

Clinical Biostatistics

Exercise: Regression and correlation

Read the following paper, "Association between raised body temperature and acute mountain sickness: cross sectional study" (*British Medical Journal*, 315, 403-4), and answer the questions.

You can ignore the references to one factor analysis of variance and Mann Whitney U test. They are equivalents of the two sample t test for more than two groups and for non-Normal data respectively.

Association between raised body temperature and acute mountain sickness: cross sectional study

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Fever has long been associated with acute mountain sickness, and the physiologist Angelo Mosso reported that Dr Jacottet, who died in 1891 of presumed high altitude pulmonary oedema on Mont Blanc, had a body temperature of 38.3°C shortly before he died.¹ We studied the association between body temperature and acute mountain sickness, and body temperature and high altitude pulmonary oedema.

Subjects, methods, and results

We studied 60 climbers (mean age 39 (range 20-64) years) at 490 m (Zurich, Switzerland), after rapid ascent within 22 hours to a mountain hut at 4559 m above sea level, and during the subsequent stay there for 72 hours. We examined the climbers at low altitude, two to six hours after arrival at the hut (4 pm to 8 pm; day 1), and each morning (6 am to 9 am) during the next three days (days 2-4). The ethics committee of the University Hospital, Zurich, approved the study.

We assessed symptoms and signs of acute mountain sickness in a clinical interview and scored them as described previously.² We classified climbers as healthy or as having mild acute mountain sickness (score ≤ 3) or as having severe acute mountain sickness (score 4-13). Climbers with at least three of the following symptoms and signs were considered to have high altitude cerebral oedema: headache resistant to paracetamol, vomiting, dizziness, and ataxia. We measured axillary body temperatures in an ambient temperature 18-24°C. Blood gas pressures were sampled from the radial artery daily, and posteroanterior chest radiography was done at low altitude and on days 2-4. The chest radiographs were analysed as previously described.³

To compare the body temperatures in climbers with and without severe acute mountain sickness, we used the value that was associated with the climber's highest score at high altitude. In climbers with cerebral oedema or pulmonary oedema, or both, we recorded the temperature measured when these conditions were diagnosed.

Because of pulmonary oedema or cerebral oedema, or both, 3/60 climbers had to be evacuated by helicopter on day 2, seven on day 3, and five on day 4. Pulmonary oedema was diagnosed by chest radiography in 22 climbers.

