Article:
Coates, LC, Savage, LJ, Chinoy, H et al. (9 more authors) (2018) Assessment of two screening tools to identify psoriatic arthritis in patients with psoriasis. Journal of the European Academy of Dermatology and Venereology, 32 (9). pp. 1530-1534. ISSN 0926-9959

https://doi.org/10.1111/jdv.14971

Title: Assessment of two screening tools to identify psoriatic arthritis in patients with psoriasis.

Manuscript Word Count: 1949

Number of Tables: 3

Number of Figures: 1

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Funding: This study was supported by an unrestricted educational grant from Abbvie and supported by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre (BRC), UK.

Conflict of Interest Disclosure: Potential conflict of interest reported by some of the authors.

Keywords: Screening, psoriasis, psoriatic arthritis, diagnosis

Abstract

Background

Many patients with psoriasis have undiagnosed psoriatic arthritis. Low specificity is found with many PsA screening tools. A new instrument, the CONTEST questionnaire, was developed utilising the most discriminative items from existing instruments.

Objective

The aim of this study was to compare the CONTEST and PEST screening tools.

Methods

People attending secondary care clinics with psoriasis, but not PsA, completed the questionnaires, were assessed for function and quality of life, and had a physical examination. Patients thought to have PsA were compared to those without. The performance of CONTEST and PEST were compared using area under the receiver operating curve (AUC), and sensitivity and specificity at the previously published cut-offs.

Results

451 dermatology patients were approached, 35% were reviewed, and 27 (17%, 95% CI 12.3 – 21.7) had unidentified psoriatic arthritis. The sensitivity and specificity (95% CI) of PEST were 0.60 (0.42 – 0.78)/0.76 (0.69 – 0.83) and for CONTEST 0.53 (0.34 – 0.72)/0.71 (0.63 – 0.79). The confidence limits for the AUC overlapped (AUC for PEST 0.72 (0.61 – 0.84), for CONTEST 0.66 (0.54 – 0.77).

Conclusions

PEST and CONTEST questionnaires performed equally well, with no superiority of the new CONTEST tool.

Introduction

Background/rationale

Psoriatic arthritis (PsA) manifests clinically in several ways including arthritis, enthesitis, dactylitis, axial disease and skin/nail involvement. The majority of people with this condition have pre-existing psoriasis[1]. A period of preclinical disease may occur, as well as cases of established disease going unidentified for some time[2]. The reason why cases of established PsA remain unidentified is not clear, but one possible cause is the lack of musculoskeletal expertise in primary care and in dermatology clinics. A simple method of screening for PsA in people with psoriasis has the potential to prevent unnecessary suffering and enable earlier treatment of this potentially disabling disease. Recent consensus guidelines for managing psoriasis published by SIGN (The Scottish Intercollegiate Guidelines Network)[3] and NICE (https://www.nice.org.uk/guidance/cg153 - accessed 14th Oct 2017) recommend using questionnaires to screen for PsA.

Several patient completed instruments are currently available for screening PsA, including the Psoriatic Arthritis Screening Evaluation (PASE[4]), the Toronto Psoriatic Arthritis Screen (ToPAS[5]), the Psoriasis Epidemiology Screening Tool (PEST[6]), and the Early Psoriatic Arthritis Screening Questionnaire (EARP[7]). A recent comparison of three of these (PASE, ToPAS and PEST) in a secondary care setting determined that they all had a good probability of detecting PsA (sensitivity~80%), but had poor specificity (~35%)[8].The PEST questionnaire had the highest area under the curve for identifying PsA[8], but is criticised for its simplicity, in particular for missing axial forms of PsA[9]. Further analysis of the results of the above study has identified the most discriminative questions from each of the three questionnaires, including questions about the back and neck, and these items have been combined to create a new single 8 item screening questionnaire (CONTEST). The aim of this

study was to evaluate the CONTEST screening questionnaire in a secondary care dermatology clinic using the PEST tool as the reference instrument.

Materials and Methods

Study Design

This was an observational, cross sectional study of patients attending dermatology clinics in 4 UK centres. Full ethical approval and informed consent were obtained.

