

Haemodynamic effects of hyperbaric hyperoxia in healthy volunteers: an echocardiographic and Doppler study

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A B S T R A C T

In the present study, we observed the haemodynamic changes, using echocardiography and Doppler, in ten healthy volunteers during 6 h of compression in a hyperbaric chamber with a protocol designed to reproduce the conditions as near as possible to a real dive. Ambient pressure varied from 1.6 to 3 atm (1 atm = 101.325 kPa) and partial pressure of inspired O₂ from 1.2 to 2.8 atm. Subjects performed periods of exercise with breathing through a closed-circuit self-contained underwater breathing apparatus (SCUBA). Subjects did not eat or drink during the study. Examinations were performed after 15 min and 5 h. After 15 min, stroke volume (SV), left atrial (LA) diameter and left ventricular (LV) end-diastolic diameter (LVEDD) decreased. Heart rate (HR) and cardiac output (CO) did not vary, but indices of the LV systolic performance decreased by 10% and the LV meridional wall stress increased by 17%. After 5 h, although weight decreased, the serum protein concentration increased. Compared with values obtained after 15 min, SV and CO decreased, but LV systolic performance, LA diameter, LVEDD and LV meridional wall stress remained unchanged. Compared with the reference values obtained at sea level, total arterial compliance decreased, HR remained unchanged and CO decreased. In conclusion, hyperbaric hyperoxia results in significant haemodynamic changes. Initially, hyperoxia and the SCUBA system are responsible for reducing LV preload, increasing LV afterload and decreasing LV systolic performance, although CO did not change. Prolonged exposure resulted in a further decrease in LV preload, because of dehydration, and in a further increase in LV afterload, due to systemic vasoconstriction, with the consequence of decreasing CO.

Key words: cardiac function, Doppler echocardiography, healthy volunteer, hyperbaric hyperoxia, sport diving.

Abbreviations: 2D, two-dimensional; ACSA, aortic cross-section area; Ao, aortic diameter; A-wave, peak velocity of atrial contraction; CO, cardiac output; DAP, diastolic arterial pressure; EF, ejection fraction; E-wave, peak velocity of early filling phase; %FS, percentage LV fractional shortening; HH, hyperbaric hyperoxia; HR, heart rate; IVRT, isovolumetric relaxation time; LA, left atrium; LV, left ventricular; LVED, LV end-diastolic; LVES, LV end-systolic; LVEDD, LVED diameter; LVESD, LVES diameter; LVEDSep, LVED interventricular septal thickness; LVESep, LVES interventricular septal thickness; LVEDPW, LVED posterior wall thickness; LVESPW, LVES posterior wall thickness; LVmWS, LV meridional wall stress; MAP, mean arterial pressure; PHT, pressure half-time of early diastolic transmitral flow; RA, right atrial; RV, right ventricular; RV/RAg, RV-RA pressure gradient; RVEDD, RV end-diastolic diameter; RVESD, RV end-systolic diameter; SAP, systolic arterial pressure; SCUBA, self-contained underwater breathing apparatus; SV, stroke volume; VTI, velocity-time integral.

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INTRODUCTION

Oxygen supplementation is widely used in many situations. During exposure to an acute reduction in ambient pressure associated with aviation or space operations, supplemental O₂ is given to limit the effects of reduced partial pressure of inspired oxygen (PiO_2). In contrast, during exposure to hyperbaric pressure, SCUBA (self-contained underwater breathing apparatus) diving or industrial activities, supplemental oxygen is given to decrease the nitrogen content of the tissues and blood thus limiting the occurrence of decompression sickness. In the particular case of military diving, 100% oxygen is given through a closed-circuit SCUBA allowing better self-sufficiency (expired gas is re-inhaled after CO₂ has been extracted by lime) and decreased detection (absence of bubbles). Hyperoxia is well known to be responsible for haemodynamic changes when PiO_2 is as low as 40% [1]. Furthermore, during a dive, subjects undergo other environmental constraints, such as increased ambient pressure, ventilation through the SCUBA, immersion in cold water, fasting and exercise. We have hypothesized that these factors may participate in the haemodynamic modifications that occur during SCUBA diving. We also hypothesized that the haemodynamic state during SCUBA diving varies and has both early and late effects.

