GRAPPA Trainees Symposium 2011: A Report from the GRAPPA 2011 Annual Meeting

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ABSTRACT. The 2011 annual meeting in Naples, Italy, of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) began with a Trainees Symposium, which has become an important aspect of the meeting. In 2011, 25 trainees currently involved in research in psoriasis or psoriatic arthritis were invited to deliver an oral abstract or poster presentation. We present a brief overview of the oral and poster presentations, which show the diversity and focus of current research performed by members and trainees of GRAPPA. (J Rheumatol 2012;39:2184–8; doi:10.3899/jrheum.120819)

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Since its inception in 2008, the Trainees Symposium has become an integral part of the annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and serves as an open forum to encourage and develop potential future researchers in this field[1,2]. Each year an increasing number of abstracts are submitted for consideration. Two types of abstracts were sought: those describing the results or progress of a primary research project and those presenting an evidence-based literature search with a proposal for a research project to follow. Abstracts submitted were judged anonymously and ranked by a committee of reviewers. The trainees who submitted the highest scored abstracts were invited to deliver an oral abstract, and the remainder of the trainees (if scoring highly enough) presented a poster that outlined the key aspects of their project.

At the 2011 GRAPPA meeting in Naples, 25 trainees representing 10 countries from North and South America and Europe presented their findings. The session was chaired by Dr. Christopher Ritchlin (University of Rochester Medical Center, Rochester, NY, USA), with an audience of about 100 GRAPPA members providing feedback and suggestions on how to develop, improve, and move current research plans or projects to the next level. Prizes for the best abstracts were presented by Prof. John Moll (retired, previously Leeds, UK), with the first prize awarded to Dr. Axel Nigg from Munich, Germany.

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Oral Presentations

Distal interphalangeal joint enthesitis (Zoe Ash, Leeds, UK)
Dr. Ash presented the results of a magnetic resonance imaging (MRI) study. Sixty patients with active disease not receiving biological treatments were recruited [27 with psoriasis and 33 with psoriatic arthritis (PsA)]. The patients underwent a clinical assessment and a high resolution MRI scan of one finger, using a 3 Tesla magnet with a dedicated finger coil and gadolinium contrast. One-third of the patients with PsA had a tender and/or swollen distal interphalangeal joint, and in those with a clinically normal joint, subclinical enthesitis was seen in 55%.

Extensor tendon enthesitis was seen only in patients with PsA (and then more commonly in those with nail disease) but not in patients with psoriasis. Collateral ligament changes were seen frequently in both PsA and psoriasis patients but were more common in older patients. While osteitis was seen in patients with psoriasis, the changes were not as severe as those seen in PsA.

Although enthesopathy and osteitis were observed in the patients with psoriasis, a relationship between extensor tendon enthesitis and nail disease was not noted; these findings raise further questions as to the pathophysiology of nail disease in psoriasis.

Enthesitis indices (Anna Caperon, Leeds, UK)
Dr. Caperon described currently available enthesitis measures and presented an analysis of data from the GRAPPA Composite Exercise (GRACE) study. In this study, 471 patients were recruited, with data available on 253 patients at 3 months. The clinical dataset included sufficient enthe-

seal points so that the majority of the existing enthesitis indices could be calculated. The methodology from the development of the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)[3] and the Leeds Enthesitis Index (LEI)[4] was also reexamined to allow the development of a new index. Frequency tables were used to score the most commonly affected entheseal site; then patients reporting tenderness at this site were discounted from the next step, an iterative process that was repeated until 80% of patients were included. This process created the GRACE Index, which includes the first costochondral joints, lateral and medial epicondyles, L5 spinous process, medial condyles of the femurs, inferior patella poles, Achilles insertions, and plantar fascia insertion (15 sites). This new index was then compared to existing enthesitis indices and to other assessments of disease state such as the swollen and tender joint counts.

