

# Third and Fourth Heart Sounds Detected by Correlated Audioelectric Cardiography Are Highly Specific Markers for Elevated Left Ventricular Filling Pressure and Reduced Ejection Fraction



Mark V Jordan, Gregory Marcus, Joshua Vessey, Ivor L Gerber, Barry H McKeown, Michele Huddleston, Elyse Foster, Kanu Chatterjee, Charles E. McCulloch, and Andrew D Michaels

The Departments of Adult Echocardiography and Invasive Cardiology, University of California, San Francisco

## Background

The presence of third (S3) and/or fourth (S4) heart sounds may reflect increased left ventricular (LV) filling pressure and is associated with adverse clinical outcomes. The aim of this study is to examine echocardiographic, neuro-hormonal and invasive correlates of an S3 and/or S4 using computerized detection assessed by audioelectric cardiography (computerized detection of heart sounds on an acoustic signal collected in the V3 or V4 position).

## Methods

Adult patients referred for cardiac catheterization were enrolled. Patients with atrial arrhythmia were excluded. Within a 4-hour period, each subject had left heart catheterization for LV end-diastolic pressure (LVEDP), measurement of serum B-type natriuretic peptide (BNP) and echocardiography for LV ejection fraction (EF) and diastolic function. E/E' ratio was computed and diastolic function was categorized according to standard transmitral and pulmonary venous patterns as normal (group 1) and impaired relaxation, pseudonormal, or restrictive patterns (group 2). The presence of an S3 and/or S4 was determined by correlated audioelectric cardiography (Audicor, Inovise Medical).

**Table 1. Hemodynamic and Neurohormonal Correlates of Elevated LV Filling Pressure (LVEDP)**

	LVEDP ≤ 15 mmHg	LVEDP > 15 mmHg	P-value
S3 (%)	8.2	41.5	0.001
S4 (%)	20.4	46.3	0.008
BNP(pg/ml)	161 ± 272	880 ± 1262	<0.001
LVEDP (mmHg)	9.0 ± 3.4	22.1 ± 4.8	0.001
LVEF (%)	62.0 ± 13.6	50.5 ± 21.1	0.004
E/E'	5.2 ± 2.0	10.4 ± 5.6	<0.001

**Table 2. Hemodynamic and Neurohormonal Correlates of Reduced Left Ventricular Ejection Fraction (LVEF)**

	LVEF ≥ 50%	LVEF < 50%	P-value
S3 (%)	11.1	53.8	<0.001
S4 (%)	27.0	46.2	0.14
BNP (pg/ml)	272 ± 612	1031 ± 1345	<0.001
LVEDP (mmHg)	12.7 ± 6.9	19.7 ± 7.2	0.002
LVEF (%)	66.7 ± 9.6	32.9 ± 9.8	<0.001
E/E'	6.2 ± 3.3	10.5 ± 6.2	<0.001

## Results

100 patients were enrolled. The mean age was 62±14 (range 24-91) years, 65 were male, 29 were diabetic, 81 had hypertension, 37 had a history of heart failure, and 68 had coronary artery disease. Accurate assessment of an S3 and/or S4 was not possible in 10 patients and therefore data is presented for 90 subjects. Forty-one subjects had abnormal heart sounds [S3 only (n=12), S4 only (n=20), or both (n=9)]. The univariate predictors of elevated LVEDP are shown in Table 1, and the predictors for reduced LVEF are shown in Table 2. By multivariate analysis, E/E' is an independent predictor for both elevated LVEDP (p<0.001) and for reduced EF (p=0.003); S3 is an independent predictor for reduced EF (p=0.024).

## Conclusions

The presence of an S3 and/or S4 determined by audioelectric cardiography reflects invasively measured increased LV filling pressure, routine echocardiographic measures of LV dysfunction (LVEF and E/E'), and elevated serum BNP levels.