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Effect of age on the presence of comet tails at high altitude

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ABSTRACT

Extravascular lung water (EVLW) increases in healthy adults upon exposure to high altitude, likely due to increased pulmonary vascular resistance (PVR). Older individuals experience increased PVR during exercise, which may be exacerbated by trekking at high altitude. This study aimed to determine whether EVLW development is greater in older versus younger adults during graded altitude exposure. Fourteen younger (32 ± 6y) and 12 older (58 ± 5y) healthy adults completed an 11-day trek of Mount Kilimanjaro. EVLW was assessed at rest via comet tails prior to the trek in Moshi (950 m), at Shira Camp (3505 m), at Barafu Camp (4837 m), and post-descent. An increase in altitude from Baseline to Barafu tended to increase the proportion of participants with mild EVLW ($p = 0.06$). A higher proportion of older versus younger individuals tended to show mild EVLW at Barafu (56 vs. 14%, $p = 0.06$). In conclusion, EVLW formation may be more common in older adults trekking at high altitude. However, the presence of EVLW in older adults was subclinical.

1. Introduction

The comet tail artifact, a hyperechoic reflection originating from the pleural surface of the lung on ultrasound, was first associated with interstitial lung fluid in 1997 by Lichtenstein et al. (1997). Clinically, comet tails on ultrasound have been found to be diagnostically comparable to radiography, particularly in cardiac and pulmonary patients, for the identification of extravascular lung water accumulation or pulmonary congestion (Agricola et al., 2005; Jambrik et al., 2004; Lichtenstein et al., 1997; Tsverava and Tsverava, 2010).

Comet tails on ultrasound have also been utilized in various remote and challenging environments, particularly mountaineering, due to the technique's ease of use, portability, and low-cost. The presence of comet tails has been shown to increase in healthy lowlanders upon ascent to altitudes ranging from ~3400 to 5100 m (Agostoni et al., 2013; Bouzat et al., 2013; Pratali et al., 2010; Strapazzon et al., 2015), though this is not always the case (Taylor et al., 2017). The presence of comet tails has also been shown to be correlated with decreases in arterial oxygen saturation at altitude (Pratali et al., 2010; Strapazzon et al., 2015), and while healthy individuals who show comet tails at altitude are often asymptomatic, the presence of comet tails can be a useful diagnostic tool in individuals with suspected high altitude pulmonary edema (HAPE) (Fagenholz et al., 2007).

The appearance of extravascular lung water at altitude is thought to occur due to hypoxia-dependent increases in pulmonary vascular resistance (PVR) and thus increased microvascular pressures within the lung (Swenson and Bartsch, 2012). Therefore, it is conceivable that older individuals, who may have increased pulmonary vascular stiffness and thus already greater PVR during exercise in comparison to younger individuals (Ehrsam et al., 1983; Emirgil et al., 1967; van Empel et al., 2014), may experience greater development of extravascular lung water while trekking at altitude. To our knowledge, however, the effect of age on the presence of extravascular lung water at altitude has not been examined. Therefore, the aim of the present study was to investigate whether the presence of comet tails is greater in older versus younger adult lowlanders during graded exposure to high altitude. We hypothesized that a greater proportion of older individuals would demonstrate comet tails, indicative of extravascular lung water, at high altitude.

2. Methods

2.1. Subjects

Fourteen younger (8 M/6 F, 32 ± 6y) and 12 older (8 M/4 F, 58 ± 5y) healthy, moderately active, non-smoking adult lowlanders participated in the study (Table 1). Each participant gave written informed consent after being provided a detailed description of the study

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Table 1
Demographics of the younger versus older cohort.

N (M/F)	Younger 14 (8/6)	Older 12 (8/4)	*P*-value
Age, y	32 ± 6	58 ± 5	< 0.001
Height, cm	177 ± 7	174 ± 10	0.348
Weight, kg	72.6 ± 17.8	75.6 ± 10.8	0.617
BMI, kg*m^{-2}	23.0 ± 4.4	25.0 ± 3.0	0.190
BSA, m^2	1.88 ± 0.25	1.91 ± 0.18	0.756
FVC, % pred.	112 ± 20	116 ± 16	0.584
FEV_1, % pred.	106 ± 18	110 ± 12	0.558
PEF, % pred.	110 ± 18	121 ± 15	0.130

BMI, body mass index; BSA, body surface area; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

requirements. The experimental procedures were approved by the Mayo Clinic Institutional Review Board and were performed in accordance with the ethical standards of the Declaration of Helsinki.

