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Comparative Overall Comorbidity Burden Among Patients With Hidradenitis Suppurativa

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IMPORTANCE The overall comorbidity burden among patients with hidradenitis suppurativa (HS) has not been systematically evaluated.

OBJECTIVES To investigate the standardized overall comorbidity burden among patients with HS and to compare it with the comorbidity burden in patients with psoriasis and a control group.

DESIGN, SETTING, AND PARTICIPANTS A cross-sectional analysis was conducted of 5306 patients with HS, 14 037 patients with psoriasis, and 1 733 810 controls identified using electronic health records data from October 1, 2013, through October 1, 2018.

MAIN OUTCOME AND MEASURE The primary outcome was the mean Charlson Comorbidity Index (CCI) score.

RESULTS Each matched cohort had 3818 patients (2789 women and 1029 men; mean [SD] age, 45.7 [15.0]). Before matching, the overall mean (SD) CCI score was highest among the psoriasis cohort (2.33 [3.13]), followed by the HS cohort (1.80 [2.79]) and control cohort (1.26 [2.35]). In matched analyses, the overall mean (SD) CCI score was highest among the HS cohort (1.95 [2.96]), followed by the psoriasis cohort (1.47 [2.43]; $P < .001$) and control cohort (0.95 [1.99]; $P < .001$) patients. A total of 516 patients with HS (13.5%) had an overall mean CCI score of 5 or greater. Mean CCI score was highest for patients with HS across all sex, race, and age groups. The most common comorbidities among patients with HS were chronic pulmonary disease (1540 [40.3%]), diabetes with chronic complications (365 [9.6%]), diabetes without chronic complications (927 [24.3%]), and mild liver disease (455 [11.9%]). Patients with HS with a CCI score of 5 or greater had 4.97 (95% CI, 1.49-16.63) times the adjusted risk of 5-year mortality compared with patients with HS with a CCI score of zero.

CONCLUSIONS AND RELEVANCE Patients with HS have a higher overall comorbidity burden compared with patients with psoriasis and a control group. A significant proportion of patients with HS have CCI scores of 5 or greater, which are associated with increased mortality. This degree of comorbidity burden may warrant multidisciplinary implementation of routine screening measures.

Author Audio Interview

Supplemental content

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Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease of the pilosebaceous unit that affects axillary, inguinal, perineal, and inframammary regions. It is characterized by painful nodules, abscesses, sinus tract formation, scarring, and disfigurement.[1] Patients with HS have a quality of life that is among the poorest of those with dermatologic diseases.[2] In addition to its locally destructive course, HS has growing recognition for its association with individual comorbid diseases,[3-7] as well as all-cause mortality.[8] However, the global comorbidity burden in patients with HS has not been established, to our knowledge. The purpose of this investigation was to estimate the standardized overall comorbidity burden in patients with HS and to compare the comorbidity burden in HS with that of psoriasis, the prototype inflammatory skin disease linked to comorbid disease.[9]

Key Points

Question What is the overall burden of comorbid disease in patients with hidradenitis suppurativa?

Findings In this cross-sectional study of 3818 patients in each of 3 matched cohorts, patients with hidradenitis suppurativa had a mean Charlson Comorbidity Index score of 1.95, which was significantly higher than mean CCI scores of age-, sex-, and race-matched cohorts of patients with psoriasis (Charlson Comorbidity Index score, 1.47) and a control group (Charlson Comorbidity Index score, 0.95).

Meaning The overall comorbidity burden in patients with hidradenitis suppurativa has implications for mortality risk and resource use, and it may warrant multidisciplinary implementation of routine screening measures.

Methods

This was a cross-sectional analysis using a multi-health system data analytics and research platform (Explorys; IBM Corp, Watson Health).[10] Clinical information from electronic medical records, laboratories, practice management systems, and claims systems is matched using the single set of Unified Medical Language System ontologies to create longitudinal records for unique patients. Data are standardized and curated according to common controlled vocabularies and classifications systems including the *International Classification of Diseases, Ninth Revision* and *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*; Systematized Nomenclature of Medicine–Clinical Terms; Logical Observation Identifiers Names and Codes; and RxNorm.[11-15] At present, the database encompasses 27 participating integrated health care organizations. More than 56 million unique individuals, representing approximately 17% of the population across all 4 census regions of the United States, are captured. Patients with all types of insurance as well as those who are self-pay are represented. The current analysis was based on a 10% random sample of the database to which access was available. This study was approved by the human subjects committee at the Feinstein Institute of Medical Research at Northwell Health, which waived patient consent owing to the deidentified nature of the data.

