

Development and validation of a graphic 2D investigator's global assessment instrument for grading the overall severity of atopic dermatitis in dogs

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Background – Clinical trials enrolling dogs with atopic dermatitis (AD) use validated instruments that aggregate the extent and severity of selected skin lesions; none of these provides a global assessment of the severity of all lesions.

Objectives – To validate an Investigator Global Assessment (IGA) instrument to globally evaluate the severity of skin lesions in dogs with AD.

Animals – Forty dogs with AD.

Methods and materials – A 2D graphic IGA (2D-IGA) instrument was created to subjectively score, with a single dot, the overall extent and severity of all cAD lesions. This tool was tested for its validity (content, construct and criterion), reliability (inter- and intraobserver) and sensitivity to change.

Results – The content of the 2D-IGA was first validated by a supportive vote by the International Committee of Allergic Diseases of Animals (ICADA) membership. Its construct was verified by positive correlations between the 2D-IGA scores and those of the Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-04) and the Canine Atopic Dermatitis Lesion Index (CADLI) (Spearman's rank-order correlation, $P < 0.0001$). The positive correlation ($P < 0.0001$) between an Owner Global Assessment of Disease Severity (OGADS) and the 2D-IGA indirectly satisfied its criterion. Scores graded by the same investigator hours apart and those between investigators were positively correlated ($P < 0.0001$), thereby validating this scale's intra- and interobserver reliabilities. Finally, the changes in 2D-IGA values during treatment were correlated positively with scores of an Owner Global Assessment of Treatment Efficacy (OGATE; $P < 0.0001$), thus showing its sensitivity to change.

Conclusions and clinical importance – This novel 2D-IGA is a simple static graphic instrument that could be useful for clinical trials testing the efficacy of interventions for cAD.

Introduction

With the publication of the first version of the Canine Atopic Dermatitis Extent and Severity Index (CADESI),¹ clinicians began using named instruments to standardize better the evaluation of skin lesions in clinical trials enrolling dogs with atopic dermatitis (AD). The four versions of CADESI^{1–4} and the later Canine Atopic Dermatitis Lesion Index (CADLI)⁵ are graded similarly by aggregating the severity scores of selected individual or grouped skin lesions at designated body areas. The extent of skin lesions is either limited to the body sites preferentially affected in canine AD [e.g. in the 4th iteration of CADESI(-04) and CADLI] or it is assessed over the entire body (e.g. in CADESI-01, -02 and -03). Both the CADLI and CADESI-04 are the recommended

instruments for the evaluation of atopic skin lesions in the 2018 Core Outcome Set for cAD (COSCAD'18) proposed by the International Committee of Allergic Diseases of Animals (ICADA).⁶

These skin lesion evaluation tools, although still subjective, have provided a valuable improvement for outcome measure assessment in clinical trials enrolling atopic dogs, yet they have one major constraint: they apply mostly to dogs with typical AD patterns and skin lesions. Indeed, both widely accepted CADESI-04 and CADLI have an evaluation of skin lesions restricted to "classic" body areas, thus limiting their usefulness in dogs exhibiting lesions elsewhere on the body. Other possible limitations are the time needed to grade all lesions in the various body areas and the possible heterogeneity in each clinician's understanding of what the various areas and skin lesions represent.

In clinical trials with human patients with AD, skin lesions are assessed with one of the two most commonly used instruments: the SCORing Atopic Dermatitis (SCORAD)⁷ and the Eczema Activity and Severity Index (EASI).⁸ Both scales rely on the evaluation of the severity of selected skin lesions and their extent within large body

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areas; the SCORAD also includes an evaluation of the perception of itch and sleeplessness.

In human medicine, global instruments (e.g. the rating of the overall AD severity on a 0–5 ordinal scale) are being reported with an increasing frequency because of their ease of use and rapidity of completion. Additionally, these Investigator Global Assessment (IGA) tools have the clear advantage that patients are more likely to understand the meaning of the words associated with each score (the most common being “clear”, “almost clear”, “mild”, “moderate” and “severe”) rather than a SCORAD or EASI value of 20. Although a systematic review confirmed the availability of numerous global scales for the evaluation of atopic skin lesions in humans, their validation is limited,⁹ and there is an unfortunate lack of standardization between tools.¹⁰

Following the performance of three systematic reviews of clinical trials enrolling dogs with AD,^{11–13} the present authors could not find any validated instruments to globally evaluate the severity of skin lesion severity in atopic dogs. The objectives were thus to design and validate such a tool, as recommended as a development need in the COSCAD’18.⁶

Methods and materials

Atopic dogs

Client-owned dogs with AD that presented to the authors clinic were eligible for enrolment. The diagnosis of cAD was based on a compatible history, characteristic clinical signs and the presence of pruritus.^{14,15} All pruritic dermatoses resembling cAD were ruled out using standard methods; the absence of visible lesions suggestive of bacterial and yeast skin infections was verified. To be eligible for enrolment, dogs had to exhibit active cAD lesions of any severity at the time of presentation; dogs were selected whether or not they were currently treated with anti-allergic drugs.

Design and grading of the 2D investigator global assessment (IGA) tool

This IGA was developed with a 2D design to simultaneously evaluate the skin lesions’ extent and intensity parameters, as these are not always positively correlated (Figure 1a; Figure S1).

The extent – that is the percentage of body surface area affected – is represented on the y-axis with 25% increment descriptors. Assessments are to be made globally (i.e. over the entire body) instead of being limited to specific body regions as for the CADESI-04 and CADLI. To better guide observers in their evaluation of the affected skin surface, a dog silhouette was added to accompany the 2D-IGA extent assessment (Figure S2). Adapted from the “Wallace rule of nines” used in human burn victims,¹⁶ the entire dog’s body is divided into sections associated with an estimated percentage of the total body surface area. On the x-axis, the intensity (i.e. the severity) of skin lesions is represented with “no lesions,” “mild,” “moderate” or “severe” written indicators. A green-to-red colour spectrum was added next to both x- and y-axes to highlight that the scoring should be on a continuum and not limited to the levels of added descriptors.

The grading of the 2D-IGA involves a two-step process. First, the clinician observes the AD skin lesions in their entirety, whereas those consistent with infections are not to be evaluated. A dot is then placed on the scale at the intersection of the clinician’s perception of the percentage of the body surface area affected and the severity of the lesions observed (Figure 1a). Second, an identically sized, coloured grading scale (ideally printed onto a transparent sheet) is overlain onto the initial sheet (Figure 1b, Figure S1). The colouring in the transparent overlay has a legend for the corresponding IGA score, as follows: 0 = “clear”; 1 = “almost clear”; 2 = “mild”;

3 = “moderate”; and 4 = “severe.” The various boxes in this grading scheme were selected so that different extent × intensity scenarios could result in the same 2D-IGA grades, as would be seen in dogs with AD of different phenotypes that would be deemed as having the same disease severity. If the dot touches the intersection of two different colours on the transparent overlay, the darkest colour should be used for a higher IGA final score.

