All-cause mortality among patients with hidradenitis suppurativa: A population-based cohort study in the United States

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Background: The mortality risk for patients with hidradenitis suppurativa (HS) is largely unknown.

Objective: To compare mortality risk among individuals with and without HS in the United States.

Methods: Retrospective cohort study in a population sample identified by using electronic health records data between January 1, 2012, and December 31, 2016. Primary outcome was incidence of 5-year all-cause mortality.

Results: The crude 5-year mortality rate among patients with HS was 2.4% (321/13 289), compared with 2.7% (18 508/685 573) among control individuals. In the fully adjusted model, the increase in HS mortality risk was 14% (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.01-1.28). Overall, excess risk of death attributable to HS was 3.1 deaths per 1000 patients (95% CI, 0.2-6.0) during the study period. Characteristics associated with mortality among patients with HS included age (OR, 1.05; 95% CI, 1.04-1.06), male sex (OR, 1.40; 95% CI, 1.09-1.79), ever-smoking status (OR, 1.48; 95% CI, 1.16-1.92), and Charlson Comorbidity Index score (OR, 1.25; 95% CI, 1.21-1.29).

Limitations: The follow-up period may not have been long enough to assess the influence of disease severity or duration on mortality.

Conclusion: HS appears to confer an independent risk of all-cause mortality. This risk is also influenced by tobacco smoking and comorbidities, which may be modifiable. (J Am Acad Dermatol 2019;81:937-42.)

Key words: comorbidities; comorbidity; hidradenitis suppurativa; mortality.

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease of the pilosebaceous unit that affects the axillary, inguinal, perineal, and inframammary regions. It is characterized by painful nodules, abscesses, sinus tract formation, scarring, and disfigurement.[1,2] In addition to its locally destructive course, HS has growing recognition for its association with individual comorbid diseases, including diabetes mellitus,[3] obstructive sleep apnea,[4] Crohn disease,[5] and substance abuse disorder,[6] among others. HS also has an overall comorbidity burden that is greater than that of psoriasis and that has been linked to mortality.[7] Patients with HS have increased circulating levels of inflammatory markers,[8-12] which may predispose them to long-term sequelae including atherosclerosis and subsequent mortality.[13-15] Although mortality has been evaluated in patients with other chronic

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inflammatory diseases of the integument,[16,17] information on mortality among patients with HS is sparse. The purpose of this investigation was to compare all-cause mortality between patients with and without HS and in a population-based sample, to identify subgroups who may be at higher risk, and to determine which clinical characteristics are most closely associated with mortality among patients with HS.

CAPSULE SUMMARY

- The mortality risk for patients with hidradenitis suppurativa is largely unknown.
- Hidradenitis suppurativa confers an independent increase in risk of all-cause mortality. Risk may be attenuated through early identification and management of comorbid conditions.

METHODS

Patient population

This was a retrospective cohort analysis using a multi—health system data analytics and research platform (Explorys) developed by IBM (Armonk, NY), Watson Health.[18] Clinical information from electronic medical records, laboratories, practice management systems, and claims systems is matched by using the single set of Unified Medical Language System (US National Library of Medicine, Bethesda, MD) ontologies to create longitudinal records for unique patients. Data are standardized and curated according to common controlled vocabularies and classification systems including International Classification of Diseases (ICD), Systemized Nomenclature of Medicine—Clinical Terms (ie, SNOMED-CT), Logical Observation Identifiers Names and Codes (ie, LOINC), and RxNorm.[19-23] At present, the database encompasses 27 participating integrated health care organizations. More than 56 million unique lives, representing approximately 17% of the population across all 4 census regions of the United States, are captured. Patients with all types of insurance and those who are self-pay are represented.

Statistical analysis

The study population was limited to patients aged 18 through 90 years having active status between January 1, 2012, and December 31, 2016, and having activity in the database at least in the year before the index date. We excluded patients who were missing data on age, sex, or race or who were missing date information for the primary exposure, outcome, or covariates. Patients with HS were identified by using at least 1 ICD-9 (705.83) or ICD-10 (L73.2) diagnosis code. In a validation study, we observed a positive predictive value of 79.3% and an accuracy of 90% for diagnosis of HS using this algorithm.[24] Information on mortality was obtained from the source health system's vital status Social Security death index. Additionally, we excluded patients who had clinically meaningful evidence of activity in the database after their recorded death year. Charlson Comorbidity Index (CCI) scores were calculated as of the index date. Disease duration was calculated as the length of time from the date of first HS diagnosis to January 1, 2012.

