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Application for the Prix de la Fondation Coeur de La Tour

Dear Members of the Jury

Enclosed please find the results of a prospective cohort study exploring the risk of latent cardiac arrhythmias in healthy individuals climbing Mount Everest for consideration for the *Prix de la Fondation Coeur de La Tour.*

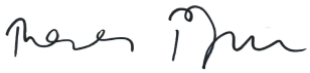
In the SUMMIT study (NCT05676398), individuals climbing Mount Everest underwent 12-lead electrocardiogram, transthoracic echocardiography, and exercise stress testing before, and ambulatory rhythm recording both before and during the expedition. A total of 41 individuals were recruited between January 25 and May 9, 2023; 32 reached an altitude of ≥7,900 meters (South Col), 23 climbed above 8,500 meters, and 14 participants reached the summit of Mount Everest. The primary endpoint, a composite of tachy- and bradyarrhythmia during the ascent to the summit, was detected in 13 out of 34 participants (38.2%) (Sherpa K et al, JAMA Cardiol. 2024;9(5):480-485).

At the same time, we recorded a gradual prolongation of the QT interval with increasing altitudes. The average prolongation of the QTc interval from baseline to the maximum achieved altitude amounted to 66±31 ms. A QTc prolongation of ≥60 ms was recorded in 17 participants (59%), while 7 (24%) had a QTc interval exceeding 470 ms, consistent with an acquired long QT syndrome. Based on our observations, individuals with inherited long-QT syndrome and patients taking medications that prolong the QT interval may be discouraged from exposure to high altitudes (Pilgrim T et al, JACC Clin Electrophysiol. 2024:S2405-500X(24)00709-6).

The SUMMIT study champions inclusive and equitable scientific collaboration between Nepali and Swiss scientists, and was funded by the Swiss Polar Institute. As the principal investigator, the SUMMIT study was a scientific endeavor for me; as a study participant it was at the same time an unforgettable adventure.

Thank you for considering the SUMMIT study for the *Prix de la Fondation Coeur de La Tour*.

Sincerely,



Thomas Pilgrim

JAMA Cardiology | Brief Report

Risk of Cardiac Arrhythmias Among Climbers on Mount Everest

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IMPORTANCE Arterial hypoxemia, electrolyte imbalances, and periodic breathing increase the vulnerability to cardiac arrhythmia at altitude.

OBJECTIVE To explore the incidence of tachyarrhythmias and bradyarrhythmias in healthy individuals at high altitudes.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study involved healthy individuals at altitude (8849 m) on Mount Everest, Nepal. Recruitment occurred from January 25 to May 9, 2023, and data analysis took place from June to July 2023.

EXPOSURE All study participants underwent 12-lead electrocardiogram, transthoracic echocardiography, and exercise stress testing before and ambulatory rhythm recording both before and during the expedition.

MAIN OUTCOME The incidence of a composite of supraventricular (>30 seconds) and ventricular (>3 beats) tachyarrhythmia and bradyarrhythmia (sinoatrial arrest, second- or third-degree atrioventricular block).

RESULTS Of the 41 individuals recruited, 100% were male, and the mean (SD) age was 33.6 (8.9) years. On baseline investigations, there were no signs of exertional ischemia, wall motion abnormality, or cardiac arrhythmia in any of the participants. Among 34 individuals reaching basecamp at 5300 m, 32 participants climbed to 7900 m or higher, and 14 reached the summit of Mount Everest. A total of 45 primary end point–relevant events were recorded in 13 individuals (38.2%). Forty-three bradyarrhythmic events were documented in 13 individuals (38.2%) and 2 ventricular tachycardias in 2 individuals (5.9%). Nine arrhythmias (20%) in 5 participants occurred when climbers were using supplemental bottled oxygen, whereas 36 events (80%) in 11 participants occurred at lower altitudes when no supplemental bottled oxygen was used. The proportion of individuals with arrhythmia remained stable across levels of increasing altitude, while event rates per 24 hours numerically increased between 5300 m (0.16 per 24 hours) and 7300 m (0.37 per 24 hours) before decreasing again at higher altitudes, where supplemental oxygen was used. None of the study participants reported dizziness or syncope.

