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Patogenetyczne i kliniczne aspekty hidradenitis suppurativa

ROZPRAWA DOKTORSKA

Cykl publikacji powiązanych tematycznie

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Pragnę złożyć najszczersze podziękowania mojemu promotorowi,
Panu prof. dr. hab. n. med. dr. h.c. Jackowi Szepietowskiemu,
Kierownikowi Katedry i Kliniki Dermatologii, Wenerologii i Alergologii
Uniwersytetu Medycznego im. Piastów Śląskich we Wrocławiu za nieustające
wsparcie, nieograniczoną chęć dzielenia się wiedzą, ogromną wyrozumiałość
oraz otwarcie drzwi do świata międzynarodowej nauki.

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nieskończoną cierpliwość i chęć pomocy na każdym etapie mojego rozwoju
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do mnogich wyjazdów i zarwanych nocy, za nieustanną pomoc i szczerą chęć
słuchania o niezliczonych projektach naukowych

Spis treści:

1. CYKL PRAC STANOWIĄCYCH ROZPRAWĘ DOKTORSKĄ

1. **Krajewski PK**, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Adv Dermatol Allergol. 2021;38(6):967-972
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2. **Krajewski PK**, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology. 2022;39(6):1053-1058.
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3. **Krajewski PK**, Marrón SE, Gomez-Barrera M, Tomas-Aragones L, Gilaberte-Calzada Y, Szepietowski JC. The use of HSQoL-24 in an assessment of quality-of-life impairment among hidradenitis suppurativa patients: first look at real-life data. J Clin Med. 2021;10(22).
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4. **Krajewski PK**, Marrón SE, Tomas Aragones L, Gilaberte-Calzada Y, Szepietowski JC. Self-reported hidradenitis suppurativa severity: is it useful for clinical practice? Dermatol Ther. 2022;12(4):899-909
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IF = 3,251; Punkty MEiN = 70

7. **Krajewski PK**, Szukala W, Lichawska-Cieslar A, Matusiak L, Jura J, Szepietowski JC. MCPIP1/Regnase-1 expression in keratinocytes of patients with hidradenitis suppurativa: preliminary results. Int J Mol Sci. 2021;22(14)
   IF = 6,208; Punkty MEiN =140

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   IF = 15,487; Punkty MEiN = 140

Sumaryczny IF: 41,509

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2. WYKAZ SKRÓTÓW

HS	Hidradenitis suppurativa
IL	Interleukina (ang. *interleukin*)
TNF-α	Czynnik martwicy nowotworu alfa (ang. *tumor necrosis factor alpha*)
DLQI	Dermatologiczny Kwestionariusz Oceny Jakości Życia (ang. *Dermatology Life Quality Index*)
MCPIP1	Białko chemotaktyczne monocytów-1 indukowane białkiem-1 (ang. *Monocyte chemotactic protein-1-induced protein-1*)
BMI	Wskaźnik masy ciała (ang. *body mass index*)
NRS	Numeryczna Skala Oceny (ang. *Numerical Rating Scale*)
VRS	Słowna Skala Oceny (ang. *Verbal Rating Scale*)
USG	Ultrasonografia
HiSQoL	Kwestionariusz jakości życia hidradenitis suppurativa (ang. *Hidradenitis Suppurativa Quality of Life*)
HSQoL-24	Kwestionariusz jakości życia hidradenitis suppurativa – 24 (ang. *Hidradenitis Suppurativa Quality of Life – 24*)
ICC	Współczynnik korelacji wewnątrzklasowej (ang. *Intraclass Correlation Coefficient*)
IHS4	Międzynarodowy system oceny ciężkości Hidradenitis Suppurativa (ang. *International Hidradenitis Suppurativa Severity Score System*)

3. OMÓWIENIE ROZPRAWY DOKTORSKIEJ

3.1. Wstęp

Hidradenitis suppurativa (HS) jest przewlekłą, wieloczynnikową, nawracającą i wyniszczającą zapalną chorobą jednostki włosowo-łojowej. Jej częstość występowania szacowana jest na około 0,1%-1% populacji. Choroba zwykle rozpoczyna się we wczesnej dorosłości, najczęściej po okresie dojrzewania, jednak coraz częściej pojawiają się doniesienia o występowaniu tej jednostki chorobowej u dzieci. Przebieg HS charakteryzuje się tworzeniem mnogich, podskórnych, bolesnych guzków zapalnych, ropni, drenujących przetok oraz blizn. Zmiany skórne lokalizują się przede wszystkim w obrębie fałdów skórnych, a także okolic pachowych, pachwinowych, pośladkowych i okolicy okołoodbytniczej. Patogeneza choroby nie została jeszcze w pełni poznana. Możliwe mechanizmy powstawania zmian skórnych obejmują hiperkeratozę i czopowanie ujść mieszków włosowych, predyspozycje genetyczne, przewlekły stan zapalny, i wtórne zakażenie bakteryjne. Często podkreślana jest rola nadprodukcji cytokin prozapalnych (w tym TNFα, IL-1β, IL-6 czy IL-17), jak i upośledzony mechanizm ich hamowania. Udowodniono, że selektywna supresja stanu zapalnego przy użyciu leków biologicznych jest korzystna w leczeniu. HS powoduje znaczne upośledzenie jakości życia pacjentów i ich rodzin, zwiększoną częstością występowania depresji, lęku, podwyższonego poziomu stygmatyzacji, aleksytymii oraz anhedonii. Choroba prowadzi do problemów socjoekonomicznych, częstszych zwolnień z pracy, a nawet do zwiększonej częstości samobójstw. Ze względu na nasilenie dolegliwości, ropną wydzielinę, zapach i ból HS jest często określana jako „najgorsza dermatoza". Ze względu na odmienne, bardzo charakterystyczne cechy obrazu klinicznego HS i powszechnie używane w dermatologii skale oceniające jakość życia pacjentów, takie jak np. Dermatology Life Quality Index (DLQI), nie mogą adekwatnie odzwierciedlać cierpienia pacjentów. Leczenie HS składa się przede wszystkim z leczenia przeciwzapalnego przy pomocy leków miejscowych, antybiotyków i leków biologicznych, a zmiany nieodwracalne opracowywane są chirurgiczne. Ze względu na postępujący przebieg choroby, długi czas do postawienia prawidłowej diagnozy i nieskuteczne leczenie wyniki terapii są często niesatysfakcjonujące zarówno dla pacjentów, jak i lekarzy.

3.2. Cel badań i problemy badawcze

Celem badań wchodzących w skład rozprawy doktorskiej jest analiza upośledzenia jakości życia i objawów subiektywnych towarzyszących pacjentom chorującym na HS, określenie nowego szlaku patogenetycznego powstawania zmian skórnych oraz analiza użyteczności badania ultrasonografii wysokiej częstotliwości w diagnostyce i leczeniu HS.

3.3. Cele szczegółowe

3.3.1. Stworzenie i walidacja polskojęzycznych wersji specyficznych dla HS instrumentów wykorzystywanych do oceny jakości życia.

3.3.2. Analiza upośledzenia jakości życia wśród pacjentów z HS przy pomocy specyficznych dla HS i dermatologii narzędzi, korelacja z nasileniem choroby i czynnikami demograficznymi.

3.3.3. Analiza objawów subiektywnych towarzyszących HS, ich korelacja z nasileniem choroby i czynnikami demograficznymi.

3.3.4. Określenia udziału białka MCPIP1 i jego ewentualnych zaburzeń w patogenezie HS.

3.3.5. Określenie użyteczności ultrasonografii wysokiej częstotliwości w diagnostyce i procesie terapeutycznym HS.

3.4. Materiał i metody

Proces tłumaczenia i walidacji polskojęzycznych wersji specyficznych dla HS narzędzi wykorzystywanych do oceny jakości życia, tj. Hidradenitis Suppurativa Quality of Life (HiSQoL) oraz Hidradenitis Suppurativa Quality of Life – 24 (HSQoL-24) przeprowadzono zgodnie z międzynarodowymi wytycznymi. Anglojęzyczne wersje kwestionariuszy uzyskano od autorów, wraz ze zgodą na ich tłumaczenie i walidację. Pierwsze tłumaczenie angielsko-polskie zostało wykonane przez dwóch niezależnych tłumaczy. Następnie dwie wersje zostały przeanalizowane pod kątem spójności i słownictwa przez trzeciego konsultanta, dwujęzycznego eksperta w dziedzinie. Następnie dokonano tłumaczenia wstecznego przez kolejnych dwóch niezależnych ekspertów, którzy nie byli zaznajomieni z anglojęzycznymi wersjami kwestionariuszy. Obie wersje następnie przesyłano autorom oryginalnych

instrumentów, po dyskusji uzgodniono ostateczną wersję danego kwestionariusza. Proces walidacji obu instrumentów przeprowadzono na grupie 30 pacjentów z HS. Wszyscy pacjenci zostali poproszeni o dwukrotne wypełnienie tych kwestionariuszy w odstępie 4–5 dni. Uważa się, że taki okres jest wystarczająco krótki, aby zapobiec zmianom rzeczywistego nasilenia HS i jego wpływu na jakość życia pacjenta, a także wystarczająco długi, aby uniknąć automatycznych powtórzeń odpowiedzi pacjentów. Ponadto każdy pacjent został poproszony o wypełnienie polskiej wersji kwestionariusza DLQI celem wykonania korelacji instrumentów. Wewnętrzną zgodność kwestionariuszy oceniono współczynnikiem Cronbacha α, zarówno dla całych kwestionariuszy, jak i dla każdej domeny. Do potwierdzenia zgodności wewnętrznej przyjęto wartość współczynnika Cronbacha α wynoszącą co najmniej 0,7. Korelację między odpowiedziami z pojedynczego wypełnienia na poszczególne pytania, a także z wynikiem łącznym ustalono za pomocą testu korelacji Spearmana. Powtarzalność kwestionariusza (rzetelność: test-retest) oceniono porównując dwie odpowiedzi każdego pacjenta za pomocą współczynnika korelacji wewnątrzklasowej (Intraclass Correlation Coefficient, ICC). Podobnie jak współczynnik spójności wewnętrznej, aby wskazać odpowiednią powtarzalność wyników, ICC powinien wynosić co najmniej 0,7. Obliczono korelacje między wynikami pierwszego wypełnienia kwestionariuszy a innymi kwestionariuszami QoL. Ponadto porównano odpowiedzi na każde pytanie z pierwszego i drugiego uzupełnienia w teście rang znaków Wilcoxona w poszukiwaniu istotnych różnic.

Następnie na grupie 342 pacjentów cierpiących z powodu HS przeprowadzono ocenę jakości życia przy użyciu kwestionariusza HSQoL-24. Od każdego pacjenta zebrano dane demograficzne, takie jak płeć, wiek, wagę, wzrost, wykształcenie, stan cywilny oraz sytuację socjoekonomiczną, a także dane dotyczące choroby, tj. nasilenie choroby wg skali Hurley, długość jej trwania i dotychczasowe leczenie. Wynik całkowity HSQoL-24 oraz wyniki 6 domen kwestionariusza, zostały następnie przeanalizowanych pod kątem różnic między płciami, grupami wiekowymi, stopniami nasilenia choroby i innymi danymi demograficznymi. Dodatkowo, w obrębie tej samej grupy pacjentów, 130 chorych oceniło samodzielnie nasilenie swojej choroby przy pomocy skali werbalnej (Verbal Rating Scale), tj.: łagodna, umiarkowana i ciężka choroba. Dane te zostały następnie porównane pod kątem upośledzenia jakości życia z nasileniem choroby ocenianym według skali Hurley.

W kolejnych dwóch badaniach wykorzystano zanonimizowaną bazę pacjentów Polsko-Niemieckiego konsorcjum ekspertów zawierającą dane 1795 pacjentów leczonych z powodu HS. Od każdego pacjenta zebrano dane demograficzne, w tym wiek, płeć, wzrost, wagę, wywiad w kierunku nikotynizmu, a także dane dotyczące choroby, takie jak nasilenie według

skali Hurley, nasilenie według skali International Hidradenitis Suppurativa Severity Score System (IHS4) i najbardziej nasilony ból towarzyszący zmianom skórnym w ciągu 24 godzin przed badaniem, który oceniano według skali numerycznej od 0 do 10 punktów (Numeric Rating Scale – NRS). Pacjenci byli także poproszeni o wypełnienie dwóch kwestionariuszy oceniających jakość życia – DLQI oraz HiSQoL. W analizie uwzględniono różnice w obniżeniu jakości życia oraz nasileniu bólu w zależności od wieku, płci, wagi, BMI, a także nasilenia choroby według dwóch skal.

Aby ocenić zależność pomiędzy zaburzeniami ekspresji białka MCPIP1 a rozwojem choroby pobrano po dwie biopsje skórne od 15 pacjentów chorujących na HS, jedną ze skóry zmienionej chorobowo, a drugą ze zdrowo wyglądającej skóry w bliskim sąsiedztwie zmian skórnych. Ponadto uzyskano także 15 wycinków zdrowej skóry od pacjentów, u których wykonywano wycięcia niezłośliwych zmian skórnych. Następnie, przy pomocy PCR w czasie rzeczywistym (real time PCR – RT-PCR oceniono ekspresję mRNA MCPIP1 w pobranych biopsjach i porównano ze zdrowymi kontrolami. Ekspresję MCPIP1 na poziomie białka oznaczono metodą Western-blot. Dodatkowo wykonano specyficzne, immunologiczne barwienia do wizualizacji dystrybucji MCPIP1 w mikroskopie fluorescencyjnym. Wyniki porównano następnie z danymi demograficznymi oraz nasileniem procesu chorobowego.

W celu oceny użyteczności ultrasonografii wysokiej częstotliwości w diagnostyce i leczeniu HS przeprowadzono prospektywne, międzynarodowe, interwencyjne badanie obejmujące 63 pacjentów chorujących na HS posiadających w obrębie zmian przetoki skórne, tzw. tunele. Od każdego pacjenta został zebrany podstawowy wywiad demograficzny oraz u każdego chorego oceniono nasilenie choroby. W całej grupie badanej wykonano USG przetok skórnych przy pomocy głowicy liniowej 18 MHz, Esaote MyLab 30 Gold. U części pacjentów potwierdzono obecność dwóch hiperechogenicznych linii wewnątrz przetoki, które nazwano „objawem torów kolejowych". Następnie pacjenci przyjmowali adalimumab zgodnie z międzynarodowymi wytycznymi (160 mg początkowej dawki i 80 mg co dwa tygodnie) i byli poddawani kontrolnemu badaniu, włączając w to badanie ultrasonograficzne, w 12 i 24 tygodniu.

3.5. Podsumowanie wyników

Polskojęzyczne wersje kwestionariuszy HiSQOL oraz HSQoL-24 wykazały bardzo dobrą spójnością wewnętrzną (współczynnik α Cronbacha wyniósł 0,96 dla HiSQoL oraz 0,91 dla HSQoL-24). Cechowały się także doskonałą powtarzalność ze współczynnikami korelacji wewnątrzklasowej (ICC) wynoszącymi dla całych skal 0,97 dla HiSQoL oraz 0,91 dla HSQoL-

24. Dobrą lub bardzo dobrą spójność wewnętrzną wykazały także podskale obu kwestionariuszy. Wykazano także umiarkowane do silnych korelacje pomiędzy pojedynczymi pytaniami i wynikiem ogólnym obu skal. Ponadto udokumentowano, że obie skale silnie ze sobą korelują (r=0.579, p=0.001), a HSQoL-24 dodatkowo koreluje silnie z DLQI (r=0.559, p=0.001).

Postrzegane upośledzenie jakości życia z powodu HS w badanej grupie oceniono jako poważne, a średni wynik w skali HSQoL-24 wyniósł 58,3 ± 21,0 punktów. Podobne wyniki zaobserwowano w każdej domenie jakości życia poza osobistą, dla której średni wynik był istotnie niższy (37,4 ± 25,1 punktów, co wskazuje na umiarkowane upośledzenie jakości życia). Kobiety zgłaszały istotnie wyższe ogólne pogorszenie jakości życia w porównaniu z mężczyznami (61,6 ± 19,2 punktów vs. 51,1 ± 23,1 punktów, p<0,001). Jeśli chodzi o sytuację mieszkaniową, pacjenci mieszkający z rodziną uzyskali wyższą punktację (wskazując na wyższy poziom upośledzenia jakości życia) niż pozostałe grupy (62,1 ± 19,7 punktów vs. 48,9 ± 22,3 punktów vs. 26,6 ± 20,91 punktów, p<0,001). Ta statystycznie istotna różnica była widoczna nie tylko w wyniku globalnym, ale także w wynikach domeny psychospołecznej, ekonomicznej, zawodowej i klinicznej. Co ciekawe, grupą, której jakość życia była najmniej obniżona, zarówno w całkowitej sumie punktów, jak i wynikami dla każdej domeny, byli pacjenci mieszkający samotnie. Poziom upośledzenia jakości życia korelował dodatnio z liczbą dotkniętych obszarów skóry (r=0,285, p<0,001). Podobnie czas trwania choroby korelował dodatnio z wynikiem całkowitym HSQoL-24 (r = 0,173, p=0,001), natomiast wiek w momencie wystąpienia pierwszych objawów chorobowych korelował ujemnie z wynikiem całkowitym HSQoL-24 (r =−0,182, p=0,001). Nasilenie HS miało duży wpływ na poziom upośledzenia jakości życia; pacjenci z ciężkim przebiegiem schorzenia uzyskali wyższą punktację (69,0 ±18,5 punktów) niż chorzy z umiarkowanym (62,1±17,6 punktów) czy łagodnym (46,0 ±19,4 punktów) nasileniem choroby (p<0,001).

Większość pacjentów oceniła swoją chorobę jako łagodną (76 pacjentów, 58,5%), następnie umiarkowaną (31 pacjentów, 23,8%), a tylko 23 pacjentów (17,7%) oceniło swoją chorobę jako ciężką. Ponadto mężczyźni istotnie częściej zgłaszali przebieg choroby o łagodnym przebiegu niż kobiety (odpowiednio 70,9% i 49,3%; p=0,014). Nasilenie HS według skali Hurley oceniono najczęściej jako Hurley II (47,7%), następnie jako Hurley III u 26,9%, a Hurley I tylko u 25,4% chorych. Samoocena nasilenia HS korelowała dodatnio z wpływem choroby na jakość życia pacjentów ocenianą za pomocą DLQI (r=0,288, p<0,001). Stwierdzono również

dodatnią, silną korelację między zgłaszanym przez pacjentów nasileniem HS a pogorszeniem jakości życia ocenianym za pomocą HSQoL-24 (r=0,404, p=0,001). Nie stwierdzono natomiast statystycznie istotnej korelacji dla stopni klasyfikacji według skali Hurley z DLQI ani HSQoL-24. Co więcej, istniała znacząca różnica zarówno w całkowitym wyniku DLQI, jak i HSQoL-24 wśród różnych nasileń HS zgłaszanych przez pacjentów. Takiej różnicy nie obserwowano dla żadnego z narzędzi badających jakość życia i nasilenia choroby według skali Hurley.

Postrzegany wpływ HS na jakość życia oceniany przy pomocy skali DLQI w badanej grupie był bardzo duży (średnia DLQI: 13,2 ± 8,1 punktów). Kobiety zgłaszały istotnie większe pogorszenie jakości życia niż mężczyźni (14,2 ± 8,0 vs. 11,5 ± 8,0 punktów, p<0,001). Zgodnie z punktami odcięcia skali DLQI, najczęściej obserwowano bardzo duży wpływ choroby na jakość życia pacjentów (36% pacjentów), a następnie ekstremalnie duży (22%), umiarkowany (21%) i mały (15%). Tylko 6% pacjentów zgłosiło, że ich choroba nie miała wpływu na jakość ich życia. Obserwowano istotnie wyższy odsetek kobiet doświadczających niezwykle dużego wpływu na jakość życia w porównaniu do mężczyzn (25% vs. 16%, p<0,001). Nasilenie HS, ocenione przy pomocy skali IHS4 korelowało dodatnio z upośledzeniem jakości życia (r = 0,306, p < 0,001). Jeśli chodzi o obszary dotknięte chorobą, wśród pacjentów z rozprzestrzeniającą się chorobą największe upośledzenie życia zgłaszali pacjenci z zajęciem szyi (14,7 ± 8,3 punktów, p < 0,001), a zajęcie kończyn dolnych powodowało najniższą redukcję jakości życia (11,9 ± 7,9 punktów, p < 0,001). Ponadto upośledzenie jakości życia wykazywało istotną dodatnią korelację z wiekiem i BMI; jednak w obu przypadkach stopień korelacji był słaby (r = 0,1, p < 0,001). Stwierdzono istotną różnicę (p < 0,001) w pogorszeniu jakości życia wśród osób palących tytoń i niepalących (odpowiednio 13,9 ± 8,1 i 12,4 ± 8,0 punktów).

Ból w ciągu ostatnich 24 godzin zgłosiło 1500 pacjentów (83,6%). Średni najgorszy ból (WP-NRS) dla całej populacji HS został oceniony na 3,9±2,9 punktów. Stwierdzono istotną statystycznie różnicę (p<0,001) pomiędzy średnim natężeniem bólu u kobiet i mężczyzn (odpowiednio 4,1±2,9 i 3,5±2,8 punktów). U ponad trzech czwartych pacjentów z HS (77,6%) ból został sklasyfikowany jako łagodny, u 15,9% jako umiarkowany, a tylko u 6,5% pacjentów był to ból silny. Dodatkowo ból był silniejszy (p<0,02) u palaczy tytoniu (4,04±2,9 punktów) niż u osób niepalących (3,7±2,8 punktów). Stwierdzono dodatnią, istotną statystycznie, choć słabą, korelację (r=0,277, p<0,001) między nasileniem bólu i ciężkością choroby ocenianą

według skali IHS4. Ponadto zaobserwowano znaczące różnice w natężeniu bólu między poszczególnymi grupami ciężkości HS (zarówno dla skali Hurley, jak i IHS4)
Nasilenie bólu było istotnie wyższe ($p<0,001$) u pacjentów z mnogimi zmianami HS (odpowiednio 4±2,9 i 3,3±2,9 punktów). Ponadto nasilenie bólu korelowało istotnie ($r=0,151$, $p<0,001$) z liczba dotkniętych obszarów skóry. Nasilenie bólu wykazywało istotną, silną korelację ($r=0,581$, $p<0,001$) z pogorszeniem jakości życia pacjentów według DLQI.

Najwyższą średnią ekspresję mRNA MCPIP1 stwierdzono w zmienionej zapalnie skórze pacjentów z HS (0,0236 ± 0,0134). Była ona znacząco wyższa niż ekspresja mRNA MCPIP1 w biopsjach zarówno zdrowych kontroli (0,0080 ± 0,0034, $p < 0,001$), jak i zdrowo wyglądającej skóry od pacjentów z HS (0,0049 ± 0,0034, $p < 0,001$). Nie wykazano statystycznie istotnych korelacji między ekspresją mRNA MCPIP1 w skórze zmienionej chorobowo a dobrze znanymi czynnikami predysponującymi do HS (otyłość i palenie). Analiza Western-blot wykazała, że ekspresja MCPIP1 była podwyższona zarówno w obrębie skóry uszkodzonej (2,5-krotny wzrost), jak i nie objętej procesem chorobowym (2,3-krotny wzrost) w porównaniu ze zdrową kontrolą. Wszystkie biopsje wykazywały podobny wzór immunofluorescencji. Specyficzne barwienie MCPIP1 było cytoplazmatyczne i obecne w naskórku, jak również w mieszkach włosowych. Immunoreaktywność MCPIP1 stwierdzono we wszystkich badanych bioptatach w ponadpodstawnych warstwach naskórka. Warstwa podstawna naskórka nie wykazywała immunoreaktywności MCPIP1. Nie było również immunoreaktywności MCPIP1 w skórze właściwej. Zarówno zmieniona, jak i niezmieniona skóra pacjentów z HS wykazywała nieprawidłową dystrybucję MCPIP1 w naskórku.

Zmiany skórne, w których obserwowano obraz „torów kolejowych” w badaniu ultrasonograficznym na początku badania wykazywały znacznie gorszą odpowiedź na terapię biologiczną (adalimumabem), z całkowitym ustąpieniem zmian (brak klinicznych i ultrasonograficznych objawów zapalenia lub drenażu) u odpowiednio 2,9% w 12. i 4,4% zmian w 24. tygodniu. Z drugiej strony, w zmianach, w których nie wykryto obrazu „torów kolejowych” na początku badania, całkowite wygojenie zmian nastąpiło w 64,7% w 12. tygodniu, a u 88,2% w 24. tygodniu. Analiza histologiczna próbek w żadnym przypadku nie wykazała obecności struktur łodygi włosa, a pozostałości komórek nabłonka wykryto w 21% przypadków. Po chirurgicznym wycięciu lub usunięciu pokrywy niereagujących na leczenie przetok, wszystkie wygoiły się bez dalszych komplikacji.

3.6. Etyka

Projekt pracy doktorskiej opartej na poniższych publikacjach został zatwierdzony przez Komisję Bioetyczną Uniwersytetu Medycznego we Wrocławiu - Nr KB 96/2023. Badanie przeprowadzono przestrzegając zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej Światowego Stowarzyszenia Lekarzy przyjętą przez 18 Zgromadzenie Ogólne Światowego Stowarzyszenia Lekarzy (WMA), w Helsinkach w czerwcu 1964 r., a zmienionej przez 64 Zgromadzenie Ogólne WMA, w Brazylii w październiku 2013 r. Badania zostały przeprowadzone z zachowaniem anonimowości uzyskanych danych.

3.7. Wnioski

3.7.1. Stworzenie polskojęzycznych wersji specyficznych dla HS kwestionariuszy HiSQoL i HSQoL-24 stwarza możliwości do rzetelnej oceny jakości życia u polskiej populacji pacjentów z HS w codziennej praktyce klinicznej i badaniach naukowych.

3.7.2. Kwestionariusz HSQoL-24 jest niezawodnym, specyficznym dla HS narzędziem do pomiaru jakości życia wśród pacjentów z HS w rzeczywistych warunkach klinicznych.

3.7.3. Samodzielna ocena ciężkości nasilenia HS wydaje się być bardziej użyteczna niż skala Hurley, szczególnie w odniesieniu do badania zależności z upośledzeniem jakości życia.

3.7.4. HS jest chorobą mającą ogromny wpływ na jakość życia chorych.

3.7.5. Codzienny ból dotyka zdecydowaną większość pacjentów z HS, a jego nasilenie koreluje z upośledzeniem jakości życia.

3.7.6. Zaburzenia ekspresji MCPIP1 na poziomie białka, jak i mRNA, mogą odgrywać rolę w powstawaniu zmian zapalnych w przebiegu HS.

3.7.7. Występowanie ultrasonograficznego obrazu „torów kolejowych” w przetokach skórnych jest samodzielnym, negatywnym czynnikiem predykcyjnym odpowiedzi na leczenie adalimumabem.