The study population was limited to patients aged 18 to 90 years with active status between October 1, 2013, and October 1, 2018, and at least 1 year of time in the database. Patients with HS were identified using at least one *International Classification of Diseases, Ninth Revision* diagnosis code (705.83) or *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* diagnosis code (L73.2). A validation study observed a positive predictive value of 79.3% and an accuracy of 90% for diagnosis of HS using this algorithm.[16] Patients with HS who also had a diagnosis of psoriasis were excluded from the HS cohort. Patients with 2 or more diagnosis codes for psoriasis[17,18] and no diagnosis code for HS comprised the psoriasis cohort. The control cohort included patients with an active status in the database who did not have a diagnosis code for HS or for psoriasis.

The Charlson Comorbidity Index (CCI) is a validated standardized measure of global comorbidity.[19-22] An individual's CCI score is composed of 17 components, each of which is assigned a weight based on the relative risks of 1-year mortality[19,23] (eTable in the Supplement). The CCI score has been shown to be associated with short-term and long-term mortality across different populations in the outpatient[24-27] and acute care settings.[28,29] Charlson Comorbidity Index scores were calculated at the time of the latest data refresh (within 1 month of data extraction) and therefore represent each patient's most current comorbidity status, rather than the comorbidity status at entry.

Statistical Analysis

Patients with HS, patients with psoriasis, and the control group were matched on age, sex, and race/ethnicity, using one-to-one exact matching. Mean CCI scores were calculated for the 3 cohorts and their subgroups before and after matching. The frequency and proportion of patients within CCI score risk categories (0, 1-2, 3-4, and ≥5) were summarized for each cohort. The Wilcoxon signed-rank test was used to compare the distribution of CCI scores between matched patients with HS, patients with psoriasis, and the control group. The proportion of patients with a CCI score of 5 or greater was compared between matched patients with HS, patients with psoriasis, and the control group using the McNemar test. All P values were from 2-sided tests and results were deemed statistically significant at $P < .05$. Analyses were performed using R, version 3.3.1 (R Foundation for Statistical Computing).

We also evaluated the association between CCI score and 5-year mortality in a subset of patients with HS. Mortality was compared across CCI risk categories during the period between January 1, 2012, and December 31, 2016. Patients with HS who were aged 18 to 90 years with an active status in 2011, and with a duration of at least 1 year in the database prior to January 1, 2012, were eligible for inclusion. Patients with no activity in the database during the 5-year study period were excluded, as well as those missing age, sex, or race/ethnicity information. Charlson Comorbidity Index scores as of January 1, 2012, were calculated for all eligible patients according to the algorithm provided in the eTable in

the Supplement, and patients were classified into 4 risk categories: CCI score 0, 1 to 2, 3 to 4, and 5 or greater. Information on mortality (yes or no) between January 1, 2012, and December 31, 2016, was obtained from the source health system's vital status social security death index. Five-year mortality was compared across CCI risk categories using multivariable logistic regression, controlling for age, sex, race/ethnicity, and smoking status (ever or never).

Results

We identified 5306 patients with HS, 14 037 patients with psoriasis, and 1 733 810 individuals in the control group who met eligibility criteria. Demographic characteristics are described in **Table 1**. The HS cohort had a lower mean (SD) age (43.7 [14.6] vs 58.0 [16.2] vs 51.9 [18.4] years), a higher percentage of women (4037 [76.1%] vs 7754 [55.2%] vs 1 004 568 [57.9%]), and a higher percentage of African American individuals (1902 [35.8%] vs 628 [4.5%] vs 216 237 [12.5%]) compared with the psoriasis and control cohorts. In unmatched analysis, overall mean (SD) CCI score was highest in the psoriasis cohort (2.33 [3.13]) followed by the HS (1.80 [2.79]) and control (1.26 [2.35]) cohorts (**Table 2**). Increasing age, male sex, and African American race/ethnicity were associated with higher comorbidity in all groups. After 1-to-1 matching, the 3 study cohorts each comprised 3818 patients and had identical age, sex, and race/ethnicity distributions (Table 1). In the matched analysis, mean (SD) CCI scores were significantly higher in the HS cohort (1.95 [2.96]) compared with those in the psoriasis (1.47 [2.43]; $P < .001$) and control (0.95 [1.99]; $P < .001$) cohorts. Patients in the HS cohort had significantly higher mean (SD) CCI scores across nearly all patient subgroups (**Table 3**).

