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ORIGINAL ARTICLE

Changes in cardiac function following a speed ascent to the top of Europe at 4808 m

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Abstract

Purpose Both prolonged exercise and acute high-altitude exposure are known to induce cardiac changes. We sought to describe the cardiac responses to speed climbing at high-altitude, including left ventricular (LV) performance assessment using the myocardial work index (MWI), a new index derived from 2D speckle tracking echocardiography (STE).

Methods Eleven elite alpinists (9 males, age: 26 ± 4 years) were evaluated before and immediately after a speed ascent of the Mont-Blanc (4808 m) by echocardiography using conventional measurements as well as STE and MWI computation with derivate parameters as global work efficiency (GWE) or global wasted work (GWW).

Results Athletes performed a long-duration (8 h 58 min ± 60 min) and intense (78 ± 4% of maximal heart rate) ascent under gradual hypoxic conditions (minimal SpO_2 at 4808 m: 71 ± 4%). Hypoxic exercise-induced cardiac fatigue was observed post-ascent with a change in right ventricular (RV) and LV systolic function (RV fractional area change: – 20 ± 23%, $p = 0.01$; LV global longitudinal strain change: – 8 ± 9%, $p = 0.02$), as well as LV geometry and RV–LV interaction alterations with emergence of a D-shape septum in 5/11 (46%) participants associated with RV pressure overload (mean pulmonary arterial pressure change: + 55 ± 20%, $p < 0.001$). Both MWI and GWE were reduced post-ascent (– 21 ± 16%, $p = 0.004$ and – 4 ± 4%, $p = 0.007$, respectively). Relative decrease in MWI and GWE were inversely correlated with increase in GWW ($r = -0.86$, $p = 0.003$ and $r = -0.97$, $p < 0.001$, respectively).

Conclusions Prolonged high-altitude speed climbing in elite climbers is associated with RV and LV function changes with a major interaction alteration. MWI, assessing the myocardial performance, could be a new tool for evaluating LV exercise-induced cardiac fatigue.

Keywords Altitude · Exercise · Cardiac fatigue · Myocardial work index · 2D speckle tracking echocardiography

Abbreviations

ABP	Arterial blood pressure
AMS	Acute mountain sickness
ANOVA	Analysis of variance
BM	Body mass
GCW	Global constructive work
GLS	Global longitudinal strain
GWE	Global work efficiency
GWW	Global wasted work
[Hb]	Hemoglobin concentration
Hct	Hematocrit
HR	Heart rate
HR_{max}	Maximal heart rate
LV	Left ventricle
LVED	Left ventricle end-diastolic
LVEF	Left ventricle ejection fraction
LVEI	Left ventricle end-systolic eccentricity index

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LLQ	Lake Louise questionnaire
mPAP	Mean pulmonary artery pressure
MWI	Myocardial work index
PEH	Postexercise hypotension
PV	Plasma volume
RPE	Rating of perceived exertion
RV	Right ventricle
RV FAC	Right ventricle fractional area change
SD	Standard deviation
SV	Stroke volume
sPAP	Systolic pulmonary artery pressure
SpO_2	Pulse oxygen saturation
STE	Speckle tracking echocardiography
TTE	Transthoracic echocardiography
$\dot{V}O_{2peak}$	Peak oxygen uptake

Introduction

Exercise at altitude as performed during ski mountaineering (Duc et al. 2011), alpine-cycling (Neumayr 2004), mountain ultramarathon (Fornasiero et al. 2018) or mountaineering (Billat et al. 2010) represents a physiological challenge for the human organism. Over the past years, speed ascent emerged as a new extreme mountaineering activity among elite mountaineers, consisting in reaching summits from the bottom as fast as possible and being associated with prolonged strenuous exercise under hypoxic conditions (Millet and Jornet 2019). The physiological impact of this new mountaineering activity remains uninvestigated while it could represent a unique model of combined hypoxic and exercise stresses. Specific studies in this population of elite climbers are also required; indeed they may exhibit specific physiological characteristics (Bernardi 2006; Puthon et al. 2016) making inappropriate the transposition of physiological observations from other populations of mountain athletes or activities at lower altitudes (Neumayr 2004; Billat et al. 2010; Duc et al. 2011; Fornasiero et al. 2018).

It is well-established that prolonged exercise such as ultra-marathon can induce acute and temporary cardiac modifications including changes in left (LV) and right (RV) ventricular dimensions and functions, a phenomenon known as exercise-induced cardiac fatigue (Elliott and La Gerche 2015; Lord et al. 2018). Acute high-altitude exposure is also known to induce substantial cardiac and hemodynamic changes, mainly associated with the hypoxia-induced elevation in pulmonary vascular resistance (Allemann et al. 2004; Naeije 2010; Maufrais et al. 2017, 2019; De Boeck et al. 2018). Hence, while both prolonged exercise and acute high-altitude exposure are known to induce cardiac modifications, the cardiac impact of combining these two factors needs to be further investigated using exhaustive echocardiography measurements (Dávila-Román et al. 1997; Boos et al. 2014; Stembridge et al. 2015). Moreover, changes in LV function induced by exercise and/or hypoxic exposure may be difficult to interpret using conventional echocardiographic measurements as LV ejection fraction (LVEF) since changes in heart rate (HR) or cardiac loading conditions associated with sympathetic activation may influence these parameters (Naeije 2010; Dalla Vecchia et al. 2014; Lord et al. 2018; Simpson et al. 2021). Therefore, conventional echocardiographic measurements may not allow to distinguish between intrinsic myocardial impairment and cardiac changes associated with systemic hemodynamic variations. Recent progress in ultrasound imaging, especially 2D speckle tracking echocardiography (STE), now allows to detect early impairments in LV function with a better sensitivity than conventional measurements in cardiac diseases (Smiseth et al. 2016) or in sports cardiology (Forsythe et al. 2018). However, longitudinal strain remains sensitive to the LV load (Smiseth et al. 2016). Approach of the myocardial efficiency through the measurement of systolic myocardial work (LV pressure–volume loops) could allow a load-independent LV mechanical assessment but requires an invasive procedure (Sörensen et al. 2020), hardly compatible with field investigations. Recently, a non-invasive and ultrasound-based myocardial work assessment using pressure–strain loops derived from STE has been developed (Russell et al. 2012; Boe et al. 2019) and has shown strong correlations with invasive measurements (Russell et al. 2012; Hubert et al. 2018). This attractive non-invasive method has been used for myocardial evaluation in patients suffering from heart diseases (Chan et al. 2019; Tadic et al. 2021) as well as in endurance athletes in three recent studies (Sengupta et al. 2020; D'Andrea et al. 2020; Tokodi et al. 2021), but never with a focus on exercise-induced cardiac muscle fatigue or in high-altitude conditions.

