Résumé and perspective

Development, exploration and testing of outcome measures in inflammatory rheumatic disorders is a continuously ongoing process in rheumatology. Results presented in this thesis are based on the considerable work that is constantly done by clinicians, methodologists and epidemiologists. These efforts are ultimately aiming at improving the daily management of patients suffering from rheumatic diseases, both in improving the methodology of clinical trials and evaluation of drugs or therapeutic strategies, and in providing better tools to monitor the disease in every day clinical practice in an individual patient.

OUTCOME MEASURES IN RHEUMATOLOGY: A CONSTANT EVOLUTION

The work conducted and reported in this thesis strengthens our conviction that a constant improvement in the metrological performance of outcome measures is possible, from conventional and traditional assessment tools like radiography in RA to innovative methods like MRI in AS. This progress systematically requires collaborative efforts involving patients, clinicians, methodologists, radiologists and others, usually in the context of organisations such as OMERACT and ASAS.

REPERCUSSION OF THE STUDIES ON RA MANAGEMENT AND EVALUATION

The results of the work that has been conducted in the field of RA may have several implications for the management of the disease as well as for the assessment of its consequences in affected patients:

In particular, validation of the **SENS method** may reasonably make objective and standardized assessment of radiographic damage in RA feasible in daily clinical practice: The reasonable amount of time required to score hands and feet radiographs in an individual patient, with the advantage of obtaining valid and standardized assessment of the damage due to RA, should help the implementation of monitoring **radiographic progression in daily clinical practice**, which is currently not done frequently. Such a monitoring may allow evaluating the impact of therapeutic strategies in clinical practice, or the consequences of joint damage on functional or professional status for example.

We have convincingly proven that repair of previously existing joint damage is a credible concept in the era of biologics. This concept has changed our

vision on the course of progression of joint damage caused by RA from an irreversible process to a more optimistic point of view including a potential reversal of erosive lesions.

The **analysis of the therapeutic behavior of rheumatologists in daily clinical practice in the ESPOIR study** has convinced us that dissemination of recommendations in the management of inflammatory disorders should be taken seriously. The heterogeneity in therapeutic approaches we have found was common in daily care and may invoke unwarranted differences with regard to the long term prognosis of individual patients: The results of our prognostic study in ESPOIR has cemented the well-known **recommendation that a DMARD should be started very early** in a patient diagnosed with RA, which was so far a general recommendation with poor evidence to support it.

Automated measurement of joint space width may, in addition to the "manual" scoring of erosions, improve accuracy of radiographic evaluation. The consequence of such an extension of radiographic assessment would be a **decreased number of patients required to be included in a trial to demonstrate efficacy of a treatment or therapeutic strategy**, as the discriminatory ability would be increased, and consequently the ability to demonstrate a difference improved. Automated joint space width measurement may bring radiographic assessment closer to small proof-of-concept trials.

CONSEQUENCES OF THE RESULTS ON AS MANAGEMENT AND EVALUATION

The evaluation of different **scoring methods of the spine of AS patients by MRI** will help the designers of clinical trials and observational research to make an educated choice for how to assess MRI-activity**.**

The development of the ASDAS has changed the world of disease activity assessment in spondyloarthritis. This method has been received extremely well by the professionals working in the field of SpA, as can be concluded from the plethora of articles that have appeared after the publication of the main paper, in which ASDAS was used to evaluate disease activity in all kinds of cohorts and trial populations. ASDAS may have impact on the design of clinical trials in AS and axial SpA, for example by **decreasing the required number of patients**, and will influence daily clinical practice because of its face validity and value in monitoring disease activity status and therapeutic response. Recent data in particular suggest that if the initiation of TNF-blockers in AS patients

with persistent disease activity would be based on ASDAS instead of BASDAI the efficiency of treatment would improve [21].

PERSPECTIVES IN FURTHER EVALUATION OF THE STUDIED OUTCOME MEASURES

With regard to radiographic assessments of RA, numerous studies might be conducted to further enhance the performance. In particular, acceptability and feasibility of the systematic scoring of radiographs in RA with SENS in the context of a daily practice could be evaluated, which might then convince non-academic rheumatologists to measure radiographic progression methodically themselves. If adopted, the collected data would consequently serve as a working tool in the evaluation of radiographic progression in RA.

With regard to repair of erosions under biological treatment, the impact of repair on long-term outcomes such as functional status should be further investigated, just as the potential susceptibility to repair of specific subgroups of patients.

Concerning the therapeutic management of early RA, the regular evaluation of the impact of periodically updated guidelines and recommendations remains necessary, and the expected and induced change in behaviors concerning the time-to-DMARD-initiation will be among the most crucial targets. This time lapse encompasses both the referral to the rheumatologist by the initially consulted health professional -usually the general practitioner- and the responsiveness of the specialist in the diagnostic process and therapeutic decision. Further efforts are needed to convince the practitioners responsible for the first contact with the patient about the -relative- emergency of the condition, as it might have an unfavorable long term outcome if not treated timely and adequately.

In the field of AS management, assessment of disease activity by ASDAS is gradually becoming a standard, and current work is conducted to confirm validity of the tool in the daily care management of individual patients. In particular, the appropriate selection of patients requiring and potentially mostly benefiting from a treatment with TNF blocking drugs might be improved if disease activity is assessed by ASDAS. Indeed, acute phase reactants have been shown to be predictive of an increased likelihood of response to TNF blockers, and are included in the assessment of the disease activity [22-24]. Confirmation of the advantage of using ASDAS in this context may then change the

recommendations about the screening of patients with regard to the decision to start a TNF blocker.

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