Ex Vivo Normothermic Limb Perfusion and Limb Specific Monitoring Evaluation of Perfusion Quality

Eliana F R Duraes, MD; Maria Madajka, PhD; Basem Soliman, MD; Cagri Cakmakoglu, MD; Stephanie Kortyka, MD; Addison Barnett, BA; Russell Frautschi, BS; Kashyap Tadisina, MD; Qiang Liu, MD; Toshihiro Okamoto, MD, PhD; Cristiano Quintini, MD; Francis Papay, MD; Antonio Rampazzo, MD; Bahar Bassiri Gharb, MD, PhD

Purpose: Ischemia time represents a significant limitation for successful extremity replantation and transplantation because of the rapid deterioration of ischemic muscle. Static cold storage (SCS) of the limb is the standard clinical practice. Normothermic ex vivo perfusion system has the potential to prolong viability providing oxygen and metabolites after limb amputation. The aim of our study was to establish a perfusion protocol with limb specific diagnostic tools to evaluate the quality and uniformity of perfusion in an ex vivo model.

Methods: A total of 18 swine limbs were perfused, five of them followed the final, optimized protocol. Limbs were perfused at 39^{O}C for twelve hours using an oxygenated colloid solution with packed red blood cells. Glucose and electrolytes were kept within physiologic range by the addition of hypertonic solution or by partial hypotonic perfusate exchanges. Limb specific perfusion quality was assessed by muscle contractility upon electrical nerve stimulation, compartment pressure, creatine kinase(CK) and myoglobin concentrations, tissue oxygen saturation (near infrared spectroscopy), indocyanine green (ICG) angiography, and infrared radiation emission by thermographic imaging.

Results: All five limbs reached the 12 hour perfusion target maintaining normal compartment pressure (16.23±7.94 mmHg), minimal weight increase (0.54%±0.07), mean muscle temperature of 33.54±1.5^{o}C, and tissue oximetry readings of 59.67%±10.21. Average values of final myoglobin and CK were 875±291.4 ng/mL, and 53344±14850.34 U/L, respectively. Muscle movement was present in all limbs until cessation of perfusion. Differences in uniformity and quality of distal perfusion were demonstrated using thermography and angiography imaging after 12 hours of perfusion. Colder areas on Thermographic imaging correlated to mal perfused areas on ICG angiography.

Conclusions: Ex-vivo normothermic limb perfusion preserves limb physiology and function for at least 12 hours. Thermography and ICG angiography are valuable tools in the assessment of limb perfusion quality with the advantage of providing an immediate evaluation which allows for the visual identification of perfusion gradients and regions of mal-perfusion. Muscle contraction upon nerve stimulation, a uniform physiologic temperature and tissue oxygenation, and the distal dye distribution on angiography identify a successful perfusion. These methods may have important future implications on the decision to transplant or replant a perfused limb. Myoglobin and CK concentration increased in all limbs during ex vivo perfusion, but the functional significance of this is still to be determined.