The aim of this study was to describe the global cardiologic response to a speed high-altitude ascent in elite climbers and specifically changes in the LV systolic function using new echocardiograph-derived myocardial work assessment. We hypothesized that a speed high-altitude ascent would induce cardiac fatigue in elite trained climbers, especially with a decrease in LV myocardial work.

Methods

Ethical approval

This study was approved by a French ethic committee (CPP Ouest VI, approval reference number 2019-A01866-51) and was conducted in accordance with the Declaration of Helsinki, except for the registration in a database. All participants signed a written informed consent before inclusion.

Participants

Elite climbers from the French national high-altitude climbing team were invited to participate in this prospective, observational, study including physiological evaluations before, during and after a direct ascent to the top of the Mont-Blanc (4808 m).

Study protocol

The study was conducted in September 2019 and consisted in three phases: 1) pre-ascent measurements consisting in anthropometric and physiological measurements, venous blood sampling, questionnaires and a transthoracic echocardiography (TTE), 2) a direct and speed ascent of the Mont-Blanc (the highest mountain of Western Europe; 4808 m), starting from the valley (Chamonix-Les Houches, France, altitude: 1000 m) with + 3808 m of altitude and about 14 km to the summit (see Fig. 1 for ascent profile), following the French normal route and 3) post-ascent measurements including anthropometric measurements, venous blood sampling, questionnaires and TTE. This study is a part of a global altitude research project aiming to study the physiological impact of a speed high-altitude ascent in elite climbers and some results about cognitive impact have been recently published (Champigneulle et al. 2022). However, except baseline subject characteristics, data presented in the present study have been never published.

Pre-ascent measurements were conducted in Chamonix-Les Houches (altitude: 1000 m). Post-ascent measurements were performed as soon as possible after arrival at the Goûter hut (3835 m), where the climbers went down as fast as possible (-973 m, about 4.1 km) after reaching the summit. During the ascent, pulse oxygen saturation (SpO_2, from a finger pulse oximeter after finger warming) and questionnaire assessments were performed at different altitude levels: 3835 m and 4362 m, corresponding to the different mountain huts along the normal route (Fig. 1), and upon arrival to the summit (4808 m). The departure was staggered between participants from 1:30 to 3:00 AM. Weather and route conditions were good and stable during the ascent. Atmospheric pressure was 683 mmHg at 1000 m during pre-ascent evaluations and 487 mmHg at 3835 m during post-ascent evaluations. The usual time of ascent to the Mont-Blanc by the same route by non-elite mountaineers is classically two days, with the first 1400-m ascent performed by using a tramway and with one night spent at the Goûter hut (3835 m) (Billat et al. 2010).

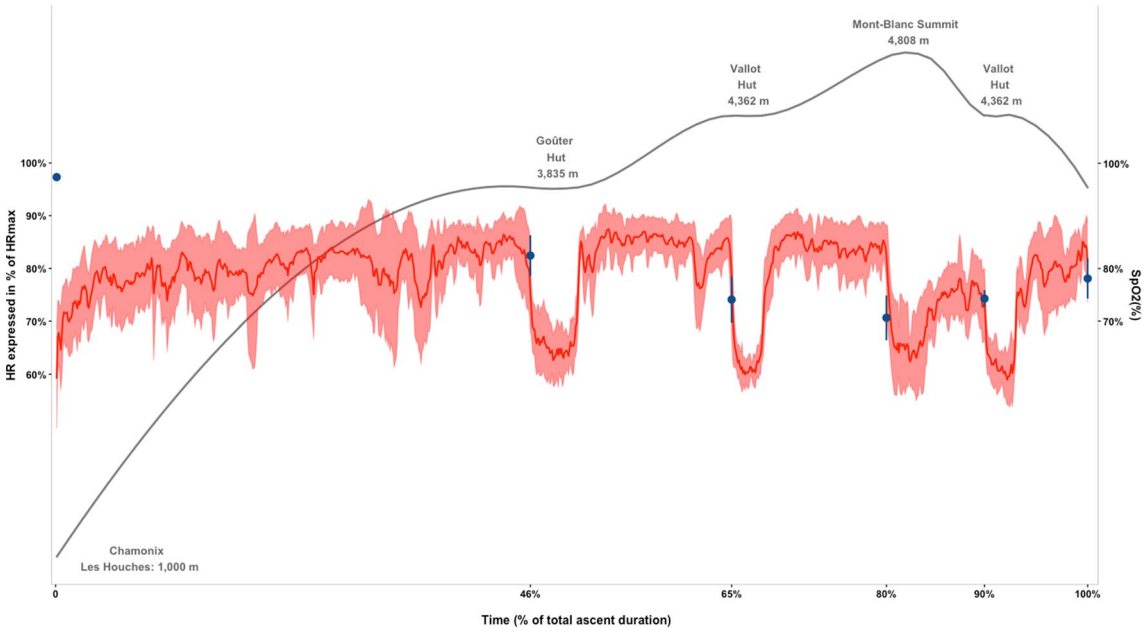

Fig. 1 Ascent profile, kinetic of average heart rate (HR) expressed in percentage of maximal HR (HR_{max}) and changes in average oxygen saturation (SpO_2) at the different checkpoints during the ascent. Gray line represents the profile of the ascent up to the top of the Mont-Blanc, with the different huts and corresponding altitudes along the route. The red line represents the average HR of the elite climbers ($n = 11$) during the ascent (left y-axis), expressed as function of the average relative total exercise duration, while the red filled zone represents its standard deviation (SD). The blue dots and bars represent the SpO_2 of the participants (mean ± SD) measured at the different checkpoints (right y-axis)

Non-cardiac assessment

Maximal exercise test

Before the ascent, a maximal incremental test was performed on a motorized treadmill (T170, Cosmed, Rome, Italy) with a constant 15% slope. After a 4-min warm-up period at 4 km·h^{-1}, speed was increased to 6 km·h^{-1} and then by 1 km·h^{-1} every 2 min, until exhaustion. During the test, HR and respiratory gas exchanges were monitored breath by breath through a facemask (Quark b^2, Cosmed, Rome, Italy). Peak oxygen uptake ($\dot{V}O_{2peak}$) as well as maximal HR (HR_{max}) were determined.

Anthropometric measurements

Body mass (BM), body fat (expressed in % of BM) and total body water (expressed in % of BM) were measured pre-ascent, then repeated post-ascent at 3835 m, by using bioelectrical impedancemetry (SC240, Tanita Corp., Tokyo, Japan).

Blood analysis

Hematocrit (Hct) and hemoglobin concentration [Hb] were measured using a microhematocrit centrifugation (Hemata STAT-II, Separation Technology Inc., Sandford, USA) and a Hb point-of-care testing (Hemocue® Hb201 +, Hemocue AB, Ängelholm, Sweden), respectively, from a venous blood sample obtained pre- and post-ascent. Relative change in plasma volume (ΔPV) between pre- and post-ascent was calculated using the Dill and Costill equation (Dill and Costill 1974).