4. ARTYKUŁ PIERWSZY:

HIDRADENITIS SUPPURATIVA QUALITY OF LIFE (HISQOL): CREATION AND VALIDATION OF THE POLISH LANGUAGE VERSION

Original paper

Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version

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Abstract

Introduction: Hidradenitis suppurativa (HS) is a chronic, inflammatory and painful cutaneous disease which often has a negative influence on patients' quality of life. Dermatology-specific instruments, such as Dermatology Life Quality Index and Skindex, are commonly used to evaluate HS patients' quality of life. However, due to the lack of specific questions, these scales may not be adequate and may not reflect the real problem.
Aim: To translate and validate the Polish version of a newly created HS-specific questionnaire – Hidradenitis Suppurativa Quality of Life (HiSQOL).
Material and methods: A forward and backward translation was conducted from the original English version of the questionnaire to Polish language according to international standards. The validation was performed on a group of 30 patients suffering from HS, who completed the questionnaire twice with a 4–5 days' interval.
Results: The Polish version of HiSQOL questionnaire showed a very good internal consistency (Cronbach α coefficient was 0.96 for total score). Excellent reproducibility with the intraclass correlation coefficient (ICC) of 0.97 was demonstrated.
Conclusions: The Polish version of HiSQOL questionnaire has high internal reliability, validity and reproducibility. It can be used as a tool to assess health-related quality of life in the patients suffering from hidradenitis suppurativa.

Key words: hidradenitis suppurativa, quality of life, questionnaire.

Introduction

Hidradenitis suppurativa (HS) is a painful chronic, multifactorial and progressive inflammatory cutaneous disease of the pilosebaceous unit. It is characterized by the formation of inflamed nodules, abscesses, tunnels and scars. It predominantly affects intertriginous areas of the body, like axillae, groins, buttocks and sub-mammary region [1]. Due to the pain, discharge, foul smell and associated pruritus, HS has documented negative influence on patients' health related quality of life (HRQOL) [2, 3]. Moreover, the disease often has correlated severe socioeconomic consequences, higher incidence of depression, fear of stigmatization, and suicide [4–7].

Numerous dermatologic instruments have been developed to evaluate impact of the disease on patients' quality of life. The most frequently used are dermatology-specific questionnaires, like Dermatology Life Quality Index (DLQI) [8]. However, there are also multiple disease-specific questionnaires. These are used for assessment of the quality of life related to, among others, psoriasis (Psoriasis Disability Index) [9], Acne (Cardiff Acne Disability Index) [10] or dermatitis (Infants' Dermatitis Quality of Life index) [11]. Dermatology-specific instruments, such as DLQI [8] and Skindex [12], were commonly used to evaluate HS patients' quality of life. However, due to the lack of specific questions, these scales may not be adequate and may not reflect the real problem [13].

Hidradenitis Suppurativa Quality of Life (HiSQOL) is a new, 17-item questionnaire developed in 2019 by Thorlacius *et al.* [13] by combined effort of Danish and

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American experts. It evaluates the impact of HS on the quality of life, patients' symptoms and emotions in the last 7 days.

Aim

The aim of this study was to translate and to validate the Polish language version of HiSQOL questionnaire. This would enable the use of HiSQOL in both clinical practice and research by Polish-speaking clinicians.

Material and methods

The Polish version of the HiSQOL questionnaire was translated and validated according to international standards [14]. The permission to translate the questionnaire was provided by the copyright holders.

Translation and validation

Firstly, the original English version of HiSQOL questionnaire was translated into Polish language by two independent translators (MS, JR). Then, the translated versions were compared in terms of inconsistencies by a third consultant, a bilingual expert in the field (JCS). After that, the unified version was created. Subsequently, the backtranslation from the Polish version was conducted (ŁM). The translator was not familiar with the original version of HiSQOL questionnaire. Afterwards, the back translation was sent to members of the team who created the original questionnaire (JSK, GBEJ). Minor changes were introduced according to the authors' recommendations. Finally, the Polish version of the HiSQOL questionnaire was created.

After the translation process, the validation was performed. The questionnaire was tested on a group of 30 people. All of the interviewed patients were diagnosed with HS by a specialist. They were asked to complete the questionnaire twice with a 4–5 days' interval. This period was considered sufficiently long to prevent the patients from remembering previous answers, as well as sufficiently short to prevent any significant changes in the clinical severity of HS.

Statistical analysis

The statistical analysis of the obtained results was performed with the use of IBM SPSS Statistics v. 26 (SPSS INC., Chicago, USA) software. The internal consistency of the questionnaire was evaluated with Cronbach α coefficient. The correlation between the responses from a single completion to each individual question, as well as to the total score, was established with Spearman correlation test. It is believed that to prove that the questionnaire is internally consistent, the Cronbach α coefficient should be at least 0.7, while the values above 0.90 stand for very good internal consistency [15]. The questionnaire reproducibility (test-retest reliability) was assessed by comparison of the two responses of each patient with the use of intraclass correlation coefficient (ICC). To indicate adequate reproducibility of the questionnaire, ICC, similarly to Cronbach α coefficient, should also be at least 0.7 [16]. The correlation between each item from the first and the second completion was analyzed. Moreover, answers to each question from the first and the second completion were compared using Wilcoxon signed-rank test in a search for significant differences. A 2-sided p-value ≤ 0.05 was considered to be statistically significant.

Results

The assessment of internal consistency of the Polish language version of HiSQOL showed that the different items from the questionnaire were correlated with one another. Cronbach α coefficient value for the HiSQOL total score was at 0.96, which indicated an excellent internal consistency of the translated questionnaire. Moreover, each of three subscales also had very good internal consistency with the Cronbach α coefficient values of 0.94 for activities-adaptations subscale, 0.87 for psychosocial subscale and 0.89 for symptoms subscale. Additionally, statistically significant, positive correlations were found between each question and the HiSQOL total score (Table 1). The Spearman correlation coefficient of each item and the total score of the scale was 0.500 to 0.934, and the Spearman correlation coefficient of each item was 0.224 to 0.654 (Table 1). Only one of the questions (question 16) did not statistically correlate with the rest of them, nevertheless, its correlation with total HiSQOL score was statistically significant ($r = 0.500$, $p < 0.001$). The above-presented results showed an excellent convergent validity of the translated version of the instrument.

The reproducibility of the studied questionnaire was determined using ICC and assessed as 0.966 for the whole HiSQOL. Furthermore, no statistically significant differences were found between the answers for each question obtained after completing the questionnaire twice (4–5 days' interval) (Table 2). Correlation coefficient assessed with Spearman test, between the answers obtained in the first and the second survey were analyzed. A statistically significant, positive correlations were found for each pair of answers (data not shown).

The Polish validated version of HiSQOL is contained in Appendix 1.

Discussion

Hidradenitis suppurativa is a burdensome disease with huge influence on patients' health-related quality of life. Due to the troublesome, often embarrassing symptoms, patients feel stigmatized and the disease frequently leads to depression, severe socio-economic problems and even suicide [4–7]. Because of this psychological impact,

Table 1. The correlation coefficients between the answers to each question and between the answers to each question and the total score of HiSQOL questionnaire

Item	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17
Q1	1																
Q2	0.747[a]	1															
Q3	0.655[a]	0.779[a]	1														
Q4	0.619[a]	0.630[a]	0.762[a]	1													
Q5	0.667[a]	0.697[a]	0.645[a]	0.722[a]	1												
Q6	0.588[a]	0.683[a]	0.616[a]	0.407[b]	0.725[a]	1											
Q7	0.571[a]	0.782[a]	0.538[a]	0.492[a]	0.753[a]	0.730[a]	1										
Q8	0.687[a]	0.863[a]	0.789[a]	0.699[a]	0.762[a]	0.796[a]	0.821[a]	1									
Q9	0.388[b]	0.497[a]	0.402[a]	0.407[b]	0.594[a]	0.528[a]	0.601[a]	0.573[a]	1								
Q10	0.608[a]	0.699[a]	0.600[a]	0.620a	0.705[a]	0.565[a]	0.814[a]	0.760[a]	0.591[a]	1							
Q11	0.449[a]	0.543[a]	0.586[a]	0.536[a]	0.549[a]	0.587[a]	0.631[a]	0.695[a]	0.718[a]	0.576[a]	1						
Q12	0.673[a]	0.693[a]	0.557[a]	0.560[a]	0.740[a]	0.728[a]	0.651[a]	0.747[a]	0.527[a]	0.535[a]	0.540[a]	1					
Q13	0.617[a]	0.693[a]	0.644[a]	0.606[a]	0.743[a]	0.714[a]	0.770[a]	0.818[a]	0.552[a]	0.674[a]	0.719[a]	0.676[a]	1				
Q14	0.516[a]	0.646[a]	0.614[a]	0.463[a]	0.660[a]	0.831[a]	0.709[a]	0.767[a]	0.621[a]	0.493[b]	0.761[a]	0.711[a]	0.832[a]	1			
Q15	0.500[a]	0.618[a]	0.531[a]	0.672[a]	0.613[a]	0.388[a]	0.562[a]	0.598[a]	0.399[b]	0.460[a]	0.250[b]	0.494[a]	0.497[a]	0.412b	1		
Q16	0.284[c]	0.348[b]	0.237[c]	0.145[c]	0.355[b]	0.477[a]	0.497[a]	0.369[b]	0.322[c]	0.276[c]	0.157[c]	0.258[c]	0.341[c]	0.430[b]	0.478[a]	[1]	
Q17	0.753[a]	0.830[a]	0.721[a]	0.720[a]	0.850[a]	0.750[a]	0.746[a]	0.922[a]	0.563[a]	0.678[a]	0.628[a]	0.817[a]	0.795[a]	0.721[a]	0.593[a]	0.337[b]	1
Total	0.762[a]	0.852[a]	0.777[a]	0.771[a]	0.843[a]	0.791[a]	0.806[a]	0.934[a]	0.658[a]	0.753[a]	0.709[a]	0.793[a]	0.855[a]	0.796[a]	0.661[a]	0.500[a]	0.919[a]

[a]p < 0.001; [b]p < 0.05; [c]p > 0.05.

Table 2. Reproducibility of the results

Item	1st assessment (points)	2nd assessment (points)	*P*-value
Q1	1.33 ±1.15	1.4 ±1.3	0.637
Q2	1.93 ±1.52	2.03 ±1.4	0.584
Q3	1 ±0.98	1.07 ±0.94	0.414
Q4	1.2 ±1.21	1.27 ±1.20	0.493
Q5	1.53 ±1.33	1.6 ±1.3	0.796
Q6	1.33 ±1.02	1.47 ±1.14	0.206
Q7	2.2 ±1.44	2.13 ±1.31	0.527
Q8	1.83 ±1.18	1.7 ±1.21	0.285
Q9	1.77 ±1.17	1.8 ±1.16	0.926
Q10	2.2 ±1.35	2.2 ±1.32	1
Q11	1.77 ±1.25	1.73 ±1.08	0.705
Q12	1.63 ±1.19	1.5 ±1.20	0.206
Q13	1.8 ±1.24	1.77 ±1.28	0.851
Q14	1.7 ±1.26	1.67 ±1.32	0.666
Q15	1.67 ±1.63	1.6 ±1.57	0.317
Q16	1.33 ±1.43	1.43 ±1.33	0.889
Q17	1.4 ±1.3	1.2 ±1.27	0.132
Total score	27.63 ±17.19	27.57 ±16.89	0.602

the psychometric assessment plays a significant role in the diagnosis and the treatment choice in these patients. The HiSQOL is a new, HS-specific, 17-item questionnaire divided into 3 subscales: activities-adaptations, psychosocial and symptoms. In comparison to the existing dermatology-specific instruments, HiSQOL identifies all the important aspects for HS patients, which are often absent in the above-mentioned questionnaires (e.g. pus drainage or odor). Besides HiSQOL, there are two HS-specific questionnaires. Hidradenitis Suppurativa Burden Of Disease (HSBOD) [17], a 19-item instrument with answers on visual analog scale, and Hidradenitis Suppurativa Quality of Life (HS-QoL) [18], a questionnaire with 44 items and a 6-month recall period. Nevertheless, HiSQOL is different from existing instruments. It is the only one for which full psychometric evaluation was performed and published. Moreover, it consists of three subscales which may be used independently or to generate a total score.

This study describes the process of development and validation of the Polish language version of HiSQOL questionnaire. The analysis of internal consistency was performed on the basis of the results obtained after a single completion of the questionnaire. Statistically significant, positive correlation was found between each question and HiSQOL total score. Additionally, the internal consistency was at a very high level, with Cronbach α value of 0.96 for HiSQOL total score and 0.87–0.94 for three subscales. Our results are similar to those obtained by the authors of the original version of questionnaire (0.94 for total score, 0.81–0.88 for subscales). The reproducibility of the instrument was evaluated with the use of ICC. We achieved an excellent reproducibility with the value of ICC of 0.97 for the whole questionnaire, which was actually even higher than in the original version (0.90) [19].

To the best of our knowledge, this is the first translation and validation of HiSQOL questionnaire from English to another language. Similar projects were conducted with other instruments. Among them, our group [20, 21] successfully created and validated Polish and Arabic versions of 6-item Stigmatization Scale and 33-item Feelings of Stigmatization Questionnaire. In both of them, we achieved the Cronbach α value of 0.94 for the Polish and 0.89 for the Arabic version [20, 21]. Moreover, Szepietowski *et al.* [22] also performed a translation and validation of Dermatology Life Quality Index (DLQI) and obtained very good results with Cronbach efficient value of 0.9.

The recently developed Polish language HiSQOL questionnaire showed a high internal consistency and a good reproducibility. Our results indicate, that this version of the instrument may be used for assessment of HRQOL, both in everyday patients care, as well as in the research programs. Moreover, in the presented paper we have shown a detailed and appropriate way of translation and validation of foreign language questionnaires. It needs to be emphasized that proper validation should be conducted for every questionnaire used in clinical practice.

Conflict of interest

The authors declare no conflict of interest.

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Appendix 1

Ten kwestionariusz jest zaprojektowany do pomiaru, jaki wpływ na Panią (Pana) ma *hidradenitis suppurativa* (HS) – trądzik odwrócony

PROSZĘ ZAPOZNAĆ SIĘ Z PONIŻSZĄ INSTRUKCJĄ:

Ważne jest, aby:

1) rozważyć wpływ HS na Pani (Pana) życie **w ciągu ostatnich 7 dni**.

2) myśleć **jedynie o HS**, nie o innych dolegliwościach.

3) w **każdej linijce proszę wybrać jedną najlepszą (najbardziej trafną) odpowiedź**.

Dla każdego punktu proszę wybrać jedną najlepszą (najbardziej trafną) odpowiedź.

W ciągu ostatnich 7 dni, jak bardzo HS sprawiał problemy z:	**Niemożliwe do wykonania z powodu HS**	**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
1) chodzeniem (nie dla ćwiczeń)	[ ]					
2) ćwiczeniem (np. pływaniem, joggingiem, jazdą na rowerze, jogą, aerobikiem)	[ ]					
3) snem						
4) myciem się						
5) ubieraniem się						
6) koncentracją						

W ciągu ostatnich 7 dni, jak obecne lub potencjalnie nowe zmiany HS wpływały na:	**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
7) wybór ubioru, aby uniknąć dyskomfortu					

W ciągu ostatnich 7 dni, jak bardzo dokuczliwy był:	**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
8) ból					
9) świąd					
10) drenaż (sączenie)					
11) nieprzyjemny zapach					

W ciągu ostatnich 7 dni, jak bardzo HS powodował odczucie:	**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
12) przygnębienia lub depresji					
13) zakłopotania					
14) niepokoju lub nerwowości					

W ciągu ostatnich 7 dni, jak bardzo HS:			**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
15) utrudniał aktywność seksualną	Nie jestem aktywny seksualnie [ ]	Niemożliwe do wykonania z powodu HS [ ]					
16) wpływał na pragnienie aktywności seksualnej							

W ciągu ostatnich 7 dni, jak bardzo HS:			**Ekstremalnie**	**Bardzo**	**Umiarkowanie**	**Nieznacznie**	**Wcale**
17) wpłynął na zdolność do pracy lub nauki	Nie pracuję i nie studiuję [ ]	Niemożliwe do wykonania z powodu HS [ ]					

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5. ARTYKUŁ DRUGI:

HIDRADENITIS SUPPURATIVA QUALITY OF LIFE 24 (HSQOL-24) NOW AVAILABLE FOR POLISH PATIENTS: CREATION AND VALIDATION OF THE POLISH LANGUAGE VERSION

Original paper

Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version

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Abstract:

Introduction: Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disorder with a well-documented impact on quality of life (QoL). Due to the very distinctive features of HS the clinical picture, and lack of specific questions, generic dermatology QoL questionnaires cannot adequately reflect patients' suffering.

Aim: To translate and validate the Polish version of the Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) questionnaire.

Material and methods: The standardized translation process included forward and backward translation from the English version of the instrument. The final version was subsequently validated on a group of 30 HS patients, who completed the questionnaire twice. Internal consistency, test-retest reliability, and reproducibility of the results were also analysed.

Results: The Polish version of HSQoL-24 showed excellent internal consistency, with a Cronbach α coefficient of 0.908. Moreover, excellent reproducibility of the results was observed, with an intraclass correlation coefficient of 0.908. The HSQoL global score correlated positively with Dermatology Life Quality Index (DLQI) and Hidradenitis Suppurativa Quality of Life (HiSQoL) questionnaire.

Conclusions: The Polish version of HSQoL-24 has excellent internal consistency, good reproducibility, and adequate validity. It may be of help in assessing QoL impairment in HS patients in daily practice and research.

Key words: hidradenitis suppurativa, quality of life, questionnaire, HSQoL-24.

Introduction

Hidradenitis suppurativa (HS) is a chronic, debilitating, inflammatory skin disease, which has an enormous influence on patients' quality of life (QoL) [1]. It is characterized by the formation of deeply seated inflammatory nodules, abscesses, perforating sinuses, and scarring in the intertriginous skin areas, like armpits, skin folds, and anogenital region [2]. Due to constant purulent discharge, unpleasant smell, debilitating pain, and associated itch, HS causes immense QoL impairment and is considered the worst dermatosis [3, 4]. It was proven that the QoL decrease in HS patients is higher or similar to those suffering from congestive heart failure or depression [5]. The assessment of QoL is a crucial part of dermatology and a holistic approach to dermatological patients. Due to very distinctive features of clinical picture of HS and the lack of specific questions, generic dermatology QoL questionnaires, including the Dermatology Life Quality Index (DLQI), cannot adequately reflect patients' suffering [6]. Currently, there are 4 properly vali-

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dated HS-specific health-related quality of life (HRQoL) instruments, among them the Hidradenitis Suppurativa Quality of Life-24 (HSQoL-24) questionnaire [1].

Aim

The aim of this study was to perform a translation of the HSQoL-24 instrument to Polish language, and its subsequent validation process.

Material and methods

The process of translation and validation of the Polish version of HSQoL-24 was performed according to international guidelines on the methods to translate health-related quality of life questionnaires [7]. The study was performed in line with guidelines for human studies and the World Medical Association Declaration of Helsinki, and it was accepted by the Ethics Committee of Wroclaw Medical University. Participation in the study was voluntary, and all patients agreed to participate. Demographic data of the patients are shown in Table 1.

Translation

The English version of the HSQoL-24 instrument was obtained from the authors with permission to translate and validate it [8]. The first English-Polish translation was performed by 2 independents translators (KT, MS). Then, those 2 versions were analysed in terms of consistency and wording by a third consultant, a bilingual expert in the field (JCS). Subsequently, a backwards translation was performed by 2 independent experts, who were not familiar with the English version of the questionnaire (KB, LM). The 2 versions were later sent to the authors of the original HSQoL-24 (SEM, LTA), who, after discussion, agreed on the final version of the questionnaire.

Table 1. Patients' characteristic

Characteristic		Results
Age [years] mean ± SD		37.47 ±10.77
BMI [kg/m^2] mean ± SD		32.12 ±7.50
Duration of the disease [years] mean ± SD		11.41 ±7.22
Professionally active, *n* (%)		24 (80.00)
Living alone, *n* (%)		2 (3.30)
Education, *n* (%)	Higher	13 (21.7)
	Professional	3 (10)
	Secondary	11 (36.7)
	Primary	3 (10)
Hidradenitis suppurativa treatment, *n* (%)		26 (86.7)
Pharmacological treatment, *n* (%)		26 (86.7)
Surgical treatment, *n* (%)		16 (53.3)

BMI – body mass index, SD – standard deviation, n – number of patients.

Validation

The validation process was conducted on a group of 30 HS patients, who were treated in the department of dermatology. All of them were previously diagnosed with HS by an expert in the field. All the patients were asked to complete the HSQoL-24 questionnaire twice, with an interval of 4 to 5 days. Such a period is thought to be short enough to prevent changes in the actual HS severity and its influence on the patients' QoL, and long enough to avoid repetition patients' answers. Moreover, each patient was also asked to complete Polish versions of the Dermatology Life Quality Index (DLQI) [9] and Hidradenitis Suppurativa Quality of Life (HiSQoL) [10] questionnaires for HSQoL-24 convergent validation.

Statistical analysis

The statistical analysis of the data was performed with the use of IBM SPSS Statistics v. 26 (SPSS INC., Chicago, USA) software. The internal consistency of the questionnaire was evaluated with Cronbach α coefficient for the whole questionnaire and for every domain. A Cronbach α coefficient of at least 0.7 was considered as confirmation of the internal consistency, while a value above 0.9 meant very good internal consistency [11]. The correlation between the responses from a single completion to each individual question, as well as to the total score, was established with the Spearman correlation test. The questionnaire reproducibility (test-retest reliability) was assessed by comparison of the 2 responses of each patient with the use of the intraclass correlation coefficient (ICC). Similarly to the internal consistency coefficient, to indicate adequate reproducibility of the results the ICC had to be at least 0.7 [12]. The correlations between results from HSQoL-24 first completion and other QoL questionnaires were calculated. Moreover, answers to each question from the first and the second completion were compared by the Wilcoxon signed-rank test to search for significant differences. A 2-sided *p*-value ≤ 0.05 was considered to be statistically significant.

Results

The results of the internal consistency calculation of the Polish language version of the HSQoL-24 questionnaire proved that all the items correlated with each other. The Cronbach α coefficient for the Polish version of HSQoL-24 global score of 0.908 reflects excellent internal consistency. Moreover, similar results were obtained for almost all of the questionnaire domains: 0.916 for psychosocial, 0.819 for economic, 0.919 for employment, 0.842 for social interaction, and 0.78 for clinical. Only the personal domain did not present satisfactory internal va-

lidity, with a Cronbach α coefficient of 0.460; however, it did not influence the internal consistency of the whole instrument. Positive, significant correlations were found between answers to each question and the HSQoL-24 global score (Table 2). The Spearman correlation coefficient for every item and the total score varied from 0.369 to 0.815, indicating moderate to strong correlations. Only Questions 4 and 22 did not show any correlation with total score, but they correlated positively with other answers (Table 2). All the above-mentioned results demonstrated very good convergent validity of the translated version of the questionnaire.

The repeatability of the results was assessed with the use of the ICC as 0.908 for the HSQoL-24 global score. Moreover, no differences in most questions were found between first and second completion (Table 3). Only answers to questions 1, 9, and 17 differed between each completion, but it did not interfere with the reproducibility of the questionnaire global score. Moreover, statistically significant, positive correlations were obtained between the answers in the first and second survey (detailed data not shown).

The convergent validity of the Polish version of the questionnaire was confirmed. Statistically significant, positive, moderate correlations were found with DLQI ($r = 0.579$, $p = 0.001$) and HiSQoL total score ($r = 0.559$, $p = 0.001$) (Figures 1, 2).

The Polish version of the validated questionnaire is shown in Supplementary material.

Table 2. Reproducibility of the results

Item (mean ± SD)	1st assessment [points]	2nd assessment [points]	*P*-value
Q1	1.8 ±1.06	1.47 ±1.01	0.033*
Q2	1.5 ±1.01	1.43 ±0.97	0.653
Q3	1.0 ±0.74	0.80 ±0.85	0.109
Q4	1.97 ±0.96	1.57 ±1.07	0.027
Q5	0.87 ±1.20	0.6 ±0.81	0.033
Q6	1.9 ±0.96	1.93 ±1.08	0.851
Q7	0.17 ±0.46	0.17 ±0.46	1
Q8	1.73 ±1.39	1.67 ±1.35	0.593
Q9	2.0 ±1.11	1.63 ±1.16	0.016*
Q10	1.47 ±1.14	1.57 ±0.97	0.499
Q11	1.43 ±1.28	1.27 ±1.28	0.449
Q12	1.9 ±1.27	1.73 ±1.20	0.244
Q13	1.97 ±1.33	1.63 ±1.30	0.083
Q14	1.3 ±0.99	1.27 ±0.91	0.705
Q15	0.97 ±1.0	0.70 ±0.95	0.065
Q16	1.43 ±1.07	1.2 ±1.06	0.108
Q17	0.5 ±0.86	0.93 ±1.14	0.013*
Q18	1.93 ±1.14	1.73 ±1.08	0.130
Q19	1.67 ±1.35	1.70 ±1.32	0.830
Q20	0.7 ±0.88	0.47 ±0.57	0.058
Q21	1.07 ±0.74	1.03 ±0.96	0.830
Q22	0.93 ±0.98	1.13 ±0.90	0.243
Q23	1.3 ±0.84	1.53 ±0.97	0.090
Q24	2.0 ±1.13	1.80 ±1.10	0.242
Total score	33.5 ±14.38	30.97 ±13.6	0.371

*Q – question, SD – standard deviation, *p-value < 0.05.*

Discussion

The huge Impact of HS on QoL is well-documented [1, 3]. The associated symptoms, frequently embarrassing and troublesome, are directly connected with the feeling of stigmatization, marginalization, and loneliness [13, 14]. HS is associated with high incidence of severe socio-economic problems with decreased work productivity and longer absence [15]. Moreover, it is associated with higher prevalence of sleep impairment or insomnia, sexual problems, depression, alexithymia, and even suicidal thoughts [4, 16–18]. Besides the obvious influence on patients who suffer from HS, the disease also affects their partners and families, and can lead to intimate partner violence and intimidation [19, 20]. Therefore, there is a need for adequate assessment of patients' QoL impairment and the creation of disease-specific QoL instruments. The HSQoL-24 instrument is a Spanish HS-specific questionnaire developed by Marrón *et al.* [21] in 2019. It consists of 24 self-administered items evaluating 6 life domains (psychosocial, economic, occupational, relationships, personal, and clinical) in a 4-week recall period. Each item is scored on a 5-point Likert scale (0 = never and 4 = always). Three items [6, 17, 22] are scored inversely. The global score is calculated by adding answers of each score. The maximum score is 96 points, while the minimum is 0 points, and the higher the score, the bigger the effect on the patient's QoL. The conversion of the score to a percentage requires the multiplication of each score by the domain coefficient: global score: 1.0412; psychosocial: 2.08; economic: 25.0; employment: 12.5; social interaction: 6.25; personal: 12.5; clinical: 8.33. total score: 1.0412; psychosocial: 2.08; economic: 25.0; employment: 12.5; social interaction: 6.25; personal: 12.5; clinical: 8.33 [21]. The questionnaire was translated and validated into English in 2021 by the same group [21].