CONCLUSION AND RELEVANCE In this study, more than 1 in 3 healthy individuals experienced cardiac arrhythmia during the climb of Mount Everest, thereby confirming the association between exposure to high altitude and incidence of cardiac arrhythmia. Future studies should explore the potential implications of these rhythm disturbances.

Supplemental content

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Arterial hypoxemia, electrolyte imbalances, and periodic breathing increase the susceptibility to cardiac arrhythmia at high altitudes.[1] However, available evidence on the occurrence of rhythm disturbances in the hypoxic hypobaric environment of high altitude is scarce. In the present study, we aimed to systematically explore the incidence of tachyarrhythmia or bradyarrhythmia in healthy individuals climbing Mount Everest.

Key Points

Question Does the hypoxic hypobaric environment of a high altitude increase the risk of cardiac arrhythmia?

Findings In this cohort study, more than 1 in 3 participants experienced bradyarrhythmia or tachyarrhythmia during the ascent from basecamp to the summit of Mount Everest. The proportion of individuals with arrhythmia remained stable across levels of increasing altitude, while the majority of arrhythmias occurred when no supplemental bottled oxygen was used.

Meaning The potential implications of the observed rhythm disturbances at high altitudes need to be explored in future studies.

Methods

Setting and Design

The SUMMIT study was a prospective cohort study involving healthy individuals who were climbing Mount Everest. Eligible climbers underwent a baseline assessment within 12 weeks before the expedition, including 12-lead electrocardiogram, transthoracic echocardiography, exercise stress testing, and ambulatory rhythm recording using a wearable continuous electrocardiogram patch (ATP-C130; ATsens) (eFigure 1 in Supplement 1). Ambulatory rhythm recording was repeated during the ascent from basecamp (5300 m) to the summit of Mount Everest (8849 m) so that every participant served as their own control.

The study was approved by the Nepal Health Research Council and the Cantonal Ethics Committee in Bern, Switzerland, and all participants provided written informed consent. The study was registered with ClinicalTrials.gov (NCT05676398). Detailed methods are described in the eMethods in Supplement 1.

Primary End Point and Definitions

The primary end point was the incidence of a composite of supraventricular (>30 seconds) and ventricular (>3 beats) tachyarrhythmia and bradyarrhythmia (sinoatrial arrest, second- or third-degree atrioventricular block) (eTable 1 in Supplement 1). Rhythm disturbances were considered as individual events when they occurred at least 5 minutes apart. The primary end point was independently adjudicated by 2 electrophysiologists blinded to the participant and the altitude of the recording. Discrepancies were resolved by joint review and mutual consensus. Secondary end points were death, high-altitude pulmonary edema, high-altitude cerebral edema, and acute mountain sickness.

Data Collection and Statistical Analysis

Data were collected using the electronic data capture web application REDCap.[2] Categorical variables are presented as frequencies and percentages, and continuous variables as mean (SD). Based on an expected event rate of 56%, a precision of 80%, and a dropout rate of 20%, we estimated a sample size of 30 participants for this study. All statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing).

Results

Between January 25 and May 9, 2023, a total of 41 individuals (mean [SD] age, 33.6 [8.9] years, 100% male) were recruited. Baseline characteristics are summarized in **Table 1.** On baseline investigations, there were no signs of exertional ischemia or wall motion abnormality in any of the participants. Ambulatory rhythm recording at baseline was completed in 35 individuals for a mean (SD) duration of 4.3 (2.3) days and revealed no supraventricular or ventricular arrhythmia in any of the study participants.

Three participants did not reach Everest basecamp and did not undergo expedition rhythm recording, 1 participant did not use the wearable continuous electrocardiogram patch for the climb, 1 participant lost the detached wearable continuous electrocardiogram patch during descent, and 2 wearable continuous electrocardiogram patches were empty on return. Among the remaining 34 individuals with rhythm recordings during the expedition, 32 reached an altitude of 7900 m or higher, 23 climbed above 8500 m, and 14 reached the summit of Mount Everest. One participant climbed to 7300 m (camp 3), and 1 participant did not climb above basecamp at 5300 m. Supplemental bottled oxygen was used during exercise by 32 individuals (94.1%) starting from an altitude of 6500 m (n = 2, 5.9%), 7300 m (n = 28, 82.4%), and 7900 m (n = 2, 5.9%). Two individuals used acetazolamide to prevent acute mountain sickness.

