Downregulation of VEGFA Impairs Post-traumatic Senile Muscle Regeneration

Presenter: Charles D Hwang, MD

Co-Authors: Yori Endo, PhD, Yuteng Zhang, PhD, Ronald L Neppl, PhD, Shailesh Agarwal, MD, Indranil Sinha, MD

Affiliation: Harvard University, Boston, MA

Purpose: The population representing trauma in adults aged >65 years alone are projected to increase financial burden on the healthcare system by nearly $375 billion. Aging is associated with frailty, a parameter that correlates significantly with mortality and muscle density. Our group demonstrated the critical regulatory function of upstream hypoxia signaling (ARNT/HIF-1ß) on skeletal muscle response to trauma. We hypothesized VEGF to critically differentiate regeneration in injured skeletal muscle.

Methods: Youn C57BL/6 mice (10-12 wks), old C57BL/6 mice, and mid-age VEGFlo and littermate controls (LC) (10mo) were subjected to a previously validated model of 10 sec muscle cryoinjury (n=3-6/group). Injured muscles were harvested after 5 or 10 days. Western blots were performed from WT whole TA muscle lysates for quantification of VEGFA.

Results: Old mice demonstrated markedly impaired ability to regenerate robust myofibers at 5 days post-injury (Young vs. Old: 526 vs. 373 mm², p<.001) and with even greater disparity by 10 days (Y v. O: 1250 vs. 833 mm², p<.001). VEGFA protein content between young and old muscle demonstrated marked reduction of this pro-vascular/differentiation signal with age. We applied the injury model within transgene mice that express 25-50% of native VEGFA activity (VEGFlo) vs. their LCs and successfully recapitulated similar trends of impaired muscle regeneration (WT vs. lo: 541 vs. 238 mm², p=.0011).

Conclusions: Muscle regeneration becomes less robust with age. This impairment in senile post-traumatic muscle regeneration is correlated with VEGFA, whose attenuation similarly leads to impaired muscle healing in age matched cohorts.

Is a Third Attempt of Breast Reconstruction Worth It? Analysis of Outcomes of Infection-associated Failed Secondary Implant-based Reconstruction

Presenter: Abbas M Hassan, MD

Co-Authors: Jackie Tran, MD, Malke Asaad, MD, Cedar Slovacek, BS, Jun Liu, PhD, Charles E Butler, MD

Affiliation: Northwestern Feinberg School of Medicine, Chicago, IL

Background: Implant-based reconstruction is the most common method of breast reconstruction in the United States. Despite ongoing advancements, periprosthetic infection is a serious problem that often results in device explantation. The objective of this study was to evaluate the outcomes of third-attempt reconstruction in patients in whom secondary implant-based reconstruction failed owing to infection.

Methods: The authors performed a retrospective review of patients who underwent mastectomy followed by implant-based reconstruction from 2000 to 2019. The outcomes of patients who had failed secondary implant-based reconstruction due to infection and ultimately underwent third-attempt breast reconstruction were analyzed.

Results: Of 6,093 patients who underwent primary implant-based reconstruction, 13 patients had third-attempt breast reconstruction following infection-related explantation (median age, 52 [51-56] years; median body mass index, 23 [22-31] kg/m²; median follow-up of 46 [16-62] months). Nine patients (70%) had implant-based reconstruction, two (15%) had implant-based reconstruction combined with pedicled latissimus dorsi flap, and two (15%) had abdominal-based free tissue transfer. Third-attempt breast reconstruction was immediate in 46% of patients and delayed in 54%. The success rate was 78% in the implant-based reconstruction group, with a 23% complication rate. The success rate for autologous breast reconstruction was 100%, with one patient developing venous congestion necessitating return to the operating room.

Conclusion: Third-attempt breast reconstruction following infection-associated failed secondary implant-based reconstruction is a safe and feasible option. Although the risk of failure is higher than that for primary implant-based reconstruction, a third attempt after secondary IBR infection had a surprisingly high 78% success rate.