Subject Review and Case Report

Cardiac Arrhythmia at High Altitude

The Progressive Effect of Aging

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To evaluate the effects of aging on cardiac rhythm at high altitude, I wore a Holter monitor at age 75 during a climb to 5,100 m on Mt. Kilimanjaro, then compared findings with those from my climb to 5,895 m at age 65. Holter leads were placed to identify left or right ventricular source of ectopy, and on the 2nd ascent arterial oxygen saturation was monitored by finger oximetry. Sea-level testing revealed no evidence of cardiac disease. During ascent from 4,710 to 5,100 m, when arterial oxygen saturation reached 70%, heart rate was higher (123 vs 116 beats per minute), and frequency of left ventricular premature complexes was greater (56 vs 50 per hour) than on the earlier ascent. Nine 3- to 5-complex runs of left ventricular tachycardia were recorded during climbing, resting, or sleeping, and there was 1 run of 14 complexes at 250 beats per minute during the climb near 5,100 m. These observations suggest that aging increases sympathetic response or sensitivity, or both, to hypoxia during exercise, and even during sleep. Also, our focus should perhaps be on sympathetic stimulation rather than on pulmonary hypertension as a cause of arrhythmia in unacclimatized older persons at high altitude. ***(Tex Heart Inst J 1999;26:258-63)***

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Prior studies in young normal subjects have documented cardiac arrhythmia under conditions of exertion at simulated high altitude or in the field, the incidence of which has correlated positively with degree of elevation and negatively with degree of acclimatization.[1-6]

Because I could not find published information on cardiac rhythm in older normal subjects who were monitored while climbing at high altitude, I recorded my own rhythm in 1986 with a Holter ambulatory electrocardiographic monitor as I ascended Mt. Kilimanjaro (5,895 m), at the age of 65.[7] Prior cardiac studies at sea level—including electrocardiography, 8-hour Holter monitoring, a thallium exercise stress test, a radionuclide gated left ventricular wall-motion study at rest and during exercise, echocardiography, and selective coronary angiography—had showed no significant abnormality. During the climb from 4,710 to 5,895 m, the recording demonstrated frequent premature ventricular complexes, predominantly of left ventricular origin, with multiple runs of ventricular bigeminy, which increased in frequency and duration until the mountain peak was reached.[7] Ventricular ectopy was reduced markedly as I began the descent, and virtually disappeared within 3 hours. The present study was undertaken 10 years later, at age 75, to determine the progressive effect of aging on cardiac rhythm under the same conditions.

Status of the Subject

I had remained free of cardiorespiratory symptoms during the 10-year interim. My electrocardiogram was normal, and sea-level 24-hour Holter monitoring showed no ST-segment change, sinus rhythm at 36 to 77 beats per minute, 13 isolated ventricular premature complexes (VPCs), 2 runs of supraventricular tachycardia (4 and 10 beats each), and one 14-beat run of idioventricular rhythm during sleep. On the Bruce treadmill test, heart rate and blood pressure were 57 beats per minute and 149/81 mmHg at rest, 156 beats per minute and 196/90 mmHg during exercise (duration 13 minutes, 13 seconds), with 3 VPCs during exercise, 2 couplets during the 2nd minute of recovery, and no ST-segment change. Echocardiography showed left atrial and ventricular dimensions of 42 and 49 mm, an ejection fraction of 60%, modest thickening of aortic and mitral valve leaflets, annular calcification of the mitral valve, and no valvular regurgitation. Changes in the cardiac

findings that had taken place in the 10-year period between studies included supraventricular tachycardia and idioventricular rhythm on Holter monitoring, reduced duration (13 minutes vs 15 minutes) on Bruce treadmill testing, higher maximum blood pressure (196/90 vs 149/81 mmHg) and ventricular ectopy on treadmill testing, and valvular lesions on echocardiography.

