GRAPPA Trainees Symposium 2009: A Report from the GRAPPA 2009 Annual Meeting

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ABSTRACT. At the 2009 annual meeting of GRAPPA (Group for Assessment of Psoriasis and Psoriatic Arthritis) in Stockholm, Sweden, 15 fellows involved in research in psoriatic disease were invited to present their work at a Trainees Symposium, which was also attended by members of the GRAPPA Faculty Committee. All of the fellows held poster sessions of their work and 4 of them gave oral presentations, including identification of soluble biomarkers for psoriatic arthritis (PsA), validation of minimal disease activity criteria for PsA, disease progression using the modified Sharp score, and discussion of a new composite disease activity score for PsA. Senior GRAPPA members also instructed the fellows on other composite scoring methods and on training videos and other GRAPPA projects to date. All of the posters and presentations from the Trainees Symposium are summarized herein. (J Rheumatol 2011;38:526–9; doi:10.3899/jrheum.101114)

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PSORIATIC ARTHRITIS PSORIASIS TRAINEE RHEUMATOLOGIST DERMATOLOGIST

A Trainees Symposium was held at the 2009 annual meeting of GRAPPA (Group for Assessment of Psoriasis and Psoriatic Arthritis) in Stockholm, Sweden. The impetus for this session arose from the marked success of the first Trainees Symposium that took place at the 2008 GRAPPA annual meeting in Leeds, UK. Fellows in training who were members of GRAPPA or nominated by GRAPPA members were invited to submit abstracts of their recent research work. Fifteen fellows involved in research in psoriatic disease were chosen to present their work at the Trainees Symposium in Stockholm. In addition to the 15 rheumatology and dermatology trainees, members of the GRAPPA Faculty Committee and other interested members were invited to the meeting, chaired by Prof. Christopher Ritchlin from the University of Rochester Medical Center, New York. Dr. Ritchlin introduced the format of the GRAPPA Trainees Symposium, and gave a brief summary of research advances by members of GRAPPA to date.

A presentation was given by Dr. Kristina Callis Duffin from the University of Utah, who is leading a group of GRAPPA members in the development of a training video for assessment of psoriasis and psoriatic arthritis (PsA) in clinical trials. A leading dermatologist, Dr. Duffin is regularly asked to provide instruction on how to perform clinical outcome measures such as the PASI (Psoriasis Area and Severity Index). With the recognition that formal training is needed for many clinicians who study psoriatic disease, she approached the GRAPPA Steering Committee regarding the development of a training video for multiple clinical outcome measures. This project is now under way with planned training videos for assessment not only for skin disease but also arthritis, enthesitis, and dactylitis to be led by GRAPPA members who are experts in these particular assessments[1].

In the next part of the symposium, 4 abstracts were selected for presentation by GRAPPA trainees: Dr. Vinod Chandran, University of Toronto, Toronto, Canada; Dr. Laura Coates, University of Leeds, Leeds; Dr. Will Tillett, Royal National Hospital for Rheumatic Diseases, Bath, UK; and Dr. Aizad Mumtaz, University College Dublin, Dublin, Ireland.

Fellow Oral Presentations

Soluble Biomarkers (Vinod Chandran, MBBS, MD, DM, University of Toronto, Canada)

Dr. Chandran presented results from a study whose objective was to identify soluble biomarkers for inflammatory arthritis in patients with psoriasis. Three groups of patients were recruited: patients with skin psoriasis only, patients with PsA according to the CASPAR (ClASsification of Psoriatic ARthritis study group) criteria, and healthy controls. All groups were age- and sex-matched, and patients with psoriasis and PsA were matched for disease duration. Analysis was performed using logistic regression to identify biomarkers that differentiated the different groups. Next, receiver operating characteristic (ROC) curves were constructed using a variety of soluble biomarkers to determine the best combination for classification of patients into disease groups.

