Effects on Lower Extremity Perfusion When the Lower Extremity Extracorporeal Distal Revascularization (LEEDR) System is Used for Arterial Shunting

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Method Article

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Abstract

Traumatic injuries to the pelvis, extremities, or extremity vessels have improved outcomes when there is early restoration of perfusion (Laverty et al, Hancock et al). An ex-vivo shunting device, such as the Lower Extremity Extracorporeal Distal Revascularization (LEEDR) system, offers a potential solution to perfuse an ischemic limb in situations where definitive repair is not available, or transfer or delay is inevitable. A large animal model is required to optimize the surgical technique and management strategies. Acknowledging the morphological differences between bipeds and quadrupeds (Edwards et al), the aim of this study is to use a model of prolonged extremity ischemia to determine whether a LEEDR system can be used to mitigate ischemia by reducing compartment pressures and the need for fasciotomies following reperfusion. We sought to develop a method where an extracorporeal shunt from the contralateral common femoral artery to the ipsilateral tibial artery in the setting of limb ischemia to provide distal perfusion. Following a period of controlled ischemia, we developed a model with a low resistance circuit and 150 mL/min pump to perfuse an ischemic extremity at a distal point utilizing the contralateral proximal femoral vessel as outflow.

Introduction

Vascular trauma injuries can cause significant destruction in military and civilian trauma settings (Morrison et al, Chipman et al). Early restoration of perfusion in patient with traumatic vascular injuries is associated with less complications and improved outcomes (Laverty et al, Hancock et al). Damage control techniques, such as intravascular shunts, can be used as temporizing measures to restore and maintain perfusion in order to manage other life-threatening injuries or physiological derangements (Laverty et al, Hancock et al, Stonko et al). Reperfusion of an injured extremity has the potential to cause devastating limb complications, such as ischemia-reperfusion injury and compartment syndrome. Such complications can be avoided through early perfusion of an injured extremity.

Complex vascular injuries, such as blast or crush injuries, may not be an optimal situation for shunt use and could increase the risk of amputation. Additionally, the acceptable duration of shunt placement has not been determined, primarily in combat care settings where long transport times or delays in transport are common (Laverty et al). Due to the limitations of open shunt placement, the ability to perfuse a limb in settings that are not amenable to shunts offers the opportunity to salvage a limb in both extreme injury and austere environments.

An ex-vivo shunting device, such as the Lower Extremity Extracorporeal Distal Revascularization (LEEDR) System, offers a potential solution to perfuse an ischemic limb in unfavorable situations. However, a large animal model is required to optimize the technique. Swine are often suitable models with similar physiology and vascular anatomy (Edwards et al.) Because swine are quadruped animals, it is important

to note there are intrinsic differences in extremity anatomy. Femoral and iliac vessels are smaller caliber in regard to both diameter and length with the femoral artery travelling medially compared to humans (Edwards et al).

The posterior tibial artery would be the ideal target for distal cannulation in humans; however, due to the morphological differences of swine, the cannulation process must be modified. **We sought to develop a swine model of an ex-vivo shunt from the contralateral common femoral artery to the ipsilateral tibial artery to provide perfusion in the setting of a model of prolonged limb ischemia.**

Reagents

1. Telazol (5 mg/kg)

2. Xylazine (2 mg/kg)

3. Isoflurane (Sigma-Aldrich, SKU 792632-250MG)

4. Heparin Sodium (10000 Units/10cc)

5. Dextrose 50% (0.5 g/mL)

6. Formalin (Sigma-Aldrich, SKU HT501128-4L)

Equipment

Access and Circuit:

1. 5 Fr micro-puncture access kit (Cook Medical, Bloomington, USA; MPIS-502-NT-U-SST)

2. 10 cm 7 Fr sheath (Terumo, Elkton, NJ; REF/Product Code RM*RS7F10PA)

3. 11 cm 8 Fr sheath connected to 38 cm large diameter tubing

4. Masterflex Digital Pump L/S (EW-07525-20; Cole Palmer, Vernon Hills, IL)

Monitoring:

1. 6mm flow probe (ADInstruments, Series MA-6-PS-ori, MA-12-PAU, and MA-16-PAU)

2. Pressure catheter (5 F, Dual, Straight, 3 cm, 120 cm, PU/WD; SPR-751S or SPR-75)

3. Rectal temperature probe (ADInstruments, Large Animal Rectal Probe (RET-1))

Imaging and Labs:

1. C-arm for fluoroscopy (OEC 9800, General Electric, Boston, USA)

2. Bedside US system, such as Phillips Lumify App and US Probes (Phillips, NV, USA; https://www.usa.philips.com/healthcare/sites/lumify/lumify-android-app)

3. iSTAT 1 (Abbott Labs; https://www.pointofcare.abbott/us/en/offerings/istat/istat-handheld#specs)

4. iSTAT test cartridges for arterial blood gas (ABG) (Abbott Labs; https://www.pointofcare.abbott/us/en/offerings/istat/istat-test-cartridges)

5. ABL800 FLEX blood gas analyzer with 18 STAT parameters (Radiometer, Brea, CA)

Anesthesia Supplies:

1. Mechanical ventilator with isoflurane vaporizer (Drager Fabius GS; DFABIUSGS).

2. Endotracheal Tube 28 French 7.0mm 10/bx Endotrol (SAM Medical: 026351)

3. Ventilator tubing, air, gas tanks, lines, and CO2 absorber (Dragersorb 800+)

Other:

1. 0.9% Normal Saline, 1L bags

2. Infusion Tubing (BD: SKU 10013365)

3. Prefilled 10 cc 0.9% Saline Syringes (BD-9104 BD PosiFlush Saline Syringe)

4. Masterflex Digital Pump L/S (EW-07525-20; Cole Palmer, Vernon Hills, IL)

5. Various sutures (Proline, 3-0 to 5-0; Vicryl, 0 to 5-0)

6. Foley bag and Foley catheter (SKU: JOR1027 and FC30X12)

Procedure

Animal Model: 50-70kg adult male Yorkshire swine

Continuous Monitoring: Mean arterial pressure, heart rate, femoral vein flow, compartment pressure, arterial blood gas, and temperature.

Control Group: Animals grouped into an interventional group (LEEDR reperfusion) or a control group (no LEEDR).

Phase 1: Animal Preparation and Instrumentation

1. Sedate the animal with Telazol (5mg/kg) and Xylazine (2mg/kg) and transport animal to procedure room.

2. Initiate isoflurane via facemask with a targeted MAC of 1.0 and FiO2 of 40%.

3. Position the animal prone and intubate with a 7.0 mm endotracheal tube.

4. Initiate general anesthesia at 10cc/kg tidal volume and respiratory rate of 12-14 with a target pCO2 of 30-45 and FiO2 of 40%.

5. Place Bovie pad and EKG leads after shaving animal as needed.

6. Place the animal in a supine position and place animal in restraints for safety and immobilization.

7. Place a 7 Fr sheath into the brachial artery percutaneously with US-guided and insert a solid-state pressure catheter in the aorta.

8. Perform a laparotomy to access the pelvis.

9. Perform a cystostomy with foley catheter placement into the bladder.

10. Expose the aortic trifurcation, dissect, and control the left iliac artery and middle sacral artery with vascular ties for later use.

11. Place an 8 Fr sheath into the right common femoral artery percutaneously using an ultrasound guided technique for LEEDR circuit inflow.

12. Expose the left tibial artery and vein through a cut-down technique and cannulate the artery with an 8 Fr catheter for LEEDR circuit outflow.

13. Place a 6mm flow probe around the left femoral vein for continuous blood flow monitoring throughout experiment.

14. Insert a pressure catheter into the anterior compartment of the lower extremity for continuous pressure monitoring.

15. Perform a timeout to identify any technical or instrumentation errors.

Phase 2: Baseline Data (30 Minutes)

1. Administer 1L of 0.9% normalized saline (NS) and 50ccs of D50 prior to baseline data collection.

2. Obtain arterial blood for an arterial blood gas (ABG) test at the start of the baseline period.

3. Initiate a timer for 30 minutes during baseline period and monitor animal physiology parameters (MAP, pH, ventilation).

