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The Effects of Ascent and Descent on Heart Rate and Rhythm at High Altitude

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Abstract

Introduction: Previous studies have reported a variable burden of cardiac arrhythmias, particularly supraventricular (SVE) and ventricular extrasystoles (VES), during hypoxic exposure. The majority of studies have either used simulated altitude and/or subjects at rest with passive ascent (eg cable car). In this study the burden and type of cardiac arrhythmias were recorded during exercise on ascent and descent to Kala Patthar (5643 m) in the Himalayas.

Methods: Ten healthy British Military servicemen aged 18-50 years were included. Health status was confirmed following a baseline history, clinical examination, electrocardiogram and transthoracic echocardiogram. Continuous ambulatory 3 lead ECG recordings (Spacelabs LifeCardTM) were made during trekking ascent to 5643 m at 2610-3840 m, 3450-3880 m, 4240-4940 m and during descent at 5140-4371 m and at 4371-3710 m.

Results: The average age of subjects was 36.1 ± 10.3 years (50% women). All subjects completed the three ascent and two descent treks that were recorded. There was a decrease in the maximal heart rates ($p<0.0001$) and oxygen saturations ($p=0.004$) with increasing HA. VEs were observed in 9/10 subjects at 2610- 3440 m, 7/10 at 3440-3710 m, 6/10 at 4270-4910 m, 9/10 at 5150-4270 m and in 6/10 at 4270-3710 m ($p=0.30$). Overall VE burden was non-significantly higher over ascent (95.0 ± 258.6/hour) versus descent (58.5 ± 171.5/hour; $p=0.58$). There was no significant change in SVEs (4/10 subjects overall) across the 5 treks ($p=0.24$). VEs (80.4 ± 226.5/hour) were more common than SVEs (0.11 ± 0.4/hour; $p<0.001$). There were no sustained pathological tachyarrhythmias.

Conclusion: In this study moderate intensity exercise to 5643 m did not lead to significant cardiac arrhythmia development in healthy subjects. VEs are common and much more prevalent than SVEs and consistently observed during both ascent and descent.

Keywords: High altitude; Heart rate; Descent; Arrhythmias; Exercise; Hypoxia

Introduction

High altitude (HA) exposure leads to a number of recognized cardiovascular responses and adaptations. These are heavily dependent upon a number of factors which include the ascent profile (speed and mode of ascent), duration of exposure and altitude achieved [1,2]. HA related hypobaria induces pulmonary arterial vasoconstriction and a consequent rise in pulmonary artery systolic pressure which contribute to the observed exercise limitation, yet left ventricular systolic function remains relatively well preserved [1,3]. There is an increase in resting heart rate and the rate of ventilation and palpitations are frequently felt, particularly at higher altitudes (>5000 m) [1,4-6].

The sensation of palpitations at HA can be worrying to the individual and can raise genuine concern as to whether they represent something more sinister. They are more common at higher altitudes where the cardiovascular risks are greater which includes the risk of sudden cardiac death (SCD) [5]. This creates further concern especially given that SCD has been cited as the commonest cause of recreational non-traumatic death at HA in adults >34 years [7]. The main mechanism of these sudden deaths is thought to be due to fatal cardiac arrhythmias suggesting a possible link between significant HA and the risk of pathological cardiac arrhythmias [5]. There are a number of factors at HA which might explain its potential pro-arrhythmic risk. These include increased sympathetic activation, the high exercise burden, reduction in heart rate variability, sleep deprivation, elevated anxiety, changes in ventricular repolarisation and a lowering of the ventricular fibrillation threshold [5,8-11].

There is some data to show that HA is linked to an increased frequency of ventricular and supraventricular extrasystoles compared with that at sea level/lower altitude [5,12,13]. However, much of the previous research into a HA-arrhythmia link have tended to focus on

the effects of short term hypoxia (<24 hours), following passive ascent (eg cable car and not trekking/climbing) and the altitudes studied have been relatively low <3500 m [12,13]. In the majority of studies subjects were studied while rested at altitude and not during actual ascent or importantly descent where a significant (>50%) proportion of non-traumatic HA deaths occur [11,14,15]. This, in part, relates to difficulties of obtaining accurate recordings without artefact during exercise and the inherent difficulties of undertaking a HA exercise study.