Validation of the 2D investigator global assessment (IGA) tool

This novel 2D-IGA instrument was evaluated for its validity, reliability and sensitivity to change according to a published method,¹⁷ a validation scheme already used for the CADESI-03 and -04 tools.^{3,4}

Evaluation of the validity of the 2D-IGA

A validated instrument is expected to measure its intended parameters effectively.¹⁷ Thus, to evaluate the validity of the 2D-IGA, the instrument’s content, construct and criterion were assessed.

Content

An instrument’s content reflects its ability to assess relevant domains, based on the judgment by one or more experts.¹⁷ The concept and design of the 2D-IGA and an anonymous online evaluation survey were sent to the then members of the ICADA. The content of the instrument was considered as validated if a majority of members voted “yes” to the question: “In your opinion, does this scale appear to be assessing all the relevant content/domains to evaluate the severity of cAD globally?”

Construct

The construct of an instrument demonstrates its ability to agree with relevant variables and measures of the same construct.¹⁷ This parameter was evaluated by having the same clinician score for the 2D-IGA, and the two validated AD skin lesion grading instruments, the CADESI-04 and CADLI, on the same dog within minutes of each other. The three instruments were assessed in a randomized order that differed between dogs.

Criterion

The criterion represents an instrument’s aptitude to correlate with other measures of the disease.¹⁷ Criterion assessment typically involves the calculation of the correlation between that instrument’s measures and those rated with a “gold standard.” Unfortunately, at present, there is no validated standard to evaluate the global severity of cAD. In such absence and as a surrogate, a decision was made to evaluate the correlation between the 2D-IGA and a subjective owner’s global disease assessment rating, as performed previously.⁴

In order to evaluate the criterion of the 2D-IGA, one clinician thus scored the 2D-IGA, and, at the same visit, one owner was asked to assess the severity of skin lesions (but not pruritus manifestations) using an Owner’s Global Assessment of Disease Severity (OGADS) scale. The OGADS was subjectively rated as follows: 1 = “no skin lesions of AD”; 2 = “mild skin lesions”; 3 = “moderate skin lesions”; and 4 = “severe skin lesions of AD.” The correlation between owner-assessed pruritus scores was calculated using the validated 10-point Visual Analog Scale (PVAS10)¹⁸ and the 2D-IGA values graded at the same visit.

Evaluation of the reliability of the 2D- investigator global assessment (IGA) tool

The reliability of a scale indicates its ability to measure what it intends to measure effectively and in a reproducible fashion;¹⁷ it consists of an assessment of both intra- and interobserver reliabilities.

Intraobserver reliability

The intraobserver reliability demonstrates that two measurements made by the same observer, on two or more distinct occasions, produce similar results.¹⁷ To evaluate this parameter, the same clinician

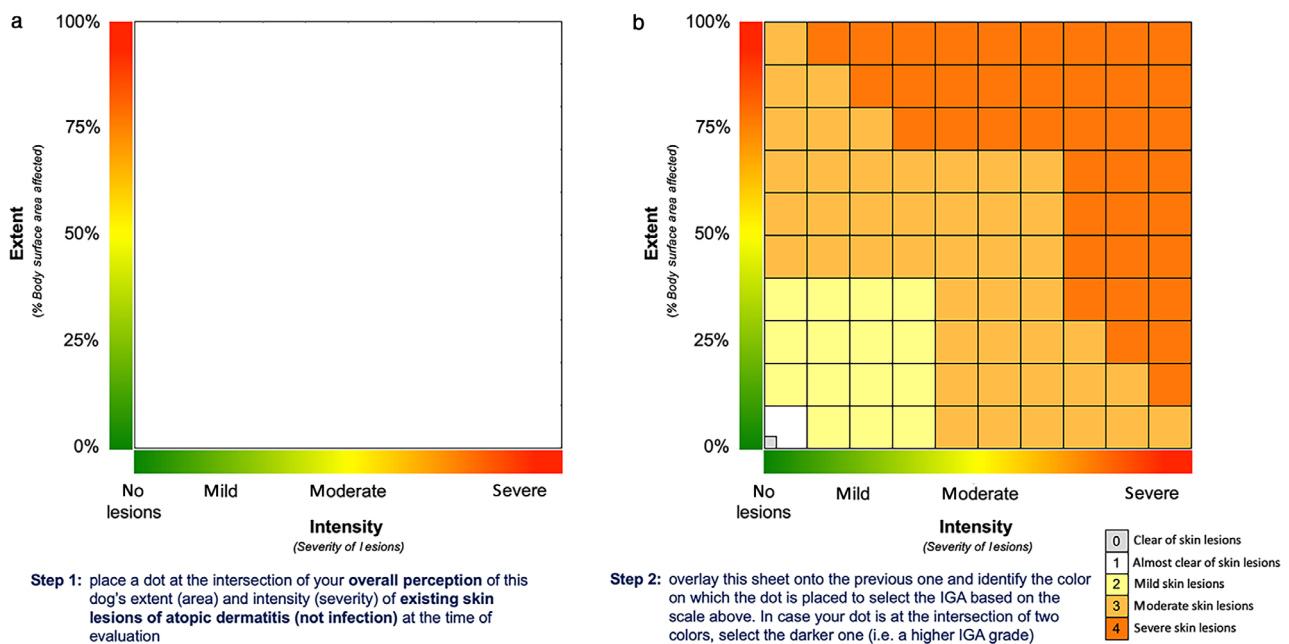


Figure 1. The 2D Investigator Global Assessment (2D-IGA) of canine atopic dermatitis skin lesions. (a) assessment scale; (b) grading overlay.

scored the 2D-IGA twice during the initial visit, ≥ 3 h apart. The clinicians were not permitted to use the transparent overlay to obtain the final IGA score before making their second assessment to limit any intrarater bias.

Interobserver reliability

The interobserver reliability demonstrates that measurements made by two or more observers produce similar results.¹⁷ To evaluate this parameter, two clinicians were instructed to rate the 2D-IGA within 1 h of one another. The clinicians were blinded to each other's results to limit bias.

