Received: 5 August 2022 | Accepted: 5 September 2022

DOI: 10.1111/ddg.14926

ORIGINAL ARTICLE

Can hidradenitis suppurativa patients classify their lesions by means of a digital lesion identification scheme?

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Summary

Background and objectives: Hidradenitis suppurativa (HS) differs widely with respect to its clinical presentation. Literature imposes different phenotypes potentially implying different treatment modalities. The aim of this study is to develop a validated scheme that enables HS patients to identify their own lesion types.

Patients and Methods: The developed schemes for physicians and patients were implemented in a specific software. Upon patient consent, the physician used the software to document the lesions identified. Patients subsequently logged into the patient-version of the software from the convenience of their home and selected the lesions they identified on themselves. Afterwards the correlation between professionals and patients was tested.

Results: For seven lesion types, correlation coefficients were statistically significant. A large/strong correlation between patients and physicians was found for the draining fistulas (0.59) and double-ended comedones (0.50). For five other lesion types, correlation was medium/moderate, namely the inflammatory nodule (0.37), abscess (0.30), accordion like-/ bridged scar (0.45), epidermal cyst (0.33) and pilonidal sinus (0.39).

Conclusions: HS-patients demonstrate high willingness to share their experiences and data. Therefore, a self-assessment scheme, as the developed LISAI, can be a valuable tool to enrich patient surveys with the identification of lesion types, for instance as a basis for phenotyping.

INTRODUCTION

Hidradenitis suppurativa (HS)/Acne inversa (Ai) is a debilitating and chronic skin disease characterized by recurrent episodes of inflammation associated with the appearance of abscesses, inflammatory nodules, pain, and drainage often ending in the formation of draining fistulas and scarring.[1] Disease onset is typically after puberty and body regions commonly affected are the axillae, breasts, groin, buttocks, and lower abdomen.[2–4]

There is no pathognomonic sign for HS that leads to an unequivocal diagnosis. Consequently, the diagnosis is based on the clinical presentation of the disease. Several validated tools assist to confirm the diagnosis and determine its severity.

However, the spectrum of disease symptoms is broad.[5,6] Most classification systems are single-lesion based systems including mainly inflammatory lesions such as inflammatory nodules, abscesses, and draining fistulas, also mentioned in the Dessau criteria, to evaluate the findings.[7,8] In 2013, Canoui-Poitrine et al. identified HS subgroups through a latent class analysis with *a priori* hypotheses in a cohort of 618 patients.[9] They designated three phenotypes, which had specific additional lesions and location specifications.[10] In 2015, van der Zee et al. revisited the issue and identified the following subtypes:

regular, frictional furunculoid, scarring folliculitis, conglobata, ectopic, and syndromic.[6] In 2022, the same group suggested that the ectopic and syndromic types do not have specific clinical features and could be categorized as one of the other phenotypes.[11]

Clinical experience suggests variability in clinical presentation and a potential phenotype-dependent response to therapies. An identification of subpopulations could, thus, improve the overall therapeutic picture and can create potential for more personalized, tailored delivery of therapy in the HS setting.[6] Kirby recently stated that multiple phenotypes have been constructed, but that all have considerable overlap especially with respect to used lesion types. Additionally, longitudinal data are needed to evaluate the predictive validity for meaningful outcomes, such as reduction in disease severity, risk of disease progression, time to flare, or flare frequency.[12,13] However, evaluating, documenting, and digitalizing lesions as a basis for phenotyping is too time consuming for professionals in the daily medical setting. In contrast, the VOICE project, a survey including 1,299 participants in 14 countries, shows that HS patients are willing to share their experiences and data on past treatments and other characteristics.[14] For future linkage of such information to phenotypes, this study aimed to develop a set of descriptive definitions and corresponding images of HS lesions that could serve as a digital tool enabling patients to identify their own lesion types.

