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# Lichen planopilaris is associated with cardiovascular risk reduction: a retrospective cohort review

Keywords: frontal fibrosing alopecia, lichen planopilaris, lichen planus, metabolic syndrome

Lichen planus (LP) is a chronic inflammatory disease that primarily affects mucocutaneous surfaces.<sup>1</sup> Lichen planopilaris (LPP) and frontal fibrosing alopecia (FFA) are important folliculocentric subtypes that result in scarring alopecia.<sup>2</sup> Previous studies linked LP with an increased risk of metabolic syndrome (MS), but how this risk varies by subtype is unknown.<sup>3,4</sup>

In this study, patients with LP were identified from outpatient dermatology/gynecology clinics by International Classification of Disease-9/10 code, diagnosis between January 1, 2015 and December 31, 2019, age at diagnosis 18 to 89 years, and 1:1 age-, race/ethnicity-, and sex-matched with patients without a diagnosis of LP ("matched cohort"). Body mass index (BMI), high-density lipoprotein (HDL), triglycerides (TG), diagnosis of hypertension (HTN), type II diabetes mellitus (DM2), coronary artery disease (CAD), and active prescription for a statin medication were obtained from the most recent visit date. Per the International Diabetes Federation's guidelines, MS was designated if a patient's BMI >30 kg/m<sup>2</sup> plus any 2 of the following: TG >150 mg/dL, HDL <50 mg/dL (females) or <40 mg/dL (males), or a diagnosis of DM2 or HTN.<sup>5</sup>

*T*-tests and Chi-square or Fisher exact tests were used to evaluate associations between continuous and categorical variables, and relative risks were calculated. All *P* values are 2-sided and evaluated at the .05 level for significance.

A total of 590 patients were identified with LP. In these patients, 15% had oral, 23% had cutaneous, 6% had genital, and 61% had LPP or FFA (Supplementary Table 1, http://links. lww.com/IJWD/A55). Of them, 481 (81.5%) were identified as female and 445 (88.6%) identified as White, and the mean age was 56.0 (standard deviation: 13.9) years.

Patients with LLP/FFA had a decreased risk of MS, HTN, CAD, DM2, and statin use versus the matched cohort; they also had lower BMI, HDL, and TG (Table 1). Patients with oral, cutaneous, or genital LP had increased or no difference in risk of these comorbidities versus the matched cohort (Supplementary Tables 2–4, http://links.lww.com/IJWD/A56). Patients with LPP/FFA demonstrated a decreased risk for HTN, DM2, CAD, MS, and statin use compared to patients with oral, cutaneous, or genital LP (Table 1). Multivariable regression demonstrated only LP subtype predicted risk of MS, not demographic factors including age, sex, or race/ethnicity (Table 2).

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Patients with LPP/FFA were less likely to be associated with MS and cardiovascular comorbidities compared to the matched cohort. This difference was even more notable when compared to patients with oral, cutaneous, and genital LP. This may be due to differences in relative systemic inflammation, and thereby, MS risk; patients with LPP/FFA have been found to demonstrate primarily localized scalp inflammation.<sup>2</sup> Behavioral factors may contribute, since oral, cutaneous, or genital LP may have a greater detrimental effect on activity or dietary habits. In contrast, patients with oral, cutaneous, or genital LP were not found to be at increased risk of MS compared to the matched cohort, a finding that diverges from prior studies.<sup>3,4</sup> It is plausible that other confounders, including hepatitis C infection, tobacco use, or the severity or treatment of the underlying LP, may influence this risk.

Limitations include the study's retrospective methodology and the overwhelmingly White female patient population. The distinction between FFA and LPP requires further investigation; due to the lack of specificity of International Classification of Disease coding and clinical documentation, these diagnoses were grouped in this study. Additionally, the matched cohort was derived from outpatients without LP, though how comorbidity rates differ from the general population is unknown.

## **Conflicts of interest**

The authors made the following disclosures: D.R.P. is a consultant for Biogen Inc. and clinical trials' principal/subinvestigator for Corbus Pharmaceuticals, Elorac, Inc., Eli Lilly and Company, Emerald Health Pharmaceuticals, Kadmon, Inc., Pfizer, Inc., and Soligenix, Inc. The other authors have no conflicts of interest to disclose.

What is known about this subject in regard to women and their families?

- Lichen Planus (LP) has previously been postulated to be associated with metabolic syndrome, which may be due to increased systemic inflammation.
- Variations in systemic and localized systemic inflammation have also been reported to correlate with LP subtype.