Moderate correlation was seen between the enthesitis indices, patient-reported measures, and tender joint counts; but poor correlation was seen with the swollen joint count, C-reactive protein (CRP), dactylitis, and Psoriasis Area and Severity Index (PASI). In an assessment of the effect size with treatment change, the greatest effect size was seen with the total index (a combined score of all enthesitis sites assessed in the GRACE clinical dataset; 0.54), followed by the SPARCC (Spondyloarthritis Research Consortium of Canada; 0.48), GRACE (0.45), LEI (0.40), and MASES (0.36). The LEI remains the only validated measure for assessing enthesitis in PsA.

Arthritis outcome measures (Laura Coates, Leeds, UK)
Dr. Coates presented data from an interim analysis of the TiCOPA trial (Tight Control of Psoriatic Arthritis) with an assessment of the differences in response measures achieved between patients with polyarticular and oligoarticular disease. This analysis of the blinded randomized controlled trial included 40 patients with recent-onset PsA (within the previous 2 yrs) who were naïve to disease-modifying antirheumatic drugs (DMARD). At baseline, 20 had polyarticular and 20 had oligoarticular disease. After being treated with DMARD for 48 weeks, patients were assessed for their response using the American College of Rheumatology (ACR) 20, 50, and 70 response, the European League Against Rheumatism (EULAR) good and moderate response, and the minimal disease activity criteria (MDA; a measure of disease state rather than a response criteria)[5]. In this analysis, the proportion of patients who achieved the response criteria was compared between those with polyarticular and oligoarticular disease.

More patients with polyarticular than oligoarticular disease achieved ACR and EULAR responses, and this difference was more marked at the higher response levels (e.g., ACR70 response). However, more patients with oligoarticular disease achieved the MDA criteria. No differences were significant, perhaps due to the small numbers in this interim analysis. Further results will be available once the study is complete. Researchers will benefit from composite measures specifically designed for PsA, but they will certainly require formal validation in oligoarticular disease.

Th17/IL-17 pathway (Bina Menon)
Dr. Menon presented an analysis of paired peripheral blood and synovial fluid samples from patients with PsA. Mononuclear cells from these samples were stimulated in the laboratory with PMA/ionomycin in the presence of GolgiStop and then analyzed for Th17, Th1, Th22, and Treg frequency using flow cytometry. CD3+CD4+ T cells and CD3+CD4− T cells were analyzed.

In the peripheral blood, an increased frequency of Th17 cells was seen in the CD3+CD4+ T cells of patients with PsA, in comparison to healthy controls. Dr. Menon also noted an enrichment of interleukin 22-positive (IL-22+), IL-21+IL-22+, and IL-17A+IL-22+ CD3+CD4+ T cells in the peripheral blood of patients with PsA compared to controls.

No significant difference was seen in Th1 cell frequency in the peripheral blood of PsA patients and controls. Patients with PsA had increased levels of CD3+CD4+ T cells producing both IL-17A and interferon-γ in the synovial fluid compared to the peripheral blood, as well as increased CD4+CD25+CD127^{low} Treg percentages.

The increase in Th17 but not Th1 in the peripheral blood was in keeping with previous work from the same group in patients with rheumatoid arthritis (RA)[6].

Ultrasound in early PsA (Axel Nigg, Munich, Germany)
Dr. Nigg described the difficulties of early diagnosis of PsA and presented the results of an ongoing study designed to evaluate the utility of ultrasound in early PsA. To be included, patients were required to have psoriasis confirmed by a dermatologist, current joint pain with a minimum visual analog scale score of 30/100, and disease duration < 5 years. Prior steroid or DMARD treatments were not permitted, nor were other coexistent rheumatological diagnoses. A total of 30 patients were recruited, with clinical and ultrasound assessments at baseline and 3, 6, and 12 months. The ultrasound assessed multiple sites for synovitis, tenosynovitis, and enthesitis.

In an analysis at the individual joint level, the positive predictive value for ultrasound abnormalities was 55% for a tender joint and 93% for a swollen joint. Subclinical synovitis was seen in 8% of clinically inactive joints. Ultrasound evidence of tenosynovitis was seen in 78% of dactylitic digits. The ultrasound synovitis score correlated well with the Disease Activity Score 28-CRP score (Spearman's rank correlation coefficient r = 0.69) and with the 68 tender joint count (r = 0.72).

