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Pilonidal sinus disease: An intergluteal localization of hidradenitis suppurativa/acne inversa: A cross-sectional study among 2465 patients

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Short title: Prevalence of Pilonidal sinus disease in hidradenitis suppurativa

Abstract

Background: Hidradenitis suppurativa (HS), also referred to as acne inversa, is a debilitating skin disease characterized by inflammatory nodules, chronic abscesses and tunnels (fistulae and sinuses). The association with pilonidal sinus disease is frequently reported but not well documented.

Objective: To determine the prevalence and characteristics of inflammatory skin lesions located in the intergluteal fold (IGF) of HS patients.

Methods: An international multicenter, retrospective cross-sectional study based on data collection of a large cohort of HS patients with and without histopathology.

Results: In a total of2465 HS patients included, 661 (27%) reported lesions in the IGF**.** These were significantly more often smokers and had more severe HS. Intergluteal-HS (IG-HS) was diagnosed in 52 (22%), and pilonidal sinus disease (PSD) in 186 (77%) of the patients with a clinical diagnosis available. IGF-HS was associated with the localization of HS in the proximity of the IGF, including the buttocks, genitals and the anus.

Limitations: Misclassification bias is possible as a clinical/imagery diagnosis, or histopathology of the intergluteal fold lesions were not always available.

Conclusions: The high prevalence of pilonidal sinus disease suggest a strong link between both entities. Common pathophysiological mechanisms and common therapeutic strategies might therefore be designed.

New statement

- The occurrence of pilonidal sinus disease has not been clearly reported among hidradenitis suppurativa/acne inversa patients.
- As the first study of its kind, we investigate the prevalence of pilonidal sinus disease among a large cohort of patients and identify patient characteristics.
- Risk factors that might help to improve the management of patients were identified.

Key words

Pilonidal sinus disease, hidradenitis suppurativa, acne inversa, prevalence, smoking, intergluteal, abscess, pathophysiology

Introduction

Pilonidal sinus disease (PSD) has been described under various names, such as pilonidal cyst, abscess or sinus. In 1880, Hodges used the word "pilonidal" by combining the word "pilus" which means hair in Latin and "nidus" which means nest [1]. The prevalence of PSD is not well documented. Histologically PSD is most often defined by an epithelial track located in the skin of the gluteal cleft generally containing hair, although alternative presentations have been described [1].Originally considered a congenital disease, the acquired origin has also been discussed by several authors. They have also highlighted the role of predisposing factors such as smoking, male gender (male-to-female ratio 3:1), obesity and local friction [2].

Hidradenitis suppurativa/acne inversa (HS) is a chronic, inflammatory, recurrent, debilitating follicular skin disease that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillary, inguinal and anogenital regions[3].

The pathophysiology of HS is not fully understood but likely includes an interaction between a complex genetic background and environment. Like HS, smoking, obesity and skin friction are risk factors for the development of PSD. Unlike PSD however, HS affects more women than men with a ratio of one to three[4,5]. PSD histology combines features of chronic and acute inflammatory skin infiltrate, abscesses, follicular occlusion and sinus tract formation [6-8].

Solitary intergluteal-HS (IG-HS) lesion may be clinically confused with PSD. Sonographic characteristics of PSD are also similar to key features observed in HS lesions suggesting that PSD may be a variant or localized form of HS [8]. In the acute phase of PSD and IG-HS, patients typically present initially with pain, erythema, and swelling in the midline gluteal cleft region. In the chronic phase, the formation of a cavity may cause chronically purulent discharge in both diseases. PSD lesions are histologically characterized by pseudocysts with granulation tissue surrounding hair shafts (not disrupted follicles) and fistulous opening to the surface; epithelial coating can be seen in severe/relapsing cases; on the other hand, HS is primarily a folliculitis. Histology cannot always help to distinguish between both entities [7]. Sharing the initial event of follicular occlusion, HS and PSD are part of the follicular tetrad with dissecting follicular of the scalp and acne conglobata [6,9]. In the phenotypical classification of Canoui-Poitrine et al, HS patients classified as LC2 had higher probabilities not only for breast and armpit involvement but also for involvement of the ears, chest, back, or legs and for follicular lesions including PSD [10]. These factors, therefore, bring up the question of whether PSD and HS represent a spectrum of one disease or are separate entities.

The aim of our study was to evaluate the prevalence of inflammatory lesion into the intergluteal fold (IG)among a large cohort of HS patients and analyze their characteristics.