To investigate the tolerance of prolonged hyperbaric hyperoxia (HH), a study was conducted by the Service de Santé des Armées and the Marine Nationale Française in a hyperbaric chamber with ten subjects exposed to HH by using a protocol employed to reproduce as closely as possible the conditions of a real dive. During this protocol, we observed the haemodynamic modifications of the ten subjects tested.

MATERIAL AND METHODS

Long-duration hyperoxia (Toulon 1999)

This study took place in the COMISMER Hyperbaric Centre, Toulon, France from October to December 1999. Ten male subjects participated in the study. They performed two periods of compression at intervals of 1 month, the first in dry conditions and the second immersed up to the neck in water at a temperature of 15°C. The experimental protocol was designed to reproduce the conditions of a real dive as closely as possible, by combining HH, SCUBA breathing, exercise, no opportunity to drink or eat, breathing 100% oxygenated gas or an inspired gas enriched with oxygen [inspired fraction of oxygen (FiO_2) = 0.6]. All subjects were exposed to the same compression profile for 6 h. The pressure was varied from 1.6 to 2 atm (1 atm = 101.325 kPa) with a short descent to 3 atm, and PiO_2 varied from 1 to 1.6 atm with a peak of 2 atm. This paper reports our observations in dry conditions.

Subjects and diving conditions

Subjects were aged 32 ± 5 years, weighed 79 ± 10 kg and were 181 ± 9 cm tall. All of them had professional military SCUBA diving experience. The ethical committee of the University Hospital of Marseille approved the protocol. Criteria for the experiment to be stopped were at the subject's request or the occurrence of convulsions or any preliminary sign of seizure.

All subjects were exposed to the same hyperbaric, breathing and exercise protocol. They performed two periods of exercise at 75 W on a cyclo-ergometer (simulating swimming during a real dive) after 3 and 5 h of exposure. During the experiment, they could neither eat nor drink, as would be normal during a real dive. Divers were in a sitting position in the hyperbaric chamber and were breathing through a closed-circuit SCUBA carried on their backs. Continuous monitoring of the ambient pressure and FiO_2 in the inspiratory circuit allowed a continuous monitoring of PiO_2 . An electroencephalogram was monitored continuously to detect any preliminary signs of seizure.

Echocardiographic and Doppler study

Technical considerations

Examinations were made using two-dimensional (2D) and M-mode echocardiography associated with pulsed- and continuous-wave Doppler with a trans-thoracic approach. The Doppler echocardiography examinations were performed using a Dasonics Vingmed CFM 750 type ultrasonography machine (GE Ultrasound, Trondheim, Norway) located outside the hyperbaric chamber and connected to a combined 3.25 MHz imaging/2.5 MHz Doppler probe inside the chamber. This technique does not expose the ultrasonographic unit to the variations in pressure. Doppler echocardiography examinations were carried out on the subjects by an investigator inside the chamber. The monitor of the ultrasonography machine was viewed by looking through a porthole. A second investigator remained outside the hyperbaric chamber, positioning the monitor in such a way that the investigator inside could see it. This second investigator also processed the ECG using the Dasonics Vingmed computer system and recorded the examinations on standard VHS videotape to be reviewed and analysed later. The two investigators communicated via a microphone. We have used this technique previously with satisfactory results during experiments in hyperbaric or hypobaric pressure [2,3]. The mean duration for each test was 15 min. Sphygmomanometric blood pressure measurements on the right arm were obtained before each examination. Mean arterial blood pressure (MAP) was calculated as $MAP = DAP + (SAP - DAP)/3$, where SAP and DAP are systolic and diastolic arterial blood pressures respectively.

