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Research Paper

Evaluation of global cardiac systolic performance and diastolic filling in central hypovolumia by lower body negative pressure with Doppler echocardiography

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Abstract

Objective: To overall evaluate the change of global cardiac systolic performance and diastolic filling in hypovoleamia by LBNP. **Methods**: 10 healthy male subjects were placed in a standard LBNP chamber. Baseline haemodynamic and echocardiographic measurements were made after a period of least 10 min resting supine within the chamber. Pressure was then decreased to −10, −20 and −30 mmHg, with each pressure maintained for 15 min. The indices of four transvalvular and SVC flow were measured using Doppler echocardiography. **Results**: The results showed that S wave, Re wave, and VTI of SVC progressively decreased with increasing LBNP. At −30 mmHg stage, S wave decreased by 35.4 %(change of 0.21+0.03 m/s, $P < 0.001$). This reduction in pre-load was associated with a progressive decrease in SV(by 21.5 ± 4.5 ml at −30 mmHg, $P < 0.001$), decrease in CO(by 1.2 ± 0.2 L min^{-1} at −30 mmHg LBNP, $P < 0.001$). The diastolic filling of mitral and tricuspid flow also reduced significantly. At −30 mmHg stage, the E wave of MVF and TVF decreased 31% and 32% respectively (change of 0.23 ± 0.05 m/s, $P < 0.001$ and 0.18 ± 0.01 m/s, $P < 0.001$). VTI of MVF and TVF decreased 27% and 27.7% respectively(change of 5.55 ± 1.41cm, $P < 0.01$ and 4.25 ± 0.44 cm, $P < 0.01$). A wave of both sides did not change significantly. **Conclusion**: Doppler indices changes in different LBNP stage can roughly reflect the degree of hypovoleamia caused by blood volume redistribution. The indices of Doppler echocardiography are more sensitive than traditional physiological indexes in evaluating cardiovascular responses of LBNP. Echocardiography techniques overall can evaluate the global cardiac function including systolic performance and diastolic filling.

Keywords: function; heart; echocardiography; lower body negative pressure

INTRODUCTION

Hypovolemia is a very common clinical pathophysiological condition, caused by dehydration, hemorrhage trauma(by traffic accident and battlefield injury, etc.). In such situations, due to the decrease of central venous flow volume, the right ventricle preload reduce and eventually cause the right cardiac output to decrease. This further influences the left systolic and diastolic performance. Therefore, it is important to reconstruct the hypovolaemic model and to investigate its hemodynamic changes. In these domains, there are a lots of studies with different methods and results [1-5]. These studies carefully observed the hemodynamic changes in left cardiac function, peripheral blood pressure and sympathetic neural activity [3,5-8], while few of them involve the right cardiac output and global heart function including its systolic and diastolic filling conditions. The present study used lower body negative pressure (LBNP) to induce acute central hypovolaemia, Doppler ultrasound was used to measure the changes of SVC flow to right ventricle and the changes to the four valvular orifices flow at different LBNP stages.

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MATERIALS AND METHODS

Subjects

Ten subjects were recruited in the experiment, all of them were healthy male volunteers aged 27 to 51 years and the mean age was 35.1 ± 8.51 years. Exclusion criteria included hypertension and other cardiovascular diseases. This study was approved by the ethic's committee of Guy's and St. Thomas' hospital, and all subjects were given written information and formal consent was obtained in writing.

Experimental protocol

To induce LBNP and reduction of the right ventricle preload, subjects were placed in a seal chamber and pressure was reduced by suction. The methods has been described in detail elsewhere [1]. Briefly, it consists of a semicircle chamber whose bottom end was closed; and the participants were put on a soft rubber bed. Suction was applied through a hole in the end of the chamber, and pressure was recorded by manometer.

A neoprene cover was placed on the subject's waist just above the iliac crest and tightened with a belt. This was then attached to the box making an airtight enclosure. Vacuum is produced by means of an electrically powered rotary vacuum pump, which can be adjusted to control the negative pressure level within the box.

All of the physiological measurements began after 5 minutes of equilibration at each pressure stage, continuing for 8 to 10 minutes, the total LBNP time was about 40-50minutes. All of the subjects were able to tolerate this protocol without any obvious adverse effects. Two dimensional echocardiography and Doppler measurements were performed at baseline and every LBNP stage. All echocardiographic images were stored in the ultrasound instrument. All parameters were measured off-line from 3 continuous waveforms to produce a mean value.

