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Psoriasis and wound healing outcomes: A retrospective cohort study examining wound complications and antibiotic use

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Abstract

Little is known about wound healing in psoriasis. We performed a cohort study examining differences in wound healing complications between patients with and without psoriasis. Psoriasis patients with traumatic wounds were matched 1:3 to non-psoriasis patients with traumatic wounds based on age, gender, and body mass index (BMI). We examined the incidence of wound complications including infection, necrosis, and hematoma as well as incident antibiotic use within three months following diagnosis of a traumatic wound. The study included 164 patients with traumatic wounds, comprised of 41 patients with psoriasis matched to 123 patients without psoriasis. No statistically significant differences were detected in the incidence of overall wound complications between wound patients with psoriasis and wound patients without psoriasis (14.6% versus. 13.0%, HR 1.18, CI 0.39-3.56). After adjustment for diabetes, peripheral vascular disease, and smoking, no statistically significant differences were detected in the incidence of overall wound complications between patients with and without psoriasis (HR 1.11, CI 0.34-3.58). Specifically, the adjusted rates of antibiotic use were not significantly different between those with and without psoriasis (HR 0.65, CI 0.29-1.46). The incidence of wound complications following traumatic wounds of the skin was found to be similar between patients with and without psoriasis.

Keywords: psoriasis; wound healing

Introduction

Psoriasis is a chronic, immune-mediated disease affecting approximately 3% of the US population [1, 2]. It is associated with various comorbid conditions such as cardiovascular, rheumatologic, and psychiatric diseases [3]. However, little is known regarding psoriasis patients and their wound healing abilities.

A critical gap exists in our understanding of the healing of traumatic wounds among psoriasis patients. Translational evidence suggests that there is upregulation of antimicrobial peptides (AMPs) including human beta-defensin 2 (HBD-2), and cathelicidin peptide LL-37 in psoriasis [4-6]. Specifically, LL-37 and HBD-2 accumulate in keratinocytes within epidermis affected by psoriasis [4, 6], and expression of both peptides is associated with a synergistic effect in enhancing microbial elimination. In contrast, there is no induction of AMPs in normal skin, and there is a decrease in AMPs in lesional skin of patients with atopic dermatitis [6].

One clinical observation that suggests cutaneous response to trauma may be different among psoriasis patients is the phenomenon of Koebnerization. The Koebner phenomenon refers to the extension of psoriasis along areas of trauma in previously uninvolved skin [7]. Along with concern regarding the Koebner phenomenon, many surgeons have deferred performing surgery on patients with active psoriatic lesions owing to the presumed risk of poor wound healing. In contrast to non-dermatologic surgeons, most dermatologists are amenable to performing surgery through psoriatic plaques and

perceive post-operative infection rates to be similar to those of surgery in uninvolved skin [8]. The literature is conflicting regarding wound healing outcomes in surgical wounds [9-13]. What is even less known is how traumatic wounds heal in psoriasis patients. This is relevant because traumatic wounds are relatively common, and their healing outcomes in lesional or non-lesional skin among psoriasis patients are unknown.

In order to optimally manage patients with psoriasis, we need to understand outcomes for traumatic wounds in psoriasis patients before developing an evidence-based approach for their management. To investigate real-world wound-healing outcomes among patients with psoriasis, we conducted a retrospective cohort study comparing incidence of wound complications, as assessed by antibiotic use and infection rates, between patients with and without psoriasis.

Methods

Study design and population

This was a retrospective cohort study using data from 164 adult patients who were seen in the University of California Davis Healthcare System between August 2001 and January 2011. A total of 41 adult psoriasis patients with wounds were matched in a 1:3 ratio to 123 adult non-psoriasis patients with wounds. The matching factors were age, gender, and body mass index (BMI). Approval for this study was obtained through the Institutional Review Board of the University of California (UC), Davis Health System.

The diagnosis of psoriasis was ascertained initially through the International Classification of Diseases, Ninth Edition (ICD-9) and then validated via manual chart review of diagnosis given by the dermatology-provider. The diagnosis of traumatic wound was ascertained initially through ICD-9 code and then further screened and validated via manual chart review of inpatient and outpatient notes. Index date was defined as the date of diagnosis of the traumatic wound and all inpatient and outpatient records were manually reviewed for the ensuing three months.

Determination of Outcomes

The primary analysis focused on the development of wound complications as outcomes. Wound complications included any one or more of the following: localized infection, wound-related systemic infection, hematoma, necrosis, malodor, or excessive exudate. Secondary analysis examined the use of wound-related antibiotics following the diagnosis of an open wound during the ensuing three months.