The Polish version of HSQoL-24 showed comparable but slightly higher internal consistency than the English version with a Cronbach α for global score of 0.908 and 0.866, respectively [21]. Moreover, additional consistency analysis was performed for each domain of the Polish version. The validity of newly translated version was comparable to its English equivalent. Both correlated positively with DLQI with Spearman coefficients of 0.579 for the Polish and 0.690 for the English version ($p = 0.001$ and $p < 0.001$, respectively). Although the authors of the original questionnaire performed the second convergent

Table 3. Correlations between answers to every question and the total score of Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24)

Spearman coefficient	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q 8	Q 9	Q 10	Q 11	Q 12	Q 13	Q 14	Q 15	Q 16	Q 17	Q 18	Q 19	Q 20	Q 21	Q 22	Q 23	Q 24	Total
Q 1	1																								
Q 2	0.179[c]	1																							
Q 3	0.735[b]	0.360[c]	1																						
Q 4	0.521[b]	0.252[c]	0.491[b]	1																					
Q 5	0.573[b]	0.337[c]	0.624[b]	0.060[c]	1																				
Q 6	0.373[a]	–0.078[c]	0.358[c]	0.279[c]	0.040[c]	1																			
Q 7	0.368[a]	0.208[c]	0.536[b]	0.151[c]	0.488[b]	0.157[c]	1																		
Q 8	0.395[a]	0.441[a]	0.408[a]	0.235[c]	0.449[a]	0.181[c]	0.265[c]	1																	
Q 9	0.417[a]	0.312[c]	0.375[a]	0.193[c]	0.254[c]	0.284[c]	0.249[c]	0.604[b]	1																
Q 10	0.377[a]	–0.078[c]	0.294[c]	–0.087[c]	0.514[b]	0.178[c]	0.394[a]	0.212[c]	0.111[c]	1															
Q 11	0.585[b]	0.241[c]	0.526[b]	–0.024[c]	0.735[b]	–0.147[c]	0.384[a]	0.403[a]	0.326[c]	0.627[b]	1														
Q 12	0.597[b]	0.175[c]	0.627[b]	0.119[c]	0.653[b]	0.109[c]	0.362[a]	0.395[a]	0.413[a]	0.615[b]	0.806[b]	1													
Q 13	0.175[c]	0.252[c]	0.430[a]	0.075[c]	0.206c	0.109[c]	0.472[b]	0.205[c]	0.402[a]	0.062[c]	0.300[c]	0.437[a]	1												
Q 14	0.483[b]	0.183[c]	0.458[a]	0.124[c]	0.493[b]	0.453[a]	0.468[b]	0.328[c]	0.500[b]	0.102[c]	0.279[c]	0.317[c]	0.507[b]	1											
Q 15	0.473[b]	0.320[c]	0.563[b]	0.135[c]	0.516[b]	0.189[c]	0.448[a]	0.507[b]	0.586[b]	0.127[c]	0.515[b]	0.506[b]	0.710[b]	0.805[b]	1										
Q 16	0.631[b]	0.170[c]	0.505[b]	0.072[c]	0.697[b]	0.287[c]	0.386[a]	0.375[a]	0.411[a]	0.609[b]	0.674[b]	0.693[b]	0.204[c]	0.421[a]	0.460[a]	1									
Q 17	0.505[b]	0.024[c]	0.460[a]	0.244[c]	0.450[a]	0.256[c]	0.110[c]	–0.025[c]	–0.150[c]	0.269[c]	0.276[c]	0.222[c]	–0.188[c]	0.299[c]	0.228[c]	0.365[a]	1								
Q 18	0.653[b]	0.244[c]	0.665[b]	0.151[c]	0.513[b]	0.371[a]	0.381[a]	0.440[a]	0.689[b]	0.364[a]	0.642[b]	0.741[b]	0.517[b]	0.607[b]	0.717[b]	0.702[b]	0.186[c]	1							
Q 19	0.442[a]	0.062[c]	0.232[c]	–0.226[c]	0.536[b]	0.196[c]	0.199[c]	0.190[c]	0.239[c]	0.645[b]	0.635[b]	0.543[b]	0.093[c]	0.229[c]	0.219[c]	0.638[b]	0.144[c]	0.598[b]	1						
Q 20	0.124[c]	0.144[c]	0.245[c]	0.074[c]	0.183[c]	0.219[c]	0.089[c]	0.437[a]	0.541[b]	0.198[c]	0.264[c]	0.214[c]	0.256[c]	0.473[b]	0.559[b]	0.221[c]	0.147[c]	0.437[a]	0.016[c]	1					
Q 21	0.246[c]	0.056[c]	0.185[c]	–0.078[c]	0.481[b]	0.091[c]	0.241[c]	–0.066[c]	0.105[c]	0.161[c]	0.310[c]	0.415[a]	0.198[c]	0.557[b]	0.310[c]	0.444[a]	0.230[c]	0.310[c]	0.359[c]	0.017[c]	1				
Q 22	0.348[c]	–0.057[c]	0.446[a]	0.385[a]	0.135[c]	0.442[a]	0.114[c]	0.050[c]	0.109[c]	0.174[c]	0.027[c]	0.148[c]	0.012[c]	0.036[c]	0.080[c]	0.126[c]	0.448[a]	0.181[c]	0.037[c]	0.043[c]	–0.103[c]	1			
Q 23	0.437[a]	0.480[b]	0.608[b]	0.360[c]	0.483[b]	0.063[c]	0.526[b]	0.428[a]	0.325[c]	–0.014[c]	0.227[c]	0.242[c]	0.240[c]	0.359[c]	0.430[a]	0.169[c]	0.243[c]	0.194[c]	–0.091[c]	–0.004[c]	0.159[c]	0.226[c]	1		
Q 24	0.397[a]	0.332[c]c	0.387[a]	0.510[b]	0.154[c]	0.138[c]	0.109[c]	0.261[c]	0.128[c]	–0.052[c]	0.072[c]	0.052[c]	0.091[c]	0.318[c]	0.348[c]	0.145[c]	0.335[c]	0.234[c]	–0.032[c]	0.156[c]	0.135[c]	0.303[c]	0.479[b]	1	
Total	0.804[b]	0.369[a]	0.815[b]	0.339[c]	0.780[b]	0.361[a]	0.520[b]	0.593[b]	0.595b[b]	0.505[b]	0.736[b]	0.778[b]	0.484[b]	0.653[b]	0.751[b]	0.784[b]	0.412[a]	0.849[b]	0.537[b]	0.417[a]	0.387[a]	0.337[c]	0.468[b]	0.402[a]	1

[a]*P < 0.001;* [b]*p < 0.05;* [c]*p > 0.05; Q – question.*

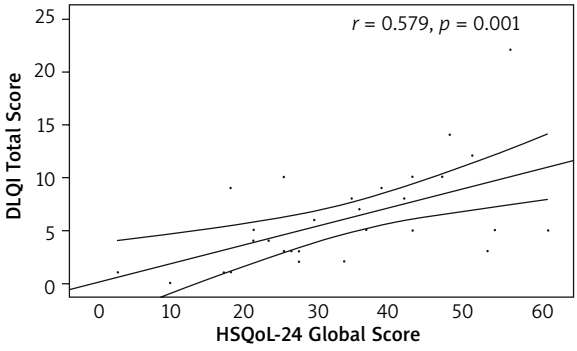

Figure 1. Correlation of the Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) global score and Dermatology Life Quality Index (DLQI) total score

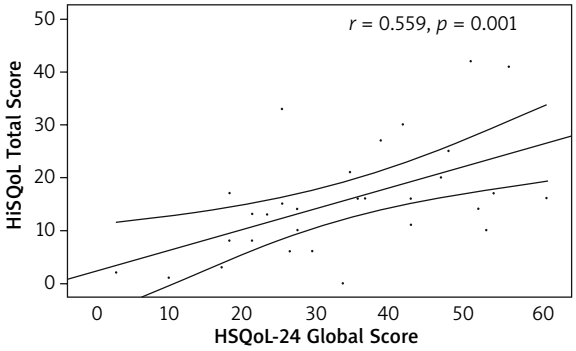

Figure 2. Correlation of the Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) global score and Hidradenitis Suppurativa Quality of Life (HiSQoL) total score

validation with Skindex-29, obtaining strong positive correlation, we used another HS-specific questionnaire. The moderate, positive correlation with HiSQoL total score ($r = 0.559$, $p = 0.001$) was obtained, indicating adequate validity of the newly translated instrument.

Our group conducted similar projects for different QoL instruments, obtaining comparable results. In 2020 we translated and validated the HiSQoL instrument, which became the first HS-specific questionnaire in Polish language [10]. HiSQoL showed excellent internal consistency, with a Cronbach α of 0.966 for total score and 0.87–0.94 for 3 subscales [10]. Nevertheless, it is important to underline that HSQoL-24 is more thorough and has a much longer recall period. Previously, Szepietowski *et al.* [9] performed translation and validation for DLQI, which is currently widely used in research and clinical practice in Poland. The group obtained very good results, with a Cronbach α of 0.9 [9]. Moreover, Polish and Arabic versions of the 6-Item Stigmatization Scale (6-ISS) were created [22, 23]. For both instruments the authors achieved very good results (Cronbach α of 0.94 an 0.89, respectively) [22, 23].

To the best of our knowledge, this is the first translation and validation of the English version of HSQoL-24. Our recently created instrument (Polish language version) showed excellent internal consistency, good reproducibility, and adequate convergent validity. This proves that the Polish version of HSQoL-24 could be of help in assessing QoL impairment in patients suffering from HS in daily clinical practice. Moreover, such a correct process of validation enables researchers to safely use the instrument in dermatological research.

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Conflict of interest

The authors declare no conflict of interest.

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6. ARTYKUŁ TRZECI:

THE USE OF HSQOL-24 IN AN ASSESSMENT OF QUALITY-OF-LIFE IMPAIRMENT AMONG HIDRADENITIS SUPPURATIVA PATIENTS: FIRST LOOK AT REAL-LIFE DATA

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Article

The Use of HSQoL-24 in an Assessment of Quality-of-Life Impairment among Hidradenitis Suppurativa Patients: First Look at Real-Life Data

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Abstract: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disorder with well-documented effects on patients' quality of life (QoL). The aim of this study was to evaluate the QoL of patients with HS via the use of a newly developed questionnaire: Hidradenitis Suppurativa Quality of Life-24 (HSQoL-24). This study was performed on a population of 342 HS patients. Their QoL was assessed via the HSQoL-24 questionnaire. The perceived impairment of QoL due to HS in the studied group was considered to be serious (mean HSQoL-24 score: 58.3 ± 21.0 points). Women tended to experience a significantly higher impact from the disease than men (61.6 ± 19.2 points vs. 51.1 ± 23.1 points, $p < 0.001$). The HS severity had an effect on the perceived QoL, with statistically significant differences being evident between the self-assessed HS severity groups. The level of QoL impairment correlated positively with the number of affected body areas ($r = 0.285$, $p < 0.001$) and the duration of the disease ($r = 0.173$, $p = 0.001$), while the patients' age at disease onset correlated negatively with the HSQoL-24 global score ($r = -0.182$, $p = 0.001$). Patients living in their family house scored higher than other groups. The least affected were patients who lived alone. The study shows that the HSQoL-24 questionnaire is a reliable, HS-specific tool for measuring the QoL among patients with HS in real-life clinical settings.

Keywords: hidradenitis suppurativa; quality of life; HSQoL-24; burden

1. Introduction

In the last few decades, there has been a significant shift in the focus of medicine and research results towards patient-reported outcomes (PROs). The concept of disease-related quality of life (QoL) has been gradually integrated into both clinical and research practices [1]. This has changed the old medicine model, which concentrated on objective measures (like laboratory results and blood pressure), into a new, holistic model that concentrates on the patient and highlights the importance of their QoL. Nowadays, disease-related QoL is an important end point of many studies and clinical trials [2].

Since 1994, when Finlay and Khan [3] developed the Dermatology Life Quality Index (DLQI), multiple dermatology- and disease-specific QoL questionnaires have been created [4]. The authors of this paper were determined to create a good instrument that would properly reflect the level of QoL impairment in patients suffering from hidradenitis

suppurativa (HS). HS is a chronic inflammatory condition that primarily affects apocrine-gland-rich regions of the body such as the axillary and groin areas. HS presents with painful nodules and abscesses that may coalesce and form fistulas where the pus has drained away. The lesions often evolve into scars that have a high physical and psychological impact on patients [5]. The above-mentioned symptoms, along with the purulent discharge and foul smell caused by the disease, make HS the most burdensome chronic dermatosis [6]. The lack of HS-specific questions in the majority of dermatology-specific QoL instruments makes them inadequate for the evaluation of QoL impairment in HS patients. Newer methods of measuring the PROs of HS patients, although they have been developed, still do not fully reflect the physical aspects of the disease [7]. Recently, a new, promising HS-specific instrument called Hidradenitis Suppurativa Quality of Life-24 (HSQoL24) was developed, validated, and translated into English by Marrón et al. [8,9].

The aim of this study was to determine the level of QoL impairment with the use of HSQoL24 among a large cohort of HS patients in a real-life setting.

2. Materials and Methods

2.1. Study Group

The study was performed on Spanish HS patients who were treated at the following hospitals in Spain between December 2018 and December 2020: the Miguel Servet University Hospital (Zaragoza), the Royo Villanova Hospital (Zaragoza), and the Barbastro Hospital (Huesca). All the patients were examined, diagnosed, and evaluated by a trained specialist in dermatology. The severity of the HS (assessed via the Hurley system and self-assessment), the duration of the disease, as well as the number of affected areas were recorded. Routine demographic data included gender, age, weight, height, education, marital status, and living situation. In line with the guidelines for studies involving human subjects and the World Medical Association Declaration of Helsinki, the anonymized data were then transferred to the Miguel Servet University Hospital of Zaragoza for a scientific evaluation. The study was accepted by the Ethics Committee of the University of Zaragoza (number PI16/020).

The studied group consisted of 342 consecutive HS patients (234 females and 108 males). The patients were 37.5 $\pm$ 10.7 years old. The mean BMI of the study participants was 29.3 $\pm$ 6.1 kg/m^2, qualifying the population as overweight. The majority of the patients were living with their families (55.3%), had reached higher education (43.9%), and were professionally active (52%) (detailed demographic data are shown in Table 1). According to Hurley staging [10], the majority of patients were assessed as Hurley II (43%), followed by Hurley III (38.3%), and Hurley I (18.7%). In addition, the self-reported HS severity was recorded. On average, every patient had more than two body areas affected by the disease (2.5 $\pm$ 1.3 localizations) (Table 1).

Table 1. Patients' characteristics.

Characteristics	Result
Sex, number of participants (%):	
• Men	108 (31.6)
• Women	234 (68.4)
Age, number of participants (%):	
• 30 years old or younger	90 (26.3)

Table 1. *Cont.*

Characteristics	Result
• 31–60 years old	247 (72.2)
• 60 years old or older	5 (1.5)
• Mean ± SD (years)	37.5 ± 10.7
Weight:	
• Mean ± SD (kg).	82.0 ± 17.3
Height:	
• Mean ± SD (cm).	167.4 ± 8.8
Body mass index (BMI):	
• Mean ± SD (kg/m^2).	29.3 ± 6.1
Living situation, number of participants (%):	
• Alone	59 (17.3)
• With family	189 (55.3)
• With partner	94 (27.5)
Education level, number of participants (%):	
• Primary	50 (14.6)
• Secondary	142 (41.5)
• College	150 (43.9)
Employment, number of participants (%):	
• Student	48 (14.0)
• Active	178 (52.0)
• Retired	20 (5.8)
• Unemployed	69 (20.2)
• Incapacitated	27 (7.9)

Table 1. *Cont.*

Characteristics	Result
Current HS severity, number of participants (%):	
• Mild	129 (37.7)
• Moderate	101 (29.5)
• Severe	112 (32.7)
Hurley stage, number of participants (%):	
• I	64 (18.7)
• II	147 (43.0)
• III	131 (38.3)
Duration of the disease, number of participants (%):	
• Less than 5 years	73 (21.3)
• Between 5 and 10 years	53 (15.5)
• More than 10 years	216 (63.2)
• Mean ± SD (years)	15.9 ± 10.7
Number of localizations:	
• Mean ± SD	2.5 ± 1.3
HSQoL-24 result:	
• Mean ± SD (points).	58.3 ± 21.0
HSQoL-24 domains, mean ± SD (points):	
• Psychosocial	58.9 ± 21.6
• Economic	50.8 ± 36.2
• Occupational	63.0 ± 31.3
• Relationships	66.0 ± 27.8
• Personal	37.4 ± 25.1
• Clinical	62.9 ± 25.7

SD—standard deviation, BMI—body mass index, HSQoL-24—Hidradenitis suppurativa Quality of life 24.

Regarding treatment, most of the patients (318 patients, 92.9%) had already been given treatment, while the rest (24 patients) had been assessed but had not yet started any kind of therapy. Among those who had already been treated, 297 patients (86.8%) had been treated pharmacologically, while 193 individuals (56.4%) had undergone surgery.

2.2. Quality of Life

In order to evaluate the influence of the disease on the patients' quality of life, all the participants were asked to complete the Hidradenitis Suppurativa Quality of Life-24 (HSQoL-24) questionnaire [8,9], a new Spanish HS-specific questionnaire which was also recently translated into and validated in English [9]. The instrument was a self-administered questionnaire consisting of 24 items that evaluate six life domains (psychosocial, economic, occupational, relationships, personal, and clinical) over a 4-week recall period [9]. Each item was scored on a five-point Likert scale. The total score was calculated by adding together the results from all the items, resulting in a maximum of 96 and a minimum of 0 points [9]. The higher the score, the bigger the impact of the disease on the patient's quality of life. To convert the score to a percentage, it was necessary to multiply the scores by the following coefficients: total score, 1.0412; psychosocial, 2.08; economic, 25.0; employment, 12.5; relationships, 6.25; personal, 12.5; clinical, 8.33. Four cut-off values were introduced to classify the effect of HS on the QoL: 0–24, no effect; 25–32, small impairment; 32–43, moderate impairment; $\geq$44, serious impairment. Both the Spanish and English versions of the questionnaire showed very good internal consistency and reliability. The instrument presented high correlation coefficients with SKINDEX-29 and DLQI [9].

2.3. Statistical Analysis

A statistical analysis of the obtained results was performed via the use of the IBM SPSS Statistics v. 26 (SPSS INC., Chicago, IL, USA) software. All data were assessed for parametric or nonparametric distribution. The minimum, maximum, mean, and standard deviation were calculated. The quantitative variables were evaluated using the Mann–Whitney U test and the Spearman and Pearson correlations. For the qualitative data, the chi-squared test was used. Differences in the DLQI total score of patients with different HS severities according to the Hurley stages system were assessed using the Kruskal–Wallis one-way analysis of variance by ranks test. A two-sided p-value lower than 5% was considered to be significant.

3. Results

The perceived impairment of QoL due to HS in the studied group was considered to be serious, with a HSQoL-24 total score mean result of 58.3 $\pm$ 21.0 points. Similar results were observed for every life domain besides personal, for which the mean score was significantly lower (37.4 $\pm$ 25.1 points, indicating moderate QoL impairment) (Table 2). Women reported a significantly higher global QoL impairment total in comparison to men (61.6 $\pm$ 19.2 points vs. 51.1 $\pm$ 23.1 points, $p < 0.001$). Similarly, female patients scored significantly higher in the psychosocial, economic, relationships, and clinical domains. There was no statistically significant difference in QoL impairment between the sexes in the employment and personal domains (Table 2).

Differences in QoL impairment were also seen between different age groups. The global score of patients aged between 31 and 60 years was significantly higher than that of the rest of the groups ($p = 0.002$). Moreover, this statistically significant difference was also confirmed for the psychosocial, employment, and personal domains. Regarding the living situation, patients living with their family scored higher (indicating a higher level of QoL impairment) than other groups (62.1 $\pm$ 19.7 points vs. 48.9 $\pm$ 22.3 points vs. 26.6 $\pm$ 20.91, $p < 0.001$). This statistically significant difference was evident not only in the global score but also in the scores for the psychosocial, economic, employment, and clinical domains. Interestingly, the group whose QoL was least affected, according to the global score and the scores for every domain, were patients who lived alone (Table 3).

Table 2. Comparison of HSQoL-24 scores between genders.

Domain, Mean ± SD (Points)	Men, *n* = 108	Women, *n* = 234	*p*
HRSQoL-24 Global	51.1 ± 23.1	61.6 ± 19.2	<0.001
HRSQoL-24 Psychosocial	51.3 ± 23.6	62.3 ± 19.7	<0.001
HRSQoL-24 Economic	39.3 ± 35.5	56.0 ± 35.3	<0.001
HRSQoL-24 Occupational	58.9 ± 33.3	64.9 ± 30.2	0.102
HRSQoL-24 Relationships	57.0 ± 27.7	70.2 ± 26.8	<0.001
HRSQoL-24 Personal	35.0 ± 27.3	38.5 ± 24.0	0.253
HRSQoL-24 Clinical	56.6 ± 25.8	65.8 ± 25.1	0.002

HSQoL-24—Hidradenitis Suppurativa Quality of Life-24; *n*—number of participants; SD—standard deviation.

Table 3. HSQoL-24 scores depending on living situation.

Domain, Mean ± SD (Points)	Alone, *n* = 59	With Family, *n* = 189	With Partner, *n* = 94	*p*(ANOVA)
HRSQoL-24 Global	48.9 ± 22.3	62.1 ± 19.7	56.6 ± 20.91	<0.001
HRSQoL-24 Psychosocial	49.6 ± 21.9	63.0 ± 20.0	56.3 ± 22.6	<0.001
HRSQoL-24 Economic	42.8 ± 37.7	57.8 ± 33.9	41.7 ± 36.9	<0.001
HRSQoL-24 Occupational	48.1 ± 31.7	66.9 ± 29.9	64.5 ± 31.3	<0.001
HRSQoL-24 Relationships	58.8 ± 38.7	69.0 ± 24.4	64.4 ± 25.3	0.04
HRSQoL-24 Personal	30.4 ± 23.7	39.9 ± 25.1	36.7 ± 25.3	0.039
HRSQoL-24 Clinical	52.5 ± 28.4	65.2 ± 23.7	64.8 ± 26.2	0.003

HSQoL-24—Hidradenitis Suppurativa Quality of Life-24; *n*—number of participants; SD—standard deviation.

The level of education and the BMI did not have any influence on HS-associated QoL (detailed data are not shown). The analysis of the results according to employment situation revealed that the highest levels of QoL impairment were among the patients who were incapacitated by the disease and those who were currently unemployed. On the other hand, students presented the lowest levels of QoL impairment most frequently.

The level of QoL impairment (based on the global score and the scores for each domain) correlated positively yet weakly with the number of affected body areas (for the global score, $r = 0.285$, $p < 0.001$). Similarly, the duration of the disease correlated positively with the HSQoL-24 total score ($r = 0.173$, $p = 0.001$), while the patients' age at HS onset correlated negatively with the HSQoL-24 global score ($r = -0.182$, $p = 0.001$). The HS severity had a large influence on the level of QoL impairment; patients with a higher severity scored higher (69.0 ± 18.5 points) than those with a moderate (62.1 ± 17.6 points) or mild (46.0 ± 19.4 points) severity of the disease ($p < 0.001$). Surprisingly, these differences were not observed between patients at different Hurley severity stages. Regarding treatment, there was no difference in QoL impairment between patients receiving any kind of treatment and those who were not receiving any treatment at all. In contrast, patients who had undergone surgical treatment in the past tended to score significantly higher than those who had not (62.4 ± 19.6 points vs. 52.9 ± 21.6, $p < 0.001$).

4. Discussion

Hidradenitis suppurativa is a chronic, painful, debilitating, and recurrent inflammatory disorder affecting the pilosebaceous unit [11]. The incidence of HS is hard to estimate, as it fluctuates from 0.03% in the Japanese population [12] to 4% among German women [13]. The disease begins in early adulthood, usually after adolescence, with the peak incidence occurring in patients aged between 20 and 30 years [14]. It is characterized by the appearance of deep, inflammatory nodules; abscesses; fistulas; and scarring, predominantly in intertriginous areas such as the axillae, the perianal and inguinal areas, and skin folds [15]. The enormous effect that HS has on the QoL of patients, their families, and their partners due to the pain, itchiness, purulent discharge, and foul smell caused by the disease has been documented [16,17]. The disease is associated with a higher incidence of depression, suicidal thoughts, stigmatization, alexithymia, and unemployment [18–21].

Numerous dermatology-specific instruments have been implemented to measure the QoL impairment associated with HS. Among the most frequently used are Skindex [22], the Dermatology Life Quality Index (DLQI) [3], the EuroQol 5 Dimensions questionnaire (EQ-5D) [23], and the Short Form 36 questionnaire (SF-36) [24]. The largest study evaluating HS-associated QoL impairment, conducted on a group of 1795 patients, was recently published by our research group. [6]. The effect of HS on the patients' QoL assessed via the DLQI was very large, with a mean DLQI score of 13.2 ± 8.1 points [6]. Similar yet slightly lower results were obtained in previous studies carried out by Matusiak et al. (12.7 ± 7.7 points) [16], Frings et al. (12 ± 7.0 points) [25], Jørgensen at al. (11.9 ± 7.6 points) [26], and Kourins et al. (11.43 ± 6.61 points) [27]. Nevertheless, it is important to underline that, due to the lack of HS-specific questions, none of the dermatology-specific QoL instruments adequately reflect the influence of HS on patients' QoL. The first HS-specific questionnaire, named Hidradenitis Suppurativa Quality of Life (HiSQOL), was created by Thorlacius et al. [28] in 2019. The instrument was subsequently validated and translated into Polish [29,30]. Nevertheless, there is still no study confirming the utility of HiSQOL for implementation in clinical settings on a significant number of patients. At present, to the best of our knowledge, there is a total of six HS-specific QoL questionnaires available. Among them, according to the new consensus on QoL in HS patients presented by Chernyshov et al. [6], HIDRAdisk, HSIA, HiSQOL, and HSQoL-24 are the most valid, yet these instruments still lack real-life implementation.

Our study was the first to use the newly developed HS-specific questionnaire HSQoL-24 in a clinical setting among a large group of patients. The results of our study confirmed the burdensome character of the disease. The mean score of 58.3 ± 21.0 points indicated a serious impairment of patients' QoL. Additionally, patients with a higher self-assessed level of HS severity tended to score significantly higher than those experiencing a mild severity of the disease. Furthermore, the number of affected areas had a significant influence on the perceived impairment of patients' QoL. This result is in accordance with the results of studies performed using dermatology-specific instruments [6,16,25,26], yet direct comparison is impossible. Similarly, as in previously mentioned studies, significantly higher scores were noted in the female population. The difference in QoL impairment between the sexes was statistically significant for the total score as well as for almost every domain. This confirms the fact that women tend to suffer more from dermatological diseases, which has previously been confirmed in the cases of multiple dermatoses including vitiligo, psoriasis, and atopic dermatitis [31–33]. Interestingly, we found that patients who lived alone scored significantly lower than those living with their families. This may have been caused by the effect of the disease on the patients' partners and family members [17]. According to the study by Włodarek et al. [17], HS has a moderate impact on the QoL of patients' partners, and the effect correlates positively with the disease severity. Therefore, it seems that patients who live alone most probably do not feel the burden of their disease being imposed on their loved ones.

We are aware of the limitations of this study. The consideration of only self-assessed disease severity may have influenced the final results; however, the Hurley staging system was also employed. Moreover, we did not compare our results with the results of other instruments, as the aim of our study was to confirm the utility of the newly developed and validated HS-specific questionnaire in a real-life clinical setting. Moreover, future studies should be conducted in order to assess the questionnaire's usefulness in measuring the treatment response.

5. Conclusions

In conclusion, this is the first study assessing the QoL impairment caused by HS using an HS-specific questionnaire. It shows that HSQoL-24 is a reliable tool for measuring the decrease in QoL in clinical settings. We believe that in the future, more studies regarding the effect of HS on patients' quality of life should be performed with disease-specific, rather than dermatology-specific, questionnaires.

