Effects of Hemorrhagic Shock and Resuscitation on Mesenteric Circulation

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Method Article

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Abstract

Vascular beds may be variably affected by hemorrhage, which may have implications for resuscitation. The vascular anatomy of swine has been described with focus on its use for vascular and endovascular research; however, current research has predominantly focused on anatomy. (1,2) There is a lack of research regarding the physiology of mesenteric circulation at baseline physiology, as well as during hemorrhagic shock and resuscitation. **The aim of this study was to develop a large animal model to characterize the implications of hemorrhage on mesenteric circulation and reperfusion.** We constructed a surgical protocol to measure intestinal perfusion, as well as pressure and flow data of the superior mesenteric artery (SMA), portal vein, inferior vena cava (IVC), and aorta.

Introduction

Reagents

1. Telazol (5 mg/kg)
2. Xylazine (2 mg/kg)
3. Heparin Sodium (10000 Units/10cc)
4. Norepinephrine (0.2-0.3 mcg/kg/min)
5. Epinephrine (0.2-0.3 mcg/kg/min)
6. Calcium carbonate (50 mEq/50 mL)
7. Dextrose 50% (0.5 g/mL)

Equipment

Access:

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. Amplatz 0.035, 180cm wire (Boston Scientific: M001465250; <https://www.esutures.com/search/in-date,short-dated/search/benson%20wire>)
4. Benson 0.035, 85 cm wire (Cook Medical: TSFB-35-80; https://www.cookmedical.com/products/di_tsfb_webds/)

Monitoring:

1. Flow probes, 6mm, 12mm, and 16mm (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-751
3. Laser doppler probe, 18-gauge needle (Transonic Corporation, Ithaca, NY; Type N-ABLPHN18)
4. 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) (available: <https://www.usa.philips.com/healthcare/sites/lumify/lumify-android-app>)
3. iSTAT 1 (Abbott Labs; available: <https://www.pointofcare.abbott/us/en/offerings/istat/istat-handheld#specs>)
4. iSTAT test cartridges for Lactate, Chemistry (Abbott Labs; available: <https://www.pointofcare.abbott/us/en/offerings/istat/istat-test-cartridges>)
5. ABL800 FLEX blood gas analyzer with 18 STAT parameters (Radiometer, Brea, CA; available: <https://www.radiometeramerica.com/en-us/products/blood-gas-testing/abl800-flex-blood-gas-analyzer>)

Anesthesia Supplies:

1. Mechanical ventilator capable of providing general anesthesia with an 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. Digital pump for medication infusion (Digipump SR31x)
4. Prefilled 10 cc 0.9% Saline Syringes (BD-9104 BD PosiFlush Saline Syringe)
5. Preprogrammable peristaltic pump (Masterflex, Gelsenkirchen, Germany)
6. Various sutures (Proline, 3-0 to 5-0; Vicryl, 0 to 5-0)
7. Foley bag and Foley catheter (SKU: JOR1027 and FC30X12)

Procedure

Order 50-70kg adult male Yorkshire swine and prepare for five study phases: (1) Animal preparation and instrumentation (2) Baseline data (3) Controlled hemorrhage (4) Hemorrhagic shock, and (5) Resuscitation.

I. Animal Preparation and Instrumentation: (Variable time)

1. Anesthetize the animal with Telazol (5mg/kg) and Xylazine (2mg/kg).
2. Transport animal to the procedure room.
3. Initiate isoflurane via facemask targeting a 1.0 MAC followed by prone intubation with a 7.0 endotracheal tube.
4. Transition to general anesthesia at 10cc/kg TV and RR of 12-14 with a target pCO₂ of 30-45 and FiO₂ of 40%, adjusted as needed.
5. Place Bovie pad and EKG leads after shaving as needed.
6. Place the animal in supine and restrain.
7. Insert percutaneous US-guided venous and arterial access with appropriate catheter placement:
 - a. 7 Fr sheath in bilateral femoral arteries.
 - i. Place an aortic pressure probe in either the right or left femoral artery line.
 - ii. Connect the Masterflex peristaltic pump to the alternate femoral artery line.
 - b. 7 Fr sheath in either femoral vein.
 - i. Place an IVC pressure probe in the femoral vein line.
 - c. 7 Fr sheath in either jugular vein.