A reference examination at sea level was performed 4–5 days before the first compression period. The presence of any cardiac abnormalities at this point led to the exclusion of the subject. At the time of the compression, the schedule of the experiment permitted two echocardiographic examinations as follows: an early examination after 15 min of compression and a late examination after 5 h of compression before the second exercise period. In both cases, ambient pressure and PiO_2 were identical (2 atm and 1.2 atm respectively). All Doppler measurements were recorded at the end of a normal expiration and were averaged from three consecutive beats. Tape recordings were obtained at a speed of 100 mm/s with simultaneous tracing of the ECG.

Echocardiographic parameters

LV systolic function

Left atrial (LA) diameter, left ventricular (LV) end-systolic (LVES) and end-diastolic (LVED) diameters (LVESD and LVEDD respectively), LVES and LVED interventricular septal thickness (LVESep and LVEDSep respectively), LVES and LVED posterior wall thickness (LVESPW, LVEDPW), right ventricular (RV) end-systolic and end-diastolic diameters (RVESD and RVEDD respectively) and aortic diameter (Ao) were measured by M-mode echocardiography from the left parasternal short- and long-axis views. Standard indexes of global LV systolic performance, including ejection fraction (EF) and percentage LV fractional shortening (%FS), were determined. %FS was taken as the ratio $(LVEDD - LVESD)/LVEDD$, and EF was calculated using the Teicholz formula. Heart rate (HR) was recorded by ECG and the rate was averaged over 60 s. Cardiac output (CO) was derived from the aortic flow. Aortic cross-section area (ACSA) was first measured by 2D echocardiography from the left parasternal long-axis view at the level of the aortic root. The aortic systolic flow velocity–time integral (AoVTI) was measured by computer-assisted determination from the pulsed-wave Doppler profile of the aortic blood flow from the apical four-chamber view. This allowed stroke volume (SV) and CO to be calculated as follows: $SV = AoVTI \times ACSA$, and $CO = SV \times HR$.

LV afterload

LV meridional wall stress (LVmWS) was used as an LV afterload index independent of the LV preload. LVmWS is a function of the inner pressure of the left ventricle at the end of the systole (considered as equal to SAP in the absence of any aortic stenosis or mitral insufficiency) and of the myocardial primary contractility. It was calculated as follows: $LVmWS = (0.33 \cdot SAP \times LVESD)/LVESPW(1 + LVESPW/LVESD)$. Total arterial compliance was calculated as SV/PP [4], where PP is the pulsed pressure (defined $SAP - DAP$).

LV filling

Transmitral blood velocities were obtained from the apical four-chamber view, positioning the sample volume at the mitral valve leaflet tips. Peak velocity and velocity–time integral (VTI) of the initial flow (E-wave), representing the early filling phase, and the late flow (A-wave), representing the atrial contraction, were measured. The peak velocities ratio (E/A) and the ratio of the A-wave VTI to the total VTI (relative contribution of atrial contraction to the total LV filling) were calculated. The deceleration pressure half-life of early diastolic transmitral flow (PHT), duration of the transmitral A-wave and isovolumetric relaxation time (IVRT) were also measured. IVRT is the interval from the aortic valve closure signal to the mitral valve opening signal.

LA filling

Pulmonary venous flow velocities were obtained in pulsed Doppler from the apical four-chamber view, positioning the sample volume 0.5 to 1 cm into the upper right pulmonary vein. Three distinct components were determined: (i) forward systolic flow (S-wave), divided into early systolic wave related to atrial relaxation and late systolic wave related to increased pulmonary vein pressure during the ventricular contraction; (ii) forward diastolic flow (D-wave) related to the decrease of LA pressure after the mitral wave opening; and (iii) the atrial reversal flow (pulmonary reversal A-wave) during the atrial contraction. Peak velocities and VTI were measured for the three components as well as the duration of the pulmonary reversal A-wave. The systolic fraction of pulmonary venous forward flow was the ratio of the systolic VTI to the sum of the systolic and diastolic VTI.