Dr. Nigg concluded that in early PsA, ultrasound is more sensitive than clinical examination in detecting joint inflam-

mation, and that ultrasound findings correlate well with other variables of disease activity both at baseline and longitudinally over the course of treatment. In future work, the group will look at predictors of clinical and radiographic outcome as well as treatment response.

Prevalence of depression in PsA patients (Lindsay Wall Burns, Vancouver, BC, Canada)
Dr. Wall Burns presented results of a study that estimated the population prevalence of diagnosed depression among patients with PsA in British Columbia. The study analyzed data from Population Data BC, which combines multiple sources of linked administrative health records for the approximately 4 million residents of British Columbia. Dr. Wall Burns looked at a PsA cohort with 5 age- and sex-matched controls for each case. A variety of depressive disorders were assessed using the International Classification of Diseases-9 (ICD-9) codes. With the primary (more stringent) PsA definition, 6096 patients were detected, while with the secondary PsA definition (any ICD-9 code of 696.0), 14,296 patients with PsA were recorded. Age- and sex-adjusted logistic regression was used to compare the odds of depressive disorders between the cases and controls. Major depression was seen in 37% of patients with PsA using the primary PsA definition, with an adjusted odds ratio of 1.30 (95% confidence intervals 1.23, 1.38).

Dr. Wall Burns demonstrated the high prevalence of depressive disorders in patients with PsA, with an increased risk of major depression compared to control subjects. Given the contribution of depression to pain levels and reduced quality of life, screening for and treatment of depression should be an important part of management of PsA.

Poster Presentations
Mariangela Atteno (Naples, Italy) described the changes in CRP measurements in 60 patients commencing treatment with tumor necrosis factor (TNF) inhibitor as monotherapy. After 1 year, 75% of patients had a significant reduction in CRP. Significantly more patients receiving etanercept than adalimumab or infliximab achieved a normal CRP.

Shiu-Chung Au (Boston, MA, USA) presented an interim analysis of a study assessing the prevalence of the metabolic syndrome in children with psoriasis compared to an age-matched population of children with warts. Analysis of the first 25 patients enrolled found that children with psoriasis or PsA had significantly lower mean high-density lipoprotein cholesterol levels than the controls. No control children fulfilled the criteria for the metabolic syndrome, while 25% of the psoriasis patients did (although this difference was not significant).

Sibel Zehra Aydin (Leeds, UK) performed ultrasound scans on 104 patients (46 with psoriasis and 58 with PsA) and 23 age- and sex-matched healthy controls. A total of 1524 entheses were scanned by a sonographer blinded to the clinical details. Higher ultrasound enthesopathy scores were seen in the patients with PsA compared to psoriasis patients ($p = 0.01$) and healthy controls ($p < 0.0001$). A higher degree of Doppler positivity was seen in PsA versus psoriasis patients (45% vs 13%), while none was seen in healthy controls. Even when assessing only asymptomatic sites, power Doppler scores were higher in patients with PsA than in psoriasis patients. The predictive value of power Doppler enthesitis needs to be assessed longitudinally in a psoriasis cohort.

Francesco Caso (Naples, Italy) evaluated arterial stiffness (a cardiovascular risk factor) in PsA patients. Twenty patients with psoriasis and 20 healthy controls matched for age, weight, height, and with a similar cardiovascular profile, were enrolled. Patients with known cardiovascular risk factors were excluded. The aortic pulse wave velocity (aPWV) was significantly higher in patients with PsA versus controls, even after adjusting for demographic factors, heart rate, and central mean pressure. The aPWV also correlated with disease duration in patients with PsA, suggesting that vascular involvement is part of the disease process in PsA.

Concepcion Castillo-Gallego (Leeds, UK) described the results of a pilot study using optical coherence tomography (OCT) to assess the nails of patients with psoriasis and PsA and healthy controls. OCT was able to clearly demonstrate abnormalities including leukonychia and pitting, with an absolute agreement between OCT and clinical findings of 69.3%.