In this study we sought to investigate the effects of exercise during incremental ascent and descent and its relationship to potential cardiac arrhythmia development. We hypothesised that exercise during ascent at HA would lead to an increasing frequency of cardiac arrhythmias which would lessen on descent.

Methods

Ten healthy British Military servicemen aged 18-50 years were included. Health status was confirmed following a baseline history, clinical examination, electrocardiogram and transthoracic echocardiogram (Sonosite M-Turbo; Sonosite Inc, Bothell, WA, USA). Oxygen saturations (SpO_2) and resting heart rate (Nellcor N-20P pulse oximeter; Nellcor Puritan Bennett, Coventry, UK) were at rest following completion of each study trek. Participation was entirely voluntary and all participants underwent detailed written informed consent. No subjects were on heart rate or rhythm controlling medication. The study was approved by the Ministry of Defence Research and Medical Ethics Committee (MODREC) and was conducted according to the standards of the declaration of Helsinki. The study was conducted during a return trek from Lukla to Kala Patthar (KP, 5643 m) in Nepal. All subjects were required to be in sinus rhythm.

High altitude ascent and descent profile

All subjects flew from the UK to Kathmandu, Nepal (1400 m) where they underwent 48 hours of acclimatization with baseline demographics, including a 10 minute continuous single lead ECG. Thereafter, they flew to Lukla (2840 m) by light aircraft and underwent a short (<1.5 h) trek to Phakding (2610 m; day 1). Thereafter detailed assessment of heart rate and rhythm was assessed during three ascent and two descent treks over the ensuing 14 days. Data was recorded during the ascent from Phakding (2610 m) to Namche Bazar (3440 m, day 2), then at 3440 to 3880 m (day 5), 4270 to 4910 m, day 8. On day 10 the trek team summited Kala Patthar 5643 m. Data was the collected during descent from 5140 m (Gorak Shep) down to 4270 m (day 11) and from 4270 to 3710 m (day 12).

Heart rate/rhythm recording

Continuous ambulatory recording of heart rate and rhythm was performed during a minimum of five minutes rest and following a minimum of 90 minutes exercise during the studied treks Lifecard CF® Digital Holter Recorder, (Spacelabs Healthcare®, Issaquah). Skin electrodes were placed over the superior anterior sternum, the left axilla and the right axilla over the 6th intercostal space following meticulous skin preparation in line with manufacturer's recommendations. All recorded ECG data was stored electronically for subsequent detailed off line full disclosure 3-channel ECG analysis. This was performed by an independent expert in Cardiac Electrophysiology via full inspection of the ECGs and Automated analysis using proprietary software application (Pathfinder 700 Holter Analyzer version 09, Spacelabs Healthcare, Issaquah, Washington) as previously described [16,17]. Arrhythmia detection criteria were as follows: pause, RR interval ≥ 2.50 s; dropped beat ≥ 180 % of RR interval; Ventricular tachycardia, minimum of 5 beats at ≥ 100 bpm; salvo, minimum of 4 beats at ≥ 100 bpm; bradycardia: minimum of 4 beats at ≤ 45 bpm; Supraventricular tachycardia, minimum of 5 beats ≥ 130 bpm fulfilling morphology criteria; premature Aberrant (ventricular extrasystole, VE), ≤ 90 % of RR interval; Isolated aberrant (ventricular extrasystole) >90% of RR interval; premature normal (supraventricular extrasystole, SVE), ≤ 66 % of RR interval; ventricular bigeminy, sinus beat followed by premature ventricular complex recurring in 1:1 pattern; ventricular trigemini. 2 sinus beats followed by a premature ventricular complex recurring in 2:1 pattern. Minimal and maximal heart rates were based on one minute averages.

Statistical analysis

Data were analysed using GraphPad InStat version 3.05 and with all graphical figures presented using GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego, CA, USA; www.graphpad.com). The Kolmogorov-Smirnov test was undertaken to assess normality of all continuous data. The Time-dependent changes in measures of heart rate and rhythm were assessed with repeated measures ANOVA for normally distributed data, with the Tukey post-test (comparing with baseline) for all significant results. Repeated measures of non-parametric continuous data were performed using the Friedman test with the Dunn post-test (comparing with baseline) for all significant results. Unpaired parametric and non-parametric continuous data were compared using an unpaired test and Mann-Whitney Tests respectively. Changes in categorical variables across the five trekking groups were assessed using the Chi-Squared test. A two tailed P value <0.05 was considered statistically significant for all comparisons.

