Spondyloarthritis and vasculitis – new perspectives on outcome.

WIN: VASCULITIS MAINTENANCE TREATMENT
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Background: Cyclophosphamide and more recently rituximab have transformed the outcome for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), resulting in survival in most cases. However, patients are at risk of frequent relapses, low grade grumbling disease, drug toxicity and worsening co-morbidity. Historically, prolonged courses of cyclophosphamide (used for both induction and maintenance) increased the risk of malignancy (especially bladder cancer). More limited use of cyclophosphamide, or the use of other agents including rituximab or methotrexate (for milder forms) offer safer but still effective options. The high relapse risk in AAV (especially in GPA) means that maintenance therapy is necessary but there is uncertainty over the most effective, safe long term choice. Maintenance RTX (fixed dose at fixed intervals of 4-6 months) is superior to azathioprine, but it is not clear if combination maintenance is superior to RTX alone. Long term side effects of RTX include hypogammaglobulinemia and potential for reactivation of JC virus. Reducing the glucocorticoid burden in AAV remains a challenge. We still do not know how long to continue therapy in AAV. Two recent studies provide conflicting opinion on the duration of maintenance therapy using azathioprine on risk of future relapse. The use of low doses of rituximab has recently explored in AAV: in thyroid eye disease, 100mg rituximab is effective. Less frequent dose intervals, as used in rheumatoid arthritis, will not control AAV. Future studies could address optimal long term management of patients with AAV, in order to improve their quality of survival and well-being.

Objectives: To assess the risk of relapse of vasculitis and to review the evidence for the use, effectiveness and toxicity of different maintenance strategies in systemic vasculitis

Methods: A review of published studies of long term outcome in vasculitis and of maintenance therapy in systemic vasculitis

Results: Once remission has been achieved, relapse is increasingly common, perhaps over 70% in some forms of ANCA associated vasculitis such as GPA. A strategy of induction therapy for one year, without any maintenance results in relapse in most cases of limited GPA. A maintenance regimen is recommended in order to avoid recurrence of the disease, but the evidence base for use of maintenance therapies remains limited. Maintenance is different from treatment of a relapse, usually aiming to prevent recurrence of clinical evidence of disease. We will show the evidence for different types of maintenance regimens and the outcomes in terms of relapse and toxicity with a focus on recently completed clinical trials and observational cohorts in a variety of forms of systemic vasculitis

Conclusion: The management disease in systemic vasculitis requires induction therapy but increasingly recognised is the importance of a maintenance regimen. Current and future strategies should explore a mechanism based approach, to selectively modify the underlying immunopathogenic mechanisms.

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CAN IMAGING PREDICT PROGRESSORS?
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Osteoarthritis (OA) is a highly heterogeneous disease with varying aetiologies, thus the manifestations of knee OA and response to treatment vary. This heterogeneity of clinical presentation and treatment response confounds interpretation of therapeutic clinical trials and complicates the care decisions for clinicians. Identifying factors to define patient profiles likely to progress more rapidly over time may help with subsequent therapeutic decision-making. Such characterisation could also help randomization strategies for clinical trials in attempting to balance comparator groups. Reasonable long-term goals among these rapid progressors would be to offer optimal quality of life and to postpone, if possible, the indication of joint replacement. Quantitative magnetic resonance imaging (qMRI) can precisely and accurately assess and quantify joint structural changes seen in OA. Such technology should logically help to identify patients with rapid OA progression and some of its predictors. This short presentation shall address whether MRI structural markers can be used to predict knee OA patient hard outcomes such as the total joint replacement. Data revealed that several articular tissue alterations have shown their potential for predicting patients with a rapid progression; global cartilage thickness/volume loss, presence and severity of meniscal damage, bone curvature, and presence of bone marrow lesions among others. However, clinical and demographics variables such as BMI, severe pain, and clinical knee synovitis and effusion are also strongly associated with articular tissue damage and should also be taken into careful consideration as they may independently also predict OA progression and potentially indication of joint replacement.

Optimizing the selection of patients for whom an intervention with a DMOAD could prevent the development of the disease should lead to better response to treatment. Imaging may assist us at identifying the rapid progressors but should be used in a context of an overall patient assessment that also integrate the co-existing demographic and clinical variables. Such context may assist us in the emergence of personalized or precision medicine for patients suffering from this disease.

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CAN IMAGING MONITOR/Demonstrate TREATMENT RESPONSE IN OA?
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Background: Treatment for osteoarthritis (OA) should ideally not be limited to ameliorating symptoms, but should include the modification of synovial joint structures that are involved in the disease process (disease modification). Imaging, particularly MRI, has unparalleled ability to evaluate joint structures qualitatively or quantitatively.

Objectives: To discuss 1) Why one should care about structure (and its modification) in OA, 2) Which joint structures may be most relevant to modify, 3) Why quantification of tissue structure is beneficial, 4) To what extent tissue structure in OA can currently be modified by intervention, and 5) Whether translation of structural modification to clinical benefits is realistic?

Methods: Narrative literature review.

Results: A public meeting for the FDA, organized by the Arthritis Foundation in March 2017, concluded that “most importantly, patients want therapies which stop progression whilst alleviating pain and improving function, yet stopping disease progression is their utmost concern and desire for new therapies”. Despite other notions, there is good evidence that structural damage of synovial tissues is related to joint pain. Quantification of synovial tissue from serial MRI can detect longitudinal changes that are too small to be detected by the naked eye. These exist surgical (e.g. joint distraction4 and high tibial osteotomy), and pharmacological approaches are in development (e.g. FGF 18 or spirinlummin5), to modify joint structure. Finally, structural change of joint tissues has been shown to be related to knee replacement (KR) as a hard clinical outcome6. Identifying factors to define patient profiles likely to progress more rapidly over time may help with subsequent therapeutic decision-making. Such characterisation could also help randomization strategies for clinical trials in attempting to balance comparator groups. Reasonable long-term goals among these rapid progressors would be to offer optimal quality of life and to postpone, if possible, the indication of joint replacement.

Conclusion: Quantitative imaging has become a powerful tool for demonstrating structure modification (treatment response) in OA. This may hopefully lead to regulatory approval of disease modifying therapy for OA in the not too distant future.

REFERENCES:


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