Journal Club 2022/10/25　　by Dr.大村

Physician Global Assessment International Standardisation COnsensus in Systemic Lupus Erythematosus: the PISCOS study

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*Matteo Piga, Elisabetta Chessa, Eric F Morand, Manuel F Ugarte-Gil, Maria Tektonidou, Ronald van Vollenhoven, Michelle Petri, Laurent Arnaud, for the PISCOS Investigator Group**

The Physician Global Assessment International Standardisation COnsensus in Systemic Lupus Erythematosus (PISCOS) study aimed to obtain an evidence-based and expert-based consensus standardisation of the Physician Global Assessment (PGA) scoring of disease activity in systemic lupus erythematosus (SLE). An international panel of 79 SLE experts participated in a three-round Delphi consensus process, in which 41 statements related to the PGA in SLE were rated, using a 0 (strongly disagree) to 10 (strongly agree) numerical rating scale. Statements with agreement of 75% or greater were selected and further validated by the expert panel. Consensus was reached on 27 statements, grouped in 14 recommendations, for the use of the PGA in SLE, design of the PGA scale, practical considerations for PGA scoring, and the relationship between PGA values and levels of disease activity. Among these recommendations, the expert panel agreed that the PGA should consist of a 0–3 visual analogue scale for measuring disease activity in patients with SLE in the preceding month. The PGA is intended to rate the overall disease activity, taking into account the severity of active manifestations and clinical laboratory results, but excluding organ damage, serology, and subjective findings unrelated to disease activity. The PGA scale ranges from "no disease activity" (0) to the "most severe disease activity" (3) and incorporates the values 1 and 2 as inner markers to categorise disease activity as mild (≥0·5 to 1), moderate (>1 and ≤2) and severe (>2 to 3). Only experienced physicians can rate the PGA, and it should be preferably scored by the same rater at each visit. The PISCOS results will allow for increased homogeneity and reliability of PGA ratings in routine clinical practice, definitions of remission and low disease activity, and future SLE trials.

Introduction

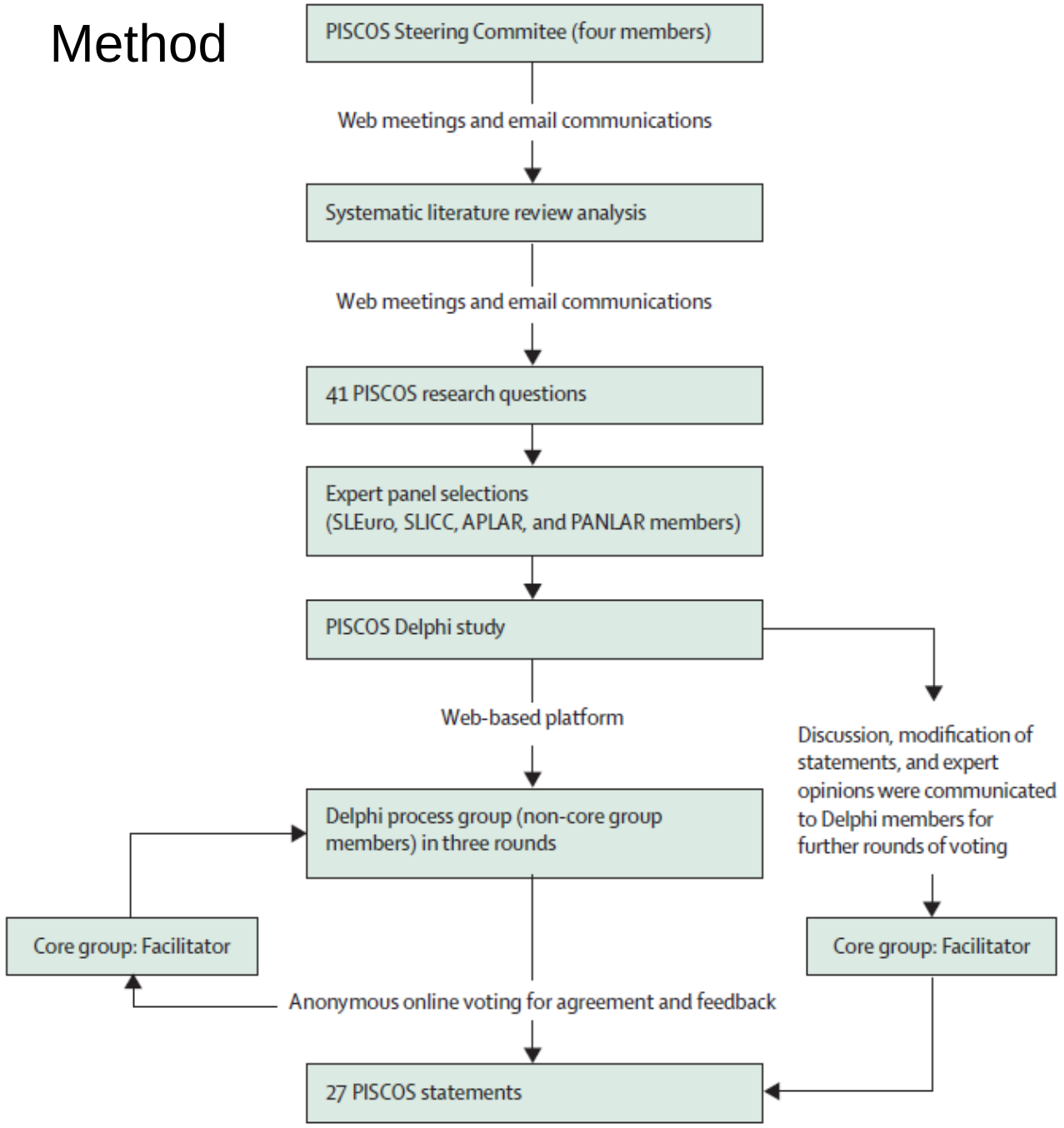
SLEでは、あまた多くの活動性指標が作られたが、PGAがEULAR recommendations 2019に含まれた唯一の指標である。