Phase 3: Limb Ischemia (1 Hour)

1. Heparinize the animal with 10K units of heparin followed by heparin every 90 minutes.

2. Clamp the left iliac artery and middle sacral artery to produce ischemia in the left limb.

3. Collect arterial blood and run the ABG test every 60 minutes.

4. Monitor animal physiologic parameters (MAP, pH, ventilation).

Phase 3a: Determining Flow Rate Prior to Study

1. Connect the tubing from the 8 Fr inflow (ipsilateral tibial artery) and 8 Fr outflow (contralateral common femoral artery) catheters utilizing connectors that are designed to preserve the flow and pressure of the circuit tubing.

2. Place circuit tubing into the digital pump.

3. Perform a stepwise progression of flow rates until the femoral vein flow returns to 60-70% of baseline values: (1) Passive, (2) 50 mL/min, (3) 100 mL/min, and (4) 150 mL/min.

4. The 150 mL/min blood flow rate proved optimal in regaining a minimum of 60-70% baseline venous flow.

Phase 4: Limb Reperfusion with LEEDR (5 Hours)

1. Connect the tubing from the 8 Fr inflow (ipsilateral tibial artery) and 8 Fr outflow (contralateral common femoral artery) catheters.

2. Insert the tubing into the digital pump and set the pump to 150 mL/min to allow blood to flow from the right common femoral artery into the left tibial artery.

3. Continue to heparinize the animal with 10K units of heparin followed by heparin every 90 minutes.

4. Collect arterial blood and run the ABG test every 60 minutes.

5. Monitor animal physiologic parameters (MAP, pH, ventilation).

6. At the end of the five-hour period prior to unclamping the left iliac and middle sacral arteries, perform muscle and nerve biopsies and store in formalin for histological analysis.

Phase 4: Post-Reperfusion Modeling (3 Hours)

1. Turn off the circuit flow and remove clamp from the left iliac artery and middle sacral artery.

2. Allow limb to recover without ex-vivo perfusion from the circuit.

3. Continue to heparinize the animal with 10K units of heparin followed by heparin every 90 minutes.

4. Collect arterial blood and run the ABG test every 60 minutes.

5. Monitor animal physiologic parameters (MAP, pH, ventilation).

Phase 5: End of Study

1. Euthanize the animal and properly dispose following protocol.

2. Clean all equipment and instruments used during the study.

Troubleshooting

Time Taken

Estimated 2 hours for instrumentation, 30 minutes for baseline, one hour for lower extremity ischemia, 5 hours of lower extremity reperfusion using the LEEDR circuit, and 3 hours of recovery with the circuit off and arteries unclamped. **Total time is a minimum of 11.5 hours per animal.**