Statistical Analysis

Baseline characteristics between patients with and without psoriasis were compared with the chi-square test or the Fisher exact test. The association between psoriasis and wound healing outcomes was summarized by calculating the hazards ratio (HR) and corresponding 95% confidence interval (CI) and adjusting for relevant confounders. Adjusted models were applied to both primary and secondary analyses and controlled for diabetes mellitus, peripheral vascular disease, and tobacco use. All calculated p-values were two-sided and considered statistically significant if $p<0.05$.

Results

A total of 164 adult patients, 41 psoriasis and 123 non-psoriasis, were matched on age, gender, and body mass index (BMI). Additional baseline characteristics showed that there were no significant differences in tobacco use (active: 14.6% versus 19.5%, former: 19.5% versus 19.5%, or never: 65.6% versus 61%, p=0.8152), peripheral vascular disease (2.4% in both groups), or diabetes mellitus (4.9% versus 6.5%, p=0.7648), (**Table 1**).

Univariate analysis revealed no statistically significant difference in the incidence of overall wound complications (which included localized infection, wound-related systemic infection, hematoma, necrosis, malodor, or excessive exudate) between patients with psoriasis and non-psoriasis controls (14.6% versus 13.0%, HR 1.18, CI 0.39-3.56, p=0.77). Adjusted analysis controlling for diabetes, peripheral vascular disease, and smoking showed no statistically significant difference in overall wound complication rates between psoriasis and non-psoriasis patients (HR 1.11, CI 0.34-3.58, p=0.87). Specifically, we examined incident use of antibiotics following diagnosis of a traumatic wound. In univariate analysis, we found that 35% of patients with psoriasis used antibiotics

Table 1. *Demographics and Patient Outcomes.*

	Psoriasis (n=41)	No Psoriasis (n=123)	P-Value
Age, years			1.0000
Mean (SD)	44 (2.6)	44 (1.5)	
BMI			0.9724
Mean (SD)	25.8 (4)	25.8 (4)	
Race			0.0406
Caucasian	16 (39.0%)	40 (32.5%)	
African American	0 (0%)	7 (5.7%)	
Asian	4 (9.8%)	2 (1.6%)	
Not specified	21 (51.2%)	74 (60.2%)	
Healing Complications			0.7942
Any Complications (One or more)	6 (14.6%)	16 (13.0%)	
No Complications	35 (85.4%)	107 (87.0%)	
Antibiotic Use			0.4601
Any Antibiotic (Topical, Oral, or IV)	14 (35.0%)	51 (42.5%)	
No Antibiotic Use	27 (65.0%)	72 (57.5%)	
Diabetes Mellitus			0.7648
Yes	2 (4.9%)	8 (6.5%)	
No	39 (95.1%)	115 (93.5%)	
Peripheral Vascular Disease			1.0000
Yes	1 (2.4%)	3 (2.4%)	
No	40 (97.6%)	120 (97.6%)	
Tobacco Use			0.8152
Active	6 (14.6%)	24 (19.5%)	
Former	8 (19.5%)	24 (19.5%)	
Never	27 (65.9%)	75 (61.0%)	

Table 2. *Univariate and Multivariate Results.*

	Hazard Ratio	95% CI	P-Value
Univariate Analysis			
Healing Complications	1.18	0.39-3.56	0.7731
Antibiotic Use	0.71	0.33-1.54	0.3858
Multivariate Analysis (controlled for DM, PVD, and smoking*)			
Healing Complications	1.11	0.34-3.58	0.8679
Antibiotic Use	0.65	0.29-1.46	0.2968

**DM = diabetes mellitus, PVD = peripheral vascular disease*

versus 42.5% of patients without psoriasis (HR 0.71, CI 0.33-1.54, p=0.39). In the adjusted analysis, there were no statistically significant differences in antibiotic use between psoriasis and non-psoriasis patients (HR 0.65, CI 0.29-1.46, p=0.3), (**Table 2**).

Discussion

Literature examining wound healing in psoriasis patients is scarce. For example, the few studies examining complications in surgical wounds have shown conflicting results [9-16]. Specifically, two retrospective chart review studies looking at outcomes of total knee arthroplasties reported delayed wound healing and significantly increased rates of post-surgical infection among patients with psoriasis [9, 10], although several other chart reviews found post-surgical healing and infection rates similar to that of the general population [11-13]. These conflicting results make it difficult for dermatologists to provide evidence-based advice to patients with psoriasis regarding expected wound healing outcomes. This study examined non-surgical wound complications not previously examined in the literature to further elucidate the relationship between wound healing and psoriasis. These results contribute to our understanding of how traumatic wounds occurring in the non-sterile environment heal among psoriasis patients.