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Institutional Review Board Statement: In line with guidelines for human studies and the World Medical Association Declaration of Helsinki, the anonymized data were then transferred to University Hospital Miguel Servet of Zaragoza for a scientific evaluation. The study was accepted by the Clinical Research Ethics Committee of Aragon (CEICA) (number PI16/020).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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7. ARTYKUŁ CZWARTY:

SELF-REPORTED HIDRADENITIS SUPPURATIVA SEVERITY: IS IT USEFUL FOR CLINICAL PRACTICE?

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ORIGINAL RESEARCH

Self-Reported Hidradenitis Suppurativa Severity: Is It Useful for Clinical Practice?

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ABSTRACT

Introduction: Hidradenitis suppurativa (HS) is considered to be the most burdensome dermatosis, with a well-documented negative influence on quality of life (QoL). The patient's perception of the disorder, assessed as the self-reported severity, has been used in other dermatoses but not in HS. The aim of this study was to evaluate the usefulness of self-reported HS severity in clinical practice.

Methods: The study was performed on a group of 130 Spanish HS patients. HS severity was assessed for all the subjects. Hurley staging and patient self-reported severity were used. Moreover, QoL impairment was evaluated using the Dermatology Life Quality Index (DLQI) and the Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) questionnaire.

Results: The severity of HS according to the Hurley staging was most commonly assessed as Hurley II (47.7%), indicating moderate disease, followed by severe disease (Hurley III, 26.9%) and mild disease (Hurley I, 25.4%). According to the patient self-reported HS severity, most of the patients reported having mild disease (76 patients, 58.5%), followed by moderate disease (31 patients, 23.8%). Only 23 patients (17.7%) assessed their disease as severe. Moreover, men reported mild disease significantly more frequently than women (70.9% and 49.3%, respectively; $p = 0.014$).The self-reported HS severity correlated positively with the effect of the disease on patient QoL assessed with DLQI ($r = 0.288$, $p < 0.001$). Likewise, a strong positive correlation was found between self-reported HS severity and QoL impairment assessed with HSQoL-24 ($r = 0.404$, $p = 0.001$). No statistically significant correlation between Hurley severity stage and DLQI or HSQoL-24 was found. Moreover, there were significant differences in both DLQI and HSQoL-24 total score between different self-reported HS severities. This was not

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seen for any of the QoL instruments or for Hurley severity staging.
Conclusion: The results show that self-assessment severity may reflect patients' subjective feelings more adequately than popular objective instruments, and there should be a place for its use in daily clinical practice.

Keywords: Hidradenitis suppurativa; Self-reported severity; Hurley; Assessment

Key Summary Points
Hidradenitis suppurativa (HS) is a chronic inflammatory dermatosis with a well-documented negative influence on quality of life (QoL).
The patient's perception of the disorder, assessed as the self-reported severity, has been used in other dermatoses, but not in HS.
The aim of the study was to assess the clinical usefulness of self-reported HS severity evaluation.
The self-reported severity correlated positively with QoL impairment assessed with the Dermatology Life Quality Index and Hidradenitis Suppurativa Quality of Life 24. Different HS severities had different effects on QoL.
The above-mentioned results were not found for Hurley staging, indicating that self-reported disease severity may more adequately reflect the patient's perspective.

INTRODUCTION

A patient-reported outcome (PRO) is defined as a type of patient health measurement that comes directly from the patient, without any interpretation of the results by a clinician or others [1]. In recent years, PROs have become an important part of a new holistic approach to the patient in both clinical and academic settings [1]. These subjective measurements allow physicians to gain an insight into the patient's perspective and to understand the patient's attitudes, burden, and feelings [2]. Dermatological disorders are often associated with disfigurement and a negative influence on the patient's quality of life (QoL), which may not be adequately reflected by an assessment of the area and the severity of the disease [3–5]. Therefore, PROs are an important part of routine dermatological care and scientific research, and are currently commonly used as endpoints in clinical trials [6].

Hidradenitis suppurativa (HS) is a burdensome, debilitating, chronic inflammatory dermatosis for which QoL impairment is well documented [5, 7–9]. The severity of the disease is commonly assessed and evaluated by a clinician using many available instruments [10–12]. The aim of this study was to assess the usefulness of a self-reported hidradenitis suppurativa (HS) severity scale and to evaluate if there is a place for it in routine dermatology practice.

METHODS

Study group

The study was performed on a group of hidradenitis suppurativa patients treated at the following hospitals in Spain between 2016 and 2017: University Hospital Miguel Servet (Zaragoza), Royo Villanova Hoaspital (Zaragoza), Barbastro Hospital (Huesca), Infanta Sofia Hospital (Madrid), Santa Creuu I Sant Pau Hospital (Barcelona), and Doctor Negrin Hospital (Las Palmas de Gran Canaria). All the patients were examined and assessed by a trained specialist in dermatology. Basic sociodemographic data were collected, including gender, age, weight, and height, as well as age at onset of the disease, its duration, and the number of affected areas. The study was conducted according to the guidelines of the Declaration of Helsinki of 1964 and its later amendments. The study was accepted by the Clinical Research Ethics Committee of Aragon

(CEICA) on 10 February 2016 (number PI16/020), and by the corresponding committees in the other participating hospitals. Moreover, a signed consent was obtained for every patient before their inclusion in the study.

Quality of life

The effect of the disease on the quality of life (QoL) of each patient was assessed using the Dermatology Life Quality Index (DLQI) and the newly developed, HS-specific Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) questionnaire. DLQI is a widely used, user-friendly, dermatology-specific tool for assessing the impacts of skin diseases on quality of life. It was developed in 1994 by Finlay and Khan [13], and has been used since then for a variety of dermatoses, including psoriasis, atopic dermatitis, and HS [9, 14, 15]. It is a 10-item instrument, and the degree of impairment is assessed on a 4-point scale (0: not at all, 3: very much) for each item within a 7-day recall period. The maximum achievable score is 30 points, and the higher the score, the bigger the impact on QoL. HSQoL-24 is a new Spanish HS-specific questionnaire that was translated into and validated in English in 2021 [16, 17]. It consists of 24 items divided into six life domains. This instrument evaluates the impact on QoL in a 4-week recall period. Each item is scored on a 5-point Likert scale. The maximum achievable score is 96 points [16, 17].

HS severity

HS severity was assessed for all the subjects. Hurley staging and patient self-reported severity were used. Hurley staging was introduced by Hurley in 1989 [10]. It divides the severity of the disease into three stages from the mildest to the most severe (Hurley I to Hurley III, respectively). Moreover, a self-reported HS severity scale was used, in which patients were asked to evaluate the severity of their disease at the time of clinical evaluation on a verbal rating scale. The subjects were asked to assess their disease severity as mild, moderate, or severe (see Supplementary Table 1).

Statistical analysis

Statistical analysis of the obtained results was performed with the IBM SPSS Statistics v. 26 (SPSS INC., Chicago, IL, USA) software. All data were assessed for a normal or abnormal distribution. The minimum, maximum, mean, and standard deviation were calculated. Quantitative variables were evaluated using the Mann–Whitney *U* test and Spearman's or Pearson's correlations. For qualitative data, the chi-squared test was used.

Differences in total DLQI and total HSQoL-24 between patients with different severities according to the self-reported severity and the Hurley staging system were assessed via Kruskal–Wallis one-way analysis of variance on ranks. A two-sided p with a value lower than 5% was considered significant.

RESULTS

The group consisted of 130 consecutive HS patients: 75 females (57.7%) and 55 males (42.3%). The patients were 37.3 ± 11.9 years old on average, with no age difference observed between the sexes. The population was characterized as overweight, with a mean BMI of 29.0 ± 5.6 kg/m^2. Women tended to have a higher BMI than men (30.1 ± 6.0 kg/m^2 and 27.5 ± 4.6 kg/m^2, respectively; $p = 0.023$). The mean age at onset of the disease was reported as 23.1 ± 10.9 years old. The disease started significantly earlier in females than in males (21.8 ± 11.2 years old and 24.9 ± 10.5 years old, respectively; $p = 0.021$). The patients had suffered from HS for 14.1 ± 11 years on average, and the disease affected about 2.2 ± 1 skin areas (Table 1).

According to Hurley staging, the severity of HS in the majority of patients was assessed as Hurley II, indicating moderate disease, followed by severe disease (Hurley III) and mild disease (Hurley I). No differences in Hurley severity assessment between the sexes were found. According to the patient self-reported HS severity, most of the patients reported having mild disease (76 patients, 58.5%), followed by moderate disease (31 patients, 23.8%). Only 23

Table 1 Patient characteristics

Characteristic	Whole group (n = 130)	Women (n = 75)	Men (n = 55)	P
Sex				
Number of men (%)	55 (42.3)	NA	NA	NA
Number of women (%)	75 (57.7)			
Age				
Mean ± SD (years)	37.3 ± 11.9	37.3 ± 11.9	37.4 ± 11.9	NS
Body mass index (BMI)				
Mean ± SD (kg/m^2)	29.0 ± 5.6	30.1 ± 6.0	27.5 ± 4.6	0.023
Age at onset of the disease				
Mean ± SD (years old)	23.1 ± 10.9	21.8 ± 11.2	24.9 ± 10.5	0.021
Duration of the disease				
Mean ± SD (years)	14.1 ± 11.0	15.6 ± 11.2	12.1 ± 10.5	
Number of locations				
Mean ± SD	2.2 ± 1.0	2.2 ± 1.0	2.3 ± 1.1	NS

SD standard deviation, *NS* not significant, *NA* not applicable, *n* number of participants

patients (17.7%) assessed their disease as severe. Moreover, men reported mild disease significantly more frequently than women (p = 0.014). This difference was not observed for other HS severities (Table 2). On average, HS had a moderate effect on the patient's life, with a mean DLQI score of 8.4 ± 7.2 points. The perceived effect was significantly greater for women than for men (p = 0.001). The impairment of QoL assessed with HSQoL-24 was considered to be serious, with a mean global score of 44.1 ± 19.2 points. Similar results were visible for every life domain aside from personal, for which QoL impairment was assessed as

Table 2 Hidradenitis suppurativa severity

Characteristics	Whole group (n = 130)	Women (n = 75)	Men (n = 55)	P
Hurley stages, number of participants (%)				
I	33 (25.4)	21 (28.0)	12 (21.8)	NS
II	62 (47.7)	31 (41.3)	31 (56.4)	NS
III	35 (26.9)	23 (30.7)	12 (21.8)	
Self-reported HS severity, number of participants (%)				
Mild	76 (58.5)	37 (49.3)	39 (70.9)	0.014
Moderate	31 (23.8)	22 (29.3)	9 (16.4)	NS
Severe	23 (17.7)	16 (21.3)	7 (12.7)	NS

N number of participants; *NS* not significant

Table 3 Quality of life impairment

Characteristic	Whole group (n = 130)	Women (n = 75)	Men (n = 55)	P
DLQI				
Total score (mean ± SD)	8.4 ± 7.2	10.1 ± 7.3	6.1 ± 6.4	0.001
HSQoL-24 (mean ± SD)				
Global	44.1 ± 19.2	49.8 ± 19.4	36.3 ± 16.1	< 0.001
Psychosocial	46.6 ± 21.5	52.9 ± 20.6	38.1 ± 19.8	< 0.001
Economic	39.6 ± 36.8	49.3 ± 38.5	26.4 ± 29.8	0.001
Occupational	45.5 ± 32.4	47.3 ± 33.2	43.1 ± 31.5	NS
Relationships	51.4 ± 31.6	58.9 ± 35.3	41.1 ± 22.2	0.001
Personal	24.9 ± 21.7	28.5 ± 22.3	20.0 ± 19.9	0.026
Clinical	46.8 ± 24.6	50.3 ± 27.3	42.0 ± 19.7	NS

DLQI Dermatology Life Quality Index, *HSQoL-24* Hidradenitis Suppurativa Quality of Life 24, *n* number of participants, *SD* standard deviation, *NS* not significant

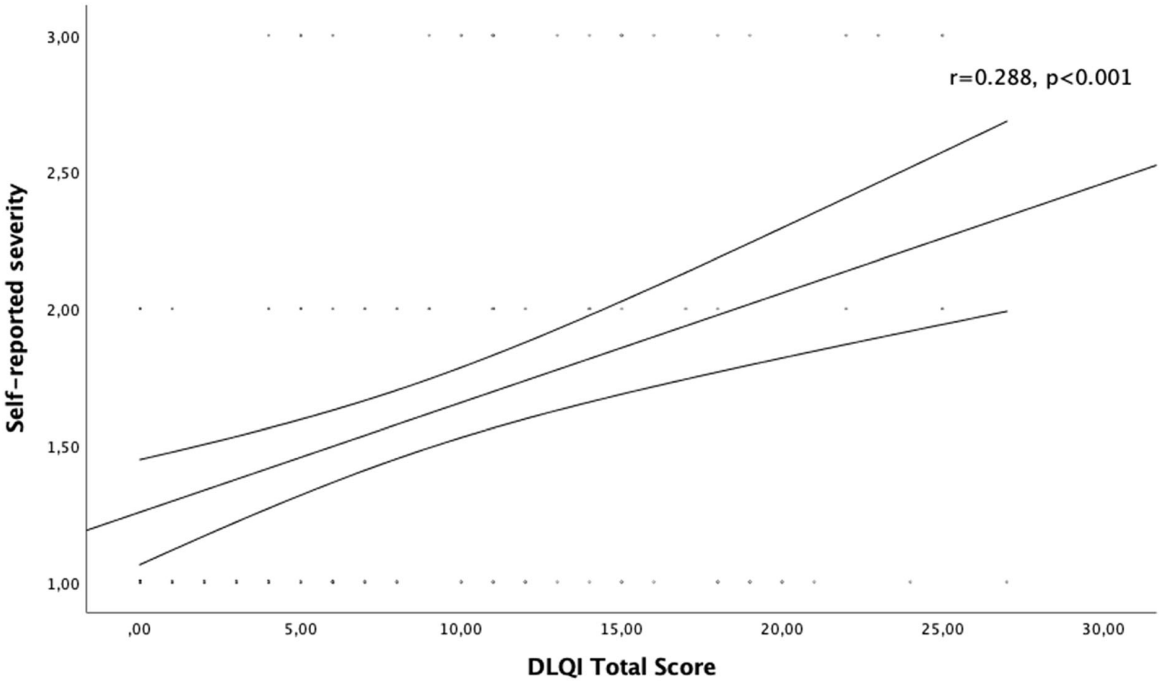

Fig. 1 Correlation of self-reported disease severity with DLQI

moderate (24.9 ± 21.7 points). As also seen for the DLQI, women scored significantly higher for the HSQoL-24 global score ($p < 0.001$), as well as for every life domain excluding the clinical and occupational domains (Table 3).

The self-reported HS severity correlated positively with the effect of the disease on patient QoL as assessed with DLQI ($r = 0.288$, $p < 0.001$) (Fig. 1). Likewise, a strong positive correlation was found between self-reported HS severity and QoL impairment as assessed with HSQoL-24 ($r = 0.404$, $p = 0.001$) (Fig. 2). No statistically significant correlation was found between Hurley severity stage and DLQI or HSQoL-24. Moreover, different self-reported HS severities showed significantly different DLQIs and HSQoL-24 total scores (Figs. 3 and 4). This was not seen for any of the QoL instruments or for Hurley severity staging (Table 4). The kappa value for the agreement between Hurley stage and self-reported severity was 0.153.

DISCUSSION

Hidradenitis suppurativa (HS) is a chronic, debilitating, recurrent inflammatory skin disorder of unknown pathogenesis that affects the pilosebaceous unit [18]. It is characterized by the formation of deep-seated inflammatory nodules, predominantly in intertriginous locations such as the groin, armpits, and anogenital area [19]. In the course of the disease, nodules progress into abscesses, sinuses, and scarring [19]. The prevalence of the disease has been reported to peak in young adults between 20 and 40 years of age. The exact incidence varies greatly among the available studies, and is currently estimated at 0.03–1% [20, 21]. Due to the resulting continuous purulent discharge, foul smell, and disease-associated pain, HS is considered the most burdensome form of dermatosis, and has a well-documented negative impact on patient QoL. This disease is associated with a high incidence of depression,

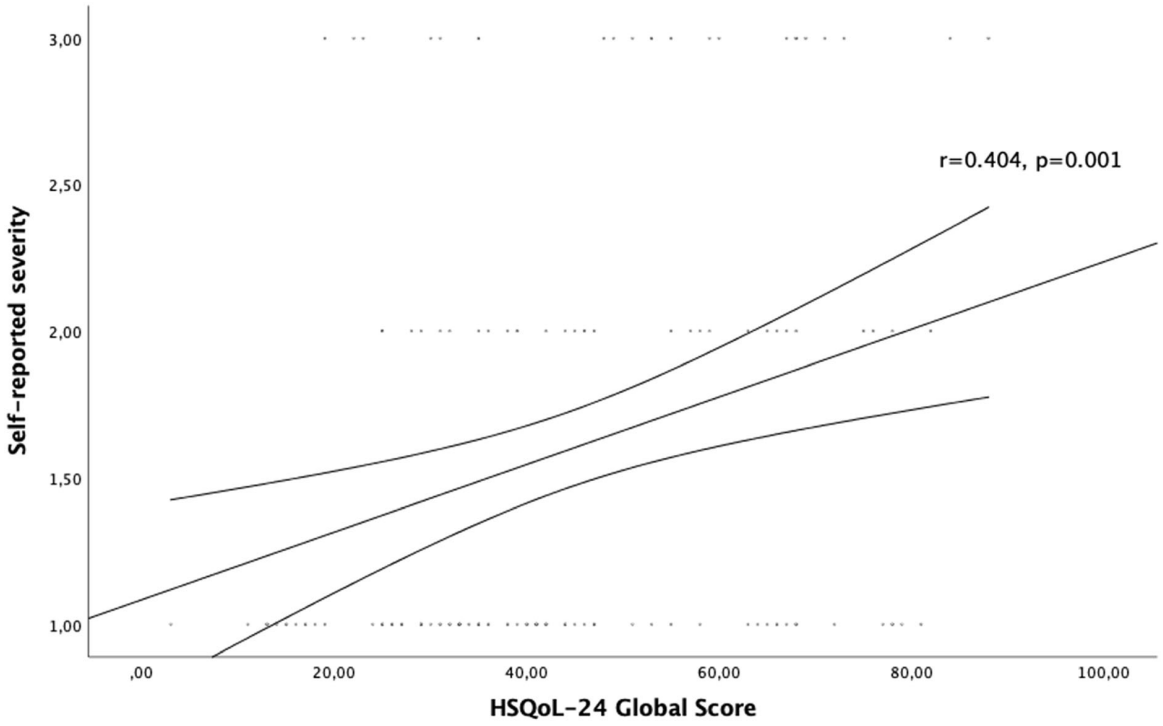

Fig. 2 Correlation of self-reported disease severity with HSQoL-24

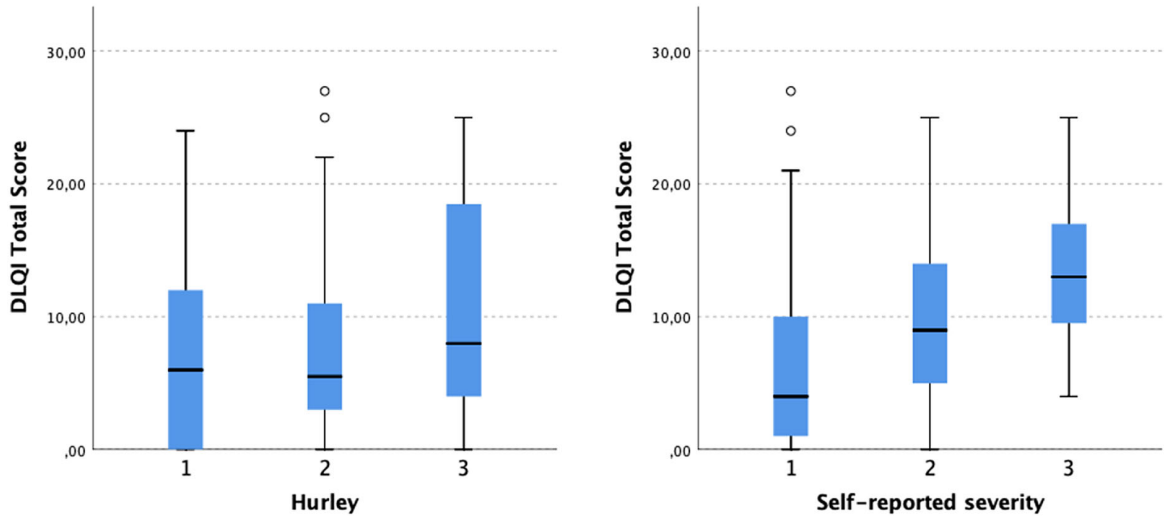

Fig. 3 Differences in DLQI total score between different self-reported HS severities and between different HS severities assessed with Hurley staging

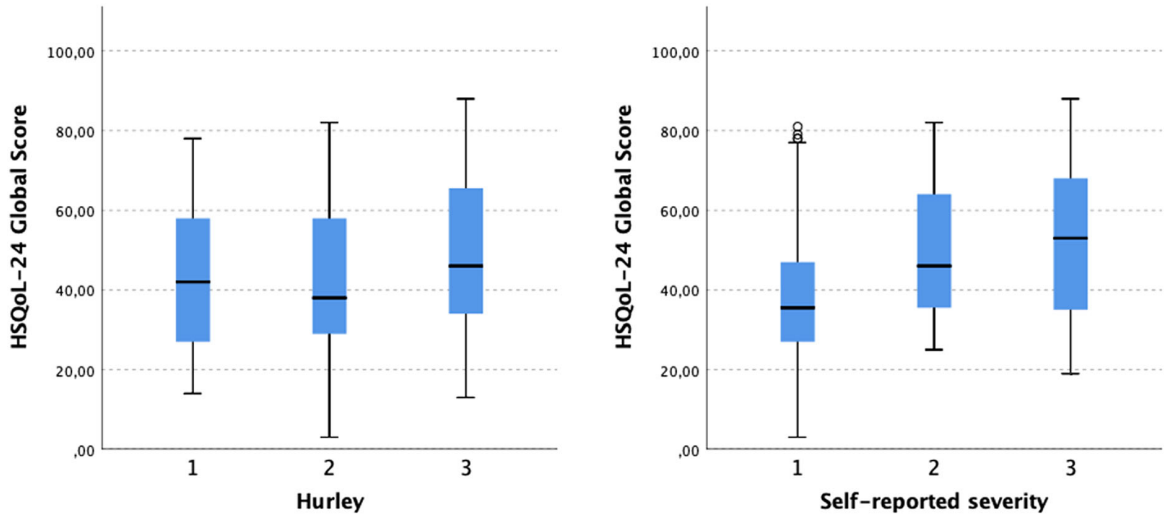

Fig. 4 Differences in HSQoL-24 global score between different self-reported HS severities and between different HS severities assessed with Hurley staging

anxiety, stigmatization, alexithymia, workplace challenges, and even suicide ideation [22–26]. Moreover, it negatively affects patients' partners and families [27].

The clinical severity of the disease may be assessed using a variety of instruments. Among the most frequently used are the Hurley staging system [10], the International Hidradenitis Suppurativa Severity Score (IHS4) [11], the Sartorius score [28], and the Physician Global Assessment (PGA) [29]. It is worth underlining that all of the previously mentioned scoring

Table 4 Differences in QoL impairment between different HS severities

Severity assessment	DLQI score (mean ± SD)	*p*	HSQoL-24 score (mean ± SD)	*p*
Hurley				
I	7.6 ± 7.2		42.8 ± 18.9	
II	7.4 ± 6.3	NS	42.6 ± 19.2	NS
III	10.91 ± 8.3		47.8 ± 19.8	
Self-assessed				
Mild	6.4 ± 6.8		39.4 ± 18.6	
Moderate	9.7 ± 6.8	< 0.001	49.1 ± 17.3	0.005
Severe	13.3 ± 6.5		52.7 ± 19.8	

NS not significant, *SD* standard deviation

systems are objective and are designed to be used by a physician. The patient's perception of the disorder, assessed as the self-reported severity, has been used for other dermatoses. Self-reported AD severity questionnaires include the Patient-Oriented SCORAD (PO-SCORAD) and Self-Administered Eczema Area and Severity Index (SA-EASI) [30, 31]. Similarly to their use in AD, patient-reported outcome measurements (PROMs) are also commonly used in psoriasis. The self-assessed Simplified Psoriasis Index (saSPI) is an instrument that combines the psychosocial impact of psoriasis, its current severity, and past history and interventions [32]. The severity assessment includes the extent of the disease and the choice of sentences that best describe the overall state of psoriasis at the time of examination [32]. The maximum achievable score for the severity of the disease is 50 points, and the higher the result, the more severe the AD. Moreover, it was proven that the results correlate strongly with the Psoriasis Severity and Area Index (PASI) [32]. Regarding HS, to the best of our knowledge, there are only three reports of attempts to use self-reported severity measurements in the literature [33–35]. The first, published by Cusack et al. [34], was performed on a group of 6 patients diagnosed with HS who were treated with etanercept [34]. The patients were supposed to assess the severity of the disease at the beginning and end of the therapy. Moreover, at the end of the treatment, all patients had to estimate the percentage improvement in HS [34]. In 2015, Deckers et al. [35] tried, for the first time, to determine the capability of patients to self-assess their Hurley stage using pictures. They found that in 76% of the cases, the results were similar to those given by a physician [35]. Moreover, a substantial agreement (with a weighted kappa of 0.63) was achieved, which was comparable to that seen in similar studies of psoriasis and atopic dermatitis [35]. The only available validation of a self-reported severity tool was published in 2019 by Senthilnathan et al. [33]. The tool consisted of 10 color photographs of different Hurley stages which 24 patients were supposed to choose from. The results, although worse than in the previous study, showed moderate agreement between assessments performed by patients and those performed by physicians (a weighted kappa of 0.57), indicating that patients may be able to assess their severity adequately [33].

The above-mentioned results clearly show that self-reported severity is a reliable tool for gaining the patient's perspective and new insight into the disease. Contrary to Hurley staging, self-reported severity correlated positively with QoL impairment. Moreover, differences in QoL impairment between different self-assessed severities of the disease were found. This may indicate that self-reported severity reflects the patient's subjective feelings more

adequately than objective severity measures such as Hurley staging.

We understand that our study has some limitations. Firstly, only Hurley staging was used to assess severity, which may not be the most detailed and reliable measurement. Nevertheless, it is necessary to underline that Hurley staging is still one of the most commonly used HS staging systems worldwide. Secondly, the self-reported severity assessment was not previously validated nor tested on smaller groups.

CONCLUSION

In conclusion, to the best of our knowledge, this is the first study to assess the usefulness of the self-reported severity of HS. The results of our study show that self-reported severity may be adequate for HS severity assessment and there should be a place for its use in daily clinical practice in the future. Nevertheless, further studies with validated objective tools for the assessment of HS are necessary before introducing this PROM into daily clinical practice.

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Author Contributions. All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Servando E Marrón, Lucía Tomas Aragones and Yolanda Gilaberte-Calzada. The first draft of the manuscript was written by Piotr K Krajewski and Jacek C Szepietowski and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Disclosures. Piotr K Krajewski, Servando E Marrón, Lucía Tomas Aragones, Yolanda Gilaberte-Calzada and Jacek C Szepietowski have nothing to disclose.

Compliance with Ethics Guidelines. The study was conducted according to the guidelines of the Declaration of Helsinki of 1964 and its later amendments. The study was accepted by the Clinical Research Ethic Committee of Aragon (CEICA) on 10 February 2016 (number PI16/020), by the corresponding committees in the other participants hospitals. Moreover, a signed consent was obtained for every patient, before including in the study.

