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Experimental Study of Acoustic Densitometry in Detecting Left Ventricular Myocardium Damage Secondary to Hypoxic Pulmonary Hypertension

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Abstract: Objective To evaluate the value of acoustic densitometry (AD) in detecting myocardium damage of the left ventricle secondry to hypoxic pulmonary hypertension (PH). **Methods** Using the rabbit model of hypoxic PH, the density of various locations of the left ventricular myocardium in the hypoxic PH group and the normal control group were detected by the technique of AD. **Results** Compared with the normal control group, average image intensity (AII) of the left ventricular anterior wall (LVA) in the hypoxic PH group increased ($P<0.05$), while the difference between the standard deviation intensity (SDI) and peak to peak intensity (CVIB) of LVA were not significantly different ($P>0.05$). The CVIB of the middle of the interventricular septum (IVSM) in the hypoxic PH group was lower than that of the normal control group ($P<0.05$). The AII of IVSM and the left ventricle posterior wall (LVPW) in the hypoxic PH group were higher than those of the normal control group ($P<0.05$). In various locations of the left ventricular myocardium, the value of AII and the left ventricle diastolic end pressure (LVDEP) were positively related ($r=0.6206-0.6311$, $P<0.01$). **Conclusions** The AD technique is useful in evaluating the extent of damage of the left ventricular myocardium in hypoxic PH. [**Chin J Contemp Pediatr, 2003, 5(5): 398-402**]

Key words: Acoustic densitometry; Pulmonary hypertension; Left ventricle; Myocardium

声学密度技术定量评价缺氧肺动脉高压对左室心肌损伤的实验研究

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[**摘 要**] **目的** 探讨声学密度定量(AD)技术定量评价缺氧肺动脉高压(PH)后左室心肌损害的应用价值。**方法** 在建立缺氧肺动脉高压兔模型的基础上,应用AD技术对PH组和正常对照组兔左室相应部位心肌密度值进行测定。**结果** 与正常组比较,缺氧PH组左室前壁的背向散射强度标准差(SDI)及背向散射强度周期性变化幅度(CVIB)差异无统计学意义($P>0.05$),但心动周期背向散射强度平均值(AII)明显升高($P<0.05$);室间隔中部CVIB明显减低($P<0.05$),AII明显升高($P<0.05$);左室后壁AII明显升高($P<0.05$)。PH组左室心肌不同部位AII值与左室舒张末压(LVDEP)成正相关($r=0.6206\sim0.6311$, $P<0.01$)。**结论** AD技术对判定缺氧PH后左室心肌损伤改变较为客观、简便,有较高的应用价值。 [**中国当代儿科杂志,2003, 5(5): 398-402**]

[**关 键 词**] 声学密度定量;肺动脉高压;左室;心肌
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Acoustic densitometry (AD) is a trauma free ultrasonic diagnosis technique. It is a quantified method based on the integral of ultrasonic backscatter. The integral of ultrasonic backscatter is the result of the interaction of ultrasound with any types of conductible medium in myocardium tissue. When the ultrasonic condition is relatively constant, the amount of scattering ultrasonic wave of a special segment of

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myocardium is a sensitive index that reflects the speciality of this segment of myocardium, and it can be expressed as decibels[1]. When there are any pathological changes in myocardium, the corresponding changes would appear in its structure. So the AD technique combined with computer automatic disposal and analysis of the ultrasonic backscatter signal of myocardium can be used to evaluate the speciality of this segment of myocardium. At present, there are some reports about the speciality of myocardium after ischemia and stroke[2] evaluated by the AD technique. But no reports about myocardium damage of left ventricle secondary to pulmonary hypertension (PH) evaluated by the AD technique both in China and overseas. On the basis of the rabbit model of hypoxic PH, the AD technique was applied to study myocardium damage of the left ventricle secondary to hypoxic PH and to probe into the possible mechanism to provide another application for AD technique in clinical and researching field.

