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Time-domain analysis of heart sound intensity in children with and without pulmonary artery hypertension: a pilot study using a digital stethoscope

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Abstract: We studied digital stethoscope recordings in children undergoing simultaneous catheterization of the pulmonary artery (PA) to determine whether time-domain analysis of heart sound intensity would aid in the diagnosis of PA hypertension (PAH). Heart sounds were recorded and stored in .wav mono audio format. We performed recordings for 20 seconds with sampling frequencies of 4,000 Hz at the second left intercostal space and the cardiac apex. We used programs written in the MATLAB 2010b environment to analyze signals. We annotated events representing the first (S1) and second (S2) heart sounds and the aortic (A2) and pulmonary (P2) components of S2. We calculated the intensity (I) of the extracted event area (x) as $I_k = \sum_{i=1}^{n} (x_k(i))^2$, where n is the total number of heart sound samples in the extracted event and k is A2, P2, S1, or S2. We defined PAH as mean PA pressure (mPAp) of at least 25 mmHg with PA wedge pressure of less than 15 mmHg. We studied 22 subjects (median age: 6 years [range: 0.25–19 years], 13 female), 11 with PAH (median mPAp: 55 mmHg [range: 25–97 mmHg]) and 11 without PAH (median mPAp: 15 mmHg [range: 8–24 mmHg]). The P2 : A2 ($P = .0001$) and P2 : S2 ($P = .0001$) intensity ratios were significantly different between subjects with and those without PAH. There was a linear correlation ($r > 0.7$) between the P2 : S2 and P2 : A2 intensity ratios and mPAp. We found that the P2 : A2 and P2 : S2 intensity ratios discriminated between children with and those without PAH. These findings may be useful for developing an acoustic device to diagnose PAH.

Keywords: auscultation, second heart sound, phonocardiography, machine learning.

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INTRODUCTION

Pulmonary artery hypertension (PAH) is a serious condition that imposes a global disease burden. If untreated, PAH has a high mortality, whether the cause of the disease is idiopathic, genetic mutation, or a complication of cardiac or pulmonary disease.[1,2] PAH is often diagnosed late because early clinical recognition is difficult, even after the onset of symptoms. There is, therefore, a need to explore or reevaluate the clinical diagnosis of PAH.

The auscultatory and phonocardiographic indicators of PAH have been described well, with plausible biological explanations for the findings.[3,4] Clinical indicators of PAH include increased loudness of the pulmonary component (P2) of the second heart sound (S2) and increased transmission of P2 to the cardiac apex. However, for the most part these descriptions predated the use of new digital stethoscopes, which are readily available and have the capability of recording and transmitting to a computer an acoustic tracing that can be optimized and analyzed later. There have been a few approaches to the noninvasive diagnosis of PAH combining phonocardiography and mathematical concepts. These investigators, for the most part, concentrated on the difficult task of identifying reliably and precisely S2, A2 (the aortic component of S2), P2, and the splitting interval between A2 and P2.[5-8] We undertook

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a pilot study to characterize the acoustic recordings of the heart sounds in children with and without PAH. Our concern was not precise localization of S2, A2, and P2 but rather a general exploration of the extracted features of the heart sounds that could provide relevant diagnostic information.

Sound signals, such as the heart sounds, may be analyzed in two modes, either the time domain or the frequency domain. Time-domain analysis quantifies the signal behavior over time and is plotted as voltage, current, or, in the case of heart sounds, intensity against time (seconds). In frequency-domain analysis, the component frequencies are spread across a frequency spectrum and are represented as peaks in the frequency spectrogram in units of hertz. We have reported the characteristics of the heart sounds in the frequency domain in children with and without pulmonary hypertensive vascular disease.[9] We hypothesized that, using recordings from a digital stethoscope, we might extract features of the heart sounds in the time domain around A2 and P2 that might differ between subjects with and those without PAH, rather than localizing A2 and P2 precisely. Therefore, we sought to extract features of the heart sounds obtained by digital stethoscope recordings from subjects with and without PAH, in an attempt to correlate these features with the simultaneously and directly measured pulmonary artery (PA) pressure at cardiac catheterization.

METHODS

The Research Ethics Board of the University of Alberta approved the study. All subjects or their parents gave informed and written consent to participate in the study. Informed assent was obtained from children who had reached sufficient developmental ability.

Clinical data collection

We approached pediatric-aged subjects undergoing right heart cardiac catheterization that was required for management of their underlying condition for inclusion in the study. We excluded subjects with congenitally abnormal aortic, pulmonary, or prosthetic valves.

The heart sounds were recorded with a 3M Littmann 3200 digital stethoscope, which works in conjunction with Zargis Cardioscan software (Zargis Medical, Princeton, NJ) to store recorded heart sounds in .wav mono audio format. Heart sound recordings were obtained over 20 seconds, with sampling frequencies of 4,000 Hz. We recorded the heart sounds sequentially at the second left intercostal space (2nd LICS) and the cardiac apex for 20 seconds. We used the MATLAB 2010b (MathWorks, Natick, MA) programming environment to implement methods for signal analysis and optimization. Heart sounds were recorded simultaneously with the direct PA pressure measurements obtained during right heart catheterization in a standard manner. Other hemodynamic data, including heart rate, PA wedge pressure (PAWp) or left atrial pressure (LAp), right atrial pressure, oxygen consumption ($\dot{V}o_2$), and systemic pressure and pulmonary blood flow, were collected within 5–10 minutes of the acoustic recordings. Pulmonary blood flow indexed to body surface area (QPI) was measured either by thermodilution catheter or by using the Fick equation with simultaneously measured $\dot{V}o_2$. The $\dot{V}o_2$ was measured by mass spectroscopy with the Ames 2000 or the Innocor (Innovision, Glamsbjerg, Denmark).[10] We calculated the pulmonary vascular resistance index (PVRI) as mean PA pressure (mPAp) minus mean PAWp (or mean LAp) divided by QPI. We measured QRS duration in lead V1 and PR interval in lead 2 from an electrocardiogram (ECG) recorded on the day of the cardiac catheterization.