PISCOS research programの最初の仕事として、systematic literature reviewを行った（Rheumatology 2020）

SLEでPGAをつける理想的な方法に関する合意はまだ得られていない

SLEのserologyをその運用に含めるかどうかに関しては明らかでない

Method



79人のExperts

PISCOS Investigator Group

Simone Appenzeller, Cynthia Aranow, Anca Askanase, Tadej Avcin, Sang-Cheol Bae, George Bertsias, Eloisa Bonfa, Ernesto Cairoli, Mario H Cardiel, Ricard Cervera, François Chasset, Carlo Chizzolini, Ann E Clarke, Fabrizio Conti, Nathalie Costedoat-Chalumeau, Laszlo Czirjak, Andrea Doria, Thomas Dörner, Gerard Espinosa, Rebecca Fischer-Betz, Mercedes Garcia, Dafna D Gladman, Luis A Gonzalez, Iva Gunnarsson, Laniyati Hamijoyo, John G Hanly, Sarfaraz A Hasni, Frederic A Houssiau, Murat Inanç, Luis S Ines, David Isenberg, Soren Jacobsen, Yeong-Jian Jan Wu, Yuko Kaneko, Yasuhiro Katsumata, Chak S Lau, Alexandra C Legge, Karoline Lerang, Maarten Limper, Worawit Louthrenoo, Shue-Fen Luo, Antonio Marinho, Loreto Massardo, Alexis Mathian, Marta Mosca, Mandana Nikpour, Jose M Pego-Reigosa, Christine A Peschken, Bernardo A Pons-Estel, Guillermo J Pons-Estel, Anisur Rahman, Simona Rednic, Camillo Ribi, Guillermo Ruiz-Irastorza, Emilia I Sato, Amit Saxena, Matthias Schneider, Gian Domenico Sebastiani, Vibeke Strand, Elisabet Svenungsson, Yoshiya Tanaka, Zoubida Tazi Mezalek, Michael L Tee, Angela Tincani, Zahi Touma, Anne Troldborg, Carlos Vasconcelos, Evelyne Vinet, Edward M Vital, Alexandre E Voskuyl, Anne Voss, Daniel Wallace, Michael Ward, Leonid D Zamora.