Material and Methods

This study was explorative, cross-sectional, descriptive, and was conducted based on case note review/interviews and clinical assessment of patients addressed to secondary/tertiary level care units (clinics or hospitals) specialized in HS management. Patients were recruited from different outpatient dermatology clinics co-operating with the Faster-and-Better research initiative of the European Hidradenitis Suppurativa Foundation e.V. (www.ehsf.eu). Centers were asked to include HS patients they were currently managing or they previously managed, provided 1) patients were consecutive within a determined period of time, and 2) the answer to the question whether there was a past or a current inflammatory lesion in the IG fold was available.We aimed to obtain the largest cohort as possible to reduce the bias of a retrospective studies and then asked several centers to participate. Similarly those centers were asked to include as exhaustively as possible within their HS patients, provided the above-described eligibility criteria.

A specific questionnaire had to be filled out, exploring gender, age, height, weight, smoking habits, family history of HS, disease activity (age at first boil, body regions involved, Hurley stage), and co-morbid conditions, such as acne, dissecting cellulitis of the scalp, joint problems, and gastrointestinal problems. Whether a current or a past inflammatory lesion in the IG was described in the patient cases was recorded. In these cases, additional data included the age of onset, a family history of inflammatory lesion in the IG, and whether the lesion has been recurrent or not.It is also important to note that the nature of lesions in the IG fold was classified as HS or PSD or undetermined, so only one possibility could be recorded.We defined 'patient diagnosis' as the diagnosis reported by the patient for a past lesion, 'clinical diagnosis' as the diagnosis reported by a physician (the one who examined the patient when filling the questionnaire or the one who cited the lesion in a medical document available in the patient's chart), and 'pathological diagnosis' as the diagnosis reported by histopathological examination of a surgical specimen obtained through excision of the lesion (whether the surgery was performed at the time of the questionnaire or mentioned in the patient's chart). Because of its retrospective nature and the lack of consensual diagnostic criteria, this study could not explore the clinical and pathologic criteria used to establish the diagnosis of each entity.Twelve centers from Europe, one center from the Middle East and one center from North America have participated in the study by sending their data from July 2016 to July 2017. The study was approved by the Ethics Committee of Erasme hospital with the following number EudraCT/ CCB B406201627010

Statistical analysis

All statistics were performed using Stata® 11.0 (College Station, Texas). Numeric data are presented with mean and standard deviation after normality checking (combination of Skewness and Kurtosis tests). Differences between groups were accordingly examined using a t-test. Categorical data are presented with frequency and percentages, comparisons between groups were done with either a Fisher's exact test (to explore the links with all comorbidities except acne vulgaris) or a Chi-squared test (for all other variables), Because of the multiple statistical tests performed, we considered a correction for multiple comparisons and used the false discovery rate Benjamini-Hochberg procedure (with a false discovery rate at 0.05). Differences were only considered significant if lower than the generated critical values.

To manage missing data in logistic regression analyses we performed multiple variable imputation using chained equations. Age at the study, age at first boil, disease duration and age at IG lesion occurrence were introduced as continuous variables in the model. All other variables were considered dichotomous (1 if present, 0 if not), except Hurley stage which was introduced as a categorical variable (stage I, II or III). To assess confounding variables in logistic regressions, a backward selection (with a p-value of 0.10) and a full multivariable model were used when distinguishing patients with or without a lesion in the intergluteal region or patients with HS or PSD. We checked and met the assumptions recommended for logistic regression, including the binary natureof the dependent variables, the linearity of independent variables (using the Stata's linktest) and the collinearity of the independent variables (because of collinearity, disease duration was consequently excluded for further regression analyses).

Results

Prevalence and characteristics of an inflammatory lesion in the IG of HS patients

We included 2465 HS patients, 1567 women (64%) and 898 men (36%). Clinical data is presented in **Table 1**. A current or past lesion in the IG was observed in 661 patients (26.8%;95% confidence interval: 25.1% - 28.6%). The mean age at IG lesion occurrence was 23.1 yrs and it occurred as the first inflammatory skin lesion in 236 patients (10% of all HS patients and 36% of patients with IG lesion) (**Table 2**). The prevalence by age is provided in **Figure 1**. These 661 patients were more frequently men and smokers (past or current smokers), as well as younger (35 *vs* 37 years) than patients without IG lesion (**Table 3**). The mean age at first boil was significantly lower (20 *vs* 23 years). The classical axilla and groin regions were involved with the same frequency in the two groups. The breast was less frequently involved in patients with IG lesions while the buttocks, genital, pubic, and anal areas were more frequently involved (**Table 3**). HS was more severe in patients with IG lesions: 22% of which had Hurley III disease, as compared to 10% in the non-IG group (**Figure 2**). No differences were observed concerning associated inflammatory rheumatic and gastrointestinal diseases but acne vulgaris andacne conglobata were more frequently associated with IG lesions(**Table 1**).To assess which factors were independent predictors of the occurrence of an IG lesion, we first managed missing data by multinomial implantation, then repeated univariate analyses with implemented data (**Table 4**), and next performed