First, patients with psoriatic disease were compared to healthy controls to identify biomarkers specific to either psoriasis or PsA. This analysis found that patients with pso-

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riatic disease had increased levels of activator for nuclear factor-κB ligand (RANKL), tumor necrosis factor superfamily member 14 (TNF SF-14), matrix metalloproteinase 3 (MMP-3), and cartilage oligomeric protein (COMP) ($p < 0.05$). Then patients with PsA were compared to those with psoriasis alone to identify biomarkers specifically related to PsA. This analysis showed that elevated concentrations of highly sensitive C-reactive protein (hs-CRP), osteoprotegerin (OPG), MMP3, and the ratio C-propeptide of type II collagen (CPII)/Col2-3/4(long mono) (C2C) were all associated with PsA ($p < 0.03$). ROC analysis using this combination of biomarkers to predict PsA found an area under the curve of 0.904[2].

Minimal Disease Activity Criteria (Laura Coates, MBChB, MRCP, University of Leeds, UK)

Dr. Coates presented work on the validation of the minimal disease activity (MDA) criteria developed for PsA. She undertook this project in collaboration with Prof. Dafna Gladman's group in Toronto, Canada, using the large longitudinal cohort of patients with PsA who are regularly reviewed at Toronto Western Hospital. MDA is defined by OMERACT (Outcome Measures in Rheumatology Clinical Trials) as "that state of disease activity deemed a useful target of treatment by both the patient and physician, given current treatment possibilities and limitations," and it encompasses both remission and low disease activity. Dr. Coates introduced the MDA criteria that were developed in collaboration with GRAPPA members. Patients are classified as being in MDA if they meet 5 of the following 7 criteria: tender joint count ≤ 1; swollen joint count ≤ 1; PASI ≤ 1 or body surface area ≤ 3; patient pain visual analog scale (VAS) score ≤ 15; patient global disease activity VAS ≤ 20; Health Assessment Questionnaire (HAQ) ≤ 0.5; and tender entheseal points ≤ 1)[3].

The objective of this study was to investigate the prognostic ability of the MDA criteria. The analysis presented data on patients who were consistently in MDA (for > 12 months) compared to controls who did not achieve MDA for this time period. Damage progression was calculated using clinically assessed damaged joint counts over this time period. Data were available for 116 patients with sustained MDA, and 200 controls. Over the followup period of 34 months, a significant difference in the mean change in damaged joint count was observed: 0.931 in the MDA group, compared to 2.245 in the controls ($p = 0.0005$)[4]. This research provided evidence that patients achieving MDA had a significant reduction in progression of joint damage, providing prognostic evidence for the validation of the MDA criteria.

Disease Progression by Modified Sharp Score (Will Tillett, MBChB, BSc, MRCP, Royal National Hospital for Rheumatic Diseases, Bath, UK)

Dr. Tillett presented work on disease progression identified by the modified Sharp score in patients with PsA, using data from a longitudinal cohort at the Royal National Hospital for Rheumatic Diseases, Bath, UK. Paired sets of radiographs with a median interval of 5.75 years were available for 139 patients. Radiologic damage was prevalent in this cohort, with over half the patients having changes evident at baseline, and nearly three-quarters at followup. The modified Sharp score showed good correlation with other clinical markers including joint counts and HAQ scores, supporting its construct validity. The study also identified ongoing progressive disease in a large cohort and quantified an annual mean change in Sharp score of around 1 point[5]. Dr. Tillett's work may assist with planning of future clinical trials that use the modified Sharp score as an outcome.

Composite Psoriatic Arthritis Disease Activity Score (Aizad Mumtaz, MBBS, MRCPI, University College Dublin, Ireland)

Dr. Mumtaz presented the development of a new composite PsA disease activity score (CPDAI). Data were collected on 71 patients who fulfilled the CASPAR criteria and were assessed for disease activity in 5 domains (joints, skin, dactylitis, enthesitis, and axial disease). In each of these domains, 2 outcome measures were used: one to assess activity directly, and one to assess the effect of the disease activity. Disease activity in each domain was graded as mild, moderate, or severe using a severity scale of 0–3 (Table 1).

