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Letter to the Editor

The amplitude ratio of the first to second heart sound is reduced in left ventricular systolic dysfunction ☆

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ABSTRACT

In animal studies, the amplitude of the first heart sound (S1) is proportional to the rate of left ventricular pressure rise (LV d*P*/d*t*). To develop a clinical application for this property, we performed phono-electrocardiographic recordings using a digital hand-held device followed by an echocardiogram within 2 hours of a clinically indicated cardiac catheterization. Compared with the group with reduced d*P*/d*t* (<1000 mm Hg/s) or ejection fraction (EF) (<55%), the median S1/S2 detected at the cardiac base was higher in those with normal d*P*/d*t* or EF. On ROC analysis, S1/S2 significantly discriminated normal from reduced d*P*/d*t* and EF. This study demonstrated that S1, corrected for S2, is decreased in patients with impaired LV systolic function. Digital phonocardiography appears promising as an adjunctive bedside tool for evaluating left ventricular systolic function.

Rapid detection of left ventricular systolic dysfunction (LVSD) is critical in the prevention and management of heart failure. Echocardiography and brain natriuretic peptide (BNP) assay are limited by technical sophistication, cost and inadequate sensitivity. One feature of the heart sounds that is a direct manifestation of the left ventricular contractile state [1] and may be used for rapid noninvasive detection of LVSD is the first heart sound (S1).

We studied consecutive patients referred to the cardiac catheterization laboratory for a left heart catheterization study and excluded those who had moderate or severe valvular disease (mitral regurgitation, mitral stenosis, aortic regurgitation, aortic stenosis), or primary pulmonary hypertension, or those who had significant hemodynamic changes during the cardiac catheterization. Sixty one eligible patients were recruited, and underwent simultaneous electrocardiographic (ECG), PCG recordings and a transthoracic echocardiogram within 2 hours of a clinically indicated cardiac catheterization, each performed by an investigator who was blinded to the results of other cardiac investigations. The study was approved by the committee for human research, all subjects gave prior informed consents. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

The ViScope™ (HD Medical Group Ltd, Portland, OR), a portal digital phonocardiogram with the capacity for simultaneous ECG was used. The data was captured using an Analog to Digital acquisition system (NIDAQ, National Instruments), sampling the heart sounds at 8000 Hz. With the patient breathing quietly in the supine position, heart sounds were recorded from each of three standard auscultatory locations, apex, right upper sternal border (RUSB), left upper sternal border (LUSB) for 20 seconds by placing the microphone head on the chest surface under its own weight without hand contact or pressure application. The amplitude of S1 was defined as the largest deflection seen within the heart sound component that follows the QRS complex, the amplitude of S2 was defined as the largest deflection seen within the component that falls between S1 and next QRS. Of the 61 patients enrolled in the study, the catheter traversed the aortic valve during the catheterization and directly measured LV d*P*/d*t* in eight patients (fluid filled system, sweep speed 100 m/s), the d*P*/d*t* for forty patients were estimated using the rising slope of the mitral regurgitant jet velocity on Doppler echocardiography with a sweep speed of 200 m/s [2]. In 14 patients, d*P*/d*t* was not available by either method. Left ventricular ejection fraction (LVEF) was obtained in all patients on echocardiogram using biplane method of disks. The d*P*/d*t* ranged from 400 to 2850 mm Hg/s, EF ranged from 11 to 78%.

We found that the amplitude of S1 recorded at LUSB modestly correlated with d*P*/d*t*, ($r = 0.31$, $p < 0.05$). When S1 was expressed as a relative amplitude with S2, the correlation with d*P*/d*t* and EF improved in both LUSB and RUSB. The absolute amplitudes of S1 and S2 at the apical location correlated with BMI and chest circumference, but not LV systolic function (Table 1). When compared with the group with normal d*P*/d*t* (≥1000 mm Hg/s, $n = 26$) or EF (≥55%, $n = 36$), those with reduced d*P*/d*t* ($n = 21$) or EF ($n = 25$) had significantly decreased absolute amplitude of S1 at the LUSB, and decreased S1/S2 ratios at the LUSB and RUSB. The BMI and PR interval did not differ between the two groups (Tables 2 and 3). On ROC analysis, S1/S2 ratios at the

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Table 1
Correlation coefficients* of heart sound amplitudes with clinical variables.

