall motion. First harmonic phase images were generated reflecting the timing of ventricular contraction. Dynamic phase displays were reviewed and graded in a blinded fashion by three independent experienced observers. Phase angle histograms of the right and left ventricle were determined for both resting and exercise images. The mean phase angle and standard deviation were also calculated for each ventricle. Visual grading of the resting phase images failed to show a significant difference between normal patients and patients with EX-LBBB. Quantitative analysis, however, revealed a significant difference in mean phase angle differences (LV–RV) in resting studies: 0.8° (±1.9° SEM) in normals versus 9.3° (±2.3° SEM) in EX-LBBB patients ($P<0.03$). Exercise accentuated the phase angle differences: 1.8° in normals vs. 31.2° in EX-LBBB patients ($P<0.001$). Quantitative phase analysis of resting RVG's permits the diagnosis of cardiac conduction disease that is not apparent on the resting EKG and may result in better monitoring and treatment.

Key words: Heart, radionuclide studies – Heart, conduction disease – Heart, phase analysis – Bundle branch block

Introduction

Effective treatment of cardiac conduction abnormalities is dependent upon early accurate diagnoses. Exercise-induced left bundle branch block (EX-LBBB) is a relatively infrequent conduction system disease which originally was felt to have no influence on mortality. However, Schneider et al. (1979) showed that 50% of patients with newly developed LBBB died of cardiovascular disease within 10 years and that EX-LBBB was strongly associated with coronary artery disease, degenerative conducting system disease, or hypertension. EX-LBBB is sometimes associated with ischemia of the septum and often progresses to LBBB or complete heart block, both associated with significant mortality (Chou 1979). By definition, EX-LBBB cannot be diagnosed on a resting ECG and may not be apparent at low work levels on a stress test. In this study, scintigraphic phase analysis was evaluated as a tool to diagnose EX-LBBB on resting radionuclide ventriculograms (RVGs).

Phase images are derived by first harmonic analysis (i.e., a cosine fit, a form of temporal Fourier transformation) of the time-activity curve for each pixel of the RVG matrix, allowing qualitative and quantitative assessment of ventricular function and contraction. Phase analysis yields a parametric image related in part to the timing of cardiac contraction. Amplitude analysis is analogous to a stroke-volume image.

In this study we used phase analysis of RVGs to evaluate four patients with normal resting ECGs, who then developed LBBB with exercise. They were then compared with normal patients who had normal rest and exercise ECGs. Qualitative visual and quantitative statistical analyses were used to evaluate differences between right (RV) and left ventricular (LV) mean resting and exercise phase angles in EX-LBBB patients and normal patients.

Materials and methods

Six normal controls were selected who had no known history of coronary artery or cardiac disease and who, at rest and exercise, had normal ECGs, ejection fractions (EFs) and wall motion by RVG. These patients were then compared with the four patients who had undergone EX-LBBB and were studied at the University of Michigan Hospitals in the last 2 years and who also had normal resting ECGs and visually normal RVGs (including normal EF response and wall motion during stress). The criteria for LBBB included: (1) QRS duration of 0.12 s or greater; (2) presence of a broad monophasic R-wave in I, V_5 and V_6 (usually notched or slurred); (3) displacement of the ST segment and T wave in a direction opposite to the major QRS deflection; (4) absence of Q waves in leads I, V_5, and V_6 (Chou 1979).

Radionuclide ventriculograms were obtained with a standard field-of-view gamma camera using a high-sensitivity, low-energy collimator that was coupled to a dedicated nuclear medicine computer. Patients were injected intravenously with 925 MBq of technetium-99m pertechnetate 20 min after 3.4 mg stannous pyrophosphate had been injected inravenously for labelling of red blood cells (Callahan et al. 1982). The RVG was then acquired in a 64 × 64 image matrix as 14 or 16 frames gated to the cardiac cycle. Approximately 300,000 counts/frame were acquired. Left ventricular ejection fractions were calculated using an automated edge detecting system (Medical Data Systems, MDS, Ann Arbor, Michigan); the raw image data were smoothed and filtered, and ventricular wall motion was

