Introduction: Healthy male volunteers were investigated for cardiopulmonary adaptations to a head-down posture (HDT).

Methods: Thirty-three volunteers were enrolled in this study. Their changes in cardiopulmonary parameters at 15° and 30° HDT, for 7.5 minutes in each posture, were studied using echocardiography. Spirometric measurements of pulmonary function were performed during sitting and supine positions, and 15° and 30° HDT, while measurements of blood pressure, carotid blood flow, and electrocardiographic (ECG) and echocardiographic examinations were performed in the supine position and under 15° and 30° HDT.

Results: A significant increase (p<0.05) in mean, systolic, and diastolic pressure, and a decrease in heart rate (p<0.05) were observed during the HDT postures. Right ventricular diameter increased (p<0.05) from supine to 15° and 30° HDT. Forced vital capacity, forced expiratory volume in 1 s, and peak flow rate decreased significantly from supine to 15° and 30° HDT. Maximum ventilatory volume decreased significantly only from the sitting to the supine posture and then remained steady in the HDT postures.

Conclusions: During short-term HDT, the cardiovascular system maintains a stable ejection fraction, with a significant increase in heart rate, and a decrease in pulmonary ventilation.

The development of space medicine during the last fifty years has prompted great interest in the physiological adaptations to postural changes. Astronauts who spend extended periods of time in a microgravity environment undergo cardiovascular adaptations, including reduced red-cell mass and hypovolemia, that leave them prone to orthostatic hypotension when they return to normal Earth gravity. As we gain greater experience of the physiological changes associated with a prolonged stay in microgravity, the development of preventive measures can be based upon experimental data, rather than conjecture.

The best way of simulating spaceflight without leaving Earth is via the 6° head-down tilt (HDT) posture. A number of studies have investigated human adaptations to microgravity exposure, to long-term bed rest, and to 6° HDT in healthy volunteers. However, there are limited data concerning the results of short-term exposure to HDT greater than 6°. Accordingly, in the present study we examined the adaptations to an HDT posture of 15° and 30° degrees in order to determine whether such a posture could provoke sufficient cardiovascular adaptations to elucidate cardiac and pulmonary reserves.

There are some reports concerning acute adaptations to 10-90° HDT in healthy
volunteers studied by two-dimensional echocardiography. No significant alterations in left ventricular end-diastolic volume, stroke volume, heart rate or blood pressure were observed, with the exception of a significant increase in diastolic blood pressure in the 60° head-down position. However, it has been suggested that, during the first 30 minutes at 6° HDT, there is an increase in ejection fraction and heart work accompanied by a decrease in heart rate. Similar increases have also been seen during the first minutes in the HDT position, accompanied by a decrease in mean blood pressure and total peripheral vascular resistance. Experimental studies in animals placed in the HDT position for three days showed an increase in systolic and diastolic blood pressure.

Other studies of changes in the pulmonary circulation as a result of the HDT position (at 30° for 45 min) showed an increase in pulmonary arterial pressure and pulmonary arterial resistance, together with an increase in right ventricular ejection time, but without any change in the peak velocity of pulmonary arterial blood flow. This suggests that an increase in pulmonary arterial resistance might be responsible for the increase in pulmonary arterial pressure.

Changes in respiratory function during HDT have also been reported. A decrease in forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), and maximum ventilatory volume (MVV), as well as an increase in the diffusion rate of carbon monoxide, have been found during 30° HDT for 30 min. These latter changes have been attributed to a uniform distribution of pulmonary blood flow and an increase in the effective pulmonary vascular bed.

The present study aimed to investigate the cardiovascular and pulmonary adaptations to short-term HDT of 15° and 30° in healthy volunteers. We evaluated the response to HDT (15° and 30°) over a period of 15 min, aiming to elucidate some of the early effects of short-term HDT on cardiopulmonary function. The results of the present study could provide baseline values for future pathophysiological studies that examine the cardiopulmonary adaptations and reserves in cardiac and pulmonary patients. They could also be a useful reference for studies that assess the potential diagnostic and therapeutic role of the head down posture in these patients.