Brachial Systolic and diastolic blood pressure(BP) were measured 3 times at all stages with oscillometric sphygnomanometer(Omron705CP, Japan) on the left arm. Mean blood pressure was calculated as diastolic BP plus 0.33 of the difference between systolic and diastolic BP.

Echocardiography study

All transthoracic echocardiographic examinations were performed by one experienced operator using a color Doppler flow imaging equipment (Siemens CV70,German) and a multi-Hertz sector probe P4-2 (H3.5mHz) at baseline and each stage of LBNP(−10, −20,−30 mmHg). With the subject in left lateral decubitus position, various view images and pulsed wave Doppler profiles were obtained from different standard projections.

SVC flows were recorded from the right supraclavicular fossa. The sample volume was in 2cm below the bifurcation of supra venous cava. The pick velocities of S wave,D wave and Re wave as well as the velocity-time integrals of S and D wave (VTIs+d)were evaluated.

Mitral and tricuspid valve flow were recorded with the pulsed-wave Doppler technique from the apical four chamber view,and parasternal four chamber view, placing the sample volume at the leaflet tips of the open atrioventricular valves; the pick velocities, the velocity-time integrals (VTI) of E and A wave were then evaluated.

The pulmonary and aortic artery flows were recorded from the parasternal pulmonary long axis view and apical five chamber view respectively. The pick velocities, the VTI of pulmonary and aortic artery were subsequently evaluated.

Cardiac output (CO) was calculated as a product of SV and HR. Stroke volume (SV) measurement was determined using VTI by the area of aorta or pulmonary artery. The arterial cross area was calculated as $\pi (D/2)^2$. D is diameter of ascending aorta in aortic valve level in left ventricle long axis view, or the diameter of main pulmonary artery in parasternal pulmonary long axis view.

Repeatability Each of 10 subjects has been completed two times scanning in baseline. Compared with all parameters of this two baseline, the coefficient variation (CV) was from 2.0% to 12.8%. Most of them were in the range of 5% to 8%. The CV results were shown in ***Tab 1***.

Statistical analysis

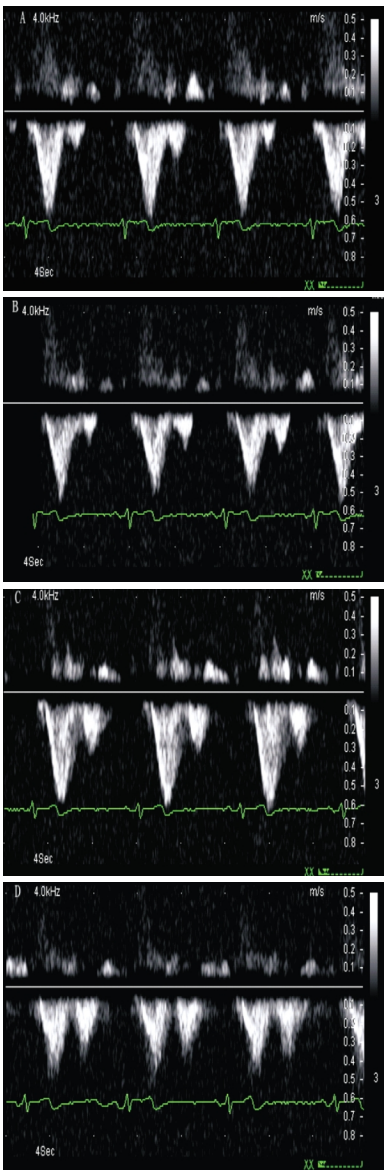
The data was analyzed with the software program SPSS12.0(SPSS Inc, Chicago, USA) and all of the data was presented as mean ± SD. Analysis of variance for repeated measures was used to assess differences to the baseline when the loading condition altered. For all statistics, a two-sided P value < 0.05 was considered statistically significant.

RESULTS

Tab 2 showed that traditional hemodynamics such as SBP,DBP,MBP and HR hadn't significantly changed in the rage of −10 to −20 mmHg LBNP, but SBP slightly decreased and HR slight increased at −30 mmHg. At the same stage, both right and left stroke volume (SV) had significantly decreased, when LBNP was up to −30 mmHg. They had re-

duced by 23%(R) and 24.7%(L), respectively.

When LBNP increased gradually, the flow of S and Re wave of SVC into right atrium significantly decreased (***Fig 1***). Half of Re waves disappeared in the -30 mmHg stage. At the same time, the VTI of SVC also significantly decreased by 22.3%, while the D wave was not significantly decreased(***Tab 2***).