Sample size calculations

In a previous study of 6 health subjects (26-57 years) Guger et al. noted a significant paired increase in resting heart rate and measures of heart rate variability with cable car ascent from 990 m to 2700 m [18]. In another study Kujanik et al. noted a significant increase in VEs on cable car ascent from 898 to 1764 m then 2632 m in 20 healthy subjects with an average VE burden of 48/hour and a an average standard deviation of ≥ 2x the mean [12]. We calculated that a sample size of 10 subjects would have ≥ 80% sufficient power to detect a >40/hour paired difference in VEs given an altitude gain of >2000 m.

Results

The average age of subjects was 36.1 ± 10.3 years, with 50% being female. All subjects completed the three ascent and two descent treks that were recorded. The average recording time was 169.7 ± 58.4 minutes with the longest being 244.3 ± 50.8 minutes during the first ascent from 2610-3450 m. The overall rate of artefact was 6.0 (14.5) % of the total recording period. Assessment of SpO_2 and resting heart rate could not be measured following the last recorded descent due to logistical reasons. There was a significant fall in SpO_2 at HA versus baseline (1400 m) for all altitudes studied (Tables 1 and 2).

Heart rate changes

Baseline minimal heart rate at 1400 m at Kathmandu (59.3 ± 8.8/minute) was significantly lower than that for all of the five HA study points (p=0.002) (Tables 1 and 2). However, there was no significant differences when only the five HA recordings were compared. There was a decrease in the maximal heart rates with increasing HA whereas there was no difference in mean heart rates across the five recordings at HA (Table 2 and Figure 1).

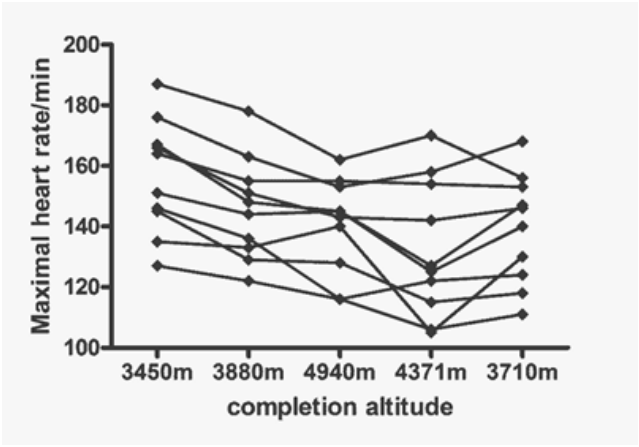

Figure 1: Changes in Maximal Heart rate during sequential trekking ascent and descent.

Heart rhythm recordings

Ventricular ectopy was observed in all participants at HA although the burden markedly differed between subjects. Ventricular ectopy was identified in 9/10 subjects during ascent from 2610 m to 3440 m, 7/10 at 3440 to 3710 m, 6/10 at 4270 to 4910 m, 9/10 at 5140 to 4270 m and in 6/10 during descent from 4270 to 3710 m with no significance of altitude on burden (Chi-Squared p=0.30). Whilst the overall VE burden was greater on the three ascents (95.0 ± 258.6) versus descents (58.5 ± 171.5) the difference was not significant (p=0.58). One or more episodes of ventricular bigeminy were observed in three subjects at HA. Ventricular trigeminy was also observed in three subjects. The burden of trigeminy was non-significantly higher during ascent (0.28 ± 0.8/hour) than descent (0.05 ± 0.1; p=0.25).

One or more SVEs were recorded in 4/10 volunteers at HA (Table 2). They were observed in 2/10, 1/10, 3/10, 3/10 and 0/10 across the five altitudes respectively (p=0.33). The SVE rate was overall non-significantly higher on ascent (0.16 ± 0.4) than descent (0.05 ± 0.20; p=0.23). The overall incidence of VEs (80.4 ± 226.5/hour) was significantly higher than that of SVEs (0.11 ± 0.4/hour; p<0.001). There were no sustained pathological tachyarrhythmias (non-sinus rhythm ≥ 5 beats at >100/minute eg atrial fibrillation, supraventricular or ventricular tachycardia). There were rare isolated dropped beats observed in ≤ 2/10 subjects at the 2nd and 4th trekking period only. There were no recorded bradycardias, observed pauses or episodes of heart block. There was no correlation between SpO_2 and ectopy burden.