multivariate analysis. While age, acne conglobata, and genital and buttocks involvement did not remain significant, male gender, smoking habits, age at first boil, Hurley stage, acne vulgaris as well as breastandanal involvement, were all confirmedas independent predictors of an IG lesion. BMI also proved to be a significant predictor (**Table 4**).

Patient, clinical and histopathological diagnosis for inflammatory lesions in the IG of HS patients

Patient diagnosis was available for 554 of the 661 patients with IG lesions (84%). Patients reported IG-HS in 11%, PSD in 83% and undetermined in 6%. A clinical diagnosis was available in 238 patients with IG lesions (36%), according to clinical observation (n = 119) or surgical exploration (with or without clinical observation; n = 119).

In those patients, the clinical diagnosis was reported as IG-HS in 52 (22%; 95%CI; 17-27%), and PSD in 186 (77%; 73-83). Patient and clinical diagnoses were consistent in 86% of the patients (208 patients among the 241 for whom both the patient and the clinical diagnoses were available). While 6% of the patients, who reported a PSD were clinically classified as HS, 6% of the patients who reported an IG-HS were clinically classified as PSD.

Histopathological diagnosis was available in 116of the 661 patients with IG lesions (18%). When available, it was reported as IG-HS in 37 (33%) and PSD in 76 (67%). Clinical and pathological diagnoses were consistent in 88% of the patients (102 patients among the 116for whom both the clinical and the pathological diagnoses were available). While 11% of the IG lesions clinically classified as PSD were eventually classified as IG-HS, none of those clinically classified as IG-HS were eventually diagnosed as PSD. The two lesions reported as IG-HS by the patients and clinically reported as PSD were eventually reclassified as HS by the pathological examination.

Factors associated with a clinical HS lesion in the IG furrow

Additionally, we investigated the characteristics of patients clinically classified as IG-HS versus PSD (**Table 5**). Patients with clinical IG-HS were significantly older (40 vs 32 yrs, p<0.001), less frequently women (29% vs 47%, p=0.019). The mean BMI was significantly lower (26 vs 29 kg/m^2, p=0.025). The prevalence of tobacco smoking and a family history of HS were not different between the two groups. Only one of the patients with a clinically-classified IG-HS had a family history of PSD (2%), while it was observed in 15% of the patients with a clinically-classified PSD (p=0.003). Both HS and IG-HS occurred later if the IG lesion was clinically-classified as HS: 25 vs 21 years (p=0.015) and 29 *vs*24years (p=0.001), respectively. Patients with clinically-classified IG-HS had more frequently HS lesions in the gluteal, genital and anal area (**Table 5**). HS severity was significantly worse in patients with IG-HS since 69% were reported as Hurley III, as compared to 25% in the PSD group. No association was found between the clinical diagnosis and the comorbidities (**Table 5**). Similar results were obtained when patients were classified in two groups (PSD *vs* IG-HS) according to pathological diagnosis (**Supplementary Table 1**).

Using multivariable regression for exploratory attempt, we found that axillary involvement (negatively), as well as Hurley stage and anal, genital or gluteal involvement (positively) proved to be independent predictors of the clinical diagnosis of IG-HS (**Table 6**).

Discussion

To the best of our knowledge, the possible association of HS and PSD has not been studied in detail. In the present cohort of 2465 HS patients, using data from 14 centers from different countries, we observed a prevalence of 27% of IG skin lesions. The exact prevalence remains elusive, but papers, using diverse cohorts, provide estimates of 4.6% to 30% of PSD in HS patients [11-17].

Direct and statistically significant comparison with the general population is, therefore, still warranted, but the proportion of PSD within this HS cohort seems largely higher than the 1% to 9% prevalence observed in the general population [18,21].

The evaluation of the prevalence of PSD among a large cohort of HS patients represent a complex challenge

Interestingly, we observed that IGF-HS lesion was associated with localization of HS in the proximity of the IGF lesion, including buttocks, genitals and anus.