Correlation between the CPDAI score and both physician and patient global assessments was significant, suggesting that the CPDAI score reflects the perception of both physicians and patients. CPDAI scores were also analyzed relative to the physician's opinion on the necessity of a treatment change. A higher median CPDAI score was found in patients whose physicians thought they needed a change in therapy. Cutpoints for the CPDAI were also proposed related to treatment change, using a tree analysis. All patients with a CPDAI < 5 were considered satisfactorily treated; however, 96% of patients with a score > 6 were felt to require treatment escalation by physicians. Scores of 5 or 6 were considered indiscriminate or borderline.

Outcome Measures in PsA (Philip Helliwell, DM, PhD, FRCP, University of Leeds)

Dr. Helliwell presented a summary of outcome measures in PsA, highlighting current and future research in the development of specific outcome measures for psoriatic disease[6]. He outlined the available outcome measures for the different aspects of psoriatic disease including peripheral arthritis, skin disease, enthesitis, and dactylitis, as well as patient-reported outcome measures. He also introduced the idea of a composite disease activity score for PsA that could encompass all aspects of the disease and provide a total score. Two of these, the CPDAI score developed in Dublin, which provides a linear score for disease activity, and the criteria for MDA in PsA developed in Leeds, are discussed above. Collection of observational data on patients with PsA

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Table 1. Composite psoriatic arthritis disease activity index (CPDAI).

Condition	None (0)	Mild (1)	Moderate (2)	Severe (3)
Peripheral arthritis		≤ 4 joints (swollen or tender); normal function (HAQ < 0.5)*	≤ 4 joints but function impaired or > 4 joints, normal function;	> 4 joints and function impaired
Skin disease		PASI ≤ 10 and DLQI ≤ 10	PASI ≤ 10 but DLQI > 10; or PASI > 10 but DLQI ≤ 10	PASI > 10 and DLQI > 10
Enthesitis		≤ 3 sites; normal function (HAQ < 0.5)*	≤ 3 sites but function impaired; or > 3 sites but normal function	> 3 sites and function impaired
Dactylitis		≤ 3 digits; normal function (HAQ < 0.5)*	≤ 3 digits but function impaired; or > 3 digits but normal function	> 3 digits and has function impaired
Spinal disease		BASDAI < 4; normal function (ASQoL < 6)	BASDAI > 4 but normal function; BASDAI < 4 but function impaired	BASDAI > 4 and function impaired

* HAQ counted only if clinical involvement of domain (joint/enthesitis/dactylitis) is present. ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire[7]; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index[8]; DLQI: Dermatology Quality of Life Index[9]; HAQ: Health Assessment Questionnaire[10]; PASI: Psoriasis Area and Severity Index[11].

is also under way as part of a GRAPPA initiative to develop a composite disease activity score. These data are being collected using similar methodology to that of the original development of the Disease Activity Score (DAS) in rheumatoid arthritis (RA), where patients are divided into those undergoing a treatment change (thought to have active disease) and those staying on the same treatment (thought to be stable and well treated). In the future, this large database will allow the development of new indices and further validation.

Poster Tour and Followup Discussions

A final session allowed all attendees to view the fellows' posters, including abstracts that were not presented earlier. Fellows explained their work and GRAPPA faculty and other trainees were invited to ask questions and gave advice and suggestions for future directions of the research. Summaries of the poster sessions are provided below.

Mariangela Atteno (Naples, Italy) outlined response data for early PsA patients (< 12 months disease duration) treated with anti-TNF in 4 Italian centers. These 19 patients showed significant reduction in DAS28 score (28-joint count status) at 12 and 24 weeks after starting treatment, confirming the potential benefit of these drugs in early disease.