	Apex S1	Apex S2	Apex S1/S2	LUSB S1	LUSB S2	LUSB S1/S2	RUSB S1	RUSB S2	RUSB S1/S2
CC	−0.41**	−0.50**	0.22	−0.11	0.03	−0.19	−0.34**	−0.24	−0.10
BMI	−0.50**	−0.46**	0.05	−0.19	−0.24	−0.05	−0.32**	−0.35**	−0.07
PR int	−0.14	0.09	−0.19**	−0.09	0.03	−0.14	−0.17	0.10	−0.25**
SBP	−0.13	−0.10	−0.01	0.29**	0.06	0.11	−0.17	−0.02	−0.14
DBP	−0.12	0.03	−0.26**	0.003	0.14	−0.13	−0.15	−0.06	−0.15
PASP	−0.13	0.007	−0.40**	−0.20	0.26	−0.47**	0.03	0.25	−0.33
d*P*/d*t*	0.13	−0.09	0.21	0.31**	−0.27	0.49**	0.10	−0.29	0.38**
LVEF	−0.04	−0.12	0.04	0.18	−0.29**	0.39**	−0.03	−0.27***	0.26**

LUSB = left upper sternal border; RUSB = right upper sternal border; CC = chest circumference; LVEF = left ventricular ejection fraction; d*P*/d*t* = rate of LV pressure rise; PR int = PR interval; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; PASP = pulmonary arterial systolic pressure.
* Spearman's rho correlation coefficient.
** *p*-value<0.05.
*** *p*-value = 0.05.

Table 2
Clinical and phonocardiographic characteristics of patient groups separated by d*P*/d*t* (mm Hg/s).

	d*P*/d*t*≥1000	d*P*/d*t*<1000	*p*-value
	n = 26	*n* = 21	
Clinical characteristics			
Age, years	68 (59–75)	73 (60–79)	0.44
Sex, % male	73	91	0.13
BMI	25 (23–29)	27 (20–28)	0.52
SBP, mm Hg	127 (115–140)	111 (102–121)	0.002
DBP, mm Hg	69 (63–72)	64 (58–69)	0.06
PASP, mm Hg	37 (30–45)	45 (37–55)	0.11
Heart rate	68 (63–74)	67 (62–77)	0.78
PR interval, ms	162 (145–190)	160 (143–195)	0.96
LVEF, %	63 (55–66)	41 (24–48)	<0.001
S1/S2 ratios			
Apex S1	0.092 (0.055–0.146)	0.091 (0.043–0.133)	0.57
Apex S2	0.047 (0.026–0.071)	0.052 (0.033–0.114)	0.32
Apex S1/S2	2.02 (1.62–2.99)	1.55 (1.00–2.66)	0.09
LUSB S1	0.086 (0.052–0.105)	0.055 (0.037–0.069)	0.01
LUSB S2	0.053 (0.033–0.091)	0.075 (0.055–0.111)	0.10
LUSB S1/S2	1.52 (0.98–2.47)	0.78 (0.57–1.14)	<0.001
RUSB S1	0.068 (0.020–0.099)	0.047 (0.025–0.060)	0.47
RUSB S2	0.042 (0.028–0.058)	0.060 (0.035–0.098)	0.08
RUSB S1/S2	1.74 (0.69–2.30)	0.78 (0.63–1.30)	0.011

Table 3
Clinical characteristics of patient groups separated by ejection fraction (%).

	EF≥55	EF<55	*p*-value
	n = 36	*n* = 25	
Clinical characteristics			
Age, years	61 (40–73)	75 (60–79)	0.013
Sex, % male	83	89	0.57
BMI	24 (23–27)	26 (22–30)	0.65
SBP, mm Hg	128 (116–140)	111 (100–121)	<0.001
DBP, mm Hg	68 (63–74)	65 (58–70)	0.07
PASP, mm Hg	37 (29–42)	45 (36–54)	0.07
Heart rate	66 (57–69)	70 (64–79)	0.03
PR interval, ms	159 (138–179)	162 (149–193)	0.28
d*P*/d*t*	1626 (1267–2533)	865 (651–1048)	<0.001
S1/S2 ratios			
Apex S1	0.079 (0.043–0.125)	0.092 (0.047–0.144)	0.48
Apex S2	0.044 (0.024–0.074)	0.056 (0.031–0.101)	0.29
Apex S1/S2	1.80 (1.43–2.22)	2.07 (1.15–3.15)	0.78
LUSB S1	0.081 (0.058–0.101)	0.054 (0.041–0.079)	0.04
LUSB S2	0.055 (0.033–0.090)	0.071 (0.042–0.105)	0.12
LUSB S1/S2	1.44 (0.97–2.19)	0.95 (0.60–1.29)	0.003
RUSB S1	0.046 (0.031–0.084)	0.049 (0.025–0.085)	0.99
RUSB S2	0.037 (0.026–0.052)	0.055 (0.033–0.094)	0.05
RUSB S1/S2	1.65 (0.80–2.19)	0.83 (0.65–1.60)	0.03

LUSB and RUSB, but not the apex significantly discriminated normal vs reduced d*P*/d*t* or EF (Fig. 1). The sensitivity and specificity of a S1/S2 ratio of more than 1 obtained at the base of the precordium (LUSB and RUSB) for detecting d*P*/d*t*≥1000 mm Hg/s ranged from 72–80% and 57–71% respectively. Using the same cutoff for S1/S2 ratio, the sensitivity and specificity of detecting EF≥55% were 74–80% and 54–61% respectively.

