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Investigation of the effects of intermediate altitude on atrial functions: A speckle tracking echocardiography study

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Abstract

Aim: Intermediate altitude (IA) is a risk factor for the development of cardiovascular disease due to low oxygen levels. At IA, adaptive mechanisms develop both in the pulmonary and systemic circulatory systems from an early period. The effects of IA on atrial functions were investigated in the present study by using speckle-tracking echocardiography.

Materials and Methods: The present study was on the subjects living at IA for 1 year. The effects of IA on atrial functions were investigated by comparing the baseline and first-year echocardiographic data of the subjects.

Results: A total of 67 subjects were included in this study. The mean age of the patients was 44.5 ± 6.2 years, and 62% of them were males. At the end of the first year, the left atrial (LA) conduit strain (p:0.011), reservoir strain (p:0.032), and contractile strain (p:0.037) rates were found to be significantly higher, whereas the left atrial volume index (p:0.005) was determined to be lower.

Conclusion: IA leads to the development of adaptive mechanisms in the cardiovascular system, and the maintenance of tissue oxygenation is not affected by these mechanisms. These adaptive changes can be detected in LA structure and functions from the first year in individuals living at high altitudes.

Introduction

The altitude between 1.500 and 2.500 meters above the sea level are defined as intermediate altitude (IA). People living at IA live in a hypoxic environment with low oxygen pressure, and it results in the development of alveolar hypoxia, hypoxemia, and polycythemia as a natural consequence of this environment. However, thanks to the development of adaptive mechanisms, people living at IA can perform similar physical activities, often at a better level in comparison to those living at sea level [1, 2].

Alveolar hypoxia and hypoxemia developing as a result of IA induce characteristic changes in the cardiovascular system; including increased pulmonary arterial hypertension (PHT), right ventricular (RV) hypertrophy, and hyperplasia in distal pulmonary arterial smooth muscles. In the studies performed from the early period, the development of RV hypertrophy was significant in individuals living at IA. This adaptation mechanism is developed to facilitate oxygen delivery into the tissues. These adaptive mechanisms result in desirable cardiac effects, particularly in athletes [3-5].

Atria have an essential role in cardiac functions. Both left atrial (LA) and right atrial (RA) disorders were shown to be associated with poor cardiac outcomes in previous large-scale studies [6-10]. Under normal conditions, RA functions in low pressure states. RA cannot generate an adequate contractile response in case of a volume or pressure overload. Subsequently, dilatation in RA develops [7,11]. LA functions in higher pressure states when compared to the RA, and it is more resistant to both increases in pressure and intravascular volumes than the RA [12]. Although the effects of IA and changes in partial oxygen pressure on ventricular functions are clearly defined [2], data about their effects on atrial functions is limited. The changes occurring in atrial volume and functions of individuals living at high altitudes at the baseline and the end of the first year were investigated in this study.

Materials and Methods

Patient selection

This study has a prospective design. Individuals aged older than 18 years were involved. Those who had not inhabited at IA and had started living at IA in the last

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month were enrolled in the present study. Individuals who applied to the cardiology outpatient clinic for routine examination and were not diagnosed with cardiovascular disease were included in the study. The altitude of our center, where the study was carried out, is 1,890 meters above sea level and is suitable for being classified as IA. Baseline and demographic records of the subjects included in the study were taken and compared with the subjects' 1st year data. Baseline data as group 1, and year 1 data as group 2.

Patients with congenital heart disease, severe valve disease, heart failure, coronary artery disease, anemia, or COPD, as well as patients, who had previously lived in IA, were excluded from the study. The local ethics committee approved the study (Afyonkarahisar Health Sciences University Clinical Research Ethics Committee, number: 2022/460). Written informed consent was obtained from all patients.

Echocardiographic evaluation

The measurements were obtained in the left lateral decubitus position by using the same echocardiography machine in all patients (Vivid 7, GE Healthcare, Horten, Norway). All cases underwent the standard echocardiographic assessment, and all images were recorded for off-line analysis.

All images used for speckle tracking echocardiographic analysis were obtained in 50–70 frames per second (FPS). The endocardial border was manually traced, and the software automatically tracked the contours on the other frames. The measurements were performed offline using the ECHOPACK software package (GE Healthcare). Three phases of the LA and RA were measured during deformation analysis (Figure 1).