PATIENTS AND METHODS

The Lesion Identification Scheme for Acne Inversa (LISAI) was developed according to the steps presented in Figure 1. Based on the literature[6], eleven lesion types were extracted as helpful for phenotyping:

1. Inflammatory nodule
2. Abscess
3. Draining fistula
4. Follicular papule and folliculitis
5. Double-ended comedones (pseudocomedones)
6. Hypertrophic scar
7. Accordion like-/ bridged scar
8. Epidermal cyst
9. Pilonidal sinus
10. Pyoderma gangraenosum
11. Acne conglobata

The first step was to use focus group interviews to develop the LISAIs, which included characteristic photos accompanied by descriptive text. They provide valuable assistance in identifying possible influencing factors. The focus group interview included ten patients with disease severities Hurley stage II and III (6 and 4 participants, respectively).

Based on the final scheme developed through the impressions of the focus group, five physicians, who were not involved in the development of the LISAI, were trained by the lead investigator of the study (see supplementary material S1_Physician-LISAI). These trained physicians assessed 27 photographs with various lesions and assigned either a 1 (present) or 0 (absent) for each lesion type for each photograph. Fleiss-Kappa was used to measure interrater reliability within six specialists (trained raters 1–5 and sample solution of leading investigator) using a significance level of 5% and Landis and Koch's (1977) guidelines for interpretation of κ defining $\kappa = 0.01–0.20$ as slight agreement, $\kappa = 0.21–0.40$ as fair agreement, $\kappa = 0.41–0.60$ as moderate agreement, $\kappa = 0.61–0.80$ as substantial agreement and $\kappa = 0.81–1.00$ as almost perfect agreement.[15]

To evaluate the agreement between physicians and patients, the scheme was implemented in the LENICURA-software (LENICURA GmbH, Wiesbaden, Germany). The LENICURA-software is used to document routine care with the LAight® therapy, ever since the latter was medically approved in 2017 for those patients who consent to this type of documentation.

Patients were recruited from the outpatient clinic of the Department of Dermatology, University Medical Center, Mainz, Germany (UMC) as well as the dermatology office of Dr. Kirschner (KI). Adult patients of any gender with

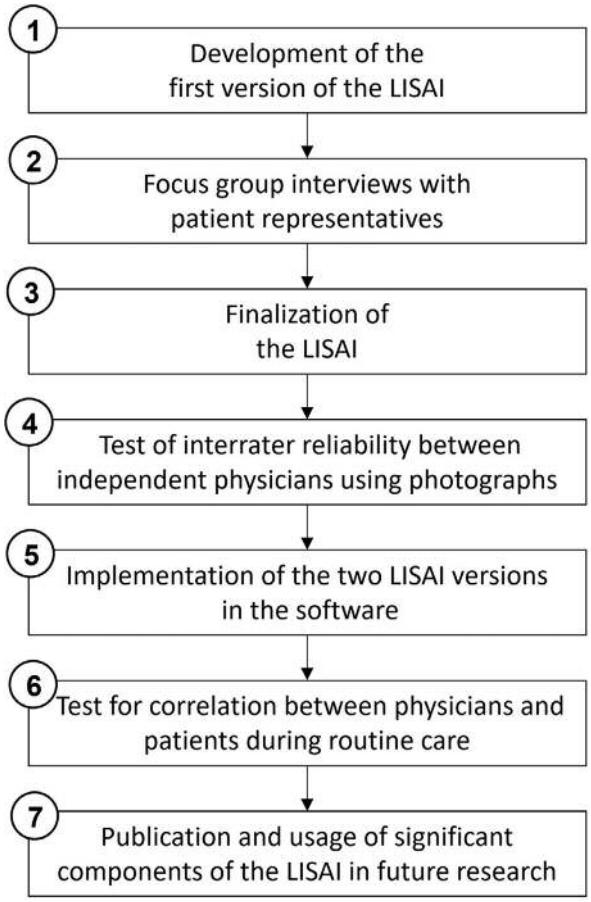

FIGURE 1 LISAI-study design

TABLE 1 Results from interrater reliability with respect to the different lesion types between professionals