Annotation of S1 and S2

We demarcated events containing S1 (the first heart sound) and from those containing S2 by identifying, from the acoustic recordings, events that were separated by intervals compatible with the relative duration of systole and diastole. Three cardiologists, blinded to the subjects' PA pressure, identified the timing of S1 and S2 independently. They listened to acoustic recordings and marked S1 and S2 on the phonocardiographic tracings. The cardiologists' interpretation was in agreement with our observation that in all of the subjects studied, the duration of diastole was longer than that of systole. Thus, the events identified as S1 and S2 occurred such that the interval between S1 and S2 was shorter than the interval between S2 and S1. Within these demarcated events, we identified the maximal positive and negative normalized amplitudes and annotated these as reference points for S1 and S2 events (Fig. 1). It is important to note that we did not identify S1 and S2 as precise points in time but rather as sound events surrounding S1 and S2.

Annotation of A2 and P2

PAH is defined as an mPAp of at least 25 mmHg and a PAWp or LAp no higher than 15 mmHg, measured at heart catheterization in subjects at rest.[11-13] Therefore, we divided the S1 and S2 events into groups, depending on whether the recording originated from subjects with mPAP of less than 25 mmHg or subjects with mPAp of at least 25 mmHg. In all subjects, the mean PAWp or

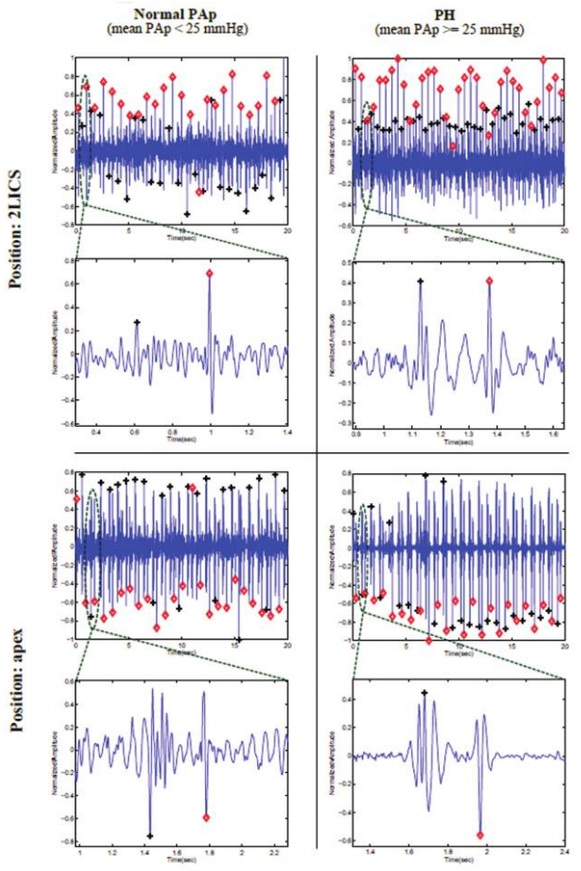

Figure 1. Annotation of S1 and S2. Normalized amplitudes (*Y*-axis) of surface acoustic recordings at the second left intercostal space (2LICS) and apex are plotted against time in seconds (*X*-axis). Black plus signs represent S1; red diamonds represent S2. PAp: pulmonary artery pressure; PH: pulmonary hypertension; S1: first heart sound; S2: second heart sound.

LAp was less than 15 mmHg. In order to find a reference point for A2 and P2 events, we superimposed all the events containing S2 recorded from the 2nd LICS and the apex (Fig. 2). We chose time 0 to coincide with the normalized amplitude peak. In subjects with mPAp of less than 25 mmHg, we observed another event occurring after the main or reference peak. In subjects with mPAp of at least 25 mmHg, we observed a secondary normalized amplitude event occurring before the main or reference peak. Thus, in subjects with mPAp of less than 25 mmHg and on the basis of timing and the assumption that A2 occurs before P2, we annotated the reference peak as A2 and the following event as P2. In subjects with mPAp of at least 25 mmHg, on the basis of timing and the assumption that A2 occurs before P2 (none of the subjects had a left bundle branch block), we designated the reference peak as P2 and the preceding event as A2.

Intensity calculation of S2, A2, P2, and S1

By visual inspection of the superimposed S2 waves (Fig. 2), we observed that the duration of the events designated A2 and P2 was 0.04 seconds, that is, 0.02 seconds on either side of the respective event peaks or reference point. Therefore, the duration of A2 and P2 events was considered to be 0.04 seconds, and the total duration of S2 events was considered to be 0.08 seconds. Similarly, the S1 event was extracted from heart sound data within 0.04 seconds on either side of the reference point or peak amplitude of S1 events.