1. Right atrial strain during reservoir phase (RASr)
2. Right atrial strain during conduit phase (RAScd)
3. Right atrial strain during contraction phase (RASct).

All echocardiographic parameters were measured according to the current guidelines [13].

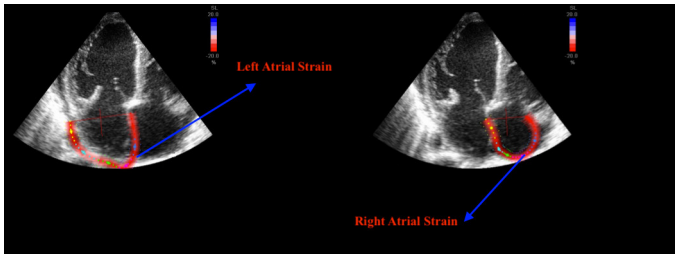

Figure 1. The demonstrative presentation of the left atrial strain(A) and right atrial strain (B) measurement.

Artificial intelligence: Artificial intelligence was not used in all parts of the study, including design, writing, and discussion.

Statistical analysis

Continuous variables were expressed as median, and categorical variables were expressed as percentage. Paired T

Table 1. Echocardiographic characteristics of the study population.

Variables	Group 1 (n=67)	Group 2 (n=67)	P value
LVEDD, mm	45±4	44±4.5	0.592
LVESD, mm	28±2.4	28±3	0.139
IVS, mm	10.2±0.6	10.7±0.4	0.482
LV-EF	65±4.8	65±5	0.993
TAPSE(mm)	17.6±3.2	17±2.1	0.089
RV, mm	42±2.5	46±4.2	0.050
TR(%)			
Trace	21	13	
Mild	0	10	0.381
Moderate	0	0	
Severe	0	0	
sPAP(mm hg)	15(12-19)	19(16-22)	0.079
LVGLS, (-%)	17(14-19)	19±3.2	0.062
Peak systolic RVSr, (%)	16±2.1	17(13-19)	0.139
LA, mm	39±3.2	35±4.2	**0.046**
LAVmax(mL/m^2)	45±2.1	42±1.2	**0.005**
LAVmin(mL/m^2)	34±2.2	30±1.8	**0.003**
LAVi(mL/m^2)	39.5±2.5	35±1.1	**0.001**
LASr, (%)	12.1±2.1	14±3.2	**0.032**
LAScd, (%)	9.2±2.4	12.5±1.8	**0.011**
LASct, (%)	11±2.9	13.6±2.6	**0.037**
pLASRr	−1.4±0.6	−1.5±0.4	0.164
pLASRcd	−1.7±0.5	−1.9±0.7	0.083
pLASRct	−1.2(1-1.4)	−1.3 (1-1.7)	0.520
RA, mm	38±4.2	43±5.2	**0.042**
RAVmax	44±3.2	45±3.2	0.067
RAVmin	31±2.1	33±2.2	0.132
RAVi	37±3.1	39±3.5	0.079
RASr, (%)	10±2.4	11±1.2	0.142
RAScd, (%)	13±2.1	13±1.5	0.158
RASct, (%)	13±2.3	13.1±1.3	0.140
pRASRr	−1.20.3	−1.10.2	0.431
pRASRcd	−1.50.4	−1.40.5	0.589
pRASRct	−1.30.5	−1.30.3	0.218

Abbreviations: LVEDD; left ventricular end diastolic diameter, LVESD; left ventricular end systolic diameter, IVS; interventricular septum, LVEF; left ventricular ejection fraction, TAPSE; Tricuspit anular plane systolic excursion, RV; right ventricle, TR; Tricuspit regurgitation, sPAP; systolic pulmonary artery pressure, LVGLS; left ventricular global longitudinal strain, RVSr; right ventricular strain, LA; left atrium, LAVmax; maximal left atrial volume, LAVmin; minimum left atrial volume, LAVi; left atrial volume index, LASr; left atrial strain during reservoir phase, LAScd; left atrial strain during conduit phase, LASct= left atrial strain during contraction phase, pLASRr; left atrial peak strain rate during reservoir phase, pLASRcd; left atrial peak strain rate during conduit phase, pLASRct: left atrial peak strain rate during contraction phase, RAVmax; maximal right atrial volume, RAVmin; minimum right atrial volume, RAVi; right atrial volume index, RASr; right atrial strain during reservoir phase, RAScd; right atrial strain during conduit phase, RASct; right atrial strain during contraction phase, pRASRr; right atrial peak strain rate during reservoir phase, pRASRcd; right atrial peak strain rate during conduit phase, pRASRct: right atrial peak strain rate during contraction phase.