- i. Reserve this line or another venous line for fluid administration.
- d. 7 Fr sheath in either carotid artery.
- i. Reserve this line for arterial blood samples.
- ii. If performing endovascular placement of the pressure catheter directly into the SMA, utilize a hydrophilic guide wire and angled catheter via the carotid artery cannula.
- 8. Administer 1L of 0.9% normalized saline (NS) prior to surgical exposures.
- 9. Perform a full abdominal laparotomy.
- 10. Perform a cystostomy with foley catheter placement into the bladder.
- 11. Perform a splenectomy to prevent autotransfusion during the hemorrhagic phase.
- 12. Perform a full left medial visceral rotation for exposure of the proximal SMA.
 - a. Place a 6mm flow probe around the SMA (adjust flow probe diameter as needed).
- 13. Perform a partial right medial visceral rotation for exposure of the IVC, SMV, and portal vein.
 - a. Place a 12mm flow probe around the distal portal vein (adjust flow probe diameter as needed).
 - b. Place a 16mm flow probe around the IVC (adjust flow probe diameter as needed).
 - c. Place a 5 Fr sheath in the portal vein directly above the flow probe, then introduce a pressure catheter.
- 14. Confirm fluoroscopically that all catheters and devices are appropriately positioned.
- 15. Perform a TIMEOUT.
 - a. Confirm appropriate line placements, confirm all sheaths are patent, confirm the timer is ready, confirm all pressure and flow data is transducing properly.
 - b. Confirm all LabChart connections and channels are appropriately labeled.

II. Baseline Phase: (60 min)

- 1. Initiate a timer of 60 minutes for baseline normalization period.
- 2. Start 0.9% NS and administer 50cc of Dextrose50 (D50).

3. Obtain a ABG and 1 tube of serum at the end of the 60 minutes.
4. Provide D50, bicarbonate, or alterations to the ventilator settings as needed for maintaining a stable physiologic state.

III. Begin Controlled Hemorrhage: (Variable time)

1. Administer 10,000 Units of Heparin intravenously prior to controlled exsanguination.
2. Connect the peristaltic pump to the femoral vein with the output end connected to a Heparinized bag.
3. Prior to beginning study protocol, program the peristaltic pump for a pressure-driven model with a target systolic blood pressure of 50 mmHg.
4. Set the peristaltic pump rate to 50mL per min until SBP of 50 mmHg is obtained.
5. Place the shed blood into a Heparinized bag.

IV. Hemorrhagic Shock Phase: (60 min)

1. Keep the animal in a state of hemorrhagic shock during this period with careful observation of SBP, MAP, and TV.
2. Collect 1 ABG and 1 serum sample per 30 minutes (Total 2 ABG, 2 Serum).

V. Resuscitation Phase: (120 min)

1. Resuscitation animal until lactic acidosis clears completely.
2. Return the shed blood to the animal via the peristaltic pump and initiate IV 0.9% NS or Lactated Ringers (LR).
3. Provide D50, calcium carbonate, norepinephrine, and epinephrine as needed throughout resuscitation to regain baseline systolic pressure.
4. Adjust ventilator settings as needed for resuscitation to normal physiologic state.
5. Collect 1 ABG and 1 serum sample per 60 minutes (Total 2 ABG, 2 Serum).
 - a. Obtain 5 samples of serum, centrifuge at 3,000 rpm for 15 minutes, aliquot into 1mL sample tubes, and freeze at -20°C for later analysis.

VI. End of Study:

1. Euthanize the animal and follow proper disposal protocol.
2. Clean all equipment used.

Troubleshooting

Time Taken

Time Taken:

1-2 hours for instrumentation, 1 hour for baseline, 30 min for hemorrhage, 1 hour for hemorrhagic shock, and 2 hours for resuscitation. **Total time is approximately 8 hours per animal.**

Anticipated Results

References

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Figures

Figure 1

Flow chart of the instrumentation process simplified and condensed into three stages: (1) Preparation of animal, (2) Vascular access, and (3) Laparotomy.

Figure 2

Study protocol timeline depicting the start at baseline data collection following instrumentation. After baseline data collection, the animal undergoes controlled hemorrhage to a target systolic blood pressure (SBP) of less than 50 mmHg. The animal is left in a state of hemorrhagic shock for 60 minutes followed by resuscitation to SBP with clearance of lactic acidosis for 120 minutes.

TABLE 1. Example data table for anticipated results following completion of protocol.

Variable	Baseline (N=#)	Shock (N=#)	Resuscitation (N=#)
Lactate T-1 (+/- SD) mmol/L			
Lactate T-2 (+/- SD) mmol/L			
MAP (+/- SD)			
SMA flow (+/- SD) mL/min			
SMV flow (+/- SD) mL/min			
IVC flow (+/- SD) mL/min			
SMA pressure (+/- SD) mmHg			
SMV pressure (+/- SD) mmHg			
IVC pressure (+/- SD) mmHg			
Intestinal LDF (+/- SD)			
Heart rate (+/- SD) bpm			
Volume exsanguinated (+/- SD) mL			
Percent blood lost			

T-1, First timepoint of lactate for study period; T-2, Second timepoint of lactate for study period; MAP, Mean arterial pressure; SMA, Superior mesenteric artery; SMV, Superior mesenteric vein; IVC, Inferior vena cava

Figure 3

Example table for anticipated results of each study phase including the lactate values, MAP, pressure data, flow data, intestinal perfusion, heart rate, and exsanguination characteristics.