Elaine Dupuis (Vancouver, BC, Canada) surveyed Canadian dermatologists and rheumatologists about their use of methotrexate in the treatment of psoriasis, PsA, and RA. Parenteral methotrexate was prescribed more frequently by rheumatologists than dermatologists. When commencing biologic therapy, the majority of rheumatologists continued methotrexate, while most dermatologists discontinued the methotrexate.

Lihi Eder (Toronto, ON, Canada) compared carotid intima-media thickness and carotid plaque area in matched pairs of patients with PsA and psoriasis, using these as a surrogate measure for cardiovascular disease. Although there were no differences in traditional cardiovascular risk factors between the groups, both of these ultrasonographic measures of atherosclerosis were significantly higher in the patients with PsA.

Leandro Ferreyra Garrott (Buenos Aires, Argentina) presented data on 54 patients with PsA followed from diagnosis for a total of 188 patient-years, with a comparison group of 108 matched controls. During the followup period, 6 cardiovascular events occurred in the patients with PsA and 9 in the controls, giving incidence rates of 3.19/100 patient-years in the PsA group and 2.2/100 patient-years in the controls. Although an increased rate was seen in PsA, this difference was not statistically significant.

Dr. Ferreyra Garrott also presented a second poster describing the prevalence of hepatic and hematological toxicity of methotrexate in 60 patients with RA and 29 patients with PsA. They found a low prevalence of discontinuation for hematological or liver toxicity (14% in the PsA group), although about 30% had abnormalities at some time.

Hillary Frankel (Boston, MA, USA) reported data from the Nurses' Health Study, validating self-reports of psoriasis and PsA using the Psoriasis Epidemiology Screening Tool and Psoriasis Arthritis Screening and Evaluation questionnaires. An 83% response rate was achieved, and 93% of patients with full data available met their criteria for a valid confirmed case of psoriasis. A significant association was seen between self-reported psoriasis severity and PsA.

Ignacio Garcia-Valladares (New Orleans, LA, USA) compared the clinical, serological, and radiological characteristics of 80 patients with PsA with and without anticitrullinated protein antibody (ACPA) positivity. ACPA were present in 10 patients, with a mean titer of 174.9 IU. Patients who were ACPA-positive were more likely to have polyarthritis and less likely to have nail involvement or axial disease. A higher proportion of ACPA-positive patients commenced TNF inhibitors. These findings suggest that ACPA could be considered a marker of disease severity in patients with PsA, although it is not evident if some or all of these patients represent true RA patients with psoriasis.

Aruna Malipeddi (Leicester, UK) described differences in disease severity, socioeconomic status, and cardiovascular events between 60 white and 60 Gujarati Indian patients with PsA. The Gujarati Indians had higher pain levels and more swollen and tender joints, with a higher physician global assessment than white subjects. The Gujarati Indians were more likely to be unemployed and receiving state benefits and they also had a higher prevalence of cardiovascular events. Dr. Malipeddi suggested that disease severity was greater in the Gujarati Indian group, and with the increased rate of cardiovascular disease, screening was particularly important.

Kory Parsi (Davis, CA, USA) compared the cost-effectiveness of standard in-office care of psoriasis with a patient-centered online model for followup. Sixty-four patients were randomized to followup visits either in-office or online for a 24-week period. No significant difference was seen between the groups in the change in Dermatology Life Quality Index or Quality Adjusted Life Expectance. The cost of online followup was 1.7 times cheaper than in-office visits, suggesting that online followup visits may be cheaper while maintaining the same standard of care.

Ana Luisa Sampaio (Rio de Janeiro, Brazil) compared human leukocyte antigen gene frequency in patients with psoriasis and seborrheic dermatitis and healthy controls, confirming the association of the alleles B*57 and C*06 with psoriasis, and finding an association of A*32 and B*18 with seborrheic dermatitis.

Raul Sueldo (Tucumán, Argentina) assessed the prevalence of psoriasis in patients with RA treated with biological agents. Of 284 RA patients assessed, 148 received treatment with biological agents, and the remaining patients received DMARD. Of the patients receiving biological agents, 5 (3.4%) developed psoriasis a mean of 32 months after commencing treatment; the majority presented with guttate psoriasis. No new cases of psoriasis developed in the RA patients receiving DMARD.

