ORIGINAL ARTICLE

PSOCUBE, a multidimensional assessment of psoriasis patients as a both clinically/practically sustainable and evidence-based algorithm

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Abstract

Background There is increasing awareness of the clinical relevance of psoriasis comorbidities and of the importance of timely and effective screening for such comorbidities in the management of psoriatic patients. Previous works have focused on assessing evidence for prevalence of comorbidities and on the best available evidence for sensitivity in diagnosing suspected comorbidities. No algorithms are available, which have been tested on large numbers of physicians concerning the acceptance of such algorithms both by practicing clinical dermatologists and by their consulting specialists from other fields.

Objective To propose a multidimensional assessment algorithm for psoriasis comorbidities which may prove at the same time enough sensitive and practically sustainable in daily clinical practice.

Methods After an exhaustive literature search, we performed a Delphi procedure involving 50 dedicated dermatological centres to obtain a standardized assessment algorithm, which would meet requirements of sustainability and acceptability both from the point of view of Evidence-Based Medicine as well as from the point of view of practical and clinical feasibility: to meet both requirements, results from the Delphi procedure were elaborated and modified by a restricted panel of experts.

Results The procedure has yielded PSOCUBE, a three-dimensional table comprising 14 clinical examination and history taking items, 32 screening laboratory and instrumental exams and 11 clinimetric scores.

Conclusion PSOCUBE, a simple algorithm, may be employed by practising dermatologists to perform standardized assessment procedures on psoriatic patients raising the chances of early recognition of patients at risk for comorbidities, thus fostering more effective prevention; PSOCUBE may therefore contribute to reduce the overall impact of this chronic, widespread disease.

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Conflicts of interest

D. Linder has received consultancy fees from the following companies: Roche (Austria), Schering-Plough (Italy), Wyeth (Italy), Abbott (Italy), Gruenenthal-Formenti (Italy), Abbvie (Italy), Leo-Pharma (Italy); Janssen –Cilag (Italy).

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Introduction

The association of psoriasis, a chronically relapsing inflammatory disease affecting mainly the skin and the joints, with several comorbidities, mainly with cardiovascular diseases, hypertension, diabetes, obesity, depression, addictions, lymphoma, uveitis and kidney affections^ is gaining increasing recognition.[1–5] For all comorbidities, prevalence rates among psoriatic patients and choice of screening – respectively management – strategies remain a matter of debate. Five exhaustive reviews,[6–10] have, to date, been published to provide indications on screening and diagnostic procedures to be initiated by the treating dermatologist (Table 1). All five publications are based on results of systematic extensive literature searches – performed according to the principles of Evidence-Based Medicine (EBM) – whereby these results are elaborated by a small group of experts. In particular, one, very exhaustive review[8] provides detailed and useful indications; these are, however, only based on the opinion of a small number of experts, without any underlying standardized consensus methodology warranting confidence in acceptability and clinical feasibility. This aspect is partly fulfilled in[9] and[10] where – on the other hand – no detailed indications concerning screening and management of the comorbidities are given.*

We endeavour to present here an algorithm for the screening of psoriasis comorbidities which, albeit still based on an extensive systematic search of all available evidence to date, would also meet the requirements of sustainability and acceptability from the point of view of practical and clinical feasibility.

Materials and methods

On the basis of what set out above we performed a Delphi poll° * involving 67 Italian dermatologists from dedicated psoriasis centres to assess the current practice and the level of acceptance, in the dermatologic community, of performing screenings and diagnostic procedures for psoriasis comorbidities. The results of the poll were subsequently to be thoroughly discussed by a restricted panel of 11 experts, and integrated by the latter with information deriving from scientific evidence to obtain a set of screening and diagnostic procedures, which are likely to cover to a reasonable extent both the requirements of EBM and Evidence-Based Practice.