Charlson Comorbidity Index risk categories are described in **Table 4**. A significantly greater percentage of patients with HS compared with patients with psoriasis and the control group had CCI scores in the ranges of 1 to 2 (1422 [37.2%] vs 1336 [35.0%] vs 1059 [27.7%]), 3 to 4 (396 [10.4%] vs 332 [8.7%] vs 201 [5.3%]), and 5 or greater (516 [13.5%] vs 356 [9.3%] vs 206 [5.4%]). The most frequent comorbid conditions among matched patients with HS were chronic pulmonary disease (1540 [40.3%]); diabetes without chronic complications (927 [24.3%]); mild liver disease (455 [11.9%]); diabetes with chronic complications (365 [9.6%]); any malignant neoplasm, including lymphoma and leukemia, except malignant neoplasm of skin (342 [9.0%]); peripheral vascular disease (319 [8.4%]); cerebrovascular disease (285 [7.5%]); renal disease (285 [7.5%]); congestive heart failure (257 [6.7%]); rheumatic disease (202 [5.3%]); and myocardial infarction (167 [4.4%]).

We identified a subset of 1269 patients with HS meeting eligibility criteria for the mortality subanalysis. These patients had a mean (SD) age of 42.4 (14.2) years and were mostly female (996 [78.5%]) and white (672 [53.0%]). The percentage of patients with a CCI risk score of 0 was 48.0% (n = 609), 1 to 2 was 36.3% (n = 461), 3 to 4 was 8.2% (n = 104), and 5 or greater was 7.5% (n = 95). There were 21 deaths during the 5-year follow-up period. Controlling for age, sex, race/ethnicity, and smoking status, patients with HS with CCI scores of at least 5 at the start of the follow-up period had 4.97 (95% CI, 1.49-16.63) times the odds of 5-year mortality compared with patients with HS with a CCI score of 0 (**Table 5**).

Discussion

In this study, we observed a 2-fold increase in standardized overall comorbidity burden as measured by CCI among patients with HS compared with the general population. Charlson Comorbidity Index scores were increased across sex, race/ethnicity, and age subgroups. Patients with HS also had higher overall and subgroup comorbidity burden compared with patients with psoriasis. Patients with HS with CCI scores of at least 5 had nearly 5 times the odds of 5-year mortality than patients with HS with CCI scores of 0.

Disease states with similar CCI indices to HS include systemic lupus erythematosus (CCI score, 1.43),[30] dermatomyositis (CCI score, 1.4),[31] and ankylosing spondylitis (CCI score, 1.33).[32] In rheumatoid arthritis, 35.4% of patients have a CCI score of at least 3,[33] compared with the nearly 1 in 4 (912 [23.9%]) patients with HS in this risk category. The mortality risk observed in our analysis is consistent with prior studies in other disease states in which CCI scores of at least 5 are associated with a 5- to 7-fold increase in 5-year mortality

Table 1. Demographic Characteristics of Patients With Hidradenitis Suppurativa, Patients With Psoriasis, and the Control Group Before and After Matching[a]

Characteristic	Patients, No. (%)			
	Hidradenitis Suppurativa (n = 5306)	Psoriasis (n = 14 037)	Control Group (n = 1 733 810)	Matched Cohorts (n = 3818 in Each Group)[b]
Age, mean (SD), y	43.7 (14.6)	58.0 (16.2)	51.9 (18.4)	45.7 (15.0)
Female sex	4037 (76.1)	7754 (55.2)	1 004 568 (57.9)	2789 (73.0)
Race/ethnicity				
White	3002 (56.6)	12 497 (89.0)	1 351 706 (78.0)	2966 (77.7)
African American	1902 (35.8)	628 (4.5)	216 237 (12.5)	505 (13.2)
Other	402 (7.6)	912 (6.5)	165 867 (9.6)	347 (9.1)

[a] The study was limited to patients 18 years or older with an active status in the database within the last 5 years and at least 1 year of total time in the database.