Table 2. Correlation between LA parameters and RA parameters.

Right atrial parameters	Left atrial parameters							
	LAVi		LASr, (%)		LAScd, (%)		LASct, (%)	
	r	p	r	p	r	p	r	p
RAVi	-0.41	**0.021**	-0.29	**0.048**	-0.22	**0.059**	-0.25	**0.052**
RASr, (%)	0.12	0.372	-0.16	0.580	-0.11	0.861	-0.17	0.329
RAScd, (%)	0.17	0.421	-0.10	0.972	-0.09	0.995	-0.13	0.968
RASct, (%)	0.11	0.893	-0.08	0.991	-0.11	0.993	-0.13	0.921

Abbreviations: LAVi; left atrial volume index, LASr; left atrial strain during reservoir phase, LAScd; left atrial strain during conduit phase, LASct;left atrial strain during contraction phase, RAVi; right atrial volume index, RASr; right atrial strain during reservoir phase, RAScd; right atrial strain during conduit phase, RASct; right atrial strain during contraction phase.

Table 3. The relationship between LAVi and RAVi in linear regression analysis.

Variables	RAVi				
	r value	Univariate OR, 95% CI	Univariate P value	Multivariate OR, 95% CI	Multivariate P value
LAVi	-0.41	0.87(0.75-0.98)	**0.021**	0.82(0.67-0.97)	**0.019**
LASr, (%)	-0.29	0.93(0.88-0.98)	**0.048**	0.89(0.75-1.03)	0.549
LAScd, (%)	-0.22	0.95(0.91-0.99)	**0.059**	0.95(0.89-1.01)	0.681
LASct, (%)	-0.25	0.89(0.83-0.94)	**0.052**	0.86(0.65-1.07)	0.429

Abbreviations: LAVi; left atrial volume index, LASr; left atrial strain during reservoir phase, LAScd; left atrial strain during conduit phase, LASct;left atrial strain during contraction phase, RAVi; right atrial volume index.

test or Wilcoxon test was used to compare continuous variables when appropriate. Additionally, Chi-square test was used for comparisons of categorical variables. Intra- and interobserver variability were assessed by intraclass correlation coefficient (ICCC). Data were evaluated with SPSS version 22 (IBM, Armonk, NY, USA).

Results

A total of 67 healthy subjects were included in this study. The median age was 44.5 ± 6.2 years, and 62% of them were males.

Considering the conventional echocardiographic characteristics of both groups, it was determined that ventricular systolic and diastolic diameters were higher in group 2 (Table 1). However, the difference between groups was not statistically significant.

Examining the left atrial deformation parameters, LASr (p:0.032), LAScd (p:0.011) and LASct (p:0.037) were found to be significantly higher in group 2. However, there were no statistical differences between RA deformation parameters (Table 2 and Figure 2). Moreover, there was a similar relationship between LAVi and RAVi. Even though there was a statistical difference between the groups in LAVi, this difference could not be observed in RAVi (Table 3). Intraobserver variability (ICCC) was found to be 0.76, 0.71, 0.79, 0.65, 0.70, and 0.76 for LASr, LAScd, LASct, SRE, LAVi, and RAVi, respectively.

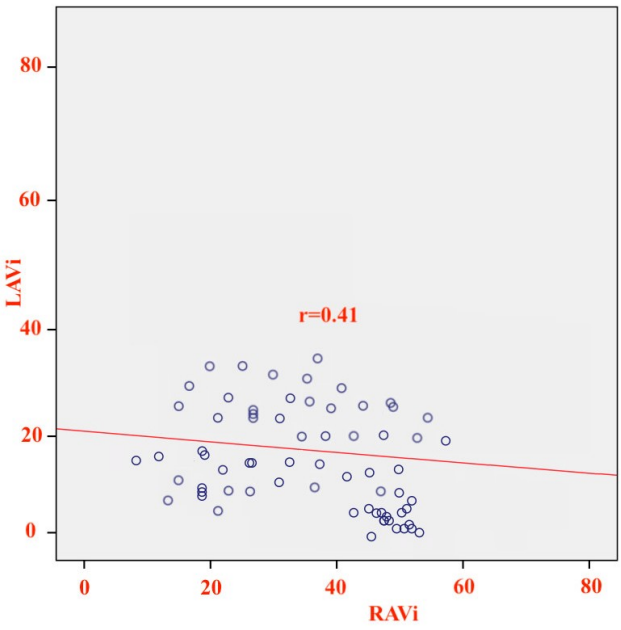

Figure 2. Error box plot of left atrial and right atrial deformation parameters.