Identifying relevant comorbidities, medical subspecialities and proposed diagnostic procedures

Articles published on indexed English or German language journals published as from January 1, 1996 on controlled trials, meta-analysis, guidelines, reviews and observational studies dealing specifically with psoriasis and its comorbidities were selected for review by the authors. The articles were identified by a MEDLINE, EMBASE and Cochrane Library systematic search up to and including January 2013, using the keywords 'psoriasis' AND 'comorbidities' OR '[*name of the single comorbidity/risk factor*]'.[§]

The research yielded initially 3387 manuscripts. After an exclusion process on the basis of titles, abstracts and full text, 131 publications were finally selected and independently reviewed by the authors of the present paper.[#] Secondary bibliographic references were accessed to obtain data on prevalence of specific comorbidities.

On the basis of the literature search, a list of comorbidities (Table 2) was obtained, yielding nine areas of competence (i.e. dermatology, rheumatology, cardiology, nephrology, psychiatry, gastroenterology, ophthalmology, metabolism/endocrinology, haematology).

For each area of competence a specialist (e.g. rheumatologist, gastroenterologist etc.) was contacted; discussions with all specialists yielded a preliminary list of 102 diagnostic procedures; procedures recommended in[6] and[8] were always considered in the discussions.

Delphi questionnaire preparation

The preliminary list of 102 diagnostic procedures was then used to set up the Delphi questionnaire: the procedures were

^There probably is less awareness of the last 3 mentioned.

*Already back in 1997 the clinician and epidemiologist Alvar Feinstein, who happened to be the scientist who coined the term 'comorbidity' in 1970[11] had expressed his concern about the applicability and validity of EBM principles in medical practice if not tested in the context of clinical reality.[12]

°The Delphi method,[13] originated in the 1960s, takes its name from the Delphic oracle's skills of interpretation and foresight. It was developed at the RAND Corporation to maximize the consensus level on a subject within a group of experts in a systematic manner.[14,15] It attempts to do this by series of well-defined questionnaires based on surveys and feedback. This consensus statement was developed using the RAND/UCLA Appropriateness Method Process,[16–18] a formal group judgment process which systematically and quantitatively combines expert opinion and scientific (systematic literature review) evidence by asking panelists to rate, discuss and then re-rate indicators. There is no intercommunication between the experts. It is the only systematic method of combining expert opinion and evidence.[19]

[§]Psoriasis AND (comorbidities OR cardiovascular risk factors OR cardiovascular risk OR cardiovascular disease OR cardiovascular OR obesity OR abdominal obesity OR waist circumference OR body mass index OR overweight OR diabetes OR hyperglycaemia OR insulin sensitivity OR insulin resistance OR metabolic syndrome OR hypertension OR blood pressure OR dyslipidaemia OR cholesterol OR hypercholesterolaemia OR triglycerides OR lipid profile OR hyperlipidaemia OR major adverse cardiac events OR infarct OR myocardial infarction OR stroke OR coronary heart disease OR ischaemia OR atherosclerosis OR alcohol abuse OR smoking OR depression OR anxiety OR psychiatric OR microalbuminuria OR renal function OR non-alcoholic fatty liver disease OR hepatic steatosis OR hepatopathy OR kidney disease OR renal OR renal abnormalities OR ocular OR ocular alterations OR prevalence of inflammatory bowel disease OR prevalence of crohn OR prevalence of ulcerative colitis OR prevalence of arthritis).

[#]German language articles were reviewed only by DL.

Table 1 Available English language review articles per 31 July 2014 on psoriasis comorbidities and their management. Review articles concerning only a subset of comorbidities (e.g. cardiovascular diseases) are excluded

Publication	Number of dermatologists involved	Delphi procedure used	Comprehensive range of comorbidities discussed	Provides detailed suggestion on screening procedures for each suspected comorbidity	Provides well-defined standard screening algorithm for all psoriasis patients	Remarks
Kimball *et al.*[6]	10	No	Yes	Yes	No	Pioneering work providing a plethora of useful suggestions
Richard *et al.*[7]	10 + 39	Yes (for expert group of 10)	No (directed only at cardiovascular events, cancer risk and alcohol use)	No	No	High adherence to principles of EBM. Focussed on collecting real evidence on comorbidities
Dauden *et al.*[8]	20 + 6 physicians of other specialities	No	Yes	Yes	No (unless one decides to perform all indicated screening procedures for all possible comorbidities)	Provides a detailed list of evidence-based screening suggestions for each single comorbidity but does not provide a general algorithm
Strohal *et al.*[9]	10 + one cardiologist and one psychologist	Yes	No (focussed on PsA, depression and cardiovascular factors)	No	No	
Kragballe *et al.*[10]	24 + one psychologist and one cardiologist	Yes (modified)	No	No	No	The work is not focussed on comorbidities, but addresses also general treatment goals and management of impact of Psoriasis on QoL
Present work: the PSOCUBE algorithm (Linder *et al.*)	67 + 8 physician of other specialities	Yes (modified)	Yes	Yes	Yes	To date, the review article on the subject involving the largest number of dermatologists and the only one providing a standard screening algorithm for all patients