Setting & Participants

Dermatology patients aged 18 and over with a confirmed diagnosis of psoriasis and no diagnosis of inflammatory joint disease from 4 UK secondary care sites (Leeds, Bradford, Salford and Bath) were approached between November 2013 and March 2017. Potential participants were invited to participate during their routine dermatology appointment, by letter from their current dermatologist, or at a routine phototherapy appointment. Those approached were given an invitation letter and detailed information sheet with local study contact details. Those who accepted or were posted study information were contacted no less than 1 week later to determine their interest to participate, and a single assessment visit scheduled, where written informed consent was obtained.

Data & Variables

At the assessment visit participants were asked to complete 2 quality of life and one functional ability questionnaires (Psoriatic arthritis quality of life questionnaire (PsAQoL), Dermatology Life Quality Index (DLQI), and Health Assessment Questionnaire, (HAQ), and the PEST and CONTEST questionnaires. Following completion, all participants were assessed by both a dermatologist (or dermatology research nurse) and a rheumatologist. Psoriasis type and symptoms were recorded, as well as demographic data and current psoriasis medication. Six clinical assessments were used to record skin and joint disease activity:

- The Psoriasis Area and Severity Index (PASI)
- The modified Nail Psoriasis Severity Index (mNAPSI)
- The Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis count
- The Leeds Enthesitis Index (LEI) enthesitis count
- The 20-digit tender dactylitis count
- the 68 tender and 66 swollen joint count

Spinal mobility measures were recorded for those with inflammatory axial symptoms. CRP and ESR were also recorded if available from patient records. The rheumatologist was asked to classify patients as PsA, no MSD (musculoskeletal disease) or other MSD. The CASPAR criteria were also assessed.

Study Sample Size

The sample size estimate was determined by the number of patients required to validate previously obtained figures for sensitivity and specificity of the CONTEST questionnaire. The sensitivity and specificity of the CONTEST questionnaire in development were 0.82 and 0.52 respectively. Assuming a prevalence of PsA of 20%, and to confirm sensitivity and specificity with a minimum accuracy of 10% and a confidence level of 95%, the minimum number required for the total sample size was 246.

Statistical methods

Data from patient completed quality of life and functional ability questionnaires were summed and/or scored according to each instruments protocol and treated as interval data after testing for normal distribution. As data from clinical measurements consisted of counts, this data was also treated as interval data and summed according to protocol.

Analysis of the sensitivity and specificity of each the questionnaire was done using receiver operator characteristic (ROC) curves, allowing for the assessment of different cut-points for the new CONTEST questionnaires.

Results

Participants

Four hundred and fifty one dermatology patients were approached across the 4 participating centres, with 43% (n=194) recruited from Leeds. Thirty five percent (n = 159) across all 4 centres consented and were assessed. Ninety five percent of participants were identified as North European. The mean age of psoriasis diagnosis was 29 years (95% C.I. 26,31). There was no age or sex recruitment bias.

Among those assessed, 27 (17%, 95% CI 12.3,21.7) were identified as having previously unidentified psoriatic arthritis (25 of these patients also fulfilled CASPAR criteria). The other participants were divided into those without any MSD (n=61) and those with other MSD (n=71) (Table 1). Those with PsA were older, more likely to be male, had a similar age of onset of psoriasis, and similar severity of skin and nail disease, although there was a trend towards more severe skin and nail disease in patients with PsA (Table 1). Further, those with PsA had worse functional ability, as measured by the HAQ, and quality of life, as measured by the PsAQoL and DLQI. Of the patients with PsA, the median tender and swollen joint counts were 3 (range 0 – 41) and 0 (range 0 – 4) respectively. Twelve (44%) had nail involvement. Median dactylitis count was 0 (range 0 - 2) and median enthesitis count was 0 (range 0 - 20). There were no significant differences in psoriasis phenotype between the patients with PsA and the other groups (data not shown). The most frequent PsA sub-group in those with PsA was oligoarthritis (n = 16, 59%) followed by axial (n = 6, 22%), polyarthritis (n = 3, 11%) and distal inter-phalangeal joint only (n = 1, 4%). In terms of treatment 10 (37%)

of people diagnosed with PsA were taking biologics or systemic treatment (methotrexate or ciclosporin); the figures for no MSD were 17 (23%) and for other MSD 18 (25%).

