INPLASY

Effects of Acute High-Altitude Exposure on Heart Rate Variability: A Systematic Review and Meta-Analysis

INPLASY202590004
doi: 10.37766/inplasy2025.9.0004
Received: 2 September 2025
Published: 2 September 2025

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ADMINISTRATIVE INFORMATION

Support - This study was supported by the Social Science Foundation of Shaanxi Province (Grant No. 2023Q014) and Natural Science Foundation of Ningxia (Grant No. 2025A1865).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590003

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 September 2025 and was last updated on 2 September 2025.

INTRODUCTION

Review question / Objective This study aims to comprehensively evaluate the effects of acute exposure to real high-altitude environments on heart rate variability (HRV) through a systematic review and meta-analysis. Unlike previous research, this study will specifically focus on high-altitude exposure above 2,500 meters, integrating multiple studies to address inconsistencies in the existing literature. We will adopt rigorous inclusion criteria, concentrating on acute exposure in authentic high-altitude settings (including altitude and duration of exposure), to ensure the reliability and generalizability of the results. Through this approach, we seek to provide more systematic and comprehensive evidence for understanding the impact of acute high-altitude exposure on the autonomic nervous system and cardiovascular health.

Condition being studied Acute high-altitude exposure is a common physiological stress state that occurs when individuals rapidly ascend to environments above 2,500 meters. Due to the significant reduction in barometric pressure and oxygen partial pressure, the body undergoes abrupt changes in autonomic nervous function, particularly reflected in fluctuations of heart rate variability (HRV). Previous studies have shown that acute high-altitude exposure is usually accompanied by increased sympathetic activity and decreased parasympathetic activity, leading to significant alterations in HRV time-domain and frequency-domain parameters (such as SDNN, RMSSD, HF, and LF/HF). These changes not only reflect the autonomic nervous system's adaptation to hypoxia but are also closely associated with the risk of acute mountain sickness (AMS). This systematic review and meta-analysis aims to comprehensively evaluate the effects of acute high-altitude exposure on HRV, thereby providing more systematic evidence for understanding

autonomic adaptation mechanisms and cardiovascular health risks.

METHODS

Participant or population The study population consisted of healthy adults from lowland areas or volunteers without severe underlying diseases who underwent HRV assessments after acute exposure to high-altitude environments (≥2,500 m) or in simulated hypobaric hypoxia chambers. The included participants encompassed males and females across different age groups, including soldiers, mountaineers, athletes, and ordinary residents. A total of 698 subjects were included, all of whom completed HRV measurements within 1–7 days of acute exposure, allowing comparisons between baseline lowland measurements and post-exposure autonomic responses.

Intervention Acute exposure to high altitude (≥2,500 m, duration ≤7 days).

Comparator Baseline at low altitude (≤600 m) or pre-exposure values.

Study designs to be included This study is a systematic review and meta-analysis, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021), and analyzed with reference to the Cochrane Handbook for Systematic Reviews of Interventions (6th edition) (Higgins et al., 2022).

Eligibility criteria

Inclusion criteria:

(1) Study type: Clinical studies, including randomized controlled trials (RCTs), non-randomized controlled trials, and prospective or retrospective cohort studies;

(2) Study population: Healthy adults or volunteers without severe underlying diseases;

(3) Exposure: Acute high-altitude exposure (or simulated hypobaric hypoxia), with altitude ≥2,500 m and exposure duration ≤7 days;

(4) Comparator: Baseline at low altitude (≤600 m) or pre-exposure data from the same participants;

(5) Outcomes: At least one heart rate variability (HRV) parameter reported, including but not limited to SDNN, RMSSD, PNN50%, LF, HF, VLF, LF/HF, SD1, and SD2.

Exclusion criteria:

(1) Reviews, case reports, conference abstracts, and animal studies;

(2) Studies involving participants with major diseases (e.g., cardiovascular disease, neurological disorders, severe infections) without separately reporting results for healthy populations;

(3) Studies lacking extractable HRV quantitative data (mean ± standard deviation or median ± interquartile range), and where data cannot be obtained by contacting the authors;

(4) Studies involving long-term high-altitude residents or chronic exposure, which do not meet the definition of "acute high-altitude exposure."

Information sources The literature search was conducted in accordance with the PRISMA guidelines, systematically retrieving studies related to acute high-altitude exposure. The databases searched included PubMed, Embase, China National Knowledge Infrastructure (CNKI), Wanfang Data, and VIP, with the search period covering inception to June 2025.

Main outcome(s) Acute high-altitude exposure (≥2,500 m, ≤7 days) significantly reduces HRV time-domain parameters (SDNN, RMSSD, PNN50) and frequency-domain parameters (HF, LF), while increasing the LF/HF ratio. This indicates a shift in autonomic nervous system balance from parasympathetic dominance to sympathetic predominance. These findings suggest that autonomic dysfunction may be one of the underlying mechanisms contributing to the development of acute mountain sickness.

Quality assessment / Risk of bias analysis To ensure the quality and reliability of the included studies, this review applied the Methodological Index for Non-randomized Studies (MINORS) to assess study quality. The MINORS scale is designed to evaluate the methodological rigor of non-randomized controlled trials (non-RCTs), covering aspects such as study design, sample size, completeness of data reporting, selection of control groups, and outcome assessment methods. In this quality assessment, all included studies were evaluated strictly according to the MINORS criteria. The scoring range is 0 to 24, with higher scores indicating better study quality.

Strategy of data synthesis Pooled effect sizes will be calculated using standardized mean differences (SMD) with 95% confidence intervals (CI). Heterogeneity will be assessed using the Q test and I^2 statistics. When I^2 0.10, a fixed-effects model will be used; otherwise, a random-effects model will be applied. Statistical analyses will be performed using Stata 17.0 and RevMan 5.4. Publication bias will be evaluated using funnel plots, Begg's test, and Egger's regression test.

Subgroup analysis
Subgroup analyses will be conducted according to:
1. Altitude of exposure (<3500 m vs. ≥3500 m);
2. Duration of exposure (≤3 days vs. 4–7 days);
3. Participant type (e.g., military personnel, athletes, college students, general residents).

Sensitivity analysis Sensitivity analyses will be conducted by sequentially excluding individual studies to assess the robustness of pooled results. In addition, sensitivity will be evaluated by comparing results from fixed-effects and random-effects models, and by excluding studies of lower methodological quality.

Country(ies) involved China.

Keywords Acute high-altitude exposure; Heart rate variability (HRV); Autonomic nervous system; Acute mountain sickness (AMS).

Contributions of each author
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