Methods
The study consisted of two separate sessions. The first session was conducted at the Laboratory of Physiology of the University of Ioannina and the second at the Michaelidion Cardiac Center of the University of Ioannina.

Subjects
A total of 33 healthy male sedentary volunteers aged 24.5 ± 4.3 years (mean body weight 76.6 ± 13.2 kg, mean height 1.79 ± 0.07 m) were enrolled in each session of the study (Table 1). A detailed medical history was obtained, which excluded cardiovascular or respiratory disease. None of the participants were taking any kind of medication, while first-visit blood pressure measurements were within the normal range. Any subject with clinical signs of respiratory or other kind of infection was excluded from the study. All subjects gave informed consent prior to their inclusion to the study. All human studies were approved by the local Ethical Approval Committee of the Michaelidion Cardiac Center and were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Procedure
All studies were performed in a quiet, temperature-controlled room (22° C) in the morning with the subjects fasting, having abstained from caffeine and alcohol for at least 12 hours so as to prevent the effects of any other form of stress apart from the HDT position. All volunteers were familiarized with the laboratory room and the study procedure. A specialized bed, automatically tilting to any position from 0° to +90° and -90° (Elba elettromedicali, Brescia, Italy), was used in the study. Subjects lay supine in the bed for 15 minutes before baseline measurements were made. The bed was then tilted to a head down position, initially -15° degrees (HDT-15°), and measurements were repeated as soon as possible after the position was acquired. Subsequently, the bed was tilted to -30° degrees (HDT-30°) and the same measurements were made. All subjects were kept in each HDT position (-15° and -30°) for 7.5 min, so that the total duration of HDT was approximately 15 min. The reason why the study involved two sessions was because it would have been infeasible to perform both cardiopulmonary and echocardiographic studies in a single session with a total duration of 15 minutes of exposure to HDT.

It should be noted that in all HDT postures the subject had to be restrained to prevent sliding. However, since shoulder restraint is known to have the po-
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Potential to alter pulmonary measurements, we used only feet and hip restraints in this study.

Cardiopulmonary studies

All cardiopulmonary studies were performed in the Laboratory of Physiology in the first session of our study. A spirometry test was performed with all subjects in a seated position after a 15-minute period of adaptation in the laboratory room. The pulmonary parameters (FVC, FEV₁, PFR, MVV) were estimated in seated, supine, HDT-15°, and HDT-30° positions using a spiroanalyzer (Fukuda Sangyo Co. Ltd. Electronic spiroanalyzer, Tokyo, Japan) between the 5th and 6th minute under both HDT-15° and HDT-30°.

The following were also recorded at the same time as the pulmonary function parameters in all volunteers in the supine, HDT-15°, and HDT-30° positions: 1) systolic and diastolic blood pressure measured in the left arm using a mercury sphygmomanometer (Tanaka Sangyo Co. Ltd., Tokyo, Japan), during the first minute of both HDT-15° and HDT-30°; 2) heart rate and mean QRS axis from a 12-lead electrocardiogram (ECAPS, Tokyo, Japan) during the 2nd minute of both HDT positions; and 3) common left and right carotid blood flow velocity using a hand-held ultrasound blood flow detector (ES – 107 PZ HAMEC, Arima, Kawasaki-Shi, Japan) during the 7th minute of both HDT positions.

Echocardiographic studies

All echocardiographic studies were performed in the Michaelidion Cardiac Center during the second session of our study. The same procedure was followed as on the previous occasion, under the same conditions, and echocardiographic studies were performed (Philips HDI 5000, Bophell, Washington, USA) in the supine, HDT-15°, and HDT-30° positions for the estimation of left ventricular ejection fraction, E and A waves of the tricuspid and mitral valves, left and right ventricular diameters, and blood flow velocity through the pulmonary and aortic valves.