Evaluation of the sensitivity to change

The sensitivity to change illustrates the ability of an instrument to detect clinically meaningful changes in the severity of a disease after a medical intervention.¹⁷ To evaluate this parameter, the 2D-IGA was scored at two time points: pre-treatment (that is during the initial visit) and post-treatment during a follow-up re-evaluation. After the first visit, atopic dogs were treated for at least one month with anti-allergic interventions, as deemed necessary by the clinician. During the second visit, the owners of these dogs were asked to subjectively rate the overall response to treatment using the five-point Owner Global Assessment of Treatment Efficacy (OGATE) scale proposed in the COSCAD¹⁸. The possible choices were as follows: 0 = "no response"; 1 = "a poor response"; 2 = "a fair response"; 3 = "a good response"; and 4 = "an excellent response". The difference between post- of pre-treatment 2D-IGA scores and the owner-reported OGATE were then compared.

Statistics

The relationship between the 2D-IGA and the CADESI-04, CADLI, PVAS10 and OGADS was calculated using the nonparametric Spearman's rank-order correlation. The same test was used to assess the correlation between the OGATE and the difference in 2D-IGA values between visits. Finally, the 2D-IGA values rated by the same and between two observers were assessed both by the Spearman's correlation and the calculation of Cohen's kappa coefficients. All correlations were calculated using PRISM software (GraphPad; La Jolla, CA, USA) and the kappa coefficients by one of GraphPad's online tools (<https://www.graphpad.com/quickcalcs/kappa2/>; accessed Oct 25, 2019).

Results

Forty dogs with active atopic skin lesions of varying degrees of severity were selected. These dogs were of both genders (a female to male ratio of 1:1), aged six months to 14 years; with 14 breeds and 12 cross-bred dogs.

Evaluation of the content

The final design of the 2D-IGA was sent to the then membership of the ICADA in January 2018. The online survey was answered by 15 of 20 members (75%) of whom 12 (80%) voted "yes" to the proposed question, thereby agreeing that the proposed instrument assessed all of the relevant content/domains to evaluate the severity of cAD globally. This clear majority vote by a committee of disease experts thus satisfied the content of the 2D-IGA.

Evaluation of the construct

The same clinician scored the 2D-IGA, CADESI-04 and CADLI in the 40 dogs within minutes of each other and in a random order of grading. The 2D-IGA values were significantly correlated to the CADESI-04 (Figure 2a) and CADLI (Figure 2b) scores with a Spearman's rank-order coefficient (r_s) of 0.79 ($P < 0.0001$). Such high correlations met the proposed criteria for construct validation used herein.

Evaluation of the criterion

During the first examination visit, the clinician graded the 2D-IGA in all dogs while their owners subjectively scored the OGADS and PVAS10. The 2D-IGA and the OGADS values were significantly correlated (Figure 2c; $r_s = 0.58$, $P < 0.0001$) but the 2D-IGA and PVAS10 scores were not so (Figure 2d; $r_s = 0.26$; $P = 0.115$). Because of the significant correlation existing between the subjective

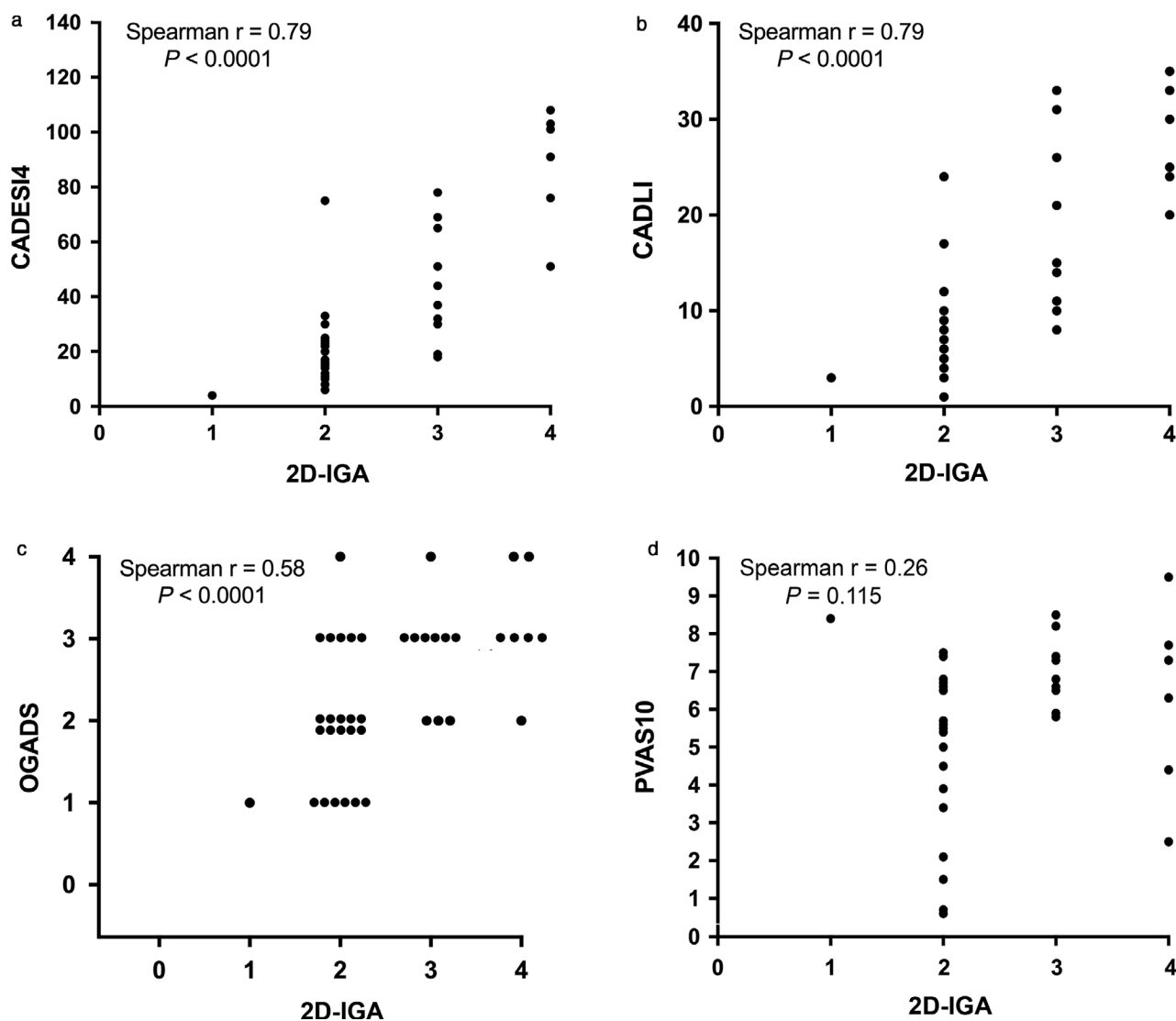


Figure 2. Assessment of the construct and criterion of the 2D Investigator Global Assessment (2D-IGA).