Acute mountain sickness (AMS)

Participants completed the 2018 version of the Lake Louise Questionnaire (LLQ), pre-ascent (1000 m), during the ascent, and immediately post-ascent at 3835 m (Roach et al. 2018). A score derived from the questionnaire ≥ 3 (with ≥ 1 point for headache symptom) indicated the presence of AMS (Roach et al. 2018).

Exercise intensity

Continuous heart rate (HR) recording during the ascent was used to assess exercise intensity. Heart rate, as well as speed ascent and GPS traces were continuously monitored for all participants during the ascent using a GPS sport-watch associated with a HR transmitter chest belt (Suunto®, Vantaa, Finland; Garmin®, Olathe, Kansas, USA; Polar®, Kempele, Finland). HR values were reported as percentage of HR_{max}. To consider the reduction of HR_{max} with altitude, HR_{max} was corrected between 3835 and 4808 m, using a single mean value of altitude of 4300 m (a preliminary analysis using a 2-level altitude correction did not show significantly different results), using the following formula:

$HR_{max}\ (\text{corrected}) = HR_{max} - 0.0024 \times (\text{altitude gain}) + 0.7296$ (Mourot 2018). To allow the graphical visualization of HR fluctuation during the ascent (Fig. 1), HR values were aggregated using a piecewise aggregate approximation algorithm function (Keogh et al. 2001) and expressed as a function of the average relative total exercise duration. To describe the exercise intensity during the ascent, four zones of intensity were used, according to the following HR values: < 70% of HR_{max} (low intensity zone), 70–80% of HR_{max} (moderate intensity zone), 80–90% of HR_{max} (high intensity zone) and > 90% of HR_{max} (very high intensity zone) (Neumayr 2004).

Perceived exertion

Rating of perceived exertion (RPE) was evaluated using the original 6–20 Borg scale during the ascent and immediately after going down to 3835 m (Williams 2017).

Echocardiography

All transthoracic echocardiographies were performed by the same experienced cardiologist (SD), before and immediately after the end of physical exertion. TTE was performed using a 3.5 MHz probe, connected to a Vivid IQ echocardiograph (GE Vingmed Ultrasound, Horten, Norway). Acquired images and cine-loops were stored for subsequent analysis using a dedicated software (EchoPAC version 203, GE Vingmed Ultrasound, Horten, Norway).

Standard 2D, M-mode and Doppler measurements were conducted according to current guidelines (Rudski et al. 2010; Lang et al. 2015; Nagueh et al. 2016). The LVEF was calculated using the biplane Simpson method. Global longitudinal strain (GLS) of LV was calculated in an 18-segment model from the apical 4-chamber, the apical 2-chamber, and the apical long-axis views. Mid LV radial strain was calculated from a mid-ventricular parasternal short-axis view. Special attention was given to image quality and frame rate (Lang et al. 2015). LV diastolic function was assessed by registration of pulsed mitral Doppler (Peak E and peak A velocities, E/A ratio) as well as the lateral annular early diastolic e' velocity using tissue Doppler, reflexing the LV intrinsic relaxation (Nagueh et al. 2016). Right ventricular global systolic function was assessed by the RV fractional area change (RV FAC), the pulsed tissue Doppler peak velocity at the tricuspid annulus (S') (Rudski et al. 2010) and by the measurement of the RV free wall longitudinal strain obtained in STE (Lang et al. 2015). Systolic pulmonary artery pressure (sPAP) was calculated from the peak velocity

of the tricuspid regurgitation using the simplified Bernoulli equation (Rudski et al. 2010). Mean pulmonary artery pressure (mPAP) was calculated from the formula: $mPAP = (0.61 \times sPAP) + 2$ (Chemla et al. 2004). Doppler velocities of the transtricuspid flow were measured using pulsed Doppler (peak E, peak A, E/A ratio). Interaction between RV and LV was assessed in parasternal short-axis view at the mid-papillary level, first by a visual assessment of the septum geometry in systole (classified as normal, intermediate or flattened) and secondly by computation of the LV end-systolic eccentricity index (LVEI), as follow: $LVEI = \frac{\text{LV anteroposterior dimension}}{\text{LV septolateral dimension}}$. An LVEI > 1 in systole may suggest a RV pressure overload (Rudski et al. 2010).

Myocardial work assessment

LV pressure–strain loops were computed from STE and the estimation of the peak of systolic LV pressure using a specific algorithm from a commercial dedicated software (EchoPAC, version 203, GE Vingmed Ultrasound, Horten, Norway), as previously described, for each myocardial segment (Chan et al. 2019; Sengupta et al. 2020; D'Andrea et al. 2020; Tadic et al. 2021). Peak of systolic LV pressure was estimated by the brachial systolic arterial blood pressure (ABP). From a global built LV pressure–strain loop, myocardial work index (MWI) was defined as the total area within the loop. Three other indices were derived: the global constructive work (GCW), corresponding to the work contributing to LV ejection (i.e. myocardial shortening in systole adding the work produced by the myocardial lengthening in isovolumetric relaxation); the global wasted work (GWW), corresponding to the work produced by LV that do not contributed to LV ejection (i.e. myocardial lengthening during systole adding myocardial shortening in isovolumetric relaxation); and the global work efficiency (GWE), corresponding to the ratio between GCW and the total work (GWW plus GCW).

Statistical analysis

Continuous variables were reported as means ± standard deviation (SD). Normality of distribution was assessed using a Shapiro–Wilk test. Pre- *vs*. post-ascent continuous variables were compared using paired Student *t*-tests. A one-way repeated measure analysis of variance (ANOVA) was performed to assess changes in continuous variables measured during the ascent. Categorical variable was expressed as number and percentage (%) and was compared using a McNemar-Bowker test of symmetry. Correlations between continuous variables and between their pre-post percent changes through the ascent were performed using Pearson correlation coefficients. All statistical analyses were performed using R version 3.4.2 for Mac OS, GNU General Public Licenses GNU (The R Foundation for Statistical Computing, Vienna, Austria) and GraphPad Prism version 9.0.2 (GraphPad Software, San Diego, CA, USA). All tests were two-sided and a p-value < 0.05 was considered statistically significant.

Results

Participants' characteristics

Eleven elite climbers (9 males and 2 females) participated in the study (Table 1). All were free of any medical history or medication and non-smokers. As shown in Table 1, mean $\dot{V}O_{2peak}$ reflected high aerobic capacities. All participants, except one, were exposed to an altitude > 3000 m during the previous month. None had previous history of severe AMS.

Speed ascent responses

Climbing performance

All climbers completed the ascent. The total ascent duration was 8 h 58 min ± 60 min, including 7 h 10 min ± 42 min to the summit. Detailed time and speed of ascent are reported in the Table 2. Among the pre-ascent physiological variables (Table 1), only $\dot{V}O_{2peak}$ was significantly correlated with the climbing performance (i.e., the total exercise duration: $r = -0.61$, $p = 0.048$).