Methods and the Climb

A 2-channel Holter monitor (Del Mar model 445 reel-to-reel recorder; Del Mar Avionics; Irvine, Calif) with a 6-mm cassette tape was used to monitor cardiac rhythm; the electrodes were positioned to facilitate distinction between left and right ventricular ectopy and measurement of P-wave amplitude (Fig. 1). Blood oxygen saturation and pulse rate were monitored continuously by a Nonin 8500 finger pulse oximeter (Nonin Medical Inc.; Plymouth, Minn), and periodic notations were recorded in a diary. Digital brachial artery blood pressure recordings with printout (Accutracker ABP; Suntech Medical Instruments, Inc.; Raleigh, NC) were made automatically, at 15- to 30-minute intervals during the climb from 1,800 to 4,100 m and hourly at night.

The route and timing for the ascent of Mt. Kilimanjaro were virtually the same as the route and timing 10 years earlier. Starting at Marangu Gate (altitude, 1,829 m), I made the 1st day's trek to the Mandara Hut (2,743 m) in approximately 4 hours and stayed the night there. The 2nd day's climb was about 16 km to Horombo Hut, at 3,758 m. On the following day, I took a side trip to a neighboring ridge at 4,000 m, then spent a 2nd night at Horombo. The 4th day's climb was a distance of about 9 km, to the Kibo Hut at 4,700 m. That night I departed the Kibo Hut at about 11 P.M., for the ascent to the peak. After 2½ hours, I had reached an altitude of 5,100 m and was rather dyspneic. The finger oximeter pulse register indicated only 70 beats per minute, although palpation of my radial pulse indicated a much faster rate. Perhaps because of hypoxic cognitive impairment, it did not occur to me that the oximeter was malfunctioning. When I recalled my run of idioventricular rhythm at 70 beats per minute during sleep at sea level, I concluded that my rhythm was abnormal and decided to turn back. Only after the Holter recording was analyzed did I learn that I had undergone an asymptomatic 14-complex run of left ventricular tachycardia at 250 beats per minute (Fig. 2) 30 minutes before this decision. Therefore I might have done the right thing for the wrong reason. I returned to the Kibo Hut, rested until 8 A.M., then descended to the Mandara Hut and spent the night there. No recordings were made on descent from the Mandara Hut to Marangu Gate on the 6th day.

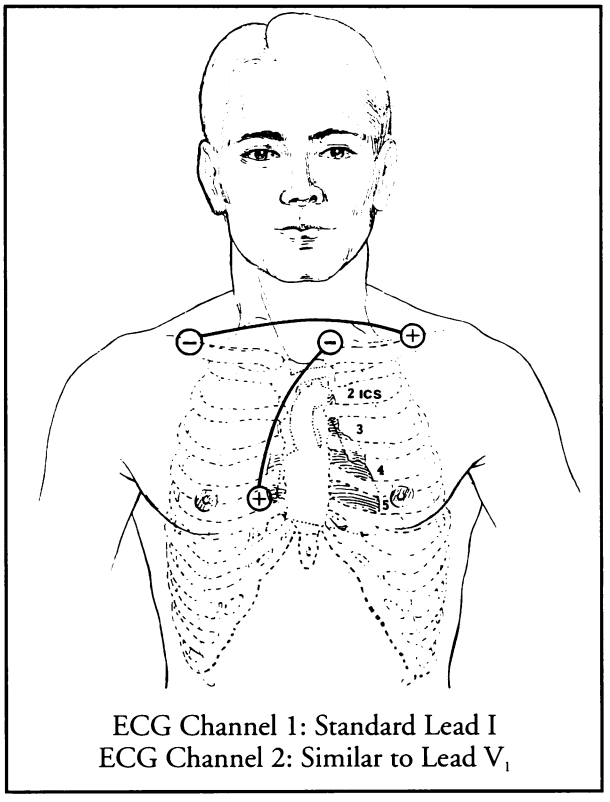

Fig. 1 *Lead placements for Holter monitor channels 1 and 2. In channel 1, left ventricular ectopic complexes will have a predominantly negative QRS deflection, and right ventricular ectopic complexes will have a predominantly positive deflection. Channel 2 measures P-wave amplitude over the right precardium.*