(a) Construct: correlation between the 2D-IGA and the Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-04); (b) construct: correlation between the 2D-IGA and the Canine Atopic Dermatitis Lesion Index (CADLI); (c) criterion: correlation between the 2D-IGA and the Owner's Global Assessment of Disease Severity (OGADS); and (d) criterion: correlation between the 2D-IGA and the pruritus Visual Analog Scale (PVAS)10.

assessments of overall disease severity by owners and clinicians, the criterion of the 2D-IGA was considered to have been met. That this novel instrument's scores did not correlate with those of the PVAS10 was expected as atopic skin lesions, especially erythema, and pruritus scores have long been known to not always evolve in unison.^{3,19}

Evaluation of the intra- and interobserver reliabilities

The 2D-IGA scores evaluated by one clinician at two different time points (≥ 3 h apart) on 34 dogs were significantly correlated (Figure 3a; $r_s = 0.96$, $P < 0.0001$). The 2D-IGA scores graded independently by two clinicians on 39 dogs were correlated to a similar degree (Figure 3b; $r_s = 0.75$, $P < 0.0001$).

Although the agreement between the same clinician's 2D-IGA values was very good [Cohen's Kappa (κ) of 0.90 (95% confidence interval: 0.77–1.00)], that between the two clinicians scores was only moderate [$\kappa = 0.53$ (0.31–0.74)].

Evaluation of the sensitivity to change

Thirty-four dogs were treated for at least one month with drugs which included oral glucocorticoids (28 dogs), ciclosporin (seven), oclacitinib (four) and lokivetmab (11), alone or in combination. The numerical differences in 2D-IGA values between those assessed after and before treatment were significantly correlated with the OGATE scores (Figure 4; $r_s = 0.78$, $P < 0.0001$); this satisfied the assessment of the sensitivity to change of the 2D-IGA.

Discussion

This paper reports the design of a graphic 2D clinician-assessed instrument to globally rate the extent and severity of cAD skin lesions. It was found that this 2D-IGA had satisfactory validity, reliability and sensitivity to change. Therefore, this tool is proposed as another validated scale for the assessment of skin lesions of cAD in clinical trials.

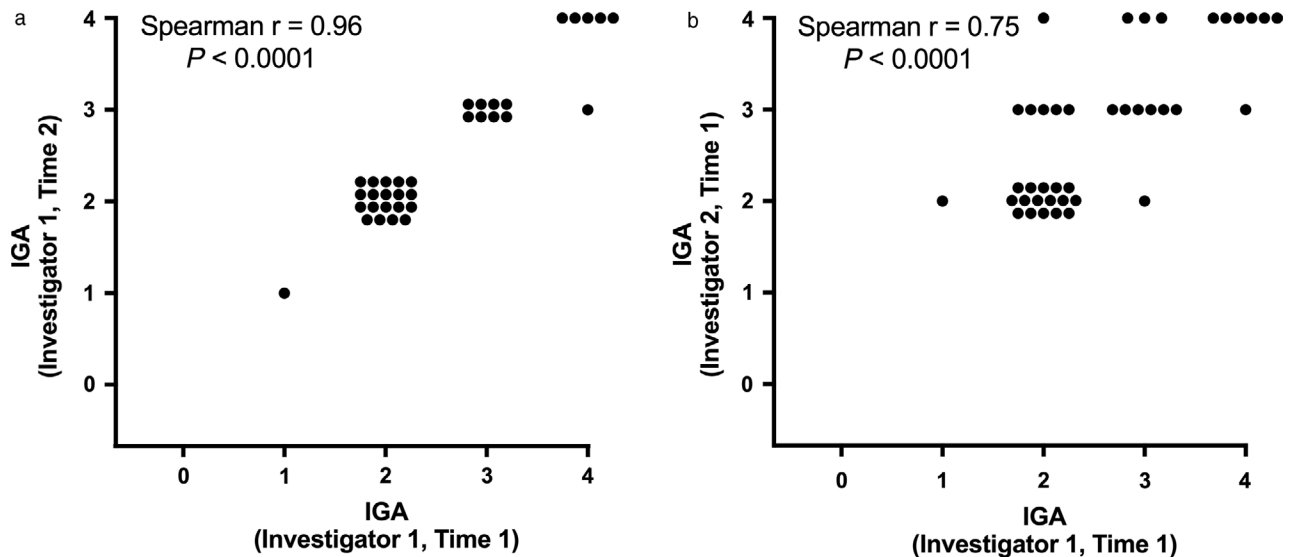


Figure 3. Assessment of the reliability of the 2D Investigator Global Assessment (2D-IGA).

(a) Intraobserver reliability: correlation between the 2D-IGA scores by the same investigator at least three hours apart; and (b) interobserver reliability: correlation between the 2D-IGA scores by two investigators within 10 min of each other.

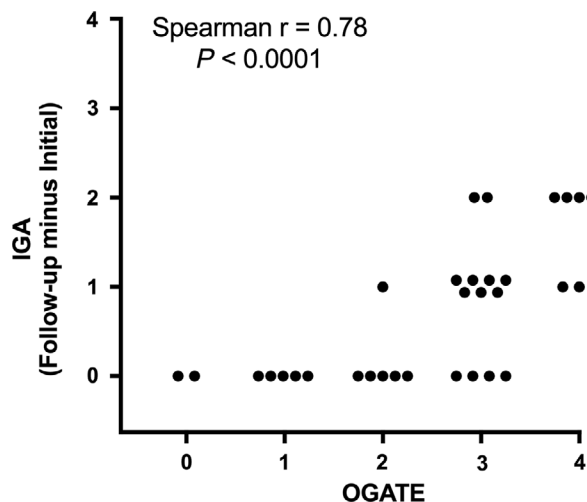


Figure 4. Assessment of the sensitivity to change of the 2D Investigator Global Assessment (2D-IGA).

Correlation between the change of the IGA during treatment and the Owner Global Assessment of Treatment Efficacy (OGATE).