Discussion

In this study 10 healthy volunteers without known cardiovascular disease were monitored during three progressive ascent and two descent treks at HA. Ventricular extrasystoles/ectopy were observed in all subjects at HA whereas supraventricular ectopics/extrasystoles were observed in less than half of the cohort. VEs was far more common than SVEs with exercise. Whilst there was a trend to higher SVE and VE burden on ascent versus descent no overall significant difference was observed. There was a progressive reduction in maximal heart rate with increasing HA which improved during descent.

The effect of increasing HA on cardiac arrhythmia development is still very poorly understood. Despite the marked increase in recreational HA exposure (skiing, trekking and climbing) over the last two decades there have been relatively few studies that have investigated the link. This is somewhat surprising given that the reported literature would appear to suggest that HA may be pro-arrhythmic and may increase the risk of SCD [5]. The results of published studies, to date, do seem to be dependent on HA environment (eg simulated or terrestrial real world, active or passive ascent and the ascent profile) as well as the studied population (age, healthy versus known coronary artery disease) [5,12,13,18]. For example in operation Everest II which investigated eight subjects over 40 days during a simulated ascent of mount Everest in a hypobaric chamber (240 torr, 8,848 m), apart from occasional VEs during exercise and minor resting ECG changes, above 3660 m, no other major abnormalities were detected [19]. However, these conclusions were based on relatively sparse data. Two of the eight subjects were removed after acute hypoxic episodes without simultaneous ECG data despite the presence of altered consciousness or acute confusional state; resting ECGs were only recorded at five altitudes above sea level; exercise ECGs only recorded at two altitudes over eight minutes and only three of the subjects exercised at the simulated peak altitude [19].

More recently Kujanik et al. noted a significant increase in ectopy development among 20 healthy men during passive ascent (800-2632 m) to terrestrial HA, followed by descent in a Cable car [12]. The number of subjects who developed ectopy was not documented. Interestingly, one of the subjects, who discovered to have had coronary disease had a short run of ventricular tachycardia. Unfortunately, the duration of this episode or whether it occurred during ascent or descent was not reported. In their study ambulatory ECG data was recorded at 800 m, 1764 m and 2632 m during ascent and at 1764 m and 898 m during descent [12]. Consistent with our study they noted a significantly higher burden of Ventricular compared with supraventricular ectopics [12]. Compared with 2.8 VEs/10 minutes at 898 m (ie16.8/hour) they observed a significant increase to 8.35/10 minutes at 1764 m (=50.1/hour) and 17.84/10 minutes at 2632 m (=107.0/hour) during ascent. Interestingly, there was still a significantly higher burden of VEs during descent at 1764 m (8.05/10 minutes=48.3/hour) [12]. In our study the highest average number of VEs was also greatest during the highest ascent (123.0 VEs/hour at 4240-4940 m). Again similar to the study by Kujanik et al. [12] we did not find a significant increase in SVEs, which were far less frequently observed than VEs, although the highest burden was at the highest altitude ascent.

Our data has shown that in a population of healthy adults trekking to moderate to extreme HA ventricular ectopy is commonly observed during exercise and is prevalent during both ascent and descent during exercise. This may be of more than of academic importance or general interest value. Whilst it well documented that that frequent VEs are

not uncommonly observed in healthy individuals, without structural cardiac abnormalities, these observations have been generally based on subjects at rest [17]. More concerning is when VEs are not supressed and triggered or actually increase with exertion. Frequent VEs (>10%, bigeminy or trigeminy) during exercise and/or recovery has been shown to be an independent predictor of longer term future adverse cardiovascular events including all cause death even in those without known cardiovascular disease [20]. However, short term follow up data among athletes with frequent VE's does appear to be more reassuring, but again relates to sea level and not the the HA environment which was assessed in our study [21].