Data Availability. The data that support the findings of this study are available from the corresponding author on reasonable request and with permission of all the authors. The data are not publicly available due to reasons of sensitivity and other reasons

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8. ARTYKUŁ PIĄTY:

QUALITY-OF-LIFE IMPAIRMENT AMONG PATIENTS WITH HIDRADENITIS SUPPURATIVA: A CROSS-SECTIONAL STUDY OF 1795 PATIENTS

life

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Article

Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients

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Abstract: The chronic, inflammatory skin disorder hidradenitis suppurativa (HS) is associated well documented negative influences on patients' quality of life (QoL). The aim of this study was to present more robust data on patients' QoL impairment by demographic data and its correlation with well-known HS risk factors on a cohort of 1795 German patients. The instrument used for measuring QoL in this study was the Dermatology Life Quality Index (DLQI). Overall, patients reported a very large effect of HS on their QoL (mean DLQI: 13.2 ± 8.1 points), and 22% of the analyzed population even reported to consider the effect as extremely large. Women tended to experience significantly higher impairment than men ($p < 0.001$). QoL impairment correlated positively with pain (r = 0.581, $p < 0.001$), HS severity (measured by the International Hidradenitis Suppurativa Severity Score System (IHS4)) as well as Hurley. Neck involvement tended to decrease QoL significantly more than any other location (14.7 ± 8.3 points). This study confirms the enormous influence of HS on patients' QoL in a large cohort. Knowledge of QoL impairment in such patients is crucial for proper understanding and holistic management of this disease.

Keywords: hidradenitis suppurativa; DLQI; quality of life

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1. Introduction

Healthy skin, due to its visibility, is an important organ for proper psychological functioning. Chronic disorders of the skin can have a devastating effect on the private and professional lives of those affected. Among the psychological problems resulting from chronic skin disorders, stigmatization, feelings of embarrassment, low self-esteem, stress, anger, shame and depression are reported most frequently [1]. Many studies confirm that visible skin disease may lead to suffering from bullying, sleep impairment and a decline in academic or work performance [2,3]. Chronic skin disorders, which are believed to cause a significant decrease in quality of life, include, among others, atopic dermatitis, psoriasis and hidradenitis suppurativa. Due to the affectation of multiple body areas, foul smell, purulent discharge and associated pain and/or pruritus, hidradenitis suppurativa (HS) has been documented to have a negative influence on patients' quality of life (QoL) [4,5]. HS is also associated with a higher incidence of depression, insomnia or decreased sleep quality, fear of stigmatization and workplace challenges [6–8]. Moreover, HS lesions often affect anogenital areas and impair sexual activity and satisfaction [4,5]. To date, several papers regarding the influence of HS on QoL have been published. However, to the best of

our knowledge, all this work was based on a limited number of patients. The aim of this study was to present more robust data on patients' QoL impairment through demographic data and its correlation with well-known HS risk factors.

2. Materials and Methods

2.1. Study Group

This study included HS patients, who were selected for LAight® therapy (a combination of intense pulsed light with radiofrequency) [9,10] in multiple dermatology outpatients' centers in Germany between April 2017 and February 2020. Patients were only included if they gave informed written consent to the collection, storage and scientific evaluation of their routine data during LAight® therapy in an electronic database hosted by LENICURA (the manufacturer of the medical device). All documented patients were examined by a doctor specifically trained on HS. The overall contraindications for LAight® therapy included pregnancy, epilepsy and an implanted electrical device. Moreover, the treatment was not initiated in patients with extreme photosensitivity, implants within 10 cm of the lesioned skin, tattoos, piercings, skin neoplasms or previous treatment with fillers in the treated HS area. Routine demographic baseline data included gender, age, body mass index (BMI) and smoking habits. In line with guidelines for human studies and the World Medical Association Declaration of Helsinki, the anonymized data were then transferred by LENICURA to the consortium of experts of this paper for scientific evaluation.

The studied group consisted of 1795 patients (1152 females and 643 males). The patients were 40.0 $\pm$ 11.8 years old. The majority of subjects were reported to be smokers (55.6%), and 10.5% of the population smoked more than 25 cigarettes a day. The mean BMI of participants was 28.1 $\pm$ 6.2 kg/m^2, qualifying the population as, on average, overweight. All patients had their HS severity assessed with the use of the Hurley staging system and affected body areas, and 634 subjects were additionally assessed according to the International Hidradenitis Suppurativa Severity Score System (IHS4) [10–12]. The worst pain in the previous 24 h was evaluated with the use of the Numeral Rating Scale (WP-NRS). In this 11-point scale, 0 implies no pain, and 10 implies the worst imaginable pain [13].

2.2. Quality of Life

In order to evaluate the actual influence of HS on the patients' QoL, all subjects were asked to complete the Dermatology Life Quality Index (DLQI) questionnaire [14]. The DLQI is a simple, dermatology-specific, quality-of-life questionnaire. Since its development, it has been widely used in a variety of dermatoses, including psoriasis, atopic dermatitis and prurigo nodularis [15–17]. It is also a routinely used instrument in assessing improvements in QoL after novel treatments with biologics [18,19]. Until 2019, before the introduction of the Hidradenitis Suppurativa Quality of Life (HiSQOL) questionnaire [20], there was no HS-specific questionnaire; therefore, the DLQI was a crucial instrument used in the evaluation of HS patients' QoL. This 10-item questionnaire was developed in 1994 by Finlay and Khan [21], and each item can receive an impairment degree on a 4-point-scale (0—not at all, 3—very much). Moreover, the questionnaire is divided into six subscales that assess the affectation of one of the QoL domains: symptoms and feeling, daily activities, leisure, work/school, personal relationships and treatment [21]. The maximum number of points achievable is 30 points, and the higher the score, the greater the impairment of QoL. The DLQI is to be interpreted with the following cut-off values for the effects on patients QoL: 0–1 = no effect at all; 2–5 = small effect; 6–10 = moderate effect; 11–20 = very large effect; 21–30 = extremely large effect [21].

2.3. Statistical Analysis

Statistical analysis of the obtained results was performed with the use of the IBM SPSS Statistics v. 26 (SPSS INC., Chicago, IL, USA) software. All data were assessed for parametric or nonparametric distribution. The minimum, maximum, mean and standard deviation were calculated. Quantitative variables were evaluated using the Mann–Whitney

U test and Spearman's and Pearson's correlations. For qualitative data, the chi-squared test was used. Differences in total DLQI between patients with different HS severities according to Hurley stages were assessed with the Kruskal–Wallis one-way analysis of variance on ranks. All analyses were performed as two-sided tests with a significance level of 5%.

3. Results

The perceived influence of HS on QoL in the studied group was found to be very large (mean DLQI: 13.2 ± 8.1 points). Female patients reported significantly higher impairment in QoL than males (14.2 ± 8.0 vs. 11.5 ± 8.0 points, $p < 0.001$). When categorized according to the DLQI cut-off values, a very large effect on patients' QoL was observed most frequently (36% of patients), followed by extremely large (22%), moderate (21%) and small (15%). Only 6% of the patients reported that their HS had no effect on their QoL. The gender difference also manifested in different cut-off areas of the DLQI since the percentage of female subjects experiencing an extremely large effect on QoL was significantly higher than that of male patients (25% vs. 16%, $p < 0.001$) (Figure 1). This finding was also confirmed for the single items of the DLQI score as well as in the DLQI domains, in which, apart from Items 6 and 7 and the domains work and school, impairment was significantly higher for females than males ($p < 0.01$) (Table 1). HS severity had a significant influence on patients' QoL, with a moderate correlation found between DLQI and IHS4 (r = 0.306, $p < 0.001$) (Figure 2). Moreover, a higher Hurley stage was associated with a greater negative impact on QoL in all DLQI-Items questions and domains (Figure 3). Interestingly, the number of affected areas seems to not decisively contribute to QoL impairment. There was a significant, but only weak, correlation (r = 0.1, $p < 0.001$) between affected areas and the DLQI and no significant difference in DLQI between single-area-affected patients and patients with multiple areas affected ($p = 0.794$). Regarding the affected areas, among subjects with spread disease, the highest life impairment was reported by those with neck involvement (14.7 ± 8.3 points, $p < 0.001$), and the lower extremities' involvement was found to cause the lowest reduction in QoL (11.9 ± 7.9 points, $p < 0.001$). For the single-area affectation, there was no difference in the decrease in QoL between affected areas (Table 2). With respect to risk factors, QoL impairment showed a significant positive correlation with age and BMI; however, in both cases, the degree of correlation was weak (r = 0.1, $p < 0.001$). There was a significant difference ($p < 0.001$) in QoL impairment comparing smokers with nonsmokers (13.9 ± 8.1 and 12.4 ± 8 points, respectively); however, we did not find any correlation with the number of smoked cigarettes per day (detailed data not shown). Finally, concerning other patients' reported outcomes, a strong positive correlation was found between mean DLQI and pain assessed by NRS (r = 0.581, $p < 0.001$).

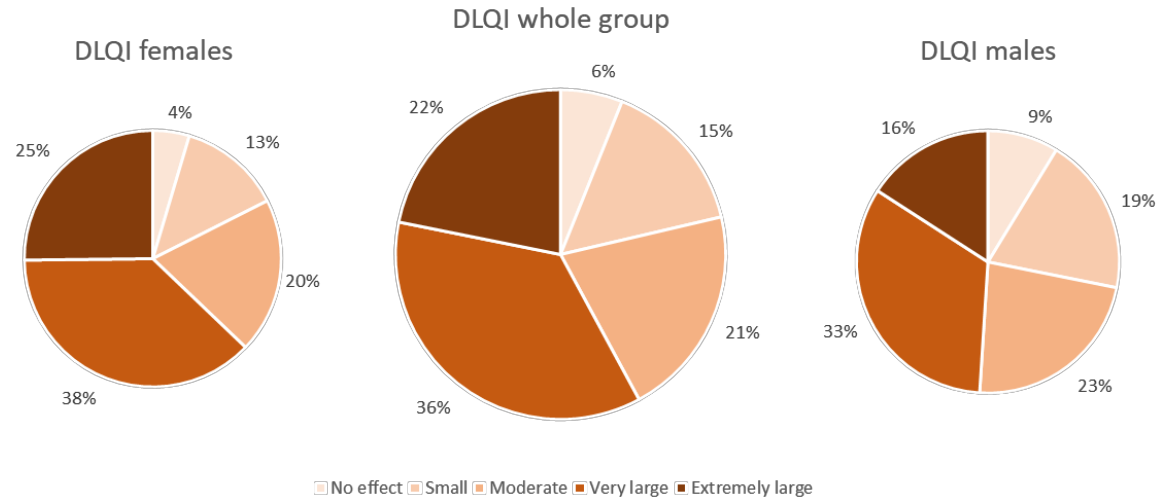

Figure 1. HS effect on patients' QoL. The diagram is based on the DLQI cut-offs. HS—Hidradenitis suppurativa; QoL—Quality of life; DLQI—Dermatology Life Quality Index.

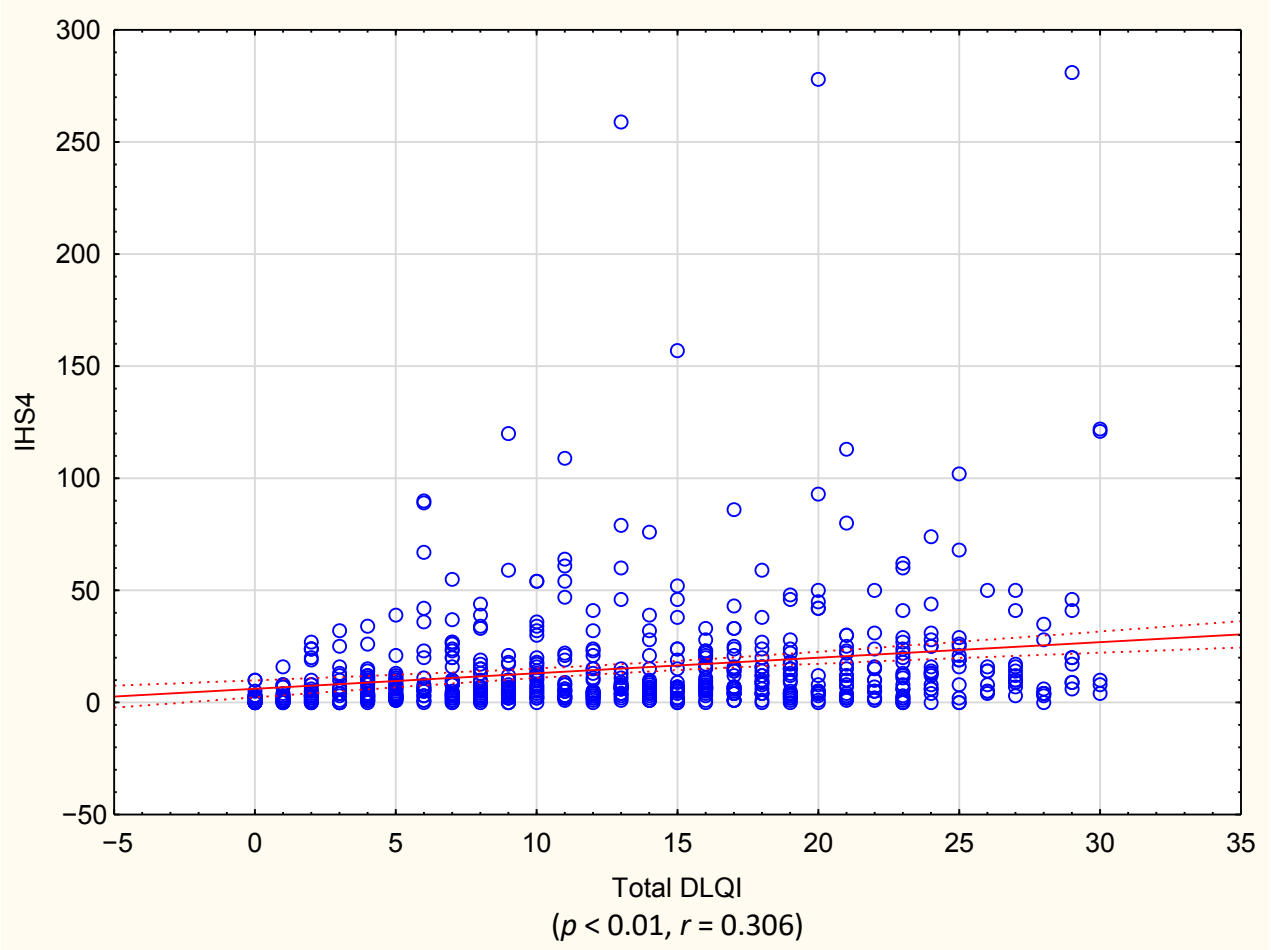

Figure 2. Correlation between disease severity (IHS 4) and quality-of-life impairment (DLQI). IHS4—International Hidradenitis Suppurativa Severity Score; DLQI—Dermatology Life Quality Index.

Table 1. Quality-of-life impairment assessed with DLQI (mean ± SD points).

DLQI	Total (n = 1795)	Female (n = 1152)	Male (n = 643)	Female vs. Male
DLQI Total	13.2 ± 8.1	14.2 ± 8.0	11.5 ± 8.0	**0.000000**
DLQI Item 1	1.7 ± 1.0	1.7 ± 1.0	1.5 ± 1.0	**0.000055**
DLQI Item 2	1.4 ± 1.2	1.5 ± 1.2	1.1 ± 1.1	**0.000000**
DLQI Item 3	1.1 ± 1.1	1.2 ± 1.1	1.0 ± 1.1	**0.001810**
DLQI Item 4	1.7 ± 1.2	1.9 ± 1.1	1.4 ± 1.2	**0.000000**
DLQI Item 5	1.4 ± 1.2	1.5 ± 1.2	1.3 ± 1.2	**0.001835**
DLQI Item 6	1.5 ± 1.3	1.6 ± 1.3	1.5 ± 1.3	0.147319
DLQI Item 7	1.1 ± 1.2	1.1 ± 1.1	1.1 ± 1.2	0.997689
DLQI Item 8	0.9 ± 1.1	1.1 ± 1.2	0.7 ± 1.0	**0.000000**
DLQI Item 9	1.2 ± 1.3	1.4 ± 1.3	0.9 ± 1.2	**0.000000**
DLQI Item 10	1.1 ± 1.1	1.2 ± 1.2	1.0 ± 1.1	**0.006825**
DOMAINS				
Symptoms and feelings	3 ± 1.8	3.2 ± 1.8	2.6 ± 1.7	**0.000000**
Daily activities	2.8 ± 2.0	3.1 ± 1.9	2.8 ± 2.2	**0.000000**
Leisure	2.9 ± 2.2	3 ± 2.2	2.4 ± 2.0	**0.010427**
Work and school	1.1 ± 1.2	1.1 ± 1.1	1.1 ± 1.2	0.997689
Personal relationships	2.2 ± 2.2	2.5 ± 2.3	1.6 ± 2.0	**0.000000**
Treatment	1.1 ± 1.1	1.2 ± 1.2	1 ± 1.1	**0.006825**

n—number of patients; DLQI—Dermatology Life Quality Index; bold—$p < 0.05$.

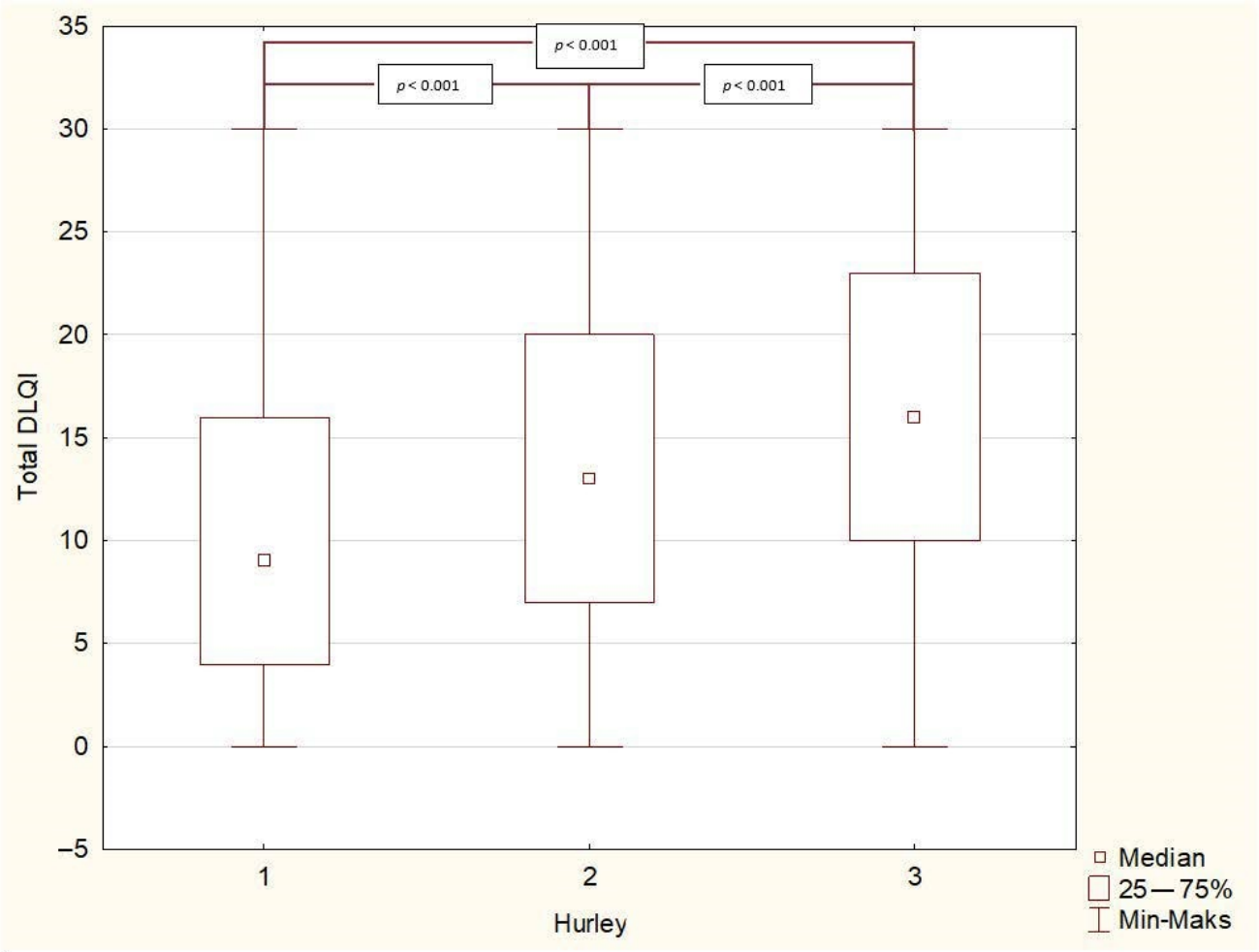

Figure 3. Total DLQI distribution among disease severity assessed with the Hurley severity score. DLQI—Dermatology Life Quality Index.

Table 2. Life impairment assessed with total DLQI regarding the affected lesions.

Affected Body Area	Singular	Multiple
Head (mean ± SD points)	14.9 ± 10.1 (n = 10)	13.3 ± 8.3 (n = 789)
Neck (mean ± SD points)	10 (n = 1)	**14.7 ± 8.3 (n = 129)**
Upper extremities (mean ± SD points)	11.3 ± 8.3 (n = 13)	13.3 ± 8.2 (n = 706)
Armpits (mean ± SD points)	12.28 ± 7.1 (n = 28)	13.3 ± 8.2 (n = 876)
Breast area (mean ± SD points)	15.1 ± 9 (n = 24)	13.3 ± 8.1 (n = 1213)
Anogenital area (mean ± SD points)	15.2 ± 7.1 (n = 16)	13.5 ± 8 (n = 1151)
Lower extremities (mean ± SD points)	9 ± 7.1 (n = 2)	**11.9 ± 7.9 (n = 347)**
Back (mean ± SD points)	7.3 ± 4.5 (n = 8)	12.5 ± 7.7 (n = 35)
Buttocks (mean ± SD points)	-	15.8 ± 10.9 (n = 4)

Bold—$p < 0.05$; n—number of patients; SD—Standard deviation.

4. Discussion

Hidradenitis suppurativa (HS) is a painful, chronic, multifactorial and progressive inflammatory skin disease of the pilosebaceous unit. It predominantly affects intertriginous zones of the body, including axillae, groins, buttocks or the submammary region in young adults, and leads to the development of inflammatory nodules, abscesses, sinuses and scarring [22]. The actual prevalence of HS is yet to be evaluated because it varies greatly between available reports. Studies report the prevalence from 0.09% among the German population up to even 4% in the population of young women [23–25]. The pathogenesis is still unclear; however, inflammation, genetic predisposition and bacterial propagation are the most often mentioned mechanisms [22].

The results of this study confirmed that HS is a burdensome disease and has a very large effect on patients' QoL. The impairment of QoL was comparable with previously conducted studies. The mean total DLQI score was similar to those reported by Matusiak et al. [5] (12.7 $\pm$ 7.7 points), Frings et al. (12 $\pm$ 7.0 points) [26], Jørgensen et al. (11.9 $\pm$ 7.6 points) [27] and Kourins et al. (11.43 $\pm$ 6.61 points) [28]. However, there are also reports on much lower QoL impairment due to the disease (8.4 $\pm$ 7.5 and 8.9 $\pm$ 8.3 points) [29,30]. We believe that such differences are mostly due to distinctions in HS severity and duration. In the above-mentioned study by Onderdijk et al. [30], HS severity assessed with the Hurley staging system was lower than among our patients (13.5% vs. 17.2% for Hurley stage 3) [30]. Moreover, in remote questionnaire studies, it is impossible to assess the actual severity of the disease and, therefore, the actual impairment of QoL [29]. It is also worth emphasizing that some of the subjects of the study by von der Werth [29] had the disease inactive for 12 months, and 21 patients (18.4%) scored 0 points. This may have biased the DLQI scores downwards. The common use of the DLQI score allows us to compare the impact of HS with the effect of other dermatoses on QoL. The results of this study confirm prior results that the burden of HS is greater than those reported among other skin conditions, including psoriasis, chronic urticaria, atopic dermatitis, acne or alopecia [31–35]. In comparison to the above-mentioned dermatoses, which are believed to cause significant disability, the DLQI scores for HS patients are markedly higher, and this indicates that, to date. HS is the most distressing dermatological condition.

We found a significantly higher perceived impairment in QoL in female than male patients. This finding was previously reported by Kluger et al. [36] in a study with 26 HS patients. Similarly, in almost every DLQI item and domain, women scored significantly higher than men. We also observed a high correlation between pain and the DLQI, known to have a significant influence on daily functioning [37]. HS-associated pain could influence females more than males due to differences in neuroimmune pain modulation. It has been shown that due to multiple mechanisms (e.g., hormonal modulation), women suffer from pain more frequently than men and are more sensitive to it [38]. Moreover, according to studies regarding QoL impairment in different dermatoses (e.g., vitiligo, psoriasis or atopic dermatitis) [39–41], women tend to suffer more from skin-associated diseases. Zhang et al. [42] tried to explain this phenomenon and stated that, compared to men, women more frequently believe that physical appearance is important to their personal or social values. It may be also attributed to patients' maladaptive assumptions about appearance and society's focus on body and beauty [42]. Interestingly, Jørgensen et al. [27] did not confirm this finding in their study of 339 HS patients. The differences in our results and the above-mentioned study may indicate that although pain is important, there are other factors that influence patients' quality of life. There are significant differences in psychological response to pain and chronic disorders between males and females. Certain coping strategies commonly used by women may be more effective with chronic pain and, therefore, diminish the difference in QoL impairment [43].

It has been well reported that obesity and smoking play an important role in the pathogenesis of HS [44]. Although the exact mechanism of smoking in HS is not well explained, a high expression of nicotine receptors was found on the follicular epithelium [45]. Regarding obesity, not only it is believed to be its own state of inflammation but also may increase

skin folds' friction, which is an important mechanism of HS development [46]. QoL was significantly lower among smokers and correlated weakly with the number of cigarettes per day. Similarly, the correlation between BMI and the DLQI was weak but significant. To the best of our knowledge, this is the second paper addressing the influence of smoking on patients' QoL. Earlier this year, Jørgensen et al. [27] did not find any relationship. However, there are too few data on the topic to draw final conclusions.

The decrease in QoL may differ regarding the affected localization. It was previously reported that psoriatic patients with anogenital localization tend to have a significantly lower QoL [47]. Similarly, HS anogenital localization was linked to a higher burden and impairment of a person's life [5,27]. However, our results are not consistent with the above-mentioned studies. Interestingly, the highest DLQI score, among our patients, was reported by those with neck involvement. We believe that, contrary to the anogenital area, which is not visible during the day, neck involvement could cause psychical distress on a daily basis. Moreover, due to the pain, tenderness and purulent flow, all head movement would be accompanied by physical and psychical discomfort.

We understand that our study has some limitations. As it concentrated on the baseline evaluation of HS patients who were selected for LAight therapy®, it may not reflect the whole population of HS patients. The use of only the DLQI and the lack of additional psychological instruments makes it impossible to assess associated psychological and psychiatric disorders (e.g., depression or anxiety). However, we believe that due to the studied sample size, which markedly exceeds the representative number of patients for the HS population, this study provides important insights into the HS-associated impairment of QoL.