Baseline covariates were summarized by using means, standard deviations, frequencies, and percentages. We calculated crude 5-year mortality for the HS and control cohorts and patient subgroups in the period between January 1, 2012, and December 31, 2016. Risk of mortality was compared between patients with HS and those without HS by using adjusted odds ratios (ORs) from 2 multivariable logistic regression models. In the first model, age, sex, and race were included as covariates. Body mass index (BMI), smoking status (ever, never), and CCI score were added as variables in the second, fully adjusted model. We assessed whether the association between HS and mortality differed across patient subgroups by including an interaction term between HS status and the subgroup variable of interest in separate covariate-adjusted logistic regression models. We also performed a separate multivariable logistic regression within the HS cohort to identify factors associated with mortality in this group.

Statistical significance was evaluated at the .05 alpha level. All analyses were performed using R, version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria). This study was approved by the human subjects committee at the Feinstein Institute of Medical Research at Northwell Health.

RESULTS

We identified 13 289 patients with HS and 685 573 control individuals who met eligibility criteria. Demographic characteristics are described in Table I. Patients with HS had a mean age of 42.6 years and were predominantly female (77%) and white (56.5%). African Americans made up 36.9% of the HS cohort. Patients with HS had higher mean BMIs and mean CCI scores than control individuals. Patients with HS were tobacco smokers more frequently than control individuals.

Abbreviations used:

BMI: body mass index
CCI: Charlson Comorbidity Index
HS: hidradenitis suppurativa
ICD: International Classification of Diseases
OR: odds ratio

Overall and subgroup-specific crude 5-year mortality incidence and adjusted ORs are presented in Table II. The overall crude 5-year mortality rate among patients with HS was 2.4% (321/13 289), compared with 2.7% (18 508/685 573) in the control cohort. After adjusting for age, sex, and race, patients with HS had a 77% (OR, 1.77, 95% confidence interval [CI], 1.62-1.93) increase in mortality risk compared with control individuals. In the fully adjusted model, which also included BMI, smoking status, and CCI score, the increase in mortality risk for patients with HS compared with control individuals was attenuated to 14% (OR, 1.14; 95% CI, 1.01-1.28). There were 3.1 more deaths per 1000 patients (95% CI, 0.2-6.0) in the HS cohort compared with the control group during the 5-year study period.

HS was associated with significantly higher mortality risk compared with control individuals in 4 patient subgroups. Among patients aged 40 to 49 years, those with HS had a 64% increase in odds of mortality compared with those without HS (OR, 1.64; 95% CI, 1.26-2.12). Among white participants, those with HS had a 25% increase in odds of mortality compared with those without HS (OR, 1.25; 95% CI, 1.07-1.46). Among obese patients, those with HS had a 20% increase in odds of mortality compared with those without HS (OR, 1.20; 95% CI, 1.03-1.40). Among patients with CCI score of at least 5, those with HS had a 31% increase in odds of mortality compared with those without HS (OR, 1.31; 95% CI, 1.08-1.59). Among the covariates, only age significantly modified the association between HS and risk of mortality (interaction *P* value, .01) (Table II).

Demographic and clinical characteristics associated with mortality in HS are described in Table III. For every 1-year increase in age, mortality increased by 5% (OR, 1.05; 95% CI, 1.04-1.06). Male sex (OR, 1.40; 95% CI, 1.09-1.79) and ever-smoking status (OR, 1.48; 95% CI, 1.16-1.92) were also significantly associated with mortality. A 1-unit increase in CCI score was associated with a 25% increase in mortality among patients with HS (OR, 1.25; 95% CI, 1.21-1.29). Body mass index and disease duration, however, were not associated with mortality.

Table I. Demographic and clinical characteristics of patients with and without HS

Variable	Patients with HS (n = 13 289)	Control individuals (n = 685 573)
Female, n (%)	10 237 (77.0)	420 559 (61.3)
Age in years at index, mean (SD)	42.6 (14.1)	50.8 (17.2)
Race, n (%)		
White	7509 (56.5)	551 975 (80.5)
African American	4906 (36.9)	77 786 (11.3)
Other	874 (6.6)	55 812 (8.1)
Body mass index in kg/m^2, mean (SD)	33.7 (8.9)	29.5 (7.3)
Tobacco smoker, n (%)	7373 (55.5)	212 054 (30.9)
Charlson Comorbidity Index score, mean (SD)	1.3 (2.1)	0.8 (1.6)
HS duration in years, mean (SD)	3.2 (3.3)	N/A

HS, Hidradenitis suppurativa; *N/A*, not applicable; *SD*, standard deviation.

