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Calculation of cut-off values based on the ABSIS and PDAI pemphigus scoring systems for defining moderate, significant and extensive types of pemphigus

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Running Head: Definition of moderate, significant and extensive types of pemphigus

Bulleted statement:

What's already known about this topic ?

* The Autoimmune-Bullous-Skin-Disorder-Intensity-Score (ABSIS) and Pemphigus-Disease-Area-Index (PDAI) are new scoring systems to measure pemphigus activity.

* The use of these scores in clinical practice is limited by the absence of cut-off values.

What does this study add ?

* Cut-off values distinguishing moderate, significant and extensive pemphigus were 15 and 45 for PDAI, and 17 and 53 for ABSIS.

* These disease activity subgroups should help physicians in the management of pemphigus patients.

Abstract

Background: Two pemphigus severity scores, Autoimmune-Bullous-Skin-Disorder-Intensity-Score (ABSIS) and Pemphigus-Disease-Area-Index (PDAI), have been proposed to provide an objective measure of disease activity. However, the use of these scores in clinical practice is limited by the absence of cut-off values which allow differentiation between moderate, significant and extensive types of pemphigus.

Objective: To calculate cut-off values defining moderate, significant and extensive pemphigus based on the ABSIS and PDAI scores.

Methods: In 31 Dermatology Departments in six countries, consecutive patients with newly diagnosed pemphigus were assessed for pemphigus severity, using the ABSIS, PDAI, Physician-Global-Assessment (PGA) and Dermatology-Life-Quality-Index (DLQI) scores. Cut-off values defining moderate, significant and extensive subgroups were calculated based on the 25th and 75th percentiles of the ABSIS and PDAI scores. Median ABSIS, PDAI, PGA and DLQI scores of the three severity subgroups were compared to validate these subgroups.

Results: Ninety-six patients with pemphigus vulgaris (n=77) or pemphigus foliaceus (n=19) were included. Median PDAI activity and ABSIS total scores were 27.5 [range:3-84] and 34.8 points [range:0.5-90.5], respectively. Cut-off values corresponding to the first and third quartiles of the scores were 15 and 45 for the PDAI, and 17 and 53 for the ABSIS. The moderate, significant and extensive subgroups were thus defined, and had distinguishing median ABSIS ($p<0.0001$), PDAI ($p<0.0001$), PGA ($p<0.0001$) and DLQI ($p=0.03$) scores.

Conclusions: This study suggests cut-off values of 15/45 and 17/53 for PDAI and ABSIS respectively, to distinguish moderate, significant and extensive pemphigus forms. Identifying these pemphigus activity subgroups should help physicians to classify and manage pemphigus patients.

Introduction

Pemphigus is a rare autoimmune disease which causes skin and mucosal blistering and erosions[1]. Two major types of pemphigus have been described, pemphigus vulgaris (PV) and pemphigus foliaceus (PF). A systematic review of outcome measures for assessing pemphigus

severity recently identified 116 different measurement systems, which were reported in 96 articles published over the last 25 years[2]. Most studies used outcome measures based on global scales such as the Physician Global Assessment (PGA), or non-specific ratings of disease activity encompassing lesion count and complete healing, or scoring systems based on semi quantitative evaluation of cutaneous and/or mucosal involvement as proposed respectively by Harman et al.[3], Ikeda et al.[4], Agarwal et al.[5], or Chams et al.[6]. The lack of uniform measurement systems has constituted a major drawback for comparing different therapeutic regimens. Additionally, there is great need for a validated and well accepted scoring system to help physicians in clinical practice to make therapeutic choices and adapt treatment according to disease activity.

Recently two new scoring systems have been proposed to provide an objective measure of disease activity in pemphigus[7]: the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS), developed by German dermatologists[8], and the Pemphigus Disease Area Index (PDAI), developed by an international panel of experts[9]. They both quantify extent of cutaneous and mucosal erosions, as well as either a measure of patient discomfort in the ABSIS score or a measure of skin damage in the PDAI score. The use of these scores in clinical practice is limited by the absence of cut-off values which allow differentiation between moderate, significant and extensive types of pemphigus. This distinction is important in clinical practice to propose adequate treatment, and in clinical trials to allow meaningful comparisons between them. The aim of this study was to propose cut-off values based on the ABSIS and PDAI scoring systems, in order to define three categories of pemphigus activity, namely moderate, significant and extensive forms.

