SHORT COMMUNICATION

Phenotypes of Psoriasis in Patients in Need of Systemic Treatment, and Correlation with Personal Habits, Treatment History and Comorbidities: A Cross-sectional Latent Class Analysis of Data from the Italian PsoReal Registry

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Accepted Mar 10, 2023; Published Apr 4, 2023
Acta Derm Venereol 2023; 103: adv5331. DOI: 10.2340/actadv.v103.5331

Latent class analysis (LCA) is a statistical instrument to uncover hidden clusters in data and to identify different subgroups within a population that share certain characteristics. Subgroups are referred to as latent groups (or classes) (1). An advantage of LCA is that it is not influenced by previously suspected connections among data. Using LCA one can estimate the proportion of subjects belonging to each class and the probability that a member of a class shows a certain characteristic (2).

Cluster analysis including LCA was previously used in psoriasis (PsO) studies to group comorbidities (3), to explore patients' choice of treatment (4), or to identify the individual optimal biologic treatment (5).

To date, no studies have been conducted by LCA to identify subgroups of PsO phenotypes and to assess their relationship with lifestyle factors, comorbidities and treatment response.

MATERIALS AND METHODS

This was a cross-sectional analysis of baseline data from a cohort of patients with moderate-to-severe PsO, candidates to receive a new systemic treatment for the disease, using data collected within the ongoing PsoReal and the former PsoCare registries, involving a network of the main hospital-based Departments of Dermatology in Italy.

All patients signed informed consent. The study was approved by the ethics committees of participating centres.

Data were collected, between January 2005 and October 2021, through an electronic data capture system. Variables used in the analysis and their categorization are listed in Table SI.

Localization and morphology of PsO lesions were employed as indicators in LCA, while patients' age, sex, body mass index (BMI), PsO area severity index (PASI), disease duration were included as covariates. In order to find the optimal classification, different LCA models were iteratively fitted by varying the number of latent classes (LCs) to be found. Lowest Bayesian information criterion (BIC) was used to estimate the best classification.

Multivariate assessment of the relationship between subclasses and selected variables was performed by using multinomial logistic regression including covariates. All tests were considered statistically significant at p-value <0.05. A detailed description of statistical methods is reported in Appendix S2.

RESULTS

Of a total of 17,598 available patients with PsO, 2,439 were excluded due to incomplete or missing information **(**Fig. S1**).**

The main characteristics of the included patients are shown in Table SI. A 5-class model best fitted our data showing the lowest BIC (Table SII)**.** Among these 5 phenotypes, 4 represent widespread PsO and 1 limited disease. Estimated class conditional probabilities of disease type and localization are shown in Table SIII and Fig. S2. Based on these results we interpreted the LCs as described in Table SIV.

The estimated class proportions were 41.8% (95% CI 39.5–44.1) in LC1, 31.4% (29.4–33.4) in LC2, 13.8% (12.9–14.7) in LC3, 8.4% (7.4–9.4) in LC4 and 4.5% (3.8–5.3) in LC5.

Some significant differences were found regarding selected demographics, lifestyle factors and comorbidities among classes, when taking LC3 as a reference in multivariate analysis (**Table I**). The generalized-erythrodermic type LC5 was more prevalent in males, while LC3 was more represented in females. The classes with frequent genital involvement LC2 and LC5 had a significantly higher prevalence of smokers/ex-smokers. Psoriatic arthritis (PsA) was significantly more frequent in the limited PsO type LC3 and in LC5. LC3 had the highest prevalence of palmoplantar pustulosis (PPP). All comorbidities, including PsA and PPP, were significantly under-represented in LC4. Comorbidities, such as diabetes, arterial hypertension, liver and kidney diseases, were more frequent in LC2 and LC5. Pruritus was significantly more severe in LC5 and LC2. The widespread and generalized classes LC1, LC2 and LC5 had a significantly higher number of previous treatments, particularly biologics. The disease duration was significantly longer in all the classes other than LC3. LC4 was the most represented phenotype among patients with a diagnosis of PsO before age 18 years, while LC3 was more frequent in the group aged ≥45 years.