ECG = electrocardiographic; ICS = intercostal space

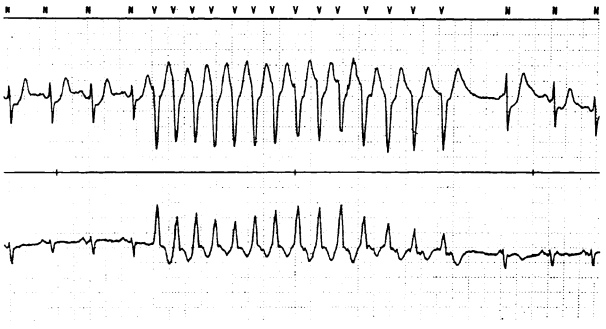

Fig. 2 *Fourteen-complex run of left ventricular tachycardia at 250 beats per minute, recorded during the climb near 5,100 m altitude. The channel 1 recording is above, and channel 2 below.*

N = sinus rhythm; V = ventricular ectopy

Results

Holter data relative to ventricular ectopy and P-wave amplitude on ascent and descent are tabulated in Table I. The maximal heart rate during the climb reached approximately 85% of the maximal rate during the treadmill test at sea level, and sinus rhythm during sleep fell to a level comparable to that at sea level. Ectopy of left ventricular origin increased progressively with higher altitude exposure during the climb, at rest, and during sleep, reaching an average of 56 complexes per hour during ascent, and falling to 10 complexes per hour during descent at the highest altitude. Ventricular complexes of right ventricular origin were relatively infrequent, and had no clear-cut pattern relative to altitude. Although short runs of left ventricular tachycardia occurred during climbing, resting, and sleeping, the incidence increased somewhat during the climb at higher altitude, with the 14-complex run occurring near 5,100 m. No right ventricular tachycardia occurred. Atrial tachycardia occurred predominately during sleep and had no clear relation to altitude. Respiratory variation in ST-segment levels was present, but no ST depression persisted as long as 30 seconds. Amplitude of the P wave in lead V_1 rose progressively during the climb, and during rest and sleep as altitude increased, but during the descent it fell to a level comparable to that at the beginning of the ascent. Figure 3 depicts the numbers of left ventricular ectopic complexes per hour and the levels of blood oxygen saturation while climbing. The incidence of ectopy rose with increasing altitude during climbing, reaching a maximum of 61 complexes per hour near 4,900 m, and fell sharply 30 minutes after descent from 5,100 to approximately 5,000 m, to 4 complexes per hour. Blood oxygen saturation levels fell from 92% at 1,800 m to 71% at approximately 5,000 m during the climb. Blood pressure levels, plotted at increasing altitude during ascent, rest, and sleep, are shown in Figure 4. Levels during ascent were not significantly different from those obtained at comparable heart rates in conjunction with treadmill testing at sea level.

Discussion

In this study, the ascent from 4,700 to 5,100 m took approximately the same length of time (2½ to 3 hours) as did the ascent 10 years earlier. Comparison

Table I. Holter Data on Ascent from 1,800 m to 5,100 m and on Descent from 5,100 m to 2,700 m (values for ventricular premature complexes and P-wave amplitude represent average numbers over the period of designated activity)