Methods

Study Population

We conducted a prospective multicentre study in 31 French, German, Italian, Swiss, Croatian and Australian Departments of Dermatology (secondary and tertiary care centres). This study was approved by the corresponding local ethics committees.

Consecutive patients aged 18 years or more with pemphigus newly diagnosed between July 2009 and May 2012 were included. All included patients had given signed informed consent. Diagnosis of either PV or PF was based on i) characteristic clinical features, and ii)

histological analysis of a skin or mucosal biopsy showing acantholysis, intraepithelial blistering, or eosinophilic spongiosis, iii) direct immunofluorescence (DIF) examination showing IgG and/or C3 deposits on keratinocyte cell membrane, and iv) detection of circulating autoantibodies by commercially available ELISA-desmoglein 3 and ELISA-desmoglein 1 assays (MBL, Japan).

Assessment of disease extent

Disease extent was evaluated using i) ABSIS[8], ii) PDAI[9] and iii) PGA scores.

The ABSIS score of cutaneous involvement is based on the extent of the body surface area (BSA) assessed using Wallace's "rule of nines" and type of skin lesions[8]. The value of the BSA affected is multiplied by an index reflecting the predominant lesions: 1.5 (erosive, exudative lesions, bullae, or Nikolsky sign positivity), 1.0 (erosive, dry lesions), or 0.5 (re-epithelialised lesions). ABSIS oral involvement is evaluated by scoring 11 mucosal sites by 1 (presence of lesions) or 0 (absence of lesions), and by completing a subjective severity scale based on discomfort during eating and drinking. Using higher scores to denote worse disease, ABSIS ranges from 0 to 206 points, with 150 points for skin involvement, 11 points for oral involvement, and 45 points for subjective discomfort.

The PDAI has a score ranging from 0 to 263 points, with 250 points representing disease activity (120, 10 and 120 points for skin, scalp, and mucosal activity, respectively) and 13 points representing disease damage[9]. However, the damage component was not included in the present analysis. For skin activity assessment, 12 anatomic sites are assigned a score according to disease extent: 0 (no lesions), 1 (1-3 lesions, up to 1 lesion > 2 cm in any diameter, all ≤ 6 cm), 2 (2-3 lesions, at least 2 lesions > 2 cm, all ≤ 6 cm), 3 (> 3 lesions, all ≤ 6 cm), 5 (> 3 lesions and/or 1 lesion > 6 cm), or 10 (> 3 lesions and/or at least 1 lesion > 16 cm or entire area affected). Scalp activity is assigned a score based on the presence of blisters, erosions or erythema of 0 (no activity), 1 (one quadrant affected), 2 (two quadrants affected), 3 (3 quadrants affected), 4 (whole skull affected) or 10 (at least 1 lesion > 6 cm). For mucosal activity assessment, 12 mucosal sites are assigned a score based on the presence of erosions or blisters: 0 (absent), 1 (1 lesion), 2 (2-3 lesions), 5 (> 3 lesions or 2 lesions > 2 cm), or 10 (entire area).

PGA is a visual analogue ten-point scale, based on a physician's subjective impression from 0 (no lesions) to 10 (worst skin and mucosae condition imaginable). It has been used in clinical trials because it is fast and easy to use [10].

Patients' quality of life was evaluated by the Dermatology Quality of Life Index (DLQI) translated into different languages[11]. It includes ten questions with a total score between 0 and 30.

Statistical analysis

The baseline ABSIS, PDAI, PGA and DLQI scores were prospectively recorded on case report forms (CRF). Observations with more than one missing score out of four were excluded from the analysis. The target sample size (n=100) was calculated for the primary objective of this study which was to assess reproducibility and inter-rater agreement.