The mean (SD) duration of rhythm recording during the climb from basecamp at 5300 m to the summit and back was 7.6 (4.3) days. Resting heart rates were stable across altitude levels. A total of 45 primary end point-relevant events were recorded in 13 individuals (38.2%). Recorded arrhythmias are summarized in **Table 2.** An illustration of the occurrence of arrhythmias as a function of altitude and use of supplemental bottled oxygen is in the **Figure.**

Forty-three bradyarrhythmic events were documented in 13 individuals (38.2%) (eFigure 2 in Supplement 1). Seven individuals had a total of 23 bradycardias at rest, and 10 individuals had 19 bradycardias during exercise (eFigure 3 in Supplement 1). P-P slowing preceded bradyarrhythmia in 18 of 43 events (41.9%) (eFigure 4 in Supplement 1). One individual had 2 episodes of third-degree atrioventricular block at rest in camp 2 (6500 m).

Two tachyarrhythmic events were recorded in 2 individuals (5.9%). There was a correlation between altitude level and maximum QTc interval duration (R^2 = 0.37) (eFigure 5 in Supplement 1). One climber had a nonsustained ventricular

Table 1. Baseline Characteristics

Characteristic	No. (%)
Age, mean (SD), y	33.6 (8.9)
Male sex	41 (100)
Ethnic group	
Nepali Sherpa	33 (80.5)
Nepali, non-Sherpa	6 (14.6)
European	2 (4.0)
History of cardiac disease	0
History of palpitations	0
No. of 8000-m peaks summitted	
1-5	20 (48.8)
6-10	9 (22.0)
>10	10 (24.4)
Unknown	2 (4.9)
Physical examination, mean (SD)	
Height, cm	161.3 (7.2)
Weight, kg	69.4 (7.6)
Body mass index[a]	26.7 (2.8)
Systolic BP, mm Hg	122.8 (9.5)
Diastolic BP, mm Hg	78.8 (9.5)
Oxygen saturation at 1400 m, %	96.5 (1.4)
Oxygen saturation at 5300 m, %	83.9 (4)
Electrocardiography (n = 36)	
Heart rate, mean (SD), /min	72.2 (10.9)
Sinus rhythm	35 (97.2)[b]
First-degree AV block	1 (2.8)
Second-degree AV block	0
Third-degree AV block	0
Left bundle-branch block	0
Right bundle-branch block	0
Early repolarization pattern	6 (16.7)
PQ interval, mean (SD), ms	161 (17)
QRS duration, mean (SD), ms	89 (5)
QTc time, mean (SD), ms	402 (19)
Transthoracic echocardiography (n = 36), mean (SD)	
Left ventricular ejection fraction, %	60 (1)
Left ventricular end-diastolic diameter, mm	43.2 (4.1)
Left ventricular end-systolic diameter, mm	29.3 (3.2)
Left ventricular mass index, g/m^2	74.3 (16.4)
Tricuspid annular plane systolic excursion, mm	21.7 (1.9)
RV/RA gradient, mm Hg	16.9 (3.3)
Systolic pulmonary artery pressure, mm Hg	23.4 (3.6)
Valvular heart disease, No. (%)	0
Exercise stress testing (n = 34), mean (SD)	
Peak exercise load, MET	10 (1.7)
Pressure rate product[c]	22 815 (6057)
Clinical symptoms suspicious of ischemia, No.	0
Maximum heart rate, /min	165 (9)
Maximum systolic BP, mm Hg	148 (13)
ST-segment depression or T-wave inversion, No.	0
Cardiac arrhythmia, No.	0
Conduction defects, No.	0
Ambulatory rhythm recording, mean (SD)[d]	
No. of days of rhythm recording	4.3 (2.3)
Maximum heart rate, /min	139 (15)
Minimum heart rate, /min	53 (8)
Tachyarrhythmia, No.	0
Bradyarrhythmia, No.	0

Abbreviations: AV, atrioventricular; BP, blood pressure; MET, metabolic equivalent of task; RV/RA, right ventricular/right atrial.