LV and LA pressure

We estimated LVED pressure from the comparison of mitral and pulmonary venous flow velocities. A duration of the A-pulmonary reversal wave flow exceeding the duration of the mitral A-wave flow indicated an increased LV late-diastolic pressure exceeding 18 mmHg [5,6]. We also predicted elevated mean LA pressure on a systolic filling fraction of pulmonary venous forward flow to be < 0.4 [6].

RV-RA (right atrial) pressure gradient (RV/RAG)

We used RV/RAG as an estimation of the systolic pulmonary artery pressure [7]. An instantaneous systolic pressure gradient from the right ventricle to the right atrium was calculated with the modified Bernoulli equation from the peak velocity of the tricuspid regurgitant flow identified in continuous-wave Doppler from the apical four-chamber view: $RV/RAG = 4V^2$, where V is the maximal regurgitant velocity (m/s).

Statistical analysis

Data are expressed as means \pm S.E.M. Statistical tests were run on Sigma Stat software. The cohorts for comparison consisted of the ten subjects at three time points, namely sea level (reference), after 15 min of exposure to HH and after 5 h of exposure to HH. Comparison between cohorts of continuous variables having a normal distribution was carried out with the parametric ANOVA (repeated measures ANOVA); comparison of dichotomous variables was then done with Tukey's test. In the case of variable cohorts not having a normal distribution, comparisons were performed with non-parametric univariate analysis (Friedmann's test); comparison of dichotomous variables was then done with Dunn's test. Differences between groups were considered significant at $P < 0.05$.

RESULTS

LV systolic function

Table 1 shows the effect on LV systolic function. HR did not vary significantly at any time points, although HR increased slightly after 15 min (+ 11 %; $P = 0.20$). AoVTI decreased significantly after 15 min and 5 h ($P = 0.006$), corresponding to a similar decrease in SV. As a result, CO remained unchanged after 15 min and decreased to approx. 20 % after 5 h ($P = 0.02$) compared with the values for reference and after 15 min exposure. SAP, MAP and DAP remained unchanged during the whole protocol. As for indices of LV systolic performance, EF and %FS decreased significantly by 10 % after 15 min ($P = 0.045$ and $P = 0.048$ respectively), with no further change between 15 min and 5 h. As for LV preload indices, left atrium decreased from 36.3 ± 3 mm (reference) to 32.5 ± 5 mm after 15 min ($P < 0.001$), with no further change between 15 min and 5 h. LVEDD was reduced significantly after 15 min ($P = 0.027$) and 5 h ($P < 0.042$), with no change between the two time points. LVESD and RVESD did not change. RVESD decreased from 17.6 mm (reference) to 16.8 mm (− 4.5 %) after 15 min and 15.6 mm (− 11 %) after 5 h, but these decreases did not reach significance. For LV afterload indices, LVmWS increased by 17 % after 15 min ($P < 0.05$), but without a further change between 15 min and 5 h (+ 22 %; $P < 0.05$) compared with reference value. Total arterial compliance tended to decrease after 15 min (not significant) and decreased significantly further after 5 h ($P = 0.017$).

LV and LA filling

Table 2 shows the effects on LV and LA filling. For indices of LV and LA filling, there were no modifications of the transmitral and pulmonary venous flow profiles after 15 min of HH exposure. After 5 h, the mitral flow showed a significant decrease in E-wave (− 20 %;

Table 1 Effects of HH on LV systolic function

* $P < 0.05$ compared with sea level (reference); § $P < 0.05$ compared with 15 min of HH.

