International Journal of Cardiology 173 (2014) 92–99

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Spectral analysis of the heart sounds in children with and without pulmonary artery hypertension

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ARTICLE INFO

Article history:
Received 23 December 2013
Accepted 13 February 2014
Available online 24 February 2014

Keywords:
Machine learning
Phonocardiography
Auscultation
Stethoscope
Fast Fourier transform

ABSTRACT

Background: Pulmonary artery hypertension (PAH) is difficult to recognize clinically. Digital stethoscopes offer an opportunity to re-evaluate the diagnosis of PAH. We hypothesized that spectral analysis of heart sound frequencies using recordings from a digital stethoscope would differ between children with and without PAH.
Methods: We recorded heart sounds using a digital stethoscope from 27 subjects (12 males) with a median age of 7 years (3 months to 19 years) undergoing simultaneous cardiac catheterization. 13 subjects had a mean pulmonary artery pressure (mPAp) < 25 mm Hg (8–24 mm Hg). 14 subjects had a mPAp ≥ 25 mm Hg (25–97 mm Hg). We applied the fast Fourier transform, power spectral analysis, separability testing, and linear discriminant analysis with leave-one-out cross-validation to the heart sounds recorded from the cardiac apex and 2nd left intercostal space (LICS) to examine the frequency domain. The significance of the results was determined using a t-test and rank-sum test.
Results: The relative power of the frequencies 21–22 Hz of the heart sounds recorded at the 2nd LICS was decreased significantly in subjects mPAp ≥ 25 mm Hg versus < 25 mm Hg.
Conclusions: Heart sound signals of patients with PAH contain significantly less relative power in the band 21–22 Hz compared to subjects with normal PAp. Information contained in the frequency domain may be useful in diagnosing PAH and aid the development of auscultation based techniques for diagnosing PAH. In the future, utilizing the diagnostic information contained in heart sounds recordings may require analysis of both the time and frequency domains.

1. Introduction

Pulmonary artery hypertension (PAH) is a serious condition that imposes a global disease burden. 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 [3]. There is, therefore, a need to explore or re-evaluate the clinical diagnosis of PAH.

The results of auscultation and phonocardiographic indicators of PAH have been described well together with plausible biological explanations for the findings [4,5]. 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, these descriptions have generally predated the use of new digital stethoscopes, which are readily available and have the capability of recording an acoustic tracing that can be optimized and analyzed later. There have been a few approaches to the non-invasive diagnosis of PAH that have been based on combining phonocardiography and mathematical analysis. These investigations, for the most part, have concentrated on the difficult task of identifying S2 and P2 reliably and precisely together with the splitting interval between the aortic component of S2 (A2) and P2 [6–9]. We undertook a pilot study to characterize the acoustic recordings of the heart sounds in children with and without PAH. Precise localization of S2, A2 and P2 was not part of our objective. Instead our goal was to explore the heart sound frequencies that might be associated with pulmonary artery hypertension.

We hypothesized that using recordings from a digital stethoscope we might demonstrate, through spectral analysis, heart sound frequencies

Abbreviations: A2, aortic component of second heart sound; LAp, left atrial pressure; LDA, linear discriminant analysis; 2nd LICS, 2nd left intercostal space; LOO, leave-one-out cross-validation; P2, pulmonary component of second heart sound; PA, pulmonary artery; PAH, pulmonary artery hypertension; PAp, pulmonary artery pressure; PAWp, pulmonary artery wedge pressure; PSD, power spectral density; QPI, pulmonary blood flow index; RAp, right atrial pressure; S2, second heart sound; VO_2, oxygen consumption.

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http://dx.doi.org/10.1016/j.ijcard.2014.02.025
0167-5273/

that would differ between subjects with and without pulmonary artery hypertension. Therefore, we sought to identify heart sound frequencies associated with the simultaneously measured pulmonary artery (PA) pressure at cardiac catheterization by spectral analysis obtained by digital stethoscope recordings from children with and without PAH.

2. Materials and methods

2.1. Ethics statement

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 were sufficiently developmentally able.

2.2. Clinical data collection

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

The heart sounds were recorded using a 3M™ Littmann^{R} 3200 digital stethoscope (3M Inc., Denmark), using Zargis Cardioscan™ software (Zargis Medical Corp., Princeton, NJ, USA) to store recorded heart sounds in *.wav mono audio format. Heart sound recordings were obtained over 20 s with sampling frequencies of 4000 Hz. We recorded the heart sounds sequentially at the 2nd left intercostal space (2nd LICS) and the cardiac apex for 20 s. We used soft ware developed in MATLAB 2010b (The MathWorks, Inc., Natick, MA, USA) 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 using fluid filled catheters and transducers zeroed at the mid thoracic level. Other hemodynamic data including, heart rate, pulmonary artery wedge pressure (PAWp) or left atrial pressure (LAp) or left ventricular end diastolic pressure, right atrial pressure (RAp), oxygen consumption (VO_2) and systemic pressure and pulmonary blood flow were collected within 5–10 min of the acoustic recordings. Pulmonary blood flow indexed to body surface area (QPI) was measured either by thermodilution catheter or using the Fick equation with simultaneously measured oxygen consumption (VO_2). Oxygen consumption was measured by mass spectroscopy using the Ames 2000 or the Innocor (Innovision, Denmark). We calculated the pulmonary vascular resistance index (PVRI) from the formula mean PAp-mean PAWp or mean LAp/QPI. We measured QRS duration in lead V1 and PR interval in lead 2 from an electrocardiogram recorded on the day of the cardiac catheterization.

