Comorbidities in palmoplantar pustulosis: a Swedish population-based register study

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Dear Editor, Palmoplantar pustulosis (PPP), a chronic relapsing skin condition characterized by pustules on the palms and soles, is often seen with psoriasis vulgaris (PV).[1,2] Smoking is a risk factor.[2] PPP has been associated with several comorbidities, including thyroid disease, metabolic disease, atopy, arthritis and depression.[3,4] However, large population-based studies with adequate control groups are lacking.

We used Swedish longitudinal register data to investigate comorbidity in PPP. Patients of all ages with a primary or secondary diagnosis of PPP ($n=15\,564$), obtained as an inpatient or at an outpatient appointment, were identified from the Swedish National Patient Register (NPR) from 2004 to 2015. These patients were matched (1 : 3) to patients with PV ($n=46\,842$) in the NPR and (1 : 5) to people from the general population ($n=77\,371$) in the Total Population Register. Matching was done based on year of birth, sex, residential area (general population) and index year (i.e. year of first PPP or PV diagnosis). In all three groups, mean participant age was 56 years; 76% were women. Among patients with PPP, 21% had concomitant PV. The occurrence of 35 diseases (selected from literature and identified by *International Classification of Diseases*, 10th Revision) were sourced from primary and secondary codes in the NPR during the entire study period. Hence, conditions may have occurred both before and after the year of the first experience of PPP. Comorbidity occurrence was compared between PPP and controls using logistic regression and expressed as odds ratios (ORs).

Among patients with PPP, 62% had at least one of the selected comorbidities vs. 44% in the general population and 61% in PV controls (Figure 1a). The most prevalent conditions in PPP were hypertension (27%), psoriatic arthritis (12%), type 2 diabetes (11%), hyperlipidaemia (8%), depression (8%), chronic obstructive pulmonary disease (COPD; 7%) and anxiety (6%).

Compared with general population controls, patients with PPP had significantly higher ORs for most ($n=32/35$) of the selected comorbidities (Figure 1b). For individual conditions, the most significant ORs were observed for allergic contact dermatitis [OR 6.25, 95% confidence interval (CI) 5.44–7.17], COPD (OR 2.54, 95% CI 2.36–2.74) and Crohn disease (OR 2.20, 95% CI 1.86–2.60). The condition 'Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue' generated a high OR; however, the prevalence was low in both groups ($<0.05\%$; Figure 1a).

The odds of having any of the selected comorbidities were similar between PPP and PV (Figure 1c); however, patients with PPP had significantly higher odds for 12 individual comorbidities and significantly lower odds for 8 (Figure 1c). The highest significant ORs for PPP compared with PV were observed for apical periodontal disease (OR 1.75, 95% CI 1.33–2.30), allergic contact dermatitis (OR 1.61, 95% CI 1.44–1.81) and coeliac disease (OR 1.55, 95% CI 1.27–1.91). Other diseases with significantly higher odds in PPP included type 1 and 2 diabetes, ulcerative colitis, hyperlipidaemia and Crohn disease; the findings for type 2 diabetes and hyperlipidaemia were consistent with the findings of a Korean study.[3] Comorbidities with significantly lower odds for PPP compared with PV included nonalcoholic fatty liver disease (OR 0.66, 95% CI 0.48–0.91), psoriatic arthritis (OR 0.74, 95% CI 0.70–0.78) and other malignant neoplasms of the skin (OR 0.80, 95% CI 0.74–0.88).

In a subgroup analysis, we limited the populations to patients with PPP without concomitant PV ($n=12\,333$) and matched PV controls ($n=36\,884$). Compared to the main