Table 1 Demographic and physiological pre-ascent characteristics of the participants

	Elite climbers ($n = 11$)
Demographic data	
Age (years)	26 ± 4
Altitude of residence (m)	606 ± 452
Anthropometric data	
Body mass (kg)	67.0. ± 9.0
Height (cm)	175.5 ± 6.8
BMI ($kg \cdot m^{-2}$)	21.7 ± 2.0
Body fat mass (%)	13.3 ± 3.8
Total body water mass (%)	61.0 ± 3.4
Maximal exercise test	
Rest HR (bpm)	59 ± 10
HR_{max} (bpm)	193 ± 8
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	61.0 ± 5.9

Data are expressed as mean ± SD

BMI body mass index, $\dot{V}O_{2peak}$ peak oxygen uptake, *HR* heart rate, HR_{max} maximal HR

Table 2 Heart rate and vertical speed during the ascent

	Uphill Section 1 1000 – 3835 m	Uphill Section 2 3835 – 4808 m	Downhill section 4808 – 3835 m
Relative time (%) in each HR zone			
< 70% of HR_{max}	18 ± 14	14 ± 3	44 ± 15
70%–80% of HR_{max}	31 ± 19	17 ± 18	34 ± 9
80%–90% of HR_{max}	47 ± 25	62 ± 17	21 ± 17
≥ 90% of HR_{max}	4 ± 6	7 ± 10	1 ± 2
Mean HR (bpm)	151 ± 11	150 ± 7	133 ± 11
Mean HR (% of HR_{max})	79 ± 5	82 ± 3	72 ± 5
Denivelation (m)	+ 2,835	+ 973	− 973
Distance (km)[a]	9.8	4.1	4.1
Vertical speed ($m \cdot h^{-1}$)	+ 626 ± 76	+ 391 ± 75	− 570 ± 144
Section duration (min)	275 ± 33	154 ± 28	109 ± 29

Data are expressed as mean ± SD

HR heart rate, HR_{max} maximal HR

[a] Approximate covered distance

Table 3 SpO_2 and questionnaires assessment during the ascent

	Pre-ascent (1000 m)	Uphill (3835 m)	Uphill (4362 m)	Summit (4808 m)	Downhill (4362 m)	Post-ascent (3835 m)	*P*
SpO_2 (%)	97 ± 1	83 ± 4	74 ± 4	71 ± 4	74 ± 2	78 ± 4	< 0.001
Borg RPE score	–	14 ± 2	15 ± 2	17 ± 2	–	14 ± 2	0.007
LLQ							
LLQ score	0.5 ± 0.5	1.6 ± 0.5	3.4 ± 1.2	3.6 ± 1.4	–	2.8 ± 1.3	< 0.001
AMS, *n* (%)	0 (0%)	0 (0%)	5 (45%)	4 (36%)	–	4 (36%)	–

Data are expressed as mean ± SD or number (percentage)

RPE, rate of perceived exertion; LLQ, Lake Louise Questionnaire; AMS, acute mountain sickness

Exercise intensity

Changes in HR during the ascent are shown in Fig. 1 and in Table 2. The average HR during the ascent was 147 ± 9 bpm (78 ± 4% of HR_{max}). Participants remained 49 ± 18% of the ascent duration above 80% HR_{max}. High exercise intensity level during the ascent was corroborated by average RPE ranging from a "somewhat hard" to "hard" perceived exertion (Table 3).

Hypoxic load

Progressive hypoxemia was observed during the ascent (Fig. 1 and Table 3), until reaching a minimal SpO_2 value of 71 ± 4% at summit arrival (4808 m). AMS occurred in some climbers during the ascent (Table 3), with a maximal prevalence of 45% at 4362 m. Neither SpO_2 nor LLQ score during the ascent were significantly correlated with the climbing performance.

Table 4 Anthropometric measurements pre- and post-ascent

	Pre-ascent (1000 m)	Post-ascent (3835 m)	*P*
Body mass (kg)	67.0 (9.0)	67.2 (9.5)	0.59
Body fat mass (%)	13.3 (3.8)	13.1 (3.6)	0.66
Total body water mass (%)	61.0 (3.4)	61.1 (3.2)	0.74

Data are expressed as mean ± SD or number (percentage)

Anthropometry

No significant change in BM, as well as body water or body fat composition were observed post-ascent (Table 4).

Hematocrit, [Hb] and PV change

Hct decreased from 46.9 ± 1.4% to 44.0 ± 1.1% ($p = 0.001$) and [Hb] also decreased from 15.2 ± 1.0 $g \cdot dL^{-1}$ to

14.5 ± 0.5 g·dL^{-1} ($p = 0.01$). Calculation of ΔPV indicated an increase of plasma volume of $10.7 \pm 8.5\%$ from pre- to post-ascent.

Cardio-vascular impact of the ascent

Post-ascent TTE was performed with a delay of 19 ± 15 min after arrival to the hut.

Hemodynamic

Post-ascent measurements (Table 5) showed an increase in mean HR (absolute change: $+35 \pm 12$ bpm, $p < 0.001$) and a decrease in systolic BP ($-8 \pm 7\%$, $p = 0.006$). CI increased by $39 \pm 38\%$ ($p = 0.003$), despite a decrease in stroke volume (SV, $-14 \pm 15\%$, $p = 0.001$). mPAP significantly increased post-ascent ($+55 \pm 20\%$, $p < 0.001$).

Right ventricle

Pre-ascent, RV was slightly dilated as classically observed in endurance athletes. RV showed a significant dilatation post-ascent: indexed RV area increased at the end of systole ($+46 \pm 56\%$, $p = 0.02$), with a similar trend at the end of diastole ($+17 \pm 26\%$, $p = 0.07$). All markers of systolic RV function (RV FAC, S' velocity and RV free wall strain) pointed towards a decrease in RV systolic function post-ascent (Table 5). In particular, RV FAC decreased by $-20 \pm 23\%$ ($p = 0.01$). Moreover, RV filling pattern (E/A ratio) was significantly modified post-ascent (Table 5). Maximal inferior vena cava diameter increased by $10 \pm 9\%$ ($p = 0.005$).