DISCUSSION

In this analysis, the 5-year mortality risk for patients with HS was increased by 77% compared with control individuals after adjustment for demographic covariates. The excess risk attributable to HS accounted for 3 additional deaths per 1000 patients in a 5-year period. The HS subgroups with significantly higher mortality risk compared with the control group included patients aged 40 to 49 years, white, obese, and with a CCI score of at least 5. Among patients with HS, increasing age, male sex, tobacco smoking, and increasing CCI score were associated with an increased risk of mortality, whereas BMI and disease duration were not. The increase in mortality risk was also substantially attenuated to 14% after further adjustment for tobacco smoking, comorbidity burden, and BMI. Although HS imparts an independent mortality risk, prevention, early identification, and management of modifiable factors may decrease mortality among patients with HS.

To date, the literature on mortality among patients with HS is sparse. In a previous analysis, we observed 12.6% mortality over a 5-year study period among patients with HS who had a CCI score of at least 5, similar to the 13.5% mortality rate among patients with HS in the same category in this analysis.[7] A Danish analysis evaluating all-cause mortality among patients with HS observed 54 deaths per 10 000 person-years.[15] This translates to an approximate crude 5-year mortality rate of 2.7%, also comparable to the mortality rate observed in this study. Before adjusting for tobacco smoking and

Table II. Risk of mortality among subgroups of patients with HS and control individuals

Subgroup	Crude 5-year mortality incidence, % (number of deaths/subgroup size)		Group-specific adjusted OR* (95% CI)	Interaction *P* value
	Patients with HS	Control individuals		
Overall	2.4 (321/13 289)	2.7 (18 508/685 573)	1.14 (1.01-1.28)	
Sex				.81
Female	2.0 (206/10 237)	2.1 (8977/420 559)	1.15 (0.99-1.33)	
Male	3.8 (115/3052)	3.6 (9531/265 014)	1.12 (0.94-1.37)	
Age in years (at index)				.01
18-29	0.3 (9/2762)	0.3 (282/100 111)	0.92 (0.46-1.84)	
30-39	0.7 (21/3148)	0.5 (433/91 677)	1.07 (0.69-1.66)	
40-49	2.1 (64/3051)	0.8 (960/114 043)	1.64 (1.26-2.12)	
50-59	3.7 (98/2651)	1.9 (2,719/144 449)	1.19 (0.96-1.47)	
60-69	6.7 (83/1230)	3.5 (4,501/126 992)	1.07 (0.84-1.35)	
70-79	10.1 (39/387)	7.6 (6401/84 400)	0.75 (0.53-1.07)	
80+	11.7 (7/60)	13.4 (3212/23 901)	0.54 (0.24-1.24)	
Race				.06
White	2.5 (185/7509)	2.7 (14 969/551 975)	1.25 (1.07-1.46)	
African American	2.4 (116/4906)	3.0 (2329/77 786)	0.95 (0.78-1.17)	
Other	2.3 (20/874)	2.2 (1210/55 812)	1.47 (0.91-2.37)	
Obesity (BMI $\geq$ 30.0 kg/m^2)				.27
Yes	2.3 (191/8253)	2.6 (7179/274 385)	1.20 (1.03-1.40)	
No	2.6 (130/5036)	2.8 (11 329/411 188)	1.05 (0.87-1.27)	
Smoking status				.35
Current or former	3.1 (226/7373)	4.3 (9175/212 054)	1.10 (0.95-1.27)	
Never†	1.6 (95/5916)	2.0 (9333/473 519)	1.24 (1.00-1.53)	
CCI category				.10
0	0.7 (46/6198)	1.1 (5075/452 435)	1.20 (0.89-1.60)	
1-2	1.5 (74/4888)	3.3 (5518/168 218)	0.91 (0.72-1.15)	
3-4	5.4 (65/1196)	8.8 (3318/37 642)	1.09 (0.84-1.41)	
≥5	13.5 (136/1007)	16.9 (4597/27 278)	1.31 (1.08-1.59)	