Inflammatory nodule (in 59% of evaluated photographs*)	Kappa	0.64	Substantial agreement
	Sig. (2-sided)	<0.001	
Abscess (in 15% of evaluated photographs*)	Kappa	0.27	Fair agreement
	Sig. (2-sided)	<0.001	
Draining fistulas (in 22% of evaluated photographs*)	Kappa	0.93	Almost perfect agreement
	Sig. (2-sided)	<0.001	
Follicular papules and folliculitis (in 18% of evaluated photographs*)	Kappa	0.58	Moderate agreement
	Sig. (2-sided)	<0.001	
Double-ended comedones (in 11% of evaluated photographs*)	Kappa	0.20	Fair agreement
	Sig. (2-sided)	<0.001	
Hypertrophic scars (in 7% of evaluated photographs*)	Kappa	0.46	Moderate agreement
	Sig. (2-sided)	<0.001	
Accordion like-/ bridged scars (in 22% of evaluated photographs*)	Kappa	0.60	Moderate agreement
	Sig. (2-sided)	<0.001	
Epidermal cysts (in 0% of evaluated photographs*)	Kappa	N/A	No photograph with this lesion evaluated
	Sig. (2-sided)	N/A	
Pilonidal sinus (in 4% of evaluated photographs*)	Kappa	1.00	Almost perfect agreement
	Sig. (2-sided)	<0.001	
Pyoderma gangraenosum (in 11% of evaluated photographs*)	Kappa	0.60	Substantial agreement
	Sig. (2-sided)	<0.001	
Acne conglobata (in 4% of evaluated photographs*)	Kappa	0.79	Substantial agreement
	Sig. (2-sided)	<0.001	

Abbr.: N/A, not available
*According to sample solution

HS of all degrees of severity who visited the centers as part of LAight® therapy were included in the study. The underlying diagnosis of HS was again confirmed at the recruiting site during a clinical examination prior to inclusion in the study. Moreover, to participate in LISAI, patients had to possess a smartphone or tablet with access to the LENICURA-software. Insufficient knowledge of the German language was an exclusion criterion.

After evaluation of the existing lesions by the physician, patients logged into the software from home and were shown the patient version of the LISAI (see supplementary material S2_Patient-LISAI). From the convenience of their home, they selected the lesions they could identify on different sites of their own bodies. The answer "I don't know" was evaluated as not identified. The inclusion of patients was terminated as soon as 50 matching data sets were obtained.

The correlation between the number of areas in which a particular lesion was identified by physicians and patients was tested via spearman rank correlation coefficient with a significance level of 5% and using Cohen's guidelines for interpretation of ρ defining $|\rho| = 0.10$ as low/weak correlation, $|\rho| = 0.30$ as medium/moderate correlation and $|\rho| = 0.50$ as large/strong correlation.[16]

Statement of ethics

The research complied with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study protocol was approved by the Ethics Committee Rhineland-Palatinate and registered in the German Register for Clinical Trials prior to recruitment (# DRKS00023511). The final approval was obtained on January 21st, 2021.

RESULTS

Outcomes of the interrater reliability between the five rating physicians and the sample solution are shown in Table 1. Epidermal cysts could not be evaluated since the presented cases did not show this lesion type and Fleiss Kappa cannot be calculated for such a scenario, even though all physicians correctly identified the absence of this lesion. For all other ten lesion types the derived κ were statistically significant.