Agnes Szentpetery (Dublin, Ireland) described the results of a study assessing periarticular bone mineral density (DXR-BMD) in very early PsA and RA patients prior to and 3 months after introducing a DMARD. In the 46 patients recruited, an inverse correlation was seen between the DXR-BMD and the age at baseline. The mean change in DXR-BMD from baseline with treatment was less marked in the PsA group than the RA group. Although the DXR-BMD correlated with various disease activity measures in RA, the same was not true in PsA, suggesting that the mechanisms for hand bone loss may be different in the 2 diseases.

Jenny Paola Varela (Bogotá, Colombia) assessed the prevalence of PsA in patients with psoriasis at their institution. A cross-sectional study using the CASPAR (ClASsification of Psoriatic Arthritis) criteria[7] found a prevalence estimate of 12.5%, with the most common psoriasis subtype being plaque psoriasis and 53% of patients having nail disease.

Cara Varley (Portland, OR, USA) investigated the relationship between *Staphylococcus aureus* colonization, subsequent infection, and TNF inhibitor use in patients with psoriasis and PsA. Patients being considered for or receiving treatment with TNF inhibitors were enrolled, surveyed, and tested for *S. aureus* colonization. At baseline, 43% of patients were colonized with *S. aureus*, of which 14% had methicillin-resistant *S. aureus*, but rates were not different between patients receiving and those not receiving TNF inhibitors. A trend was seen for persistent colonization in those patients exposed to TNF inhibitors. Of the patients with complete medical records available, 51% developed infections, most commonly skin infections. Subsequent *S. aureus* infections were associated with persistent *S. aureus* colonization. Dr. Varley raises the question of whether colonization status should be assessed before initiating TNF inhibitor therapy.

Ine Westhovens (Leuven, Belgium) reported data from a large cohort of patients with spondyloarthropathies (SpA) treated with TNF inhibitors, comparing the incidence of malignancy with that in the general population. The retrospective study included 231 patients, with 1199.83 patient-years of followup. Of the SpA cohort, 6 patients (2.6%) developed malignancy. A suggestion of a higher incidence of malignancy was observed in the TNF inhibitor–treated SpA population compared to the general population, but further study is needed to determine the cause.

Jamie Woodcock (Salt Lake City, UT, USA) described efforts to develop MDA criteria for psoriasis. They compared the Psoriasis Area and Severity Simplified (PASS) with the DLQI score[8] in 729 patient visits by 264 patients. A significant difference was seen in the PASS score for patients with a DLQI score ≤ 5 compared to those with a score between 6 and 10. An analysis to determine the optimal cutoff to define psoriasis MDA with the PASS suggested that this should be 4.25.

Conclusion

With encouragement from Dr. Ritchlin, GRAPPA members took the opportunity to discuss the research projects further with the oral and poster presenters during the GRAPPA meeting. A ceremony was held during the gala dinner when prizes were awarded to the trainees by Prof. John Moll. It is anticipated that the Trainees Symposium will continue to be an important part of the GRAPPA annual meeting in years to come. The next meeting will be in June 2012 in Stockholm, at which 28 trainees are due to present their research.

REFERENCES

1. Coates LC, Ritchlin CT. GRAPPA Trainees Symposium 2009: A report from the GRAPPA 2009 annual meeting. J Rheumatol 2011;38:526-9.
2. Ritchlin CT. GRAPPA Trainees Symposium 2010: A report from the GRAPPA 2010 annual meeting. J Rheumatol 2012;39:394-7.
3. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A, Landewe R, van der Tempel H, Mielants H, et al. Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis 2003;62:127-32.
4. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: Assessment of existing measures and development of an instrument specific to psoriatic arthritis. Arthritis Rheum 2008;59:686-91.
5. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: A proposed objective target for treatment. Ann Rheum Dis 2010;69:48-53.
6. Gullick NJ, Evans HG, Church LD, Jayaraj DM, Filer A, Kirkham BW, et al. Linking power Doppler ultrasound to the presence of th17 cells in the rheumatoid arthritis joint. PLoS One 2010;5:9.
7. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
8. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) — A simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.