We calculated the intensity (I) of the extracted event area (x), as $I_k = \sum_{i=1}^{n} (x_k(i))^2$, where n is the total number of heart sound samples in the extracted event and k is A2, P2, S1, or S2. We compared the relative intensity of the heart sound recordings at the apex and at the 2nd LICS in subjects whose mPAp was less than 25 mmHg (normal) with that in subjects whose mPAp was at least 25 mmHg (pulmonary hypertension) by comparing the ratios of the heart sound intensity S2 : S1, P2 : A2, and P2 : S2 (Figs. 3–5).

Statistical methods

The clinical and hemodynamic data from subjects with mPAp of less than 25 mmHg and mPAp of at least 25 mmHg were compared using the Mann-Whitney U test for two independent groups, since the data were not normally distributed. A P value of less than .05 was considered significant. We used Pearson's correlation coefficient to define the correlation between the heart sound intensity ratios P2 : S2 or P2 : A2 and the mPAp. We used Fisher's linear discriminant to test the separability of the extracted features between subjects with and those without PAH.

RESULTS

We collected recordings from 26 subjects. In 22 subjects, recordings were sufficiently free of background noise, artifacts, and low-amplitude signals to analyze at least one complete 20-second recording from either the 2nd LICS or the cardiac apex. Thus, we analyzed heart sound recordings from 22 children (9 males and 13 females). Twenty-two recordings obtained at the apex were suitable for analysis (11 subjects with mPAp of less than 25 mmHg and 11 subjects with mPAp of at least 25 mmHg). In 17 of the 22 subjects, the heart sound recordings from 2nd LICS were of sufficient quality to be analyzed. These included 10 subjects with PAH and 7 subjects with normal

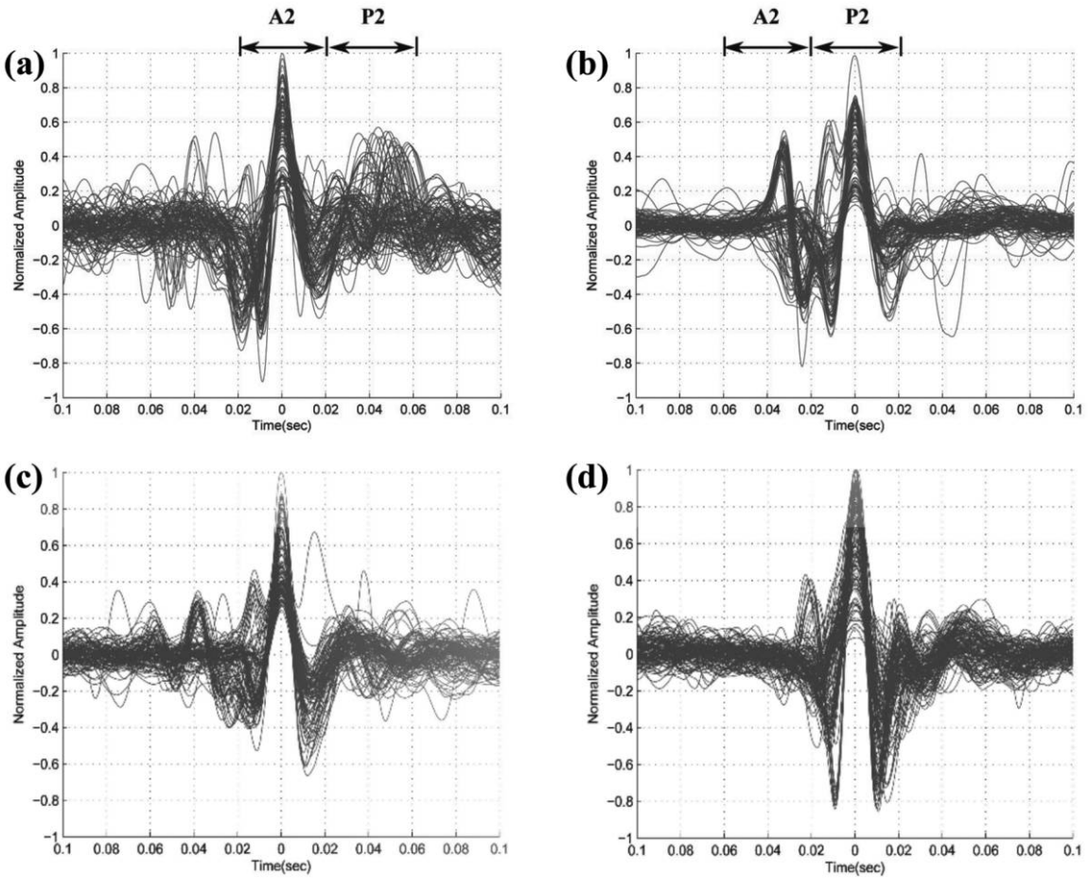

Figure 2. Analysis of A2 and P2 durations. The normalized amplitude (*Y*-axis) is plotted against time in seconds (*X*-axis). Time 0 is defined as the peak of S2. In subjects with mPAp $<$ 25 mmHg, the taller peak is considered to be A2. In subjects with mPAp $\geq$ 25 mmHg, the taller peak is considered to be P2. *a*, Recordings from second left intercostal space (2nd LICS) in subjects with mPAp $<$ 25 mmHg. *b*, Recordings from the apex in subjects with mPAp $\geq$ 25 mmHg. *c*, Recordings from the 2nd LICS in subjects with mPAp $<$ 25 mmHg. *d*, Recordings from apex from subjects with mPAp $\geq$ 25 mmHg. A2: aortic component of S2; mPAp: mean pulmonary artery pressure; P2: pulmonary component of S2; S2: second heart sound. A color version of this figure is available online.