	Altitude						
	1,800 m to 2,700 m	2,700 m to 3,720 m	3,720 m to 4,000 m	4,000 m to 4,700 m	4,700 m to 5,100 m	5,100 m to 4,700 m	4,700 m to 2,700 m
Max HR during climb (beats/min)	132	138	121	121	123	120	130
Min HR during sleep (beats/min)*	45	38	48	56			
LV, VPCs/hr							
Climb	4	8	7	16	56	10	21
Rest*	1	8	8	11			
Sleep*	2	3	4	6			
RV, VPCs/hr							
Climb	4	2	2	1	6	2	5
Rest*	0	4	1	4			
Sleep*	1	1	3	2			
LV, Ventricular Tachycardia**	4 (105) Sleep		3 (135) Rest	3 (192) Climb 6 (170) Sleep	3 (121) Climb 14 (251) Climb	4 (207) Climb 3 (105) Climb 4 (108) Climb	
Atrial Tachycardia**		6 (145) Sleep	5 (165) Rest 3 (133) Sleep 9 (163) Sleep	7 (200) Climb 8 (168) Sleep 6 (158) Sleep			
P-wave Amplitude (mm)***	0.7/0.5/0.5	1.0/0.7/1.0	1.2/1.0/1.0	1.5/1.0/1.1	1.5	1.0	1.0/0.7/0.5

*Data secured at the higher altitude.
**First figure refers to number of complexes, second (in parentheses) to beats per minute.
***Measurements are from lead V_1 during climb, at rest, and during sleep, respectively. Values in column 7 were recorded during descent.

HR = heart rate; LV, VPCs = ventricular premature contractions of left ventricular origin; RV, VPCs = ventricular premature contractions of right ventricular origin

of heart rates and incidences of left ventricular ectopic complexes during the 2 climbs indicates that the average heart rate and the incidence of ectopy were somewhat higher in this later study (123 vs 116 beats per minute and 56 vs 50 VPCs per hour). During the 1st 2 hours of descent from the highest altitude, the heart rate fell much less than in the earlier study (120 vs 102 beats per minute), but the incidence of ectopy was virtually the same on both occasions—dropping sharply to 10 and 9 VPCs per hour, respectively. The multiple runs of ventricular bigeminy observed in the earlier study during the climb above 4,700 m did not occur in this study. However, in contrast to the 9 episodes of left ventricular tachycardia that occurred in this study, ventricular tachycardia was not manifest in the earlier study. Similarly, there were 7 episodes of atrial tachycardia in this study, in comparison with a single episode in the previous study. The incidences of right ventricular ectopy were comparable in the 2 studies. In both studies, the P-wave magnitude increased during the climb: in the prior study, P-wave amplitude, monitored in V_2, rose from 0.1 to 0.2 mm early in the climb, without further change; in this study, P-wave amplitude, monitored in lead V_1, increased more significantly during the climb, from 0.5-0.7 mm to 1.5 mm at highest altitude.

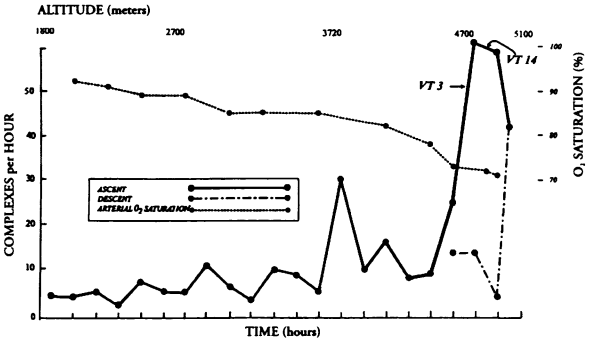

Fig. 3 *Hourly numbers of left ventricular ectopic complexes and levels of blood oxygen saturation while climbing.*

VT = ventricular tachycardia of left ventricular origin, followed by number of complexes