[b] After exact 1-to-1 matching, the 3 study groups had identical age, sex, and race/ethnicity distributions, with 3818 patients in each group.

Table 2. Mean (SD) Charlson Comorbidity Index Scores for Cohorts and Subgroups Prior to Matching

Cohort	Hidradenitis Suppurativa (n = 5306)	Psoriasis (n = 14 037)	Control Group (n = 1 733 810)
Overall	1.80 (2.79)	2.33 (3.13)	1.26 (2.35)
Sex			
Male	2.14 (3.26)	2.49 (3.28)	1.40 (2.51)
Female	1.69 (2.61)	2.20 (3.00)	1.16 (2.23)
Race/ethnicity			
White	1.77 (2.77)	2.31 (3.11)	1.27 (2.35)
African American	1.83 (2.77)	2.89 (3.31)	1.40 (2.50)
Other	1.90 (3.02)	2.29 (3.19)	1.05 (2.12)
Age, y			
18-29	0.60 (1.01)	0.47 (0.94)	0.28 (0.68)
30-39	0.90 (1.46)	0.70 (1.41)	0.40 (1.00)
40-49	1.60 (2.36)	1.06 (1.79)	0.64 (1.42)
50-59	2.54 (3.16)	1.77 (2.50)	1.08 (2.01)
60-69	3.78 (3.91)	2.60 (3.09)	1.71 (2.62)
70-79	4.67 (4.16)	3.75 (3.64)	2.59 (3.20)
80-89	5.71 (4.31)	4.98 (4.06)	3.41 (3.52)

Table 3. Mean (SD) Charlson Comorbidity Index Scores for Age-, Sex-, and Race/Ethnicity-Matched Cohorts and Subgroups

Cohort	Hidradenitis Suppurativa (n = 3818)	Psoriasis (n = 3818)	*P* Value[a]	Control Group (n = 3818)	*P* Value[b]
Overall	1.95 (2.96)	1.47 (2.43)	<.001	0.95 (1.99)	<.001
Sex					
Male	2.27 (3.39)	1.59 (2.58)	<.001	1.16 (2.24)	<.001
Female	1.84 (2.77)	1.42 (2.37)	<.001	0.87 (1.88)	<.001
Race/ethnicity					
White	1.79 (2.78)	1.31 (2.29)	<.001	0.87 (1.92)	<.001
African American	2.89 (3.59)	2.51 (3.06)	.06	1.52 (2.44)	<.001
Other	2.04 (3.16)	1.26 (2.16)	<.001	0.80 (1.67)	<.001
Age, y					
18-29	0.59 (1.05)	0.46 (0.91)	.008	0.24 (0.65)	<.001
30-39	0.83 (1.28)	0.71 (1.30)	.004	0.44 (1.03)	<.001
40-49	1.55 (2.31)	1.07 (1.73)	<.001	0.61 (1.25)	<.001
50-59	2.61 (3.27)	1.92 (2.73)	<.001	1.13 (2.18)	<.001
60-69	3.82 (3.98)	2.66 (3.13)	<.001	1.84 (2.55)	<.001
70-79	4.62 (4.15)	3.94 (3.74)	.05	2.89 (3.58)	<.001
80-89	5.71 (4.23)	5.16 (3.87)	.34	4.61 (3.96)	.24

[a] Comparisons between patients with hidradenitis suppurativa and patients with psoriasis based on Wilcoxon signed-rank test.

