Degeneration of the lumbar spine

Preclinical concepts for clinical questions

Rustenburg, C.M.E.

Citation for published version (APA):
Chapter 8
English summary
‘Degeneration of the lumbar spine: preclinical concepts for clinical questions’
Degeneration of the lumbar spine is one of the known causes of chronic low back pain. It is an ongoing, progressive process and is believed to start with degeneration of the intervertebral discs which may eventually result in *de novo* degenerative lumbar scoliosis. Unfortunately, there are currently no therapies available that are able to slow down, halt or even reverse this process. Therefore, the **general aim** of this thesis was to provide a pre-clinical foundation for a better understanding of the degeneration of the lumbar spine and for the development and implementation of therapies.

*Evaluating current surgical treatments for degenerative lumbar scoliosis*

When lumbar spine degeneration progresses, *de novo* degenerative lumbar scoliosis may develop, mostly causing disabling symptoms such as radiculopathy and neurogenic claudication due to degenerative lumbar spinal stenosis. A laminectomy procedure followed by short posterior instrumentation may provide alleviation of these symptoms. In Chapter 2 and 3, our aim was to study the flexibility and stiffness of lumbar spines with degenerative scoliosis and how these parameters, defined by range-of-motion (ROM) and stiffness around the neutral orientation (i.e. neutral zone; NZ stiffness) of the spinal segment, alter after laminectomy on the level of the apex and posterior instrumentation. We found that spines with degenerative scoliosis tend to be stiffer and less flexible compared to non-scoliotic spines. When laminectomy was performed, there was a small increase in range-of-motion (ROM) and small decrease in NZ stiffness. However, when posterior instrumentation was applied, there was a major decrease in ROM and strong increase in NZ stiffness in most directions of both the whole lumbar spine and the levels around the apex. This implies that laminectomy partly restores the level of flexibility and stiffness in lumbar spines with degenerative scoliosis towards that of lumbar spines without degenerative scoliosis, while relieving patients from their disabling symptoms. Posterior instrumentation only deteriorates the flexibility and increases the stiffness of the lumbar spine.

*Determining the degree of degeneration*

Since degenerative lumbar scoliosis is one of the features of end-stage degeneration of the lumbar spine, the cascade of degeneration, interference should optimally occur in an early stage of the disease. Our
aim in **Chapter 4** was to identify prognostic clinical, environmental and imaging factors for the progression of intervertebral disc degeneration, in order to predict which patients will likely proceed towards end-stage degeneration and should be prioritized for targeting with regenerative therapies. Strong evidence was found that disc herniation is associated with progression of intervertebral disc degeneration, while most clinical and environmental causal factors (e.g. BMI, smoking and occupation) were not associated with progression. Limited or conflicted evidence was found though for most of the identified prognostic factors, as there was a lot of diversity in determinants and outcome parameters between the included studies. This implies that there is no clear and universally used definition of intervertebral disc degeneration.

When there is no clear definition of intervertebral disc degeneration, this may also have implications for the way we measure the degree of degeneration. In **Chapter 5**, we compared the two most common used system for grading intervertebral disc degeneration, which are the method by Pfirrmann et al. and Thompson et al. We found that their reliability is low, which has a direct effect on patients as many of them are probably misdiagnosed. Thus, we need a new, more reliable and valid classification system for intervertebral disc degeneration. Since the conventional classification systems rely on the interpretation of the observer, this new, improved classification system should consist of a more objective method and be able to distinguish the small changes that occur during degeneration. We recommend that this classification system takes the multifactorial character of the disease into account by combining two or more measures for degeneration and not consist of five pre-determined grades to determine the degree of degeneration.

**Stepping stones for future therapies**

To serve in the need for evidence-based therapies, we developed a disease model for moderate intervertebral disc degeneration in **Chapter 6**, by injecting an optimized mixture of collagenase and chondroïtinase ABC (cABC) into whole caprine intervertebral discs. After ten days, consistent but mild degeneration was found. Once the intervertebral discs are degenerated, regenerative therapies that have been designed and tested in vitro can be applied to the intervertebral discs in order to study
their therapeutic capacities in an ex vivo setting under physiological mechanical loading using this method, to thoroughly screen its potential before moving to in vivo testing.

When a therapy is found to be safe and successful, it is time to implement it in clinical practice. Besides the earlier mentioned lack of prognostic factors, there are multiple problems to overcome to find the right treatment for the right patient. For instance, no clear clinical algorithm for diagnosis or treatment is present for intervertebral disc degeneration. We could however adapt this from a well-studied degenerative joint disease with a clear, consecutive schedule of evidence-based therapies, like osteoarthritis. In Chapter 7, we compared intervertebral disc degeneration and osteoarthritis. We found that both conditions are surprisingly similar, both in the composition of their healthy, non-degenerated matrix as well as their process of degeneration, but there is a strong imbalance between osteoarthritis and intervertebral disc degeneration in terms of awareness and knowledge among clinicians, patients and society. While osteoarthritis is a well-known health problem, intervertebral disc degeneration is often disregarded as a cause of low back pain. When the similarities between the two conditions are emphasized, the imbalance might be reduced. This may facilitate the development of sufficient therapies by facilitating cross-fertilization of clinicians and scientists in both fields.

In short, in this thesis we determined the natural range of motion of lumbar spines with degenerative scoliosis, tested and optimized current surgical treatment, gathered the evidence for progression of degeneration, validated the golden standard measures for intervertebral disc degeneration, set a new methodology to test early regenerative treatments, and found new insights by studying the degenerative diseases in other joints.