Incompleted questionnaires for the PEST and CONTEST instruments occurred in 14 cases (9%) for PEST, primarily question #4 concerning heel pain, and 30 cases (19%) for CONTEST, again primarily for a question concerning heel pain, but also for questions related to nail changes. Sensitivity and specificity for PEST were 0.60 (95% CI 0.42,0.78)/0.76 (95% CI 0.69,0.83) and for CONTEST 0.53 (95% CI 0.34,0.72)/0.71 (0.63,0.79). The ROC curve analysis is presented in Table 2. The confidence limits for the AUC (area under the receiver operating curve) overlap between questionnaires so, although the PEST had the higher AUC, statistically there was no difference between them.

The ability of the screening questionnaires to identify all the sub-groups of PsA is given in Table 3. The analysis is partly obscured by the number of missing questionnaire item responses but, nevertheless, from this table it is clear that the CONTEST does not have an obvious superiority in identifying the axial sub-group of PsA.

Discussion

The CONTEST questionnaire was developed using the best performing items from three other screening questionnaires in the hope that it would perform better than its originators. In development this was partly correct but the current study does not support this – statistically there was no difference between PEST and CONTEST in terms of ability to detect psoriatic arthritis in patients with psoriasis.

The performance of both questionnaires is acceptable at the given cut-offs. It is, however, worth noting the discrepancy in sensitivity/specificity of these questionnaires across different studies. For example, the CONTEST study found lower specificity for all tested questionnaires[8] while maintaining acceptable sensitivities. On the other hand a study from

Dublin found the opposite – acceptable specificities with lower sensitivities[9]. Some of these discrepancies will be due to subject selection (excluding people with any known rheumatic disease will improve specificity) and the research environment (for example offering unselected subjects a chance to have a consultation with a rheumatologist may increase the proportion of those with all categories of musculoskeletal disease). Some of the differences may also be explained by those cases of PsA with axial disease which may favour one questionnaire over another.

The relative simplicity of the PEST questionnaire has raised concerns that the tool is not able to detect pure axial forms of the disease. The CONTEST questionnaire includes items specific to back and neck pain, and so it was hoped it would better detect this subgroup. In this study this is not the case (see Table 3), although the numbers were small and imaging of the spine was not part of the study. The pure axial subgroup is uncommon (less than 10%); up to 40% of cases of PsA have axial involvement with additional peripheral disease activity, and this may explain the success of the PEST in identifying axial forms of the disease.

A proportion of the participants were already receiving systemic treatment for their psoriasis which may have suppressed the presentation of musculoskeletal symptoms. But a higher percentage of people diagnosed with PsA were already receiving systemic treatment would argue against this theory, and is consistent with a recent report from Italy which reported a large cohort of patients in whom PsA had developed while already taking biologic drugs[10]. The higher prevalence of systemic drug use in the PsA group may represent a more severe form of psoriasis; traditionally the association between psoriasis severity and onset of PsA has been weak but there has been a recent report that the onset of PsA is related to the more severe forms of psoriasis[11].

The prevalence estimate of previously undiagnosed PsA is within the range encountered in other studies, but probably less than would be expected in a secondary care setting[2, 8, 12]. The reasons for this are likely multifactorial. Firstly, other screening studies have previously been performed at two out of the three sites that participated in this study, and it is possible that the 'pool' of unrecognised PsA was reduced by these previous efforts. Secondly, in the main participating site, a triage clinic for new psoriasis referrals was introduced towards the latter half of the current study – this is also likely to have impacted the prevalence of unrecognised PsA in this population. As with many such studies the results should be interpreted with caution for the above reasons and because only a minority of invitees agreed to take part.

In addition to the aforementioned problem (heterogeneity across sites) a further limitation of this study was the failure to achieve the planned sample size of 246 participants. Therefore it is possible that this study was underpowered to validate the pre-existing performance of the CONTEST questionnaire. However, the sensitivity and specificity were different to those anticipated: the specificity exceeded that found in the original study and sensitivity was lower and, although the confidence intervals of the estimate were wide, they did not encompass the original estimate for sensitivity.