Table 2 Comorbidities selected for screening in psoriatic patients

Psoriatic arthritis	Metabolic syndrome	Obesity
Diabetes mellitus	Arterial hypertension	Non-alcoholic fatty liver
Psychosocial impairment	Dyslipidaemia	Depression/ anxiety
Crohn's disease	Ulcerative colitis	Coeliac disease
Lymphoma	Smoking	Alcohol abuse
Coronary disease	Cerebrovascular disease	Peripheral vascular disease
Uveitis and other inflammatory ocular disease	Renal disease	

divided according to the area of competence (e.g. cardiology etc.) and for each item the following question was set up: 'According to you, how relevant is this procedure for a first-degree assessment (respectively second-degree assessment) of comorbidities in psoriasis patients?' (s.u.).

Selection of the expert panel size

Participants for the Delphi poll were selected among practising clinical dermatologist working in 50 different dedicated psoriasis centres in Italy (former PSOCARE centres[20]). Sixty-seven dermatologists finally agreed to take part to the poll. Participants were sent a standardized information package containing a synopsis of the study and a description of the Delphi process.

The survey

Between February 2013 and July 2013, the questionnaire concerning the diagnostic procedures was submitted to the 67 dermatologists selected. At least two Delphi rounds were planned. If consensus (s.u.) was not reached after two rounds, additional rounds were to be performed until consensus was reached.[^] In the first Delphi round, each member of the panel evaluated the clinical relevance of each of the diagnostic procedures on a 9-point scale. For each procedure, the experts were asked to answer the following question: 'According to you, how relevant is this procedure for a first-degree (respectively second-degree) assessment of comorbidities in psoriasis patients?'. A 9-point scale with the anchors 'not relevant at all' at 0 and 'extremely relevant' at 9 was available for responding. Participants were also encouraged to suggest additional procedures, not included in the questionnaire, which they nonetheless might deem appropriate in screening psoriasis patients for comorbidities; such procedures were included in the subsequent round provided the medical specialist 'in charge' for the respective field did not consider them redundant because of analogue procedures already dealt with in the survey.

In the second round, participants were sent for assessment the same diagnostic procedures, and were also informed of each procedure rating at the first round reporting. They were asked to rate again each procedure in light of the responses at the first round.

The criteria of agreement and disagreement between experts were defined as follows:

1 Agreement – 80% of panelists rating inside one of the 3-point region (1–3; 4–6; 7–9);
2 Disagreement – 90% of panelists ratings are within one of two extra wide regions (1–6 or 4–9).

This level of consensus was decided *a priori*. The collected assessments were evaluated for internal consistency and aggregated to obtain a composite judgment.

After completion of the Delphi procedure, all 67 participants were summoned to a 1-day meeting where the outcome of the poll was made public and discussed. Further diagnostic procedures were brought up and came into discussion in the course of the meeting.

Elaboration of the outcome of the Delphi survey combined with the results of the '1 day 67 experts meeting': setting up the final algorithm

At this final stage, the authors of the present paper ('restricted experts panel') compared both (i) the direct results of the Delphi procedure and (ii) the results of the subsequent 67 experts 1-day meeting with (iii) the prevalence values available from literature – for instance[9] – and in cross-talk with the medical specialists' opinion: diagnostic procedures stemming from the original 102 items deemed necessary by the restricted experts panel and leading to the assessment of comorbidities with a well assessed prevalence but not included in the final list obtained by the Delphi method (or brought into discussion during the multidisciplinary large expert meeting) were identified and added to the final list. The flow chart of the whole work is described in Fig. 1.