PA pressure. The clinical and hemodynamic details of the subjects are included in Tables 1–6. The only statistically significant differences between the two groups were hemodynamic measurements that reflected the presence or absence of PAH. Of note, there was no difference in the LAp (or PAWp) or QPI between the two groups. The two groups did not differ by age, weight, height, body surface area (BSA), or body mass index (BMI; Table 7).

Extraction of A2 and P2

We found that in subjects with normal PA pressure, the normalized amplitude of the recordings obtained from the cardiac apex position clearly differentiated a defined peak before a more diffuse and lower-amplitude peak, which we annotated as A2 and P2, respectively (Fig. 2). In contrast, in subjects with PAH, 2 peaks are seen. The earlier and lower-amplitude peak we annotated as A2, and the later and higher-amplitude signal we annotated as P2.

Comparison of the intensity of S2, A2, and P2

We constructed box plots of 3 time-domain features from both groups of subjects by comparing the ratios of the normalized intensity of the heart sounds S2 : S1, P2 : A2, and P2 : S2. In Figure 3, it can be seen that S2 : S1 discriminates less well between subjects with PAH and those with normal PA pressure, particularly at the apex. Statistically significant differences in the heart sound intensity ratios P2 : A2 ($P = .0001$) and P2 : S2 ($P = .0001$) are found between the two groups from sounds recorded at both the 2nd LICS and the apex.

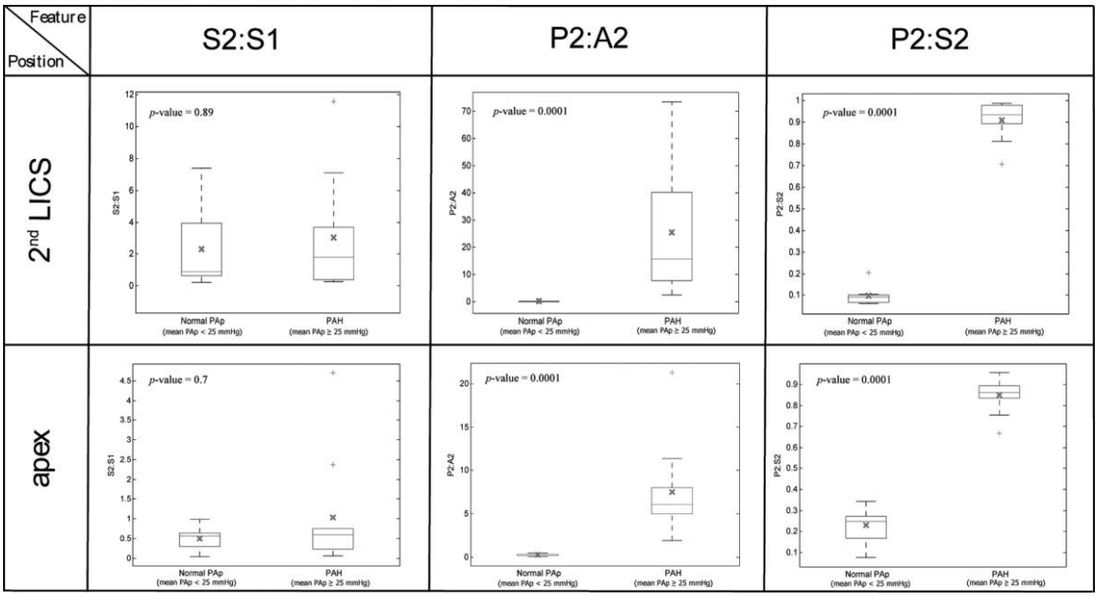

Figure 3. Boxplot of 3 time-domain features calculated from auscultation at the 2nd LICS and apex. The ratios of the intensity of the heart sounds P2 : A2 and P2 : S2 can be used to discriminate between mean PAp $\geq$ 25 mmHg ($P = .0001$) at 2nd LICS and that at apex. S2 : S1 ratios do not discriminate between subjects with and those without PAH. A2: aortic component of S2; PAH: pulmonary arterial hypertension; PAp: pulmonary artery pressure; P2: pulmonary component of S2; S1: first heart sound; S2: second heart sound; 2nd LICS: second left intercostal space.

In Figure 4, we have plotted the medians of the ratios of the intensities of the extracted features, P2 : S2 and P2 : A2, recorded from the 2nd LICS and the apex against mPAp. There is a linear correlation ($r > 0.7$) between the ratio P2 : S2 and mPAp from recordings at the 2nd LICS and the apex. However, for the intensity ratio P2 : A2, a linear correlation is seen only in the apical recordings.

In Figure 5*a* and 5*b*, we have plotted the intensity of P2 against that of S2 for each heartbeat for all subjects at the 2nd LICS and the apex. In Figure 5*c* and 5*d*, we have plotted the intensity of P2 against that of A2 for each heart beat for all subjects at the 2nd LICS and the apex.

DISCUSSION

The main finding of our investigation is that we can discriminate between the intensity of heart sound events that we annotated as P2 and A2 in children with PAH and that in children without PAH in the recordings taken simultaneously with direct PA pressure measurements (Figs. 3, 5). We found that P2 events have increased intensity in children with PAH. In addition, in children with PAH, the increased intensity of P2 events is transmitted to the apex and overshadows A2 events, in contrast to children without PAH. Experienced clinicians diagnose PAH by auscultation if they hear a loud P2 at the 2nd LICS and hear the transmission of P2 to the apex, where usually only A2 is heard in the absence of PAH.[3,4,14] These observations add credibility and biological plausibility to our findings in children and raise the potential for the interpretation of digitally recorded heart sounds by medical personnel without years of experience in auscultation.