Materials and methods

Establishment of the rabbit model of hypoxic PH and grouping

Thirty healthy adult rabbits were provided by the Experiment Animal Center of the First and Third Military Medical University. After being catheterized in the right ventricle through the right common carotid and the right external jugular vein, the mean artery pressure (MAP) and shrinking right ventricle pressure (SRVP), which represented the pulmonary artery pressure (PAP), were measured and recorded. The rabbits were intubated and connected with baby artificial respirators (PIP 18 cmH_2O, PEEP 2 cmH_2O, FiO_2 20% – 30%). The rabbits were incubated divided into 2 groups: 10 rabbits of the normal control group were aerated with FiO_2 of 25% – 30%; 20 rabbits of the hypoxic PH group were aerated with FiO_2 of 9% – 15%. Blood gas was measured after the SRVP ascending.

The measurement of quality control indexes of the hypoxic PH group model

At the end of the experiment, the mean RVP, the mean PAP, the maximium ascending velocity of the right ventricle (RVdp/dt max), the left ventricle shrinking pressure (LVSP), the left ventricle diastolic end pressure (LVDEP) and the maximium ascending and descending velocity of the left ventricle (+ LVdp/dt max) were measured by cardiac catheterization and the multi-conductor physiological instrument.

At the end of the experiment, the oxygen content of pulmonary aorta was also measured.

The hearts were removed and put in the pre-cold PBS (0.02 mmol/L, pH 7.4). After the hearts were washed and wrapped up in filter paper, their weight was measured. The atrium and free wall of right ventricle along the ring between the atrium and ventricle were cut off. The weight of the remaining interventricle septum and the free wall of the left ventricle were regraded as the weight of the left ventricle. The ratio of the left ventricle weight to the body weight was then used as the index of the left ventricle weight (LVWI).

The speciality of myocardium detected by the AD technique

The diagnostic ultrasonic instrument was an American Hewlett-Packard SONOS 5500. It had an acoustic densitometry, an ultrasonic backscatter software (AD-IBS) package and a compact disc recording system. The frequency of phased-array detector was 2.0~2.4 MHz.

Before examining the rabbits, the chest hair was removed by 1% sulfuric natrium and a 3.3 cm × 2.0 cm space was left for ultrasonic examination. The rabbits were examined in the left lateral position.

The standard two-dimensional images were acquired at the short axial layer of left ventricle and 4 cavities layer of apex of heart. Such conditions as the depth, general gain, time gain compensation (TGC), lateral gain compensation (LGC), transmit power compression were constant. The images were recorded on the CD system.

The sampling box (oval, 21 pixel × 21 pixel) was put on the middle of interventricular septum (IVSM), the ring of mitral valve, the middle of left ventricular cavity, the inferior and posterior wall of the left ventricle (LVPW) at short axial layer of the left ventricle. The images were followed closely with

cardiac cycle to keep the sampling's location unchanged. The interference of the signals of endocardium and epicardium was avoided.

The automatic analysis system of AD-IBS was used to analyse the images. The results included 3 indexes. Peak to peak intensity (PPI), also called CVIB, was the periodical chang of ultrasonic backscatter intensity with the cardiac cycle. The average image intensity (AII) was the average value of ultrasonic backscatter intensity in one or several cardiac cycles. The standard deviation intensity (SDI) was the standard deviation of ultrasonic backscatter intensity.

Statistical anaysis

All data were shown as the mean value and the standard deviation. The statistical analysis of paired design t test and regression analysis were used.

Results

Blood gas analysis

Compared with the normal control group, the value of pH in the hypoxic PH group was higher ($P<0.01$), but the value of PaO_2 and $PaCO_2$ decreased ($P<0.01$). See Table 1.