41のResearch Questionに対して各Expertが0-10でRatingし、Delphi法を用いて改訂を加え、75%以上の同意が得られた(7点以上）Research Questionより最終27のstatementを採用した

Overarching Principles

		Level of agreement (0–10)*	Percentage of votes ≥9/10
1. Overarching principles for scoring PGA			
1.1	The PGA is an outcome instrument for measuring disease activity in SLE	9·7 (0·9)	94·9%
1.2	The PGA is a visual analogue scale for measuring disease activity in SLE	9·8 (0·4)	97·5%
1.3	The PGA should be used to rate overall disease activity in SLE	9·7 (0·8)	96·2%
1.4	The PGA rating should reflect the severity of active manifestations	9·6 (1·4)	93·7%
1.5	The PGA should be used to rate disease activity only (not organ damage)	9·8 (0·9)	96·2%
1.6	The PGA reflects the clinician's judgement about disease activity in SLE	9·9 (0·5)	96·2%
1.7	The PGA should be scored independently of prespecified thresholds used in other scores	9·6 (0·9)	93·7%
1.8	The PGA should assess disease activity according to the physician's perspective	9·8 (0·5)	97·5%
1.9	The PGA should be rated only by a medical doctor	9·6 (1·0)	94·9%
1.10	Only physicians with expertise in SLE can rate disease activity using the PGA	9·5 (0·9)	91·1%
1.11	The PGA scoring should not take into account subjective findings (eg, headache, arthralgias, fatigue) if those are not clearly related to disease activity	9·5 (1·4)	93·7%
1.12	The PGA scoring should take into account common clinical laboratory parameters such as urinalysis, serum creatinine level, and blood cell count	9·6 (1·1)	93·7%

2. PGA scale design			
2.1	The PGA is rated on a 0–3 scale	9·7 (0·5)	94·9%
2.2	The PGA should incorporate inner markers for 1 and 2 (with a graph showing a PGA and 0, 1, 2, 3) without any additional comment regarding whether this is mild, moderate, etc	9·5 (1·0)	93·6%
3. Practical considerations for PGA scoring			
3.1	Preliminary training on a set of training cases is mandatory before a physician can rate the PGA	9·2 (1·8)	89·8%
3.2	For a given patient, the PGA should be preferably scored by the same rater at each visit	9·6 (1·1)	94·9%
3.3	The PGA should preferably be scored during the consultation and, if needed, amended as soon as all elements for PGA rating are available	9·7 (0·8)	92·4%
3.4	The timeframe to consider when rating the PGA should be explicitly stated	9·5 (1·3)	91·1%
3.5	The timeframe to consider when rating the PGA is the last month	9·5 (1·4)	89·8%
3.6	The PGA should be rated by putting a vertical tick (recommended in trials by the European Medicines Agency and US Food and Drug Administration)	9·9 (0·3)	100%
3.7	The PGA can be scored either on a printed sheet or using a web or app-based scale	9·9 (0·3)	100%
3.8	The PGA score should be expressed using a continuous measure with one decimal (eg, 2·3 on a 0–3 scale)	9·5 (1·4)	93·7%
4. Relationship between PGA values and severity of disease activity			
4.1	On the PGA scale, the anchor "0" refers to "no disease activity"	9·9 (0·2)	100%
4.2	On the PGA scale, the anchor "3" refers to "most severe disease activity"	9·9 (0·2)	100%
4.3	A PGA score ≥0·5 and ≤1 reflects mild disease activity	9·7 (1·0)	93·7%
4.4	A PGA score >1 and ≤2 reflects moderate disease activity	9·8 (0·5)	96·2%
4.5	A PGA score >2 and ≤3 reflects severe disease activity	9·8 (0·5)	96·2%

