Arthrofibrotic remodeling after knee replacement surgery – a stress-related disease?

- Clinic, biochemical model, therapy, research -

Introduction

The predicted incidence of arthrofibrosis after knee replacement surgery is 5 - 10%. Arthrofibrosis is defined as painful impairment of joint flexibility occurring postoperatively. To counteract symptoms and to accomplish quality standards (E/F 0-0-90) several therapeutic strategies as for instance physiotherapy or mobilization under anaesthesia are applied. Although it is known that mechanical and emotional stress induce myofibroblast differentiation, extracellular matrix (ECM) synthesis and xylosyltransferase (XT) activity, biochemical processes of fibrotic diseases receive little attention in orthopaedics. Until today, neither an adequate disease model nor a diagnostic marker for arthrofibrosis has been described.

Mechanical strain

Surgical procedures (e.g. endoprosthesis, cruciate ligament replacement) initiate physiological wound healing and the release of inflammatory mediators from platelets, damaged tissue and other cells of the immune system. Secreted cytokines such as transforming growth factor-β1 (TGF-β1) or platelet derived growth factor (PDGF) promote myofibroblast proliferation and differentiation.

Mechanical strain (stretching exercises with pain inhibition) leads to activation of latent TGF-β1, which triggers scarring via ECM/XT synthesis and prevents myofibroblast apoptosis. Our recent study carried out a decreased platelet count in arthrofibrosis patients compared to healthy controls. Thus, an elevated platelet consumption might take place. Analogous to TGF-β1, PDGF also inhibits myofibroblast apoptosis and expression of matrix metalloproteinase expression, which degrade ECM.

Emotional stress

Emotional stress might not only matter in other fibrotic diseases e.g. tako-tsubo cardiomyopathy (TTC) but also in arthrofibrosis. Sympathicotonic destabilization (due to pain, frustration or social burden) results in increased catecholamine synthesis and sympathetic activity. These effects are recognizable by vegetative symptoms (e.g. insomnia, sweating, muscle tension). Catecholamines directly activate fibroblasts and increase ECM synthesis by binding to β2-adrenergic receptors. In TTC, a decrease in catecholamines and profibrotic cytokines restores organ functionality.

Causal therapy

Several therapeutic approaches might exert a positive influence on degradation of fibrotic tissue: less of postisometric stretching, avoidance of emotional workload, positive expectations due to medical consultation about reversibility of fibrotic mechanisms, appropriate medication as well as osteopathy.

Research

Operating surgeons are able to detect an unfavorable development of arthrofibrosis relatively early. Nevertheless, they are afraid to name the possible complication. Therefore, quantification of a reliable biomarker would bring great advantages for diagnostics of pre- and after-treatment. Our current studies examine whether increased XT activity might display a biomarker in synovial fluid.