[a] Calculated as weight in kilograms divided by height in meters squared.

[b] One patient had ectopic atrial rhythm.

[c] Calculated as systolic BP × maximum heart rate.

[d] Rhythm recordings were performed in Kathmandu (1400 m) or Bern (540 m).

tachycardia with 9 consecutive ventricular beats at a rate of 240/min during descent from camp 4 (7900 m). One climber had a slow monomorphic sustained ventricular tachycardia with a rate of 137/min during the ascent from camp 2 (6500 m) to camp 3 (7300 m). Examples of recorded arrhythmias are shown in eFigure 6 in Supplement 1.

The proportion of individuals with arrhythmia remained stable across levels of increasing altitude, while event rates per 24 hours numerically increased between 5300 m (0.16 per 24 hours) and 7300 m (0.37 per 24 hours) before decreasing again at higher altitudes, where supplemental oxygen was increasingly used (Figure and Table 2). Nine arrhythmias (20%) in 5 participants occurred when climbers were using supplemental bottled oxygen, whereas 36 events (80%) in 11 participants occurred at lower altitudes when no supplemental bottled oxygen was used. Individuals detected to have cardiac arrhythmia were comparable with those who did not with regard to baseline characteristics (eTable 2 in Supplement 1). None of the participants reported dizziness, palpitations, or chest pain. One participant experienced symptoms consistent with acute mountain sickness; none of the participants experienced high-altitude pulmonary edema or high-altitude cerebral edema (eTable 3 in Supplement 1).

Discussion

The SUMMIT study systematically explored the incidence of cardiac arrhythmia in healthy young men climbing Mount Everest and confirmed the association between exposure to high altitude and the occurrence of cardiac arrhythmia.[1,3] Distinct patterns of arrhythmia can be differentiated at high altitude, for which a combination of several pathophysiological mechanisms may be accountable. A decrease in atmospheric pressure at high altitude results in hypobaric hypoxia and arterial hypoxemia. In the Caudwell Xtreme Everest research expedition, arterial blood samples obtained from 4 climbers at an altitude of 8400 m revealed an oxygen saturation of 54% (range, 34%-70%).[4] Autonomous nervous system mechanisms are thought to play a key role in the

Table 2. Arrhythmias at Altitude

Type of arrhythmia	Everest basecamp, 5300 m (n = 34)[a]		Base to camp 2 (n = 33)[b]		Camp 2 to camp 3 (n = 33)[c]		Camp 3 to camp 4 (n = 32)[d]		Camp 4 to summit (n = 28)[e]	
	No. of events	No. of participants	No. of events	No. of participants	No. of events	No. of participants	No. of events	No. of participants	No. of events	No. of participants
Composite of tachyarrhythmia and bradyarrhythmia	13	6	9	6	13	5	8	5	2	2
Tachyarrhythmia	0	0	0	0	1	1	1	1	0	0
Supraventricular	0	0	0	0	0	0	0	0	0	0
Ventricular	0	0	0	0	1	1	1	1	0	0
Bradyarrhythmia	13	6	9	6	12	5	7	5	2	2
Sinoatrial block	6	4	1	1	2	2	1	1	1	1
Atrioventricular block	7	3	8	5	10	4	6	4	1	1
Second-degree										
Mobitz type 1	5	2	4	3	5	2	5	3	1	1
Mobitz type 2	2	2	2	2	5	3	1	1	0	0
Third-degree	0	0	2	1	0	0	0	0	0	0

[a] Supplemental oxygen: 0 participants.