[b] Comparisons between patients with hidradenitis suppurativa and control group based on Wilcoxon signed-rank test.

risk,[23,24] as well as a 5-fold increase in annual health care expenditures.[34,35]

As a chronic inflammatory disease characterized by inflammatory nodules, suppuration, and abscess formation resulting in pain and disfigurement, HS represents a prime candidate to bridge disease of the integument and comorbid systemic disease. To our knowledge, this is the first primary analysis on standardized overall comorbidity burden in a population of patients with HS. In a primary analysis on health care use, Israeli patients with HS had a mean CCI score of 1.1, compared with scores of 0.97 among age- and sex-matched patients with psoriasis and 0.9 among an age- and sex-matched control group.[36] However, the difference in mean CCI scores between patients with HS and patients with psoriasis was not statistically significant in the Israeli study. We also observed higher mean CCI scores among US patients with HS and psoriasis in our study. There were no black patients in the Israeli cohort, so their results may not be generalized to the United States, where HS disproportionately affects black patients,[37] and where black patients generally have a greater comorbidity burden and poorer health outcomes than white counterparts.[38]

Biomarker expression in tissue and serum of patients with HS appears complex and its description at present likely remains incomplete. Cytokine expression profiles in lesional skin have demonstrated increased levels of tumor necrosis factor, interleukin 1β (IL-1β), IL-6, IL-8, IL-10, IL-12, IL-17, and IL-23.[39-44] Serum of patients with HS has also shown elevated levels of tumor necrosis factor, IL-17, and IL-6.[45-48] The chronic inflammatory state in HS may represent shared pathways, yet to be characterized, that link HS with comorbid conditions.

Limitations

This retrospective analysis has important limitations that warrant consideration when interpreting the results. We could not capture patients with HS who did not seek care in health systems included in the database. We could not assess the potential influence of HS disease severity on the CCI score in this code-based analysis. The CCI does not capture all comorbid conditions or states, such as mood disorder[49] and substance abuse,[5] which are more prevalent among patients with HS compared with the general population. We were not able to perform Cox proportional hazards regression for mortality because exact dates of death are removed to preserve anonymity. Despite these limitations, this population-based analysis describes important data on the standardized overall comorbidity burden in HS. Given the size and heterogeneity of the HS cohort, we believe these results may be generalized.

Conclusions

Hidradenitis suppurativa is associated with a significant overall comorbidity burden across age, sex, and race/ethnicity groups. This comorbidity burden is higher for patients with HS than it is for patients with psoriasis. A significant proportion of patients with HS have CCI scores of at least 5, which is associated with increased 5-year mortality. The degree of comorbidity burden among patients with HS may warrant multidisciplinary implementation of counseling and screening measures, with the goals of prevention and early detection of

Table 4. Frequency of CCI Risk Categories for Age-, Sex-, and Race/Ethnicity-Matched Cohorts

CCI Risk Category	Hidradenitis Suppurativa, No. (%) (n = 3818)	Psoriasis (n = 3818), No. (%)	*P* Value[a]	Control Group, No. (%) (n = 3818)	*P* Value[b]
0	1484 (38.9)	1794 (47.0)	<.001	2352 (61.6)	<.001
1-2	1422 (37.2)	1336 (35.0)	.04	1059 (27.7)	<.001
3-4	396 (10.4)	332 (8.7)	.01	201 (5.3)	<.001
≥5	516 (13.5)	356 (9.3)	<.001	206 (5.4)	<.001

Abbreviation: CCI, Charlson Comorbidity Index.

[a] Comparisons between patients with hidradenitis suppurativa and patients with psoriasis.

[b] Comparisons between patients with hidradenitis suppurativa and control group.

Table 5. Five-Year Risk of Mortality Among Patients With Hidradenitis Suppurativa According to CCI

CCI Risk Category	Patients, No.	Deaths, No. (%)	Adjusted OR (95% CI)[a]	*P* Value
0	609	5 (0.8)	1 [Reference]	
1-2	461	4 (0.9)	0.60 (0.15-2.36)	.46
3-4	104	0	[b]	.99
≥5	95	12 (12.6)	4.97 (1.49-16.63)	.01

Abbreviations: CCI, Charlson Comorbidity Index; OR, odds ratio.

[a] Derived from a logistic regression model, adjusting for age, sex, race/ethnicity, and smoking status.

[b] Could not be estimated with adequate precision owing to 0 deaths within this subgroup.

identified comorbidities. Future studies may evaluate cardiovascular, rheumatologic, and malignant associations with HS, because these conditions comprise many of the comorbidities in the CCI. Whether comorbidity burden in HS is reduced with systemic treatments that may modulate shared inflammatory pathways also warrants investigation.

ARTICLE INFORMATION

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Drafting of the manuscript: Reddy, Garg.
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