Discussion

The findings of this study can be summarized as follows:

1. Exposure to IA causes changes in cardiac structure and functions.
2. Despite decreased O_2 concentrations at IA, LA functions were not reduced and even increased.

IA causes various adaptive reactions in the cardiovascular system due to reduced partial O_2 concentration, and these mechanisms aim to facilitate the delivery of O_2 into the tissues. These adaptive mechanisms begin to appear after months following the birth of an infant. In an autopsy series, increases were detected in the right ventricular muscle mass in infants born at high altitudes who continued to live there. This increase in RV muscle mass also continues in later periods and results in an increase in pulmonary

artery pressure in people living at IA compared to those living at sea level [1,2,5,14].

Left heart physiology and adaptive conditions are well known in individuals living at IA [12, 15, 16]. In a previous study, healthy participants camping at higher altitudes were reported to have increased left ventricular global strain after 10 days of follow-up [17]. In a study carried out by Sareban et al [4] examining the LA functions of individuals living at 4559 meters, no statistically significant decreases were observed in LA volumetric and Doppler parameters. However, analyzing the deformation, an increase was determined in LASr, LAScd, LASct, LASct, and strain rates after 44 hours at high altitudes. In the present study, similar to the aforementioned study, decreases observed in Doppler parameters were not statistically significant. However, the decrease in LAVi parameters and the increase in strain parameters in the deformation analysis were statistically significant. It might have been caused by the relatively longer follow-up period, and cardiac adaptations occurring during this period in this study.

There is conflicting information about the right heart physiology. It was frequently reported that RV dilatation and PHT develops in individuals living at IA. It was suggested that this condition might be an adaptation mechanism to hypoxia [1,8,17,18]. In a study carried out by Faoro et al. [3], it was reported that a mild deterioration might occur in the RV functions of individuals living at IA. This condition was also observed by Naeije [1]. In the etiology of this condition, reduced preload, reduced sympathetic nervous system activation, and decreased oxygen concentrations were thought to be responsible. In the present study, similar to a previous study carried out by Faoro et al. [3], right atrial volume increased and this increase was accompanied by a decrease in right atrial deformation parameters. Chronic hypoxia causes myocardial depression and PHT in the long term. These changes are well-known in patients with congenital heart disease. Myocardial depression, endothelial dysfunction, and PHT develop as a result of the stimulation of various cytokines and the sympathetic nervous system [18-22]. In the present study, similar to the aforementioned adaptive mechanism, this mild impairment in right atrial function is likely to be mediated by hypoxia. This statistically nonsignificant decrease in RA functions found in the present study is consistent with the current literature data. However, there are some conflicting results in current literature and larger-scale studies are required for further clarification. Moreover, since atrial strain measurement is not a frequent investigation performed routinely, it may show individual and inter-individual variability.

The present study has several limitations. The small number of patients involved in the main limitation, and having 1-year follow-up data and not having longer-term data can be considered as a limitation. The lack of a control group is another limitation, and it is not clear when these adaptive mechanisms emerge or through which pathway they occur from. The lack of basal O_2 saturation due to technical inadequacy is a limitation. Finally, evaluation with regression models would have provided more useful information. In this case, it can be considered as a limitation.

Conclusion

Oxygen levels are markedly lower at IA. Despite this decrease, a hypoxic condition does not occur clinically and hemodynamically by means of adaptive mechanisms. While a mild deterioration is observed in the right atrial volume and functions at high altitude, the exact opposite situation is observed in the left atrium. Left atrial functions are found to not deteriorate and even increase in IA.

Conflict of interest

The authors have no conflicts of interest to declare.

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Ethical approval

Ethical approval was obtained for this study from the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee (Number: 2022/460).

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