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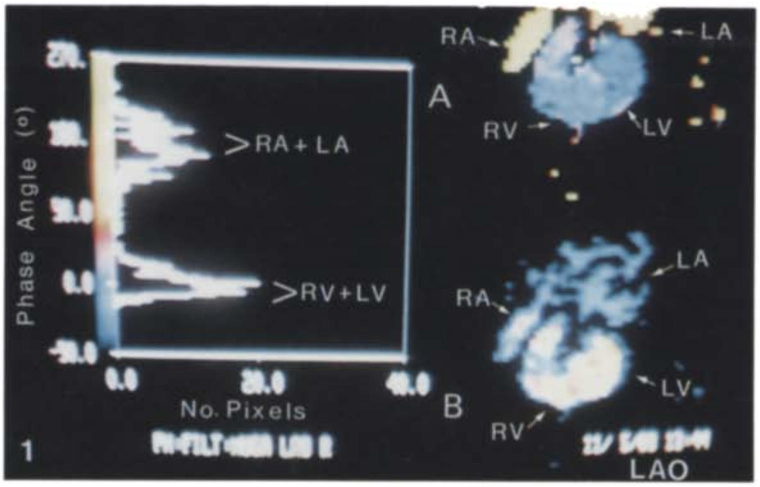

Fig. 1. Normal patient. LAO phase image (*A*) showing LV and RV to be "isophase" (i.e., as shown by same color). Normal LAO amplitude image (*B*). Phase angle distribution histogram (*C*) showing two peaks, one for the atria (*LA* + *RA*) and one for the ventricles (*LV* + *RV*). *LA* Left atrium; *RA* right atrium; *LAO* left anterior oblique; *RV* right ventricle; *LV* left ventricle

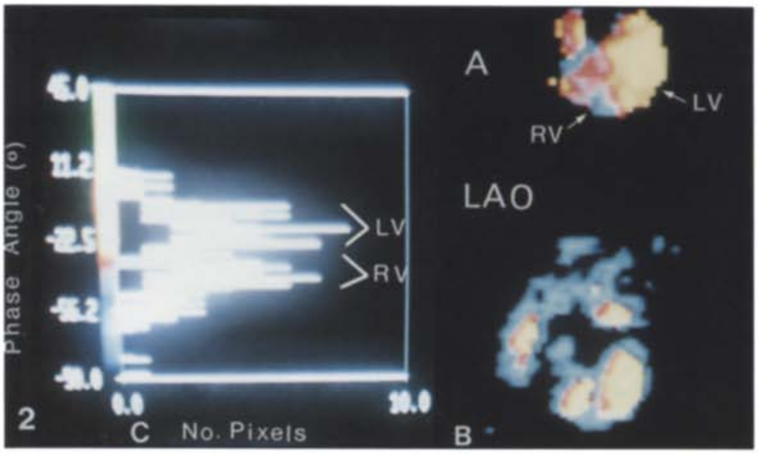

Fig. 2. An exercise-induced left bundle branch block (EX-LBBB) patient at exercise. Phase image of the ventricles only (*A*) shows marked phase shift between the LV and RV as manifested by different colors, indicating non-synchrony of ventricular contraction. Normal LAO amplitude image (*B*), including the atria. Phase angle distribution histogram, of the ventricles only (*C*), showing separate peaks for the LV and RV (contrast with Fig. 1, where the LV and RV have a single peak)

