Association Between Hidradenitis Suppurativa and Lymphoma

The chronic inflammatory state in hidradenitis suppurativa (HS) may result in development of clonal immune cell populations which give rise to malignant lymphomas. Our objective was to investigate prevalence of non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), and cutaneous T-cell lymphoma (CTCL) among patients with HS.

Methods | This cross-sectional cohort analysis used standardized electronic health record information of the IBM Explorys database for 55 million patients from 27 integrated health systems across the United States.[1] The analysis was limited to adults aged at least 18 years with active status between July 16, 2013, and July 16, 2018, who had complete information on sex and age. The Systemized Nomenclature of Medicine-Clinical Terms *hidradenitis*, *non-Hodgkin's lymphoma*, *Hodgkin's disease*, and *primary cutaneous T-cell lymphoma* were used to identify cohorts.[2] Use of electronic health data to identify lymphoma cohorts has been performed in prior studies evaluating associations between lymphoma and other conditions, including psoriasis.[3,4] We assessed overall lymphoma prevalences among patients with and without HS, and within demographic subgroups. Prevalences were compared using a logistic regression model controlling for age and sex. All hypothesis tests were 2-tailed and conducted at the .05 significance level. This study was approved by the human subjects committee at the Feinstein Institute for Medical Research at Northwell Health, which waived the need for informed consent for deidentified data.

Results | We identified 62 690 patients with HS whose demographic characteristics are described in **Table 1** (25.6% men and 74.4% women). Crude prevalences of NHL, HL, and CTCL among patients with HS compared with patients without HS (N = 28 937 880) were 0.40% vs 0.35%, 0.17% vs 0.09%, and 0.06% vs 0.02%, respectively (**Table 2**). In multivariable analysis, patients with HS had increased overall odds of having NHL (odds ratio [OR], 2.00; 95% CI, 1.76-2.26), HL (OR, 2.21; 95% CI, 1.83-2.68), and CTCL (OR, 4.31; 95% CI, 3.09-6.01).

Subgroup lymphoma prevalences are shown in Table 2. Males with HS had higher prevalences of NHL, HL and CTCL; crude prevalences in males with HS compared with females with HS were 0.62% vs 0.32% for NHL, 0.28% vs 0.13% for HL, and 0.09 vs 0.04% for CTCL. Significant effect modification was observed in the association between HS and HL across sex subgroups. For example, the ORs for the association between HS and HL were higher in males (OR, 2.97; 95% CI, 2.22-3.99) than in females (OR, 1.86; 95% CI, 1.44-2.39) (P = .02). Patients with HS aged 65 years or older had higher prevalences of NHL and CTCL than those aged 45-64 or 18-44 years. Prevalence of NHL was 1.2%, 0.52%, and 0.20% for patients with HS aged 65 years or older, 45-64 years, and 18-44 years, respectively. Prevalence of CTCL was 0.17%, 0.07%, and 0.03% for patients with HS aged 65 years or older, 45-64 years, and 18-44 years, respectively. Age was a significant effect modifier in the association between HS and NHL. Patients with HS aged 18-44 years had 3.64 (95% CI, 2.87-4.60) times the odds of NHL compared with patients without HS in the same age-group. Patients with HS aged 45-64 years (OR, 1.38; 95% CI 1.09-1.74) and greater than or equal to 65 years (OR, 1.99; 95% CI, 1.65-2.41) also had increased odds of NHL compared with patients without HS of the same age-group (P < .001 for the interaction of HS with age).

Table 1. Demographic Characteristics

Variable	No. (%)	
	Patients With HS (N = 62 690)	Patients Without HS (N = 28 937 880)
Sex		
Male	16 030 (25.6)	12 557 910 (43.4)
Female	46 660 (74.4)	16 379 970 (56.6)
Age, y		
18-44	35 800 (57.1)	11 767 990 (40.7)
45-64	21 070 (33.6)	9 398 000 (32.5)
≥65	5820 (9.3)	7 771 890 (26.9)

Abbreviation: HS, hidradenitis suppurativa.

Table 2. Prevalence of Lymphomas

Variable	Type of Lymphoma, No./Total No. (%)					
	Non-Hodgkin Lymphoma		Hodgkin Lymphoma		Cutaneous T-Cell Lymphoma	
	HS (N = 62 690)	Non-HS (N = 28 937 880)	HS (N = 62 690)	Non-HS (N = 28 937 880)	HS (N = 62 690)	Non-HS (N = 28 937 880)
Overall	250/62 690 (0.40)	102 570/28 937 880 (0.35)	105/62 690 (0.17)	25 335/28 937 880 (0.09)	35/62 690 (0.06)	5920/28 937 880 (0.02)
Sex						
Male	100/16 030 (0.62)	54 080/12 557 910 (0.43)	45/16 030 (0.28)	12 575/12 557 910 (0.10)	15/16 030 (0.09)	3200/12 557 910 (0.03)
Female	150/46 660 (0.32)	48 490/16 379 970 (0.30)	60/46 660 (0.13)	12 760/16 379 970 (0.08)	20/46 660 (0.04)	2720/16 379 970 (0.02)
Age, y						
18-44	70/35 800 (0.20)	6850/11 767/990 (0.06)	50/35 800 (0.14)	7000/11 767 990 (0.06)	10/35 800 (0.03)	700/11 767 990 (0.01)
45-64	110/21 070 (0.52)	26 090/9 398 000 (0.28)	40/21 070 (0.19)	9750/9 398 000 (0.10)	15/21 070 (0.07)	1740/9 398 000 (0.02)
≥65	70/5820 (1.2)	69 630/7 771 890 (0.90)	10/5820 (0.17)	8480/7 771 890 (0.11)	10/5820 (0.17)	3480/7 771 890 (0.04)

Abbreviation: HS, hidradenitis suppurativa.