5. Conclusions

In conclusion, to the best of our knowledge, this is the biggest study assessing the impairment of QoL in HS patients. Moreover, it presents a correlation with demographic data and clinical parameters. Our study highlights the enormous impact of HS on QoL. It is important to remember that, to date, HS seems to be a most burdensome dermatosis. Knowledge of QoL impairment in such patients is necessary for the proper understanding and holistic management of this disease.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Wroclaw Medical University (number KB-520/2018, 26.09.2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

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9. ARTYKUŁ SZÓSTY:

PAIN IN HIDRADENITIS SUPPURATIVA: A CROSS-SECTIONAL STUDY OF 1,795 PATIENTS

Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients

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Hidradenitis suppurativa is a chronic, inflammatory skin disorder that affects the pilosebaceous unit of the intertriginous body areas. Pain is one of the most important problems in patients with hidradenitis suppurativa. The aim of this study, which included 1,795 patients, was to evaluate the prevalence and characteristics of pain. The intensity of pain was assessed with a numerical rating scale. In addition, pain intensity was correlated with various clinical features. Pain was reported by 83.6% of subjects. The majority of patients (77.6%) experienced mild pain; women and smokers tended to experience more intense pain. Pain intensity was greater in patients with multiple affected skin areas and correlated positively with the number of those affected areas ($r = 0.151$, $p < 0.001$). There was no difference in pain intensity between affected locations. The worst pain was observed in the patients with the most severe disease and it would weaken significantly along with the severity of hidradenitis suppurativa (assessed using the Hurley staging system and the International Hidradenitis Suppurativa Severity Score System).

Key words: pain; hidradenitis suppurativa; acne inversa; numerical rating scale.

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SIGNIFICANCE

This cross-sectional study assessed the prevalence and characteristics of hidradenitis suppurativa-related pain in 1,795 patients with confirmed hidradenitis suppurativa. Most patients (83.6%) reported pain in the last 24 h. In most subjects the pain was mild; female sex and smoking were found to correlate with higher intensity of pain. Moreover, patients with multiple affected areas of skin experienced more pain, and their pain intensity correlated with the number of affected areas. In addition, the intensity of pain was found to depend on the severity of hidradenitis suppurativa, and the pain had a negative influence on patients' quality of life. The results of this large study provide an important insight into hidradenitis suppurativa-related pain, a topic that requires further research to be completely understood.

Hidradenitis suppurativa (HS), or acne inversa, is a chronic, multifactorial recurrent, debilitating inflammatory skin disorder that affects the pilosebaceous unit (1). The reported prevalence of HS varies widely; from 0.03% to 0.09% (2, 3) in Germany and 4% in young women (4). The pathogenesis of HS is not fully understood; possible mechanisms include follicular plugging, inflammation, genetic predisposition and bacterial propagation (1). The disease usually begins in early adulthood, commonly after puberty, and predominantly affects the skin folds of axillary, inguinal, gluteal and perianal areas of the body. HS is characterized by the formation of multiple inflamed nodules, abscesses, draining sinus tracts, fistulas, and scars (5). Due to the extent of the disease, foul smell, purulent discharge and pain, HS has a negative influence on patients' health-related quality of life and sexual activity (6, 7). Moreover, HS correlates with a higher incidence of depression and increased level of stigmatization (8, 9).

Pain is one of the most important burdening symptoms of HS. It is usually linked to inflammatory lesions located deep within and under the skin. The sensation varies among patients and is described as hot, pressing, cutting, sharp, gnawing, sore, or aching (1). HS-associated pain has been reported to have a negative influence on patients' quality of life (10, 11). However, the available literature on pain in HS in a representative population is limited (10–14). The aim of this study was to evaluate HS-related pain in a large sample of patients with HS in order to broaden our knowledge on this topic and to understand the relevance of pain management in the holistic approach to patients with HS.

MATERIALS AND METHODS

The study included all patients who were selected for LAight® therapy (a combination of intense pulsed light with radiofrequency) (14, 15) in multiple dermatology outpatients' centres in Germany between April 2017 and February 2020. Patients were only included if they gave informed written consent to the collection, storage and scientific evaluation of their data in an electronic database. All included patients were examined by a doctor specifically trained to determine the Hurley stage in patients with HS. The overall contraindications for LAight therapy

included pregnancy, epilepsy, and implanted electrical devices. Moreover, the treatment was initiated in patients with extreme photosensitivity, implants within 10 cm of the lesioned skin, tattoos, piercings, skin neoplasms, infection, or previous treatment with botulinum toxin in the treated HS area. In addition, baseline data, including sex, age, body mass index (BMI), Dermatology Life Quality Index (DLQI) scores, smoking habits and affected body areas, were collected.

In line with guidelines for human studies and the World Medical Association Declaration of Helsinki, the anonymized data was then transferred for evaluation.

Demographic characteristics

A total of 1,795 patients (1,152 females and 643 males; mean ± standard deviation (SD) age 40.0 ± 11.8 years) with confirmed diagnosis of HS were included in the study. The majority of subjects were active smokers (55.6%), and 10.5% smoked more than 25 cigarettes a day (heavy smokers). According to the estimated mean ± SD BMI of participants (28.1 ± 6.2 kg/m^2), the population was categorized as overweight (**Table I**).

Hidradenitis suppurativa assessments

Disease severity stage was evaluated in all patients during dermatological examination, using the Hurley staging system. Patients were then divided into groups, from Hurley stage I to III (15). In addition, after establishment of the International Hidradenitis Suppurativa Severity Score System (IHS4) as a validated severity assessment tool (17), the subjects (n = 634) were assessed accordingly and were subsequently divided into 3 groups (mild, moderate, and severe disease). The most intense pain that occurred in the last 24 h was assessed with a numeral rating scale (WP-NRS), where 0 = no pain and 10 = worst imaginable pain. Cut-off points were employed for mild (≤ 6 points), moderate (> 6 and ≤ 8 points) and severe pain (> 8 points) (16).

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics v. 26 (SPSS Inc., Chicago, IL, USA) software. All data were assessed for parametric or non-parametric distribution and minimum, maximum, mean and SD numbers were calculated. Analysed quantitative variables were evaluated using Mann–Whitney U test, Spearman's and Pearson's correlations, while for qualitative data test χ^2 was used. Changes between patients with a Hurley score of I–III and IHS4 mild, moderate and severe were assessed by Kruskal–Wallis 1-way analysis of variance on ranks. A 2-sided p-value ≤ 0.05 was considered statistically significant.

Table I. Patients' characteristics

Characteristics	All patients (n=1,795)
Sex, *n* (%)	
Men	643 (35.8)
Women	1,152 (64.2)
Age, years, mean ± SD	40.03 ± 11.81
Body mass index, kg/m^2, mean ± SD	28.08 ± 6.17
Smoking, *n* (%)	
Smokers	998 (55.6)
Non-smokers	797 (44.4)
Cigarettes/day), mean ± SD	8.07 ± 9.22
Hurley stage, *n* (%)	
I	425 (23.7)
II	1,061 (59.1)
III	309 (17.2)
IHS4, *n*, mean ± SD (range 0–281 points)	634, 14.9 ± 26
Mild, *n* (%)	180 (28.4)
Moderate, *n* (%)	222 (35)
Severe, *n* (%)	232 (36.6)
WP-NRS (last 24 h) (points), mean ± SD (range 0–10 points)	3.89 ± 2.89
Mild, *n* (%)	1,393 (77.6)
Moderate, *n* (%)	285 (15.9)
Severe, *n* (%)	117 (6.5)
Dermatology Life Quality Index (points), mean ± SD	13.2 ± 8.1

IHS4: International Hidradenitis Suppurativa Severity Score System; WP-NRS: Worst Pain Numeric Rating Scale; SD: standard deviation.

RESULTS

A total of 1,500 patients with HS (83.6%) reported pain in the last 24 h. Mean WP-NRS for the whole HS population was 3.9 ± 2.9 points. There was a statistically significant difference (p < 0.001) between mean pain intensity in women and men (4.1 ± 2.9 and 3.5 ± 2.8 points, respectively). Pain was classified as mild in 77.6% of patients, moderate in 15.9%, and severe in 6.5% (**Fig. 1**). In addition, pain was of higher intensity (p < 0.02) in smokers (4.04 ± 2.9 points) than in non-smoking patients (3.7 ± 2.8 points). There was no correlation between pain intensity and age, BMI and number of cigarettes smoked per day (detailed data not shown).

The severity of HS in the majority of patients (59.1%) was assessed as Hurley stage II, in 23.7% as Hurley stage I, and in 17.2% as Hurley stage III. As for IHS4, 36.6% of patients presented with severe HS, followed by moderate and mild HS (35.0% and 28.4%, respectively). A positive, statistically significant, but weak, correlation (r = 0.277, p < 0.001) was found between WP-NRS and IHS4 scores. Moreover, significant differences were observed in pain intensity between HS severity groups (for both Hurley and IHS4) (**Fig. 2**a, b). The most severe pain was observed in the Hurley stage III group (4.9 ± 2.8 points), and pain intensity reduced significantly with HS severity, being 3.9 ± 2.9 points for Hurley stage II group and 2.9 ± 2.7 points for Hurley stage I patients (Fig. 1a). Similar findings were noted for the IHS4 scoring system. Patients with severe HS reported pain of highest intensity (4.4 ± 2.8 points), followed by those with moderate HS (3.7 ± 2.9 points) and mild HS (2.6 ± 2.5 points) (Fig. 2b).

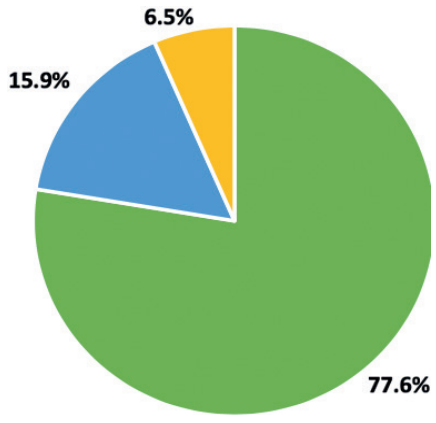

Fig. 1. Hidradenitis suppurativa-related pain intensity among patients, based on the numerical rating scale cut-offs.

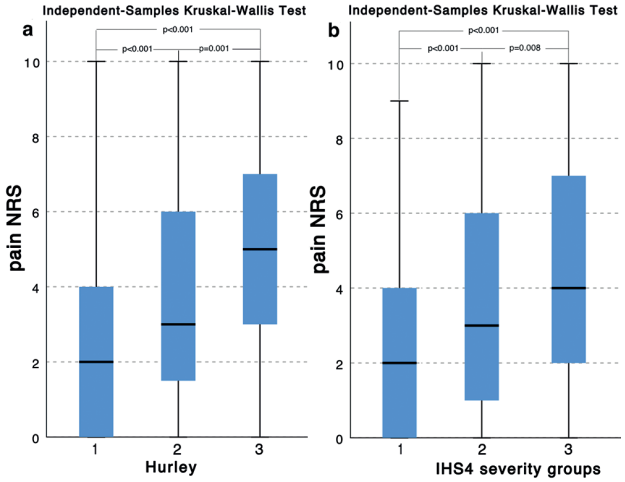

Fig. 2. Pain numerical rating scale (NRS) points differences: (a) between Hurley severity groups; and (b) between International Hidradenitis Suppurativa Severity Score System (IHS4) severity groups.

In 350 patients (19.5%) lesions were limited to a single localization, while the remainder (80.5%) had multiple affected skin areas. WP-NRS was significantly higher ($p<0.001$) in patients with multiple HS lesion locations (4 ± 2.9 and 3.3 ± 2.9 points, respectively) Moreover, intensity of pain correlated significantly ($r=0.151$, $p<0.001$) with the number of affected skin areas. Among the most commonly involved single localizations were the armpits, anogenital area, groins and buttocks. Analysis of variance did not reveal any difference in pain intensity between those locations (detailed data not shown). Mean DLQI for the whole studied population was 13.2 ± 8.1 points. The WP-NRS for the last 24 h showed significant strong correlation ($r=0.581$, $p<0.001$) with impairment in quality of life (DLQI).

DISCUSSION

HS-associated pain is the most burdensome symptom of HS, affecting up to 97% of patients during the course of the disease (11). The pain is frequently described as sharp, acute, gnawing, tenderness, or throbbing (17, 18). Although the pain appears to be mainly nociceptive, recent studies suggested an important role of the associated neuropathic component (19). The researchers indicate that overexpression of IL-1β may play a significant role in the pathogenesis of HS-associated pain (20, 21).

To the best of our knowledge, HS-related pain has not been evaluated previously in such a large population. The results of the current study confirm that pain is reported by most patients with HS (83.6%). The prevalence of pain in the current group was slightly higher than in a study by Matusiak et al. (11) (77.5%), which was one of the first studies to assess the clinical characteristics of pain and pruritus in a group of 103 patients with HS. Similarly, in the study by Kaaz et al. (10), on the influence of itch and pain on quality of sleep in patients with HS, fewer people experienced pain (79.6%) than in the current study population. Furthermore, in the above-mentioned studies, the authors assessed the prevalence of pain over longer periods of time (the previous 7 and 3 days, respectively), which may complicate the interpretation in direct comparison with our results. Due to the recurrent course of HS, it was not surprising that the estimated prevalence of pain during the whole course of the disease in these 2 studies was higher (97.1% and 86%, respectively) (10, 11).

Pain intensity assessed with a NRS did not differ greatly from previous reports (10–12, 22). Similar to the results of studies mentioned above, most subjects had mild pain symptoms (77.6%). However, the current study also found that pain in women was reported as significantly more severe than in men. Another finding of the current study, which was in accordance with the study by Matusiak et al. (11) is that the intensity of pain was significantly higher for more advanced HS. The results were independent of the severity assessment method (Hurley staging system or IHS4). Moreover, pain intensity correlated positively with IHS4 scores. Similar results were reported previously for Hurley staging, Hidradenitis Suppurativa Score, and Hidradenitis Suppurativa Severity Index (10).

HS characteristically begins as follicular plugging in a single area, which later progresses to inflammatory nodules. Nevertheless, during its course, HS tends to affect multiple body areas (23). Among the most frequently affected body zones in the current study population were the armpits, groins, buttocks and anogenital region. Involvement of multiple skin areas was proven to have stronger negative influence on patients' quality of life (7). In addition, it has been shown that involvement of the anogenital region has the strongest impact on patients' quality of life and psychological status (7). Similarly, in the current study, patients with multiple involved skin areas had statistically more severe pain. However, the current study did not find any differences in pain perception between patients with different body areas affected.

A significant role in the pathogenesis of HS is attributed to smoking and obesity (5). A connection was established between disease severity and both smoking and high BMI (24). The mechanism of influence of nicotine on the pathogenesis of HS is yet to be determined; however, nicotine receptors are highly expressed on follicular epithelium (25). Obesity may contribute to the pathogenesis, since obesity itself is considered a state of inflammation (26). In addition, obesity may increase friction in the skin folds, which plays a role in the pathophysiology of the disease. Due to increased knowledge of the possible role of mechanical stress in the pathogenesis of HS, patients should be educated regarding the best fabrics and styles of undergarments (27). The correlations between these risk factors and pain have not been studied until now. Although the current study population was overweight (mean BMI >25 kg/m^2) no

correlation was found between BMI and pain intensity. More than half of the patients were active smokers, and they reported significantly higher pain levels than non-smokers. Nevertheless, no correlation was found between pain and number of cigarettes smoked per day.

The negative influence of HS on quality of life of patients is well documented (9). In a qualitative study by Esmann et al. (28) responders indicated pain as one of the significant factors in impaired daily functioning and poor quality of life. Moreover, multiple studies have found pain to be one of the most important contributors to decreased quality of life (4, 22, 29, 30). More than one-third of patients in the current study reported a very large effect on their quality of life. Moreover, comparable to the study by Matusiak et al. (11), pain intensity correlated positively with DLQI scores, indicating the importance of pain perception in patients' well-being.

This study has some limitations. Only basic evaluation of the patients selected for LAight® therapy treatment was performed. Since this did not include all necessary questions about HS-related pain, this study was unable to fully characterize the pain. However, due to the large sample size of the study, which markedly exceeds the representative number of patients in the HS population in Germany, the results provide an important insight into HS-related pain.

In conclusion, to the best of our knowledge, this is the largest study to date to assess intensity of pain in patients with HS, and its relationships with demographic data and clinical parameters. The results clearly show that pain is an important and frequent burden for patients with HS. Although published data on the characteristics and prevalence of pain in HS is scarce, the impact of HS-related pain on quality of life was well documented. During the diagnosis and treatment of HS, clinicians should pay close attention to the management of accompanying pain.

The authors have no conflicts of interest to declare.

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10. ARTYKUŁ SIÓDMY:

MCPIP1/REGNASE-1 EXPRESSION IN KERATINOCYTES OF PATIENTS WITH HIDRADENITIS SUPPURATIVA: PRELIMINARY RESULTS

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Article

MCPIP1/Regnase-1 Expression in Keratinocytes of Patients with Hidradenitis Suppurativa: Preliminary Results

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Abstract: The pathogenesis of hidradenitis suppurativa (HS) is yet to be fully understood. However, inflammation is a key element in the development of skin lesions. The aim of this study was to evaluate the expression of monocyte chemotactic protein-1-induced protein-1 (MCPIP1) in the skin of patients suffering from HS. Skin biopsies of 15 patients with HS and 15 healthy controls were obtained and processed for immunohistochemistry, western blot, and real time PCR. The highest mean MCPIP1 mRNA expression was found in the inflammatory lesional skin of HS patients. It was significantly higher than MCPIP1 mRNA expression in the biopsies from both healthy controls and non-lesional skin of HS patients. Western blot analysis indicated that expression of MCPIP1 was elevated within both lesional and non-lesional skin compared to the healthy control. The increased MCPIP1 mRNA and protein expression level in HS lesions may indicate its possible role in the disease pathogenesis.

Keywords: MCPIP1; hidradenitis suppurativa; Regnase-1

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1. Introduction

Inflammation is a basic immune response of our organism that enables survival during infections or injuries. On the molecular level, it is a set of interactions between inflammatory factors and cells, often described as a stress response of tissue or organism to noxious conditions [1,2]. Although usually beneficial and life-preserving, disturbances of the innate immune system may lead to development of immune-mediated diseases [3]. Moreover, failure in neutralizing acute response often causes chronic inflammation and severe metabolic consequences [4]. Many of the important immune responses are carried out in the skin [5].

Hidradenitis suppurativa (HS) is a debilitating skin disorder of a complex pathogenesis, which remains unclear [6]. The role of overproduction of inflammatory cytokines and an inability of its inhibition has been mentioned by many authors [7]. The possible suppression of inflammation is of benefit for the treatment of HS [8–10].

Monocyte chemotactic protein-1-induced protein-1 (MCPIP1), also known as Regnase-1, is an RNase protein encoded by the ZC3H12A gene. It regulates the inflammatory activation and maintains immune homeostasis by selectively promoting the destabilization of mRNAs of certain proinflammatory cytokines (e.g., IL-6 and IL-1β) and transcription factors [11–15]. The lack of MCPIP1 in mice resulted in systemic inflammation leading to growth retardation, anemia, splenomegaly, lymphadenopathy, and premature death [11,16–18]. Recent studies indicated that in the skin, MCPIP1 functions as an important regulator of epidermal homeostasis. The ZC3H12A gene is induced by many inflammatory mediators including

IL-17 and IL-36 [19–21]. Our previous studies on the influence of MCPIP1 on keratinocytes showed that its deficiency leads to the skin barrier impairment and spontaneous cutaneous inflammation [22]. On the other hand, MCPIP1 was shown to be upregulated in human psoriatic skin [20,23], whereas its deficiency in mice led to the much aggravated psoriasis-like inflammation phenotype induced by imiquimod [21,23,24].

We hypothesized that MCPIP1 may be involved in the pathogenesis of other than psoriasis skin disorders of inflammatory background, like HS. The aim of this study was to evaluate the expression of MCPIP1, both on mRNA and protein level, in the skin of patients suffering from HS. To the best of our knowledge, this is the first study to investigate the possible association between MCPIP1 and the pathogenesis of HS.

2. Results

MCPIP1 Is Aberrantly Expressed in Hidradenitis Suppurativa

To investigate potential association of MCPIP1 with HS, we analyzed the expression of MCPIP1 on both mRNA and protein levels in the lesional and non-lesional skin of HS patients, and healthy controls. The highest mean MCPIP1 mRNA expression was found in the inflammatory lesional skin of HS patients (HS-1: lesional skin) (0.0236 ± 0.0134). It was significantly higher than MCPIP1 mRNA expression in the biopsies from both healthy controls (CTR) (0.0080 ± 0.0034, $p < 0.001$) and non-lesional skin of HS patients (HS-2: non-lesional skin) (0.0049 ± 0.0034, $p < 0.001$) (Figure 1A). There were no statistical correlations between MCPIP1 mRNA expression in lesional HS skin and well-known HS predisposing factors (obesity and smoking), as well as between sexes, those with and without family history of HS or those who had or had not suffered from juvenile acne in their adolescence (detailed data not shown). We next determined MCPIP1 protein expression in the lysates of control and HS skin. Western blot analysis indicated that expression of MCPIP1 was elevated within both lesional (2,5-fold increase) and non-lesional skin (2,3-fold increase) compared to the healthy control (Figure 1B,C). Subsequently, we determined the in situ expression of MCPIP1 in the skin. Generally, all biopsies showed a similar pattern of immunostaining. Specific MCPIP1 immunostaining was cytoplasmic and present in the epidermis, as well as in hair follicles. MCPIP1 immunoreactivity was found in all studied biopsies (HS-1: lesional skin, HS-2: non-lesional skin and healthy control skin) in the suprabasal layers of the epidermis. The basal layer of the epidermis showed no MCPIP1 immunoreactivity. There was also no MCPIP1 immunoreactivity in the dermis. Both lesional and non-lesional HS skin showed aberrant distribution of MCPIP1 within epidermis (Figure 1D).

In parallel to the analyses of MCPIP1 expression, we investigated the level of inflammatory influx within HS skin. Haematoxylin and eosin staining showed a large inflammatory cell infiltration into the dermis of HS lesional skin (Figure 2A). This correlated with increased gene expression level of selected inflammatory mediators: IL-1β, IL-6, TNFα and S100A8 (Figure 2B). The non-lesional HS skin did not show any signs of inflammatory reaction (Figure 2A,B).

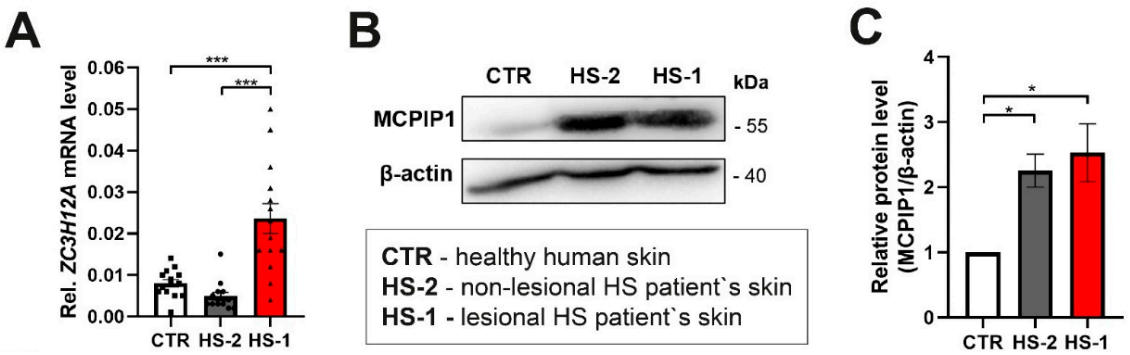

Figure 1. *Cont.*

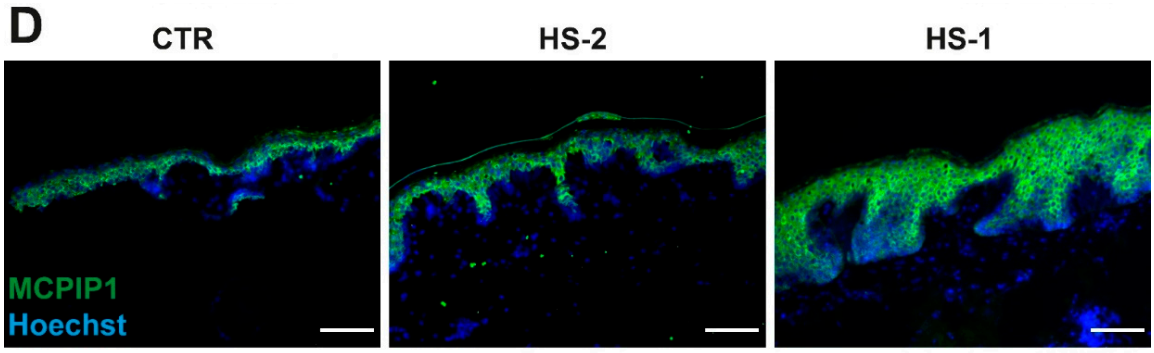

Figure 1. Increased expression of monocyte chemotactic protein-1-induced protein-1 (MCPIP1) in the hidradenitis suppurativa skin. (**A**) qRT-PCR analysis of MCPIP1 (ZC3H12A) transcript level in the healthy human skin (CTR), non-lesional hidradenitis suppurativa patients' skin (HS-2) and lesional HS patients' skin (HS-1) (n = 14). (**B**) Representative Western blot for MCPIP1. β-actin was used as the loading control. (**C**) Densitometric quantification of MCPIP1 protein level (n = 4). (**D**) Representative MCPIP1 immunofluorescence staining of the skin sections. Scale bar 100 μm. Data represent the mean ± SEM. * $p < 0.05$, *** $p < 0.001$ by one-way ANOVA.

