**ABSTRACT INTRODUCTION:**

Muscle injury is a disabling condition in sport medicine and a challenging problem in current traumatology. Insufficiency of skeletal muscle regeneration often impedes the healing process with functional deficiencies and scar formation (1). The goal of our study was to evaluate the regenerative capacity of peripheral muscle tissue upon injury of different severity.

**METHODS:**

For this purpose we used 90 male Wistar rats (275-325 g body weight) and under pentobarbital sodium anesthesia we induced a blunt injury of the left soleus muscle by using an instrumented clamp. The injury severity was stepwise increased by increasing the locking level of the clamp, resulting in three different experimental groups (1x lock; 2x lock; 3x lock; n=30 animals per group). Subsequent observations were performed at day 1, 4, 7, 14 and 42 after injury induction. After bilateral stimulation of the sciatic nerve fast twitch and tetanic forces of the left soleus muscle were analyzed and were given as percentage of the corresponding values of the contralateral non-injured muscle (2).

Sampling of muscle tissue served for analysis of cell proliferation (BrdU-immunohistochemistry and PCNA-western blot analysis), cell apoptosis (TUNEL-analysis), leukocyte infiltration (CAE-analysis) and muscle tissue area (HE histology - planimetric analysis). In addition, we analyzed the proliferating satellite cells and interstitial cells in the transitional zone between injured and non injured muscle tissue (BrdU/laminin double immunohistochemistry) as well as the ratio of fast and slow myofibers (fast myosin heavy chains and slow myosin heavy chains immunohistochemistry). All data are expressed as mean±standard error of the mean. Differences between groups and time points were assessed using a 2-way ANOVA and the statistical significance was set at p<0.05.

**RESULTS SECTION:**

Contraction force analysis demonstrated one day after trauma in all animals minimal values of muscle strength (fast twitch and tetany <20%) reaching a maximum at day 42. Significantly higher values of relative muscle strength was observed in the 1x group compared to the 2x and 3x group over 42 days.

Furthermore, as given by the quantitative analysis of BrdU-positive cells (Figure 1) and the densitometric western blot analysis of PCNA, during the first 4 days the cell proliferation was found to be significantly dependent on the severity of the muscle injury, in that the higher the severity, the higher the proliferation. A significant increase of satellite cell proliferation was noted 4 days after injury in 3x lock group compared to the 1x lock group. The interstitial cell proliferation was significantly and comparably increased in all groups regardless of the severity of the injury at day 4. At the same time, however, cell apoptosis was found increased in the 3x lock group compared to the 1x lock group (Figure 2). Local leukocyte infiltration was significantly increased at day 1 after trauma in the 3x lock group compared to the 1x lock group and the visible muscle tissue area was found significantly decreased during the first 7 days in 2x lock and 3x lock group compared to 1x lock group. At later time points the local leukocyte infiltration and the visible muscle tissue area was found comparably equal between the groups.

**DISCUSSION:**

Severe muscle injury causes incomplete restoration of the muscle force, is accompanied with a higher twitch-to-tetanic force ratio and results in a transient switch to a fast twitching phenotype of muscle. The degree of injury determines the increase of both proliferating cell activity and cell apoptosis. Furthermore the injury severity is relevant to the degree of leukocyte infiltration and the quantity of muscle tissue during the first days after trauma. These results indicate, that the increased cellular turnover after severe muscle injury is not always accompanied with increased muscle function.

**REFERENCES:**