A:baseline; B:10 mmHg;C:20 mmHg; D:30 mmHg

Fig 1 Blood flow of SCV at different stages

During LBNP, blood volume decentralized to the lower body and right ventricular filling was reduced. The peak velocity of E wave of TVF was significantly decreased by 32%, VTI was decreased by 27% at -30 mmHg, while A wave of TVF was not changed. Similar results were observed in left ventricular filling(***Fig 2***). The peak velocity of E wave of MVF was reduced by 31%, and the VTI of MVF was reduced by 27.7% when pressure was -30 mmHg. As the A wave of TVF, the A wave of MVF was not changed(***Tab 2***).

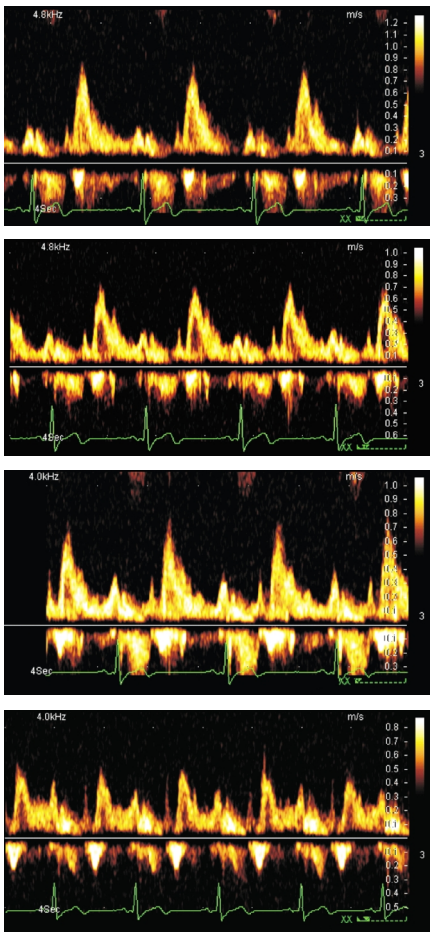


Fig 2 From top to bottom, the flow of MVF reduced gradually at baseline,-10,-20, and -30 mmHg stages

The parameters of cardiac output had changed in LBNP. The pick velocity, VTI of pulmonary artery flow and SV of right ventricle decreased significantly at different stages. The pick velocity, VTI of aortic artery and SV of left ventricle also decreased significantly at different stages. SV reduction was similar in both sided ventricles. The SV of right ventricle and left ventricle decreased by 23% and 24.7% at -30 mmHg(***Tab 2***).

DISCUSSION

Lower body negative pressure (LBNP) was firstly reported by Stevens in 1965 [1], It used a physical method of suction to the circular blood volume causing a shift of fluid from the upper body to lower extremities, resulting in central hypovolemia. As a nonpharmacological and noninvasive hypovoleamic model, LBNP is used to study orthostatic intolerance in aviation in order to observe the compensatory a-

Tab 1 **The coefficient variation of echocardiographic parameters**

parameters	Mean	Diff	SD	CV
Dpa(mm)	20.75	0.18	0.60	2.0
Vmaxpa(m/s)	0.93	0.04	0.12	8.9
VTIpa(cm)	19.63	0.88	1.46	5.8
Dao(mm)	21.49	0.03	0.91	2.8
Vmaxao(m/s)	1.13	0.02	0.10	6.3
VTIao(cm)	23.17	0.20	2.99	8.6
Emvf(m/s)	0.71	0.03	0.05	5.6
Amvf(m/s)	0.38	0.001	0.07	12.8
VTImvf(cm)	18.64	0.83	1.49	6.2
Etvf(m/s)	0.55	0.02	0.05	6.3
Atvf(m/s)	0.30	0.03	0.04	10.1
VTItvf(cm)	14.56	0.19	0.93	4.3
S(m/s)	0.56	0.02	0.07	8.7
D(m/s)	0.27	0.01	0.04	10.2
VTIs+d(cm)	17.87	0.59	1.76	7.0
Re(m/s)	0.20	0.01	0.02	7.5

Dpa=diameter of pulmonary artery; Vmaxpa=peak velocity of pulmonary flow; VTIpa=velocity time integral of pulmonary flow; Dao =diameter of aorta; Vmaxao =peak velocity of aortic flow; VTIao=velocity time integral of aortic flow; Emvf=early transmitral filling velocity; Amvf=late transmitral filling velocity; VTImvf=velocity time integral of Emvf+Amvf; Etvf=early transtricuspid filling velocity; Atvf=late transtricuspid filling velocity; VTItvf=velocity time integral of Etvf+Atvf; S=systolic velocity of SVC; D=diastolic velocity of SVC; Re=atrial reversal velocity of SVC.

bility of the cardiovascular control system [9,10]. Recently LBNP has also been used to estimate progress into shock due to hemorrhagic trauma and to evaluate the effects of acute reduction in ventricular volume on QT interval dispersion with and without heart failure[3,11].