Left ventricle

Decrease in left ventricle end-diastolic (LVED) volume was marked ($-17 \pm 10\%$, $p = 0.001$) and was negatively correlated with the increase in mPAP ($r = -0.93$, $p < 0.001$) but not with the change in HR ($r = 0.05$, $p = 0.88$). LV GLS decreased by $8 \pm 9\%$ ($p = 0.02$) and mid LV radial strain by $-28 \pm 24\%$ ($p = 0.004$). MWI decreased by $21 \pm 16\%$ ($p = 0.004$, Fig. 2a) and GWE decreased by $4 \pm 4\%$ ($p = 0.007$, Fig. 2b), without significant variation of both global constructive and wasted work (Fig. 2c, d, respectively). Post-ascent, LV filling pattern was significantly modified (Table 5). The decrease in MWI was inversely correlated with the changes in GWW ($r = -0.86$, $p = 0.003$) but not with those in GCW ($r = 0.38$, $p = 0.32$). The decrease in GWE was also inversely correlated with the changes in GWW ($r = -0.97$, $p < 0.001$) but not in GCW ($r = 0.13$, $p = 0.73$). The changes in MWI were significantly correlated with changes in both LV GLS ($r = 0.71$, $p = 0.03$) and systolic ABP ($r = 0.71$, $p = 0.03$), but not with the changes in the E/A mitral ratio ($r = 0.63$, $p = 0.07$) or HR ($r = 0.56$, $p = 0.12$). The decrease in LV GLS was inversely correlated with the changes in GWW ($r = -0.78$, $p = 0.01$), but not in GCW ($r = 0.10$, $p = 0.80$). No significant correlation between changes in mid LV radial strain and in MWI (and derived indexes) were observed (all $p > 0.05$).

RV and LV interaction

LVEI increased by $27 \pm 14\%$ ($p < 0.001$) from pre- to post-ascent together with emergence of a septal flattening in about 50% of the participants (Fig. 3 and Electronic Supplementary Material Video S1), suggesting a RV pressure overload.

Correlations of TTE variables with performance and AMS

Neither markers of ventricular systolic functions (LVEF, RV FAC, STE and myocardial work indices) in pre- or post-ascent conditions, nor their changes across the ascent were significantly correlated with the aerobic capacities ($\dot{V}O_{2peak}$), the climbers' performance (i.e. total exercise duration), or the LLQ scores (Table 3) measured during the ascent.

Discussion

In this exploratory study, we characterized the changes in cardiac function induced by a mountaineering speed ascent in elite climbers. We showed a significant cardiac impact of combined high-intensity prolonged exercise and hypoxic exposure, including an enlargement of RV associated with a decrease in LV volumes, a geometric change in bi-ventricular interaction and a bi-ventricular decrease of both systolic and diastolic functions. Moreover, MWI, a new non-invasive tool for myocardial work assessment, was significantly decreased after the speed ascent.

A fast and intensive ascent

Physiological data obtained during the ascent confirmed that mountaineering speed ascent represent a high-intensity exercise. Furthermore, the exertion was prolonged and associated with a severe hypoxemia. Occurrence of AMS in this study likely reflected the effect of severe exertion during speed climbing on the perception of the non-specific symptoms characterizing AMS (Rupp et al. 2013), according with the fact that AMS is generally considered to develop after > 6 h at high altitude (Hackett and Roach 2001).

Table 5 Hemodynamic and echocardiographic parameters recorded during pre- and post-ascent measurements

	Pre-ascent (1000 m)	Post-ascent (3835 m)	*P*
Systemic hemodynamic variables			
Systolic BP (mmHg)	124 ± 10	115 ± 13	0.006
Diastolic BP (mmHg)	72 ± 5	66 ± 12	0.07
Mean BP (mmHg)	90 ± 7	82 ± 11	0.02
HR (bpm)	61 ± 9	95 ± 7	<0.001
Left and right atria			
LA volume (mL m^{-2})	33.4 ± 4.7	32.9 ± 8.2	0.82
RA volume (mL m^{-2})	30.3 ± 4.7	32.1 ± 6.6	0.23
Left ventricle			
LV morphology			
LV ED diameter (mm)	49.3 ± 4.4	45.6 ± 4.7	<0.001
LV ES diameter (mm)	32.4 ± 2.5	31.7 ± 3.1	0.32
Septal wall thickness (mm)	9.1 ± 1.0	9.7 ± 1.0	0.03
Posterior wall thickness (mm)	8.9 ± 1.2	9.4 ± 1.3	0.05
LV ED volume (mL)	115.9 ± 17.7	96.6 ± 19.2	0.001
LV ES volume (mL)	47.5 ± 8.3	42.6 ± 9.7	0.04
Indexed LV mass (g m^{-2})	96.4 ± 20.3	96.9 ± 23.1	0.91
LV systolic function			
LV shortening fraction (%)	34.2 ± 4.0	30.9 ± 2.3	0.02
LVEF - Simpson (%)	59.2 ± 2.4	55.6 ± 6.5	0.06
Stroke volume (mL)	68.3 ± 10.4	53.7 ± 12.8	0.001
Cardiac index (L min^{-1} m^{-2})	2.9 ± 0.7	4.0 ± 0.8	0.003
LV GLS (%)	−19.5 ± 1.3	−17.9 ± 2.4	0.02
Mid LV radial strain (%)	−19.3 ± 2.6	−13.6 ± 5.0	0.004
LV diastolic function			
Peak E	74.1 ± 9.1	60.5 ± 8.2	0.001
Peak A (cm s^{-1})	45.3 ± 9.3	60.5 ± 15.1	0.01
E/A ratio	1.7 ± 0.5	1.0 ± 0.2	0.002
Peak e' (cm s^{-1})	17.5 ± 2.6	14.9 ± 2.6	0.02
Right ventricle			
RV morphology			
Indexed RV ED area (cm^2 m^{-2})	13.3 ± 1.9	15.2 ± 2.5	0.07
Indexed RV ES area (cm^2 m^{-2})	7.1 ± 2.0	9.6 ± 2.3	0.02
RV pressure estimation			
Maximal IVC diameter (mm)	20.5 3.1	22.3 ± 2.8	0.005
mPAP (mmHg)b	19.1 1.5	29.7 ± 4.7	<0.001
RV systolic function			
RV FAC (%)	47.7 8.0	37.2 ± 8.8	0.01
S' velocity (mm s^{-1})	15.2 1.8	13.7 ± 1.4	0.02
RV free wall strain (%)	–23.9 2.6	–20.6 ± 3.4	0.04
RV diastolic function			
Peak E (cm s^{-1})	50.2 ± 8.7	43.0 ± 10.4	0.14
Peak A (cm s^{-1})	25.1 ± 3.4	45.6 ± 10.5	<0.001
E/A ratio	2.1 ± 0.6	1.0 ± 0.2	<0.001
RV-LV interaction			
LVES eccentricity index	1.2 ± 0.1	1.4 ± 0.2	<0.001
Septum geometry in systole			
Normal	11 (100 %)	1 (9.0%)	
Intermediate	0 (0 %)	5 (45.5%)	<0.001
Flattened	0 (0 %)	5 (45.5%)	

Data are expressed as mean ± SD or number (percentage)

