Repetitive Reduction Leads to Significant Elevated IL-6 Levels in Femoral Fractures: A Quantitative Analysis of a Robot-Assisted Reduction Process in a Rat Model

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Purpose: The field of robot-assisted fracture reduction has been developed by several research groups over more than one decade by now. The main goals are to increase the fracture reduction accuracy by reaching anatomically correct bone alignments, and also to relieve the surgeon from x-ray exposure as well as from the exhausting task of fracture manipulation against strong soft tissues, especially in the femur. Robotized procedures, with their precise and well-controlled motions, have the potential to achieve a more gentle and soft-tissue-preserving operation outcome. However, the influence of different reduction paths to the patients' physiology is not yet fully known. The aim of our study was to compare in an in vivo rat model the impact of a robot-assisted direct reduction path to the impact of an artificially prolonged reduction path by measuring the cytokine responses.

Methods: We developed a robotic testing environment for femur fracture reduction in a rat model. The developed system uses an industrial robot, a Stäubli RX 90, with its standard robot control unit, a CS7B. The robot is controlled from a Windows PC with self-made control software written in C++. The direct reduction path used for our tests consisted of a distraction of 2 mm followed by a vertical displacement of first 10 mm up and then 20 mm down. Finally, the bone is moved back to the starting position for an anatomically correct reconstruction of the fracture. The prolonged reduction path consisted of the same steps, but these steps were repeated 10 times. For the study, 36 male rats were divided equally and randomly assigned into three groups (A, B, and C). A reference blood sample was collected from all rats 1 hour before operation procedure started. Afterwards all rats were anesthetized and an external fixator was attached to the left femur. Next, an osteotomy of the femur was performed between the two inner pins of the external fixator using a Gigli wire. Three days later the robot was attached in rats of the group A and B to the distal femur part and a mechanical holding device was attached to the proximal femur part. Group A received a fracture reduction on a direct path, whereas group B received the prolonged reduction path using 10 repetitions. The third group (C) was the control group. In this group, the external fixator was attached to the femur, but no reduction was performed. 0, 6, 24, and 48 hours, after the reduction process blood samples were collected. The following markers where analyzed via ELISA (enzyme-linked immunosorbent assay) or cytometric bead assay: interleukin (IL)-1, IL-4, IL-6, IL-8, IL-10, IL-17, MCP (monocyte chemotactic protein)-1, interferon gamma, and TNF (tumor necrosis factor) alpha. Statistical significance was set at $P < 0.05$. Furthermore, muscle biopsies in the area of the osteotomy were collected 48 hours after the reduction process for histologic analyses.

See pages 47 - 108 for financial disclosure information.

Results: Analysis of the cytokines showed that the pr-inflammatory cytokine IL-6 of group B (prolonged reduction) had a significant rise 6 hours after reduction compared to the control group. IL-6 further showed markedly elevated levels 6 and 24 hours after operation in group B compared to the direct reduction of group A. On the anti-inflammatory side, IL-10 showed a significant decrease in group B 6 and 48 hours after reduction compared to group A or C. Furthermore, the muscle biopsies showed a significant increased soft-tissue damage in group B compared to group A.

Conclusion: It could be shown that the developed robotic test bench is suitable for comparing the physiologic impact of different fracture reduction procedures utilizing cytokine measuring in a rat model. Different reduction procedures produce different responses in the measured cytokine markers. In particular, it was possible to distinguish between a direct and a prolonged reduction procedure. The response of IL-6 was considerably higher in the prolonged procedures 6 and 24 hours after operation compared to the performed direct reductions. Therefore, it can be concluded that a direct and gentle reduction procedure is preferable over a prolonged and straining reduction and might potentially support the postoperative healing process of the patient.