[^]The process was conducted via email, two reminders were sent during each round in case of non-response. The group responded by e-mail or fax using the Likert scale: the experts assessed each procedure using a score ranging from 1 to 9 based on increasing appropriateness. Agreement was defined as assignment of a score by at least 80% of the expert appraisers in three subsequent questionnaire rounds. All panel members were invited by email to complete the first round questionnaire within 14 days, and two email reminders were sent prior to the round deadline. Due to requests for a longer period for response, the round 1 deadline was extended by 8 days, and 21 days was provided for response to the round 2 questionnaire. One contact attempt was made by telephone at least 5 days before the closure date of rounds 1 and 2.

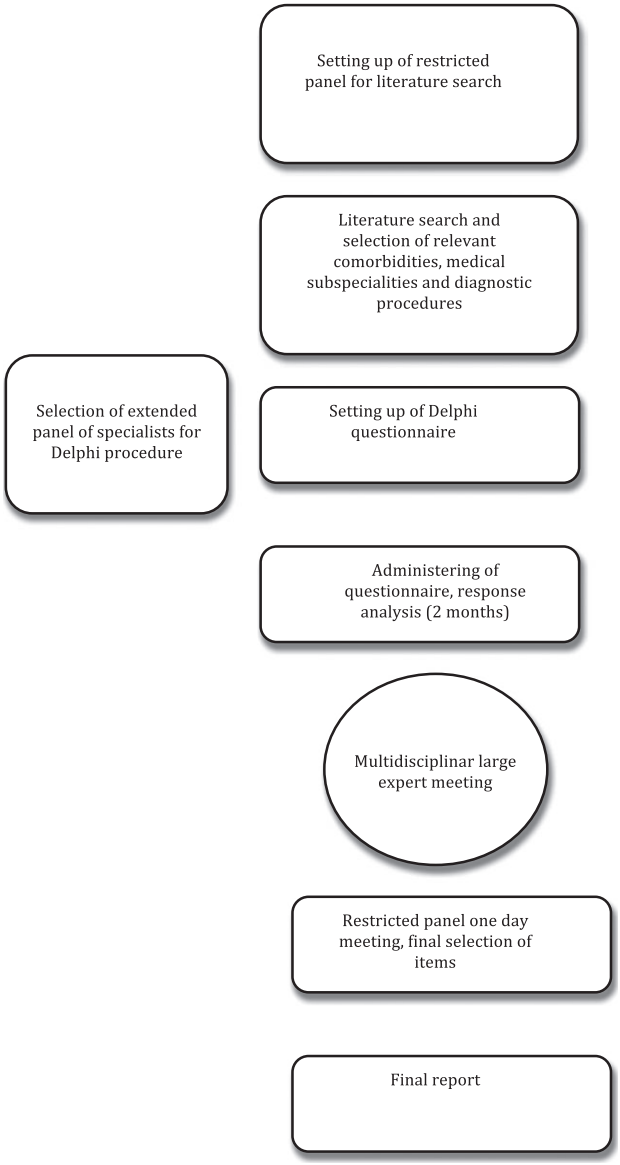

Figure 1 Flow chart of the modified Delphi procedure.

Statistical analysis

Calculations were performed using the Office 2007 software package.[^]

Results

The final list of recommended assessment procedures, i.e. the outcome of the Delphi survey, of the 67 experts meeting and the final meeting of the restricted experts panel, is shown in Table 3. Each procedure has been classified, according to the type of outcome, as item of the medical history/clinical examination, screening item or clinimetric* index ('score'): the final procedure set can be seen as a three-dimensional algorithm, hence the name PSOCUBE.

Procedure assessments were divided during the final 1-day meeting of the restricted panel into first- and second-level assessments, whereby second-level assessments are defined as those, which should be prescribed in a second stage by the dermatologist whenever findings within the first-level assessments support the need for such prescription.

Discussion

The elaboration and completion of the gross results of the Delphi survey by means of a restricted panel of experts yielded an algorithm which might prove at once both better accepted by the dermatological community and effective in terms of providing the treating physician with a more comprehensive understanding of the global patients' condition.