2.3. Definition of pulmonary artery hypertension

Pulmonary artery hypertension is defined as a mean PA pressure ≥ 25 mm Hg and a PAWp or LAp ≤15 mm Hg measured at heart catheterization in subjects at rest [10–12]. Therefore, we divided the recordings into 2 groups depending on whether the recording originated from subjects with a mean PA pressure < or ≥25 mm Hg. In all subjects the mean PAWp or LAp was <15 mm Hg.

2.4. Heart sound analysis

We analyzed the heart sound recordings with spectral feature extraction, in particular the relative power of the heart sound frequency bands. We performed separability tests to discover which recording site (the 2nd LICS or the apex) was more informative in diagnosing PAH. We applied linear discriminant analysis (LDA) to each spectral feature separately, with the aim of distinguishing subjects with and without PAH.

2.5. Spectral analysis

We applied fast Fourier transform on the heart sounds recorded from the cardiac apex and 2nd LICS to examine the frequency domain.

2.6. Spectral feature extraction

We investigated the power spectrum of heart sounds recorded at two positions (2nd LICS and apex). Power spectral density (PSD) analysis was undertaken. To answer the question which auscultation position and which frequency band provided the best detection of PAH, we explored systematically different heart sound frequency bands [F: (F + W)] Hz as follows:

Bandpass filter: a bandpass filter is applied to each heart sound recording to extract the heart sound data in a specific frequency band [F: (F + W)] Hz. We used Butterworth filters (3rd order) as they offer good transition band characteristics at low coefficient orders; as a result, they can be implemented efficiently.

Relative power (RP): the relative power of a certain frequency band (extracted in the previous step) is obtained by dividing the power of this frequency band by the power of the total frequency band:

$$RP_i = \frac{P_i(F, F+W)}{P_i(F_{min}, F_{max})}, \quad (1)$$

where P is the power of the frequency band [F, F + W] Hz and P (Fmin, Fmax) is the power of the wide frequency range [1,80] Hz at the auscultation position.

2.7. Separability test

The separability test was carried out to determine which auscultation position (2nd LICS or apex) was more informative for diagnosing PAH. After calculating the RP for all subjects within a certain frequency band [F: (F + W)] Hz, we computed the average RP for PAH subjects ($\mu \geq 25$) and subjects with normal pulmonary artery pressures ($\mu < 25$). The subscripts ≥ 25 and <25 indicate PAH subjects and subjects with normal PA pressure, respectively. Then we computed the standard deviation of RP within both populations, denoted by ($\sigma \geq 25$) and ($\sigma < 25$), respectively. The linear separability criterion J was computed as follows:

$$J(F, F+W) = \frac{|\mu \geq 25(F, F+W) - \mu < 25(F, F+W)|}{\sigma \geq 25(F, F+W) + \sigma < 25(F, F+W)}. \quad (2)$$

We calculate the index J (F, F + W) over a range of frequency bands, i.e., F = 1, 2,..., 79 Hz and W = 1, 2,..., 79 Hz, corresponding to 6241 different frequency bands within [1,80] Hz; we depict the value J as a function of F and W.

2.8. Linear discriminant analysis (LDA)

We assessed the classification performance with LDA through leave-one-out (LOO) cross-validation. We created each training set by taking all the samples except one with the corresponding test set being the sample left out. Thus, for n samples, we have n different training sets (each yielding a coefficient vector w) and n different test sets. We conducted this procedure for each spectral feature. We analyzed the discriminative power of each feature in terms of LDA classification error. We selected the spectral features

Table 1
Demographic data for subjects #1–14 with pulmonary artery hypertension and mean pulmonary artery pressure ≥ 25 mm Hg.

Subject #	Age (years)	Height (m)	Weight (kg)	BSA ($m^{2)}$	BMI (kg/m^2)	Gender	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
12	12	1.54	77.6	1.76	32.7	F	Repaired CDH
13	11	1.55	54.8	1.53	22.8	M	IPAH
14	1.7	0.85	11.6	0.55	16.1	M	IPAH
Median	8.5	1.31	30.8	1.06	17.7	7M:7F	
Minimum	0.8	0.64	5.9	0.31	14		
Maximum	15	1.62	77.6	1.76	32.7		

Abbreviations: m = meters, kg = kilograms, BSA = body surface area, BMI = body mass index, M = male, F = female, CDH = congenital diaphragmatic hernia, CHD = congenital heart disease, IPAH = idiopathic pulmonary hypertension.