In order to determine the overall severity of human AD, instruments typically score a global domain on an ordinal scale that is simple to comprehend and rapid to administer. Because of their ease of use, this type of scale has proliferated since the report of an IGA for human AD in 2002.²⁰ As of 2015, there were variants of such scales published under 20 different names with the term "IGA" used most commonly.¹⁰ These instruments were designed as "static", that is that their evaluation referred to a single time point, or "dynamic" if they referenced the disease severity before treatment (e.g. a "50% reduction from baseline").¹⁰ Over time, such IGAs have varied considerably in their design and composition. For example, the number of categories to be chosen ranged between four and seven points with a six-point tool being reported most frequently.¹⁰ These scales also differ in their content, incorporating the evaluation of signs (i.e.

skin lesions), or signs and symptoms (i.e. itch) with an array of different descriptors. Most clinical trials have used these IGAs to report the proportion of patients in each severity category, whereas others have defined "treatment success" in a "yes/no" manner depending on whether or not a specific benchmark had been met during treatment.¹⁰ An example of the latter is a trial in which one of the secondary outcome measures was "an IGA of 0/1 [i.e. "clear or almost clear"] with at least a two-grade reduction from baseline."²¹ One caveat of such an outcome measure, however, is that it might underestimate treatment success, as shown in two large clinical trials testing the efficacy of dupilumab for the treatment of human AD.²² Despite their lack of homogeneity, variants of global scales have been used in about one-third of randomized controlled trials of treatments for human AD published between 2000 and 2014.¹⁰ In fact, the US Federal Drug Administration recommends that an IGA serves as the primary end-point for trials supporting new drug applications, but this recommendation became the subject of controversy.²³

The 2D-IGA was designed and validated as a response to COSCAD'18's report of a need for the development of an instrument to globally assess the severity of AD in dogs.⁶ The question rapidly rose on how to define the severity of cAD: By skin lesions, pruritus manifestations, or a combination of both? As clinicians and pet owners would likely answer this question differently, the tool herein was developed as a global instrument of signs – that is a tool to overall assess the severity of cAD skin lesions.

A second challenge arose while designing this IGA: deciding whether a dog with mild erythema over its entire body would have milder or more severe AD skin lesions than one with very localized but intense erythema and excoriations. A consensus was reached on the notion that the severity of cAD skin lesions depends most often on a combination of their extent (i.e. the surface area affected) and intensity (that is their severity in a strict sense). This

led to the concept of a 2D instrument using a simple square with four or five descriptors on both x- and y-axes. To limit the grading at the intersection of written descriptors, green-to-red continuous colour scales were added on each axis, as they are the symbolic colours implying a continuum from the milder (green) to the most severe (red) skin lesions. The grading square was left blank, not to influence the rating itself. To help reduce the variability of extent assessment between investigators, a typical German shepherd dog silhouette was added, separated into regions that mirror those of the “rule of nines” used to assess the percentage of affected body surface area in human patients with burns.¹⁶ This silhouette was incorporated to help reassure clinicians of the logic of their lesion extent evaluation. This newly designed 2D-IGA is straightforward and fast to administer, as it requires only a single dot to be made by the clinician with the final score being determined after the overlay of a grading sheet with five levels of severity.

As reported originally for the validation of instruments to rate skin lesions of human AD,¹⁷ an evaluation was made of the 2D-IGA tool’s content, construct and criterion, which all assess its validity, as well as its intra- and inter-rater reliabilities and sensitivity to change. Such a methodology had been employed previously for the validation of the CADESI-03 and -04 scales.^{3,4} After evaluation, the 2D-IGA tool was found to have similar properties to those of the two other CADESI lesion-assessment scales. These steps are thus sufficient for considering this new instrument validated.

As part of the study of the scale’s criterion, an assessment was made that the 2D-IGA scores were correlated with the owner’s pruritus grades, although this was not possible to demonstrate. Although disappointing, this observation was not surprising in light of the occasional discrepancies existing between pruritus and skin lesion scores, even though they are usually correlated.^{19,24} One also sees such varied response in clinical trials in which some of the recently approved treatments have led to a faster improvement in pruritus manifestations than skin lesions;^{25,26} these interventions would thus lead to different 2D-IGA and PVAS scores, especially at early re-evaluation time points. Altogether, these considerations suggest that the validation of future instruments to grade atopic skin lesions should not require a significant correlation with pruritus scores.

Finally, another parameter traditionally evaluated to assess an instrument’s reliability is its internal consistency; that is, the study of how the different items scored in the scale correlate with each other and with the total score.¹⁷ As the 2D-IGA scale does not include separately graded individual components, its internal consistency was not evaluated.

There are several limitations to the use of this 2D-IGA that could impact upon its precision.

- 1 The lack of a validated tool to use to compare this new instrument to that of a “gold standard” for the assessment of global skin lesions; the 2D-IGA values correlated with those of a surrogate subjective evaluation by owners and thus only provides an imperfect validation of the criterion parameter.

- 2 Variations in the assessment of the extent of skin lesions between clinicians. Although the proposed silhouette, albeit with unvalidated body surface percentages, applies to a German shepherd dog and similarly shaped dogs, it is likely less translatable to dogs of brachycephalic breeds.

- 3 Lesions to be rated should be limited to those of cAD. Unfortunately, atopic skin lesions are commonly infected with *Staphylococcus* bacteria with the ensuing superimposition of lesions of folliculitis or epidermal collarettes onto those of typical AD; the same could be said about cutaneous colonization with *Malassezia* yeast that could worsen clinical signs of AD. These infected lesions, which can be widespread, could lead to a greater extent or intensity ratings, and thus to a higher IGA score. To limit this interference, it was specified in the narrative written below the scale that lesions of superinfection should not be graded. In summary, it is probably best to rate the 2D-IGA in dogs visibly free or cleared of bacterial skin infections; this is usually, and luckily, the case in clinical trials testing novel interventions in dogs with AD.

It is proposed that this 2D-IGA be utilized in clinical studies in different situations. For example, it could be used as a selection criterion, such as: “We will enrol untreated atopic dogs with a 2D-IGA of 3/4 (moderate-to-severe AD skin lesions) at baseline”. Additionally, this instrument could be used as an outcome measure of treatment success, for example: “We will define treatment success as a final 2D-IGA of 0/1 (clear-to-almost-clear) with at least a two-grade improvement from the baseline score”. A close variant would be: “The primary outcome measure will be the percentage of dogs with a final 2D-IGA of 0/1 (clear-to-almost-clear) with at least a two-grade improvement from the baseline score”.

In summary, a novel, graphic, 2D static IGA is designed herein that is simple to complete and rapid to administer. It is proposed that this newly validated instrument is used as an additional scale to grade canine atopic skin lesions in clinical trials.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1. Downloadable 2D-IGA rating and grading sheets.

Figure S2. Downloadable German shepherd silhouette for extent estimation.

Résumé

Contexte – Les essais cliniques incluant des chiens avec dermatite atopique (AD) utilisent des outils validés qui totalisent l'extension et la sévérité des lésions cutanées sélectionnées; aucun d'eux ne fournit une évaluation globale de la sévérité de toutes les lésions.

Objectifs – Valider un IGA (Investigator Global Assment) pour évaluer globalement la sévérité des lésions cutanées chez les chiens avec AD.