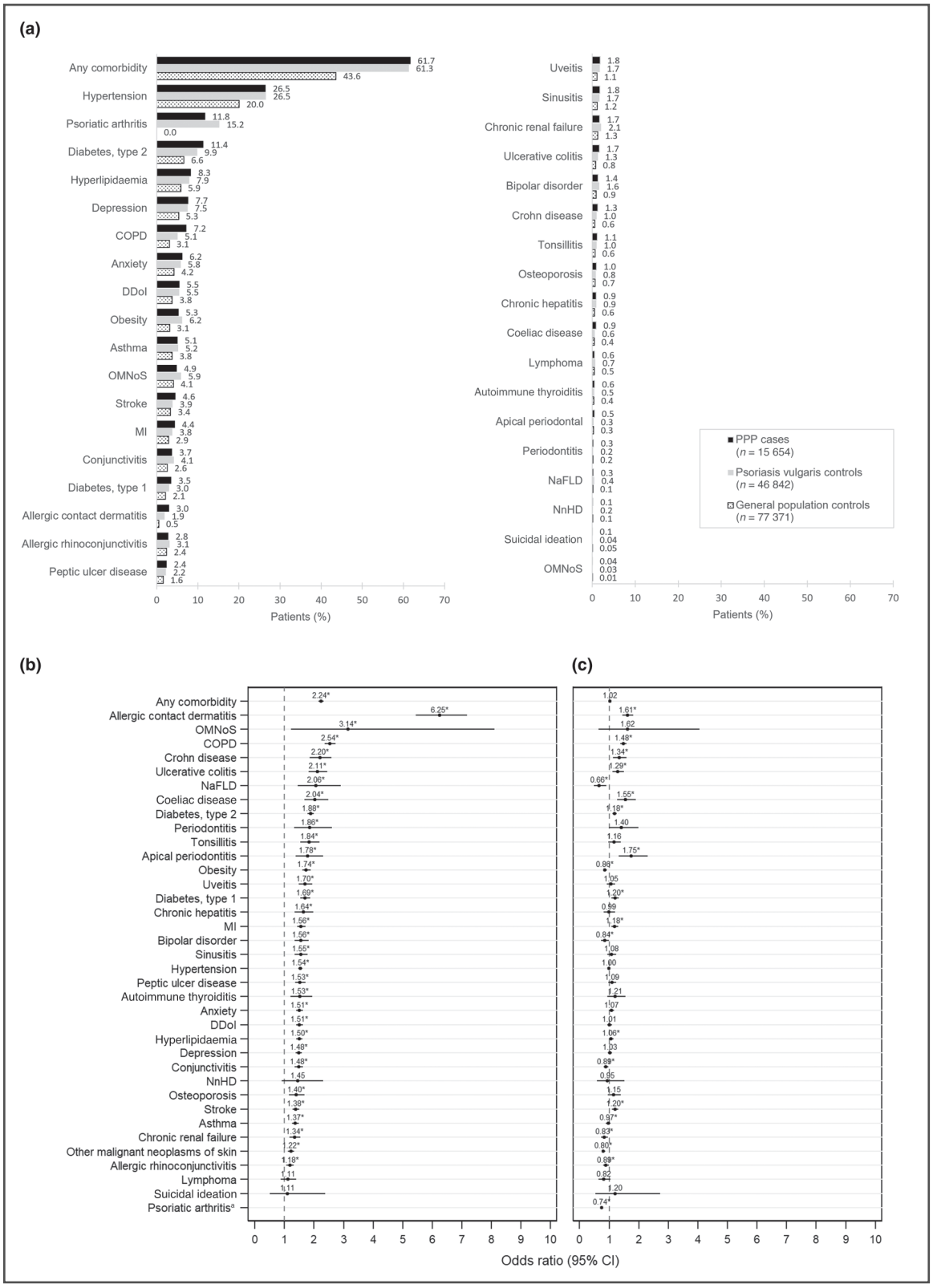

Figure 1 (a) Prevalence of selected comorbidities in patients with palmoplantar pustulosis (PPP) and matched controls from the general population and patients with psoriasis vulgaris (PV). (b) Odds ratios [ORs; 95% confidence interval (CI)] for comorbidities in patients with PPP vs. matched controls from the general population. (c) ORs (95% CI) for comorbidities in patients with PPP vs. matched PV controls. COPD, chronic obstructive pulmonary disease; DDoI, diverticular disease of the intestine; OMNoS, other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue; MI, myocardial infarction; NaFLD, nonalcoholic fatty liver disease; NnHD, nephritic nonhypertensive disease. [a]Nonapplicable in the comparison of patients with PPP vs. the general population. The conditions are sorted by order of magnitude of the OR (from highest to lowest) for PPP vs. the general population. *$P < 0.05$.

analysis, this subanalysis showed a similar prevalence of the most common comorbidities in PPP. The highest odds for PPP vs. PV controls were observed for apical periodontal disease (OR 1.63, 95% CI 1.20–2.22), followed by COPD (OR 1.44, 95% CI 1.32–1.57) and allergic contact dermatitis (OR 1.43, 95% CI 1.25–1.64).

The data that support the findings of this study are available from the Swedish National Board of Health and Welfare and the Swedish Tax Agency. Restrictions apply to the availability of these data, which were used under licence for this study. This study was conducted according to the principles of the Declaration of Helsinki and approved by the Regional Ethical Review Board at Umeå University.

We found a significantly higher comorbidity burden in patients with PPP compared with the general population, represented by higher odds for disease across different categories (metabolic, cerebrovascular, cardiovascular, psychiatric). Although patients with PPP and PV showed similar comorbidity burdens overall, the comorbidity profiles differed significantly. Comorbidities such as type 2 diabetes and COPD, which showed both a high prevalence (> 5%) in PPP and higher odds than in PV, may be of particular importance for the specific comorbidity burden of PPP. With regard to PPP, smoking is a risk factor for both type 2 diabetes and COPD. Upregulation of interleukin-36γ, which can be induced by smoking, has been implicated in the pathogenesis of all three diseases,[5–7] and may represent a common mechanism of PPP comorbidity. Limitations of the study include the potential misdiagnosis of PPP and underestimation of comorbidities due to the lack of a Swedish definition for the diagnosis of PPP and also primary care information. That some results were mediated by trigger factors for PPP (e.g. metal allergy or treatment with tumour necrosis factor inhibitors) cannot be ruled out.[4,8] Data on potential confounders (smoking) would have improved interpretation of the observed associations.

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Conflicts of interests: M.S.-E. is responsible for dermatology in the project management for the national guidelines for psoriasis at the Swedish Board of Health and Welfare. J.M.N. and S.L. have been involved in the health economic analyses of the national guidelines for psoriasis at the Swedish Board of Health and Welfare.

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