BP blood pressure, *HR* heart rate, *LA* left atrial, *RA* right atrial, *LV* left ventricle, *ES* end-systolic, *ED* end-diastolic, *EF* ejection fraction, *GLS* global longitudinal strain, *RV* right ventricle, *IVC* inferior vena cava, *mPAP* mean pulmonary artery pressure, *RV FAC* right ventricle fractional area change

[a]Missing value for 1 subject (9%). [b] Missing value for 3 subjects (27%)

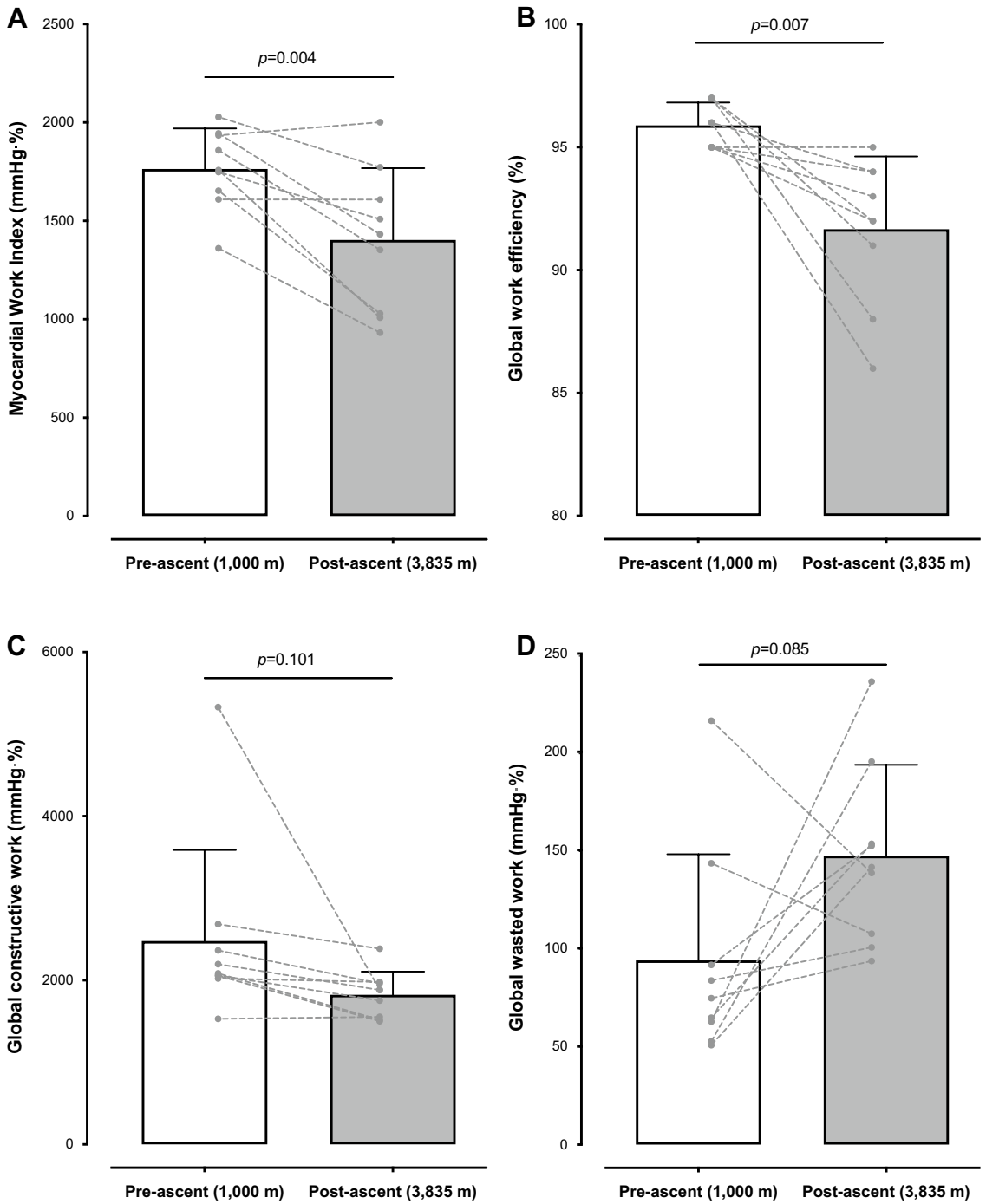

Fig. 2 Myocardial work indices measured pre- and post-ascent. Bar plots and errors bars represent means values and standard deviation whereas connected dots represent individual variations (data missing for 2 participants, $n = 9$ participants)

A major RV impact

As shown in Fig. 3, Video S1 and in Table 5, we observed substantial changes at the RV level post-ascent, which seemed greater (when considering RV FAC) than previously reported following prolonged exercise (Elliott and La Gerche 2015). An important mechanism that could explain the greater decrease in RV systolic function is the large increase in mPAP, leading to a prolonged RV pressure overload. Exercise alone is well-known to increase PAP and RV end-systolic stress especially in high-level athletes (La Gerche et al. 2011) and may induce a significant albeit transitory