Sujets – Quarante chiens avec AD.

Matériels et méthode – Un outil 2D-IGA (2D graphic IGA) a été créé pour évaluer subjectivement, en un seul point, l'étendue et la sévérité globale de toutes les lésions d'AD canine (cAD). Cet outil a été testé pour sa validité (contenu, construction et critères), la fiabilité (inter et intra-observateur) et la sensibilité au changement.

Résultats – Le contenu de 2D-IGA a d'abord été validé par un vote de soutien par les membres de l'ICADA (International Committee of Allergic Diseases of Animals). La construction a été vérifiée par des corrélations positives entre les scores 2D-IGA et ceux du CADESI-04 (Canine Atopic Dermatitis Extent and Severity Index, 4th iteration) et le CADLI (Canine Atopic Dermatitis Lesion Index) (Spearman's rank-order correlation, $P < 0.0001$). La corrélation positive ($P < 0.0001$) entre OGADS (Owner Global Assessment of Disease Severity) et le 2DIGA satisfaisait indirectement ses critères. Les scores gradés par le même investisseur en quelques heures et entre investigateurs, étaient positivement corrélés ($P < 0.0001$), validant ainsi les fiabilités intra et inter-observateur. Enfin, les changements des valeurs 2D-IGA au cours du traitement étaient corrélés positivement avec des scores de OGATE (Owner Global Assessment of Treatment

Efficacy $P < 0.0001$), montrant ainsi ces sensibilités au changement.

Conclusions et importance clinique – Ce nouveau 2D-IGA est un graphique statique simple qui pourrait être utile pour les essais cliniques testant l'efficacité des interventions pour la cAD.

Resumen

Introducción – los ensayos clínicos que incluyen perros con dermatitis atópica (AD) utilizan instrumentos validados que agregan la extensión y la gravedad de las lesiones cutáneas seleccionadas; pero ninguno de ellos proporciona una evaluación global de la gravedad de todas las lesiones.

Objetivos – validar un instrumento de evaluación global del investigador (IGA) para evaluar globalmente la gravedad de las lesiones cutáneas en perros con AD.

Animales – Cuarenta perros con AD.

Métodos y materiales – se creó un instrumento gráfico 2D IGA (2D-IGA) para puntuar subjetivamente, con un solo punto, la extensión y la gravedad general de todas las lesiones caninas de AD (cAD). Esta herramienta fue probada para su validez (contenido, construcción y criterio), fiabilidad (entre observadores e intraobservadores) y sensibilidad al cambio.

Resultados – el contenido del 2D-IGA fue validado inicialmente con un voto de apoyo por parte del Comité Internacional de Enfermedades Alérgicas de los Animales (ICADA). Su construcción se verificó mediante correlaciones positivas entre las puntuaciones 2D-IGA y las del índice de extensión y severidad de la dermatitis atópica canina, cuarta versión (CADESI-04) y el índice de lesiones de dermatitis atópica canina (CADLI) (correlación de orden de rango de Spearman, $P < 0.0001$). La correlación positiva ($P < 0.0001$) entre una evaluación global del propietario de la gravedad de la enfermedad (OGADS) y el 2D-IGA indirectamente satisfizo su criterio. Los valores calificados por el mismo investigador con horas de diferencia y entre los investigadores se correlacionaron positivamente ($P < 0.0001$), validando así la fiabilidad intra e interobservador de esta escala. Finalmente, los cambios en los valores de 2D-IGA durante el tratamiento se correlacionaron positivamente con los valores de una evaluación global del propietario de la eficacia del tratamiento (OGATE; $P < 0.0001$), lo que muestra su sensibilidad al cambio.

Conclusiones e importancia clínica – este novedoso sistema 2D-IGA es un instrumento gráfico estático simple que podría ser útil para ensayos clínicos que prueben la eficacia de las intervenciones para tratar la cAD.

Zusammenfassung

Hintergrund – Klinische Studien mit Hunden mit atopischer Dermatitis (AD) verwenden validierte Methoden, um das Ausmaß und den Schweregrad der Hautveränderungen in der Gesamtheit zu betrachten; keine dieser Methoden erfasst global das Ausmaß aller Veränderungen.

Ziele – Die Evaluierung eines Investigator Global Assessment Instruments (IGA), um global die Schwere von Hautveränderungen bei Hunden mit AD zu beurteilen.

Tiere – Vierzig Hunde mit AD.

Methoden und Materialien – Es wurde ein grafisches 2D IGA (2D-IGA) Instrument kreiert, um subjektiv, mit einem einzigen Punkt, das Gesamtausmaß aller AD Veränderungen von Hunden (cAD) zu bewerten. Dieses Instrument wurde auf seine Validität (Inhalt, Aufbau und Bewertungsgrundlage), seine Verlässlichkeit (Inter- und IntraobserverInnen) und Empfindlichkeit in Bezug auf Veränderungen getestet.

Ergebnisse – Der Inhalt des 2D-IGA wurde zuerst mittels Zustimmung eines International Committee of Allergic Diseases of Animals (ICADA) validiert. Sein Konstrukt wurde mittels positiver Korrelation zwischen den 2D-IGA Werten und jenen des Canine Atopic Dermatitis Extent and Severity Index, 4. Ausgabe (CADESI-04) und dem Canine Atopic Dermatitis Lesion Index (CADLI) (Spearman's Rangordnungskorrelation, $P < 0.0001$) verifiziert. Die positive Korrelation ($P < 0.0001$) zwischen einem Owner Global Assessment of Disease Severity (OGADS) und dem 2D-IGA stützte indirekt seine Kriterien. Beurteilungen durch dieselben UntersucherInnen im Abstand von mehreren Stunden und jenen zwischen den UntersucherInnen waren positiv korreliert ($P < 0.0001$), wodurch die Intra- und InterobserverInnen Verlässlichkeit dieser Bewertungsskala validiert wurde. Letztlich waren die Veränderungen der 2D-IGA Werte während der Behandlung positiv korreliert mit den Werten der Owner Global Assessment of Treatment Efficacy (OGATE; $P < 0.0001$), was seine Empfindlichkeit gegenüber Veränderungen zeigte.

Schlussfolgerungen und klinische Bedeutung – Dieses neue 2D-IGA ist ein einfaches grafisches Instrument, welches für klinische Versuche, die die Effektivität von Interventionen bei cAD austesten, nützlich sein kann.