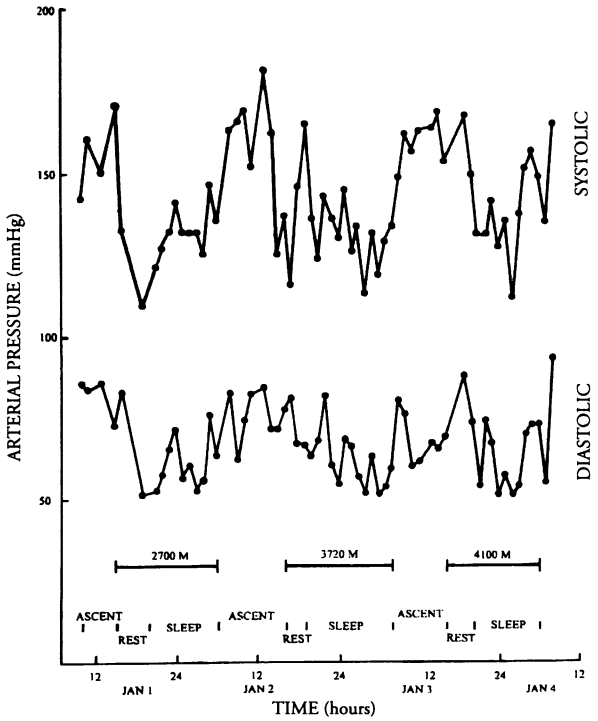

Fig. 4 *Blood pressure levels during ascent, rest, and sleep at increasing altitude, from 1,800 to 4,100 m.*

Of note relative to the blood oxygen saturation findings in this study is a comparison with observations of younger subjects. In a study of young, normal, partially acclimatized male subjects[8] at rest under a simulated altitude of 4,600 m in a barometric chamber (barometric pressure = 429 torr, inspired oxygen partial pressure [PIO_2] = 80 torr, arterial blood pH [pHa] = 7.445), arterial blood pressure of oxygen (PaO_2) and oxygen saturation (SaO_2) were 52 and 85%—in contrast with this study's PaO_2 of 41.5 (assuming the same pHa) and SaO_2 of 73% (Fig. 5). In the younger subjects, PaO_2 and SaO_2 fell to these levels only after a simulated altitude of 6,140 m was reached. These findings are similar to those reported on an older and a younger subject, which indicated comparable arterial blood gas and oxygen saturation levels at a much higher altitude for the younger subject (6,140 vs 3,380 m).[9]

Arrhythmia has not been observed at rest in partially or well acclimatized younger men at altitudes as high as 8,848 m.[2,10-12] However, VPCs, ventricular bigeminy, and premature atrial complexes have been recorded during ordinary activity or brief exercise, and after exercise, in healthy men over an age range of 20 to 53 years at altitudes from 4,600 to 7,620 m.[5,6,13] The postulate that this ectopy is caused by increased sympathetic neural activity has some experimental support. In young subjects, direct intraneural recordings demonstrate increased sympathetic activity during exposure to ambient hypoxia under laboratory conditions.[14] Further, hypoxia has a synergistic effect on exercise-induced sympathetic neural activation, with a rapid rise in norepinephrine levels.[15] In turn, sympathetic stimulation and catecholamine release can cause delayed after-depolarizations and triggering of arrhythmia in atria or ventricles.[16,17] In older normal subjects, exercise-induced ventricular arrhythmia is frequent[18]

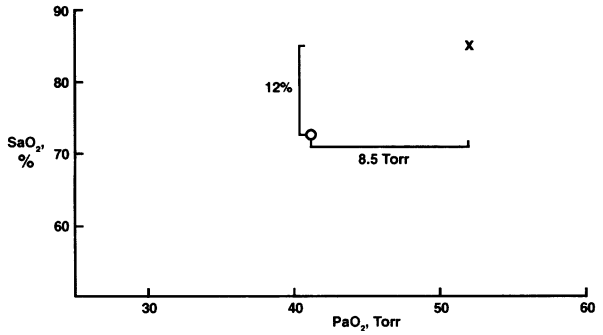

Fig. 5 *Arterial blood partial pressure of oxygen (PaO_2) and oxygen saturation (SaO_2) at rest in young normal subjects, at an altitude of 4,600 m, and in the study subject, at 4,700 m. For young normal subjects, the barometric pressure is 429 torr, the inspired oxygen partial pressure (PIO_2) is 80 torr and the arterial blood pH (pHa) is 7.445. A comparable pHa has been assumed for the study subject, whose PaO_2 is 8.5 torr lower and whose SaO_2 is 12% lower than observed in young normal subjects.*

