Alopecia areata: Mortality trends from a population-based cohort study reflect increased survival

To the Editor: A recent population study suggested a decreased risk of dermatologic and internal malignancies and all-cause mortality in patients with vitiligo.[1] These observations are purportedly related to elevated immune surveillance and clearance of potentially neoplastic processes.[1] Alopecia areata (AA) is an autoimmune condition governed by pathologic mechanisms akin to vitiligo for which similar survival benefits have not been studied.

A population-based cohort study was performed using an anonymized database (TriNetX Network) to investigate potential survival benefits in patients with AA between 2006 and 2024. A case cohort was identified using ICD-9 code 704.01 and ICD-10 code L63.X for AA diagnoses. A control cohort was created by matching for age, sex, and comorbidities (Table I). These cohorts were further stratified using the Charlson comorbidity index (CCI; the most extensively studied assessment tool that predicts long-term mortality by scoring comorbidities) and the presence of end-organ disease.

A total of 99,116 patients with AA were identified. The mean age was 33.6 years (SD: 20.7) with 61% female and 39% male (Table I). The most common comorbidities were hypertension (12.9%), dyslipidemia (9.1%), and diabetes (5.2%) like the vitiligo cohort reported by Ju et al[1] (Table I). The overall adjusted hazard ratio (aHR) of mortality for the AA cohort compared with controls was 0.498 (95% CI: 0.473-0.526, P value $< .0001$), despite matching based on the demographics and comorbidities listed in Table I. The presence of end-organ disease yielded an aHR of mortality for AA of 0.519 (95% CI: 0.486-0.555), which was similar to the aHR in the absence of end-organ disease of 0.479 (95% CI: 0.436-0.527). Likewise, the prediction of mortality scoring indicates that the aHR for a CCI of 0, where no comorbidities were found, is 0.52 (95% CI: 0.44-0.614), which is almost identical to a CCI of 1 or more, which is 0.51 (0.48-0.55; Table II).

These results disclose a mortality benefit for patients with AA very similar to those recently described in patients with vitiligo.[1] The mechanisms of this observed benefit in AA potentially mirror those described in the vitiligo studies whereby T-cell recruitment to areas of inflammation provides additional defense against infections, neoplasms, and oxidative stress.[2] This conjecture contrasts autoimmune conditions marked by widespread chronic inflammation and tissue damage, like systemic lupus erythematosus and psoriasis.[3,4] These conditions are associated with higher rates of comorbidities, more frequent systemic

Table I. Characteristics of alopecia areata study population and covariate-matched cohort

	Alopecia areata, *n* (%)	Matched controls, *n* (%)	*P* value*
Number of subjects	99,116	99,116	
Female sex, *n* (%)	60,896 (61.43)	60,766 (61.3)	.55
Age at index	33.6 (20.7)	33.5 (20.6)	.23
Smoking, *n* (%)	2444 (2.5)	2381 (2.4)	.36
Comorbidities			
Hypertension	12,794 (12.9)	12,652 (12.8)	.34
Diabetes	5130 (5.2)	5082 (5.1)	.63
Dyslipidemia	9014 (9.1)	8787 (8.9)	.075
CAD	2781 (2.8)	2667 (2.7)	.12
Stroke or TIA	1241 (1.25)	1143 (1.2)	.043
COPD	1363 (1.4)	1313 (1.3)	.33
Liver cirrhosis	405 (0.4)	368 (0.4)	.18
CKD	1764 (1.8)	1708 (1.7)	.34

CAD, Coronary artery disease; *CKD*, chronic kidney disease; *COPD*, chronic obstructive pulmonary disease; *SD*, standard deviation; *TIA*, transient ischemic attack.
**P* values between cohorts indicate the degree of propensity score matching.

Table II. Mortality risk for patients with alopecia areata according to sex, age, Charlson comorbidity index, and presence of end-organ disease

	Alopecia areata*	Matched control*	aHR (95 % CI)	*P* value
Overall	212 (2094/98,828)	416 (4119/98,956)	0.498 (0.473-0.526)	<.0001
Sex				
Female	224 (1362/60,673)	452 (2749/60,773)	0.485 (0.466-0.518)	<.0001
Male	193 (675/34,958)	407 (1,424/34,986)	0.464 (0.433-0.519)	<.0001
Age (y)				
<40	531 (275/51,815)	877 (455/51,861)	0.603 (0.519-0.701)	<.0001
40-59	132 (364/27,568)	247 (682/27,593)	0.528 (0.464-0.606)	<.0001
>60	697 (1454/20,858)	1440 (3022/20,918)	0.444 (0.415-0.512)	<.0001
CCI				
0	35.8 (210/58653)	68.7 (403/58684)	0.52 (0.44-0.614)	<.0001
1 or more	946 (1440/15,211)	1700 (2,589/15,253)	0.51 (0.48-0.55)	<.0001
End-organ disease				
Absent	75.1 (635/84,609)	155 (1316/84,696)	0.479 (0.436-0.527)	<.0001
Present	1100 (1626/14,748)	1930 (2848/14,786)	0.519 (0.486-0.555)	<.0001

aHR, Adjusted hazard ratio; *CCI*, Charlson comorbidity index.
*Mortality outcomes reported as incidence rate of mortality per 10,000 person-years; (number of events/person-years).

immunosuppressive therapies, and worse mortality outcomes.[5] Although cutaneous conditions, such as AA and vitiligo, confer a survival benefit via a proposed mechanism of targeted immune hypervigilance in skin disorders marked by more chronic systemic inflammation, such as psoriasis, detrimental effects lead to poorer health outcomes. It will be interesting to see how the emergence of novel immunosuppressive therapies for both vitiligo and AA will impact these mortality trends and in which direction. Limitations of this study include the retrospective nature of data collection and the potential for clinician-based misclassification of diagnoses using ICD-10 codes.

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Conflicts of interest

None disclosed.

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