要約

背景 – アトピー性皮膚炎(AD)の犬を登録した臨床試験では、選択した皮膚病変の程度および重症度を集計する検証済みの手法を使用している。しかしながら、これらのいずれもすべての病変の重症度の包括的評価を提供していない。

目的 – 本研究の目的は、AD犬の皮膚病変の重症度を世界的に評価するため、Investigator Global Assessment(IGA)手法を検証することである。

被験動物 – 40頭のAD犬。

材料と方法 – 2DグラフィックIGA(2D-IGA)装置を作成し、すべての犬AD(cAD)病変の全体的な範囲および重症度を単一ドットで主観的に評価した。その有効性(コンテンツ、構成、基準)、信頼性(観察者間および観察者内)および変化に対する感度について、2D-IGA装置をテストした。

結果 – 2D-IGAの内容は、国際動物疾病アレルギー委員会(ICADA)会員による支持投票により最初に検証された。その構造は、2D-IGAスコアと犬のアトピー性皮膚炎の程度および重症度指数(CADESI-04)および犬のアトピー性皮膚炎病変指数(CADLI)(スピアマンの順位相関、 $P < 0.0001$)との正の相関によって検証された。オーナーによる疾病重症度の包括的評価(OGADS)および2DIGA間の正の相関($P < 0.0001$)は、間接的にその基準を満たした。同じ調査者によって時間ごとに格付けされたスコアおよび調査者間のスコアは正の相関があり($P < 0.0001$)、それによってこのスケールの観察者内および観察者間の信頼性が検証された。最後に、治療中の2D-IGA値の変化は、オーナーによる治療効果の包括的な評価(OGATE; $P < 0.0001$)のスコアと正の相関があり、変化に対する感受性を示した。

結論と臨床的重要性 – この新しい2D-IGAは、cADの介入の有効性をテストする臨床試験に役立つ可能性のある単純な静的グラフィック機器である。

摘要

背景 – 异位性皮炎(AD)臨床試験使用一些经过验证的仪器,用于统计皮肤病变的范围和严重性;这些都不能全面评估所有病变的严重性。

目的 – 验证一种调查者整体评估(IGA)仪器,是否能够整体评估AD犬皮肤病变的严重性。

动物 – 40只AD患犬。

方法和材料 – 我们制作了一个二维图形IGA (2D-IGA)仪器,用单点对犬AD (cAD) 所有病变的总体范围和严重性进行主观评分。测试该工具的有效性(内容、结构和标准)、可靠性(观察者间和观察者自身重复)和对变化的敏感性。

结果 – 通过国际动物过敏疾病委员会(ICADA)成员投票支持,2D-IGA的内容首先被验证。通过2D-IGA评分与第4代犬异位性皮炎范围和严重性指数(CADESI-04)和犬异位性皮炎病变指数(CADLI)的正相关(Spearman 秩序相关, $P < 0.0001$)来验证其结构。疾病严重性宠主整体评估(OGADS)与2DIGA之间的正相关($P < 0.0001$)间接满足其标准。同一调查者间隔数小时重复评分与调查者之间的评分存在正相关($P < 0.0001$),从而验证了该量表的观察者自身和观察者间的可靠性。最后,治疗期间2D-IGA值的变化与疗效的宠主整体评估(OGATE; $P < 0.0001$),显示出对变化的敏感性。

结论和临床重要性 – 2D-IGA是一种全新的简单静态图形仪器,可用于临床试验,以测试干预cAD的有效性。

Resumo

Contexto – Ensaios clínicos envolvendo cães com dermatite atópica (DA) utilizam instrumentos validados que agregam a extensão e a gravidade de lesões cutâneas selecionadas; nenhum deles fornece uma avaliação global da gravidade de todas as lesões.

Objetivos – Validar um instrumento de Avaliação Global do Investigador (IGA) para avaliar globalmente a gravidade das lesões cutâneas em cães com DA.

Animais – Quarenta cães com DA.

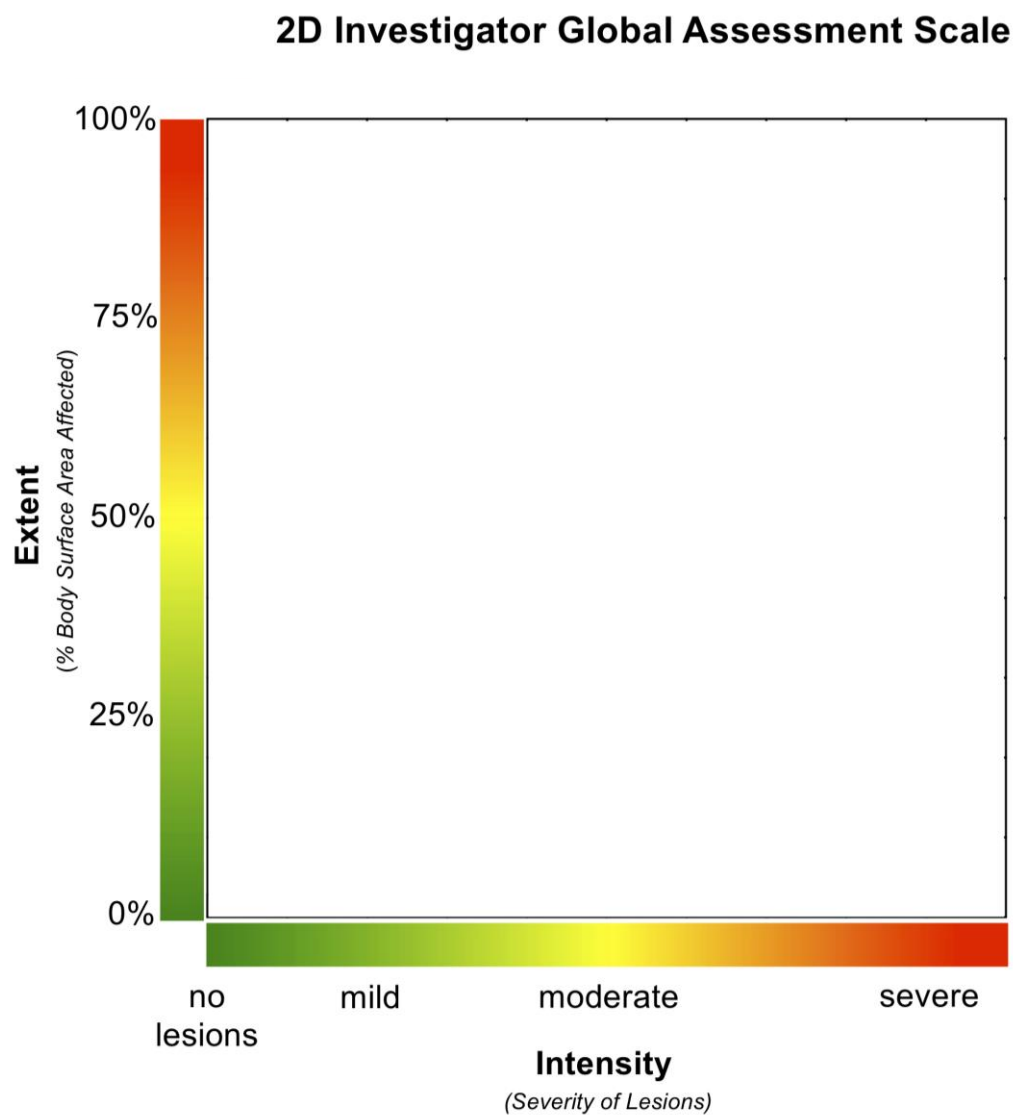
Métodos e materiais – Um instrumento gráfico de IGA 2D (2D-IGA) foi criado para pontuar subjetivamente, com um único ponto, a extensão e a severidade gerais de todas as lesões caninas AD (cAD). Esta ferramenta foi testada quanto à validade (conteúdo, construto e critério), confiabilidade (inter e intraobservador) e sensibilidade à mudança.