and plasma catecholamines for given exercise level (% VO_2 maximum) are higher than those in younger subjects,[19] due to reduced uptake at the nerve ending, with spill-over from the neuron-effector cell synapse into the blood.[20] However, this is associated with ß-adrenoceptor down-regulation,[21] which makes for an apparent paradox in relation to the predisposition to arrhythmia. Three hypothetical explanations have been advanced.[7] The most attractive hypothesis, in my view, relates to α-adrenoceptor activity. Although down-regulation of α_2-adrenoceptors takes place with aging, there is no loss of response to α_1 adrenoceptor stimulation, so the response to the nonselective α-agonist norepinephrine is preserved by α_1 activation.[22] Since adrenoceptors in the myocardium are virtually all of the α_1 type,[23] and a specific α_1 subtype modulates catecholamine-induced increases in ventricular automaticity,[24] aged subjects with higher norepinephrine levels during exercise would be more vulnerable to development of ventricular ectopy.

In both my 1986 and 1996 climbs, the incidence of ectopy at comparable altitudes declined significantly upon descent, in comparison with the incidence upon ascent. Hence the degree of exertion appeared to have a similar effect in the 2 studies. The subsequent development of ventricular tachycardia in 1996, under conditions similar to conditions in 1986 that did not provoke ventricular tachycardia, suggests that sympathetic response or sensitivity, or both, increased over the 10-year period. Further, while the combination of pulmonary hypertension and sympathetic stimulation might predispose to right ventricular ectopy, the incidence of left ventricular ectopy was much higher in my case, presumably as a consequence of a greater susceptibility to sympathetic stimulation. The predisposition to ectopy of left ventricular origin was present not only during the climb, but also during sleep, with an episode of left ventricular tachycardia during sleep at 4,700 m (Table I). This observation is noteworthy because, in 1 study, electrocardiographic recordings in partially acclimatized young normal subjects during sleep at altitudes as high as 7,620 m demonstrated no ventricular ectopy, only cycling of heart rate associated with periodic breathing.[25] Although the modest degree of acclimatization in my case may have been a factor, a predisposition to ectopy of left ventricular origin suggests that the sympathetic response to hypoxic stimulus, as well as to exercise, might be augmented in the older subject.

Some consideration of the implications of these findings is warranted. In a survey of deaths from all causes among mountain hikers in Austria during the period from 1985 through 1992,[26,27] it was found that 210 deaths (30% of the total) were sudden, that over 50% of these occurred in men older than 60 years, and that risk increased with physical exertion.[28] In a survey of deaths occurring in British expeditions at altitudes greater than 6,500 m during the period from 1968 through 1987, 3 of 15 deaths were of uncertain cause.[29] These observations suggest that cardiac arrhythmia may account for a significant percentage of fatalities at high altitude, as well as for syncopal episodes, and perhaps some of the deaths attributed to falls.

Conclusions

During 2 climbs with a 10-year interim, at high altitude and under comparable circumstances of time and place, this older normal subject observed that the degree of exertion (during ascent vs descent) had a significant and similar effect on both occasions. Yet I found that at age 75 the incidence of left ventricular ectopic complexes increased and episodes of ventricular tachycardia developed, which had not been present at age 65. Hence the exaggerated sympathetic response to exercise under hypoxic conditions in older subjects appears to progress with aging. In addition, at age 75 there was a short run of left ventricular tachycardia during sleep at 4,700 m, which was not present 10 years earlier, and which has not previously been reported in healthy normal subjects under conditions of simulated altitude or in the field. This development of episodic ventricular tachycardia during sleep also suggests that there is increased sympathetic sensitivity to the hypoxic stimulus with advancing age.

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