HS is a multifaceted disease and one of the main challenge is to determine a clinical classification that mirrors pathophysiological mechanisms and theranostic significance. Whether HS patients with PSD constitute a particular subgroup has been suggested when integrating PSD in the so-called HS follicular phenotype or in the follicular tetrad [6]. The main limitations of our study is its retrospective nature: clinical diagnosis was based on the diagnostic conclusion reported in the medical charts but the criteria used to obtain this diagnosis were quite never mentioned. In fact, a precise definition of PSD and a consensual list of criteria to ascertain the diagnosis are still lacking. The presence of a midline dimple and the presence of hair within a cyst or an abscess are usually reported as diagnostic criteria but both are not necessarily present. Even clear pathological criteria are still warranted. Similar ultrasonographic features have been reported for both HS and PSD [9], suggesting that distinction between IG-HS and PSD can be difficult. The major limitation of our work is the retrospective design of the study which could be associated with a lack of accuracy of the recorded data. Imaging and/or histopathology analysis were not always found in the medical charts depending on variable managment of the included centers and represent another limiting factor of our work. We found that 77% and 67% of the IG lesions observed in HS patients were considered as PSD upon clinical and pathological examinations, suggesting that the prevalence of PSD is around 20% in HS patients.

By contrast to its relative high prevalence, the factors associated with the primary occurrence of PSD has only been scarcely explored. Suggested factors are overweight, excess hair in the IG, stiff hair, male gender, prolonged sitting time, family history of PSD and poor hygiene [22-25]. In our series, when compared to those without lesion in the IG, HS patients with such lesions were more frequently men. A male predisposition was observed when comparing PSD and HS lesions within the group of patients with an IG lesion. While clearly associated with HS[3] smoking has been reported as a prognostic factor for recurrence and delayed healing after surgery but not as a predisposing factor to PSD[26]. IG-HS patients were more frequently smokers but we could not associate smoking habits with a clinical diagnosis of IG-HS or PSD. HS patients with an IG lesion were significantly younger at HS onset. They suffered from the disease for a longer time and the risk of an IG lesion in HS increases with time. However, although we cannot exclude a bias due to the retrospective nature of the evaluation, our results rather suggest that IG lesions occur early (Figure 1). Among HS patients with an IG lesion, this lesion occurred earlier and more frequently in a family context of PSD if it was classified as a PSD. By contrast, true IG-HS lesions recurred more frequently after surgery

than PSD lesions. We identified a new phenotype of HS patients having an IG lesion as first manifestation of the disease and presenting risk factors such asmalegender, smoking, late onset, no family history of PSD, recurrence after surgeryand could be indicative of the possibility of future HS occurrence. Further studies are needed to compare HS-associated and HS-free PSD and confirm the contribution of a genetic background component involved in the etiopathogenesis.

Whether a precise distinction between PSD and HS is clinically relevant when managing a lesion of the IG in HS patients remains matter of discussion. The occurrence of an inflammatory IG lesion has to be reconsidered among the surgeons. Patients with recurrent flares of IG lesions(with or without a confirmed diagnosis of PSD) with no other skin involvement have to be followed up in dermatologyto track the diagnosis of an HS disease.Interstingly, surgery would be preferred for PSD while systemic therapiescould be offered for HS. The high prevalence of PSD in HS patients is in fact not inconsistent with the acquired theory of PSD. The Karydakis' concept of *HxFxV* formula in PSD pathophysiology is now widely accepted and suggests that PSD occurs due to the association of free hair (H-hair), the vacuum effect that drives hair embedding in the IG during movement of the gluteal region (F-force), and the vulnerability of the skin (V-vulnerability) [27]. HS may predispose to PSD by weakening the skin (folliculitis for example) and thereby increasing the V parameter of Karydakis' formula.

We conclude from our work that IG lesions occur in about one fourth of the HS patients. These lesions are not always PSD: about one third correspond clinically to real HS lesions. We identified a new clinicalphenotype of HS patients with IG lesions (male predominance, younger age, smoking, family history of PSD, higher recurrence rate, more severe disease) that probably deserve to be considered when attempting to dismember the complex and multifaceted HS.