Quantitative variables were reported as median [range], and qualitative variables as frequency and percentages. Correlations between the different scoring systems (ABSIS, PDAI activity, PGA, DLQI) were assessed using Spearman's rank correlation coefficient. Separately for the ABSIS and PDAI scoring systems, three subgroups of severity, moderate, significant and extensive, were arbitrarily defined based on the first and third score quartiles (Q1 and Q3). Moderate, significant and extensive pemphigus corresponded to cases with a score lower than the 25^{th} percentile of the sample, higher than or equal to the 25^{th} and lower than the 75^{th} percentile, and higher than or equal to the 75^{th} percentile, respectively. From these defined categories, the median scores of the three severity subgroups (moderate, significant and extensive) were compared between these three subgroups, separately for each score (i.e., median PDAI activity scores were compared between the three severity subgroups from the PDAI and similarly for the ABSIS). In order to validate the classification in the three severity subgroups, we first compared the median PDAI scores of the three subgroups defined by the ABSIS cut-off values and vice versa. Then, we compared the median PGA and DLQI scores of the three subgroups of disease extent defined by the cut-off values calculated from the PDAI and the ABSIS scoring systems. All these comparisons relied on the non-parametric Kruskal-Wallis test. Statistical analyses were performed using Graph Pad Prism Version 5.0 (San Diego, CA, USA).

Results

Patient characteristics

A total of 96 patients (59 female and 37 male) were enrolled in the study. Nineteen patients had PF and 77 PV (22 with exclusive mucosal involvement, 6 with exclusive cutaneous involvement and 49 with mucosal and cutaneous lesions). Median age was 50.5 years [19-84 years]. Median duration of disease before diagnosis was 4.4 months [0.3 – 107.5 months].

Disease activity scores of the whole population were distributed over the first 34% (3 to 84 points) and 44% (0.5 to 90.5 points) of PDAI and ABSIS scales, respectively (Fig.1, Fig. 2). Median PDAI activity and ABSIS scores of the whole population were 27.5 out of 250 points [3-84 points], and 34.8 out of 206 points [0.5 – 90.5 points], respectively. Median PGA score was 6 out of 10 points [1 - 10 points] and median DLQI score was 9 out of 30 points [0 - 30 points]. Median PDAI activity, ABSIS, PGA and DLQI scores of PV and PF subpopulations are shown in table1.

Spearman's coefficient correlation was r=0.52 ($p<0.0001$) between PDAI and ABSIS scores, r=0.69 ($p<0.0001$) between PDAI and PGA scores and r=0.56 ($p<0.0001$) between ABSIS and PGA scores.

Calculation of cut-off values defining three subgroups of pemphigus activity

Cut-off values (first and third quartiles) for PDAI and ABSIS scores were respectively 15 and 45 for the PDAI score, and 17 and 53 for the ABSIS score.

Median PDAI activity scores in the three subgroups (moderate, significant and extensive) defined by the two cut-off values from the PDAI scoring system were 10.0 [3-14], 26.5 [15-44], and 61.0 [45-84] ($p<0.0001$). Median ABSIS scores in the three subgroups defined by the two cut-off values from the ABSIS scoring system were 6.0 [0.5-15.3], 34.8 [17.0-52.8] and 56.0 [53.0-90.5] ($p<0.0001$) (Table 2).

Validation of the three pemphigus activity subgroups

To validate the classification in the three activity subgroups and determine if they were interchangeable, we compared the median ABSIS scores of the three subgroups defined by

the two cut-off values from the PDAI scoring system, and vice versa. Median ABSIS scores of the three subgroups (moderate, significant and extensive) defined by the 15 and 45 point cut-offs from the PDAI scoring system were 19.5 [0.5-39.5], 35.8 [1.5-90.5] and 52.8 [12.0-83.5] ($p<0.0001$). Conversely, median PDAI activity scores of the three severity subgroups defined by the 17 and 53 point cut-offs from the ABSIS scoring system were 16 [3-45], 25 [5-80] and 45 [23-84] ($p<0.0001$) (Table 2).

In order to identify among patients with moderate pemphigus a subgroup of patients with very few lesions who might be treated without corticosteroids, we calculated the cut-off values corresponding to the 10^{th} percentile of the population. These cut-off values defining a fourth subgroup of patients with “limited extent” were 10 and 4 points on the PDAI and ABSIS scores respectively. However, the median PDAI and ABSIS scores of this fourth subgroup of patients with “limited extent" were not statistically different from those of patients with “moderate extent” (corresponding to patients from the 10^{th} to the 25^{th} percentile), which did not strongly argue for the definition of a fourth subgroup of patients.