We found that the heart sound intensity ratios P2 : S2 and P2 : A2 were useful for discriminating subjects with PAH. In our study, we were interested in discovering whether extracted sound features around S1 and S2 would be useful in the diagnosis of PAH and whether it would be possible to demarcate these events without a simultaneous ECG, echocardiogram, or pressure tracing on the same platform as the heart sound recordings. The finding that extracted features that make up S2 in the time domain distinguish subjects with PAH from those with normal PA pressure is encouraging and is further substantiated by the finding that the ratios of the intensity of the components that make up S2, that is, P2 and A2, are also discriminatory for PAH. The precise origin of the extracted features of S2, P2, and A2 cannot be identified in our study, but there is sufficient evidence to suggest that PAH may be identified quantitatively by S2.

We divided the subjects into two groups, based on whether mPAp was less than 25 mmHg or not. In ad-

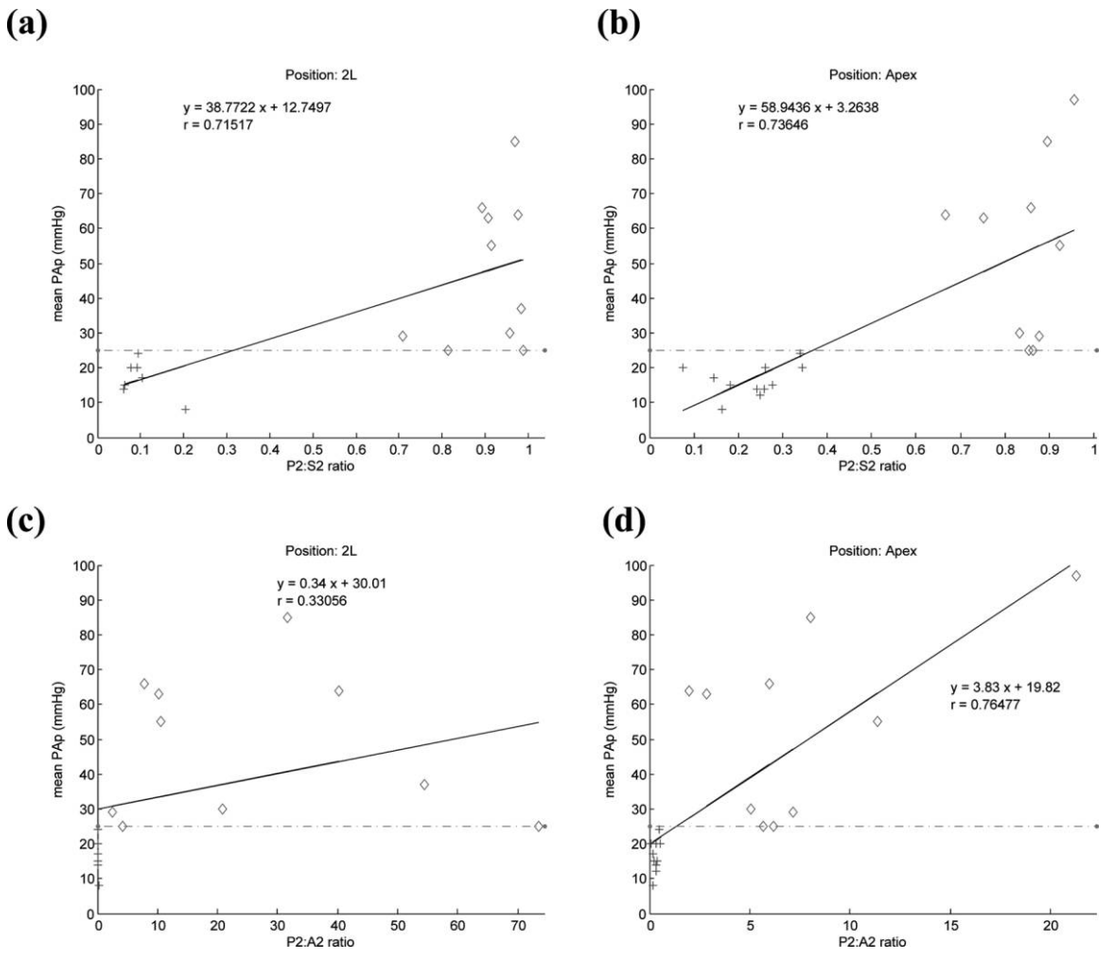

Figure 4. Individual patients mean PAp (*Y*-axis) plotted against the median of the heart sound intensity ratios of P2 : S2 and P2 : A2 (*X*-axis). *a*, P2 : S2 heart sound intensity ratio at the second left intercostal space (2L). *b*, P2 : S2 heart sound intensity ratio at the apex. *c*, P2 : A2 heart sound intensity ratio at 2L. *d*, P2 : A2 heart sound ratio intensity at the apex. Plus signs indicate subjects with mean PAp $<$ 25 mmHg. Diamonds indicate subjects with mean PAp $\geq$ 25 mmHg. The dot-dashed line represents the mean PAp of 25 mmHg. Values on or above this line indicate pulmonary artery hypertension, and values below it indicate normal PAp, according to the internationally recognized definition of pulmonary artery hypertension. The correlations of the heart sound intensity ratio at 2L for P2 : A2 with mean PAp (*c*) were poor in comparison with those of the P2 : A2 intensity ratio at the apex (*d*) and the S2 : P2 intensity ratios at 2L (*a*) and the cardiac apex (*b*). A2: aortic component of S2; PAp: pulmonary artery pressure; P2: pulmonary component of S2; S2: second heart sound.

dition, all of our subjects in both groups had an LAp or PAWp of less than 15 mmHg. This is in keeping with the current definition of and recommendations for the diagnosis of PAH.[11,13,15] The only statistically significant differences in the hemodynamic measurements between the two groups were mPAp (55 vs. 15 mmHg; $P < .001$) and PVRI (10.7 vs. 2 Wood units/m^2; $P < .001$). This supports our finding that the S2 (A2 and P2) events were largely influenced by pulmonary vascular hemodynamic measurements; see Tables 3–7.