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	Number of subjects with available data	Mean (SD) or N (%)	95% confidence interval of the mean or the proportion
Female	2465	1567 (64)	62 – 65
Mean age (yrs)	2249	36.8 (12.6)	36.3 – 37.3
BMI (kg/m^2)	2285	27.8 (6.3)	27.6 – 28.1
Current or past smokers	2416	1852 (77)	75 – 78
Family history of HS	2437	713 (29)	27 – 31
Mean age at first boil (yrs)	2391	22.3 (10.0)	21.9 – 22.7
Mean HS duration (yrs)	2364	14.4 (10.6)	14.0 – 14.9
Hurley stage			
I	2372	1044 (44)	42 – 46
II		1011 (43)	41 – 45
III		317 (13)	12 – 15
Regions involved			
Axilla	2384	1608 (67)	66 – 69
Breast	2324	522 (22)	21 – 24
Buttocks	2330	916 (39)	37 – 41
Groin	2394	1843 (77)	75 – 79
Pubis	1586	376 (24)	22 – 26
Genitals	2295	647 (28)	26 – 30
Anus	2300	398 (17)	16 – 19
Elsewhere	2343	539 (23)	21 – 25
Comorbidities			
Joints	2306	133 (6)	5 – 7
Gastrointestinal	2299	63 (3)	2 – 3
Acne vulgaris	2465	223 (9)	8 – 10
Acne conglobata	1633	98 (6)	5 – 7
Dissecting folliculitis	1650	34 (2)	1 – 3
Psoriasis	2465	44 (2)	1 – 2
Inflammatory lesion in the intergluteal fold	2465	662 (27)	25 – 29

Table 1: Description of the population (n=2465)

	No inflammatory lesion in the intergluteal furrow N = 1804 (73%)		Description of an inflammatory lesion in the intergluteal furrow N = 661 (27%)		Statistical analysis*
	Mean (SD) or N (%)	95% CI of the mean or the proportion	Mean (SD) or N (%)	95% CI of the mean or the proportion	
Female	n=1264 (70)	68 – 72	n=303 (46)	42 – 50	**p < 0.001**
Mean age (yrs)	37.3 (13.0)	37 – 38	35.4 (11.3)	35 – 36	**p < 0.001**
BMI (kg/m^2)	27.8 (6.5)	27 – 28	28.0 (6.3)	28 – 28	p = 0.470
Current or past smokers	1320 (77)	75 – 79	532 (84)	81 – 87	**p < 0.001**
Family history of HS	528 (30)	27 – 32	185 (28)	25 – 32	p = 0.523
Mean age at first boil (yrs)	23.1 (10.7)	23 – 24	20.1 (7.8)	20 – 21	**p < 0.001**
Mean HS duration (yrs)	14.2 (10.8)	14 – 15	15.2 (10.1)	14 – 16	p = 0.032
Regions involved					
Axilla	1164 (67)	65 – 69	444 (69)	65 – 73	p = 0.309
Breast	410 (24)	22 – 26	112 (18)	15 – 21	**p = 0.002**
Buttocks	629 (37)	35 – 39	287 (46)	42 – 50	**p < 0.001**
Groin	1347 (77)	75 – 79	496 (77)	74 – 81	p = 0.847
Pubis	234 (22)	19 – 24	142 (27)	24 – 31	**p = 0.015**
Genitals	441 (26)	24 – 28	206 (34)	30 – 37	**p < 0.001**
Anus	240 (14)	13 – 16	158 (26)	22 – 29	**p < 0.001**
Elsewhere	373 (22)	20 – 24	166 (26)	22 – 29	**p = 0.029**
Comorbidities					
Joints	97 (6)	5 – 7	36 (6)	4 – 8	p = 0.924

Gastrointestinal	52 (3)	2 – 4	11 (2)	1 – 3	p = 0.077
Acne vulgaris	138 (8)	6 – 9	85 (13)	10 – 15	**p < 0.001**
Acne conglobata	50 (5)	3 – 6	48 (9)	7 – 12	**p < 0.001**
Dissecting folliculitis	22 (2)	1 – 3	12 (2)	1 – 4	p = 0.686
Psoriasis	32 (2)	1 – 2	12 (2)	1 – 3	p = 0.945

Table 2: Characteristics of the patients with hidradenitis suppurativa and an inflammatory lesion in the intergluteal furrow (IGF)

*: p values are bolded when considered as significant after Benjamini-Hochberg correction (false discovery rate at 0.05)

	Number of subjects with available data	Mean (SD) or N (%)	95% CI of the mean or the proportion
Mean age at IGF lesion occurrence (yrs)	447	23.1 (8.4)	22 – 24
IGF lesion as the first occurring lesion	661	236 (36)	32 – 39
Family history of IGF lesion	508	70 (14)	11 – 17
Recurrent IGF lesion (after surgery)	597	163 (25)	24 – 31
Patient diagnosis			
Hidradenitis suppurativa	554	61 (11)	8 – 14
Pilonidal sinus disease		493 (89)	84 – 94