Statistical analysis

Group means for each parameter were compared among the body positions and tested for significance using analysis of variance (ANOVA) for repeated measures. Multiple comparisons among group means between body positions were performed using Pillai’s Trace, Wilk’s Lambda, Hotteling’s Trace, and Roy’s largest Root method. All computations were performed using SPSS 14.0 for Windows (SPSS Inc., Chicago, USA). The level of significance was set at p<0.05.

Results

Cardiovascular parameters

Heart rate

There were no significant changes in heart rate from the supine to the HDT-15° position. A significant decrease of 4.5% was recorded from HDT-15° to HDT-30° (p<0.05). Heart rate also decreased significant-
Blood pressure

Systolic blood pressure (SBP) increased significantly from the supine to the HDT-15° posture by 3.2% (p=0.03), from the HDT-15° to the HDT-30° posture by 3.9% (p<0.05), and from the supine to the HDT-30° posture by 7.3% (p<0.05). Diastolic blood pressure (DBP) also increased significantly from the supine to the HDT-15° posture by 10.4% (p<0.05), from the supine to the HDT-30° posture by 17.7% (p<0.05), and from HDT-15° to HDT-30° posture by 6.6% (p<0.05). In addition, mean arterial pressure (MAP) also increased significantly from the supine to the HDT-15° posture by 7% (p<0.05), from the HDT-15° to the HDT-30° posture by 5.6% (p<0.05), and from the supine to the HDT-30° posture by 13% (p<0.05) (Table 2).

Carotid blood flow velocity

There were no significant changes in peak systolic blood flow velocity in either the left or the right carotid artery during any posture (Table 2).

Left ventricular ejection fraction, left ventricular end-systolic and end-diastolic diameter

There were no significant changes in left ventricular ejection fraction during any posture. Nor were there any significant changes in left ventricular end-diastolic or end-systolic diameter (Table 2).

Right ventricular diameter

There was a significant increase of 7.5% (p<0.05) in the right ventricular diameter from the supine to the HDT-30° position. There were no significant changes from the supine to the HDT-15° or from the HDT-15° to the HDT-30° posture (Table 2).

Tricuspid valve A and E waves

There were significant changes in the A wave of the tricuspid valve (p<0.05). There was a significant increase of 7% (p<0.05) from the supine to the HDT-15° posture and a significant increase of 10.9% (p<0.05) from the supine to the HDT-30° posture. However, there was no significant change from the HDT-15° to the HDT-30° posture. There were no significant changes in the E wave of the tricuspid valve during any posture (Table 2).

Mitral valve A and E waves

There were significant changes in the E wave of the mitral valve (p<0.05). There was a significant increase of 4.6% (p<0.05) from the supine to the HDT-15° posture and a significant increase of 5.5% (p<0.05) from the supine to the HDT-30° posture. However, there was no significant change from the HDT-15° to the HDT-30° posture. There were no significant changes in the A wave of the mitral valve during any posture (Table 2).

Blood flow velocity in the pulmonary and aortic valves

There were no significant changes in blood flow velocity in either the pulmonary or the aortic valve. However, the blood flow velocity in the pulmonary valve increased non-significantly from the supine to the HDT-15° posture and finally stabilized in the HDT-30° posture at a higher level than in the supine position. On the other hand, the blood flow velocity of the aortic valve decreased non-significantly in the HDT-15° posture and then increased in the HDT-30° position, finally stabilizing at the same level as in the supine position (Table 2).

Respiratory function parameters

Spirometry was performed in the sitting, supine, HDT-15°, and HDT-30° positions for all 33 volunteers.

Forced vital capacity

There was a significant decrease in FVC from the sitting to the supine posture by 9.1% (p<0.05). A significant decrease was also observed between the sitting and HDT-15° postures by 11.8% (p<0.05), and between sitting and HDT-30° postures by 12.4% (p<0.05). Between the supine and HDT-15° postures FVC significantly decreased by 2.8% (p<0.05). Between supine and HDT-30° postures FVC significantly decreased by 3.6% (p<0.05), whereas there was no significant decrease in FVC from the HDT-15° to the HDT-30° posture (Table 3).