The QRS complex duration was shorter in subjects with PAH (77 vs. 103 ms; $P = .02$). The children without PAH had repaired congenital heart disease or had undergone heart transplants and may often have had a widened QRS postoperatively. A longer QRS or prolonged right-heart conduction time might influence the splitting interval between A2 and P2 but not the intensity of S2.

There were no statistically significant differences in age, body weight, BSA, or BMI between the two groups, suggesting that the differences in the intensity of P2

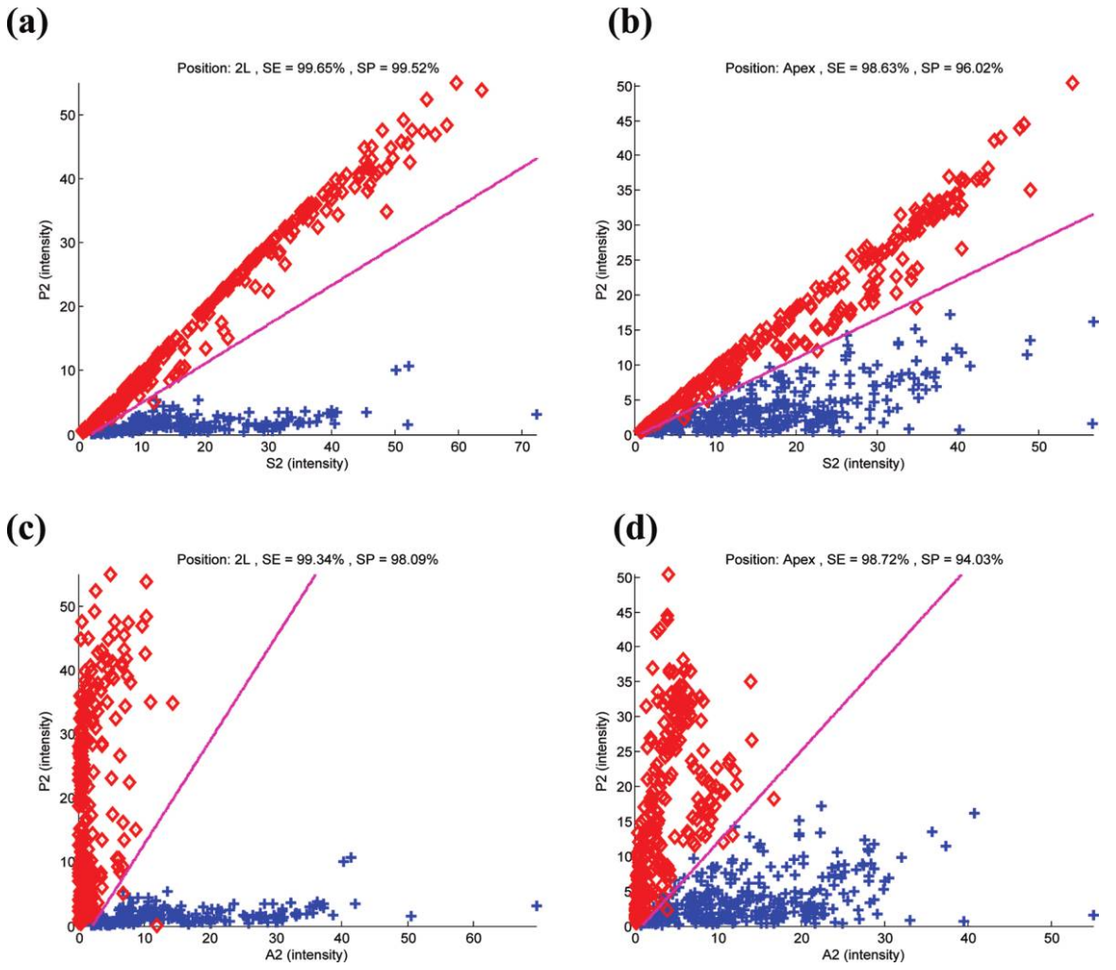

Figure 5. Intensity of P2 plotted against intensity of S2 or A2 for each heartbeat contained in each acoustic recording. *a*, Intensity of P2 against that of S2 recorded at the second left intercostal space (2L). *b*, Intensity of P2 against that of S2 recorded at the apex. *c*, Intensity of P2 against that of A2 at 2L. *d*, Intensity of P2 against that of A2 at the apex. Blue plus signs indicate heartbeats recorded in subjects with mean PAp $<$ 25 mmHg. Red diamonds indicate heartbeats recorded in subjects with mean PAp $\geq$ 25 mmHg. A2: aortic component of S2; PAp: pulmonary artery pressure; P2: pulmonary component of S2; SE: sensitivity; SP: specificity; S2: second heart sound.

events were unrelated to age, body size, or habitus. However, further studies are needed to reproduce our findings in subjects with an increased BMI, as increased body fat or muscle may impair the transmission of heart sounds from body surface microphones.