In studies of cardiovascular responses to LBNP in recent times some researchers have used echocardiographic techniques to estimate the cardiac function [2,4,5]. Jie Liu et al found that the filling of SVC and TVF was decreased as LBNP increased [2]. Giovanna P reported LBNP caused a significant decrease in end diastolic volume, stroke volume and systolic artery pressure [4]. In the present study, it was found that the filling flow of right atrium and ventricle(that reflects preload of right ventricle) decreased with the acute blood volume decentralization. all of S wave, Re wave of SVC and E wave of TVF as well as VTI of SVC and TVF decreased by about 20-30% as LBNP at −30 mmHg. Cooke et al summarized the relation between levels of LBNP and acute hemorrhage severity in humans(***Tab 3***)[3]. From Tab 3, we can see that −20~−40 mmHg LBNP is equivalent to moderate hemorrhage, which equals 500-1000 ml

Tab 2 **Effect of LBNP on hemodynamic and echocardiographic indices** ($\bar{x} \pm s, n = 10$)

	Lower body negative pressure			
	baseline	−10 mmhg	−20 mmhg	−30 mmhg
Basic homodynamics				
HR(bpm)	61 ± 7	62 ± 5	63 ± 7	67 ± 10*
SBP(mmhg)	118 ± 8	116 ± 9	115 ± 9	113 ± 7*
DBP(mmhg)	70 ± 7	71 ± 6	72 ± 6	73 ± 6
MAP(mmhg)	84 ± 6	83 ± 6	84 ± 7	84 ± 6
SV(ml)	85 ± 16	75 ± 11*	67 ± 10△	64 ± 16△
CO(l/min)	5.22 ± 0.93	4.65 ± 0.47*	4.23 ± 0.47△	4.24 ± 0.87★
SVC				
S(m/s)	0.58 ± 0.11	0.51 ± 0.11*	0.43 ± 0.10★	0.37 ± 0.07△
D(m/s)	0.27 ± 0.07	0.26 ± 0.08	0.25 ± 0.07	0.28 ± 0.08
RE(m/s)	0.21 ± 0.03	0.19 ± 0.02*	0.16 ± 0.06*	
VTIs+d(cm)	18.40 ± 6.32	16.99 ± 5.78*	16.30 ± 4.26*	14.44 ± 4.08*
TVF				
E(m/s)	0.56 ± 0.08	0.49 ± 0.08△	0.43 ± 0.06△	0.38 ± 0.07△
A(m/s)	0.33 ± 0.06	0.31 ± 0.06	0.30 ± 0.07	0.28 ± 0.07
VTI(cm)	15.44 ± 3.13	13.68 ± 3.50*	13.10 ± 2.61*	11.19 ± 2.69★
MVF				
E(m/s)	0.73 ± 0.11	0.64 ± 0.09△	0.59 ± 0.12★	0.50 ± 0.06△
A(m/s)	0.39 ± 0.10	0.35 ± 0.09	0.39 ± 0.13	0.33 ± 0.07
VTI(cm)	18.46 ± 4.32	16.64 ± 2.52★	15.23 ± 3.35△	12.91 ± 2.91★
PA				
Vmax(m/s)	0.95 ± 0.19	0.86 ± 0.14	0.88 ± 0.18*	0.78 ± 0.08△
VTI(cm)	19.19 ± 3.99	17.87 ± 2.53	18.22 ± 2.25★	15.38 ± 1.22★
AO				
Vmax(m/s)	1.16 ± 0.16	0.99 ± 0.12★	0.96 ± 0.12△	0.94 ± 0.11△
VTI(cm)	23.66 ± 4.26	20.64 ± 2.82★	18.49 ± 2.31△	17.55 ± 4.36△

HR=heart rate; SBP=systolic blood pressure; DBP=diastolic blood pressure; MAP=mean arterial blood pressure; SV=stroke volume; CO=cardiac output; SVC=superior vena cava; S=systolic flow velocity of SVC; D=diastolic flow velocity of SVC; Re=atrial reversal flow velocity of SVC; VTIs+d= velocity time integral of S+D; TVF=tricuspid valvular flow; E=ealear filling velocity in diastole; A= later filling velocity in diastole; VTI= velocity time integral; Vmax=peak velocity of flow. Compared with baseline $^{*}P < 0.05$; $^{\triangle}P < 0.01$; $^{\star}P < 0.001$;