Several limitations have to be considered when interpreting the results of this study. First, we did not distinguish M1 from T1, A2 from

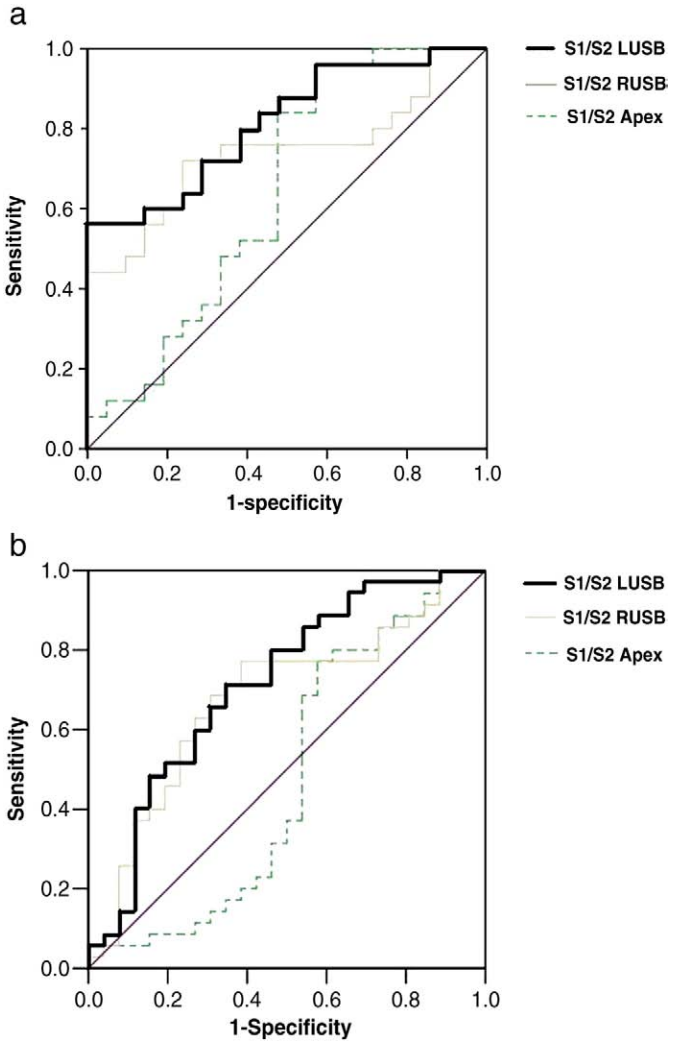

Fig. 1. Receiver operating characteristics curves showing the ability of S1/S2 ratio to detect (a) d*P*/d*t*≥1000 and (b) EF≥55 at each of the three auscultatory locations.

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P2, instead the largest positive to negative deflections in each of the heart sound components were assumed to correspond to M1 and A2. The contributions of T1 and P2 to the amplitude of the S1 and S2 respectively are known to be relatively small except in disease states such as tricuspid stenosis [3] atrial septal defect [4], or severe pulmonary hypertension which were not present in our study population. Second, the dP/dt of eight patients were obtained from non-simultaneous, direct catheter measurement and the majority was derived non-invasively from Doppler echocardiography. Although this methodology deviates from the standard simultaneous catheter and PCG measurements, we have taken steps such as eliminating subjects with significant hemodynamic shift after catheterization and cross examination of high sweep speed, mitral regurgitant Doppler velocity signal by two independent investigators, to ensure close representation of the true dP/dt. Third, because there were no patients with extremely prolonged PR interval and other factors influencing S1 amplitude, such as LV function were not controlled, the effect of PR prolongation on S1 amplitude could not be demonstrated. Nevertheless, PR interval remains an important factor of consideration when interpreting S1 amplitude.

Using a digital phonograph, we showed that at the cardiac base, LUSB and RUSB, S1 amplitude and its ratio with S2 amplitude, S1/S2 are reduced in patients with LV systolic dysfunction expressed as reduced dP/dt or EF. S1/S2 modestly discriminated normal from abnormal left ventricular systolic function defined as dP/d$t \geq 1000$ mm Hg/s or EF $\geq 55\%$. The diagnostic accuracy of S1 for LV systolic dysfunction may be further optimized by improved calibration methods. A hand-held digital phonocardiograph confers the advantage of being accessible and portable as a diagnostic tool and therefore appears promising as an adjunctive bedside tool for evaluating left ventricular systolic function.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [5].

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