Anticipated Results

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Figures

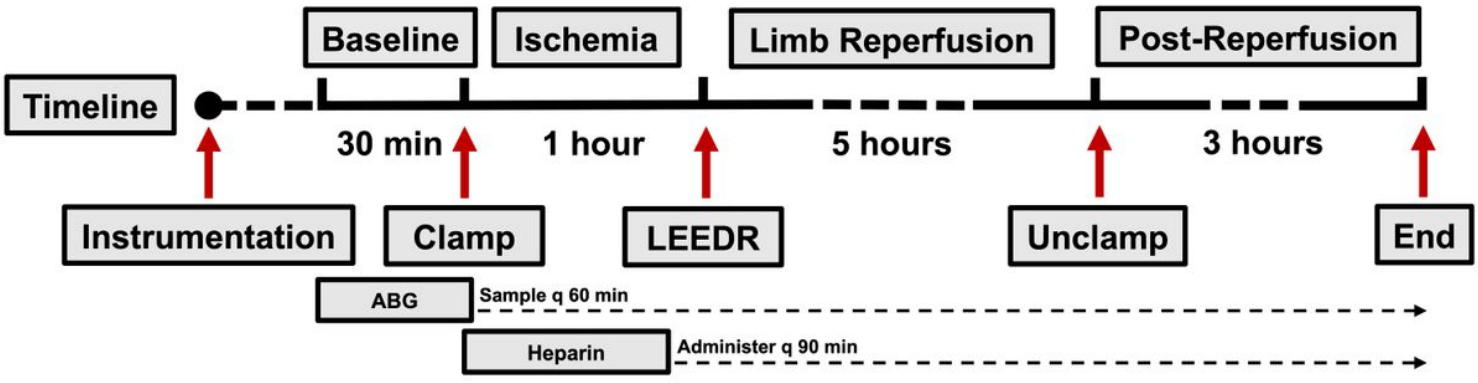

Figure 1

Study protocol timeline for animals who received arterial shunting with the Lower Extremity Extracorporeal Distal Revascularization (LEEDR) system. The protocol begins with instrumentation, a baseline period, one hour of ischemia, five hours of LEEDR circuit reperfusion, and three hours of post-reperfusion. Arterial blood gas samples were taken every (q) 60 minutes and heparin was administered every 90 minutes. Animals who did not receive LEEDR remained in the ischemia phase until unclamping prior to post-reperfusion phase.

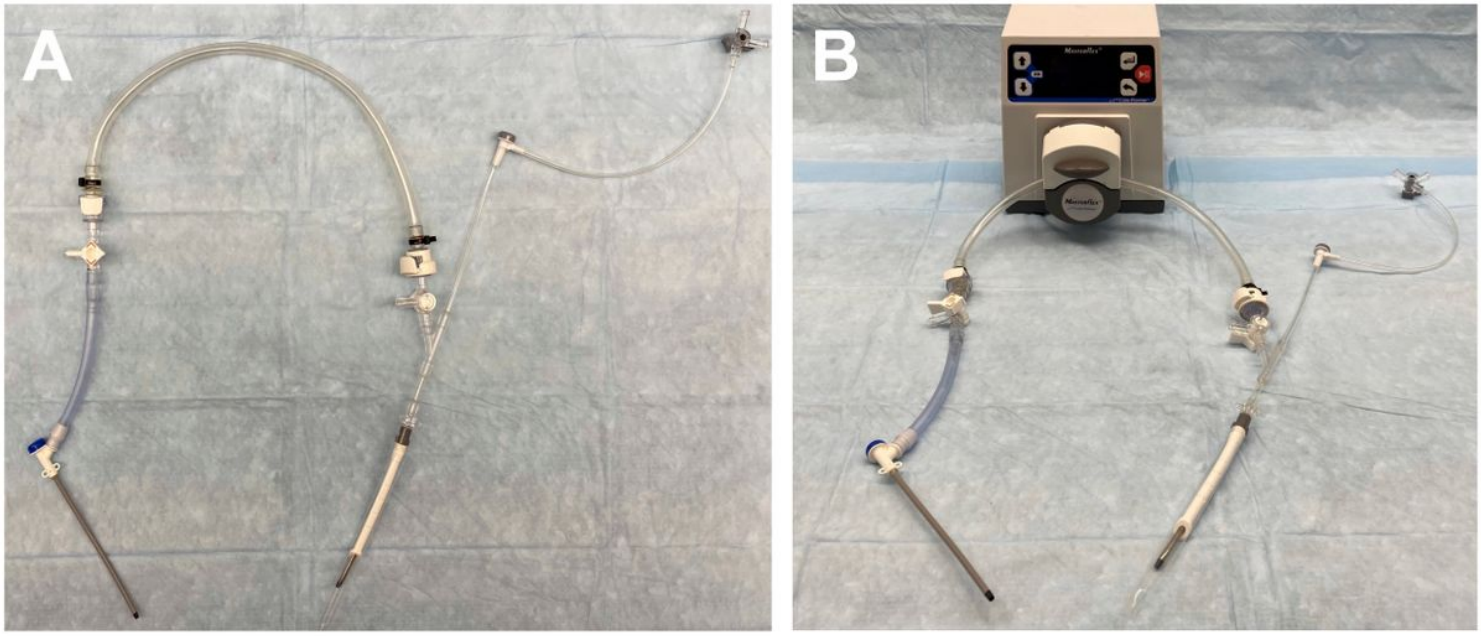

Figure 2

The LEEDR circuit set up (A) with outflow cannula on the right and inflow cannula on the left and (B) the digital pump connected to the LEEDR circuit.