Luisa Costa (Naples, Italy) reported on a study investigating arterial wall stiffness in 11 patients with PsA and 11 healthy controls. Hemodynamic assessment was performed using the noninvasive tonometry technique. An increased arterial wall stiffness was observed in patients with PsA compared to controls, highlighting the systemic characteristic of PsA and potential for cardiovascular morbidity.

Patrick Dominguez (Boston, MA, USA) reported on validation work for the psoriasis screening tool (PST), a self-report questionnaire designed to collect data on psoriasis in large epidemiological studies. In this particular study, it was sent to 1886 women from the Nurses Health Study who had previously reported a physician diagnosis of psoriasis. Over 1500 people responded, and 93% were diagnosed with psoriasis according to the PST, suggesting high validity in this large sample.

Lihi Eder (Toronto, Canada) described the response to anti-TNF in 100 patients followed in the observation cohort of PsA patients in Toronto. Nearly 80% of patients saw a reduction in their swollen joint count, with 56% of patients achieving a PASI50 (50% reduction in PASI) at 3 months. Interestingly, the improvements at 12 months were very similar, suggesting that most patients will respond within the first 3 months of treatment. Multivariate analysis found that a higher baseline swollen joint count increased the likelihood of response, while previous anti-TNF failure was a negative predictor of response.

Christina Jonckheere (Amsterdam, The Netherlands) presented a biopsy study investigating the role of interleukin 20 (IL-20) in PsA. Paired skin and synovial biopsies were taken pre- and post-treatment with alefacept that showed raised levels of IL-20 in both tissues at baseline. Following alefacept therapy, IL-20 expression in the skin decreased significantly, although there was no significant change in the synovial biopsy samples.

Lotus Mallbris (Stockholm, Sweden) described the results of a case-control study using nearly 500 patients with recent onset of psoriasis recruited for the Stockholm Psoriasis Cohort, matched to controls taken from the Swedish Population Registry. At baseline, psoriasis patients had higher levels of obesity and dyslipidemia compared to controls. After 3–5 years of disease duration, in addition to these differences, there was also a higher rate of hypertension and diabetes mellitus in patients with psoriasis, suggesting that the presence of psoriasis may have an increasing influence on development of metabolic syndrome with increasing disease duration.

Natalia Palmou (Leeds, UK) outlined work on nail disease phenotypes in psoriasis and PsA. In a sample of 130 patients, 75 with PsA and 55 with skin psoriasis only, no significant differences were observed in the type of psoriatic nail disease. In particular, linear pitting, which was hypoth-

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esized to be linked to enthesitis, was not more prevalent in patients with PsA.

Susanne Pedersen (Copenhagen, Denmark) introduced preliminary work looking at whole-body magnetic resonance imaging (WBMRI) scanning in 8 patients with active PsA. Improvements in scanning technique during the study improved the image quality, particularly in peripheral areas such as the hands and the feet. WBMRI identified synovitis, bone marrow edema, soft tissue inflammation, and sacroiliitis in this cohort, suggesting that this technique may be useful. Further validation work comparing WBMRI to established imaging techniques is required before this can be recommended for future research.

Jessica Walsh (Salt Lake City, UT, USA) presented data on the prevalence of obstructive sleep apnea (OSA) in patients with PsA and ankylosing spondylitis (AS). Of the 24 patients screened with polysomnography, 75% were diagnosed with OSA. This is much higher than in the general population and previous studies in AS. The high prevalence in this cohort may be linked to a high body mass index that was also identified. She highlighted the importance of screening for OSA in patients with spondyloarthritis.

Following the poster presentations, Dr. Ritchlin summarized some of the major findings presented at the Trainees Symposium. He encouraged those trainees who were not members to consider joining GRAPPA or at least to collaborate with other trainees and faculty in GRAPPA projects. Trainees attending the session gave positive feedback about the symposium and agreed that future events that highlight research in psoriatic disease at the trainee level should become a regular feature of the annual GRAPPA meeting.

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