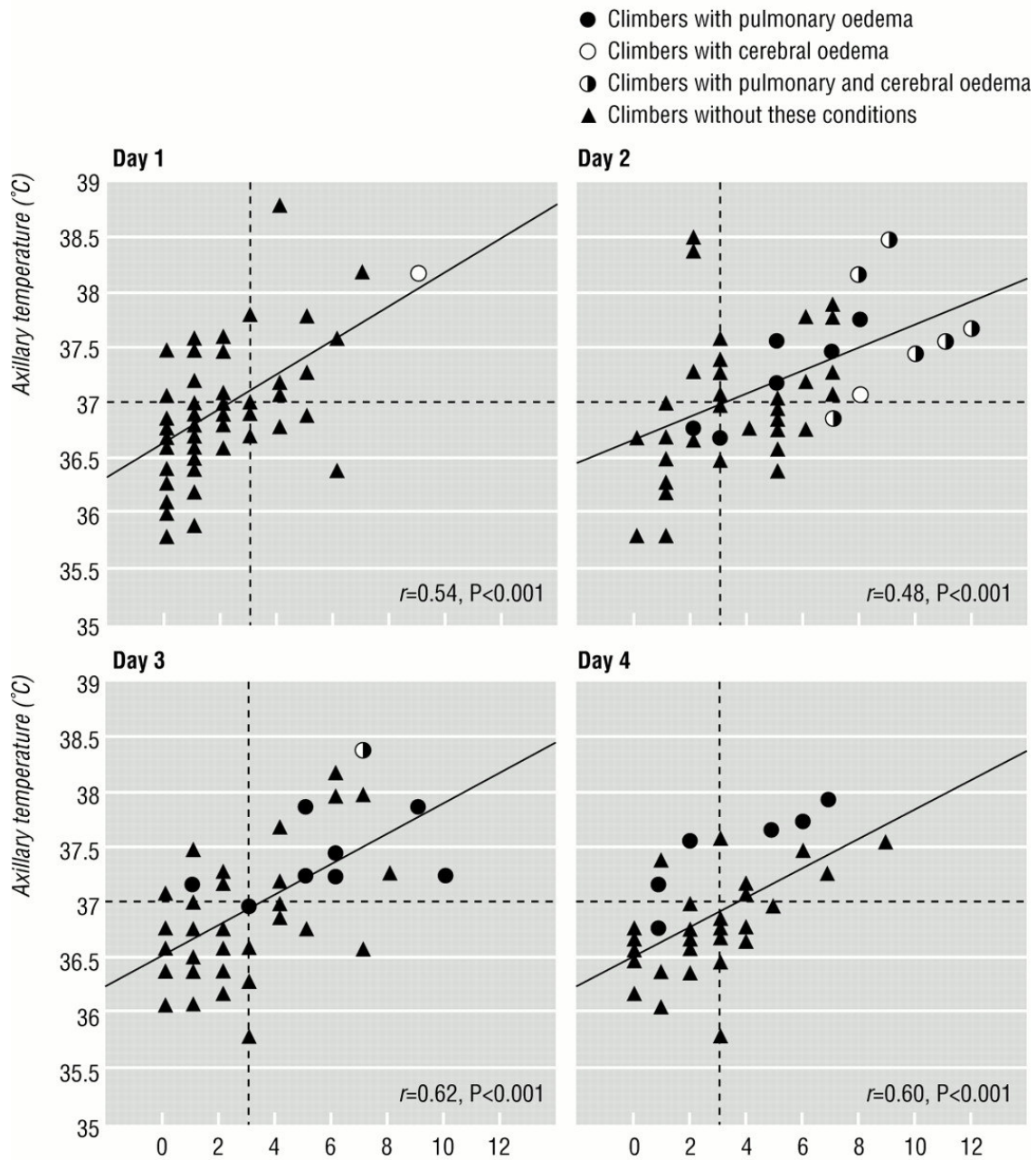


Fig 1 Body temperatures and scores for mountain sickness at high altitude on day 1 (n=60), day 2 (n=57), day 3 (n=50), and day 4 (n=44). Some climbers had same body temperature and same score. Oblique line is regression line.

Climbers' body temperatures and scores for acute mountain sickness are plotted in figure 1. The mean (SD) increase in body temperature between low and high altitude was 0.5°C (0.6) in climbers with a score ≤ 3 , 1.2°C (0.6) in those with a score >3 , and 1.7°C (0.5) in those with cerebral oedema (one factor analysis of variance, $P<0.001$). The mean body temperature was 37.9°C in climbers with cerebral oedema, compared with 36.9°C in climbers with a score ≤ 3 (mean difference 1.0°C (95% confidence interval 0.5 to 1.5)), and 37.7°C in climbers with a score >3 and pulmonary oedema, compared with 37.2°C in those without pulmonary oedema (0.4°C (0.2 to 0.7); Mann-Whitney U test, $P = 0.005$). The correlation coefficients between the body temperature and arterial oxygen pressure as well as between the body temperature and the radiographic assessment were -0.52 ($P < 0.001$) and 0.42 ($P < 0.001$) respectively (simple regression analysis).

Comment

We show a strong relation between body temperature, hypoxaemia, and the severity of acute mountain sickness in 60 climbers studied at low and high altitude. The correlations between the body temperature, the score for acute mountain sickness, and the arterial oxygen pressure suggest that a rise in temperature after rapid ascent to high altitude is a sign of acute mountain sickness and is associated with the severity of hypoxaemia.

Changes in the local vasomotor tone and exercise may have influenced our temperature measurements on the first day but not on subsequent days.

The aetiology of raised body temperature in acute mountain sickness remains unclear. Raised concentrations of thromboxane B₂ and leukotriene B₄, as well as C5a have been measured in the bronchoalveolar lavage fluid of subjects with high altitude pulmonary oedema.⁴ These findings, together with recent data from our group, showing a significant increase of C reactive protein and plasma concentrations of interleukin 6 and interleukin 1 in climbers with high altitude pulmonary oedema,⁵ suggest that such pulmonary oedema could be a systemic inflammatory disease. The findings here suggest that such a reaction could also occur in acute mountain sickness.

We are most grateful to all hut keepers and the Sezione Varallo of the Italian Alpine Club. We thank Ms J Hofmann and Mrs H Boeschstein-Manner for their excellent assistance.

Funding: The study was supported by a grant (3200-0092.85) from the Swiss National Science Foundation.

Conflict of interest: None.

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(Accepted 17 February 1997)

QUESTIONS ABOUT THIS REPORT:

1. "The mean body temperature was 37.9°C in climbers with cerebral oedema, compared with 36.9°C in climbers with a score ≤ 3 (mean difference 1.0°C (95% confidence interval 0.5 to 1.5))". What does this mean and what method could be used to calculate the 95% confidence interval?
2. "The correlation coefficient between the body temperature and arterial oxygen pressure ... [was] -0.52 (P<0.001)". What does this mean?
3. Figure 1 shows axillary temperature plotted against mountain sickness score, with correlation coefficients and associated P values. What condition must the data meet for the P value to be valid? Do you think the condition is met for Day 1?
4. Do you think this study was ethical?