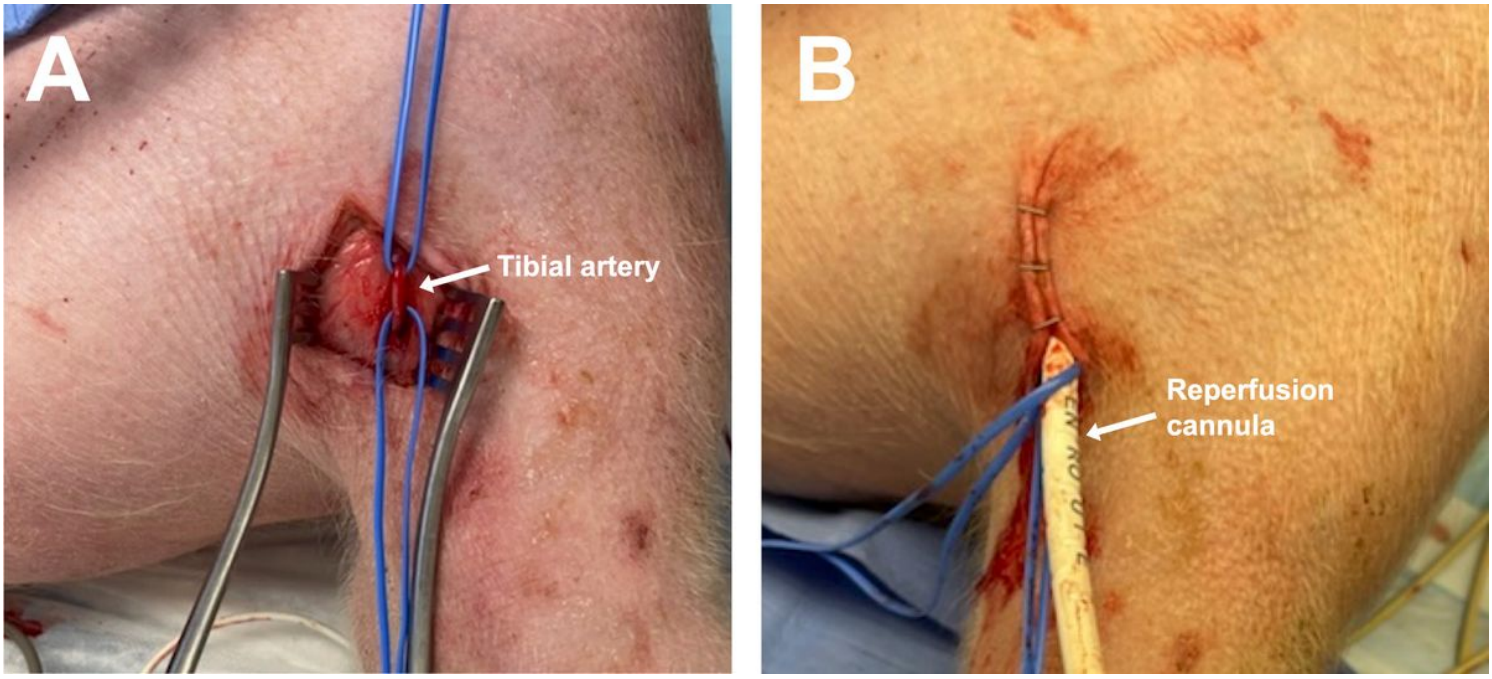

Figure 3

(A) Surgical exposure of the left tibial artery and (B) cannulation of the tibial artery for reperfusion of the limb.

Figure 4

Angiogram of the left tibial artery with the reperfusion cannula in place demonstrating reperfusion.