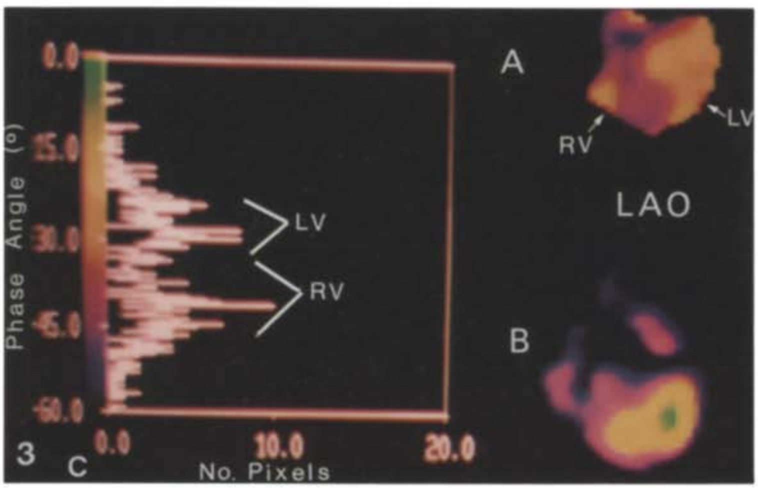

Fig. 3. Same EX-LBBB patient as in Fig. 2 but at rest. LAO phase image of ventricles only (*A*) shows that the LV phase is visibly different (delayed) compared to the RV (note different colored ventricles). LAO amplitude image, including the atria (*B*), is normal. Ventricular phase angle distribution histogram (*C*) again shows separate peaks for the LV and RV (the Y-axis is expanded compared to Fig. 2). The mean phase shift (*LV–RV*) was 21.8° at exercise and was 10.4° at rest (both significantly more than the normal mean phase shifts of 1.8° and 0.8° respectively)

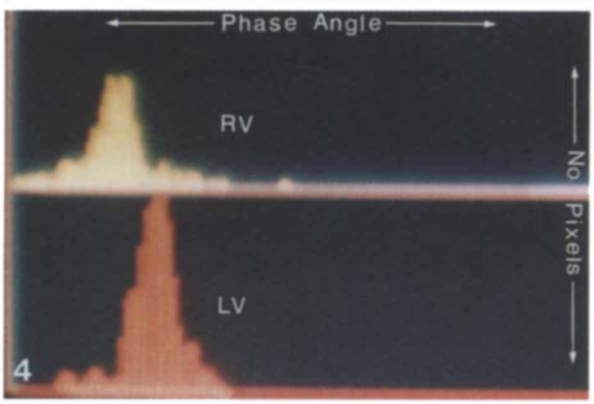

Fig. 4. Same EX-LBBB patient at rest. Manually drawn regions of interest (ROIs) were drawn for the LV and RV. These LV and RV ROIs were then used to generate the isolated right (*RV*) and left (*LV*) ventricular phase angle distribution histogram curves. A significant delay in the phase distribution of the left ventricle was noted despite the fact that the resting EKG was normal. Similar curves were drawn for the ventricles in all patients for statistical analysis