Forced expiratory volume in 1 s

The changes observed in FEV₁ in various positions
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Table 2. Cardiovascular parameters in different positions.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Supine</th>
<th>HDT-15°</th>
<th>HDT-30°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>71.1 ± 12.6</td>
<td>71.5 ± 11.2</td>
<td>68.3 ± 11.9*†</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>102.26 ± 9.85</td>
<td>109.49 ± 10.03*</td>
<td>115.6 ± 14.45*†</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>136 ± 15.2</td>
<td>140.3 ± 18.7*</td>
<td>145.9 ± 19.2*†</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>85.4 ± 8.6</td>
<td>94.3 ± 11.4*</td>
<td>100.5 ± 13.5*†</td>
</tr>
<tr>
<td>Left CBFV (cm/s)</td>
<td>44.9 ± 15.2</td>
<td>40.9 ± 12.8</td>
<td>40.8 ± 14.8</td>
</tr>
<tr>
<td>Right CBFV (cm/s)</td>
<td>46.1 ± 19.2</td>
<td>41.3 ± 15.3</td>
<td>35.7 ± 14.8</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>63.4 ± 7.4</td>
<td>62 ± 7</td>
<td>63.1 ± 6.9</td>
</tr>
<tr>
<td>Right ventricular diameter (mm)</td>
<td>16.92 ± 5.28</td>
<td>17.58 ± 6.27</td>
<td>18.19 ± 6.03*</td>
</tr>
<tr>
<td>Left ventricular end systolic diameter (mm)</td>
<td>32.11 ± 4.03</td>
<td>31.61 ± 4.07</td>
<td>31.5 ± 4.02</td>
</tr>
<tr>
<td>Left ventricular end diastolic diameter (mm)</td>
<td>48.65 ± 4.78</td>
<td>47.81 ± 4.78</td>
<td>47.92 ± 4.82</td>
</tr>
<tr>
<td>Tricuspid valve E wave</td>
<td>57.78 ± 14.86</td>
<td>60.39 ± 12.47</td>
<td>60 ± 12.62</td>
</tr>
<tr>
<td>Tricuspid valve A wave</td>
<td>39.44 ± 10.08</td>
<td>42.24 ± 11.77*</td>
<td>43.72 ± 10.4*</td>
</tr>
<tr>
<td>Mitral valve E wave</td>
<td>47.69 ± 14.79</td>
<td>48.34 ± 10.91*</td>
<td>50.83 ± 13.32*</td>
</tr>
<tr>
<td>Mitral valve A wave</td>
<td>87.07 ± 16.55</td>
<td>91.04 ± 11.49</td>
<td>91.92 ± 17.9</td>
</tr>
<tr>
<td>Pulmonary valve blood flow velocity (cm/s)</td>
<td>111.37 ± 26.88</td>
<td>113.81 ± 27.59</td>
<td>113.57 ± 26.75</td>
</tr>
<tr>
<td>Aortic valve blood flow velocity (cm/s)</td>
<td>111.9 ± 22.99</td>
<td>109.91 ± 21.14</td>
<td>111.19 ± 20.04</td>
</tr>
</tbody>
</table>

Data are mean ± SD.
*Statistically significant difference compared to supine (p<0.05); †statistically significant difference compared to HDT-15° (p<0.05).
SBP/DBP – systolic/diastolic blood pressure; MAP - mean arterial pressure; CBFV – carotid blood flow velocity; LVEF – left ventricular ejection fraction.