In conclusion this study in a secondary care setting has shown equivalent performance of the PEST and CONTEST questionnaires, with no superiority of the more comprehensive CONTEST tool. PEST is a short and simple screening tool which should be used to assess the possibility of psoriatic arthritis in patients with psoriasis. A positive response requires further assessment of the musculoskeletal symptoms.

Acknowledgements

Mrs Julie Bush, Dermatology Research Nurse, Leeds Teaching Hospital NHS Trust; Mrs Catherine Lambe, Clinical Trials Nurse Specialist and Mr Will Gregory, Highly Specialist Physiotherapist, Salford Royal NHS Foundation Trust, Salford, Manchester M6 8HD, UK. This publication was supported by researchers at the National Institute for Health Research (NIHR) Biomedical Research Unit. The views expressed are those of the authors and not necessarily those of the (UK) National Health Service (NHS), the NIHR or the (UK) Department of Health.

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Figure 1: Screening for Arthritis in Psoriasis study flow diagram for participants

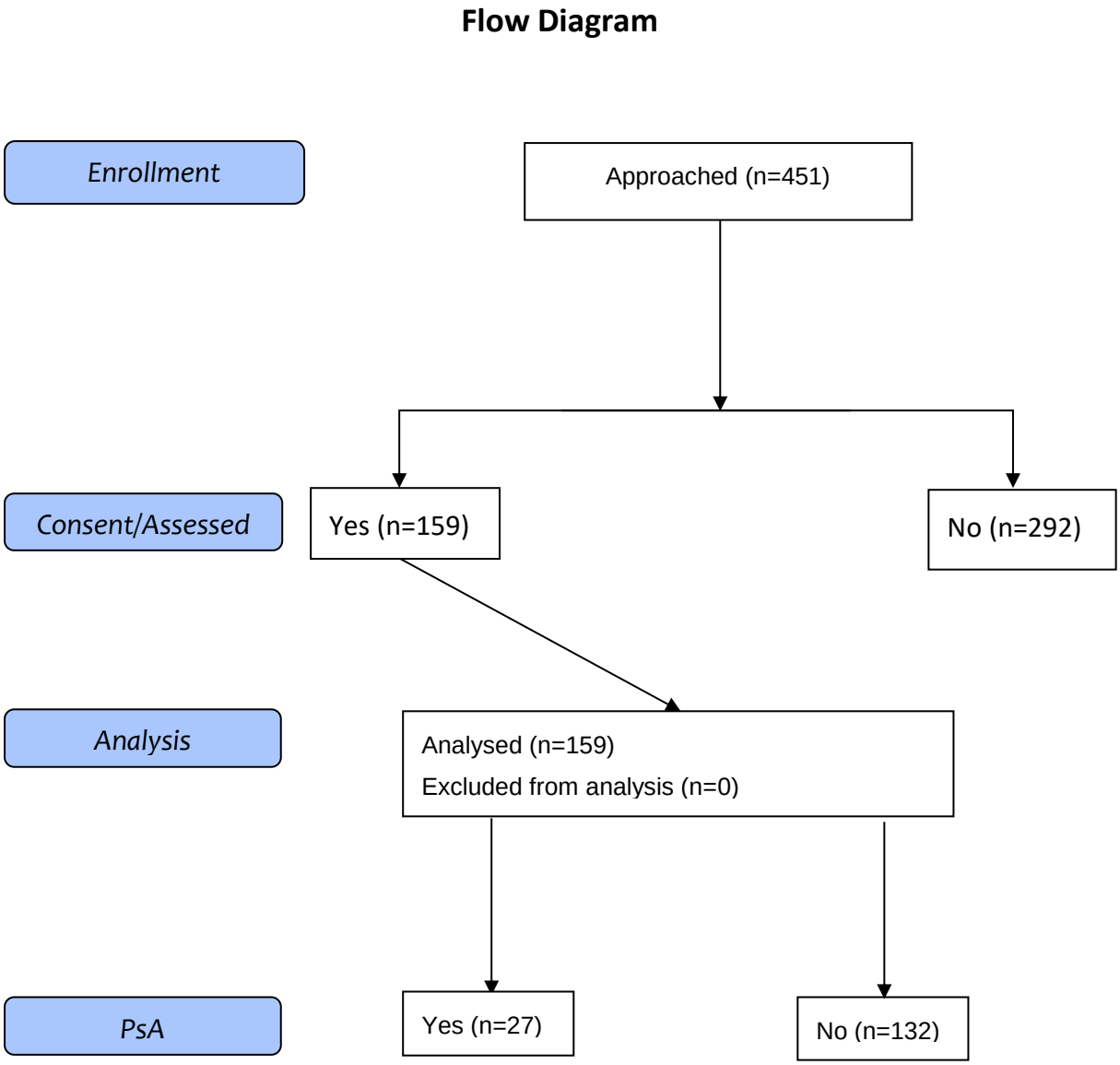

Table 1. Demographic and clinical characteristics of participants.

	Psoriatic arthritis	No MSD	Other MSD+	Statistic	P
n	27	61	71		
Age, y	52.7 ± 12.0	43.5 ± 13.0	49.7 ± 15.1	5.4	0.006
Duration psoriasis, y	33.8 ± 17.3	28.2 ± 14.7	27.1 ± 17.2	1.5	ns
Gender M/F	18/9	40/21	33/38	6.1*	0.05
PASI	7.2 ± 8.7	6,3 ± 6.2	4.7 ± 4.9	2.0	ns
mNAPSI	10.7 ± 16.6	5.3 ± 9.7	7.2 ± 10.8	2.6	0.08
HAQ	0.52 ± 0.54	0.10 ± 0.30	0.30 ± 0.40	9.7	0.0001
PsAQoL	7.0 ± 6.0	2.5 ± 4.2	5.6 ± 6.0	8.8	0.0001