To further validate classification in the three disease activity subgroups defined either by the cut-off values of PDAI or ABSIS scoring systems, we calculated the median PGA and DLQI scores of these three subgroups for both scoring systems.

Median PGA scores of moderate, significant and extensive subgroups defined by the 15 and 45 point cut-off values of the PDAI score were 4 [1-6], 6 [2-9] and 8 [5-10] ($p<0.0001$), respectively. When using the 17 and 53 point cut-off values of the ABSIS score, the median PGA scores of moderate, significant and extensive subgroups were similar to the corresponding previous values: 4 [1-8], 6 [3-9] and 8 [5-10] ($p<0.0001$), respectively. (Table 2)

Median DLQI scores of moderate, significant and extensive subgroups defined by the 15 and 45 point cut-off values of the PDAI score were 6 [0-30], 10 [0-30] and 12 [0-24] ($p=0.02$), respectively. When using the 17 and 53 point cut-off values of the ABSIS score, the median DLQI scores of moderate, significant and extensive subgroups were 6.5 [0-22]), 10 [0-30] and 13 [0-30] ($p<0.03$), respectively. (Table 2)

Then, we determined the proportion of PF patients, and PV patients (overall, and according to clinical form: exclusive cutaneous involvement, exclusive mucosal involvement,

cutaneous and mucosal involvement) among the moderate, significant and extensive subgroups. Results are shown in table 3.

Finally, we calculated cut-off values defining moderate, significant and extensive pemphigus according to the three clinical presentations of pemphigus: exclusive cutaneous involvement, exclusive mucosal involvement or both. The cut-off values differentiating moderate from significant, and significant from extensive subgroups on the PDAI scale were rather close irrespective of the exclusive cutaneous or exclusive mucosal presentation of patients (12 points versus 11.5 points, and 37 points versus 35 points). These cut offs were higher in patients with both skin and mucosal lesions (19 and 54 points, respectively). Conversely, these cut-off values on the ABSIS scale were close in patients with exclusive mucosal involvement or both mucosal and skin involvement, whereas they were much lower in the subgroup of patients with exclusive skin presentation (Table 4).

Discussion

The main objective of this study was to propose cut-off values based on ABSIS and PDAI scoring systems, allowing classification of patients into three pemphigus extent subgroups (moderate, significant and extensive disease). It must be underlined that these scores assess disease extent which is not identical to disease severity, since the prognostic relevance of these scores and their consequences in term of treatment options have not yet been evaluated.

Our results suggest that a PDAI activity value of 15 points and an ABSIS value of 17 points allow differentiation between moderate and significant pemphigus forms, whereas a PDAI activity value of 45 points and an ABSIS value of 53 points allow differentiation between significant and extensive pemphigus forms.

The three subgroups defined by these cut-off values differed from each other not only by their respective median ABSIS ($p<0.0001$) and PDAI scores ($p<0.0001$), but also by their median PGA ($p<0.0001$) and DLQI scores ($p<0.005$ or $p<0.017$). Moreover, using ABSIS cut-off values allowed excellent separation between PDAI score and vice-versa.

The extensive pemphigus subgroup defined by the 45 and 53 point cut-off values based on PDAI and ABSIS scores, respectively, had a high median PGA score (8 out of 10

points) and high median DLQI score (12 or 14 out of 30 points). These figures closely reflected both the investigator's and the patient's evaluation of disease extent. In contrast, the moderate subgroup defined by the 15 and 17 point cut-off values, had rather low median PGA and DLQI scores of 4 and 6 respectively, which again correlated well with the evaluation of both investigators and patients. Therefore, despite the fact that the 25th and 75th percentiles used to calculate the cut-off values were somehow arbitrary although often used, the three disease activity subgroups defined by this means correlated well and fitted with the quick overall assessment of the patient made by the investigator. In fact, median PGA scores were 4, 6 and 8 out of 10 points, corresponding to the moderate, significant and extensive subgroups defined by the percentile method.