Table 3. Respiratory parameters in different positions.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sitting</th>
<th>Supine</th>
<th>HDT-15°</th>
<th>HDT-30°</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>4.6 ± 0.77</td>
<td>4.2 ± 0.6*</td>
<td>4 ± 0.7*†</td>
<td>4 ± 0.6*†</td>
</tr>
<tr>
<td>FEV1 (L/s)</td>
<td>4 ± 0.5</td>
<td>3.7 ± 0.7*</td>
<td>3.5 ± 0.5*†</td>
<td>3.5 ± 0.4*†</td>
</tr>
<tr>
<td>PFR (L/s)</td>
<td>8.9 ± 1.5</td>
<td>8.2 ± 1.7*</td>
<td>7.7 ± 1.4*†</td>
<td>7.8 ± 1.4*†</td>
</tr>
<tr>
<td>MVV (L/min)</td>
<td>118.3 ± 24.3</td>
<td>105.2 ± 24.4*</td>
<td>105.7 ± 23*</td>
<td>105.9 ± 20.2*</td>
</tr>
</tbody>
</table>

FVC – forced vital capacity; FEV1 – forced vital capacity in 1 s; PFR – peak flow rate; MVV – maximum ventilatory volume. Data are mean ± SD.
*Statistically significant difference compared to sitting position (p<0.05); †statistically significant difference compared to supine (p<0.05).

were similar to those of FVC. There was a significant decrease of 8% in FEV1 from the sitting to the supine posture (p<0.05). A significant decrease of 13.8% was also observed between the sitting and HDT-15° (p<0.05) and HDT-30° (p<0.05) postures. From the supine to HDT-15° and HDT-30° postures a significant decrease of 6.25% (p<0.05) was observed, whereas there was no decrease in FEV1 between HDT-15° and HDT-30° (Table 3).

Peak flow rate

There was a significant decrease in PFR among the various postures (<0.05) except for between HDT-15° and HDT-30°. There was a significant decrease of 7.9% in PFR (p<0.05) from the sitting to the supine posture. Furthermore, PFR significantly decreased between sitting and HDT-15° posture by 12.6% (p<0.05), and between sitting and HDT-30° posture by 12.2% (p<0.05). A significant decrease of 5.2% (p<0.05) from the supine to the HDT-15° posture, and of 4.6% (p<0.05) from the supine to the HDT-30° posture was also observed. There was no significant decrease in PFR between HDT-15° and HDT-30° (Table 3).

Maximum ventilatory volume

There was a significant decrease of 11.04% (p<0.05) in MVV from the sitting to the supine posture, of 10.7% (p<0.05) from sitting to HDT-15° posture, and of 10.5% (p<0.05) from sitting to HDT-30° posture. There were no significant changes in MVV from supine to HDT-15° and HDT-30° postures, or between HDT-15° and HDT-30° (Table 3).

Discussion

The findings of the present study suggest that, in healthy males, the cardiopulmonary system adapts to
head-down positions (-15° and -30°) by altering various cardiac and pulmonary parameters. More specifically, a significant increase in systolic, diastolic and mean BP was observed in all HDT positions. This finding is in contrast with previous reports in which only a slight increase in diastolic BP at -60° HD position was demonstrated,13,16 while others have reported a decrease in diastolic BP in the same HD positions as those in the present study.19 Nevertheless, experimental studies in rats demonstrated a significant increase in BP and heart rate.17

We observed a significant decrease in heart rate in HDT postures, mainly HDT-30°, without a notable change in ejection fraction. A decrease in heart rate has also been previously reported in -15° and -30°15 and in -6° HD positions.22 However, an increase in stroke volume has been reported after 10 min at -90°13,16 and after 30 min at -6° HDT,14 suggesting that stroke volume may increase either at extreme (-90°) or after prolonged (30 min) though mild HDT. In this study, volunteers were studied at -15° and -30° HDT positions and the total time in both positions did not exceed 15 minutes.

