Maastricht University

# Prognosis of chronic clinical pain conditions : the example of complex regional pain syndrome 1 and low back pain

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# Summary

Non-specific low back pain (LBP) and complex regional pain syndrome 1 (CRPS 1) are two important examples of non-specific pain conditions. While non-specific LBP is common, CRPS 1 is less known but economically very important. Both illnesses share a high patient burden and lead to substantial healthcare expenditures for pain management.

Non-specific LBP is defined as lumbar pain without a specific morphological correlate and accounts for over 90 percent of all LBP cases. In the absence of a structural abnormality explaining the patient complaint, the diagnosis is solely based on the clinical findings. Further examinations—in particular imaging—do not give a causal explanation. CRPS 1 is defined as a pain state following injury, which exceeds in magnitude and duration the expected clinical course when other underlying diseases are excluded. Clinical manifestations include a broad spectrum of sensory, autonomic, motor, and trophic changes usually associated with significant impairment of motor function. For diagnosis, the use of the "Budapest criteria" is recommended. These criteria consider signs and symptoms of the clinical manifestation.

While in specific pain conditions a targeted therapy of the underlying somatic anomaly may be initiated, in non-specific LBP and CRPS 1, no causal derived therapies are possible and the therapy remains symptom-based. In order to avoid chronicity, it is important to identify early those patients at risk for delayed recovery. However, when no clear underlying cause can be found, the identification of patients at risk represents a major challenge in clinical practice.

The results presented in this thesis should be seen as a contribution to the problems outlined above. The research presented in this thesis comprises a series of projects that were performed at the Horten Centre, University of Zurich, Zurich, Switzerland, and at the Occupational and Industrial Orthopaedic Center (OIOC), New York University Hospital for Joint Diseases (NYU-HJD), New York, U.S.A, in collaboration with the University Hospital Balgrist, Zurich, Switzerland.

In Chapter 2 we demonstrated that in LBP studies many important prognostic factors are incompletely assessed or reported. Even 10 years after the publication of the CONSORT statement which aimed at improving the reporting in RCTs, on average only half of the prognostic factors identified by Hayden and colleagues are reported. We therefore concluded that the influence of prognostic factors on the course of LBP and

treatment efficacy is not fully understood. Future research should systematically assess and report prognostic factors.

In Chapter 3 we studied the influence of fear avoidance beliefs on the prognosis of LPB. High fear avoidance beliefs were associated with poor work-related outcome in patients with persisting LBP of less than three months duration. Further, important gaps in the literature are highlighted in this review.

In Chapter 4 we analyzed how fear avoidance beliefs influenced treatment efficacy in various treatment strategies. While the findings were consistent, the heterogeneity of outcomes measured, the various analyses conducted and the different study protocols used impeded us from conducting meta-analyses. The results presented in this study should inspire future research to assess the influence of various prognostic factors on treatment outcome.

In Chapter 5 we systematically assessed the diagnostic accuracy of bone scintigraphy for the Diagnosis of CRPS 1. Our analysis showed that a positive finding is not necessarily concordant with and a negative scan does not necessarily rule out CRPS 1.

Whereas clinical LBP management involves early prognostic screening for delayed recovery, these concepts are largely lacking in CRPS 1. The systematic analysis of prognostic factors in In Chapter 6 we identified 28 potentially relevant factors for the outcome of CRPS 1. Most consistently associated with poor prognosis were cold skin temperature (5 studies) and the presence of sensory disturbances (3 studies). However, the study quality was poor in many studies. The measurement of prognostic factors or potential confounders and the statistical methods used were often inappropriate. While in patients with LBP, maladaptive cognitive behaviors are considered to play a significant role in the development of chronicity, in CRPS their influence is not clear. In the systematic analysis of prognostic factors, only one study identified previous psychological problems associated with poor prognosis.

In patients with CRPS 1, treatment recommendations include a magnitude of options. The wide variety of treatment options reflects the uncertainty and dilemma regarding the optimal choice. In Chapter 7 we used a network-meta-analytic approach of 16 randomized controlled trials to establish a rank order of treatment efficacy for pain management. Based on the results, a rational therapeutic strategy should consider illness duration. Further bisphosphonates (disease duration less than 12 months, follow-up 2 months and more) or short-term calcitonin (for disease duration 12 months and more, follow-up less than 2 months) were most effective. However, there are some limitations that need to be addressed in future studies. For many treatments, only a few studies and small patient samples were available. Future research should further investigate the pathway of action of pharmacological agents. Further treatment regiments and administration routes should be studied. Finally, studies should use reliable and comparable outcome measures so clinicians and researchers will be able to compare study outcomes.

In conclusion, prognostic factors may play an important role in chronic non-specific pain conditions. Future research should aim at understanding the influence of prognostic factors and how they affect treatment efficacy and prognosis. With our research activities we expect to make a sustained contribution to the emerging recognition of the importance of prognostic factors in chronic pain. We hope that clinicians, researchers, and patients affected with LBP and CRPS can benefit from our findings.