Resultados – O conteúdo do 2D-IGA foi validado pela primeira vez com apoio da associação do Comitê Internacional de Doenças Alérgicas de Animais (ICADA). O seu construto foi verificado por correlações positivas entre os escores 2D-IGA e os do Índice de Extensão e Gravidade da Dermatite Atópica Canina, 4ª versão (CADESI-04) e o Índice de Lesão da Dermatite Atópica Canina (CADLI) (correlação de Spearman, $P < 0,0001$). A correlação positiva entre a Avaliação Global da Gravidade da Doença pelo proprietário (OGADS) e o 2D-IGA satisfaz indiretamente o seu critério. Houve correlação positiva entre os escores classificados pelo mesmo investigador com uma hora de diferença e as entre investigadores, validando, assim, a confiabilidade intra e interobservadores desta escala. Finalmente, as alterações nos valores de 2D-IGA durante o tratamento foram correlacionadas positivamente com os escores de uma Avaliação Global da Eficácia do Tratamento pelo Proprietário (OGATE; $P < 0,0001$), mostrando assim sua sensibilidade à mudança.

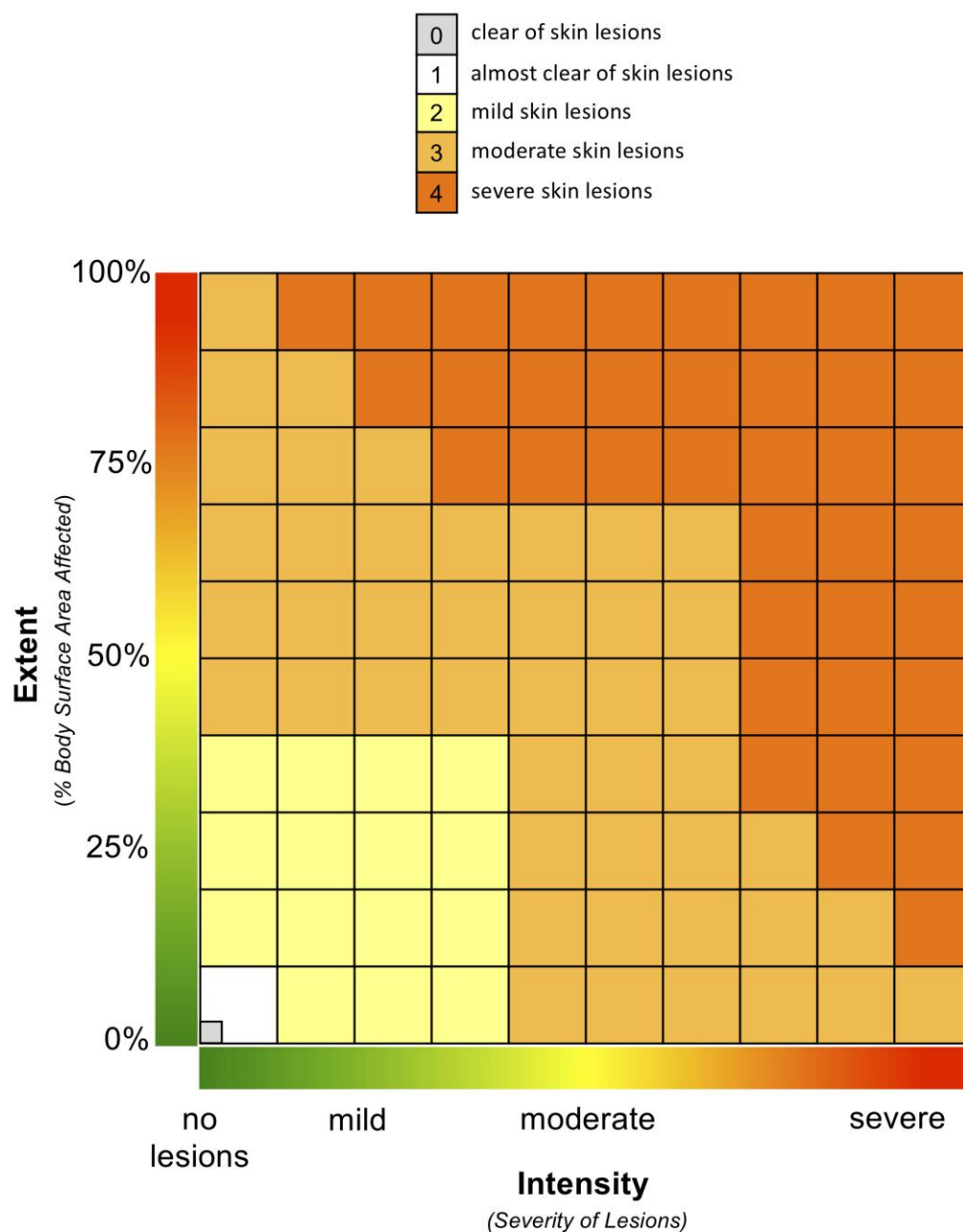
Conclusões e importância clínica – Este novo 2D-IGA é um instrumento gráfico estático simples que pode ser útil para ensaios clínicos que testam a eficácia de intervenções para cAD.

Supporting Information

Figure S1 Downloadable 2D-IGA rating and grading sheets



Step 1: place a dot at the intersection of your **overall perception** of this dog's extent (area) and intensity (severity) of **existing skin lesions of atopic dermatitis (not infection)** at the time of evaluation



Step 2: overlay this sheet onto the previous one and identify the color on which the dot is placed to select the IGA based on the scale above. In case your dot is at the intersection of two colors, select the darker one (i.e. a higher IGA grade)

Figure S2 Downloadable German shepherd silhouette for extent estimation