As expected, most PV patients with both cutaneous and mucosal involvement were classified in the significant to extensive subgroups, whereas most PV patient with exclusive mucosal involvement were found in the moderate to significant subgroups, which strengthens the validity of the proposed cut-off values. Interestingly, these cut-off values also allowed classification of three and six PV patients with exclusive but extensive mucosal involvement in the extensive subgroup (according to the ABSIS and PDAI cut-off values respectively). Similarly, whereas most PF patients were classified in the moderate to significant subgroups, five and four PF patients with a mean 50% body surface area involvement were classified in the extensive subgroup.

However, one could ask whether the proposed cut-offs are valid for all clinical subtypes of pemphigus (exclusive cutaneous involvement, exclusive mucosal involvement and involvement of both). Although this complementary analysis of cut-off values in each clinical subgroup was performed in a limited number of patients, we observed that the PDAI cut-off values were slightly lower in the subgroups of patients with exclusive mucosal or exclusive skin involvement than in the subgroup of patients with both skin and mucosal involvement. Conversely, the ABSIS cut-off values were much higher in patients with exclusive mucosal or muco-cutaneous involvement than in those with exclusive cutaneous involvement. This is most likely due to the presence of a subjective component in the ABSIS mucosal assessment but not in the PDAI scoring system. Since the PDAI cut-off values were close for the whole pemphigus population (both PF and PV), they could be used for all forms of pemphigus. However, since there were higher thresholds for mucosal involvement with ABSIS, it might be useful to have different cut-off scores for cutaneous and mucosal involvement.

The 15 and 45 point cut-off values proposed for the PDAI severity score in the present study are somewhat higher than the 9 and 25 points proposed by Shimizu et al., in a Japanese study which enrolled 37 pemphigus patients[12]. This difference might be due to the fact that the latter study included both newly diagnosed and previously treated patients, with few severe cases. Indeed, two thirds of the evaluations in the Japanese study were performed in already treated and / or relapsing patients with only 11 of the 110 assessments which were considered as severe according to the physician's subjective impression. Therefore, it is likely that this particular recruitment may have been responsible for the inclusion of a higher number of patients with limited disease extent than in our series, which only recruited newly diagnosed non treated incident cases. Additionally, we cannot exclude that some particularities of pemphigus patients in Japan may differ from those in our multicentre international study.

A selection bias is unlikely in our prospective multicentre study, since it included a large number of consecutive newly diagnosed patients recruited both in secondary and tertiary care centres. One may hypothesize that some patients could have been treated by a general practitioner and never needed to be referred to a dermatology department, thus leading to underestimation of the proportion of limited and moderate types of pemphigus. This is unlikely since in Europe where most patients in this study are from, all pemphigus patients are referred to the in- or out-patient clinic of dermatology departments, especially for diagnosis and to discuss treatment options. In fact, the present study included patients with a wide range of severity, whereas previous studies only included a limited number of patients, most of them already treated and with limited lesions[9]. Despite the recruitment of consecutive incident cases of pemphigus, we observed that severity scores of the whole group of patients were distributed over the lowest third of PDAI and ABSIS scales. A prospective longitudinal study is currently being conducted to determine if this usage of a limited portion of ABSIS and PDAI scales impairs the sensitivity of these scores in detecting improvement or worsening of the patient's condition. We did not assess here the reproducibility of these scores between investigators. However, good correlation between ABSIS and PDAI scoring systems, as well as between these scores and PGA and DLQI scores suggests acceptable reproducibility of these scoring systems. Moreover, the observation that the Spearman correlation coefficients calculated in the present study (r=0.69 for PDAI/PGA and r=0.56 for ABSIS/PGA) were close to those reported by Rosenbach et al. (r=0.60 for PDAI/PGA and r=0.43 for

ABSIS/PGA)[9] and by Rahbar et al. (r=0.67 for PDAI/PGA and r=0.33 for ABSIS/PGA)[13] also suggests the acceptable reproducibility of these scores.

Conclusion

In conclusion, identifying three subgroups of moderate, significant and extensive pemphigus should help physicians to classify and manage affected patients. Furthermore, this should facilitate reporting of outcome as well as enable direct comparisons between treatment regimens in future prospective trials.

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Figures legends

Figure 1: Distribution of PDAI total activity and ABSIS total scores. Thick lines correspond to the median of PDAI and ABSIS values of the whole population. Thin lines correspond to the 25^{th} and the 75^{th} percentiles.