2.2. Study overview

The experimental procedures were performed during an 11-day trek of Mount Kilimanjaro in Tanzania, Africa (Fig. 1). Baseline measures were collected in Moshi ('Baseline,' 950 m) prior to beginning the trek, at Shira Camp ('Shira,' 3505 m) on days 3 and 4, at Barafu Camp ('Barafu,' 4837 m) on days 8 and 9, and post-descent in Moshi ('Post,' 950 m) on days 12 and 13. Participants were tested on the same day and in the same order over the course of the two testing days at each of the four testing sites. At each test site, extravascular lung water was quantified via ultrasound comet tails (Philips Lumify with 12 MHz linear array transducer, Andover, MA). Additionally, systolic pulmonary artery pressure (sPAP) was estimated at rest via cardiac ultrasound, and resting arterial oxygen saturation (SaO_2) and end-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$) were also measured at each test site.

2.3. Extravascular lung water via ultrasound comet tails

Comet tails were observed via lung ultrasound with subjects in the supine position for at least 20 min. Briefly, a comet tail was defined as a hyperechoic reflection on a 2-D ultrasound image of the lung that originated from the pleural line and spread away from the transducer (i.e., 'B-lines') (Summerfield and Johnson, 2013). All 2-D images were acquired from standardized sonographic windows with system settings adjusted to optimize signal-to-noise ratio and held constant throughout the experimental testing session and across testing days. Comet tails were totaled over 28 sonographic windows, including intercostal spaces 2–5 on the right and 2–4 on the left in the parasternal, mid-clavicular, anterior axillary, and mid-axillary positions (Jambrik et al., 2004). Based on a semi-quantitative classification proposed by Picano and colleagues, subjects were considered to show mild or moderate levels of extravascular lung water if the total number of comet tails was between 5 and 15 or between 15 and 30, respectively (Picano et al., 2006).

2.4. Statistical analyses

Only two individuals ever showed moderate levels of extravascular lung water; therefore, all further analysis was restricted to whether or not subjects showed at least mild levels of extravascular lung water. The effect of increasing altitude (from Baseline to Barafu) on the proportion of all participants that showed at least mild levels of extravascular lung water was analyzed using Cochrane's Q Test. The difference in proportions of younger versus older individuals that showed lung water at each test site was analyzed using Fisher's Exact Test. The effect of altitude and age on SaO_2, sPAP, and $P_{ET}CO_2$ were determined using a two-way ANOVA with repeated measures for altitude. Statistical analyses were performed in GraphPad Prism 7.02 (GraphPad Software, Inc., La Jolla, CA) and significance was set at $p < 0.05$.

3. Results

27 individuals participated in the trek; however, one participant was not assessed for comet tails for technical reasons. The remaining 26 subjects were assessed for comet tails throughout the trek, except for three data points that were not collected at altitude for various reasons (Fig. 1). The missed data points included one older individual who had to descend early prior to Barafu Camp for reasons not related to the altitude exposure; the remaining 25 subjects completed the trek. Thus, the altitude was generally well-tolerated and there were no clinical cases of HAPE or HACE.

The proportion of younger and older individuals at each test site with five or more comet tails, indicative of at least mild levels of extravascular lung water, is shown in Fig. 2. An increase in altitude from Baseline to Barafu tended to increase the proportion of participants with at least mild levels of extravascular lung water; however, Cochran's Q test did not indicate a statistically significant effect of altitude ($p = 0.06$) (Fig. 2). Regarding the effect of age, a higher proportion of

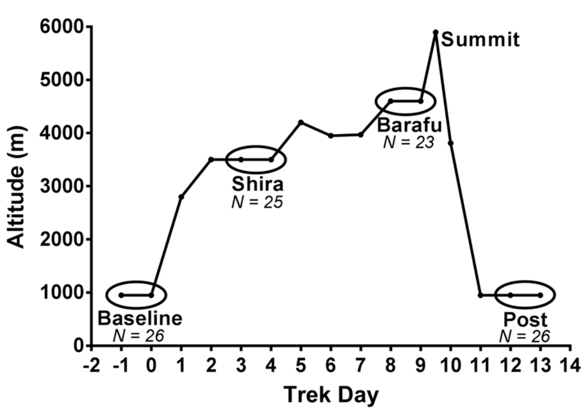

Fig. 1. Ascent profile for the 11-day trek of Mount Kilimanjaro. Participants were tested in Moshi ('Baseline,' 950 m) prior to beginning the trek on days −1 and 0, at Shira Camp (3505 m) on days 3 and 4, at Barafu Camp (4837 m) on days 8 and 9, and after descending back to Moshi ('Post,' 950 m) on days 12 and 13.

