International Journal of Clinical Rheumatology

in

Lessons learned from Canadian databases in RA, SLE and systemic sclerosis: highlights from the Canadian Rheumatology Association Annual Scientific Meeting

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Several important topics were presented at the Canadian Rheumatology Association meeting in Quebec City, 2015. This conference report focuses on Canadian database research in rheumatoid arthritis (RA) and connective tissue disease. Many patients with RA are lost to follow-up and this affects their future care as they frequently discontinue their disease modifying antirheumatic drug. Treating to a target has been well described in RA, whereas in systemic lupus erythematosus, there is both undertreatment (patients in a high or moderate disease activity state) and also the ability in others to demedicate include stopping immune suppressants. The utility of the recently published criteria for systemic sclerosis was debated as applying the criteria could classify many more patients than those who truly have systemic sclerosis.

Keywords: classification criteria • database • demedication • DMARDs • immune suppressants • longitudinal cohort • rheumatoid arthritis • systemic sclerosis • systemic lupus erythematosus • treat to target

Access to chronic rheumatology care for patients with RA is lacking & results in discontinuation of DMARDs

Diane Lacaille (University of British Columbia, Canada) presented data from a large British Columbia provincewide administrative database with incident rheumatoid arthritis (RA) patients followed over time [1]. A staggering two-thirds do not return to see their rheumatologist consecutively annually by 5 years for their RA. Sadly these patients also drop off from disease modifying antirheumatic drug (DMARD) treatment, especially in the year prior to returning to see the rheumatologist and we know that this does not allow optimal care.

The importance of ongoing follow-up with a rheumatologist is likely needed to be explicitly expressed by rheumatologists for a chronic disease such as RA as when DMARDs are stopped, patients will not maintain remission in the majority of cases, and prescriptions for new and ongoing DMARDs are strongly correlated with seeing a rheumatologist.

Lacaille has published prior papers that demonstrate the use of DMARDs in RA patients not seeing a rheumatologist can be as low as 10%. Her previous work showed that care by a rheumatologist increased DMARD use in more than 27,000 patients with RA 31-fold [2]. Specifically, the published research demonstrated that only 48% saw a rheumatologist by 5 years and 34% by 2 years of RA. DMARD use was significantly more frequent and persistent, and more often used as combination therapy with continuous rheumatologist care. DMARDs were used in RA patients followed by rheumatologists continuously or intermittently (73–84%), internists (40%) and family physicians (10%), respectively. The current study she presented at the Canadian Rheumatology Association (CRA) meeting included 9224 RA patients seen in British Columbia by rheumatologists who started DMARD treatment. She found that in the 6th year of follow-up, only a third had seen a rheumatologist yearly for the preceding 5 years; and only a third were followed by 9 years. At year 6, 14% had not

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seen a rheumatologist in the preceding 5 years, and this rate increased to 19, 23 and 25% at years 7, 8 and 9, respectively. At year 6, the rate of DMARD use was 92% for those with continuous rheumatologist care over the prior 5 years compared with only one in five for those without any rheumatologist care in the preceding 5 years.

This may be the most important justification of the specialty of rheumatology, as patients with RA (the most common noncrystal inflammatory arthritis) are not treated appropriately if they do not continue to have clinical encounters with their rheumatologist. There is also a need for rheumatologists to determine who is lost, in order to follow-up and encourage the patients to return. There may also be other co-sharing models of care that continue adherence in this chronic disease, which usually needs lifelong DMARD treatment.

Treating to a target in SLE may include demedication but there is also high disease activity. Are we treating SLE well enough?

Appropriate treatment of lupus may include discontinuation of treatment

Zahi Touma (University of Toronto, Canada) presented at the CRA meeting in Quebec City an oral paper titled 'Successful Withdrawal and Discontinuation of Immune suppressants in Lupus Patients: Outcomes and Predictors' [3]. Patients from the Toronto Lupus Clinic were followed from 1987 to 2012 and included in this study and also if they were in clinical remission and taking 7.5 mg of prednisone daily or less. Out of the 1678 patients followed, there were 973 patients on immune suppressants. Of these, 179 had some tapering and 99 were able to stop immune suppressants. The length of time from tapering to stopping treatment was 1.8 ± 1.8 years in the no flare and 0.9 ± 0.9 years in the flare group. This demonstrates that we should taper very slowly to decrease the chance of systemic lupus erythematosus (SLE) flaring. The longer duration that patients were followed, the more likely they were to flare, at least in the first 3 years, with one in six at year 1, one in three at year 2, and one in two over years 3, 4 and 5. If on prednisone, those patients were more likely to flare, which is possibly due to the fact that the patients previously required prednisone, but it also shows us that being on chronic prednisone is a predictor of decreased chance of stopping immune suppressants successfully. The importance of this analysis is that it shows some patients can successfully decrease and stop their treatment in SLE but there is a 50/50 chance of flare by 3 years, especially if on stable chronic low-dose steroids.