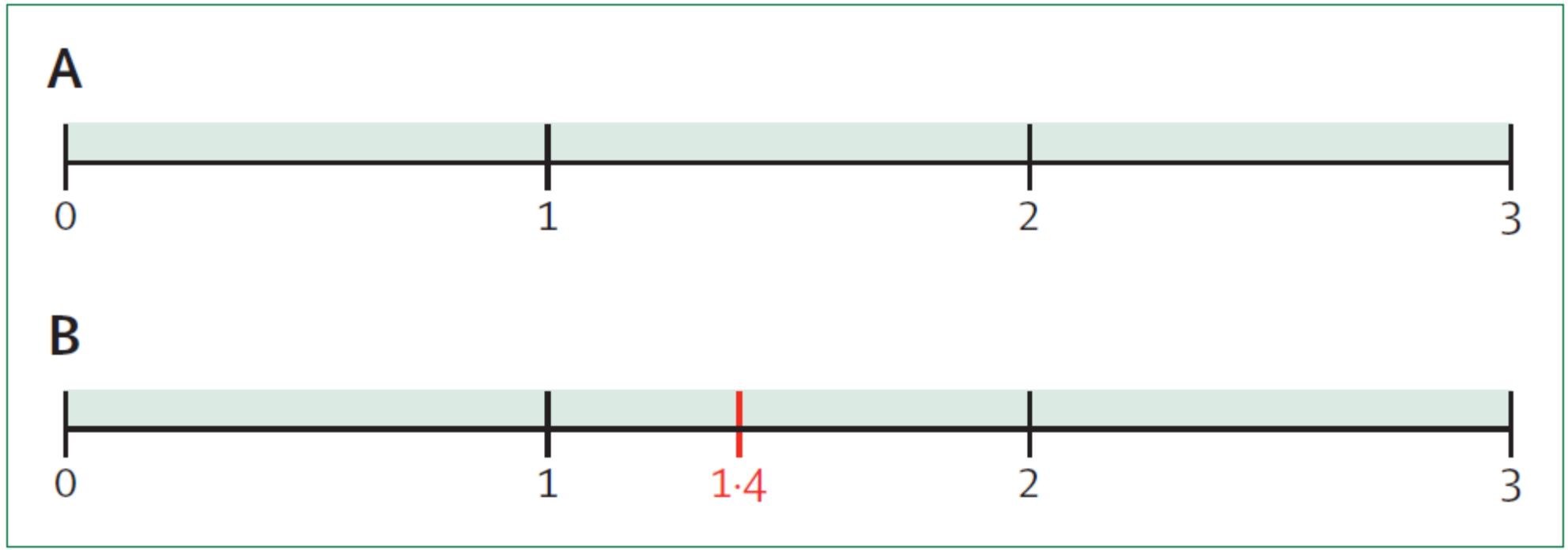


Figure 3: The PGA graph and scoring recommended by the PISCOS experts

Discussion

PISCOS studyはPGA scoringの標準化を目指している。
Evidence-based およびconsensus-basedのmethodologyによって。
Extensive literature reviewとDelphi consensus processを経て統合した。
PGAは現在、endpointとして使われているSRIやBICLA、LLDASに組み込まれているので重要。

疲労感や筋肉痛、うつや不安などの主観的な所見やSLEのserologyをPGAをつけるときに考慮するかどうかは、非常に重要な問題。
重要な点は内科医はこれらの症状が臓器障害や合併症や薬の副作用からきているのではなく、SLEの活動性からきていかどうかを判断しないといけない、ということ。
一方、疾患活動性を正確に反映させなくてはならないということもあり、PGAは通常の臨床検査所見を考慮してよいということになっている。とはいえ、SLE serologyを考慮するかどうかに関してはコンセンサスが得られなかった。補体と抗DNA抗体は役に立つことはわかっているが。このような点を頭において、多くの専門家はovertreatmentにつながるoverestimationのリスクを避けるため、PGAはSLEの血清学的異常やその程度に影響されてはいけないということに同意した。この背景にはSLE患者の中には抗DNA抗体が上昇していて、補体が低くても、臨床的には落ち着いていてさらなる治療を要しない患者がいる、というエビデンスに基づいている。
かと思うと急激に抗DNA抗体が上昇したりfluctuateし再燃につながることもある。後者のケースは臨床のclinical Decision makingや免疫抑制治療を変えたり、受診頻度に影響を与えるが、PGA scoreに反映させてはいけない。
PGAは現時点の疾患活動性を測定するものだからである。

Future studiesは血清学的異常をPGAに組み込むことが、ダメージ蓄積などのしっかりしたアウトカムと関連するかを明らかにして将来の改訂をevidence-basedになるようにしたい。

Limitations

- 一般的にデータに基づくよりも同意に基づく内容に多くがなってしまっている。
- PGAの長さに関するコンセンサスが得られなかったことはminorなlimitationだ。