Almost perfect agreement was observed for draining fistulas (0.93) and pilonidal sinus (1.00) while substantial agreement was reached for inflammatory nodules (0.64),

TABLE 2 Results from Spearman rank correlation analysis with respect to the different lesion types between professionals and patients

Inflammatory nodule (identified by physicians in 96% of patients)	Coefficient	0.37	Medium/moderate correlation
	Sig. (2-sided)	0.009	
Abscess (identified by physicians in 32% of patients)	Coefficient	0.30	Medium/moderate correlation
	Sig. (2-sided)	0.032	
Draining fistulas (identified by physicians in 38% of patients)	Coefficient	0.59	Large/strong correlation
	Sig. (2-sided)	<0.001	
Follicular papules and folliculitis (identified by physicians in 32% of patients)	Coefficient	0.11	Low/weak correlation
	Sig. (2-sided)	0.450	
Double-ended comedones (identified by physicians in 42% of patients)	Coefficient	0.50	Large/strong correlation
	Sig. (2-sided)	<0.001	
Hypertrophic scars (identified by physicians in 38% of patients)	Coefficient	0.27	Low/weak correlation
	Sig. (2-sided)	0.061	
Accordion like-/ bridged scars (identified by physicians in 16% of patients)	Coefficient	0.45	Medium/moderate correlation
	Sig. (2-sided)	0.001	
Epidermal cysts (identified by physicians in 2% of patients)	Coefficient	0.33	Medium/moderate correlation
	Sig. (2-sided)	0.021	
Pilonidal sinus (identified by physicians in 2% of patients)	Coefficient	0.39	Medium/moderate correlation
	Sig. (2-sided)	0.005	
Pyoderma gangraenosum (identified by physicians in 4% of patients)	Coefficient	–0.05	No correlation
	Sig. (2-sided)	0.722	
Acne conglobata (identified by physicians in 0% of patients)	Coefficient	N/A	No patient with Acne conglobata in study population
	Sig. (2-sided)	N/A	

Abbr.: N/A, not available

acne conglobata (0.79) and pyoderma gangraenosum (0.60). Moderate agreement was shown for hypertrophic scars (0.46), follicular papules and folliculitis (0.58) as well as accordion like-/ bridged scars (0.60). For abscesses and double-ended comedones only fair agreement could be reached between the participating physicians (0.27 and 0.20, respectively).

Between of September 23rd, 2021, and of May 19th, 2022, a total of 85 patients were enrolled by the two centers and were evaluated by physicians trained on the physician version of LISAI. Of those patients, 50 completed the patient version of the LISAI at home (21 UMC and 29 KI). Of the participants, 41 were female (82%) and nine were male (18%). They had a mean age of 39 (SD = 10.8) and varied in disease severity (Hurley I: 10%; Hurley II: 66%; Hurley III: 24%). On average, patients completed their version of the LISAI 5 days after the evaluation of the physician.

Results of the correlation analysis between patients and physicians are shown in Table 2. The most common lesion type found in participants was the inflammatory nodule (in 96% of cases). The other two IHS4 (International Hidradenitis Suppurativa Severity Score System) components, abscesses and draining fistulas, were found in 38% and 32% of patients, respectively. Among the other defined lesion types, double-ended comedones were the most common (42%) followed by hypertrophic scars (38%).

A large/strong correlation between patients and physicians was found for draining fistulas (0.59) and double-ended comedones (0.50). For five other lesions correlation was medium/moderate, namely inflammatory nodules (0.37), abscesses (0.30), accordion like-/ bridged scars (0.45), epidermal cysts (0.33) and pilonidal sinus (0.39). All seven coefficients were found to be statistically significant. Insignificant, low/weak correlations were found for follicular papules and folliculitis (0.11) and hypertrophic scars (0.27), while pyoderma gangraenosum (–0.05) showed no correlation and acne conglobata could not be evaluated since this lesion type was not found by physicians in any participant.

For all lesion types with a significant correlation coefficient, the proportion of patients who identified this lesion type on themselves following prior identification by physicians was higher than 80% (Figure 2).