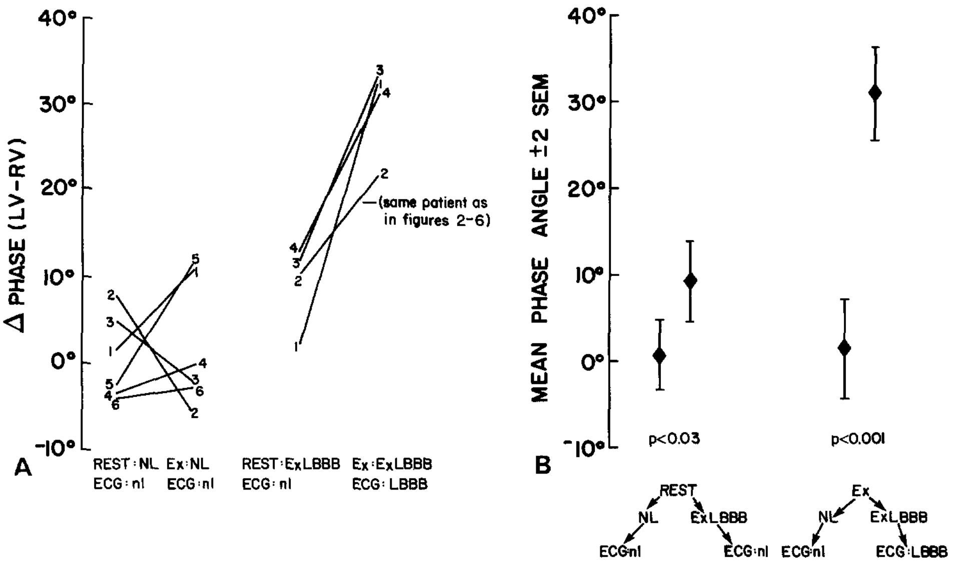

Fig. 5. A Scatter-plot diagram of difference (LV–RV) in mean phase angles for normal and EX-LBBB patients at rest and exercise. **B** The mean ±2 SEM (standard error of the mean) of LV–RV mean phase angle was plotted for normal and EX-LBBB patients at rest and at exercise. *P* values indicating significant differences between group means are shown at rest ($P<0.03$) and exercise ($P<0.001$). *ECG* electrocardiogram; *EXLBBB* exercise-induced left bundle branch block; *LBBB* left bundle branch block; *nl* normal; *NL* normal control group

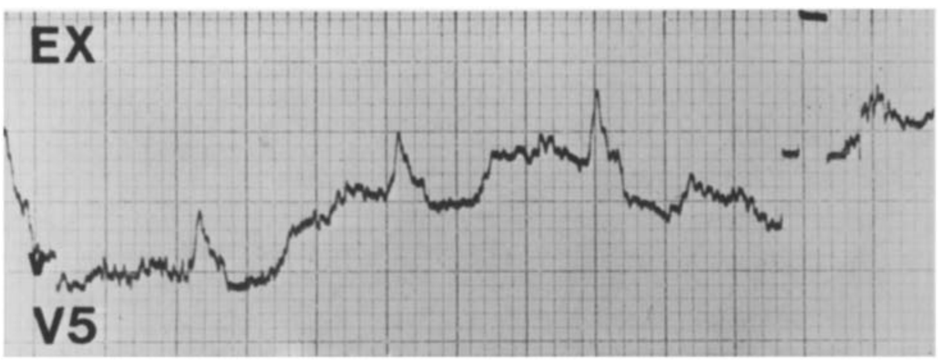

Fig. 6. Resting and exercise electrocardiogram of the same EX-LBBB patient. As can be seen, the QRS complex is of normal width at rest (0.08 s) (*arrowhead 1*). With exercise, however, the QRS duration increased to 0.13 s (*arrowhead 2*); broad monophasic R-waves are noted, and the ST and T wave segments are deflected opposite to the major QRS direction compatible with LBBB

visually analyzed by three experienced nuclear physicians (RW, JJ, AB). Phase and amplitude images were then created for display (Figs. 1–3). Dynamic display of the phase angles was evaluated by the three observers on a six-point scale with normal equalling one and complete (or "extreme") LBBB (i.e., marked asynchrony between ventricles) equalling six. Regions of interest (ROIs) were then manually drawn around the left and right ventricle without knowledge of the patient's clinical history (Fig. 4) with reference to end-diastolic, end-systolic, dynamic phase, and amplitude images. These ROIs were used to generate histograms of the RV and LV phase angle distribution of the normal and EX-LBBB patients for statistical analysis (Fig. 4). The interventricular difference in men a phase angle, standard deviations of phase angle, and standard error of the mean of the men a phase angle differences were calculated for each patient at rest and exercise. The differences between means were analyzed by Student's *t*-test, corrected for small sample size.

Results

Visual differentiation of phase images between normal patients and the patients with EX-LBBB at exercise was not difficult (Figs. 1, 2). Although in some cases (Fig. 3) it was possible to visually detect EX-LBBB patients on the resting phase image, visual grading by three experienced observers gave resting phase images a mean score of 1.6 for normal controls and 2.4 for EX-LBBB patients ($P=$NS). There was, however, a statistically significant difference in mean phase angle differences between LV and RV [Δ(LV–RV)] of normal and EX-LBBB patients at rest (0.8°±1.9° SEM for controls, 9.3°±2.3° SEM for patients with EX-LBBB; $P<0.03$), despite the fact that the resting ECG was normal in all patients (Figs. 4–6). This difference is, as expected, more apparent at exercise (1.8°±2.4° SEM for controls, 31.2°±2.7° SEM for patients with EX-LBBB; $P<0.001$) when LBBB was apparent on the ECG (Fig. 6).