Table 3: Characteristics of the inflammatory lesion in the intergluteal furrow when present (n=661)

	Univariate analyses			Multivariate analysis		
	Odds ratio	95% confidence interval	p value*	Odds ratio	95% confidence interval	p value**
Female	0.36	0.30 – 0.43	< **0.001**	0.40	0.32 – 0.49	< **0.001**
Age	0.99	0.98 – 0.99	**0.001**	0.99	0.98 – 0.99	0.040
BMI	1.00	0.99 – 1.02	0.542	1.02	1.00 – 1.04	**0.028**
Smokers	1.50	1.19 – 1.88	< **0.001**	1.61	1.25 – 2.06	< **0.001**
Family history of HS	0.93	0.76 – 1.14	0.496	0.80	0.64 – 1.00	0.052
Age at first boil	0.97	0.96– 0.98	< **0.001**	0.96	0.95 – 0.97	< **0.001**
Hurley stage	1.69	1.49 – 1.93	< **0.001**	1.56	1.35 – 1.81	< **0.001**
Axilla	1.10	0.91 – 1.33	0.331	0.87	0.70 – 1.09	0.230
Breast	0.72	0.57 – 0.90	**0.005**	0.66	0.51 – 0.87	**0.003**
Buttocks	1.42	1.18 – 1.70	< **0.001**	1.12	0.91 – 1.38	0.289
Groin	1.01	0.81 – 1.26	0.903	1.08	0.84 – 1.39	0.759
Pubis	1.23	0.97 – 1.56	0.091	1.11	0.83 – 1.47	0.476
Genitals	1.39	1.14 – 1.68	< **0.001**	1.24	0.99 – 1.55	0.058
Anus	2.05	1.64 – 2.57	< **0.001**	1.68	1.29 – 2.17	< **0.001**
Elsewhere	1.26	1.02 – 1.56	0.034	0.89	0.70– 1.14	0.369
Joints	0.99	0.68 – 1.47	0.998	1.24	0.80 – 1.91	0.331
Gastrointestinal	0.56	0.28 – 1.12	0.102	0.57	0.27 – 1.22	0.149
Acne vulgaris	1.78	1.34 – 2.37	< **0.001**	1.65	1.21 – 2.26	**0.002**
Acne conglobata	2.02	1.40 – 2.91	< **0.001**	1.26	0.82 – 1.95	0.288
Dissecting folliculitis	1.12	0.52 – 1.42	0.759	0.69	0.28 – 1.37	0.415
Psoriasis	1.02	0.52 – 2.00	0.945	0.78	0.37 – 1.62	0.506

Table 4: Clinical factors influencing the occurrence of an inflammatory lesion in the intergluteal furrow of 2465 patients with hidradenitis suppurativa (univariate and multivariate regression analyses after multinomial imputation of missing data)

*: p values are bolded when considered as significant after Benjamini-Hochberg correction (false discovery rate at 0.05)

**: p values are bolded (meaning significance) when < 0.05

	Pilonidal sinus disease N = 186 (78%)		Hidradenitis suppurativa in the intergluteal fold N = 52 (22%)		Statistical analysis*
	Mean (SD) or N (%)	95% CI of the mean or the proportion	Mean (SD) or N (%)	95% CI of the mean or the proportion	
Female	n=87 (47)	40 – 54	n=15 (29)	16 – 42	**p = 0.019**
Mean age (yrs)	32.2 (9.8)	31 – 34	40.2 (12.6)	37 – 44	**p < 0.001**
BMI (kg/m^2)	28.8 (7.1)	28 – 30	26.4 (5.1)	25 – 28	**p = 0.025**
Current or past smokers	142 (77)	71 – 83	44 (88)	79 – 97	p = 0.078
Family history of HS	38 (21)	15 – 27	10 (19)	8 – 30	p = 0.794
Mean age at first boil (yrs)	21.1 (8.7)	20 – 22	24.9 (10.4)	22 – 28	**p = 0.015**
Mean HS duration (yrs)	11.3 (7.9)	10 – 13	15.4 (11.8)	12 – 19	**p = 0.007**
Hurley stage					
I	69 (38)	31 – 45	4 (8)	0 – 15	**p < 0.001**
II	68 (37)	30 – 44	12 (23)	11 – 35	
III	46 (25)	19 – 31	36 (69)	56 – 82	
Regions involved					
Axilla	130 (77)	71 – 83	32 (62)	48 – 75	p = 0.032
Breast	37 (25)	18 – 32	6 (12)	3 – 21	p = 0.033
Buttocks	54 (35)	27 – 43	37 (71)	59 – 84	**p < 0.001**
Groin	131 (78)	72 – 84	39 (75)	63 – 87	p = 0.657
Pubis	48 (32)	24 – 40	18 (35)	21 – 48	p = 0.730
Genitals	38 (26)	19 – 34	31 (60)	46 – 73	**p < 0.001**
Anus	25 (17)	11 – 24	23 (44)	30 – 58	**p < 0.001**
Elsewhere	60 (37)	30 – 45	17 (33)	20 – 47	p = 0.630