	Sea level	Duration of HH	
		15 min	5 h
HR (beats/min)	62 \pm 7	69 \pm 12	63 \pm 11
CO (l/min)	6.1 \pm 1.1	6.3 \pm 0.9	4.9 \pm 0.7*§
SV (ml)	98 \pm 15	93 \pm 20*	78 \pm 14*§
EF (%)	74 \pm 4	68 \pm 6*	68 \pm 4*
%FS (%)	36 \pm 3	32 \pm 5*	31 \pm 3*
Cardiac diameters			
Left atrium (mm)	36.3 \pm 3.8	29.5 \pm 3.0*	28.6 \pm 4.2*
LVEDD (mm)	53.5 \pm 3.5	50.9 \pm 3.5*	50.6 \pm 3.7*
LVESD (mm)	34.2 \pm 3.0	34.3 \pm 3.6	34.6 \pm 2.6
RVESD (mm)	22.2 \pm 2.4	22.2 \pm 3.6	21.1 \pm 2.3
RVESD (mm)	17.6 \pm 2.0	16.7 \pm 2.8	15.5 \pm 1.4
LV afterload indices			
MAP (mmHg)	91 \pm 7	93 \pm 13	93 \pm 9
SAP (mmHg)	124 \pm 9	131 \pm 15	130 \pm 9
DAP (mmHg)	74 \pm 8	74 \pm 15	75 \pm 10
Total arterial compliance	1.97 \pm 0.38	1.74 \pm 0.57	1.49 \pm 0.30*
LVmWS (dynes/cm ²)	69 \pm 11	81 \pm 13*	84 \pm 16*

$P < 0.05$), A-wave (− 10 %; $P = 0.018$) and E/A ratio (− 14 %; $P = 0.048$). The relative contribution of atrial contraction to total LV filling increased from 22.5 % (reference) to 25 % after 5 h (+ 12 %; not significant). PHT, IVRT and the pulmonary venous flow profiles did not vary significantly. For the indices of LV end-diastolic pressure and mean LA pressure, the duration of the mitral A flow, the duration of the A-pulmonary reversal wave and the difference between the two did not change. The systolic filling fraction of pulmonary venous forward flow remained above 0.4 for all subjects at all of the time points. RV/RAG remained unchanged throughout the experiment.

DISCUSSION

In the present study, the protocol was employed to reproduce, as closely as possible, real diving conditions, and this is the novelty of our study. Regarding the protocol conditions, the study of ten subjects should be regarded as satisfactory, even though some physiological changes may have been missed. We used 2D and M-mode pulsed- and continuous-wave Doppler echocardiography, because they are techniques practised widely and featured on most echocardiographic apparatuses. Recently, other ultrasound modes, such as colour M-mode Doppler or tissue-Doppler imaging, have been proposed, but these are used by only a few specialized teams.

Table 2 Effects of HH on LV and LA filling**P* < 0.05 compared with sea level (reference). D-wave, forward diastolic flow; S-wave, forward systolic flow.

	Sea level	Duration of HH	
		15 min	5 h
Transmitral flow			
E-wave max (cm/s)	73.1 ± 11.3	76.2 ± 11.8	58.2 ± 8.5*
A-wave max (cm/s)	44.1 ± 11.3	48.0 ± 13.3	39.6 ± 7.2*
E/A	1.75 ± 0.50	1.66 ± 0.44	1.51 ± 0.35*
Contribution of atrial contraction to LV filling (%)	22.5 ± 6.3	24.6 ± 6.0	25.2 ± 6.5
PHT (cm/s)	57.7 ± 9.9	61.6 ± 11.1	64.7 ± 11.0
IVRT (ms)	90. ± 7	90 ± 8	91 ± 11
Pulmonary venous flow			
D-wave max velocity (cm/s)	51.8 ± 10.7	54.4 ± 10.4	51.4 ± 8.4
VTI D (cm)	14.4 ± 4.3	14.8 ± 3.6	15.2 ± 4.4
S-wave max velocity (cm/s)	46.8 ± 9.8	45.6 ± 9.3	42.8 ± 4.4
VTI S (cm)	12.3 ± 3.7	11.4 ± 2.7	12.3 ± 2.5
Systolic VTI fraction	46.1 ± 4.5	43.9 ± 5.0	45.5 ± 7.5
LA and LV pressure indices			
RV/RAg (mmHg)	9.9 ± 1.5	13.9 ± 5.3	10.5 ± 2.4
A-wave mitral duration (ms)	128 ± 14.7	135.0 ± 20.1	135.0 ± 18.4
A-pulmonary reversal wave duration (ms)	93.3 ± 10.0	88.0 ± 10.3	92.0 ± 9.2
A-wave mitral duration–A-wave pulmonary duration (ms)	33.3 ± 19.3	46.0 ± 22.2	42.0 ± 18.7
A-pulmonary reversal wave max velocity (cm/s)	24.3 ± 2.7	26.3 ± 3.1	25.3 ± 3.4