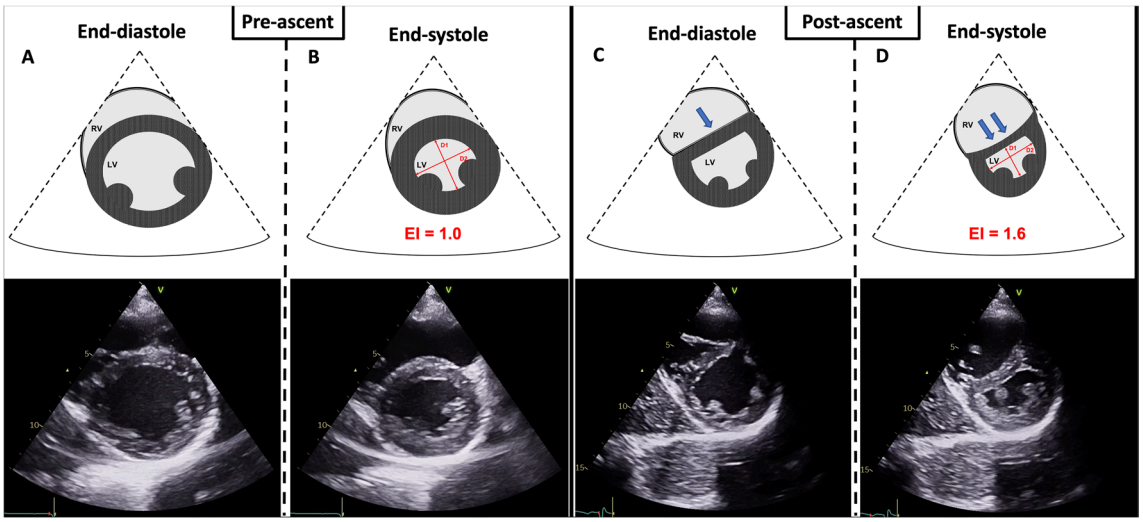

Fig. 3 Change in RV–LV interaction from pre- to post-ascent TTE in one participant, representative of the 50% of the participants in whom a septal flattening was observed post-ascent (see also Video S1). Each panel provides a schematic representation of a TTE parasternal short-axis view (at the papillary muscle level), obtained pre-ascent at the end of diastole (panel A) and at the end of systole (panel B); post-ascent at the end of diastole (panel C) and at the end of systole (panel D). LV EI was computed as the ratio between D2 (LV anteroposterior dimension) and D1 (LV septolateral dimension) as represented in red in the panel B et D (Rudski et al. 2010). The combination of both post-ascent increase in RV afterload and decrease in RV systolic function induced a RV dilatation associated with a flattening septum, leading to a D-shaped LV. The emphasis of the D-shaped LV at the end of systole post-ascent (with a reversal septal curvature as shown in the TTE view and represented by the blue arrows, panel D) as well as the large increase in LV end-systolic EI suggest a RV pressure overload post-ascent (Rudski et al. 2010). *RV* right ventricle, *LV* left ventricle, *TTE* transthoracic echocardiography, *EI* eccentricity index

decrease in the RV systolic function after long-endurance exercise (Elliott and La Gerche 2015). Acute high-altitude exposure is also known to induce hypoxic pulmonary vasoconstriction but does not classically lead by itself to RV systolic change at rest (Naeije 2010; Maufrais et al. 2017, 2019; De Boeck et al. 2018). However, the present results highlight that the additive effects of exercise and hypoxia on RV afterload and RV end-systolic stress can induce a decrease in RV systolic function in trained and partially acclimatized elite climbers after a high-altitude speed ascent, as shown in a previous study (Dávila-Román et al. 1997), in particular because the thin RV wall is not built to counterbalance the increase in PAP and the wall stress associated with exercise (La Gerche et al. 2011).

Appraisal of LV systolic changes could benefit from the use of MWI

Decrease in LV systolic function has previously been well-described in many studies after long-duration exercise (Lord et al. 2018). The proposed main mechanisms pertaining the post-exercise decrease in LV systolic function include beta-adrenergic receptor downregulation, myocardial damage or stunning, and load changes (which cannot explain the changes in TTE observed in the present study by themselves) (Lord et al. 2018). As high-altitude exposure alone does not seem to decrease LV systolic function (Maufrais et al. 2017, 2019; De Boeck et al. 2018) or may even be associated with an increase in LVEF (Allemann et al. 2004; Stembridge et al. 2015), we postulate that the changes in LV systolic function observed in the present study (Table 5 and Fig. 2) are mostly the consequence of the sustained exercise. When considering LVEF calculated by the biplane Simpson method (Lang et al. 2015), change in LV systolic function seemed less marked. LVEF is known to be highly sensitive to changes in LV load conditions (Cikes and Solomon 2016) which varied significantly in the present study. LV GLS, a more sensitive and less load-dependent index of LV function (Cikes and Solomon 2016), well-validated in the context of both high altitude and endurance exercise (Maufrais et al. 2017, 2019; Lord et al. 2018), decreased significantly post-ascent in the present study. Thus, the use of a sensitive TTE marker for LV systolic assessment in conditions combining exercise and hypoxic exposure as in the present study appears relevant. Furthermore, due to the systemic hemodynamics changes induced by both hypoxia and exercise (Naeije 2010; Lord et al. 2018), the preferred LV systolic marker should be also as much load-independent as possible.

In this context, MWI (and its derivate's indices), which correlates well with invasive measurements and reflects myocardial metabolism (Russell et al. 2012; Hubert et al. 2018), could represent a promising marker of LV impairment and LV performance (Boe et al. 2019). The significant correlation observed between MWI variation and both

LV GLS and systolic ABP variation through the ascent was expected, since MWI calculation is computed from these 2 parameters (Manganaro et al. 2020). The tendency of GWW to increase (Fig. 2d) post ascent, as well as the significant inverse correlation between the change in GWW and changes in MWI, GWE and LV GLS, suggests that the observed post-ascent reduction in systolic myocardial performance is more likely a consequence of a larger myocardial wasted work than a decrease in myocardial constructive work. These mechanisms remain to be further investigated in athletes. The present MWI data are difficult to compare with previous published studies since, to the best of our knowledge, this is the first study using MWI in the context of high-altitude exposure to describe exercise-induced cardiac fatigue. No global change in MWI was previously reported after a half-marathon (Sengupta et al. 2020), but the duration and intensity of this exercise performed by recreational athletes were hardly comparable with the conditions of the present study. Finally, using highly trained athletes we did not find any association between the myocardial efficiency (reflected by pre-ascent MWI or its variations through the ascent) and the $\dot{V}O_{2peak}$ or the sport performance as others shown in endurance athletes or hypertensive patients (D'Andrea et al. 2020; Tadic et al. 2021; Tokodi et al. 2021). If MWI could represent a new sensitive ultrasound index to assess myocardial fatigue, its superiority compared to LV GLS, as a more sensitive or early marker, needs to be further confirmed.

A change in right diastolic pattern

RV filling pattern was substantially modified post-ascent, with an increase in late filling, as already observed with a lower magnitude after acute (Maufrais et al. 2017) and prolonged (Maufrais et al. 2019) high-altitude exposure, and which may be explained at least in part by tachycardia (Naeije 2010). In the present study, tachycardia was likely the consequence of an activation of the sympathetic nervous system secondary to both hypoxia and prolonged strenuous exercise (Naeije 2010; Lord et al. 2018). In addition, the vascular volumetric changes associated with the ascent may play a role on RV filling. It is reasonable to assume that the calculated ΔPV represents a valid estimate of the post-ascent PV expansion, assuming that total red blood cell volume was affected neither by the short altitude exposure (Siebenmann et al. 2017) nor by the prolonged exercise and exercise-induced hemolysis (Robach et al. 2014). Although this result may seem contrasting with the early PV reduction seen at high altitude, here the exposure to altitude was likely too short to initiate such change. It is more plausible that PV expansion was induced by prolonged exercise, as shown after a mountain ultramarathon (Robach et al. 2014). In summary, we postulate that the increase in PV combined with the concomitant reduction in RV systolic function could increase the RV preload, as suggested, otherwise, by the increase in the inferior vena cava diameter after the ascent.