Three of the four EX-LBBB patients had a phase angle difference [Δ(LV–RV)] at rest that was greater than 2 SD above the mean for normals. There were no significant differences in the standard deviations of the RV and LV phase angle distributions between control patients and EX-LBBB patients either at rest or at exercise.

Discussion

Rate-dependent (or exercise-induced) LBBB occurs when the cardiac impulse finds the left bundle branch system in its refractory period during a critical accelerated ventricular rate (Shearn and Rytand 1953). When the rate slows enough for the left bundle branch system to recover from its refractory period, normal ventricular conduction can again result. This sudden failure of conduction is typical of the diseased His-Purkinje system (Moe et al. 1965). Most patients with this form of intermittent LBBB eventually develop complete LBBB (Chou 1979).

Although intermittent bundle branch block was first described by Lewis as early as 1913, there have been relatively few studies related to this phenomenon. Several mechanisms, including alterations in autonomic tone and changes in coronary perfusion, have been suggested as an explanation for rate-dependent bundle branch block (El-Sherif 1974). Comeau et al. (1983) studied 60 patients with intermittent LBBB and found that 42 had evidence of hypertensive heart disease or coronary artery disease. Other studies have confirmed these observations (Shearn and Rytand 1953; Bauer 1964). Therefore, the finding of exercise-induced LBBB may be a clue to underlying disease of the His-Purkinje system or structural cardiac disease.

The left conducting bundle derives blood supply from both the right coronary artery and the left anterior descending artery so that a conduction disturbance in this bundle (when due to coronary artery disease) may imply involvement of both vessels (Chou 1979). Fixed or transient LBBB can be seen in patients with acute myocardial infarction (Chou 1979). Other cardiac diseases associated with left bundle branch block include rheumatic heart disease, calcific aortic stenosis, primary and secondary cardiomyopathy, and symphilitic heart disease (Chou 1979). Rate-dependent or exercise-induced LBBBs generally have the same etiology as the the stable or complete variety, including degenerative conduction system disease, ischemia, and hypertension (Chou 1979). There is an especially poor prognosis in patients with acute myocardial infarction and LBBB. Transient LBBB also occurs during angina and heart failure (Chou 1979). In a patient recently reported by Meyer-Pavel and Logic (1982), EX-LBBB was associated with a ^{201}Tl myocardial perfusion scan showing a reversible defect in the anteroseptal region (consistent with reversible ischemia) and a significant left anterior descending artery stenosis at cardiac catheterization. In the patient group we evaluated, there was no convincing evidence to suggest coronary artery disease.

Phase analysis of RVGs has been shown to be useful in the diagnosis of coronary artery disease (Turner et al. 1983; Ratib et al. 1982), aiding in localizing bypass tracts in Wolff-Parkinson-White syndrome (Chan et al. 1983), quantifying regional wall motion abnormalities (Pavel et al. 1983), and detecting and defining complete bundle branch blocks (Frais et al. 1982; Botvinick et al. 1982). Frais et al. (1982) and Swiryn et al. (1981) demonstrated and quantified the delayed mean phase angle of the right ventricle in patients with right bundle branch block and the left ventricle in patients with LBBB compared with patients with normal conduction. It must be noted that the statistical analysis of phase angle differences involves the potential for propagation of statistical errors, which must be considered in assessing the statistical separation of RV and LV mean phase angles (Mancini et al. 1985; Schwaiger et al. 1984).

The present study shows that in patients who have visually normal wall motion and normal rest and exercise ejection fractions, phase analysis can be used to detect a phase delay between the left and right ventricles alerting the clinician to the possibility of an exercise-inducible LBBB. In addition, this study has shown quantitative phase analysis to be superior to experienced observers in making this diagnosis. The ability of phase analysis to detect occult conduction abnormalities may indicate that phase imaging should be performed routinely.

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