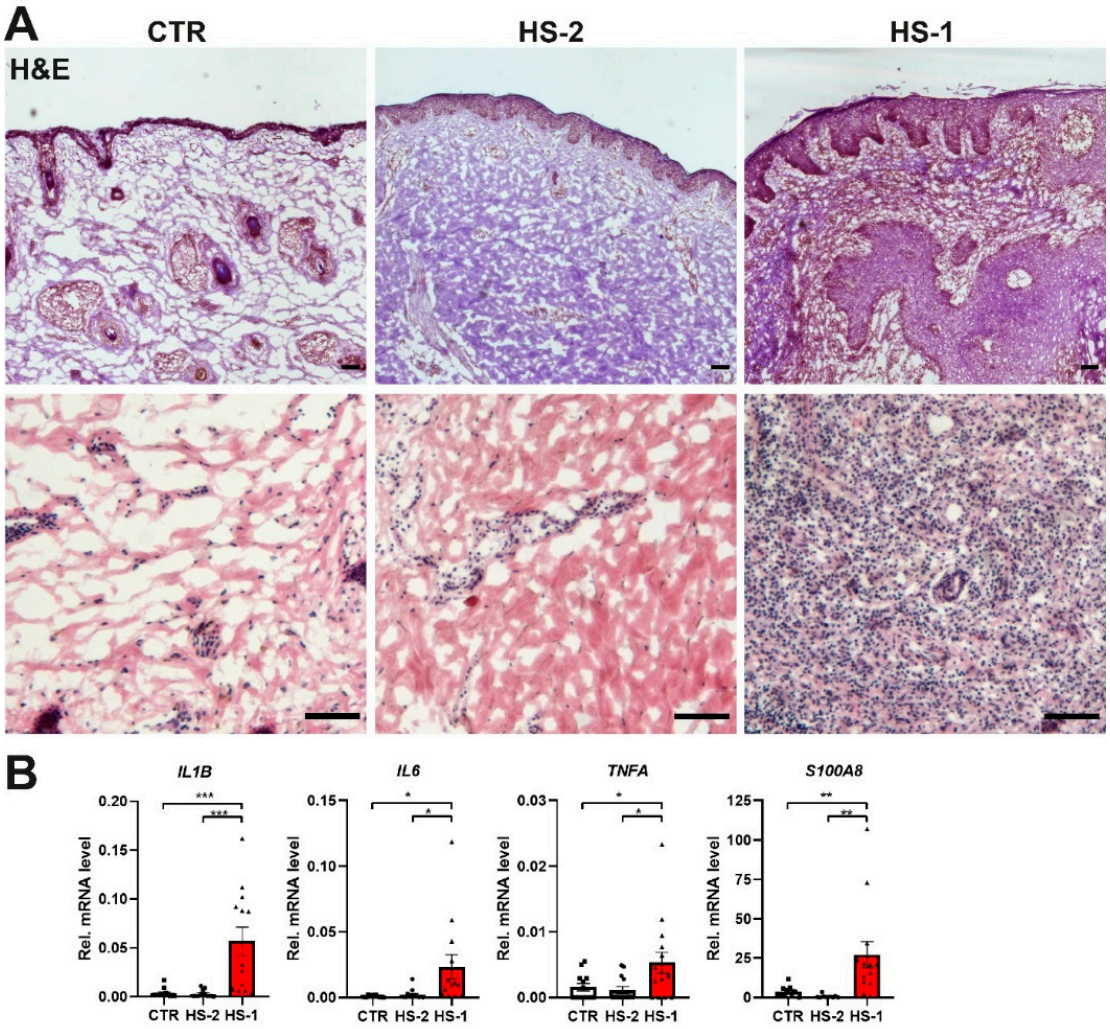

Figure 2. Abundant inflammation in the hidradenitis suppurativa skin. (**A**) H&E staining of the CTR, HS-1, and HS-2 skin sections at different magnification. (**B**) qRT-PCR analysis of IL1B, IL6, TNFA and S100A8 transcript level. Scale bar 100 μm. Data represent the mean ± SEM. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by one-way ANOVA.

3. Discussion

The pathogenesis of HS is yet to be fully understood. Among several proposed pathogenetic factors (obesity, smoking, hormonal disbalance, genetic predisposition) immunological disturbances are considered crucial for the development of HS lesions. The involvement of the immune system and disruption in the immune response have been confirmed with the favorable outcome of anti-inflammatory biologic treatment [8–10].

The results of our study clearly demonstrate the increased MCPIP1 mRNA and protein expression in the lesional skin of HS patients. Our results are comparable with those reported in psoriatic plaques [20,23]. Similarly to our study, MCPIP1 mRNA and protein expression was significantly increased in psoriatic skin than in healthy control skin samples. The similarities between both studies confirm a possible mutual immune-pathogenetic pathway of HS and psoriasis. Higher MCPIP1 expression and its function in inflammatory regulation may play an important role in the pathogenesis of both disorders. As hypothesized by Monin et al. [23] it is likely that the increased MCPIP1 mRNA expression reflects the ongoing inflammatory milieu, and particularly the high IL-17A levels, demonstrated in lesional skin of both HS and psoriasis. This is not surprising as the resemblances between HS and psoriasis have already been found in pathogenesis and treatment in both disorders [25].

We observed that the level of MCPIP1 protein was elevated not only within lesional skin, but also in the skin surrounding the HS lesion. In that region MCPIP1 was stabilized, most likely as a result of a highly inflammatory environment. This, however, did not correlate with increased transcriptional expression of ZC3H12A. This may be explained by the fact that MCPIP1 RNase regulates, among many other mRNAs, also its own transcript half-live [26].

To the best of our knowledge, this is the third study in which MCPIP1 expression was assessed in human skin. Ruiz-Romeu et al. [20] in healthy skin found the expression of MCPIP1 exclusively present in the granular layer of the epidermis. A similar pattern of MCPIP1 immunoreactivity was found in atopic dermatitis [20]. In contrast, Monin L et al. [23] demonstrated MCPIP1 expression distributed in the whole epidermis of the healthy skin. Our study clearly showed MCPIP1 immunoreactivity in the suprabasal layers of the epidermis of healthy controls. In HS lesional skin we demonstrated abundant MCPIP1 immunoreactivity in the suprabasal layers of the epidermis with comparable immunostaining pattern as in non-lesional HS skin and healthy control skin. In lesional psoriatic skin MCPIP1 immunoreactivity was also predominantly found in the epidermis, distributed equally in the entire epidermis [23] or in its upper layers [20]. In both studies MCPIP1 immunoreactivity was similarly localized both in lesional and non-lesional psoriatic skin [20,23].

In the lesional skin of HS, MCPIP1 is elevated on both transcriptional and translational level and it is not sufficient to resolve inflammatory processes. We noticed high inflammatory influx and elevated transcriptional expression of selected HS-related factors: IL-1β, IL-6, TNFα and S100A8. Enhanced expression of IL-6 and IL-1β was demonstrated in the lesional skin of HS patients [27]. Expression of S100A8/A9 was also shown to be elevated in HS [28]. Moreover, increased levels of TNFα in HS patient serum and skin have been reported [29–32].

Another molecule that may be important in HS pathogenesis is the seventh subunit of P2X receptor (P2 × 7R), which is plasma membrane channel gated by adenosine triphosphate (ATP) [33]. It is widely distributed, especially in immune system cells. Its role is to activate the NLRP3 inflammasome and promote IL-1β maturation and release. The receptor have been previously described in psoriasis, rosacea, and HS [34–36]. Manfredini et al. [35] found that P2X7R protein level is higher in keratinocytes, lymphocytes, and monocytes of HS skin in comparison to healthy controls [35]. Moreover, authors presented, that P2X7R has significant, yet weak association with NLRP3 inflammasome [35].

We are aware of limitations of our study. Firstly, our group consisted only of 15 people suffering from HS. Although the population of well diagnosed HS patients is small, the

number of patients in future studies should be bigger in order to provide more accurate data. Moreover, we have focused on MCPIP1 and its expression in the skin of HS patient. Future studies aiming for correlation between MCPIP1 and well-known proinflammatory molecules, including newly described P2X7R, would play an important role in discovering the pathogenesis of HS.

4. Materials and Methods

The study was approved by the local Bioethics Committee of Wroclaw Medical University. The studied group included 15 patients with HS: 7 females (46.67%) and 8 males (53.55%). The mean age of the group was 35.8 ± 11.2 years. According to the mean BMI (30.1 ± 6.31 kg/m^2) the population was considered obese. The majority (8 people, 53.6%) of the subjects were active smokers with the mean of 9.6 ± 6.1 pack-years. 7 people (46.7%) reported to suffer from juvenile acne during adolescence, while only 2 (13.3%) had a positive family history of HS. A total 86.7% (13) of patients were treated previously, with unsatisfactory results. All included patients have not been treated for HS for at least of two months before the enrollment to the study. All the patients were examined by the dermatologists experienced with HS, in order to properly assess HS severity. According to Hurley staging [37] the severity of the disease in the majority of the patients was assessed as Hurley II (8 patients, 53.3%), in 4 subjects (26.7%) as Hurley III and in the rest (3 people, 20%) as Hurley I. As for IHS4 assessment [38], on average the patients scored 15.9 ± 8.9 points, indicating severe disease. Among the HS–associated subjective symptoms, assessed with 11-point Numeral Rating Scale (NRS), pain was the most severe (4.4 ± 2.9 points), then purulent discharge (4.2 ± 2.9 points), foul smell (3.4 ± 3.4 points) and pruritus (2.5 ± 2.6 points). 9 patients (60%) had multiple body areas affected by HS, while 6 (40%) presented HS limited to one area. Among the most frequently affected areas were armpits (11 patients, 73.3%), while buttocks affectation was present in only 1 subject (6.7%).

Additionally, 15 control healthy skin samples were collected from the age and sex-matched patients who underwent surgical procedures for non-malignant skin lesions or blepharoplasty.

4.1. Biopsy

Prior to the biopsy, the patients got locally injected the mixture of anesthetic (2% lidocaine) and adrenaline to diminish pain and impede bleeding. Two 5-mm punch biopsies were obtained from every HS patient. One of the biopsies was taken from the active, inflammatory lesion, while the other from the healthily looking skin in close proximity from the first one (at least 2 cm).

4.2. RNA Isolation and Quantitative Real-Time PCR

All collected skin samples were frozen in RNAlater (Sigma-Aldrich, Saint Louis, MO, USA) and stored at −80 °C. Total RNA was extracted from tissues by homogenization in Fenozol (A&A Biotechnology, Gdynia, Poland) using a tissue homogenizer (Miccra D-1, Miccra GmbH, Germany). The purity and concentration of total RNA were assessed using a NanoDrop 1000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA). Subsequently, 1 µg of total RNA was reverse-transcribed with oligo(dT) primer and M-MLV reverse transcriptase (Promega, Madison, WI, USA). The cDNA was diluted 5 times, and real-time PCR was performed using a QuantStudio 3 system (Applied Biosystems, Thermo Fisher Scientific, Waltham, MA, USA) with SYBR Green qPCR master mix (A&A Biotechnology, Gdynia, Poland). The mRNA level of MCPIP1 transcript was determined relative to elongation factor-2 (EF2) by the $2^{-\Delta Ct}$ method. The following gene-specific primer pairs were used: for ZC3H12A: GGAAGCAGCCGTGTCCCTATG and TCCAGGCTGCACTGCTCACTC, for EF2: GACATCACCAAGGGTGTGCAG and TCAGCACACTGGCATAGAGGC, for IL1B: GATGTCTGGTCCATATGAACTG and TTGGGATCTACACTCTCCAGC, for IL6: GTGAAAGCAGCAAAGAGGCA and

TCACCAGGCAAGTCTCCTCA, for TNFA: TAGCCCATGTTGTAGCAAACC and TGATGGCAGAGAGGAGGTTG, for S100A8: GAATTTCCATGCCGTCTACAGG and GCCACGCCCATCTTTATCACCAG.

4.3. Western Blot Analysis

The protein lysate from skin tissues was isolated in RIPA (Radioimmunoprecipitation assay buffer) solution with protease and phosphatase inhibitors (Roche, Basely, Switzerland) using a tissue homogenizer and then centrifuged for 20 min, 4 °C, 14,000× g. The protein concentrations in the tissues lysates were measured with the bicinchoninic acid assay. The electrophoresis separation was carried out in 10% polyacrylamide gel and electrotransferred to PVDF (Polyvinylidene fluoride) membranes (Merck-Millipore, Burlington, MA, USA). After the transfer, membranes were blocked for 1 h in 3% milk in Tris-buffered saline with 0.05% Tween (BioShop, Burlington, ON, Canada) followed by an overnight incubation in the primary antibody at 4 °C. On the following day, the membranes were rinsed and incubated for 1 h with the secondary antibody. The Immobilon TM Western Chemiluminescent HRP Substrate (Merck-Millipore, Burlington, MA, USA) and the ChemiDoc system (Bio-Rad, Hercules, CA, USA) were used for signal detection. Densitometric quantification was performed using ImageLab (Bio-Rad, Hercules, CA, USA). The MCPIP1 protein level was normalized to β-actin level. The following antibodies were used: rabbit anti-MCPIP1 (GTX110807; 1:2000; GeneTex, Inc., Irvine, CA, USA), mouse anti-β-actin (A1978; 1:2000; Sigma-Aldrich), peroxidase-conjugated anti-rabbit (A0545; 1:20,000; Sigma-Aldrich, St. Luis, MO, USA) and peroxidase-conjugated anti-mouse (1:20,000; BD Pharmingen).

4.4. Immunofluorescence Staining

Skin tissues were embedded in Tissue-Tek O.C.T. Compound (Scigen Scientific Gardena, Gardena, CA, USA) and stored at −80 °C. Then, 8 µm cryosections were cut and stained with hematoxylin and eosin (H&E) using standard protocol. For immunofluorescence staining, antigen retrieval was performed in 10 mM citrate buffer (pH 6.0) for 30 min at 95 °C. Subsequently, skin samples were blocked with 5% horse serum, 1% BSA and 0.05% Tween in PBS for 1 h and incubated with primary rabbit antibodies against MCPIP1 (1:100; GeneTex) overnight at 4 °C in blocking buffer. Bound primary antibodies were detected by incubation with secondary goat antibodies Alexa Fluor 488 anti-rabbit (A11008; 1:600; Invitrogen, Darmstadt, Germany) for 1 h at room temperature, followed by counterstaining with Hoechst 33,258 (1:2500; Thermo Scientific). After incubation, the sections were mounted in fluorescent mounting medium (Dako) and visualized in Leica DMC5400B microscope (Leica Microsystems, Wetzlar, Germany). All figures were prepared using ImageJ (National Institutes of Health, Bethesda, MD, USA).

4.5. Statistical Analysis

The statistical analysis of the obtained results was performed with the use of IBM SPSS Statistics v. 26 (SPSS INC., Chicago, IL, USA) software. All data were assessed for parametric or non-parametric distribution. The minimum, maximum, mean and standard deviation numbers were calculated. Analyzed quantitative variables were evaluated using Mann–Whitney U test, Spearman and Pearson correlations, while for qualitative data test Chi2 was used. One-way ANOVA was used for the comparison of mRNA and protein expression levels between two HS samples and healthy skin. A 2-sided p value of ≤ 0.05 was considered to be statistically significant.

5. Conclusions

As far as we know, this is the first study assessing the expression of MCPIP1 in the skin of HS patients. Our preliminary results may be of benefit for the deeper understanding of the possible immunopathogenesis of this chronic and recurrent inflammatory dermatosis. Nevertheless, though our study sheds light on possible involvement of MCPIP1 in HS

pathogenesis, further studies are necessary to clarify the exact role of MCPIP1 in the pathogenesis of HS.

Author Contributions: Conceptualization, J.J., J.C.S. and Ł.M.; methodology, J.J., J.C.S. and Ł.M.; investigation, P.K.K., W.S., A.L.-C., Ł.M., J.J. and J.C.S.; resources, P.K.K., W.S. and A.L.-C.; data curation, P.K.K., W.S., A.L.-C., Ł.M., J.J. and J.C.S.; writing—original draft preparation, P.K.K., W.S., A.L.-C., Ł.M., J.J. and J.C.S.; writing—review and editing, J.J., J.C.S. and Ł.M.; visualization, W.S. and A.L.-C.; supervision, J.J., J.C.S. and Ł.M.; project administration, P.K.K., J.C.S. and J.J. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was performed based on the statutory activity of the department, in accordance with the previously obtained approval of the Institutional Review Board of Wrocław Medical University (KB-520/2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data obtained in this study may be available from the corresponding authors upon a reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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11. ARTYKUŁ ÓSMY:

ULTRASONOGRAPHIC RAILWAY SIGN IN TUNNELS AS A NEW INDEPENDENT RISK FACTOR OF ADALIMUMAB FAILURE IN HIDRADENITIS SUPPURATIVA

Research letter

Ultrasonographic railway sign in tunnels as a new independent risk factor of adalimumab failure in hidradenitis suppurativa

To the Editor: Cutaneous ultrasound is a valuable tool for assessing, staging, and monitoring hidradenitis suppurativa (HS). The implementation of ultrasound in HS assessment allows for the detection of tunnels and optimizes both surgical and medical approaches.[1]

In 2016, Wortsman et al[2] published a study on the assessment of tunnels in HS using ultrasound. The authors mentioned the presence of hyperechogenic, linear structures within tunnels that could be suggestive of hair shafts.[2,3] During our daily practice in our HS and ultrasound unit, we noted the following similar characteristics: multiple yet parallel hyperechogenic structures inside dermoepidermal tunnels (Figs 1 and 2). Despite this, no hair tracts were found during surgery or identified in histopathologic reports. We hypothesized that, because of the similar echogenicity of the epidermis, the structures might also correspond to a granulation membrane and pseudoepithelialization within the tunnels.

Therefore, we conducted a prospective observational study in the Dermatology Department of the Hospital de Manises between January 2020 and April 2021. Our goal was to evaluate the correlation between linear hyperechogenic parallel lines along the tunnel, we called the "railway sign," and the response to adalimumab. The study included 102 HS lesions assessed with ultrasound (Esaote MyLab 30 Gold, 18 MHz) as dermoepidermal tunnels in 63 adult patients of Hurley stages II to III who were surgery naïve and at least 12 weeks without systemic intervention. In 68 out of 102 lesions (66.67%), ultrasound examination revealed the presence of the railway sign. All patients started biologic therapy with adalimumab 160 mg initial dose and 80 mg every 2 weeks and were subsequently assessed using ultrasound on the 12th and 24th week of treatment.

Patients with the railway sign lesions on ultrasound examination at baseline showed significantly worse response to biologic therapy, with complete lesion resolution (no signs of clinical and ultrasonographic inflammation or drainage) of 2.9% and 4.4% on the 12th and 24th week, respectively. By contrast, 64.7% of the patients in whom the railway sign was not detected at baseline exhibited complete lesion healing at week 12 and 88.2% at week 24. Pathologic analysis of the surgical samples detected no hair shaft structures in any case, and remnant epithelial cells were detected in up to 21% of the cases. After surgical excision or deroofing of unresponsive lesions, all remnant cases healed without further complications.

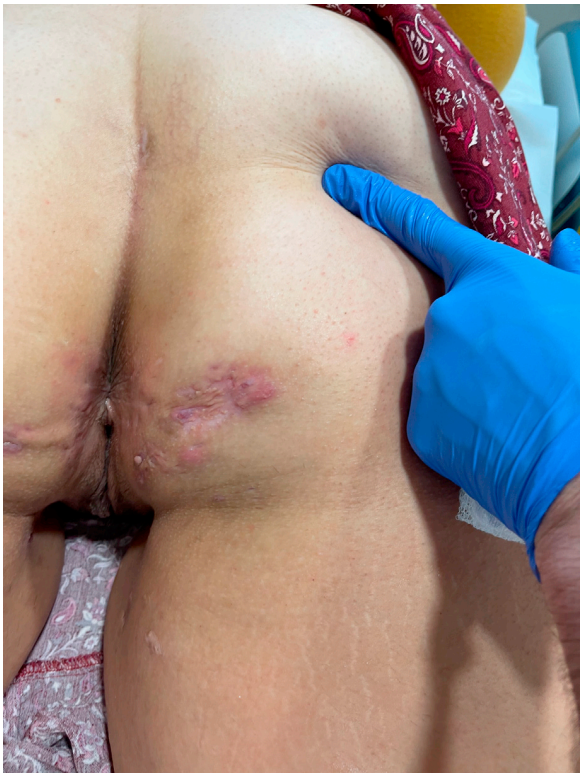

Fig 1. A 43-year-old patient with an inflammatory area on the right buttock.

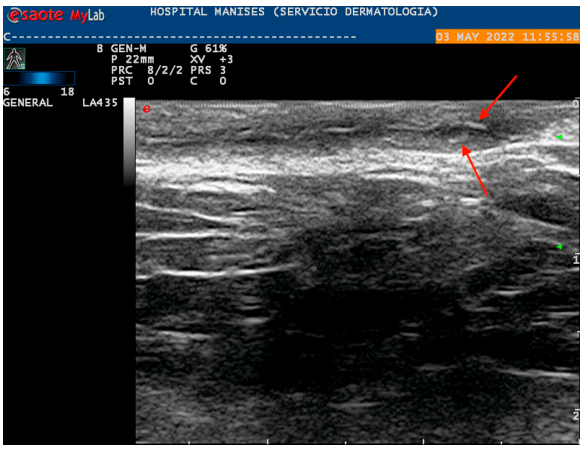

Fig 2. Ultrasonographic railway sign in a dermoepidermal tunnel, the longitudinal plane of B-mode (18 MHz).

Cutaneous ultrasound is a noninvasive, cost-effective technique that can easily be mastered by dermatologists and used in HS clinics. Its use can improve both the staging and management outcomes of patients with HS. In addition to showing

that not all HS lesions are entirely resolved using adalimumab, our study demonstrates that detecting the railway sign of tunnels is an independent risk factor of adalimumab failure for individual lesions. This may be helpful in managing patients' expectations of adalimumab use and planning early surgical excision of less likely responsive lesions. Further, extensive cohort studies regarding the implementation of ultrasound in patients with HS on treatment are necessary to confirm our observations.

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Funding sources: None.

IRB approval status: Not applicable.

Key words: Adalimumab; biologics; failure; fistulas; hidradenitis suppurativa; imaging; tunnel; ultrasonography.

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Conflict of interests

Dr Martorell Calatayud has served as a consultant for and received speaker fees from AbbVie, Celgene, Janssen, Novartis, MSD, UCB Pharma, Lilly, Leo Pharma, Isdin, and Pfizer. The rest of the authors have no conflict of interest to declare.

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2. Wortsman X, Castro A, Figueroa A. Color Doppler ultrasound assessment of morphology and types of fistulous tracts in hidradenitis suppurativa (HS). *J Am Acad Dermatol*. 2016;75:760-767. https://doi.org/10.1016/j.jaad.2016.05.009
3. Wortsman X, Wortsman J. Ultrasound detection of retained hair tracts in hidradenitis suppurativa. *Dermatol Surg*. 2015;41:867-869. https://doi.org/10.1097/DSS.0000000000000388

https://doi.org/10.1016/j.jaad.2022.08.064

12. STRESZCZENIE W JĘZYKU POLSKIM

Na rozprawę doktorską składa się cykl 8, monotematycznych artykułów opublikowanych w międzynarodowych czasopismach naukowych indeksowanych w bazie MEDLINE i uwzględnionych na liście Journal Citation Reports by Web of Science oraz znajdujących się w wykazie czasopism naukowych Ministerstwa Edukacji i Nauki (MEiN).
Łączny współczynnik wpływu (impact factor – IF) artykułów wchodzących w skład rozprawy doktorskiej wynosi 41,509, a punktacja MEiN 830 punktów. We wszystkich artykułach jestem pierwszym i wiodącym autorem.

Sześć pierwszych artykułów skupia się na aspekcie psychodermatologicznym hidradenitis suppurativa (HS), jakości życia pacjentów oraz towarzyszących objawach subiektywnych.

Dwa pierwsze artykuły dotyczą tworzenia polskich wersji językowych instrumentów specyficznych dla HS wykorzystywanych do pomiary jakości życia. Zgodnie z międzynarodowymi standardami stworzono polskie wersje językowe oraz dokonano walidacji kwestionariuszy Hidradenitis Suppurativa Quality of Life (HiSQoL) oraz Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24). Oba kwestionariusze, zarówno jako całe instrumenty, jak i podskale, charakteryzowały się wysoką spójnością wewnętrzną (Cronbach alfa), powtarzalnością oraz bardzo wysokimi współczynnikami korelacji wewnątrzklasowej (Intraclass Correlation Coefficient). Ponadto, wykazano zadawalającą korelację wyników obu kwestionariuszy z powszechnie używanymi instrumentami oceniającymi jakość życia w dermatologii, jak np. Dermatology Life Quality Index (DLQI).

We współpracy z autorami oryginalnej wersji kwestionariusz HSQoL-24 przeprowadzono także analizę pierwszych na świecie danych dotyczących użyteczności tego narzędzia w praktyce klinicznej na grupie 342 pacjentów z HS (artykuł trzeci). Udowodniono, że upośledzenie jakości życia pacjentów z HS koreluje pozytywnie z liczbą zajętych obszarów ciała, czasem trwania choroby, a negatywnie z wiekiem pojawienia się pierwszych objawów. Ponadto pacjenci pozostający w związkach rodzinnych lub z partnerami osiągali wyższe wyniki niż pacjenci bez bliskiej osoby.

W kolejnej pracy, na grupie 130 pacjentów z HS oceniano, czy pacjenci adekwatnie potrafią określić ciężkość swojej choroby, oraz czy samoocena pacjenta lepiej odzwierciedla wpływ choroby na jego życie. Wykazano pozytywną korelację upośledzenia jakości życia, ocenianą za pomocą HSQoL-24 oraz Dermatology Life Quality Index (DLQI), z nasileniem

choroby ocenianym przez pacjentów. Podobnej korelacji nie udokumentowano dla stopni nasilenia choroby według Hurley. Co ciekawe, nie obserwowano także różnic w upośledzeniu jakości życia pomiędzy różnymi stopniami nasilenia choroby według skali Hurley.

Prace piąta i szósta powstały jako współpraca w ramach Polsko-Niemieckiego konsorcjum ekspertów z zakresu HS. Do analizy włączono dane 1795 niemieckich pacjentów leczonych z powodu HS. W pierwszej pracy, na największej dotychczas opisanej grupie pacjentów, określono przy pomocy kwestionariusza DLQI upośledzenie jakości życia. Udowodniono, że choroba wywiera bardzo duży wpływ na jakość życia pacjentów, który rośnie wraz ze wzrostem nasilenia zmian chorobowych oraz odczuwanego bólu. Ponadto wykazano, że HS ma istotnie większy wpływ na jakość życia kobiet niż mężczyzn. W kolejnej pracy na tej samej kohorcie pacjentów przeanalizowano częstość występowania bólu i jego charakterystykę. Ponad 80% pacjentów odczuwało ból w ostatnich 24 godzinach przed badaniem, a większość z nich odczuwała ból o nasileniu łagodnym. Osoby o wyższym nasileniu zmian chorobowych, większej liczbie zajętych okolic skóry i palacze raportowali ból o istotnie wyższym nasileniu.

Siódma praca jest oryginalną pracą badawczą, w której określono zaburzenia ekspresji białka MCPIP1 w skórze pacjentów z HS. MCPIP1 jest białkiem regulującym aktywację zapalną i utrzymującym homeostazę immunologiczną poprzez hamowanie niektórych cytokin prozapalnych. Bioptaty skóry pobrane od pacjentów z HS ze zmian skórnych i ze skóry sąsiadującej ze zmianami skórnymi porównano ze zdrowymi kontrolami. Najwyższą średnią ekspresję mRNA MCPIP1 stwierdzono w skórze zmienionej zapalnie. Była ona istotnie wyższa niż ekspresja mRNA MCPIP1 w skórze niezmienionej chorobowo, jak i u zdrowych kontroli. Analiza Western-Blot wykazała, że w porównaniu do zdrowych kontroli, ekspresja MCPIP1 na poziomie białka jest istotnie podwyższona u pacjentów z HS, zarówno w skórze zmienionej i niezmienionej chorobowo. Specyficzne barwienia immunologiczne wykazały nieprawidłową dystrybujcję MCPIP1 w skórze chorych zmienionej i niezmienionej chorobowo.

Ostatnia praca jest międzynarodowym projektem badającym użyteczność ultrasonografii (USG) wysokiej częstotliwości w diagnostyce i leczeniu HS. Po raz pierwszy opisano występowanie „obrazu torów kolejowych" wewnątrz tuneli, który odpowiada procesowi pseudoepitelializacji. Udowodniono, że tunele, w których obserwowano ten obraz nie odpowiadały na leczenie adalimumabem i wymagały wykonania zabiegu chirurgicznego.

Podsumowując, hidradenitis suppurativa jest przewlekłą, wyniszczającą i bolesną jednostką chorobową, której patogeneza nie jest do końca poznana. Wyniki prac zawartych w rozprawie doktorskiej wskazują na ogromny wpływ choroby i towarzyszącego jej bólu na

jakość życia pacjentów. Ponadto wskazują na potrzebę holistycznego podejścia do pacjenta, indywidualizacji terapii oraz prowadzenia dalszych badań mających na celu dalsze zgłębianie patomechanizmu powstawania zmian skórnych.