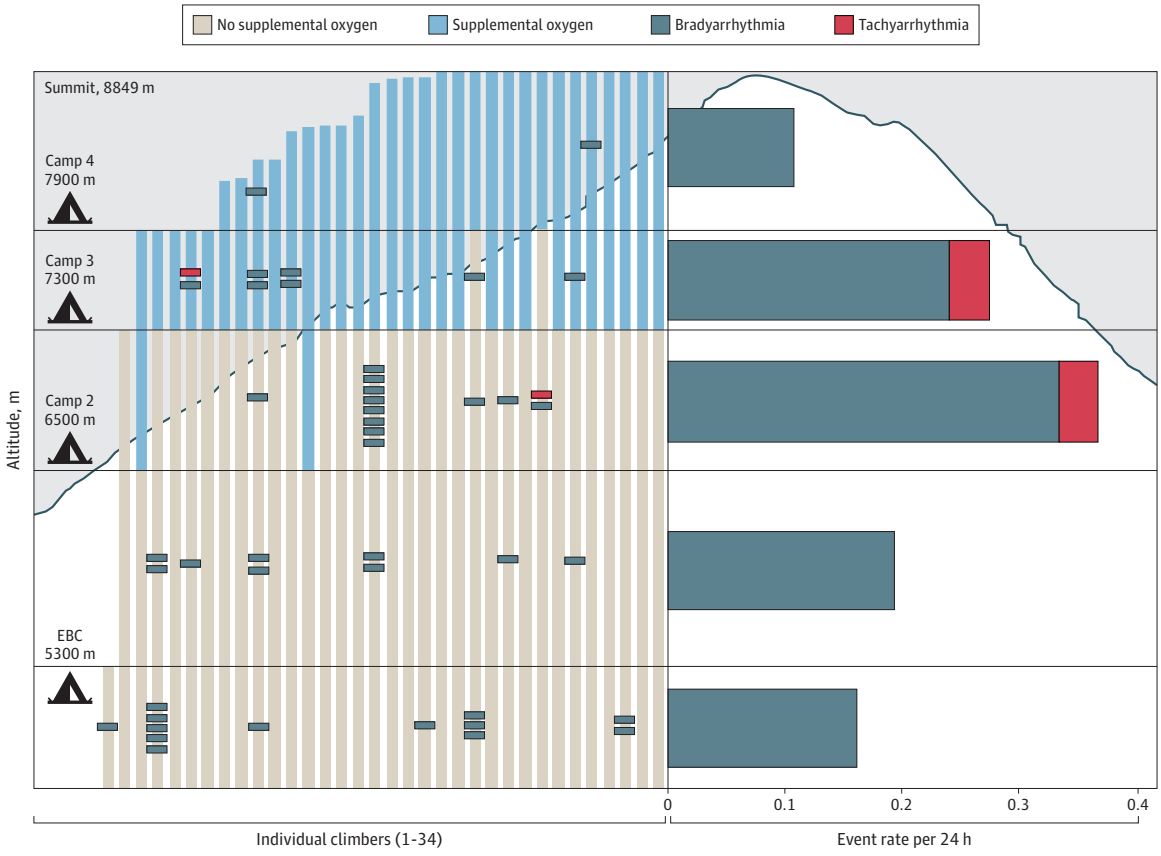
[b] Altitude, 5300-6500 m; supplemental oxygen: 0 participants.

[c] Altitude, 6500-7300 m; supplemental oxygen: 2 participants.

[d] Altitude, 7300-7900 m; supplemental oxygen: 30 participants.

[e] Altitude, 7900-8849 m; supplemental oxygen: all participants (n = 28).

Figure. Occurrence of Arrhythmias as a Function of Altitude and Use of Supplemental Bottled Oxygen



Each column represents 1 study participant and indicates the maximum altitude climbed without oxygen (beige) and with the use of supplemental oxygen (light blue). Arrhythmias are indicated by blue (bradyarrhythmia) or red (tachyarrhythmia) bars. The position of the bar relative to the y-axis indicates the altitude at which the arrhythmia occurred. EBC indicates Everest basecamp.

development of bradyarrhythmia in the hypobaric hypoxic environment. Periodic breathing, which is frequently observed in healthy mountaineers at high altitude during sleep, is thought to exacerbate antagonistic autonomic responses to hypoxemia and promote a conflict between the parasympathetic pathway and the sympathetic driver mediated by the peripheral chemoreflex.[5] In an experimental model of healthy individuals, voluntary apnea at an altitude of 5050 m unmasked the cardiac autonomic conflict and was shown to induce bradyarrhythmia.[6] Hypoxia-related periodic breathing in healthy individuals at high altitude shares mechanistic similarities with sleep apnea syndrome, which has been strongly associated with the incidence of bradyarrhythmia.[7] Moreover, the physiologic response to altitude features mechanistic parallels with the diving reflex involved in the occurrence of bradyarrhythmia in breath-hold divers.[8]