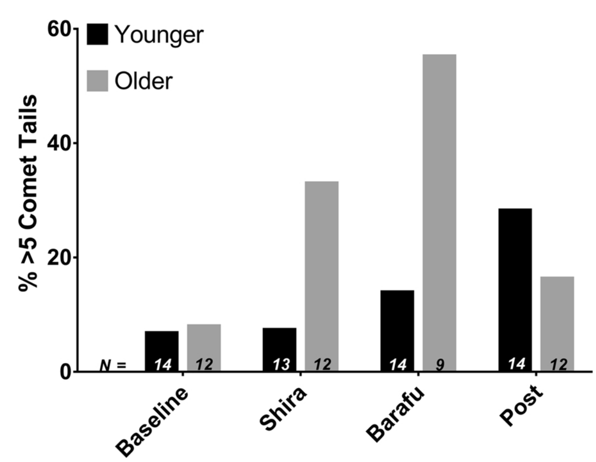

Fig. 2. Comet tails with increasing altitude. Proportion of younger and older participants with five or more comet tails, indicating at least mild levels of extravascular lung water, at each testing site. An increase in altitude tended to increase the proportion of participants with five or more comet tails ($p = 0.06$). At Barafu, the proportion of older individuals with five or more comet tails tended to be greater than that of the younger individuals ($p = 0.06$).

Table 2
Physiological variables of interest at each altitude in the younger versus older cohort.

	Younger	Older
Baseline		
SaO_2, %	97 ± 1	98 ± 2
sPAP, mmHg	17.8 ± 4.4	19.7 ± 4.6
$P_{ET}CO_2$, mmHg	31.8 ± 3.1	30.7 ± 2.9
Shira		
SaO_2, %	91 ± 6	92 ± 4
sPAP, mmHg	27.2 ± 8.0	26.4 ± 8.5
$P_{ET}CO_2$, mmHg	28.0 ± 1.8	26.4 ± 2.0
Barafu		
SaO_2, %	84 ± 6	85 ± 5
sPAP, mmHg	32.6 ± 6.8	33.5 ± 10.1
$P_{ET}CO_2$, mmHg	22.0 ± 1.2	20.3 ± 1.4
Post		
SaO_2, %	98 ± 1	97 ± 5
sPAP, mmHg	17.3 ± 5.3	18.5 ± 5.4
$P_{ET}CO_2$, mmHg	27.8 ± 1.7	26.1 ± 2.1

SaO_2, arterial oxygen saturation; sPAP, systolic pulmonary artery pressure; $P_{ET}CO_2$, end-tidal partial pressure of carbon dioxide. All variables demonstrated a significant effect of altitude ($p < 0.001$). $P_{ET}CO_2$ demonstrated a significant effect of age ($p = 0.021$).

older individuals tended to show at least mild levels of extravascular lung water at Barafu (4837 m) vs. the younger cohort; however, this comparison did not reach statistical significance (56 vs. 14%, p = 0.06) (Fig. 2). In general, the location of comet tails was relatively homogenous across the surface of the lung.

Two individuals showed moderate levels of extravascular lung water, defined as 15–30 comet tails, during the trek (Picano et al., 2006). Thirteen of 26 participants showed at least mild levels of extravascular lung water at some point during the climb; three participants showed greater than 5 comet tails at both altitude testing sites (Shira and Barafu Camps). The presence of comet tails was assessed in relation to potential causes and/or outcomes of extravascular lung water, including systolic pulmonary artery pressure (sPAP), arterial oxygen saturation (SaO_2), end-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$), and acute mountain sickness (AMS) scores. However, no associations between either the number or presence of comet tails and sPAP, SaO_2, $P_{ET}CO_2$, or AMS scores were observed at any test site, likely due to the slow acclimatization profile used presently. SaO_2, sPAP, and $P_{ET}CO_2$ are shown in Table 2; there was a significant effect of altitude for each variable ($p < 0.001$), and $P_{ET}CO_2$ demonstrated a significant effect of age ($p = 0.02$), suggesting higher ventilation in the older individuals.