Interestingly, the final changes made by the restricted experts panel concerned, in the first level, only the medical history taking and five laboratory values (Homocysteine, Hb1A, Azotemia, RF and Vitamin D). All other additions were second-level assessments: laboratory/instrumental assessments and the NAPSI. This encouraging result suggests a not too wide discrepancy between the attitudes of practising clinicians and protocols deriving more from scientific evidence.

A first limit of the study is having been carried in Italy only. Medical practice and 'beliefs' of specialists tend to differ from country to country and, notwithstanding progressing globalization, clinical practice is far from having achieved equal standards and patterns throughout the EU, let alone throughout the whole Western world. Also the role of GPs differs widely from country to country. Hence, PSOCUBE as presented here may prove practicable and effective screening algorithm for dermatologists for a country – like Italy – where patients enjoy a comparatively easy access to specialists' consultations, while for a country – like the UK – where GPs often manage common dermatological diseases, the development of the same algorithm should probably have ideally involved a representative number of GPs.

A further weakness of this work is that, despite all efforts to precisely define ahead the procedure by which the final algorithm was to be established, some arbitrariness is inevitably bound to 'have sneaked' into the final result. Nonetheless, if compared to the other similar works published so far (Table 1), all based on the collaboration of smaller groups of experts, PSOCUBE is the – admittedly, modified – outcome of a very broad Delphi consultation, which thus has yielded a list of procedures

[^]Microsoft Corporation, Redmond, WA, USA.

*According to Feinstein,[21] 'clinimetrics' indicates a domain concerned with indexes, rating scales and other expressions that are used to describe or measure symptoms, physical signs and other distinctly clinical phenomena.

Table 3 The three-dimensional PSOCUBE algorithm

Assessment type	Parameter	Procedure	Level
1st Dimension: medical history and first clinical examination			
Medical history	Age, sex, time of onset and duration of disease	Medical history	1
Medical history	Medical history – recent and remote	Medical history	1
Medical history	Previous treatments for psoriasis	Medical history	1
Medical history	Life style	Smoking habits, alcohol consumption, physical activity, sleep quality	1
Medical history	Current pharmacological treatment	Medical history	1
Medical history	Pregnancy respectively intention to become pregnant	Medical history	1
Medical history	Stools (consistency, frequency) (*)	Medical history	1
Medical history	Familiarity for: psoriasis, renal disease, neurological or psychiatric disease (*)	Family medical history	1
Medical history	Lacrimation patterns, sensation of burning, other discomforts or abnormalities (*)	Ophthalmologic medical history	1
Clinical examination	Prognostic factors for major cardiovascular adverse events	BMI	1
Clinical examination	Nail abnormalities	Clinical examination	1
Clinical examination	Overweight and obesity	Waistline	1
Medical history	*Fatigue, night sweating, loss of weight and/or appetite, fever*	*Medical history*	*2*
Clinical examination	*Lymphadenopathy*	*Palpable superficial lymph nodes (submandibular, nuchal, axillary, inguinal)*	*2*
2nd Dimension: laboratory and instrumental assessment			
Screening	General state	Complete blood count	1
Screening	Prognostic factors for major cardiovascular adverse events	Complete lipid assessment (Chol.Tot., HDL, LDL, triglycerides)	1
Screening	Risk for cardiovascular disease (*)	Homocysteine	1
Screening	Arterial pressure	Measurement of arterial pressure	1
Screening	Sugar metabolism	Basal glycaemia	1
Screening	Sugar metabolism (*)	Hb1Ac	1
Screening	Renal functioning	Creatinine	1
Screening	Renal functioning	Protein electrophoresis	1
Screening	Renal functioning	Complete urine examination	1
Screening	Renal functioning	Uric acid	1
Screening	Renal functioning (*)	Azotemia	1
Screening	Renal functioning/inflammation	Microalbuminuria	1
Screening	Inflammation	High sensitivity CRP	1
Screening	Liver functioning	Transaminases	1
Screening	Liver functioning	Gamma-GT	1
Screening	Rheumatoid arthritis (*)	Rheumatoid factor	1
Screening	Vitamin D deficiency (*)	Vitamin D	1
Screening	*Arterial hypertension*	*Blood pressure diary*	*2*
Screening	*Cardiovascular disease* (*)	*Cardiologic exam + ECG* (*+ECO*)	*2*
Screening	*Liver disease* (*)	*Abdomen echography*	*2*
Screening	*Renal functioning* (*)	*Electrolytes*	*2*
Screening	*Renal functioning* (*)	*24 h proteinuria*	*2*
Screening	*Renal functioning*	*Creatinine clearance in 24 h urine*	*2*
Screening	*Joint involvement*	*Muscle bone echography*	*2*
Screening	*Joint involvement* (*)	*RX standard*	*2*
Screening	*Joint involvement* (*)	*MRI*	*2*
Screening	*Folic acid deficiency* (*)	*Folic acid*	*2*