Haemodynamic effects of HH after 15 min

After 15 min, we observed a decreased LV preload, as shown by a significant reduction in LA diameter, LVEDD and SV. This decrease in LV preload was secondary to the increased ambient pressure. Indeed, elevated ambient pressure increases the intrathoracic and intrapleural pressure and decreases central venous pressure [8]. Furthermore, it leads to an increased breathing gas density, with a consecutive increase in the bronchial dynamic resistance and positive end-expiratory pressure (internal PEEP) [9]. Venous return flow was also reduced by an external PEEP, due to the resistance of the breathing apparatus of approx. 5 cm of water at a depth of 10 m (F. Galland et al., unpublished data from the French "Marine Nationale").

Although there was a decrease in LV preload, we did not observe reflex tachycardia, which would normally be the case, as the baroreceptor reflex should be involved [10]. A reason for this was the negative effect of hyperoxia on HR [11–13], as HR decreases semi-logarithmically as a function of PiO_2 [14]. The mechanism is via an increase in parasympathetic tone [13,15], which is diminished or absent when the sympathetic tone is increased [16]. This was the case in our subjects, where the baroreceptor reflex was stimulated, and the blood level of noradrenaline increased [17]. As a result, SV decreased ($P < 0.05$), HR tended to increase (not significantly) and CO did not vary significantly.

Other than the effects on LV preload and HR, we observed a decrease in LV systolic performance, as shown by the approx. 10% reduction in EF and %FS. The mechanism responsible for this might be increased LV afterload or decreased primary cardiac contractility. An increased LV afterload is demonstrated by the significant increase in LV end-systolic wall stress by 17% and the decrease in the total arterial compliance (non significant), suggestive of arterial vasoconstriction. A negative inotropic effect of hyperoxia should also be considered. It has been demonstrated during exposure to normobaric hyperoxia [11,16,18,19]. However, the negative inotropic effect of oxygen generally does not persist during exposure to HH [20,21], as increased ambient pressure causes the elevation in cardiac contractility [8,22,23]. In our subjects, the decreased LV systolic performance did not permit the maintenance of a normal SV, even through reflex adrenergic stimulation. However, this adrenergic stimulation was sufficient to increase HR and maintain CO.

At least, in our subjects, Doppler echocardiography permitted the assessment of LV filling. In normal young adults, LV elastic recoil is vigorous and myocardial relaxation is swift, so most LV filling is completed during early diastole with only a small contribution of filling during atrial contraction. This results in an elevated transmitral E velocity peak, a smaller transmitral A velocity peak and an E/A ratio > 1 [24], which we observed in our subjects at

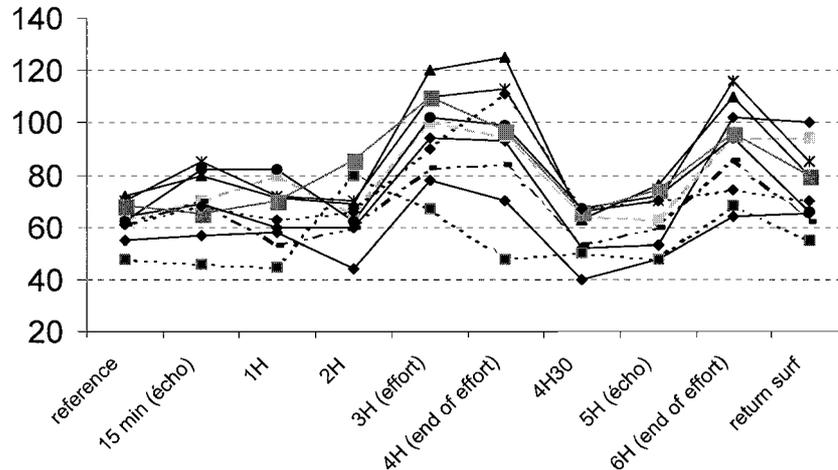


Figure 1 Evolution of HR in the ten subjects during the compression and exercise period

