

Abstract

Background: Asthma is a chronic and heterogeneous inflammatory airway disease, characterized by variable airflow obstruction. About 5-10% of all asthma patients have severe asthma. These patients may be referred for Alpine Altitude Climate Treatment (AACT), provided by the Dutch Asthma Center Davos (NAD) in Switzerland. The NAD offers pulmonary rehabilitation (PR) at altitude, which consists of a multidisciplinary team and combines minimal exposure to environmental triggers with an individualized PR program. To date, it remains unclear what characterizes patients who repeat PR and which factors contribute to the need to repeat PR at altitude in patients with severe or difficult-to-treat asthma. Additionally, we do not know if repeated PR at altitude is as successful as a first rehabilitation.

Aim: To identify and compare the characteristics of patients with severe or difficult-to-treat asthma who completed a single AACT versus patients who repeated AACTs. Additionally, to assess the effectiveness of readmissions on the outcome measurements.

Methods: A total of 930 patients from the prospectively maintained database of the Dutch Asthma Centre Davos, admitted between 2008 and 2025 were included in this retrospective study. These patients accounted for 1498 admissions. Two databases were constructed, one on a patient level and one containing all admissions. Depending on data distribution, Kruskal-Wallis, Mann-Whitney U test or Pearson's chi-square test was used to compare outcomes between groups based on repeater status (repeater vs non-repeater), number of admissions (≤ 3 admissions vs ≥ 4 admissions) and admission period (before 2016, since 2016, mixed in both periods). These outcomes included patient-reported outcome measures (PROMs) such as the Asthma Control Questionnaire (ACQ), the Asthma Quality of Life Questionnaire (AQLQ), the Sino-Nasal Outcome Test-22 (SNOT-22), as well as objective biomarkers such as fractional exhaled nitric oxide (FeNO). Logistic regression analysis was performed to assess the baseline characteristics which predict the likelihood of AACT readmission. Linear mixed-effect model analysis was conducted to assess whether readmissions are still associated with beneficial outcome measurements.

Results: The multivariable logistic regression analysis showed that patients with higher ACQ score at baseline (OR=1.48, 95% CI: 1.21-1.80, $p < .001$), a lower ACQ score at the end of admission (OR=0.82, 95% CI: 0.69-0.99, $p = .035$) and patients who discontinue OCS at the end of admission (OR=2.21, 95% CI: 1.47-3.31, $p < .001$) are associated with an increased risk of AACT readmission. Additionally, the mixed-effect model analysis for diverse dependent variables showed that there was no association between PR admission order and outcome measurements and that baseline values for most dependent variables are the strongest predictors.

Conclusion: We concluded that outcomes of PROMs (ACQ, AQLQ and SNOT-22), physical capacity (ISWT) and medication use (OCS/ICS dose) were important factors in identifying repeaters, whereas no association between asthma phenotypes or objective biomarkers (FeNO, SIgE, total IgE, BEC) and readmission was found. ACQ was the most important factor in identifying repeaters, as patients presenting with

high and therefore worse ACQ scores at baseline, low and therefore better ACQ scores at the end of the first admission and patients who discontinued OCS at the end of the first admission are associated with an increased risk of AACT readmission. Furthermore, this study showed that repeating AACT is effective, as there is no significant association between PR admission order and outcome measurements. Patients showed improvement in asthma control (ACQ) in each subsequent admission and repeaters even showed a greater improvement in asthma control compared to non-repeaters.