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The impact of underlying disease state on outcomes in patients with pyoderma gangrenosum: A national survey

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Abstract

Background—It is unclear if the underlying disease affects the outcomes in pyoderma gangrenosum.

Objectives—To determine the impact of comorbid disease associations and concomitant procedural treatments on patient outcomes in PG patient-hospitalizations.

Methods—A cross-sectional analysis of the Nationwide Inpatient Sample (NIS) for PG patient-hospitalizations from years 2002–2011, analyzing in-hospital mortality rate and health care resource utilization.

Results—Inflammatory bowel disease was the most frequent comorbid association, followed by inflammatory arthritis, hematologic malignancies/dyscrasias, and vasculitis. Multivariable modeling showed that vasculitis and hematologic malignancy/dyscrasia, when compared to subjects with IBD, were associated with a 4–6 fold increased risk of in-hospital mortality while increasing healthcare resource utilization. Inpatient procedural interventions including skin grafts, biopsies, and debridement did not impact mortality and were associated with an increased length of stay.

Limitations—The database does not account for outpatient follow-up, additionally there was a low rate of coded comorbid conditions.

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Conclusions—Comprehensive evaluation to determine the underlying comorbidity for patients with PG is important for patient risk stratification.

Introduction

Pyoderma gangrenosum (PG) has multiple underlying disease associations including inflammatory bowel disease, rheumatoid arthritis, monoclonal gammopathy, vasculitis, streptococcal infections, multiple myeloma, and acute myelogenous leukemia.[1–8] It is unclear if the underlying comorbidities impact the prognosis or treatment course. Therefore, the primary objective is to evaluate if survival in PG is influenced by comorbidity.

While long thought that debridement and grafting are strictly contraindicated,[3,9] there is some evidence to support skin grafting and gentle debridement once the inflammation is quiescent.[1,10] Secondary objectives include the determination of whether skin biopsies and procedural techniques such as debridement or grafting, are associated with improvements in mortality, hospital length of stay, and hospital costs.

Methods

Patient Database

The study utilized de-identified data and was exempt from the Institutional Review Board of The Ohio State University Wexner Medical Center. Variables of interest were queried from the Nationwide Inpatient Sample (NIS) from 2002–2011. The NIS is maintained as part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality.[11] This is the largest all-payer inpatient care database in the United States and approximates a 20% stratified sample of nonfederal, acute-care hospitals encompassing over 8 million discharges per year. Each discharge entry includes demographic features on the patient, hospital characteristics, primary and secondary diagnoses, in-hospital mortality, hospital cost, and length of stay.

Study Population

The study population consisted of all adult discharges, >17 years of age, hospitalized with pyoderma gangrenosum. This diagnosis was selected using the International Classification of Diseases, Ninth revision, Clinical Modifications codes (ICD-9CM) of 686.01 as a primary or secondary diagnosis during the hospitalization. Comorbidities of interest were defined as inflammatory bowel disease (IBD), inflammatory arthritis (IA), small vessel vasculitis, and leukemia and gammopathies (classified as hematologic dyscrasia). We chose to include small vessel vasculitis as an associated condition for pyoderma gangrenosum based on case reports and experience, particularly given that IgA paraproteinemias may link both morphologies and that lymphocytic vasculitis can be a diagnostic criterion. They underwent an algorithm in that order for attribution to PG (Supplemental Table 1). Patients with pregnancy related codes, and concomitant codes related to a potential misdiagnosis including, medium vessel vasculitis, deep fungal infections, cutaneous T and peripheral T-cell lymphomas, leukemia cutis, Langerhans cell histiocytosis, anti-phospholipid antibody syndrome, and livedoid vasculopathy and related codes were excluded. Procedures were included in this analysis if they were listed on the patient discharge and were based on

appropriate ICD-9-CM codes including skin biopsy, debridement, skin graft, and ostomy management (Supplemental Table 1). Typical demographic patient variables were included and comorbidity was assessed using the Elixhauser score, a validated instrument for assessing inpatient data for patient outcomes from a set of 30 comorbid conditions.[12] The comorbidity score was dichotomized as <3 vs ≥3 comorbidities. Hospital procedure volume was categorized as high for those at or above the 75th percentile for skin biopsies, low for those between 1–74%, and none for those that billed for 0 skin biopsies during the years analyzed.

Statistical Analysis

SAS 9.4 (SAS Institute, Cary, NC) was used to perform all analyses, employing appropriate survey estimation commands and strata weights. Sample data for continuous variables were stated as means with standard deviations (SDs). Categorical variables were tested for statistical significance with χ^2 tests, whereas differences in continuous variables were analyzed with *t*-tests. Statistical significance was defined by $P<0.05$. Linear regression was used to evaluate the effect of underlying comorbidities and procedures on LOS and hospital cost and logistic regression was used to calculate odds ratios (OR) and corresponding 95% confidence intervals (CI) for inhospital mortality. Multivariable regression models were developed using stepwise methodology where all variables in supplemental table 2 with the exception of the individual Elixhauser comorbidities were eligible for inclusion and adjusted for variables significantly associated with mortality, length of stay, and cost in the models.