There are a number of plausible explanations as to why we did not observe a statistically significant increase in ventricular ectopy at the higher altitudes versus lower altitudes. Apart from recording heart rate at 1400 m in Kathmandu a sea level/low altitude baseline exercise recording was not performed. This is unfortunate but was not possible given the trekking itinerary and geography of Kathmandu. Consequently the first prolonged ambulatory recording commenced at 2610 m which is considerably higher than several other studies [12,13]. However, we have previously failed to identify significant cardiac arrhythmias during lower level trekking (near sea level to maximum of 1346 m (Ben Nevis and Three Peaks Challenge) in nine healthy volunteers fitted with an implantable cardiac Monitor (Reveal Model 9525 ILR, Medtronic®) [4]. Secondly, with a sample size of 10 subjects, albeit at five recording time points our study may be underpowered, however a detailed sample size/power calculation was undertaken but the variation (standard deviation) in both VEs and VES between individuals was great. Our study is unique in that we not only investigated subjects during exercise but also during both ascent and descent and the definitions of VEs and the recording times are accurately defined. Recording during exercise is a fundamental aspect of this study given the strong link between SCD and exercise. Whilst a similar average heart rate was observed across the five treks the overall exercise intensity/duration did obviously vary with each trek and the descent was not simply the ascent in reverse. The first trek was the longest and subjectively the hardest and could have minimized the ability to detect true differences related to the effects of HA alone that might have been appreciated with more prolonged recording at rest. Another confounder worth considering was that the first descent started at a marginally higher altitude (5140 m) than the highest recording started during ascent (max 4940 m). Finally, our study was performed over more than a week which brings in the added effect of acclimatisation which could potentially mitigate potential pro-arrhythmic effects of increasing HA [22]. Indeed there is some albeit limited data to support this concept [23,24].

We observed a decrease in the maximal heart rate with increase HA ascent and this effect appeared to reverse on descent with the maximal heart rate increasing on greater descent. It is well documented that compared with sea level or lower altitude, HA leads to an increase in resting heart rate, as observed in this study [6]. Yet paradoxically, despite the rise in resting heart rate it has been consistently observed that increasing HA leads to a fall in the maximal/peak heart rate on exercise [25]. This data has been largely derived from acute hypoxia studies typically using a normobaric or hypobaric chamber [26,27]. The fall in peak heart rate has been shown to correlate with the fall in oxygen saturation (Benoit 2003). The limited data available, published from genuine non-simulated HA studies, suggest that terrestrial HA does lead to a fall in maximal heart rate versus sea level, and that the fall is greater with increasing HA [28]. We were unable to examine this relationship directly as SpO_2 was recorded while rested after each study trek and not during. Acclimatisation appears to attenuate the magnitude of the decline [26]. Furthermore, the maximal heart rate appears to be higher at genuine HA than that observed with acute hypoxia [26,27]. This may relate to the greater physiological stimulus of terrestrial HA (cold, dehydration, and greater anxiety) but also to the effects of acclimatisation. Our study is unique in that it documents the changes in maximal heart rate on descent and has shown that the blunting of maximal heart rate is reduced with descent.

This study has some additional limitations that need to be acknowledged. There was clearly artefact on the ECG recordings which varied by subject and altitude (Table 2). Whilst the overall percentage artefact is lower (9.8-30. 4%) than that reported in previous terrestrial HA studies this could have led to under-appreciation of the true arrhythmia incidence [28]. The artefact appeared to be greater at times of more vigorous exertion which is not unsurprising given the heavy exercise while carrying rucksacks. Data was only collected during exercise following a brief rest period prior to the start of exercise due to competing research. The relationship of ectopy and arrhythmias to markers of acute mountain sickness and perceived exertion were not recorded.

In conclusion in this study it was found that moderate intensity exercise to HA at ≥ 5140 m does not lead to significant cardiac arrhythmia development in healthy subjects. VEs are common and much more prevalent than SVEs and consistently observed during both ascent and descent.

Demographic	Result
Number	10
Age, years (range)	36.1 ± 10.3 (22-50)
Males N, %	5, 50%
Height, cm	174.7 ± 6.1
weight	75.0 ± 11.8
Body mass index kg/m^2	24.5 ± 2.4
Resting mean Heart rate	70.4 ± 8.9
Resting Minimal heart rate	59.3 ± 8.8
Systolic blood pressure	132.0 ± 17.7
Diastolic blood pressure	77.4 ± 9.2
Oxygen saturations, %	95.7 ± 2.3
Current smokers n, %	1, 10%

Table 1: Baseline Demographics at Kathmandu (1400 m).