Tachyarrhythmias were less frequently documented in our study and may be related to electrolyte imbalances due to hyperventilation. Premature ventricular complexes and nonsustained ventricular tachycardias have been reported under strenuous exercise at high altitudes in previous studies.[9-11] Respiratory alkalosis is associated with hypokalemia and hypocalcemia. Early afterdepolarizations in hypokalemia induce premature ventricular complexes, which precipitate ventricular tachycardia.[12] At the same time, hypocalcemia prolongs the QT-interval and predisposes to ventricular arrhythmia.[13] Dehydration may further exacerbate the pro-arrhythmic milieu by augmenting existing electrolyte imbalances.

The proportion of individuals with arrhythmia was stable across altitude levels. Supplemental bottled oxygen may have blunted the effect of hypoxia during exercise at extreme altitudes. Most rhythm disturbances were recorded at an altitude less than 7300 m at which a majority of climbers did not use supplemental bottled oxygen, whereas numerically fewer rhythm disturbances occurred on supplemental bottled oxygen, despite higher altitude.

Limitations

The current analysis must be understood in light of a number of constraints. First, the use of supplemental bottled oxygen during exercise may have mitigated the risk of tachyarrhythmia, whereas more than half of all bradyarrhythmias occurred during periods of rest when no supplemental oxygen was used by a majority of participants. In addition, all study participants underwent acclimatization over several weeks before the climb; the risk of rhythm disturbances may be even higher during acclimatization to high altitude and in people less conditioned to high altitude. Second, the study included only men and climbers with previous exposure to extreme altitude, which may have introduced selection bias. The latter may have favored individuals who tolerated altitude well in the past. Third, the sample size of the SUMMIT study was modest, and we found no association of cardiac arrhythmia with clinical events.

Conclusions

The results of the SUMMIT study showed a substantial incidence of cardiac arrhythmia at extreme altitude. The potential implications of the observed rhythm disturbances need to be explored in future studies.

ARTICLE INFORMATION

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Author Contributions: Drs K. Sherpa and Pilgrim had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Rothenbühler, Reichlin, Pilgrim.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: P. Sherpa, Sherchand, Pilgrim.
Critical review of the manuscript for important intellectual content: K. Sherpa, T. Sherpa, Rothenbühler, Ryffel, D. Sherpa, D. R. Sherpa, Galuszka, Dernektsi, Reichlin.
Statistical analysis: Rothenbühler.
Obtained funding: Pilgrim.
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Supervision: Reichlin, Pilgrim.

Conflict of Interest Disclosures: Dr Reichlin reported grants from Medtronic, Biotronik, Boston Scientific, Biosense Webster, Swiss National Science Foundation, Swiss Heart Foundation, and the sitem-insel Support Fund outside the submitted work; speaker/consulting honoraria or travel support from Abbott/SJM, Biosense Webster, Biotronik, Boston Scientific, and Medtronic; and support for his institution's fellowship program from Abbott/SJM, Biosense Webster, Biotronik, Boston Scientific, and Medtronic. Dr Pilgrim reported research, travel, or educational grants to their institution without personal remuneration from Biotronik, Boston Scientific, Edwards Lifesciences, and ATsens and speaker fees and consultancy fees to their institution from Biotronik, Boston Scientific, Edwards Lifesciences, Abbott, Medtronic, Biosensors, and HighLife outside the submitted work. No other disclosures were reported.

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LETTERS

RESEARCH LETTER

QT Prolongation and Acquired Long QT Syndrome in Climbers on Mount Everest

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Excessive prolongation of the QT interval is a manifestation of delayed cardiac repolarization associated with an increased risk of life-threatening cardiac arrhythmias. Acquired long QT syndrome is caused by a variety of factors such as electrolyte imbalances, thyroid hormone disturbances, cardiovascular comorbidities, and certain drugs. In the ANDES (Altitude Non-Differentiated ECG Study) study, people permanently living at moderate or high altitudes had longer heart-rate corrected QT intervals as compared to sea-level residents.[1] In this subanalysis of the SUMMIT (Cardiac Arrhythmias at Extreme Altitude; NCT05676398) study, we aimed to quantify the effect of extreme altitude on the prolongation of the QT interval in healthy individuals.

