Continuous testosterone administration prevents skeletal muscle atrophy and enhances resistance to fatigue in orchidectomized male mice

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Androgens promote anabolism in skeletal muscle; however, effects on subsequent muscle function are less well defined because of a lack of reliable experimental models. We established a rigorous model of androgen withdrawal and administration in male mice and assessed androgen regulation of muscle mass, structure, and function. Adult C57Bl/6J male mice were orchidectomized (Orx) or sham-operated (Sham) and received 10 wk of continuous testosterone (T) or control treatment (C) via intraperitoneal implants. Mass, fiber cross-sectional area (CSA), and in vitro contractile function were assessed for fast-twitch extensor digitorum longus (EDL) and slow-twitch soleus (SOL) muscles. After 10 wk, Orx+C mice had reduced body weight gain (P < 0.05), seminal vesicle mass (P < 0.01), and levator ani muscle mass (P < 0.001) compared with Sham+C mice, and these effects were prevented with testosterone treatment. Orx+T mice had greater EDL (P < 0.01) and SOL (P < 0.01) muscle mass compared with Orx+C mice; however, median fiber CSA was not significantly altered in these muscles. EDL and SOL muscle force was greater in Sham+T compared with Orx+C mice (P < 0.05) in proportion to muscle mass. Unexpectedly, Orx+T mice had increased fatigue resistance of SOL muscle compared with Orx+C mice (P < 0.001). We used a rigorous model of androgen withdrawal and administration in male mice to demonstrate an essential role of androgens in the maintenance of muscle mass and force. In addition, we showed that testosterone treatment increases resistance to fatigue of slow- but not fast-twitch muscle.