DISCUSSION

Disease patterns of HS and coherences are still poorly known mainly due to the complexity of the disease also represented in its inhomogeneous appearance and expression. Commonly accepted definitions of key HS lesions are vital in the development of standardized examination

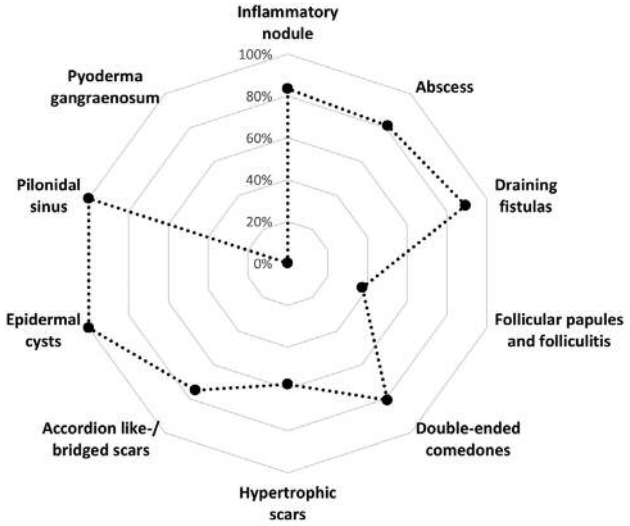

FIGURE 2 Graphical depiction of correlation between professionals and patients

techniques to improve clinical care and create a comparable study landscape.[17]

From a practical point of view, it is crucial that developed schemes and the resulting phenotypes allow predictions of HS progression and response to treatment. Only one study examined correlations between phenotype and genotype, but few significant correlations were found.[18] Given the chronic, but also waxing and waning nature of HS, it is moreover important to assess the stability of phenotypes during the course of the disease. It has been shown that the appearance of HS can change within 5 years in up to 45% of cases.[19]

The *Lesion Identification Scheme for Acne Inversa* (LISAI) for physicians and patients developed in this study includes eleven main skin lesions of HS. Several descriptions of lesions have been developed through European Consensus.[17] The descriptions of skin lesions in the LISAI are broadly consistent with the recent definitions of Frew et al. 2021. The only difference is that the cut-off size of a nodule is larger (at least 1 cm) than in the LISAI, where it is set to 0.5 cm according to existing literature.[20]

To the best of our knowledge, there is no study to date that defines and evaluates specifications of lesions for the purpose of patient self-examination. The VOICE project shows that HS patients are willing to share their experiences and data on past treatments and other characteristics. Therefore, a self-assessment scheme, as the developed LISAI in this study, can be a valuable tool to enrich patient surveys by the identification of lesion types, for example, as a basis for phenotyping.[14] In a recent study, the agreement between patients and physicians regarding affected body parts in psoriasis was analyzed.[21] This emphasizes the research interest of the dermatological community in this topic.

The interrater reliability analysis showed that the LISAI results obtained from healthcare professionals exhibited a sound agreement for draining fistulas (0.93), pilonidal sinus (1.00), inflammatory nodules (0.64), acne conglobata (0.79), pyoderma gangraenosum (0.60), hypertrophic scars (0.46), follicular papules and folliculitis (0.58) as well as accordion like-/ bridged scars (0.60). However, for abscesses and double-ended comedones only fair agreement could be reached between the participating physicians (0.27 and 0.20, respectively). The main reason for this low agreement is most likely attributable to the method, since photographs do not enable a palpation of the lesion. This made it hard to differentiate a fluctuant, compressible abscess from a nodule. Moreover, even in the literature, the classical definition of abscess does not seem to be uniformly understood.[17]

The low agreement with respect to double-ended comedones in turn might result from the fact that those lesions are so small, that raters might not have seen them on the photographs, especially if they did not zoom in. This reemphasizes the importance of palpating the skin lesion during examination of HS patients for the most accurate assessment.