Although the epidermal barrier is altered in psoriasis patients, the present study did not find a statistically significant difference in the incidence of wound complications between patients with and without psoriasis. This is possibly related to biochemical similarities between psoriatic plaques and normal skin undergoing healing. After injury to the skin, growth factors have been shown to induce the expression of antimicrobial peptides in human keratinocytes. The growth factors IGF-1 and TGF-alpha are elevated in both psoriatic plaques and cutaneous wounds [17]. Likewise, antimicrobial peptides such as hCAP-18 and SLPI are also detectable in both sites. Furthermore, the increased rate of keratinization and the metaplasia phenomenon observed in psoriasis may promote wound closure [18]. Psoriasis, with its sustained inflammatory response and excessive proliferation of keratinocytes, bears semblance to an exaggerated wound healing process.

Although not statistically significant, the rates of antibiotic use were numerically lower in psoriasis patients as compared to non-psoriasis patients (**Table 1**). Several studies have found AMPs such as LL-37 and HBD-2 to be elevated in psoriatic lesions [4-6, 19, 20]. LL-37, a cathelicidin, promotes chemotaxis and angiogenesis, enhances wound repair following injury, and has both pro-inflammatory and anti-inflammatory actions [20]. HBD-2, a beta-defensin, displays cytokine-like behavior in addition to antimicrobial activity [19]. The roles of AMPs are complex, but overall these peptides may be helpful in reducing infection rates.

Although traumatic wounds are common, their documentation in the medical history as a main reason for a visit is relatively uncommon. Thus, one limitation of the study is the limited sample size, which may affect detection of smaller differences in wound healing outcomes between psoriasis and non-psoriasis patients. The relatively small sample size also contributes to the inability to capture subsets of participants with psoriasis-specific wound

complications such as Koebnerization. Other factors include the retrospective nature of the study, which limits data collection to ICD coding and chart review, as well as the paucity of Koebner phenomenon documentation during wound care follow-up visits.

Our understanding of wound healing among psoriasis patients is limited, especially in the setting of traumatic wounds. This study found no significant differences in healing of traumatic wounds among patients with psoriasis, which corroborates translational findings that antimicrobial properties may even be increased in psoriasis patients. Additionally, findings from this study complement the small existing body of literature on surgical wounds in psoriasis patients. Based on the results of this study, future research can explore wound healing outcomes in larger populations to detect whether small differences in wound healing exist between psoriasis versus non-psoriasis patients. These larger studies may be able to examine the incidence of Koebnerization as a wound complication in psoriasis patients with cutaneous wounds. Alternatively, future research can also explore whether differences exist in wound healing between lesional and non-lesional skin within the same psoriasis patient.

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Appendix

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[page 1]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[page 1]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[pages 1 & 2]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 2]**
Methods		
Study design	4	Present key elements of study design early in the paper **[page 3]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 3]**
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **[page 3]** *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls **[ ]** *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants **[ ]**
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed **[page 3]** *Case-control study*—For matched studies, give matching criteria and the number of controls per case **[ ]**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[pages 3 & 4]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[page 3]**
Bias	9	Describe any efforts to address potential sources of bias **[pages 3 & 4]**
Study size	10	Explain how the study size was arrived at **[page 3]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[N/A]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[pages 3 & 4]**
		(*b*) Describe any methods used to examine subgroups and interactions **[N/A]**
		(*c*) Explain how missing data were addressed **[N/A]**
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed **[N/A]** *Case-control study*—If applicable, explain how matching of cases and controls was addressed **[ ]** *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy **[ ]**
		(*e*) Describe any sensitivity analyses **[N/A]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[page 4; table 1]**
		(b) Give reasons for non-participation at each stage **[N/A]**
		(c) Consider use of a flow diagram **[N/A]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[page 4; table 1]**
		(b) Indicate number of participants with missing data for each variable of interest **[table 1]**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) **[page 3]**
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time **[page 4; table 1]**
		Case-control study—Report numbers in each exposure category, or summary measures of exposure **[ ]**
		Cross-sectional study—Report numbers of outcome events or summary measures **[ ]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **[page 4; table 2]**
		(*b*) Report category boundaries when continuous variables were categorized **[N/A]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[N/A]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[pages 4 & 5]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[page 5 & 6]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[pages 5 & 6]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[pages 5 & 6]**
Other information		
Funding	22	**Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [N/A]**

Continued on next page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.