Tab 3 **Classification of hemorrhage severity in humans and magnitudes of LBNP**

LBNP	hemorrhage
10-20 mmHg	mild
400-500 ml fluid displaced	= 10% of total blood volume
20-40 mmHg	moderate
500-1 000 ml fluid displaced	=10-20% of total blood volume
> 40 mmHg	severe
>1 000 ml fluid displaced	>20% of total blood volume

Hemorrhage data were from human and represent approximations and ranges from literature LBNP=lower body negative pressure.

fluid displaced or 10-20% of total blood volume lost. Our experimental results showed that the decreased degree of filling flow is consistent with the degree of blood redistribution. This relation can be roughly reflected through the change of Doppler flow, either filling flow to ventricle or out flow of ventricle(see below).

Because of insufficient preload of the right ventricle, the output of right ventricle is also decreased. This is not mentioned in prior studies of Doppler echocardiography[2,4], while these phenomenon were observed clearly from our experiment. The pick velocity, VTI of pulmonary artery flow and SV of right ventricle have decreased significantly at different stages. When LBNP was –30 mmHg, peak velocity of pulmonary artery reduced by 17.9%, VTI of pulmonary artery reduced by 19.8%, stroke volume of right ventricle reduced by 23%, and cardiac output of right ventricle reduced by 14%. These decreases were consistent with the mild-moderate hemorrhage of 10-20% total blood volume[3].

Due to the right cardiac output decrease, the flow of return to left ventricle decreased inevitably, so transmitral orifice filling flow was reduced. In this study, E wave and VTI of MVF decreased by 31% and 27% at –30 mmHg, respectively. Similar results of decreases of left ventricular filling had also been found in other studies[2,4,5,12].

As to left ventricular output change in LBNP, there are lots of studies[13-16]. Gasiorowska A et al reported that stroke volume and cardiac output decreased significantly in LBNP in both high tolerance group and lower tolerance group. They found that this decrease was significant from the beginning of LBNP test in lower tolerance group, while in high tolerance groups significant decreases were found at the start of 30 mmHg[6]. Another author reported that SV and CO decreased both in nomotensives and hypertensive patients in LBNP [5]. The present study found that the pick velocity, VTI of aortic artery and SV of left ventricle and CO have decreased significantly at different stages of LBNP. These results indicated that Doppler echocardiography can conclusively be used to evaluate the cardiac output condition in central hypovolemia, caused by LBNP.

According to our results, it is obviously that the indices of Doppler echocardiography are more sensitive than other traditional physiological measurements. As Table 2 showed,physiologic indices SBP, DBP,MAP and HR were not changed in –10 mmHg, –20 mmHg, while SV of both sides were significantly changed. When LBNP increased to –30 mmHg, the SV decreased more significantly, but DBP, MAP didn't change, although SBP and HR slightly changed(***Tab 2***).

Comparing the decreased degree of SV and CO, it was found that SV of both sides decreased 23% and 24.7% at –30 mmHg LBNP respectively,while CO of both sides just decreased 14% and 18.9%. The prior decreased degree is more obvious than that of the posterior. It indicated that increased HR may play a compensatory role to some degrees, while this increase in heart rate seen during LBNP could not fully compensate for the decrease in stroke volume, so the cardiac output also fell[5]. As to compensator mechanisms, beside increased HR effects, the neuroendocrine responses also play an important role in compensating the hypovolaemia by LBNP[6-8,19,20].

In the present study, both peak velocities of A wave in trans-mitral and trans-tricuspid flow were not significantly changed at all LBNP stages. These results are consistent with other studies [2,17,18]. The reason is that atrial dynamics were not altered during late filling phase. Because in spite of a reduction of preload, the atrioventricular pressure gradient and the amount of ventricular filling, in later diastole are kept constant by a parallel afterload reduction to atrial contraction[18].

Our experiments manifested that: (1)Doppler indices changes at different LBNP stages can roughly reflect the degree of central hypovolemia caused by blood volume redistribution. (2)The indices of Doppler echocardiography are more sensitive than traditional physiological indices in evaluating the cardiovascular responses of LBNP. (3)Echocardiography techniques can overall evaluate the global cardiac function including systolic performance and diastolic filling.

The present study has some limitations. Firstly, the subjects are all male healthy persons. Secondly, the experimental parameters are lacking of supporting and simultaneous related invasive indices. And

lastly, the present study only used the morphology of echocardiography to evaluate the cardiac responses in LBNP. When there is more supporting evidence of blood hormorindocrine changes, the interpretation of these morphologic changes will undoubtedly become more evident and revealing.

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