Results

Demographics

After excluding similar ulcerative conditions, 31 885 hospitalizations for patients with a diagnosis of pyoderma gangrenosum were identified during years 2002–2011. The patients were predominately female, with a mean age of 55 ± 0.31 years. The groups spanned the spectrum of race, insurance type, and hospital region (Supplemental Table 2). Most patients had 2 or fewer Elixhauser comorbidities. The most common underlying disease was IBD with over 26% of patient hospitalizations followed by patients with inflammatory arthritis, hematologic malignancy and dyscrasias, and small vessel vasculitis, while 61% of patient-hospitalizations did not have a coded well-described comorbidity. The incidence of streptococcal infections and intestinal blind loop syndromes were < 1%. Multiple complications were associated with hospitalizations for PG: a chronic wound in 28%, cellulitis in 27%, sepsis and systemic inflammatory response syndrome (SIRS) in 7% and 5% respectively. Stoma complications were noted in 6%. The vast majority of hospitalizations did not have cutaneous procedures documented, however, 12% underwent a skin biopsy, 11% had debridement, and 3% had a skin graft. There was a disproportionate amount of PG diagnosed in the top quartile of hospitals for skin biopsies with nearly 60% of the diagnoses. Lastly, 731 patients expired in this cohort comprising 2% of the population. The hospitalization outcomes for the entire cohort include a mean hospitalization of 8.15 ± 0.14 days and mean cost of $13 159 ± 300.

Multivariable Logistic Regression Modeling for Mortality

The diagnosis of small vessel vasculitis, OR 6.0, 95% CI [2.63–13.69] and hematologic dyscrasias, OR 4.31, 95% CI [1.78–10.43] and all others, OR 2.23, 95% CI [1.21–4.11] in comparison to IBD were associated with increased risk of hospitalized patient mortality, while inflammatory arthritis was not. In addition, sepsis OR 12.43, 95% CI [8.65–17.86] and increasing age OR 1.04, 95% CI [1.03–1.05] were associated with patient mortality. In comparison, cellulitis was inversely associated with mortality risk OR 0.58, 95% CI [0.39–0.86] (Table 1).

Multivariable Linear Regression Modeling for Length of Stay

Patients with high Elixhauser comorbidity scores were associated with longer hospitalizations by 2.14 days, 95% CI [1.51–2.78], as were sepsis by 8.89 days, 95% CI [6.88–10.91], stoma complications by 2.67 days, 95% CI [0.74–4.61], chronic wound codes by 1.76 days, (1.11–2.40), and the diagnosis of an underlying small vessel vasculitis by 2.17 days [0.12–4.23] or hematologic dyscrasia by 2.22 days [0.14–4.29] as compared to IBD. When looking at procedures, all were associated increased length of hospitalization, patients that received skin biopsies by 2.87 days [1.82–3.91], debridement by 5.32 days [3.96–6.68], or skin grafts by 7.93 days [4.14–11.72] (Table 2).

Multivariable Linear Regression Modeling for Hospital Cost

Hospitalizations with higher Elixhauser comorbidity scores were associated with increased hospitalization costs of $4 321 [2 948– 5 694], while the comorbidities vasculitis $5 981 [67 – 11896], hematologic dyscrasia $7 715 [1 775 – 13 655] also increased the costs respectively compared to the IBD reference patients. Hospitalizations involving debridement, skin biopsy, and skin grafting were consistently more expensive. In addition, hospitalization costs were increased with sepsis $22 448 [17 659 – 27 237], post-surgical complications $11 463 [2 319 – 20 608] and patients at centers that were categorized as high skin biopsy volume $1 874 [293 – 3 454]. (Table 3).

Discussion

Previous studies have demonstrated the high mortality rate in patients with PG, over 15% in an 8 year longitudinal study.[1] The present study demonstrates an in-hospital mortality risk of around 2% with significant variation based on comorbidities. It confirms that there is important prognostic value that is lost in the event that a patient is not thoroughly evaluated for a monoclonal gammopathy, myeloma, or leukemia. Interestingly, cellulitis was associated with a decreased mortality risk, but similar associations are reported in psoriasis hospitalizations.[14] This may indicate that there is a high rate of misdiagnosis or an overstated systemic risk from the coded diagnosis of cellulitis.

From the procedure analyses, skin biopsies were performed in a minority of patient-hospitalizations, however, many patients may have already carried the diagnosis of PG. In the hospital setting, the skin biopsy was associated with longer hospitalization and higher costs. This may be a surrogate for an initial or more thorough evaluation. Previous studies have also demonstrated the association of skin biopsies with longer hospitalizations.[15]

Similar to skin biopsies, skin grafts and debridement were actually associated with increased lengths of stay and costs without benefits in mortality.