DISCUSSION

To the best of our knowledge, this is the first study using LCA to identify clinical subgroups of PsO patients requiring a systemic treatment.

The most frequent class was characterized by widespread PsO without inverse locations and no nail involvement (LC1), while the generalized-erythrodermic type (LC5) represented the smallest group. This is in concor-

Table I. Description of the 5 latent classes

Latent class	Description
LC 1	Widespread psoriasis, mainly plaque type lesions sparing nails and inverse localizations
LC2	Widespread psoriasis, mainly plaque type lesions with nail, head and inverse localizations
LC3	Limited psoriasis, with mostly plaque type lesions on the extremities and palmoplantar lesions
LC4	Widespread psoriasis, not fitting largely into the classic plaque type with head, face and nail involvement and limited inverse localizations
LC5	Generalized psoriasis, with mainly plaque type lesions and erythrodermic features

dance with the low prevalence of generalized-erythrodermic PsO in clinical series, where it represents 1–6% of all PsO patients (6). In LC5 there was a male predominance and 31% of patients could be classified as having erythrodermic features, defined by skin involvement of at least 80–90% (7). The severity and extent of disease in this class, as well as the high rate of severe pruritus, the higher number of comorbidities and the longer disease duration could explain the reported higher number of previous systemic treatments, especially biologics, in this class compared with the others. Furthermore, a treatment resistant course and a smaller drug survival of biologics could be hypothesized, as already described by others (8). The high rate of comorbidities in erythrodermic PsO is well known (9). PsA, hypertension and kidney disease were remarkably more prevalent in LC5 compared with other classes. Arterial hypertension is known to be more prevalent in erythrodermic PsO (7). Comorbidities may be partially explained by lifestyle factors, such as drinking alcohol and smoking, that were more prevalent in patients with generalized erythrodermic PsO (7). The relationship between smoking and severity of PsO as well as treatment resistance is already well known (10).

In the current cohort, patients in LC3 had a higher prevalence of PsA compared with widespread non-erythrodermic classes (LC1, LC2 and LC4). The correlation of PsO extension with the risk of PsA has been described by some authors, but it is still controversial (6, 11). The observation that patients in LC3 with limited skin involvement had also a high prevalence of PsA may contradict such an association. LC2, with fold and genital involvement, showed a trend to be more itchy and more frequent in obese patients and smokers. In addition, the reduced efficacy of biologics in obese patients (12, 13) could explain the higher number of previous therapies in this group.

Patients in LC3, are a peculiar group of predominant females with late disease diagnosis, limited PsO involvement, nail lesions and palmoplantar locations. The female predominance in palmoplantar PsO has been already described (14). The short disease duration may reflect the limited efficacy of topical therapies and the high demand for effective systemic treatments. Besides PsA, the frequent involvement of "critical" areas is also a reason for the initiation of a systemic treatment in this group, as also recommended by international expert panels (15).

The study was limited by restricting the population to PsO patients requiring systemic treatment, hence those with mild disease were not included. Moreover, our classification was not validated in an independent psoriasis cohort. In addition, there may be a non-negligible heterogeneity between patients included from 2005 to 2021, which was not considered in the analysis.

In conclusion, the use of LCA in the current study identified 5 clinical sub-classes of PsO patients in need of systemic treatment. These sub-classes, characterized by specific clinical features, showed differences in demographics, personal habits, comorbidities, and history of previous treatment. Besides confirming already described associations, the current analysis identified a few new ones. Dermatologists should be aware of the existence of important clusters in their PsO population. Of course, further analyses, possibly including additional variables and biomarkers, are required to better characterize PsO phenotypes.

ACKNOWLEDGEMENTS

The authors are grateful to all members of the PsoReal registry for contribution of data collections.

Datasets related to this article can be found at: https://data.mendeley.com/datasets/mhrzbc58p7, hosted at Mendeley.

LN has received honorarium as a scientific consultant for Abbvie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo, Lilly, Novartis, Sanofi.

SC and KH have no conflicts of interest to declare.

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