BMI, Body mass index; *CCI*, Charlson Comorbidity Index; *CI*, confidence interval; *HS*, hidradenitis suppurativa; *OR*, odds ratio.
*ORs compare the risk of mortality in patients with HS versus control individuals, with control as the referent. Group-specific ORs are adjusted for age, sex, race, CCI, BMI, and smoking status.
†The lower limit of the 95% CI for the adjusted ORs in this subgroup equals 1.002.

comorbidities, the incidence rate ratio in the Danish analysis was 1.96, similar to the age-, sex-, and race-adjusted OR in our study. In their fully adjusted model, which accounted for tobacco smoking and comorbidities, the incidence rate ratio for mortality was attenuated to 1.35, similar to the attenuation in our fully adjusted model. Although the results appear to be similar, there are important distinctions between the 2 analyses. The Danish analysis did not evaluate potentially important covariates, such as obesity and disease duration. Most importantly, the 2 populations have significantly different racial and ethnic compositions, and so their results may not be generalized to the United States, where black patients are disproportionately affected by HS.[25]

The mechanism by which HS confers an independent mortality risk is unclear. Other chronic inflammatory diseases, including psoriasis,[16] rheumatoid arthritis,[17] ankylosing spondylitis,[26] and periodontal disease,[27] have also been independently associated with increased mortality risk. It has been proposed that chronic inflammation as part of the disease state, through shared pathophysiologic pathways, may predispose to accelerated atherosclerosis and increased cardiovascular mortality.[14] Moreover, comorbid conditions such as diabetes mellitus, obstructive sleep apnea, and Crohn's disease, linked to the disease state through shared inflammatory pathways, may further increase the risk of cardiovascular or other organ-related death.

This retrospective analysis has important limitations that warrant consideration when the results are interpreted. Our analysis is subject to the limitations inherent to research based on electronic health record data. Causation of mortality could not be established because information on cause of death was not available and because the analysis is retrospective. We could not capture patients with HS who did not seek care in health systems included in the database. Accordingly, our cohort may be

Table III. Demographic and clinical characteristics of patients with HS associated with mortality

Variable	Adjusted OR	95% CI	*P* value
Age*	1.05	(1.04-1.06)	<.001
Sex			
Male	1.40	(1.09-1.79)	.01
Female	—	—	—
Race			
White	—	—	—
African American	0.95	(0.74-1.22)	.68
Other	1.10	(0.65-1.75)	.71
Body mass index*	1.01	(0.99-1.02)	.25
Smoking status			
Current or former	1.48	(1.16-1.92)	.002
Never	—	—	—
Charlson Comorbidity Index score*	1.25	(1.21-1.29)	<.001
Disease duration*	1.00	(0.97-1.03)	.87

CI, Confidence interval; *HS*, hidradenitis suppurativa; *OR*, odds ratio.
*OR associated with a 1-year increase in age, 1-unit increase in CCI, 1-unit increase in body mass index, and 1-year increase in disease duration.

selected for patients with more severe HS, who may be more likely to seek care and have a diagnosis of HS. It is also possible that this analysis underestimates mortality because patients with more severe disease may be more likely to receive systemic treatment, which may modify mortality. There is potential for misclassification of exposure, outcome, or covariates due to erroneous documentation or misdiagnosis. To mitigate the influence of possible misclassification bias, we used validated case definitions to identify patients with HS and other comorbidities. Data on potentially relevant covariates, such as socioeconomic status, that are not typically collected in the course of routine health care are generally unavailable in electronic medical records or claims data. We could not assess the influence of disease severity in HS on the strength of the association with mortality. The follow-up period in this analysis may not have been long enough to assess the influence of disease duration on mortality. Finally, subgroup results should be interpreted with caution because these are generally dependent on group sizes, and they may represent chance findings resulting from multiple testing.

Despite these limitations, this population-based analysis describes important data on mortality among patients with HS, which are sparse in the medical literature. The quantity of lives included in the analysis permitted the evaluation of an uncommon occurrence, as well as subgroup analyses that allowed identification of groups at highest risk. Because the population sample was drawn from various health care settings across US census regions, this study overcomes selection biases associated with tertiary single-center or multicenter investigations. Given the size and demographic heterogeneity of the HS cohort, we believe these results may be generalized to the US health care–seeking population.

In conclusion, HS appears to confer an independent increase in risk of all-cause mortality. Mortality in HS is also partly attributable to tobacco smoking and comorbid conditions, which may be modifiable through prevention, early identification, and management. The results reported here may support future areas of study, including elucidating the causes of mortality among patients with HS and determining whether systemic treatment aimed at reducing inflammation in HS reduces the risk of mortality.

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