Parameter	Altitude					P value
-	2610-3450 m	3450-3880 m	4240-4940 m	5140-4371 m	4371-3710 m	-
Total recording time, minutes	244.3 ± 50.8	135.6 ± 39.9	184.2 ± 18.3	165.6 ± 52.6	119.0 ± 27.9	0.0004[ad]
Artefact, % overall recording time	0.95 ± 0.4	6.1 ± 12.2	1.1 ± 0.3	14.5 ± 23.0	7.5 ± 18.2	0.003[d]

Max heart rate/ minute	156.4 ± 18.8	145.9 ± 16.9	140.3 ± 15.7	132.4 ± 22.5	139.3 ± 18.1	<0.0001[abcd]
Average Heart rate/ minute	114.2 ± 16.2	112.5 ± 18.3	109.1 ± 13.0	108.8 ± 17.7	106.4 ± 15.7	0.2
Minimal heart rate/ minute	77.4 ± 11.50	83.8 ± 19.6	74.5 ± 11.0	80.1 ± 13.6	76.7 ± 13.8	0.28
SVEs/hour	0.08 ± 0.25	0.04 ± 0.14	0.36 ± 0.66	0.1 ± 0.32	0	0.24
Isolated aberrant, hour	18.8 ± 59.2	24.9 ± 67.2	48.5 ± 152.6	39.4 ± 120.8	31.3 ± 94.4	0.92
Premature aberrants/hour	35.9 ± 76.2	11.4 ± 20.6	46.9 ± 124.6	17.3 ± 45.9	11.6 ± 23.1	0.75
Ventricular Bigeminy/hour	4.5 ± 13.4	6.8 ± 18.7	5.8 ± 18.0	8.3 ± 20.7	6.0 ± 18.9	0.57
Ventricular trigeminy/hour	0.46 ± 1.2	0.20 ± 0.52	0.15 ± 0.4	0.10 ± 0.20	0	0.33
Total aberrants (VEs)/hour	79.8 ± 193.0	82.1 ± 214.1	123.0 ± 362.0	35.1 ± 81.3	81.9 ± 233.0	0.93
Dropped beats/ hour	0	0.06 ± 0.2	0	0.17 ± 0.4	0	0.26
Oxygen saturations, %	85.7 ± 5.2	87.5 ± 4.6	80.3 ± 4.0	86.5 ± 3.0	-	0.004[b]
Resting heart rate/min	93.8 ± 17.8	84.5 ± 13.5	88.6 ± 12.8	83.2 ± 10.4	-	0.33
Results are displayed as mean ± standard deviation; results of post hoc test compared with baseline 2610-3450 m, a vs 3450-3880 m; b vs 4240-4940 m, c vs 5140-4371 m, d vs 4371-3710 m						

Table 2: Changes in Heart Rate and rhythm with increasing then decreasing altitude.