13. STRESZCZENIE W JĘZYKU ANGIELSKIM

The doctoral dissertation consists of a series of 8 monothematic articles published in international scientific journals indexed in the MEDLINE database and included in the Journal Citation Reports by Web of Science list, as well as in the list of scientific journals of the Ministry of Education and Science (MEiN). The total impact factor (IF) of the articles included in the doctoral dissertation is 41.509, and the MEiN score is 830 points. In all articles, I am the first and lead author.

The first six articles focus on the psychodermatological aspect of hidradenitis suppurativa (HS), patients' quality of life, and the accompanying subjective symptoms.

The first two articles concern the creation of Polish language versions of HS-specific instruments used to measure the quality of life. In accordance with international standards, Polish language versions were created, and the Hidradenitis Suppurativa Quality of Life (HiSQoL) and Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) questionnaires were validated. Both questionnaires, as whole instruments and subscales, were characterized by high internal coherence (Cronbach alpha), repeatability, and very high intraclass correlation coefficients (ICC). In addition, a satisfactory correlation of the results of both questionnaires with commonly used instruments assessing the quality of life in dermatology, such as the Dermatology Life Quality Index (DLQI), was demonstrated.

In cooperation with the authors of the original version of the HSQoL-24 questionnaire, an analysis of the world's first data on the usefulness of this tool in clinical practice was conducted on a group of 342 patients with HS (third article). It has been proven that the impairment of the quality of life of patients with HS correlates positively with the number of affected body areas and the duration of the disease and correlates negatively with the age of the first symptoms. In addition, patients with a family or partner relationship scored higher than patients without a significant one.

In the next study, on a group of 130 patients with HS, it was assessed whether the patients were able to determine the severity of their disease adequately and whether the patient's self-assessed severity better reflected the impact of the disease on their lives. There was a positive correlation between the impairment of quality of life, assessed by HSQoL-24 and the Dermatology Life Quality Index (DLQI), with the severity of the disease assessed by patients. A similar correlation was not documented for Hurley severity grades. Interestingly, there were also no differences in quality-of-life impairment between different severity grades according to the Hurley scale.

The fifth and sixth works were created as cooperation within the Polish-German consortium of experts in the field of HS. The data of 1795 German patients treated for HS were included in the analysis. In the first study, on the largest group of patients described so far, impairment of the quality of life was determined using the DLQI questionnaire. It has been proven that the disease has a very large impact on the quality of life of patients, which increases with the severity of the lesions and the pain experienced. In addition, it has been shown that HS has a significantly more significant impact on the quality of life of women than men. In another study on the same cohort of patients, the incidence of pain and its characteristics were analyzed. More than 80% of patients experienced pain in the last 24 hours before the examination and most experienced mild pain. People with higher severity of lesions, more affected skin areas, and smokers reported significantly higher pain intensity.

The seventh paper is an original research paper in which disturbances of MCPIP1 protein expression in the skin of HS patients were determined. MCPIP1 is a protein that regulates inflammatory activation and maintains immune homeostasis by inhibiting some pro-inflammatory cytokines. Skin biopsies taken from HS patients from lesional and non-lesional skin were compared with healthy controls. The highest mean MCPIP1 mRNA expression was found in inflamed skin. It was significantly higher than MCPIP1 mRNA expression in normal skin and the skin of healthy controls. Western-blot analysis showed that, compared to healthy controls, MCPIP1 protein expression was significantly elevated in HS patients in both lesional and non-lesional skin. Specific immunostaining showed an abnormal distribution of MCPIP1 in HS patients' lesional and non-lesional skin.

The latest paper is an international project investigating the use of high-frequency ultrasonography (USG) in diagnosing and treating HS. For the first time, the occurrence of a "railway image" inside the tunnels, which corresponds to the pseudo-epithelialization process, was described. It was proven that the tunnels in which this image was observed did not respond to treatment with adalimumab and required surgery.

To summarize, hidradenitis suppurativa is a chronic, debilitating, and painful disease whose pathogenesis is not fully understood. The results of the work included in the doctoral dissertation indicate the enormous impact of the disease and the accompanying pain on patients' quality of life. In addition, they indicate the need for a holistic approach to the patient, individualization of therapy, and conducting further research to explore the pathomechanism of skin changes further.

14. OPINIA KOMISJI BIOETYCZNEJ

KOMISJA BIOETYCZNA
przy
Uniwersytecie Medycznym
we Wrocławiu

OPINIA KOMISJI BIOETYCZNEJ Nr KB – 96/2023

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 278/XVI R/2020 z dnia 21 grudnia 2020 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 514 z 2020 r.) w składzie:

dr Joanna Birecka (psychiatria)
dr Beata Freier (onkologia)
dr hab. Tomasz Fuchs (ginekologia, położnictwo)
prof. dr hab. Dariusz Janczak (chirurgia naczyniowa, transplantologia)
prof. dr hab. Krzysztof Kaliszewski (chirurgia endokrynologiczna)
dr prawa Andrzej Malicki (prawo)
dr hab. Marcin Mączyński, prof.UMW (farmacja)
Urszula Olechowska (pielęgniarstwo)
prof. dr hab. Leszek Szenborn (pediatria, choroby zakaźne)
prof. dr hab. Andrzej Szuba (choroby wewnętrzne, angiologia
ks. prof. Andrzej Tomko (duchowny)
prof. dr hab. Mieszko Więckiewicz (stomatologia)
dr hab. Andrzej Wojnar, prof. nadzw. (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

pod przewodnictwem
prof. dr hab. Jerzego Rudnickiego (chirurgia, proktologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z projektem badawczym pt.

„Patogenetyczne i kliniczne aspekty hidradenitis suppurativa"

zgłoszonym przez lek. Piotra Krajewskiego, zatrudnionego w Katedrze i Klinice Dermatologii, Wenerologii i Alergologii Uniwersytetu Medycznego we Wrocławiu oraz złożonymi wraz z wnioskiem dokumentami, w tajnym głosowaniu postanowiła **wyrazić zgodę** na przeprowadzenie badania w Katedrze i Klinice Dermatologii, Wenerologii i Alergologii Uniwersytetu Medycznego we Wrocławiu pod nadzorem prof. dr hab. Jacka Szepietowskiego, **pod warunkiem zachowania anonimowości zgromadzonych danych.**

UWAGA: Jeśli projekt/badanie wymaga ubezpieczenia na podstawie Rozporządzenia Ministra Finansów, Funduszy i Polityki Regionalnej z dnia 23.12.2020r. w sprawie obowiązkowego ubezpieczenia odpowiedzialności cywilnej podmiotu przeprowadzającego eksperyment medyczny, Wnioskodawca zobowiązany jest do złożenia wniosku o zawarcie umowy ubezpieczenia odpowiedzialności cywilnej zgodnie z procedurą przyjętą w Uniwersytecie Medycznym we Wrocławiu. W takim przypadku pozytywna opinia Komisji Bioetycznej ma charakter warunkowy i będzie uprawniała do prowadzenia Badania pod warunkiem zawarcia przez Uniwersytet umowy ubezpieczenia OC zgodnie z Rozporządzeniem wskazanym w zdaniu poprzednim.

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu.

Opinia powyższa dotyczy projektu badawczego będącego podstawą rozprawy doktorskiej

Przewodniczący Komisji Bioetycznej
przy Uniwersytecie Medycznym

prof. dr hab. Jerzy Rudnicki

Wrocław, dnia 01 02 2023

15. CURRICULUM VITAE

Piotr Krajewski

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DOŚWIADCZENIE ZAWODOWE

07/10/2021 – OBECNE Wrocław
ASYSTENT KATEDRA I KLINIKA DERMATOLOGII, WENEROLOGII I ALERGOLOGII,

11/01/2021 – OBECNE Wrocław, Polska
LEKARZ REZYDENT UNIWERSYTECKI SZPITAL KLINICZNY IM. JANA MIKULICZA-RADECKIEGO

30/06/2020 – OBECNE Wrocław, Polska
SAMODZIELNY REFERENT PROJEKTU AZON - DIGITALIZACJA MULAŻY UNIWERSYTET MEDYCZNY IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

30/09/2019 – 30/10/2020
STAŻYSTA UNIWERSYTECKI SZPITAL KLINICZNY IM. JANA MIKULICZA-RADECKIEGO

Adres Wroclaw, Polska

WYKSZTAŁCENIE I ODBYTE SZKOLENIA

30/09/2019 – OBECNE Wroclaw, Polska
SZKOŁA DOKTORSKA Katedra i Klinika Dermatologii, Wenerologii i Alergologii

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30/09/2016 – 31/05/2019 Wroclaw, Polska
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30/09/2015 – 31/08/2016 Malaga, Hiszpania
ERASMUS University of Malaga - Faculty of Medicine

Adres Malaga, Hiszpania

30/09/2013 – 31/05/2019 Wroclaw, Polska
KIERUNEK LEKARSKI Uniwersytet Medyczny im. Piastów Śląskich we Wrocławiu

Adres Wroclaw, Polska

ZNAJOMOŚĆ JĘZYKÓW

Język ojczysty / języki ojczyste: **POLSKI**

Inny język / inne języki:

	ROZUMIENIE		MÓWIENIE		PISANIE
	Słuchanie	Czytanie	Samodzielne wypowiadanie się	Porozumiewanie się	
ANGIELSKI	C2	C2	C2	C2	C2
HISZPAŃSKI	C1	C1	C1	C1	C1
WŁOSKI	A2	A2	A1	A1	A1

Poziomy: A1 i A2: poziom podstawowy; B1 i B2: poziom samodzielności; C1 i C2: poziom biegłości

INFORMACJE DODATKOWE

PUBLIKACJE

Publikacje

- **66 artykułów** zarówno w Polskich, jak i międzynarodowych czasopismach (28 jako 1 autor)
- Całkowity **IF = 267,08** punktów, punktacja **MEiN = 5615**
- IF jako 1 autor **IF = 142,98** punktów.
- **Hirsh index** według**:** Google Scholar = 12; ResearchGate = 13; Web of Science Core Collection = 11
- **Liczba cytowań** według: Google Scholar = 605; ResearchGate = 585; Web of Science Core Collection = 389

GRANTY, STYPENDIA, NAGRODY, WYRÓŻNIENIA

Granty, stypendia, nagrody, wyróżnienia

Granty, stypendia:

- **„Dolnośląscy liderzy medycyny"** – Europejskie stypendium wspierające doktorantów medycyny. Czas trwania 10.2019 - 12.2020. Kwota 25000 PLN. Kwota na poszerzenie i rozwój umiejętności bezpośrednio związanych z prowadzonymi badaniami
- **Stypendium dla Młodych Naukowców** Uniwersytet Medyczny we Wrocławiu 2020. Czas trwania 1.2020 - 12.2020. Kwota 15000 PLN. Na badania nad mechanizmem powstawania zmian w hidradenitis suppurativa i udziału cząsteczki MCPIP1 we współpracy z Uniwersytetem Jagiellońskim
- **Stypendium RID (Regionalnej Inicjatywy Doskonałości)** Uniwersytetu Medycznego we Wrocławiu. Czas trwania 3.2020 - 3.2022. Kwota 50000 PLN. Grant na badania dotyczące patogenezy świądu mocznicowego u pacjentów po przeszczepieniu nerki
- **Grant Uniwersytet Przyszłości** Uniwersytetu Medycznego im. Piastów Śląskich we Wrocławiu pod moim kierownictwem na kwotę 50000 PLN na 24 miesiące. W ramach grantu prowadzę badania dotyczące zaburzeń stężeń i ekspresji adipokin w skórze chorych na hidradenitis suppurativa.
- **Grant Polskiego Towarzystwa Dermatologicznego** na kwotę 20000 PLN na okres 24 miesięcy. W ramach grantu prowadzone są badania dotyczące zaburzeń stężeń adipokin w surowicy chorych na hidradenitis suppurativa
- **Clinical Fellowship 2021 European Academy of Dermatology and Venereology** - grant przyznany przez Europejską Akademię Dermatologii i Wenerologii na zagraniczny staż kliniczny. Kwota 6000 €
- **International Society of Dermatology Mentorship Program 2023** - grant przyznany przez Międzynarodowe Towarzystwo Dermatologii na zagraniczny staż kliniczny. Kwota 2000 USD
- **Eli Lilly Scholarship** European Academy of Dermatology and Venereology 2021
- Wielokrotne **stypendia rektora** dla najlepszych studentów i doktorantów

Nagrody, wyróżnienia:

- Finalista 21. edycji Nagród Naukowych Polityki 2021 rok
- Laureat konkursu "Uniwersytet Przyszłości" i ambasador Uniwersytetu Medycznego we Wrocławiu w roku 2022.
- Finalista nagród Młode Talenty 2021 roku w kategorii sukces naukowy
- Laureat (2022 rok) oraz wyróżnienie (2021 rok) w stypendium im. Ludwika Hirshfelda Wrocławskiego Centrum Akademickiego 2021
- I miejsce w sekcji prac oryginalnych, VIII Międzynarodowa Konferencja Naukowa Interdyscyplinarne aspekty chorób skóry i błon śluzowych 11-12.03.2022
- Kierunek lekarski ukończony z wyróżnieniem rektora

STAŻE ZAGRANICZNE

Staże zagraniczne

1. Roczny Program Erasmus+ w Universidad de Malaga (10.2015 - 9.2016)
2. 4 - tygodniowy staż w University Hospital Miguel Servet, Department of Dermatology (19.07-16.08.2021), Hiszpania
3. 3 - miesięczny staż w Hospital de Manises kwiecień-lipiec 2022 roku (finansowany z grantu Europejskiej Akademii Dermatologii i Wenerologii)

WSPÓŁPRACA MIĘDZYNARODOWA

Współpraca międzynarodowa

- Współpraca z University of Mainz, Niemcy - 3 opublikowane prace
- Współpraca z University Hospital Complex of Granada, Hiszpania - 1 opublikowana praca
- Współpraca z Hospital Universitario Miguel Servet, Zaragoza, Hiszpania - 2 opublikowane prace
- Współpraca z LENICURA GmbH, Wiesbaden, Niemcy - 3 opublikowane prace
- Współpraca z Hospital de Manises, Valencia, Hiszpania - opublikowane 2 prace, kolejne w przygotowaniu

TOWARZYSTWA NAUKOWE

Towarzystwa naukowe

- Członek European Academy of Dermatology and Venereology
- Członek International Society of Dermatology
- Członek Polskiego Towarzystwa Dermatologicznego
- Członek European Hidradenitis Suppurativa Foundation
- Członek European Society for Dermatology and Psychiatry

16. DOROBEK NAUKOWY

(z wyłączeniem prac stanowiących cykl publikacji do Rozprawy Doktorskiej)

16.1. Lista publikacji

1. Wojciechowska J, Krajewski W, **Krajewski P**, Krecicki T. *Granulomatosis with polyangiitis in otolaryngologist practice: a review of current knowledge*. Clin Exp Otorhinolaryngol. 2016;9(1):8-13.
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16.2. Autorstwo rozdziałów w podręcznikach

1. **Krajewski P**, Matusiak Ł. Nowoczesne leczenie zachowawcze hidradenitis suppurativa. [w:] Nowe Metody Leczenia Chorób Skóry. Lublin 2022, Wydawnictwo Czelej, s.197-208, ISBN: 9788375633351

16.3. Doniesienia zjazdowe

1. **Piotr Krajewski**, Wójcicka Karolina, Szepietowski Jacek. Hidradenitis suppurativa surgical treatment - three years single center experience. 9th Conference of the European Hidradenitis Suppurativa Foundation, Athens, Greece 05-07.02.2020
2. **Piotr Krajewski**. Cutaneous hyperestesia: novel manifestation of SARS-CoV-2 infection. 29th Congress of European Academy of Dermatology and Venereology, Virtual 28.10-1.11.2020
3. **Piotr K. Krajewski**, Lukasz Matusiak, Esther von Stebut, Michael Schultheis, Uwe Kirschner, Georgios Nikolakis, Jacek C. Szepietowski. DLQI scores in hidradenitis suppurativa patients 10th European Hidradenitis Suppurativa (EHSF) e.V. Conference, Virtual 10-12.02.2021
4. **Piotr K. Krajewski**, Lukasz Matusiak, Esther von Stebut, Michael Schultheis, Uwe Kirschner, Georgios Nikolakis, Jacek C. Szepietowski. Pain assessment in patients suffering from hidradenitis suppurativa. 10th European Hidradenitis Suppurativa (EHSF) e.V. Conference, Virtual 10-12.02.2021
5. **Piotr K. Krajewski**, Weronika Szukała, Agata Lichawska-Cieslar, Lukasz Matusiak, Jolanta Jura, Jacek C. Szepietowski MCPIP1/Regnase-1 expression in the skin of hidradenitis suppurativa patients. 10th European Hidradenitis Suppurativa (EHSF) e.V. Conference, Virtual 10-12.02.2021
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7. **Piotr Krajewski**. Zastosowanie światła w leczeniu Hidradenitis Suppurativa. Hidradenitis Suppurativa day, Wrocław 26.03.2021
8. **Piotr Krajewski**, Maj Joanna, Szepietowski Jacek C. Cutaneous hyperesthesia in SARS-CoV-2 infection: rare but not unique clinical manifestation. European Academy of Dermatology and Venereology Spring Symposium 2021, Virtual 06-07.05.2021.
9. **Piotr K Krajewski**, Łukasz Matusiak, Esther von Stebut, Michael Schultheis, Uwe Kirschner, Georgios Nikolakis, Jacek C Szepietowski. Decrease in quality of life among patients with hidradenitis suppurativa: a cross-sectional study of 1,795. The Virtual 19th European Society for Dermatology and Psychiatry Conference, London, 11-12.06.2021

10. **Piotr Krajewski**, The burden of itch in renal transplant recipients. 2022 Annual Conference of Association for Psychocutaneous Medicine of North America, Boston, USA 24.03.2022
11. **Piotr Krajewski**, Fatima Mayo, Virginia Sanz, Gema Ochando, Antonio Martorell. Deroofing: a safe, effective, and well-tolerated procedure in patients with hidradenitis suppurativa. 2022 SHSA Symposium on hidradenitis suppurativa advances, Miami, USA, 7-9.10.2022
12. **Piotr Krajewski**. Basic surgical procedures in dermatology. Dermatology Without Borders 2022, Liepaja, Latvia, 29.07.2022
13. **Piotr Krajewski**. Przydatność ultrasonografii w hidradenitis suppurativa. IV Bieszczadzkie Spotkania z Dermatologią, Arłamów, Polska, 31.08-02.09.2022
14. **Piotr Krajewski**. Deroofing: a safe, effective, and well-tolerated procedure in patients with hidradenitis suppurativa. 31st Congress of European Academy of Dermatology and Venereology, Milan, Italy, 7-10.09.2022
15. **Piotr Krajewski**. Controversies VIII: Surgical treatment for hidradenitis suppurativa in adolescents. 31st Congress of European Academy of Dermatology and Venereology, Milan, Italy, 7-10.09.2022
16. **Piotr Krajewski**. Itch and its psychosocial burden in renal transplant recipients. 31st Congress of European Academy of Dermatology and Venereology, Milan, Italy, 7-10.09.2022
17. **Piotr Krajewski**, Antonio Martorell. Ultrasonograficzny obraz "torów kolejowych" jako niezależny czynnik braku odpowiedzi na leczenie biologiczne u pacjentów z hidradenitis suppurativa. Zjazd Sekcji Forum Młodych Polskiego Towarzystwa Dermatologicznego, Łódź, Polska, 20-21.10.2022.

17. OŚWIADCZENIA WSPÓŁAUTORÓW

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Jacek Szepietowski, wyrażam zgodę na włączenie poniższych prac naukowych, których jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

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Krajewski PK, Marrón SE, Tomas Aragones L, Gilaberte-Calzada Y, Szepietowski JC. Self-Reported Hidradenitis Suppurativa Severity: Is It Useful for Clinical Practice? Dermatol Ther (Heidelb). 2022 Apr;12(4):899-909

Uniwersytet Medyczny we Wrocławiu
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09/01/2023

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UNIWERSYTET MEDYCZNY
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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Łukasz Matusiak, wyrażam zgodę na włączenie poniższych prac naukowych, których jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

Krajewski PK, Matusiak L, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients. Acta Derm Venereol. 2021;101(1):adv00364.

Krajewski PK, Matusiak Ł, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. Life (Basel). 2021 Jan 8;11(1):34

Krajewski PK, Szukala W, Lichawska-Cieslar A, Matusiak L, Jura J, Szepietowski JC. MCPIP1/Regnase-1 Expression in Keratinocytes of Patients with Hidradenitis Suppurativa: Preliminary Results. Int J Mol Sci. 2021;22(14)

Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

02.01.2023 .....

Data i podpis

UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Abdulhadi Jfri, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Jfri A, Ochando-Ibernón G, Martorell A. Ultrasonographic railway sign in tunnels as a new independent risk factor of adalimumab failure in hidradenitis suppurativa. J Am Acad Dermatol. 2022 Oct 4:S0190-9622(22)02789-X

January 29, 2023. .....

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Agata Lichawska-Cieślar, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Szukala W, Lichawska-Cieslar A, Matusiak L, Jura J, Szepietowski JC. MCPIP1/Regnase-1 Expression in Keratinocytes of Patients with Hidradenitis Suppurativa: Preliminary Results. Int J Mol Sci. 2021;22(14)

3/01/2023 Lichawska-Cieślar

Data i podpis

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Antonio Martorell, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Jfri A, Ochando-Ibernón G, Martorell A. Ultrasonographic railway sign in tunnels as a new independent risk factor of adalimumab failure in hidradenitis suppurativa. J Am Acad Dermatol. 2022 Oct 4:S0190-9622(22)02789-X

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Esther von Stebut, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak L, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients. Acta Derm Venereol. 2021;101(1):adv00364.

Krajewski PK, Matusiak Ł, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. Life (Basel). 2021 Jan 8;11(1):34

Jan 8, 2023 Esther von Stebut
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Date and signature

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CO-AUTHOR DECLARATION

I, Gema Ochando-Ibernón, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Jfri A, Ochando-Ibernón G, Martorell A. Ultrasonographic railway sign in tunnels as a new independent risk factor of adalimumab failure in hidradenitis suppurativa. J Am Acad Dermatol. 2022 Oct 4:S0190-9622(22)02789-X

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Georgios Nikolakis, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak L, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients. Acta Derm Venereol. 2021;101(1):adv00364.

Krajewski PK, Matusiak Ł, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. Life (Basel). 2021 Jan 8;11(1):34

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Gregor B Jemec, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

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3 Jan 2023

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Jolanta Jura, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Szukala W, Lichawska-Cieslar A, Matusiak L, Jura J, Szepietowski JC. MCPIP1/Regnase-1 Expression in Keratinocytes of Patients with Hidradenitis Suppurativa: Preliminary Results. Int J Mol Sci. 2021;22(14)

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Joslyn S Kirby, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Kinga Tyczyńska, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego..

Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

22.01.23 K. Tyczyńska

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Klaudia Bardowska, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

23.01.2023 Bardowska

Data i podpis

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Lucia Tomas Aragones, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Marrón SE, Gomez-Barrera M, Tomas-Aragones L, Gilaberte-Calzada Y, Szepietowski JC. The Use of HSQoL-24 in an Assessment of Quality-of-Life Impairment among Hidradenitis Suppurativa Patients: First Look at Real-Life Data. J Clin Med. 2021;10(22).

Krajewski PK, Marrón SE, Tomas Aragones L, Gilaberte-Calzada Y, Szepietowski JC. Self-Reported Hidradenitis Suppurativa Severity: Is It Useful for Clinical Practice? Dermatol Ther (Heidelb). 2022 Apr;12(4):899-909

Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Manuel Gomez-Barrera, hereby agree that below mentioned scientific paper, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Marrón SE, Gomez-Barrera M, Tomas-Aragones L, Gilaberte-Calzada Y, Szepietowski JC. The Use of HSQoL-24 in an Assessment of Quality-of-Life Impairment among Hidradenitis Suppurativa Patients: First Look at Real-Life Data. J Clin Med. 2021;10(22).

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Marta Szepietowska, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Michael Schultheis, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak L, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients. Acta Derm Venereol. 2021;101(1):adv00364.

Krajewski PK, Matusiak Ł, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. Life (Basel). 2021 Jan 8;11(1):34

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Wrocław, 28.12.2022

DEKLARACJA WSPÓŁAUTORA

Ja, Julia Rymaszewska, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS, Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of the Polish language version. Postepy Dermatol Alergol. 2021 Dec;38(6):967-972

03/02/2023 Rymaszewska

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e-mail: dermwen@umw.edu.pl http://www.derm.umed.wroc.pl

Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Servando E Marrón, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Marrón SE, Gomez-Barrera M, Tomas-Aragones L, Gilaberte-Calzada Y, Szepietowski JC. The Use of HSQoL-24 in an Assessment of Quality-of-Life Impairment among Hidradenitis Suppurativa Patients: First Look at Real-Life Data. J Clin Med. 2021;10(22).

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Krajewski PK, Bardowska K, Matusiak Ł, Szepietowska M, Tyczyńska K, Marrón SE, Tomas Aragones L, Szepietowski JC. Hidradenitis Suppurativa Quality of Life 24 (HSQoL-24) now available for Polish patients: creation and validation of the Polish language version. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2022;39(6):1053-1058.

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Uve Kirschner, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Matusiak L, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Pain in Hidradenitis Suppurativa: A Cross-sectional Study of 1,795 Patients. Acta Derm Venereol. 2021;101(1):adv00364.

Krajewski PK, Matusiak Ł, von Stebut E, Schultheis M, Kirschner U, Nikolakis G, Szepietowski JC. Quality-of-Life Impairment among Patients with Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. Life (Basel). 2021 Jan 8;11(1):34

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January 3rd, 2023
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DEKLARACJA WSPÓŁAUTORA

Ja, Weronika Szukała, wyrażam zgodę na włączenie poniższej pracy naukowej, której jestem współautorem, do serii publikacji, na podstawie których będzie oparta praca doktorska głównego autora, Piotra Krajewskiego.

Krajewski PK, Szukala W, Lichawska-Cieslar A, Matusiak L, Jura J, Szepietowski JC. MCPIP1/Regnase-1 Expression in Keratinocytes of Patients with Hidradenitis Suppurativa: Preliminary Results. Int J Mol Sci. 2021;22(14)

22.01.2023, Szukała Weronika

Data i podpis

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Wrocław, 28.12.2022

CO-AUTHOR DECLARATION

I, Yolanda Gilaberte-Calzada, hereby agree that below mentioned scientific papers, which I have co-authored, may be incorporated into a series of publications on which the doctoral thesis of the main author, Piotr Krajewski, will be based.

Krajewski PK, Marrón SE, Gomez-Barrera M, Tomas-Aragones L, Gilaberte-Calzada Y, Szepietowski JC. The Use of HSQoL-24 in an Assessment of Quality-of-Life Impairment among Hidradenitis Suppurativa Patients: First Look at Real-Life Data. J Clin Med. 2021;10(22).

Krajewski PK, Marrón SE, Tomas Aragones L, Gilaberte-Calzada Y, Szepietowski JC. Self-Reported Hidradenitis Suppurativa Severity: Is It Useful for Clinical Practice? Dermatol Ther (Heidelb). 2022 Apr;12(4):899-909

12/JAN/2023

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