The effect of non-severe dorsal burn injury on the contractile properties of fast-twitch hind limb skeletal muscle of the mouse

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Loss of skeletal muscle function is the most common reason that prevents burn patients from returning to work (Cronan, Hammond & Ward. 1990). It is generally accepted that severe burn injury affects muscle function, possibly through systemic inflammatory changes. However the effect of non-severe burn injury on skeletal muscle function has not been investigated, despite this type of burn accounting for over 90% of the burn injuries in western countries (Chipp *et al.*, 2008; Morgan, Bledsoe & Barker, 2000). In this study, we examined the effect of non-severe dorsal burn injury on muscle mass and contractile function in the predominantly fast-twitch, *extensor digitorum longus* (EDL) muscle of the mouse.

Mice were anaesthetized with 4% isoflurane in O_2. The dorsal area was shaved and animals received a full-thickness, 2 cm diameter burn (6% of total body surface area) by contact for 9 seconds with a brass rod heated to 95°C. Buprenorphine (0.1 mg/kg) was administered immediately post-burn and additional analgesia was provided in drinking water (paracetamol, 0.01 mg/mL) for 5 days following the procedure. At 7, 28 or 84 days after burn injury, mice were anaethetized with pentobarbitone (40 mg/kg) and EDL muscles were excised and mounted onto a force transducer system. The muscles were bathed in Krebs Ringer solution (in mM; NaCl 137, $NaHCO_3$ 24, glucose 11, KCl 5, $CaCl_2$, NaH_2PO_4 1, $MgSO_4$ 1) with 0.025 mM d-tubocurarine chloride. The bath solution was bubbled with carbogen (5% CO_2 in O_2) and maintained at pH 7.3 and 25°C. Twitch force characteristics, maximum specific force levels and the rate of muscle fatigue were determined in EDL muscles from control and burn-injured mice. The effects of burn-injury on the contractile apparatus of EDL fibres was determined using the skinned fibre technique. EDL fibres were isolated under paraffin oil, tied to a sensitive force transducer and chemically skinned by exposure to Triton X-100 for 12 minutes. Fibres were then exposed to highly Ca^{2+}-buffered EGTA-based solutions of increasing, known free Ca^{2+} concentration and the resulting force responses measured.

The mean mass of the EDL muscles from burn injured and control mice were not significantly different at any time point. At day 7, maximum specific force (N/cm^2) was significantly elevated in EDL muscles from burn injured mice (116% of controls, P<0.05). However, after 28 days maximum specific force was found to be significantly lower in EDL muscles from burn injured mice compared to controls (82% of controls, P<0.01). After 84 days, maximum specific force was still significantly lower in EDL muscles from burn injured mice compared to controls (86% of controls, P<0.05). No significant difference in the rates of muscle contraction or relaxation or the rate of muscle fatigue were found between EDL muscles from burn-injured and control mice, at any time point. Skinned fibres from burn injured EDL muscles exhibited significantly greater maximum force at day 7 ($P \leq 0.01$) compared to controls. However, no differences in maximum specific force were found between groups at day 28 and day 84 post-injury.

These results indicate that non-severe burn injuries cause significant long-term contractile deficits in remotely located hind-limb skeletal muscles. These effects were not related to skeletal muscle atrophy or direct effects on the contractile apparatus. If similar effects occur in humans, non-severe burn injury-related muscle weakness may be an important factor impeding patient recovery.

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Cronan T, Hammond J, Ward CG. (1990) The value of isokinetic exercise and testing in burn rehabilitation and determination of back-to-work status' *Journal of Burn Care and Rehabilitation* **11:** 224-7.

Morgan ED, Bledsoe SC, Barker J. (2000) Ambulatory management of burns. *American Family Physician* **62:** 2015-26, 2029-30, 2032.