Table 3 *(Continued)*

Assessment type	Parameter	Procedure	Level
Screening	*Genetic predisposition* (*)	*HLA haplotype*	*2*
3rd Dimension: clinimetric scores			
Score	Arthritis	EARP questionnaire	1
Score	Clinical severity	PASI	1
Score	Clinical severity	BSA	1
Score	Quality of life	DLQI	1
Score	Psychosocial impact of disease	PSODISK	1
Score	Psoriatic arthritis	CASPAR criteria	1
Score	*Psoriatic arthritis*	*Number of swollen joints – clinical exam*	*2*
Score	*Psoriatic arthritis*	*Number of painful joints – clinical exam*	*2*
Score	*Psoriatic arthritis*	*Number of enthesis involved – clinical exam*	*2*
Score	*Psoriatic arthritis*	*Dactilitis – clinical exam*	*2*
Score	*Nail psoriasis* (*)	*NAPSI*	*2*

Items marked with (*) were not included in the list obtained through the Delphi poll, but added to the final list by the restricted experts panel. Items deemed to belong to the 1st level assessment are listed first. Second-level procedures are printed in *italics*.

more likely to be well received by the dermatological community.

Also, the PSOCUBE algorithm presented here still needs to be tested in daily practice, to prove its efficacy in detecting at an early – respectively still silent – stage the various comorbidities, facilitating thus treatment decisions that may reduce the number of manifest comorbidities or at least modulate their severity and progression.

Finally, implementing PSOCUBE in daily practice may be incompatible with prescribed cost limits or local guidelines.

Nonetheless, the development of the PSOCUBE algorithm has yielded a selection of well-established diagnostic procedures and clinical scores. By implementing the algorithm in a network of dedicated centres, once enough clinical data will have been made available, statistical correlations with the risk for specific comorbidities of appropriate combinations of subsets of the values measured[^] should be searched for, to indicate automatically to the treating dermatologist the need to proceed either to second-degree assessments or to further examinations by medical specialists in other fields.

The PSOCUBE algorithm might therefore eventually yield a multidimensional clinimetric index providing to dermatologists indications as to which comorbidities need to be better investigated: a statistically sound 'PSOCUBE scale' and its correlation with the risk for the various comorbidities might therefore add further dimensions to the (one-, at best – when joints are involved – two dimensional) severity of Psoriasis, again simplifying diagnosis and paving the way to a global (and better) assessment of the psoriatic patient.

[^]Of course, some procedures – like for instance medical history – will need to be translated into numerical scales.

Conclusion

Dermatologists are increasingly becoming aware of the risk for psoriasis patients to present with comorbidities; this will make them more receptive to indications as to how to proceed with diagnostic steps aiming at assessing the severity of already presenting comorbidities (on one side) and the risk of developing new ones (on the other side). The PSOCUBE algorithm is likely, thanks to the innovative approach that guided its completion, to represent a first step towards a synthesis of rational, evidence-based data relating to the diagnostic procedures useful for assessing psoriasis comorbidities on one side and, on the other side, of the availability of practising dermatologists to implement these data into clinical practice. It may hence have paved the way to the development of new strategies increasing the mutual understanding between researchers using mainly epidemiological tools and clinicians confronted with the difficulties of daily medical care.

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