DLQI	8.4 ± 6.5	6.6 ± 6.9	6.4 ± 5.3	1.1	ns
PEST ≥ 3	15/25 (60)	6/58 (10)	23/62 (37)	22.7*	0.0001
CONTEST ≥ 4	10/19 (53)	8/54 (15)	24/56 (43)	13.9*	0.001

MSD: musculoskeletal disease

PASI: psoriasis area and severity index

mNAPSI: modified nail psoriasis severity index

HAQ: health assessment questionnaire

PsAQoL: psoriatic arthritis quality of life

DLQI: dermatology life quality index

Statistic is F (analysis of variance) unless indicated with an asterix (chi squared test)

+ osteoarthritis (n = 40); soft tissue disorder (n = 12); mechanical low back pain (n = 6); hypermobility syndrome (n = 4); injury (n = 3); gout (n = 2); fibromyalgia (n = 2); missing (n = 2).

Table 2. Sensitivities and specificities of selected cut offs for the questionnaires (usually applied cut off in bold). Figures derived from the ROC curves. AUC: area under the ROC curve. Sens: sensitivity. Spec: specificity.

Questionnaire				AUC	95% CI
PEST	Cut point	Sens	Spec	0.723	0.609 – 0.836
	2	0.80	0.49		
	3	**0.60**	**0.76**		
	4	0.40	0.88		
CONTEST				0.655	0.536 – 0.774
	3	0.63	0.54		
	4	**0.53**	**0.71**		
	5	0.32	0.80		

Table 3. PsA sub-type and number of questions answered affirmatively in each of the questionnaires.

The darker grey shading indicates that the score range in which the questionnaire would have deemed to be positive, given usual cut offs.

Questionnaire	Number of questions answered positive						
PEST	0	1	2	3	4	5	Total
Oligoarthritis	0	2	3	3	6	1	15
Polyarthritis	0	0	0	1	1	1	3
Axial	1	1	2	1	1	0	6
DiP	1	0	0	0	0	0	1
CONTEST	1	2	3	4	5	6	
Oligoarthritis	1	3	0	3	4	2	13
Polyarthritis	0	0	0	0	0	0	0
Axial	2	0	2	1	0	0	5
DiP	0	1	0	0	0	0	1