4. Discussion

This study aimed to explore whether the development of extravascular lung water should be further investigated in older individuals during active trekking to high altitude, particularly when incorporating a faster – and therefore more typical – ascent profile. Our preliminary findings suggest that, in general, both younger and older participants showed limited development of extravascular lung water, likely due to the exceptionally slow acclimatization profile of our trek. However, we demonstrate that older adults likely experience greater levels of extravascular lung water at high altitude. These data, when compared with existing reports, demonstrate the importance of adequate acclimatization time during a trek to high altitude, particularly in older recreational climbers. Furthermore, these results highlight an important avenue of research moving forward, especially as recreational trekking to altitude becomes more accessible to individuals of all ages.

In general, the number of comet tails observed in our participants was low, and the individuals that showed comet tails at any given testing site was inconsistent. These data would suggest that the presence of extravascular lung water was subclinical and sporadic in our participants. However, it is well established that a slower ascent limits the negative physiological impacts of altitude exposure. For example, one of the potential negative impacts of altitude exposure is the development of high altitude pulmonary edema (HAPE), a serious condition that occurs when accumulation of extravascular lung water is severe. However, HAPE only occurs in the first days at altitude prior to pulmonary vascular adaptations taking effect (Hackett and Roach, 2001). Also, comet tails are measured in a resting state and thus may underestimate the level of extravascular lung water present in the lung during exercise (i.e., active trekking), particularly due to a greater PVR during exercise in older adults (Ehrsam et al., 1983; Emirgil et al., 1967; van Empel et al., 2014). Therefore, lung water formation is likely more substantial during active trekking while participating in a faster ascent profile.

While comet tails have been shown to be indicative of extravascular lung water, the threshold at which their presence transitions from subclinical to a potential HAPE diagnosis is not well established (Wimalasena et al., 2013). It is well accepted that under five comet tails is entirely normal, and according to the semi-quantitative threshold proposed by Picano et al. (2006), less than fifteen comet tails is indicative of only mild levels of extravascular lung water. In the present study, only two individuals ever showed moderate levels of extravascular lung water, defined as 15–30 comet tails. Thus, the subclinical nature of comet tails in the present study likely explains their lack of association with other potential outcomes of extravascular lung water development, such as decreased arterial oxygen saturation, which has been demonstrated in previous studies at altitude (Fagenholz et al., 2007; Pratali et al., 2010; Strapazzon et al., 2015).

A limitation of the current study is the lack of statistical power associated with a dichotomous measure; in other words, the presence *or* absence of comet tails. This semi-quantitative nature of comet tail assessment required the application of a simple yes/no statistical approach. Several previous investigations have treated the comet tail score as a continuous number; however, this mischaracterizes the clinical meaning of extravascular lung water when assessed via the comet tail score. Thus, while the rate of extravascular lung water formation was likely greater in older versus younger individuals, this finding did not reach statistical significance due to our strictly clinical interpretation of the comet tail score.

Future studies in which a faster ascent profile is utilized should measure comet tails in both younger and older adults. In this way, whether the slow acclimatization profile is responsible for the low level of extravascular lung water formation seen presently can be assessed. Additionally, other portable measures should be employed to help define whether the appearance of comet tails and extravascular lung water development is clinically relevant. For example, measures of lung diffusing capacity are able to quantify the rate at which gases are able to transfer from the pulmonary alveoli into capillary blood (Roughton and Forster, 1957). An increase in extravascular lung water may not be meaningful if gas transfer within the lungs is not substantially impeded. Nevertheless, studies incorporating measures of both comet tails and lung diffusing capacity are limited (Taylor et al., 2017), and to our knowledge do not exist in the realm of aging.

In conclusion, older adults may experience greater levels of extravascular lung water formation during a trek to high altitude. These data support the commonly held notion that a slow acclimatization profile should be implemented whenever possible, particularly in an older population. Nevertheless, additional studies are needed to fully understand the formation of extravascular lung water in older individuals while trekking at high altitude.

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