Multiple limitations exist in this current study, 60% of patients did not have a classically associated diagnosis by coding. This could represent coding error, unevaluated comorbidities, or even misdiagnosis. The validation of this disease using cross-sectional data is challenging, but coding data by general physicians in England has demonstrated a 50–75% positive predictive value in the coded diagnosis of PG, and we suspect our outcomes may be higher with the benefit of more specialists.[7] Further, 68% of patient hospitalizations for PG were within hospitals that were in the top quartile for skin biopsies volume, indicating that most probably had access to dermatologists to make this specialized diagnosis. From the procedural aspect, its value may be understated without being able to follow patients longitudinally. Lastly, we hoped to study rare associations such as pneumonitis and PG, but such complications were so rarely coded, that we could not reliably quantify outcomes in this setting.

In conclusion, mortality risk varied substantially among patients with small vessel vasculitis and hematologic malignancy/dyscrasia in comparison with patients with IBD and inflammatory arthritis. This emphasizes the need for comprehensive diagnostic evaluation. Procedural treatments did not show a benefit in this setting but ought to be studied further using longitudinal databases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of Abbreviations

AHRQ	Agency for Healthcare Research and Quality
AIDS	Aquired immunodeficiency syndrome
IA	Inflammatory Arthritis
IBD	Inflammatory Bowel Disease
NIS	Nationwide Inpatient Survey
PG	pyoderma gangrenosum
SIRS	Systemic Inflammatory Response Syndrome

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What is known

Pyoderma gangrenosum has many underlying disease associations.

What this adds

Pyoderma gangrenosum patients who have underlying hematologic cancers, dyscrasias, and vasculitis, have worse hospital outcomes compared to patients with inflammatory bowel disease or inflammatory arthritis.

Impact on care

There is a need for comprehensive evaluation for risk stratification in patients with pyoderma gangrenosum.

Table 1

Multivariable logistic regression model for in-hospital mortality in patient hospitalizations for PG. Abbreviations: IBD – Inflammatory Bowel Disease

	OR	95% CI	p-value
Age	1.04	(1.03, 1.05)	<0.001
Comorbidities			<0.001
IBD	Reference		
Inflammatory Arthritis	0.89	(0.31, 2.57)	
Vasculitis and Henoch Schonlein Purpura	6.00	(2.63, 13.69)	
Hematologic malignancy and Dyscrasia	4.31	(1.78, 10.43)	
Others	2.23	(1.21, 4.11)	
Sepsis	12.43	(8.65, 17.86)	<0.001
Cellulitis	0.58	(0.39, 0.86)	0.007

Table 2

Multivariable linear regression model for length of stay in patient hospitalizations for PG. Abbreviations: IBD – Inflammatory Bowel Disease

	Days	95% CI	p-value
Elixhauser comorbidity score			<0.001
<3	Reference		
≥3	2.14	(1.51, 2.78)	
Comorbidities			0.014
IBD	Reference		
Inflammatory Arthritis	−0.52	(−1.42, 0.38)	
Vasculitis and Henoch Schonlein Purpura	2.17	(0.12, 4.23)	
Hematologic malignancy and Dyscrasia	2.22	(0.14, 4.29)	
Others	−0.02	(−0.64, 0.60)	
Sepsis	8.89	(6.88, 10.91)	<0.001
Stoma complications	2.67	(0.74, 4.61)	0.007
Chronic Wound	1.76	(1.11, 2.40)	<0.001
Skin graft	7.93	(4.14, 11.72)	<0.001
Skin biopsy	2.87	(1.82, 3.91)	<0.001
Debridement	5.32	(3.96, 6.68)	<0.001

Table 3

Multivariable linear regression model for cost in patient hospitalizations for PG

	$	95% CI	p-value
Hospital region			<0.001
Northeast	Reference		
Midwest	−3,373	(−5,281, −1,465)	
South	−3,870	(−5,705, −2,035)	
West	1,482	(−1,151, 4,114)	
Elixhauser comorbidity score			<0.001
<3	Reference		
≥3	4,321 (2,948, 5,694)		
Comorbidities			0.037
IBD	Reference		
Inflammatory Arthritis	365	(−1,633, 2,364)	
Vasculitis and Henoch Schonlein Purpura	5,981	(67, 11,896)	
Hematologic malignancy and Dyscrasia	7,715	(1,775, 13,655)	
Others	61	(−1,258, 1,381)	
Sepsis	22,448	(17,659, 27,237)	<0.001
Stoma complications	6,717	(2,532, 10,903)	0.002
Post Surgical Complication	11,463	(2,319, 20,608)	0.014
Skin graft	7,836	(2,549, 13,124)	0.004
Skin biopsy	3,952	(2,062, 5,842)	<0.001
Debridement	8,513	(6,174, 10,852)	<0.001
Biopsy procedure volume			0.027
None	Reference		
Low (1–10 per year)	704	(−941, 2,348)	
High (>10 per year)	1,874	(293, 3,454)	