In our cohort of children, we had 2 subjects with a mean PA pressure of 25 mmHg and 1 with a mean PA pressure of 24 mmHg. In Figure 4, the dashed line represents an mPAp of 25 mmHg, which demarcates normal from abnormal mPAp. It can be seen that the P2 : S2 and P2 : A2 intensity ratios are less discriminatory for mPAp close to 25 mmHg. Differentiating subjects with borderline signs of PAH will be challenging. Nevertheless, Figure 5 demonstrates that if all recorded heartbeats are included, then the estimation of the intensity of S2, A2, and P2 events reveals an easily visible separation between recordings from children with PAH and those from children without PAH. The sensitivity and specificity to discriminate between PAH and normal PA pressure are both high.

In contrast to a recent report,[16] we did not find that the intensity of the ratio S2 : S1 discriminated between PAH and non-PAH. We found the intensity ratios of the heart sounds P2 : S2 and P2 : A2 to be more indicative of PAH. However, Chan et al.[16] used the term "complexity" of S1 and S2, which may differ from intensity. In addition, we

Table 1. Subjects 1–11, with pulmonary artery hypertension (mean PAp $\geq$ 25 mmHg)

Subject	Age, years	Height, m	Weight, kg	BSA, m^2	BMI, kg/m^2	Sex	Diagnosis
1	0.8	0.66	6.1	0.32	14.0	M	Repaired CDH
2	0.9	0.64	5.9	0.31	14.4	F	Unrepaired CHD
3	2	0.88	11.9	0.53	15.5	M	IPAH
4	3	0.90	12.3	0.55	15.2	M	Unrepaired CHD
5	7	1.23	23	0.89	15.2	F	IPAH
6	12	1.62	62	1.66	23.6	F	Repaired CHD
7	8	1.33	33.2	1.1	18.8	M	IPAH
8	9	1.34	29.9	1.06	16.7	F	Repaired CHD
9	12	1.62	62	1.66	23.6	F	Repaired CHD
10	12	1.49	59	1.53	26.6	M	IPAH
11	15	1.30	31.7	1.06	18.8	F	IPAH
Median	8	1.3	29.9	1.06	16.7		
Minimum	0.8	0.64	5.9	0.31	14.0		
Maximum	15	1.62	62	1.66	26.6		

Note: There were 5 male and 6 female subjects in this group. BMI: body mass index; BSA: body surface area; CDH: congenital diaphragmatic hernia; CHD: congenital heart disease; IPAH: idiopathic pulmonary artery hypertension; PAp: pulmonary artery pressure.

studied children, who may have acoustic precordial characteristics different from those of adults.

We did not assess the effect of right versus left ventricular function or right-left ventricular interactions in PAH on the acoustic recordings. One of the aims of our study was to determine whether one could separate A2 from P2 and S1 from S2 without a simultaneous electrocardiographic or pressure tracing on the same platform as the heart sound recording. We did, however, measure the PA pressure simultaneously with the acoustic recordings.

The fidelity of the recordings at the cardiac apex was sufficient for analysis in only 22 of 26 subjects and that

Table 2. Subjects 12–22, with normal PAp (mean PAp $<$ 25 mmHg)

Subject	Age, years	Height, m	Weight, kg	BSA, m^2	BMI, kg/m^2	Sex	Diagnosis
12	0.8	0.71	8.3	0.39	16.5	M	Unrepaired CHD
13	2	0.77	9.8	0.44	16.7	M	Repaired CHD
14	3	1.01	18.1	0.7	17.7	M	Unrepaired CHD
15	0.25	0.52	4.5	0.24	16.6	F	Repaired CHD
16	2	0.87	11.4	0.51	15.1	F	Unrepaired CHD
17	5	1.17	19	0.79	13.9	F	Post–heart transplant
18	3	0.89	12.8	0.55	16.2	F	Post–heart transplant
19	10	1.29	31.5	1.06	18.9	F	Post–heart transplant
20	17	1.58	59	1.6	23.6	F	Repaired CHD
21	17	1.62	42	1.4	16.0	F	Repaired CHD
22	19	1.75	59	1.72	19.3	M	Post–heart transplant
Median	3	1.01	18.1	0.7	16.6		
Minimum	0.25	0.52	4.5	0.24	13.9		
Maximum	19	1.75	59	1.72	23.6		

Note: There were 4 male and 7 female subjects in this group. BMI: body mass index; BSA: body surface area; CHD: congenital heart disease; PAp: pulmonary artery pressure.

Table 3. Pulmonary vascular hemodynamic data for subjects 1–11, with pulmonary artery hypertension (mean PAp $\geq$ 25 mmHg)

Subject	Mean PAp, mmHg	Systolic PAp, mmHg	Diastolic PAp, mmHg	Mean LAp or PAWp, mmHg	PVRI,[a] WU/m^2	QPI, L/min/m^2
1	29	48	13	6	4.8	4.8
2	25	38	12	2	5.2	4.4
3	64	89	34	9	13.1	4.2
4	66	92	47	7	10.7	5.5
5	25	31	19	7	5.5	3.3
6	97	140	66	10	27.2	3.2
7	37	49	26	10	9.3	2.9
8	30	46	14	5	7.4	3.4
9	85	119	57	6	27.2	2.9
10	63	95	37	7	19.3	2.9
11	55	99	37	6	16.7	2.9
Median	55	89	34	7	10.7	3.3
Minimum	25	31	12	2	4.8	2.9
Maximum	97	140	66	10	27.2	5.5

Note: LAp: left atrial pressure; PAp: pulmonary artery pressure; PAWp: pulmonary artery wedge pressure; PVRI: pulmonary vascular resistance index; QPI: pulmonary blood flow index; WU: Wood units.