References

1. Boos CJ, Mellor A, Begley J, Stacey M, Smith C, et al. (2014) The effects of exercise at high altitude on high-sensitivity cardiac troponin release and associated biventricular cardiac function. Clin Res Cardiol 103: 291-299.
2. Bärtsch P, Swenson ER (2013) Clinical practice: Acute high-altitude illnesses. N Engl J Med 368: 2294-2302.
3. Naeije R, Huez S, Lamotte M, Retailleau K, Neupane S, et al. (2010) Pulmonary artery pressure limits exercise capacity at high altitude. Eur Respir J 36: 1049-1055.
4. Woods DR, Allen S, Betts TR, Gardiner D, Montgomery H, et al. (2008) High altitude arrhythmias. Cardiology 111: 239-246.
5. Woods DR, Boos C, Roberts PR (2011) Cardiac arrhythmias at high altitude. J R Army Med Corps 157: 59-62.
6. Boos CJ, O'Hara JP, Mellor A, Hodkinson PD, Tsakirides C, et al. (2016) A Four-Way Comparison of Cardiac Function with Normobaric Normoxia, Normobaric Hypoxia, Hypobaric Hypoxia and Genuine High Altitude. PLoS One 11: e0152868.
7. Burtscher M, Ponchia A (2010) The risk of cardiovascular events during leisure time activities at altitude. Prog Cardiovasc Dis 52: 507-511.
8. Roth WT, Gomolla A, Meuret AE, Alpers GW, Handke EM, et al. (2002) High altitudes, anxiety, and panic attacks: is there a relationship? Depress Anxiety 16: 51-58.
9. Cakici M, Dogan A, Cetin M, Suner A, Caner A, et al. (Negative effects of acute sleep deprivation on left ventricular functions and cardiac repolarization in healthy young adults. Pacing Clin Electrophysiol 38: 713-722.
10. Horii M, Takasaki I, Ohtsuka K, Tsukiyama H, Takahashi A, et al. (1987) Changes of heart rate and QT interval at high altitude in alpinists: analysis by Holter ambulatory electrocardiogram. Clin Cardiol 10: 238-242.
11. Windsor JS, Firth PG, Grocott MP, Rodway GW, Montgomery HE, et al. (2009) Mountain mortality: a review of deaths that occur during recreational activities in the mountains. Postgrad Med J 85: 316-321.
12. Kujaník S, Snincák M, Galajdová K, Racková K (2000) Cardiovascular changes during sudden ascent in a cable cabin to the moderate altitude. Physiol Res 49: 729-731.
13. Kujaník S, Snincák M, Vokál' J, Podracký J, Koval' J (2000) Periodicity of arrhythmias in healthy elderly men at the moderate altitude. Physiol Res 49: 285-287.
14. Firth PG, Zheng H, Windsor JS, Sutherland AI, Imray CH, et al. (2008) Mortality on Mount Everest, 1921-2006: descriptive study. BMJ 337: a2654.
15. McIntosh SE, Campbell AD, Dow J, Grissom CK (2008) Mountaineering fatalities on Denali. High Alt Med Biol 9: 89-95.
16. Grond M, Jauss M, Hamann G, Stark E, Veltkamp R, et al. (2013) Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study. Stroke 44: 3357-3364.
17. Hingorani P, Karnad DR, Rohekar P, Kerkar V, Lokhandwala YY, et al. (2016) Arrhythmias Seen in Baseline 24-Hour Holter ECG Recordings in Healthy Normal Volunteers During Phase 1 Clinical Trials. J Clin Pharmacol 56: 885-893.
18. Guger C, Domej W, Lindner G, Pfurtscheller K, Pfurtscheller G, et al. (2005) Effects of a fast cable car ascent to an altitude of 2700 meters on EEG and ECG. Neurosci Lett 377: 53-58.
19. Malconian M, Rock P, Hultgren H, Donner H, Cymerman A, et al. (1990) The electrocardiogram at rest and exercise during a simulated ascent of Mt. Everest (Operation Everest II). Am J Cardiol 65: 1475-1480.
20. Jouven X, Zureik M, Desnos M, Courbon D, Ducimetière P (2000) Long-term outcome in asymptomatic men with exercise-induced premature ventricular depolarizations. N Engl J Med 343: 826-833.
21. Delise P, Sitta N, Lanari E, Berton G, Centa M, et al. (2013) Long-term effect of continuing sports activity in competitive athletes with frequent ventricular premature complexes and apparently normal heart. Am J Cardiol 112: 1396-1402.
22. Asemu G, Papousek F, Ostádal B, Kolár F (1999) Adaptation to high altitude hypoxia protects the rat heart against ischemia-induced arrhythmias. Involvement of mitochondrial K(ATP) channel. J Mol Cell Cardiol 31: 1821-1831.
23. Meerson FZ, Ustinova EE, Manukhina EB (1989) Prevention of cardiac arrhythmias by adaptation to hypoxia: regulatory mechanisms and cardiotropic effect. Biomed Biochim Acta 48: S83-88.
24. Zhang P, Downey HF, Chen S, Shi X (2014) Two-week normobaric intermittent hypoxia exposures enhance oxyhemoglobin equilibrium and cardiac responses during hypoxemia. Am J Physiol Regul Integr Comp Physiol 307: R721-730.
25. Lundby C, van Hall G (2001) Peak heart rates at extreme altitudes. High Alt Med Biol 2: 41-45.
26. Lundby C, Araoz M, van Hall G (2001) Peak heart rate decreases with increasing severity of acute hypoxia. High Alt Med Biol 2: 369-376.
27. Benoit H, Busso T, Castells J, Geyssant A, Denis C (2003) Decrease in peak heart rate with acute hypoxia in relation to sea level VO(2max). Eur J Appl Physiol 90: 514-519.
28. Kao WF, Huang JH, Kuo TB, Chang PL, Chang WC, et al. (2013) Real-time electrocardiogram transmission from Mount Everest during continued ascent. PLoS One 8: e66579.