The second paper (British Medical Journal, volume 311, pages 1668, 23-30 December 1995) describes a research exercise carried out by a GP. Epi-Info is a public domain statistical program developed by the Centres for Disease Control, Atlanta, Georgia, for investigating outbreaks of infectious disease.

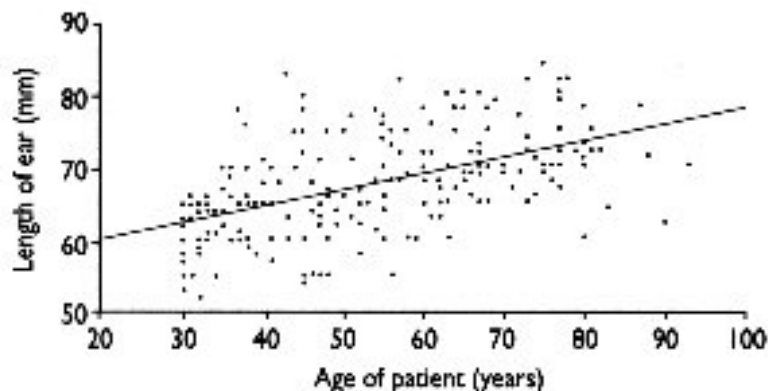
Why do old men have big ears?

James A Heathcote

In July 1993, 19 members of the South East Thames Faculty of the Royal College of General Practitioners gathered at Bore Place, in Kent, to consider how best to encourage ordinary general practitioners to carry out research. Some members favoured highly structured research projects; others were fired by serendipity and the observations of everyday practice. Someone said, “Why do old men have big ears? Some members thought that this was obviously true – indeed some old men have very big ears – but others doubted it, and so we set out to answer the question “As you get older do your ears get bigger?”

Methods and results

Four ordinary general practitioners agreed to ask patients attending for routine surgery consultations for permission to measure the size of their ears, with an explanation of the idea behind the project. The aim was to ask consecutive patients aged 30 or over, of either sex, and of any racial group. Inevitably it was sometimes not appropriate – for example, after a bereavement or important diagnosis – to make what could have seemed so frivolous a request, and sometimes (such as when a surgery was running late) patients were not recruited. The length of the left external ear was measured from the top to the lowest part with a transparent ruler; the result (in millimetres), together with the patient's age, was recorded. No patients refused to participate, and all the researchers were surprised by how interested (if amused) patients were by the project. The data were then entered onto a computer and analysed with Epi-Info; the relation between length of ear and the patient's age was examined by calculating a regression equation.



In all, 206 patients were studied (mean age 53.75 (range 30-93; median age 53) years). The mean ear length was 67.5 mm (range 52.0-84.0 mm) [decimal points added to original text], and the linear regression equation was: ear length = 55.9+(0.22 x patient's age) (95% confidence intervals for B coefficient 0.17 to 0.27). The figure shows a scatter plot of the relation between length of ear and age.

It seems therefore that as we get older our ears get bigger (on average by 0.22 mm a year).

Comment

A literature search on Medline by the library at the Royal College of General Practitioners that looked for combinations of “ears, external,” “size and growth,” “males,” and “ageing” produced no references.

A chance observation – that older people have bigger ears – was at first controversial but has been shown to be true. For the researchers the experience of involving patients in business beyond their presenting symptoms proved to be a positive one, and it was rewarding to find a clear result. Why ears should get bigger when the rest of the body stops growing is not answered by this research. Nor did we consider whether this change in a particular part of the anatomy is a marker of something less easily measurable elsewhere or throughout the body.

I acknowledge the generous help of Drs Colin Smith and David Armstrong and Ms Sandra Johnston with the data analysis; the work of my fellow data collectors, Drs Ian Brooman, Keren Hull, and David Roche; and the support of all members of the Bore Place group.

QUESTIONS ABOUT THIS REPORT:

5. What will be the effects of using patients attending their general practice?
6. Will the dropping of patients due to the seriousness of their presenting problem or the late running of the surgery have any effect?
7. Is this study blind? Does this have any implications for the interpretation of the results?
8. Is the distribution of ear size skew or symmetrical, and why?
9. What is a regression equation? What does the one in the paper tell us?
10. Can we conclude that the mean ear size at birth is 55.9 mm?
11. What assumptions about the data are required for regression analysis and do you think they satisfied here?
12. What are the conclusions and are they justified by the data?
13. What further investigations could be done?