The results demonstrate that patients evaluating their affected body-sites with the help of the developed LISAI, are able to identify seven HS lesions with at least medium/moderate correlation to physicians. A large/strong correlation between patients and physicians was found for draining fistulas (0.59) and double-ended comedones (0.50). Correlation was medium/moderate for inflammatory nodules (0.37), abscesses (0.30), accordion like-/ bridged scars (0.45), epidermal cysts (0.33) and pilonidal sinus (0.39).

There are a few limitations of this study. First, there was an average time lag of about 5 days between physician and patient examinations. For developing lesions in HS, an abscess can evolve on the base of an inflammatory nodule and might develop into a draining fistula or spontaneously regress. Since the lesions were assessed by patients five days after the physician assessment, this could potentially bias the results, since the evolution or normal course of the lesions during this time might lead to discrepancies between the patient and the physician group. However, it was important to provide the patients with the set-up at home where they had the time and privacy to examine themselves thoroughly, especially since this will be the manner of data collection once the LISAI is used in further studies. A second bias may stem from the fact that visual self-examination may be hard to perform by some patients due to the specific areas of HS skin lesions.

Looking ahead, the LISAI may contribute to research by providing a more comprehensive survey of the disease expression, a better understanding of the time course of the disease, phenotyping, and therefore hopefully lead to a more tailored assessment of the patient's condition. Moreover, if affected individuals are empowered to identify their own lesions and their assessment matches that of physicians, this could further facilitate efficient teleder-

matology consultation and treatment tailoring if in-person consultation and physical examination are not possible.

A further survey-based study called EPICAI (Epidemiology and Care in Acne Inversa) already includes the LISAI – among other questionnaires – to assess patients' lesions and link these to the burden of disease as well as comorbidities and treatment experiences and response. With the help of the LISAI, EPICAI will hence link phenotype information to longitudinal data.

In the present study, the focus was on examining reliability and agreement only. The LISAI has not yet been tested for its potential applicability for the exact number, size, and localization of lesions, which could be a valuable additional field of application for gaining a better understanding of the structures in flares and for assessing treatment effects.

ACKNOWLEDGEMENT

The authors wish to thank all the patients who participated in LISAI despite the extraordinary Covid-19 situation.

Open access funding enabled and organized by Projekt DEAL.

FUNDING SOURCES

The implementation of the LISAI in the LENICURA-software was provided free of charge by LENICURA GmbH. No other funding was received.

CONFLICT OF INTEREST

Michael Schultheis: Speaker for AbbVie, travel funding and assumption of congress fees by Pfizer, Controller for LENICURA GmbH. Petra Staubach: Advisor/Consultant AbbVie, Allergika, Almirall-Hermal, Amgen, Beiersdorf, Biocryst, Biogen Idec, BMS, Boehringer-Ingelheim, Celgene, CSL-Behring, Eli-Lilly, Galderma, Hexal, Janssen, Klinge, Klosterfrau, LEO-Pharma, LETI-Pharma, L'Oréal, Novartis, Octapharma, Pfizer, Pflüger, Pharming, Regeneron, Shire, Takeda, Regeneron, Sanofi-Genzyme und UCB Pharma. Stephan Grabbe: Advisor/Consultant: AbbVie (also travel funding), BMS (also travel funding), MSD (also travel funding), SUN Pharma, Roche (also travel funding), Pfizer, Sanofi-Pasteur-MSD, Takeda, Novartis, Merck, Guidepoint Global, Merck Serono; Research support: Novartis, Pierre Fabre. Katharina Hennig: CEO of LENICURA GmbH. Fareed Khoury: Nothing to declare. Georgios Nikolakis: Nothing to declare. Uwe Kirschner: Speaker for/consultant to Mylan, Germany; travel funding LENICURA.

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How to cite this article: Schultheis M, Staubach-Renz P, Grabbe S, et al. Can hidradenitis suppurativa patients classify their lesions by means of a digital lesion identification scheme?. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2023;21:27–32. https://doi.org/10.1111/ddg.14926