Figure 2: Distribution of PDAI (panel A), ABSIS (panel B), and PGA (panel C) scores for each patient in the three extent subgroups with mean (thick bar) and standard variation (thin bar).

Table 1: Median [range] PDAI total activity score, ABSIS total score, PGA and DLQI scores of the whole population (n=96) and pemphigus vulgaris and pemphigus foliaceus subpopulations.

	PDAI total activity score (0-250)	ABSIS total score (0-206)	PGA score (0-10)	DLQI score (0-30)
	Median [range]	Median [range]	Median [range]	Median [range]
Whole population (n=96)	27.5 [3 - 84]	34.5 [0.5 - 90.5]	6 [1 - 10]	9 [0 - 30]
PF (n=19)	18.0 [3 - 68]	12.0 [0.5 - 83.5]	5 [1 - 8]	6.5 [2 - 22]
PV (n=77)	29.0 [4 - 84]	36.7 [0.5 - 90.5]	6 [1 - 10]	9 [0 - 30]
PVmc (n=49)	35.0 [9 - 84]	36.7 [7.4 - 90.5]	6 [1 - 10]	11 [0 - 30]
PVm (n=22)	22.5 [5 - 74]	39.0 [4 - 56]	6 [3 - 10]	7 [0 - 22]
PVc (n=6)	20.5 [4 - 36]	1.9 [0.5 - 9.5]	3.5 [2 -6]	7.5 [1- 12]

PF: Pemphigus Foliaceus, PV: Pemphigus Vulgaris, PVm: with exclusive mucosal involvement , PVc: with exclusive cutaneous involvement, PVmc: with both mucosal and cutaneous involvement

Table 2: Median [range] PDAI, ABSIS, PGA and DLQI scores according to pemphigus severity (moderate, significant or extensive) defined from PDAI or ABSIS scoring systems

	subgroups defined according to PDAI score*				subgroups defined according to ABSIS score**			
	moderate (n=21)	significant (n=50)	extensive (n=25)	*P****	moderate (n=23)	significant (n=50)	extensive (n=23)	*P****
PDAI total activity median [range]	10.0 [3.0-14.0]	26.5 [15.0-44.0]	61.0 [45.0-84.0]	*<0.0001*	16.0 [3.0-45.0]	25.0 [5.0-80.0]	45.0 [23.0-84.0]	*<0.0001*
ABSIS median [range]	19.5 [0.5-39.5]	35.8 [1.5 - 90.5]	52.8 [12.0-83.5]	*<0.0001*	6.0 [0.5-15.3]	34.8 [17.0-52.8]	56.0 [53.0-90.5]	*<0.0001*
PGA median [range]	4 [1-6]	6 [2-9]	8 [5-10]	*<0.0001*	4 [1-8]	6 [3-9]	8 [5-10]	*<0.0001*
DLQI median [range]	6 [0-30]	10 [0-30]	12 [0-24]	*0.02*	6 [0-22]	10 [0-30]	13 [0-30]	*0.03*

* cut-off values differentiating moderate, significant and extensive pemphigus forms based on PDAI score were 15 and 45 points

** cut-off values differentiating moderate, significant and extensive pemphigus forms based on ABSIS score were 17 and 53 points

*** Kruskal-Wallis non parametric test

Table 3: Distribution of clinical types of pemphigus (pemphigus vulgaris, pemphigus foliaceus) among moderate significant and extensive pemphigus forms defined from PDAI or ABSIS scoring systems

	subgroups defined according to PDAI score* No (%)			subgroups defined according to ABSIS score** No (%)		
	moderate (n=21)	significant (n=50)	extensive (n=25)	moderate (n=23)	significant (n=50)	extensive (n=23)
Pemphigus foliaceus (n=19)	6 (32%)	8 (42%)	5 (26%)	12 (63%)	3 (16%)	4 (21%)
Pemphigus vulgaris (n=77)	15 (19%)	42 (55%)	20 (26%)	11 (14%)	47 (61%)	19 (25%)
- skin only (n=6)	2 (33%)	4 (67%)	0 (0%)	6 (100%)	0 (0%)	0 (0%)
- mucosal only (n=22)	7 (32%)	12 (55%)	3 (13%)	2 (9%)	14 (64%)	6 (27%)
- skin and mucosal (n=49)	6 (12%)	26 (53%)	17 (35%)	3 (6%)	33 (67%)	13 (27%)