Care gaps in SLE

Christine Peschken (University of Manitoba, Canada) presented a poster at the CRA titled 'Residual Lupus Disease Activity in a Large Canadian Cohort of Prevalent Patients' where she analyzed patients with SLE from the 1000 Faces of Lupus cohort (a prevalent and incident cohort of patients followed annually at many Canadian sites) [4]. The premise for this study is that if we can effectively control SLE disease activity, there should be less damage. There were 1454 SLE patients studied, with a mean age of 44 years and 11 years of disease duration, of whom 90% were women and two-thirds caucasians and an astounding one in five had not obtained a high school diploma. Half the patients were in low disease activity, a fifth were in moderate activity and a sixth were in high disease activity as measured by the SLE Disease Activity Index. The low and moderate versus active and highly active groups did not differ in age, sex or education, whereas the SLE disease duration was lower in those with high disease activity. As expected, cyclophosphamide and steroids were used more in high disease activity but antimalarials were less in the highly active group. Somewhat unexpectedly, just over half of the low and moderate disease activity patients were using prednisone at greater than 7.5 mg/day. SLE damage as measured by the SLE Damage Index were slightly higher in the groups with higher disease activity (suggesting an accumulation of damage over time from previous disease activity). This study raises questions, especially about the use of steroids. Are we using too many steroids? As steroids are lowered will SLE flare? Are other immune suppressants under utilized that could allow for steroid sparing? Steroids may maintain a low disease state in many SLE patients, but this can result in complications over the long term. We do know from SLE RCTs (where patients are enrolled with active disease) that steroid use occurs in 50% of patients. Future research should consider ways to limit steroid use (dose and duration) while maintaining low disease states.

Is the new American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) SSc classification a waste of time or not? Scleroderma classification criteria may be overly inclusive

The usefulness of the new ACR/EULAR 2010 classification criteria for scleroderma (systemic sclerosis) was debated by Drs Sindhu Johnson and Marie Hudson. Johnson, who was instrumental in developing the new criteria, commented that the previous preliminary American Rheumatism Association criteria were weighted toward established disease, as there were clinical and chest x-ray features [5]. The old criteria were; one major (sufficient): skin thickening of the fingers

and proximal to the metacarpophalangeal joints, or if not present: two of three minor: sclerodactyly, digital pits or tuft resorption, pulmonary fibrosis. The new criteria reflect the various components of the disease including vascular, fibrosis and autoantibodies. They are more sensitive and specific both in the validation of the criteria that was performed in the classification paper, published in *Arthritis & Rheumatology and Annals of Rheumatic Disease* simultaneously [6,7], and they have been externally validated including using the Canadian Scleroderma Research Study Group [8].

Patients with limited SSc and early SSc were less likely to be classified. The calculator for determining the score for the new SSc criteria can be found on the RheumInfo website [9]. The criteria can inform the constructs of the SSc disease. Some limitations that were mentioned [10] were that the classification criteria are meant as a research tool and they are not diagnostic criteria. She demonstrated the false positive rate if applied in a Canadian population which could over classify 35,000 individuals. The gold standard for diagnosis is still the clinician. Making a very early diagnosis is being studied in 'pre-SSc'. Not all the patients will develop full SSc or have lead time bias if they are enrolled in a research study where outcomes are better if the patients do not progress to clinical disease. We do not know if an early identification changes clinical outcomes. Perhaps as the genetics and phenotypes are so varied, we should concentrate on SSc subsets.

The take home message depends on what you want to use the criteria for. Good clinical judgement trumps all, but the criteria are an excellent teaching construct for SSc including what is not included, such as scleroderma renal crisis and tendon friction rubs, where some items are too rare or redundant and cluster with other included features. So, common sense trumps all, but the criteria do identify more patients with SSc who are early, mild or of the limited subset.

Conclusion

Databases in rheumatic diseases inform best practices and also identify care gaps. These conference highlights illustrate that in RA, a large proportion of patients cease to be followed by rheumatologists over time resulting in poor care. SLE patients may be able to decrease their immune suppressant use but others are likely under treated where they remain in high disease activity. The new SSc classification criteria are more sensitive and specific than previous criteria but could result in many false positives with consequences of over labeling patients with SSc.

Financial & competing interests disclosure

J Pope is an author on the ACR/EULAR SSc classification criteria and is a member of the 1000 Faces of Lupus research group. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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