[a] PVRI calculated from pressure at the time of QPI measurement, not acoustic recording.

Table 4. Pulmonary vascular hemodynamic data for subjects 12–22, with normal pulmonary artery pressure (mean PAp $<$ 25 mmHg)

Subject	Mean PAp, mmHg	Systolic PAp, mmHg	Diastolic PAp, mmHg	Mean LAp or PAWp, mmHg	PVRI,[a] WU/m^2	QPI, L/min/m^2
12	20	29	17	11	2.8	3.2
13	20	32	11	8	3.1	3.9
14	15	25	10	4	.8	14.4
15	15	25	7	6	2.0	4.4
16	24	34	15	9	4.8	3.1
17	14	27	7	7	NA	NA
18	20	30	12	10	2.6	3.8
19	8	11	5	5	1.3	2.3
20	17	31	9	7	2.8	3.6
21	12	22	4	5	1.6	4.5
22	14	20	8	10	1.5	2.7
Median	15	27	9	7	2	4
Minimum	8	11	4	4	.8	2.3
Maximum	24	34	17	11	4.8	14.4

Note: LAp: left atrial pressure; NA: not available; PAp: pulmonary artery pressure; PAWp: pulmonary artery wedge pressure; PVRI: pulmonary vascular resistance index; QPI: pulmonary blood flow index; WU: Wood units.

[a] PVRI calculated from pressure at the time of QPI measurement, not acoustic recording.

Table 5. Systemic vascular hemodynamic and electrocardiographic data for subjects 1–11, with pulmonary artery hypertension (mean PAp $\geq$ 25 mmHg)

Subject	Mean BP, mmHg	Systolic BP, mmHg	Diastolic BP, mmHg	Mean RAp, mmHg	Heart rate, beats/min	QRS duration, ms	PR interval, ms
1	59	83	41	2	130	62	66
2	68	93	47	1	130	75	91
3	48	70	34	8	99	97	98
4	70	82	56	7	115	77	92
5	70	97	50	3	66	71	88
6	93	122	73	5	107	71	71
7	96	44	67	3	75	110	106
8	62	93	42	4	65	110	88
9	88	106	71	6	90	71	71
10	78	110	56	4	70	77	71
11	68	99	53	3	80	132	110
Median	70	93	53	4	90	77	88
Minimum	48	44	34	1	65	62	66
Maximum	96	122	73	8	130	132	110

Note: BP: systemic blood pressure; PAp: pulmonary artery pressure; RAp: right atrial pressure.

at the 2nd LICS in 17 of those 22. This drawback will have to be resolved in future studies.

We made assumptions about S1 and S2 that, although biologically plausible and consistent with the known descriptions of S1 and S2, remain to be validated. Future studies may improve the accuracy by including simultaneous recordings of pressure, ECG, and echocardiogram on the same platform as the acoustic recordings.

Conclusion. The main finding of our investigation is that there is a clear separation between the intensities of

Table 6. Systemic vascular hemodynamic and electrocardiographic data for subjects 12–22, with normal PAp (mean PAp $<$ 25 mmHg)

Subject	Mean BP, mmHg	Systolic BP, mmHg	Diastolic BP, mmHg	Mean RAp, mmHg	Heart rate, beats/min	QRS duration, ms	PR interval, ms
12	54	92	36	11	130	77	84
13	60	95	39	6	78	111	116
14	60	71	46	1	111	120	114
15	52	67	37	1	134	99	87
16	63	80	50	8	108	91	97
17	42	63	32	8	82	101	98
18	75	97	53	3	105	101	92
19	55	65	45	1	96	134	80
20	73	108	56	7	78	147	136
21	67	93	51	1	90	108	96
22	116	72	96	1	70	103	116
Median	60	80	46	3	96	103	97
Minimum	42	63	32	1	70	77	80
Maximum	116	108	96	11	134	147	136

Note: BP: systemic blood pressure; PAp: pulmonary artery pressure; RAp: right atrial pressure.

Table 7. Comparison of clinical and hemodynamic data between subjects with pulmonary artery hypertension (mean PAp $\geq$ 25 mmHg) and those with normal PAp (mean PAp $<$ 25 mmHg)

Variables	*P* value
Age	.8
Height	.6
Weight	.5
Body surface area	.6
Body mass index	.9
Systolic PAp	<.001*
Diastolic PAp	<.001*
Mean PAp	<.001*
Pulmonary vascular resistance index	<.001*
Pulmonary blood flow index	.9
Mean left atrial pressure	.6
Mean right atrial pressure	.8
Systolic blood pressure	.2
Diastolic blood pressure	.2
Mean blood pressure	.1
Heart rate	.5
QRS duration, lead V1	.02*
PR interval, lead 2	.07

Note: PAp: pulmonary artery pressure.
* Significant result ($P < .05$).

P2 and A2 in children with PAH and those in children without PAH in acoustic recordings collected with a handheld digital stethoscope simultaneously with direct PA pressure measurements. The ratios of the heart sound intensities P2 : A2 and P2 : S2 discriminate between subjects with and those without PAH. These findings may be of value in the development of an acoustic device to diagnose PAH with more accuracy than conventional auscultation.

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