Table 1 Results of the blood gas analysis ($\bar{x} \pm s$)

Groups	n	pH	PaO_2(kPa)	$PaCO_2$(kPa)	HCO_3^-(mmol/L)
Normal conrol	10	7.40±0.02	13.60±0.47	5.42±0.37	25.57±1.14
Hypoxic PH	20	7.48±0.00[a]	5.89±0.55[a]	4.61±0.18[a]	25.41±1.45

Note: a vs control group $P<0.01$

The kinetics of blood flow and the weight of left ventricle

The LVWI, LVSP and +dp/dt max in the hypoxic PH group were not significantly different from those of the normal control group. But the −dp/dt max in the hypoxic group was much lower than that of the normal control group ($P<0.05$). The LVDEP in the hypoxic PH group was higher than that of the normal control group ($P<0.05$). See Table 2.

Table 2 Changes of the kinetics of blood flow and LVWI ($\bar{x} \pm s$)

Groups	n	LVWI(g/kg)	+dp/dt max(kPa/s)	LVSP(kPa)	−dp/dt max(kPa/s)	LVDEP(kPa)
Normal control	10	1.49±0.11	619.8±23.0	18.1±0.3	574±16.9	0.18±0.08
Hypoxic PH	20	1.53±0.12	621.3±24.1	18.9±0.7	426.1±15.2[a]	1.09±0.04[a]

Note: a vs control group $P<0.05$

The results analysed by the AD-IBS system

The SDI and CVIB of LVA (the left ventricular anterior wall and LVPW in the hypoxic PH group were not different from those of the normal control group ($P>0.05$), but the AII was higher than that of the normal control ($P<0.05$). The CVIB of IVSM in the hypoxic PH group was lower than that of the normal control, while the AII of IVSM increased compared with that of the normal control group ($P<0.05$). The difference of SDI of IVSM between the normal control group and the hypoxic PH group was not significant ($P>0.05$). See Table 3.

Table 3 AII, SDI, CVIB in various locations of 2 groups ($\bar{x} \pm s$, dB)

Groups	n	LVA			IVSM			LVPW		
		AII	SDI	CVIB	AII	SDI	CVIB	AII	SDI	CVIB
Normal control	10	3.34±0.53	0.40±0.21	1.12±0.73	10.34±1.33	0.70±0.21	4.36±1.33	10.34±1.33	0.70±0.21	3.85±1.22
Hypoxic PH	20	4.36±1.33[a]	1.2±0.7	2.1±2.34	22.1±2.34[a]	1.1±0.7	2.12±0.73[a]	22.7±1.91[a]	0.9±0.22	3.12±0.73

Note: a vs normal control group $P<0.05$

The correlation analysis of AII and LVDEP in different locations of left ventricular myocardium in the hypoxic PH group

In different locations of the left ventricular myocardium of the hypoxic PH group, the value of AII was positively related to LVDEP ($r = 0.6206 - 0.6311$, $P < 0.01$). See Table 4.

Table 4 Relationship between AII and LVDEP in various locations of PH group

	LVDEP	
	r	*P*
LVA	0.6206	<0.01
IVSM	0.6219	<0.01
LVPW	0.6311	<0.01

Discussion

In this study it was found that there was a significant difference in the value of pH and PaO_2 between the normal control group and the hypoxic PH group. In the hypoxic PH group, the left ventricular myocardium was not thickened and its shrinking function was almost normal (+ dp/dt max, LVSP and LVWI in the hypoxic PH group were not significantly different from those of the normal control group). But the diastolic ability of the left ventricular myocardium was disabled (− dp/dt max decreased, LVDEP increased). This suggested that the diastolic disability of the left ventricle was caused by PH, but the shrinking function of the left ventricle was not significantly affected. The mechanism that the left ventricular diastolic function (LVDF) was disabled by PH is not completly clear. Nelson, et al[3], thought that hypoxic PH increased the pressure of the right ventricle. Then, during the diastolic period the interventricular septum moved to the left, the diameter of the left ventricle shortened asymmetrically and the geometry shape changed. Other researches however have reported that the disfunction of left ventricle secondary to hypoxic PH did not combine with the drift and flesh of interventricular septum[4]. With the breakthrough recognition that the change in the kinetics of blood flow is not the deciding factor in causing the reformation and fibrosis of myocardium, it is postulated that hypoxic PH causes the right ventricle to become thickened and outstretched. This might lead to the reformation and fibrosis of left ventricular myocardium by the effects of hypoxia, stress nerve and body fluid. To prove the above hypothesis the rabbit model of hypoxic PH was used to study the speciality of left ventricular myocardium by AD.