RV–LV interdependency may drive a LV diastolic impairment

In all participants but one, we observed a significant change in LV geometry associated with an abnormal septum motion induced by the increase in PAP (De Boeck et al. 2018). This observation has been reported after strenuous exercise at altitude (Dávila-Román et al. 1997) and may explain the LV diastolic change and the post-ascent decrease in LVED volume observed in the present study, as suggested by the strong inverse correlation between mPAP and LVED volume changes. Conversely, the absence of statistical relationship between HR and LVED volume changes, suggests that the increase in HR (leading to shorter LV filling time) had no major effect on the LV preload change post-ascent. Similar modified pattern of LV filling was previously described after prolonged exercise (Lord et al. 2018) and high-altitude exposure (Allemann et al. 2004; Maufrais et al. 2019). At high altitude, the decrease in mitral E/A has been shown correlated with the elevation in PAP (Allemann et al. 2004) and could be the consequence of an altered relaxation induced by the modified LV geometry and flattening septum (Maufrais et al. 2017, 2019). These assumptions have been corroborated by a recent RV–LV interaction physiological study highlighting an alteration of the LV diastolic compliance and then a decrease in LVED volume following pulmonary artery occlusion (Pinsky 2020).

Some compensatory hemodynamic mechanisms

In our study, the important decrease in LVED volume post-ascent participated, alongside the intrinsic decrease in LV systolic function, in the decreased SV. Despite this reduced SV, the increased HR and the decreased LV afterload (as reflected by ABP) allowed an increased cardiac output post-ascent. According to the literature, these hemodynamics post-ascent changes seem mainly triggered by a change in the sympathetic vagal balance that could have been induced by both hypoxia and strenuous exercise (Naeije 2010; Dalla Vecchia et al. 2014; Lord et al. 2018; Simpson et al. 2021). However, if the post-ascent HR increase may be the consequence of sympathetic activation induced by both hypoxia and exercise, the impact of hypoxia on the post-ascent decrease in ABP remains to investigate, as hypoxic exposure usually induces an increase in ABP through sympathoexcitation (Simpson et al. 2021). Postexercise hypotension (PEH) is a well-known phenomenon after exercise and involves notably a postexercise baroreflex resetting (for review, see Halliwill et al. 2013). The effect of hypoxia on PEH remains

mostly under investigated, but at identical workload, a recent study highlighted that a hypoxic exercise (simulated altitude ~ 3000 m), compared to a normoxic condition, was associated with a similar but longer PEH (thus evoking a delayed cardiac autonomic recovery), and with a decrease in cardiac baroreflex sensitivity (Fornasiero et al. 2021).

Based on previous reports (Dávila-Román et al. 1997; Allemann et al. 2004; Naeije 2010; Halliwill et al. 2013; Boos et al. 2014; Elliott and La Gerche 2015; Stembridge et al. 2015; Maufrais et al. 2017, 2019; De Boeck et al. 2018; Lord et al. 2018; Fornasiero et al. 2021), we propose in Fig. 4 a schematic overview of the cardiac changes observed after a speed ascent at high altitude as in the present study.

Our study has several limitations. The sample size was small (corresponding to the entire French national high-altitude climbing team) which may have limited the statistical power (for GWW changes for example); however, despite a small sample, the pre-post ascent changes were both clinically and statistically significant, especially regarding the RV and LV-RV interaction parameters. Although climbing at high altitude represents a unique stress combination for the heart, this field study did not allow to detangle the respective effects of a prolonged endurance exercise and of an acute hypoxic exposure on cardiac function. However, these two factors are nevertheless imbricated as exercise is well-known to increase hypoxemia at high altitude (Rupp et al. 2013), and the combination of these two factors on the field (when speed mountaineering is performed) offers a unique model of cardiac stress. Further studies are required to investigate the mechanisms underlying cardiac fatigue following speed ascent at high altitude as performed by numerous elite-mountaineers in the Alps and other high-altitude regions throughout the world. In particular, quantification of myocardial injury (e.g. using troponin) or investigation of the autonomic cardiovascular balance (e.g. using HR variability and baroreflex sensitivity measurements) associated with cardiac fatigue should be of interest in this setting. Moreover, since only two females were included in the present study, sex-specificity of cardiac changes associated with hypoxic prolonged sustained exercise remains to be investigated.

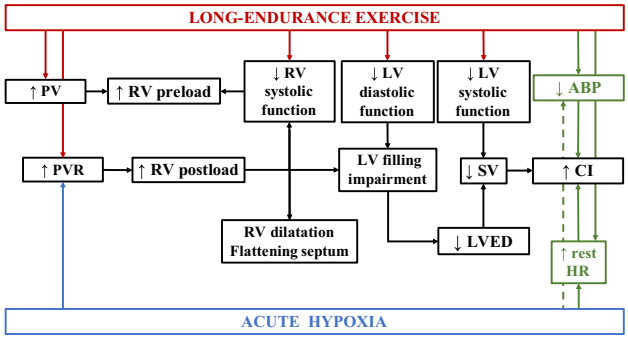

Fig. 4 Proposed schematic explanation of observed cardiac changes after a speed ascent at high altitude according to the present results and previous findings from the literature (Dávila-Román et al. 1997; Allemann et al. 2004; Naeije 2010; Halliwill et al. 2013; Boos et al. 2014; Elliott and La Gerche 2015; Stembridge et al. 2015; Maufrais et al. 2017, 2019; De Boeck et al. 2018; Lord et al. 2018; Fornasiero et al. 2021). Both acute hypoxia and sustained exercise contribute to the RV dilatation and associated decrease in systolic function, mainly by a mechanism of pressure overload. Decrease in LV systolic function is triggered by the exercise without further influence of hypoxia. RV dilatation then RV–LV interaction can participate to the LV filling impairment (leading to a decrease in LVED volume and thus in stroke volume). Hemodynamic changes post-ascent (increase in HR and decrease in ABP), assumed to be triggered by changes in sympathetic vagal balance, allow an increase in CI. Red arrows show changes induced by long-endurance exercise whereas blue arrow shows changes attributed to acute hypoxia. Hemodynamic changes attributed to autonomic nervous system balance modification are depicted in green. Dotted arrow represents uncertain mechanism. *PV* plasma volume, *PVR* pulmonary vascular resistance, *RV* right ventricle, *LV* left ventricle, *LVED* left ventricle end-diastolic, *SV* stroke volume, *ABP* arterial blood pressure, *CI* cardiac index, *HR* heart rate

Conclusion

Prolonged speed climbing at high altitude in elite climbers is associated with bi-ventricular diastolic and systolic changes, notably with a RV enlargement and pressure overload, a major alteration in RV–LV interaction and a decrease in LV systolic function and performance, highlighted by both GLS and MWI changes post-ascent.

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Author contributions BC, SD, SB, JVB, PR, PB and SV designed the study and acquired the data. BC and SD performed the statistical analysis. BC, SD, SB and SV analyzed and interpreted the data. BC, SD and SV wrote the manuscript; PB, PR, JVB and SB revised it critically for important intellectual content. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Availability of data and materials The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the French Ethics Committee CPP Ouest VI (approval reference number 2019-A01866-51).

Consent to participate Written informed consent was obtained from all individual participants included in the study.

Consent to publication The authors affirm that human research participants provided informed consent for publication.

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