What is new from this article as messages for women and their families?

• Our study investigates the risk for several cardiovascular comorbidities and metabolic syndrome in lichen planopilaris, frontal fibrosing alopecia, and other lichen planus subtypes.

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## Table 1

Comorbidities and metabolic syndrome for patients with LPP/FFA compared to the matched cohort and oral, cutaneous, and genital subtypes

	LPP/FFA	Matched cohort (LPP/FFA)	RR, LPP/FFA vs matched cohort [[95% Cl]] { <i>P</i> value}	LPP/FFA only <sup>a</sup>	All other LP subtypes	RRª, LPP/FFA only vs other LP subtypes [[95% Cl]] { <i>P</i> value}
BMI, mean (SD) [n]	27.7 (6.3) [211]	29.5 (7.5) [254]	N/A <b>{.006</b> }	27.3 (6.3) [197]	29.1 (6.7) [201]	N/A <b>{.022}</b>
HDL, mean (SD) [n]	63.8 (20.3) [94]	57.7 (19.6) [117]	N/A <b>{.03}</b>	62.8 (20.2) [347]	57.6 (19.6) [240]	N/A <b>{.064}</b>
TG, mean (SD) [n]	117.5 (88.5) [94]	148.7 (89.0) [119]	N/A <b>{.01}</b>	118.8 (87.9) [347]	136.1 (83.9) [240]	N/A <b>{.154</b> }
HTN, n (%)	59 (16.3)	135 (37.2)	0.44 [[0.33-0.57]] {<.001}	55 (15.9) [347]	102 (42.5) [240]	0.37 [[0.28-0.50]] {<.001}
DM2, n (%)	19 (5.2)	49 (13.5)	0.39 [[0.23-0.65]] {<.001}	17 (4.9) [347]	50 (20.8) [240]	0.24 [[0.14-0.40]] {<.001}
MS <sup>b</sup> , n (%) [N]	15 (8.6) [174]	28 (14.2) [197]	0.61 [[0.34–1.10]] {.093}	13 (7.9) [347]	38 (23.5) [240]	0.34 [[0.19-0.61]] {<.001}
Statin Rx, n (%)	100 (27.5)	112 (30.9)	0.89 [[0.71–1.12]] {.327}	96 (27.7) [347]	86 (35.8) [240]	0.77 [[0.61-0.98]] {.035}
CAD, n (%)	6 (1.7)	10 (2.8)	0.60 [[0.22–1.63]] {.312}	6 (1.7) [347]	11 (4.6) [240]	0.35 [[0.13–0.93]] {.043}

Relative risk and P values are highlighted in bold to demonstrate differences across comorbidities.

P values were calculated using t-tests.

BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; DM2, type II diabetes mellitus; HDL, high-density lipoprotein cholesterol; HTN, hypertension; LP, lichen planus; LPP/FFA, lichen planopilaris/frontal fibrosing alopecia; MS, metabolic syndrome; N/A, not applicable; RR, relative risk; Rx, prescription; SD, standard deviation; TG, triglycerides.

<sup>a</sup>Subset of LPP/FFA including 347 patients who had LPP/FFA and no other LP subtypes.

<sup>b</sup>Defined per IDF criteria.

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## Study approval

This study was approved by the University of Minnesota's Institutional Review Board.

### **Author contributions**

AR and DRP wrote and revised the manuscript. RF and VR contributed to the data collection and analysis.

## **Supplementary data**

Supplementary material associated with this article can be found at http://links.lww.com/IJWD/A55 and http://links.lww. com/IJWD/A56.

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#### Table 2

Multivariable logistic regression for risk of MS, adjusting for diagnosis, age, sex, and race/ethnicity

	RR coefficient (95% CI)	<i>P</i> value
Intercept	0.119 (0.034–0.365)	.001
Diagnosis, LPP/FFAª	0.308 (0.159-0.553)	<.001
Age <sup>b</sup>	1.014 (0.995-1.033)	.167
Sex, Female	0.988 (0.557-1.965)	.969
Race/ethnicity, non-White/Hispanic or Latinx	0.863 (0.351-1.701)	.707

Relative risk and *P* values are highlighted in bold to demonstrate differences across comorbidities. Cl, confidence interval; LPP/FFA, lichen planopilaris/frontal fibrosing alopecia; MS, metabolic syndrome; RR, relative risk.

aVersus other lichen planus subtypes.

<sup>b</sup>Continuous variable.