sea level. After 15 min, the LV filling pattern seemed to be unchanged; however, this should be analysed in the light of our results mentioned above. Among our subjects, a decrease in LV preload should have led to a decrease in early LV filling and E/A ratio; however, the decrease in LV systolic performance by increasing LA pressure and LA/LV gradient might have increased early LV filling and E/A ratio [25]. As a result of these two opposite effects, the LV filling pattern appeared unchanged. At least, no indications suggesting elevated LA or end-diastolic LV pressure were noticed.

HH after 5 h

During hyperbaric exposure, our subjects did not have access to food or drink. They were exposed to a temperature of 20–24 °C and performed two periods of exercise. This resulted in an average weight loss of 2.21 ± 0.39 kg and increases in haematocrit and total serum protein concentration level by $7 \pm 1\%$ and $11 \pm 1\%$ respectively [17,26]. This is very suggestive of hypovolaemia. In other respects, subjects tolerated the experimental conditions very well, even if they felt tired at the end of the study period.

During the experiment, similar HR modifications were observed in all subjects (Figure 1). Bradycardia, which occurred after 60–90 min, was masked during the exercise period and disappeared again after 4.5 to 5 h of exposure, the time of our second examination. At this time, the hyperoxia-induced bradycardia was masked by the current hypovolaemia-induced tachycardia.

The main result observed after 5 h was a decrease in CO of almost 20%, due to a decrease in SV of 16% with an unchanged HR. This might be due to hypovolaemia with a consequential decrease in LV preload, but the absence of changes in LA diameter and LVEDD between the two examinations suggested that the LV preload varied little. Similarly, LV systolic performance did not

vary either. We thought that the decrease in SV was due to a large increase in LV afterload, secondary to an intense peripheral arterial vasoconstriction, as shown by the important decrease in total arterial compliance (–24%). Indeed, systemic vasoconstriction is observed constantly during exposure to hyperoxia [11,12], predominantly in the peripheral, renal and splanchnic areas [27], and this vasoconstriction is independent of the sympathetic system [11]. The sympathetic response to orthostasis or hypovolaemia is maintained, resulting in a greater vasoconstrictor response [28], which explains the very important decrease in total arterial compliance observed in our subjects.

Finally, we demonstrated after 5 h of exposure to HH a decrease in LV filling volume due to hypovolaemia, with a greater decrease in early (V_{\max} E-wave) than late (V_{\max} A-wave) filling and a decreased E/A ratio.

In conclusion, we would like to make two comments. First, the question persists in our subjects does the decreased CO limit the cardiovascular tolerance during effort, or is the decreased CO a consequence of the elevated arterial oxygen content, i.e. adapted tissue oxygenation needs lower arterial flow? As we did not perform haemodynamic measurements during the exercise periods or measure lactate blood levels we cannot answer this question. However, we observed that our subjects tolerated the exercise very well. We can also state that, during the second part of the experiment when the subjects were immersed, although LV preload, LV contractility and LV afterload were quite different, CO fell by the same degree, due to a decreased HR with normal SV [29]. We think this is suggestive of a regulation of O_2 delivery, i.e. CO, function of arterial partial pressure of O_2 , independently of the cardiac preload or afterload conditions, sympathetic or parasympathetic tone.

The second comment concerns the practical implications of our results. We observed in our young,

healthy, and very well trained subjects, 10–20 % changes in haemodynamic measurements, which did not result in clinically relevant symptoms. However, our findings suggest that a risk may exist of cardiovascular events in subjects with latent cardiovascular disease or mild hypertension. This has been reported by Wilmshurst et al. [30], who described pulmonary oedema during SCUBA diving in subjects without demonstrable cardiac abnormalities, but with a latent abnormal vascular reactivity, 70 % of whom became hypertensive during a follow-up for an average of 8 years.

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