Comorbidities					
Joints	5 (3)	0 – 7	3 (6)	0 – 12	p = 0.488
Gastrointestinal	1 (1)	0 – 2	1 (2)	0 – 6	p = 0.478
Acne vulgaris	28 (15)	10 – 20	6 (12)	3 – 21	p = 0.513
Acne conglobata	11 (8)	3 – 12	8 (15)	5 – 26	p = 0.121
Dissecting folliculitis	3 (2)	0 – 4	3 (6)	0 – 12	p = 0.214
Psoriasis	4 (2)	0 – 4	3 (6)	0 – 12	p = 0.207
Mean age at IGF lesion occurrence (yrs)	23.7 (7.8)	22 – 25	28.9 (10.9)	26 – 32	**p = 0.001**
IGF lesion as the first occurring lesion	55 (30)	23 – 36	25 (48)	34 – 62	**p = 0.014**
Family history of IGF lesion	22 (15)	9 – 21	1 (2)	0 – 6	**p = 0.003**
Recurrent IGF lesion (after surgery)	52 (36)	28 – 44	28 (58)	44 – 73	**p = 0.008**

Table 5: Exploration of the factors related to hidradenitis suppurativa or pilonidal sinus disease (as assessed by clinical observation) in patients with an inflammatory lesion in the intergluteal fold.

*: p values are bolded when considered as significant after Benjamini-Hochberg correction (false discovery rate at 0.05)

	Univariate analyses			Multivariate analysis		
	Odds ratio	95% confidence interval	p value*	Odds ratio	95% confidence interval	p value**
Female	0.46	0.24 – 0.90	0.023	2.01	0.71 – 5.70	0.186
Age	1.06	1.03 – 1.09	< **0.001**	1.05	0.99 – 1.10	0.052
BMI	0.94	0.89 – 0.99	0.042	0.98	0.90 – 1.07	0.611
Smokers	2.41	0.93 – 6.25	0.070	2.32	0.63 – 8.51	0.204
Family history of HS	0.90	0.42 – 1.97	0.799	0.83	0.26 – 2.69	0.760
Age at first boil	1.04	1.01 – 1.07	0.017	0.97	0.92 – 1.04	0.411
Hurley stage	3.90	2.36 – 6.45	< **0.001**	3.79	1.99 – 7.19	< **0.001**
Axilla	0.48	0.25 – 0.92	0.028	0.43	0.15 – 1.30	0.136
Breast	0.38	0.15 – 0.97	0.043	0.17	0.04 – 0.69	**0.013**
Anal, genital and/or buttocks	7.58	2.63 – 21.9	< **0.001**	6.50	1.85 – 22.9	**0.004**
Elsewhere	0.47	0.21 – 1.05	0.066	0.60	0.16 – 2.28	0.450
Acne vulgaris	0.74	0.29 – 1.89	0.523	1.08	0.29 – 4.06	0.904
Acne conglobata	2.43	0.94 – 6.27	0.067	2.52	0.47 – 13.5	0.278
Dissecting folliculitis	3.53	0.76 – 16.3	0.107	8.80	0.99 – 77.5	0.050
Family history of IG lesion	0.19	0.04 – 0.91	0.038	0.19	0.02 – 1.49	0.113
Recurrent IG lesion (after surgery)	2.32	1.12 – 4.85	0.025	1.79	0.65 – 4.95	0.255

Table 6: Clinical factors influencing the HS nature (rather than a pilonidal sinus disease) of an inflammatory lesion in the intergluteal furrow of 238 patients with hidradenitis suppurativa (univariate and multivariate regression analyses after multinomial imputation of missing data ; exploratory study)

*: p values are bolded when considered as significant after Benjamini-Hochberg correction (false discovery rate at 0.05)