* cut-off values differentiating moderate, significant and extensive pemphigus forms based on PDAI score were 15 and 45 points

** cut-off values differentiating moderate, significant and extensive pemphigus forms based on ABSIS score were 17 and 53 points

Table 4: Cut-off values defining moderate, significant and extensive pemphigus according to the three clinical presentation of pemphigus (exclusive cutaneous involvement, exclusive mucosal involvement and both involvement)

	PDAI		ABSIS	
	25^{th} percentile	75^{th} percentile	25^{th} percentile	75^{th} percentile
Whole population (n=96)	15	45	17	53
pemphigus with exclusive cutaneous involvement (n=25)	12	37	3	31
pemphigus with exclusive mucosal involvement (n=22)	11.5	35	29	53
pemphigus with both cutaneous and mucosal involvement (n=49)	19	54	26	53

Figure 1

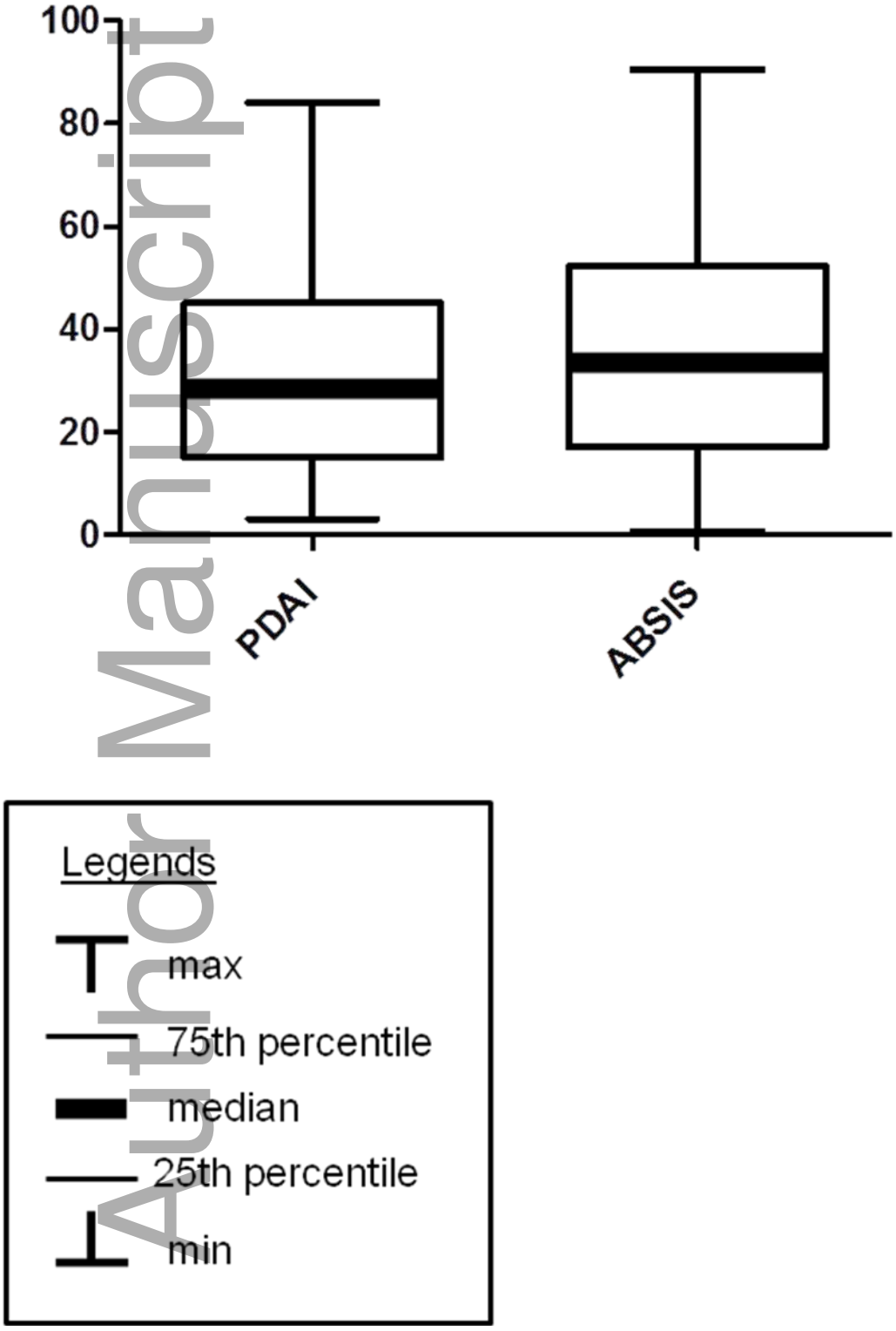
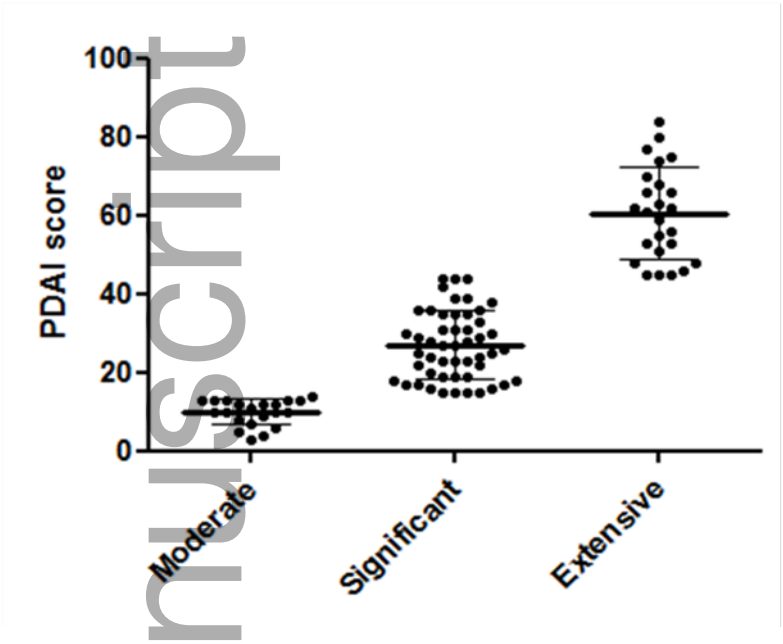
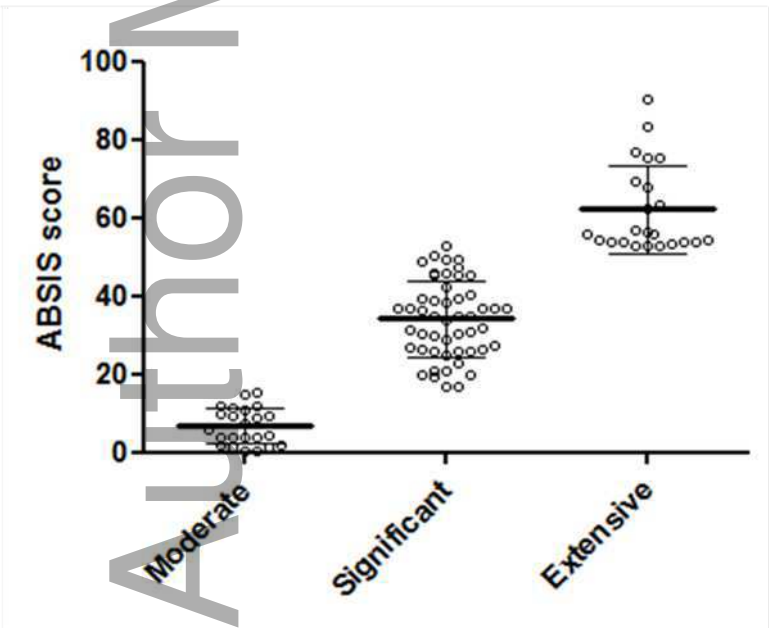


Figure 2

PANEL A: Distribution of PDAI in the 3 subgroups according to PDAI cut-offs



PANEL B: Distribution of ABSIS in the 3 subgroups according to ABSIS cut-offs



PANEL C: Distribution of PGA in the 3 subgroups according to PDAI or ABSIS cut-offs