The decrease in heart rate, increase in BP, and unchanged ejection fraction demonstrated in our study suggest that total peripheral vascular resistance may increase in the -15° and -30° HDT postures. This is further supported by our finding that no significant changes in carotid blood flow velocity were observed in any of the HDT postures, despite the significant increase in BP. All these changes indicate that a reactive vasoconstrictive mechanism was probably activated in the HDT postures studied, inducing an increase in total peripheral vascular resistance.23 However, Loeppky et al reported that common carotid artery blood flow velocity decreases after a transient initial increase, but with prolonged (after 20 min) HDT at -30°.24 An increase in carotid blood flow velocity has also been demonstrated in humans at about 3 minutes of HDT-10°, which was restored after almost 10 minutes in this posture.25 The measurements of carotid blood flow velocity in our study were performed at about 7th min at the HDT-15° and HDT-30° postures. At that time it is possible that carotid blood flow velocity may have returned to the values of the supine posture.

In our study the A wave of the tricuspid valve increased in HDT postures. The A wave of the tricuspid valve represents the contraction of the right coronary sinus. This finding is consistent with an increase in cardiac preload, something that has been demonstrated by other studies in terms of increased central venous pressure in the first minutes of the HDT position.19 This is also in agreement with the increased right ventricular diameter observed in our study.

However, there was a significant increase in the E wave of the mitral valve, which represents the blood flow in the left ventricle, despite the insignificant alterations in the mitral A wave. The preloading of the left heart is not increased, in contrast to that of the right heart. Considering all the heart alterations in the HDT posture we can conclude that the ultimate goal is the achievement of an unchanged left ventricular ejection fraction, as demonstrated in our study.

We should also mention that the mitral E wave values in our study were higher than those predicted for the 3rd decade of life.26,27 This may have been the result of the postural changes during our echocardiographic studies.

In our study the blood flow velocity in the pulmonary valve increased non-significantly from the supine to the HDT-15 position and finally stabilized in the HDT-30 position, at a value higher than in the supine position. On the other hand, the blood flow velocity of the aortic valve decreased non-significantly in the HDT-15 position and then increased in the HDT-30 position, finally stabilizing at same level as in the supine position. These differences between the pulmonary and aortic valves may be caused by the increased pulmonary vessel bed and increased pulmonary arterial pressure in HDT positions.

Spirometric evaluation revealed that FVC significantly decreased from the sitting to the supine position and from the supine to the -15° HDT position, while no differences in FVC were recorded between the -15° and -30° HDT positions; these findings are in agreement with previous results.20 Similar changes were also recorded for FEV1 and PFR; there was an initial decrease from the sitting to the supine position and a further decrease from the supine to the -15 HDT position, while no change was observed between the -15° and -30° HDT positions. Previous clinical studies have shown a slight, non-significant increase in PFR, but only during a prolonged stay in the HDT position for 120 days.28 These changes in pulmonary function could be attributed to a decrease in lung compliance and an increase in pulmonary resistance taking place during the transition from the sitting to the supine position.20

MVV significantly decreased from the sitting to the supine position but remained unchanged between the supine and the HD positions (-15° and -30°).
There are data indicating that in the sitting position resting tidal volume is accomplished mainly by ribcage motion, whereas in the supine position tidal volume is predominantly generated by diaphragm-abdominal displacement. This breathing pattern, which is also maintained in HDT postures, may explain the changes in MVV recorded in the present study. Pulmonary functional parameters decrease during short-term HDT and stabilize at a lower level than normal after 7.5 min of HDT.

In conclusion, healthy males appear to adapt acutely to head-down positions with hemodynamic and functional pulmonary alterations, such as changes in blood pressure, heart rate, FVC, FEV1, PFR, and MVV. These adaptations could be used in future pathophysiologic studies in cardiac and pulmonary patients to reveal cardiovascular and respiratory reserves, or to investigate the diagnostic or therapeutic role of the HDT posture. Further research is needed to investigate whether the acute cardiovascular and pulmonary adaptations to HDT may vary with age, sex, or disease. There is also a need for further investigation into whether this behavior is related to the time remaining in HDT or to the posture change from the 15° to 30° HDT.

References

27. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-