**: p values are bolded (meaning significance) when < 0.05

Fig. 1

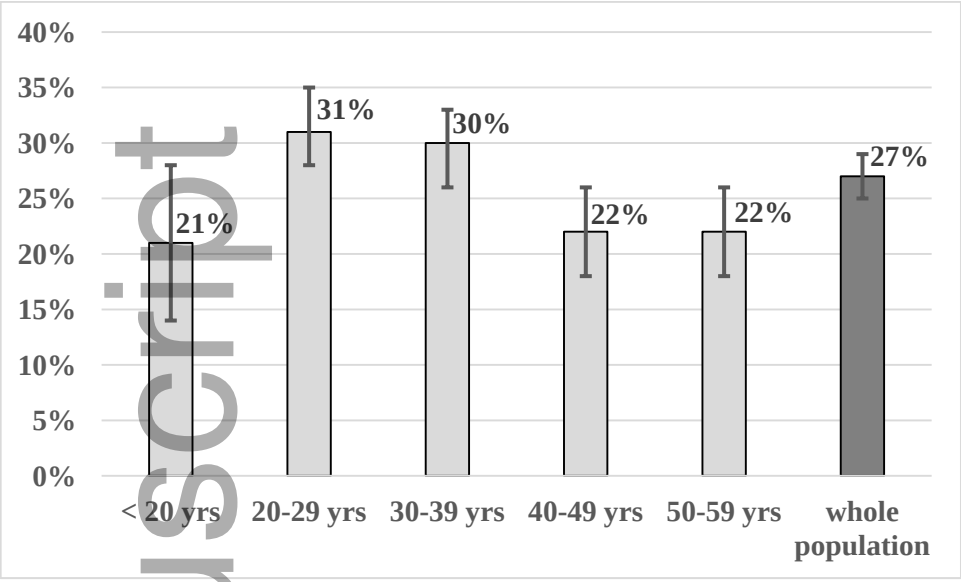

Figure 1. Prevalence of an inflammatory lesion in the intergluteal furrow of patients with hidradenitis suppurativa depending on age.

95% confidences intervals for each age group and the whole population are presented as error bars

Fig. 2

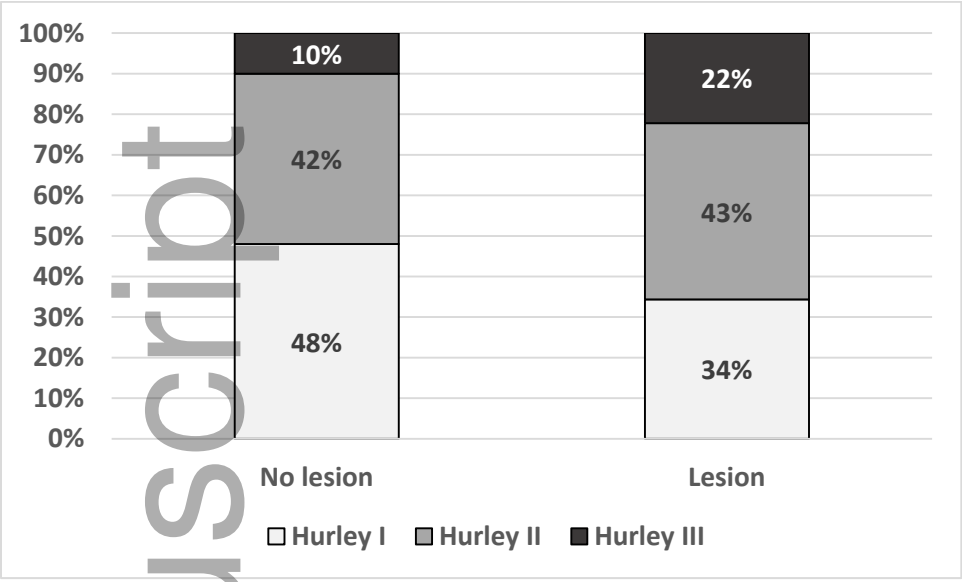

Figure 2. Classification of HS patients according the Hurley Staging in presence or absence of an inflammatory lesion in the intergluteal furrow

The p value < 0.001 was considered as significant after Benjamini-Hochberg correction (false discovery rate at 0.05)

95% confidences intervals for Hurley I, II and III are as following:
'No lesion' group: I=45.2-50%; II=40.1-44.8%; III=8.6-11.5%
'Lesion' group: I=30.8-38.2%; II=39.2-47.0%; III=19.3-25.9%

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