Discussion | Patients with HS have malignant lymphomas more frequently than the general population. Rates of NHL, HL, and CTCL in the general population are low. However, patients with HS appear to have 2 to 4 times the overall risk of developing lymphomas.

Overall and subgroup associations between HS and lymphoma subtypes have not been evaluated previously in a population. A single-center retrospective series identified 1776 patients with HS in whom frequency of unspecified lymphoma was 1.8%.[5] In a Swedish retrospective analysis including 2119 patients hospitalized for HS, 6 cases of any hematopoietic cancer, which may include lymphomas, were identified.[6] Neither study observed greater risk of malignant lymphoproliferative disease among patients with HS.

A limitation of our study was that we could not assess the disease duration or severity in this claims analysis. The uncommonness of the event did not permit us to evaluate systemic treatment or other exposures and the association between HS and lymphoma. To our knowledge, this is the first investigation to systematically evaluate this association in a US population of patients with HS. Size and diversity of our cohort may overcome selection biases and limitations inherent to smaller cohorts recruited with specialty centers.

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Concept and design: Strunk, Garg.
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Supervision: Garg.

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1. Explorys IBM. https://www.ibm.com/watson/health/explorys/. Accessed August 8, 2018.

2. Strunk A, Midura M, Papagermanos V, Alloo A, Garg A. Validation of a Case-Finding Algorithm for Hidradenitis Suppurativa Using Administrative Coding from a Clinical Database. *Dermatology*. 2017;233(1):53-57. doi:10.1159/000468148

3. Kamstrup MR, Skov L, Zachariae C, Thyssen JP, Egeberg A. Psoriasis and risk of malignant lymphoma: a population-based cohort study. *Br J Dermatol*. 2018;178(6):1435-1436. doi:10.1111/bjd.16245

4. Lemaitre M, Kirchgesner J, Rudnichi A, et al. Association between use of thiopurines or tumor necrosis factor antagonists alone or in combination and risk of lymphoma in patients with inflammatory bowel disease. *JAMA*. 2017;318(17):1679-1686. doi:10.1001/jama.2017.16071

5. Shlyankevich J, Chen AJ, Kim GE, Kimball AB. Hidradenitis suppurativa is a systemic disease with substantial comorbidity burden: a chart-verified case-control analysis. *J Am Acad Dermatol*. 2014;71(6):1144-1150. doi:10.1016/j.jaad.2014.09.012

6. Lapins J, Ye W, Nyrén O, Emtestam L. Incidence of cancer among patients with hidradenitis suppurativa. *Arch Dermatol*. 2001;137(6):730-734.

Multiple Cutaneous Squamous Cell Carcinoma in Immunosuppressed vs Immunocompetent Patients

Squamous cell carcinoma (SCC) is the second most common skin cancer in the United States and is an important cause of morbidity in immunosuppressed patients.[1] Studies demonstrate an increased risk of developing a subsequent SCC after the first incidence.[1-3] Levine et al[4] linked multiple SCCs to increased poor outcomes; however, their study cohort consisted of primarily immunocompetent patients. Immunosuppressed patients are believed to have a 65- to 100-fold increase in the incidence of SCC.[4] In this study, we aimed to determine the association between multiple SCCs and the risk of poor outcomes in the immunosuppressed population.

Methods | This is a case-control study of primary invasive SCCs treated at a tertiary academic center from January 1, 2005, and December 31, 2015. The study was approved by the Tufts University Health Sciences Campus institutional review board and a waiver of written informed consent was granted owing to the minimal risk involved in the study. Overall, 106 mixed-cause immunosuppressed patients with 412 primary invasive SCCs were matched by age, sex, and race to immunocompetent controls on a 1:2 basis. Demographics, tumor characteristics, and outcome data including local recurrence, nodal metastases (NM), in-transit metastases (ITM), distant metastases (DM), any disease-specific poor outcome, and disease-specific death were recorded. Each cohort was categorized based on number of SCCs (1, 2-9, ≥10). Outcomes were compared using χ^2 and Fisher exact statistics. Logistic regressions were used to estimate the effects of immunosuppression on poor outcomes, stratified by number of SCCs (1 or 2-9) and adjusted for tumor stage according to Brigham and Women's Hospital (BWH) and American Joint Committee on Cancer (8th edition) (AJCC-8) criteria (limited to head and neck tumors) with each stage as a covariate.

Results | The most common causes of immunosuppression were organ transplantation (58%; 61 of 106) and inflammatory disease (16%; 17 of 106). A significantly higher proportion of immunosuppressed patients had multiple tumors: 57% (60 of 106) vs 25% (53 of 212) (odds ratio [OR], 3.91; 95% CI, 2.39-6.41; $P < .001$) for immunocompetent patients. No immunocompetent patient had 10 or more SCCs.

Patients were stratified based on number of tumors. In the immunosuppressed cohort, those with 2 to 9 and 10 or more