METHODS

The SUMMIT study was a prospective cohort study exploring the incidence of cardiac arrhythmias in climbers on Mount Everest. Details on setting, design, and conduct of the study have been reported previously.[2] In brief, participants underwent 12-lead electrocardiogram (ECG), transthoracic echocardiography, exercise stress testing according to the standard Bruce protocol, and ambulatory rhythm recording within 12 weeks before the expedition in their home environment (<1,500 meters). Ambulatory rhythm recording was repeated during the ascent from Everest Base Camp (EBC) (5,300 meters) to the summit of Mount Everest (8,849 meters) using a wearable continuous electrocardiogram patch (ATP-C130, ATsens). Analysis of the QT interval was conducted automatically and verified manually using Kubios HRV software (Kubios Oy). QT interval was corrected for heart rate using the Fridericia formula (QTc). Continuous variables are presented as mean values ± standard deviation. Between-group comparison was performed by Kruskal-Wallis test with Bonferroni-adjusted Mann Whitney-U post hoc testing. The study was approved by the Nepal Health Research Council and the Cantonal Ethics Committee in Bern, Switzerland, and all participants provided written informed consent.

RESULTS

Among 41 study participants enrolled between January 25 and May 9, 2023, 29 individuals (mean age 33.8 ± 9.0 years, 100% male) had an adequate ECG signal to measure QT intervals at altitude and represent the study population for the present analysis. None of the individuals had a history of cardiac disease. Twelve-lead ECG showed sinus rhythm in all participants, first-degree atrioventricular block in 1,

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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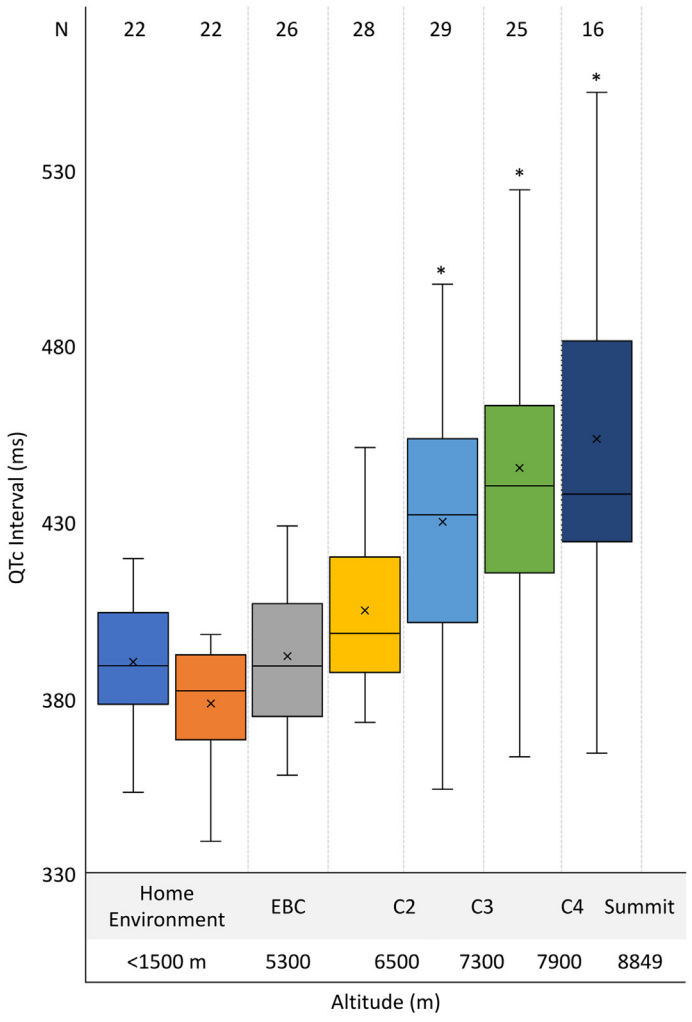
FIGURE 1 Box-Whiskers Plot Showing Friderica's Corrected QT Interval (ms) (y-axis) According to Different Altitude Levels (x-axis)