The results showed that the difference of SDI and CVIB of LVPW between the hypoxic PH group and the normal control group was not significant, but the difference of AII was significant. Compared with the normal control group, the CVIB of IVSM of the hypoxic PH group decreased, while the AII value increased but the difference of SDI between the 2 groups was not obvious. In the hypoxic PH group, the value of AII in the left ventriclar posterior wall increased greatly and the values of AII and LVDEP in different locations of the left ventricular myocardium were positively related. These suggested that the myocardium density of the left ventricle and the interventricular septum increased in the hypoxic PH group, that the shrinking function of myocardium weakened or disappeared, and that the diastolic function of myocardium was abnormal. Past researches[5] has shown that the CVIB decreased quickly and that the shrinking time was delayed when the myocardium lacked blood supplement. This was accorded with the authors' present research.

The mechanism responsible for the increase of myocardium density might be that hypoxia or the element of nerve and body fluid stimulate the growth of fibroblast and increase the production of I type collagen. This has cytotoxic effect and cause the collagen aggradation and fibrosis. At present, the quantified evaluation of the myocardium fibrosis is an unsolved and difficult clinical problem. The ultrasonic backscatter is caused by very tiny scattering bodies such as collagenous tissue and other large molecular matter. These kinds of scattering component and other matter without scattering ability all exist in the ultrastructure. The area of the tiny scattering body decides its ability to send out the ultrasound. So, the ultrasonic scattering intensity of all scattering bodies in a fixed volume is the total back-scatter intensity. Past research has proved that the changes of IBS and CVIB

have close relationship with the pathological changes of the myocardium, especially the myocardium fibrosis[6,7]. The authors's research found that AII and CVIB of the myocardium and interventricular septum changed significantly on the basis of the changes of blood flow kinetics and diastolic ability of the left ventricle after hypoxic pulmonary hypertension. This suggested that there was a relationship between AII, CVIB and myocardium pathological changes, especially the degree of myocardium fibrosis. So the ultrasonic back-scatter of myocardium is a sensitive and effective way without any trauma to evaluate the degree of myocardium fibrosis.

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·消息·

关于举办《新生儿脑损伤学习班》的通知

(国家继续医学教育项目　项目编号:2003-06-03-001)

经卫生部继续教育委员会批准,由中南大学湘雅医院主办的《新生儿脑损伤学习班》定于2003年11月在长沙举办。同时由中国当代儿科杂志社召开新生儿脑损伤专家研讨会(此会议的专家讲座为学习班内容之一)。现将学习班有关事项通知如下:

一、学习对象

各级医疗单位从事围产医学、新生儿科、儿科和产科医师。

二、授课内容

新生儿脑损伤概况,颅高压与脑水肿,HIE研究近况,颅内出血,颅内感染,胆红素脑病、遗传代谢疾病所致的脑损伤,脑损伤的检测,高压氧治疗、亚低温疗法、神经干细胞脑内移植治疗的实验研究等。

三、学分与学习时间

学习班时间:2003年11月8日~11月15日。学习结束后可取得国家级继续教育I类学分16分。

四、联系方式

参加者请按下列方式联系,索取正式通知。湖南省长沙市湘雅路141号中南大学湘雅医院中国当代儿科杂志社。电话:0731-4327402;0731-4327208。传真:0731-4327402。E-mail:xyped@public.cs.cn。网址:www.cjcp.org。联系人:李清香,邓芳明。

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