Respective numbers (N) of measurements available per altitude are provided in the top row. Home environment differentiates between measurement in 12-lead electrocardiogram (blue) and wearable continuous electrocardiogram patch (orange). Asterisks indicate a significant difference ($P < 0.05$) compared to QTc interval at baseline. EBC = Everest basecamp; C2 = camp 2; C3 = camp 3; C4 = camp 4.

and an early repolarization pattern in 4 individuals. The mean QTc interval at baseline was 390 ± 17 ms as assessed by 12-lead ECG and 379 ± 17 ms as assessed by continuous electrocardiogram patch, respectively. Echocardiography showed normal left and right ventricular function and normal left ventricular dimensions and mass in all participants. Exercise stress testing revealed no exertional angina or changes suspicious of ischemia, and ambulatory rhythm monitoring documented no supraventricular or ventricular arrhythmias in any of the participants.

All 29 individuals climbed from EBC to an altitude of ≥7,900 meters (South Col); 21 climbed above 8,500 meters, and 12 reached the summit of Mount Everest. Supplemental bottled oxygen was used by all individuals starting from 6,500 meters (n = 2), 7,300 meters (n = 26), and 7,900 meters (n = 1). Acetazolamide was used by 2 participants.

The mean QTc interval became gradually longer along the climb from EBC (391 ± 21 ms) to camp 2 at 6,500 meters (405 ± 21 ms), to camp 3 at 7,300 meters (431 ± 33 ms), to camp 4 at 7,900 meters (441 ± 29 ms), and to the summit (446 ± 38 ms) (Figure 1). At the level of the individual participant, the average prolongation of the QTc interval from baseline to the maximum achieved altitude amounted to 66 ± 31 ms. A QTc prolongation of ≥60 ms was recorded in 17 participants (59%), whereas 7 (24%) had a QTc interval exceeding 470 ms, consistent with an acquired long QT syndrome. One individual with a massively prolonged QTc of 504 ms recorded at 7,900 meters (QTc 385 ms at EBC) experienced nonsustained ventricular tachycardia during the descent from camp 4. Another climber with a monomorphic sustained ventricular tachycardia during the ascent from camp 2 to camp 3 had a QTc of 439 ms at 7,300 meters (QTc 391 ms at baseline). Both tachyarrhythmias were asymptomatic. None of the study participants experienced a syncopal event or cardiac arrest.

DISCUSSION

In a prospective cohort study of healthy individuals climbing Mount Everest, we recorded a gradual prolongation of the QT interval with increasing altitudes. Hyperventilation in the hypoxic, hypobaric environment leads to respiratory alkalosis with hypokalemia and hypocalcemia, both of which have been associated with a delay in cardiac repolarization. Hypokalemia may be exacerbated by the use of the carbonic anhydrase inhibitor acetazolamide frequently used for the prevention of acute mountain sickness at high altitudes. Hypothermia and the use of energy drinks may further prolong the QT interval.[3]

Autonomous nervous system activity modulates cardiac repolarization and QT interval duration independently from changes in heart rate. There is a mechanistic interaction between respiratory dynamics and autonomous nervous system activity mediated by the peripheral chemoreflex. Hypoxia stimulates the sympathetic nervous system whereas pure oxygen inhalation increases parasympathetic activity.[4] High-altitude periodic breathing begets a

conflict between the sympathetic driver and the parasympathetic pathway which may exacerbate long-QT-associated ventricular arrhythmias.[5]

The present analysis must be interpreted in light of several limitations. First, the QT interval was measured in a rhythm strip rather than a 12-lead ECG and may hence have been underestimated. Second, the use of supplemental bottled oxygen at high altitudes attenuated hyperventilation and respiratory alkalosis. Finally, the study sample included only men and was too small to corroborate an association between QT prolongation and the occurrence of ventricular arrhythmias in this population. Nevertheless, the findings of the present subanalysis of the SUMMIT study have important implications. Based on our observations, individuals with inherited long-QT syndrome and patients taking medications that prolong the QT interval may be discouraged from exposure to high altitudes.

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