Journal of Surgical Research **152,** 249–257 (2009)
doi:10.1016/j.jss.2008.02.058

Establishment of an Acute Superior Mesenteric Artery Injury Model for Damage Control Surgery

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Submitted for publication November 25, 2007

Background. **Managements of superior mesenteric artery (SMA) injuries are difficult and often result in a disappointing outcome. Damage control surgery (DCS) has been approved to be an effective and reliable strategy for severe trauma victims. We aimed to build up a severe trauma-shock-hypothermia model of SMA injuries for DCS study and determine the optimal time to institute DCS.**

Methods. **Pigs were anesthetized and instrumented with arterial and a thermodilution cardiac output catheter. SMA flow was interrupted while animals were hemorrhaged to 45% estimated blood volume. Pigs were maintained shock and intestine ischemia for three durations: intestine ischemia for 30 min (I-30; $n = 6$), 60 min (I-60; $n = 6$), and 90 min (I-90; $n = 6$). Cold lactated Ringer's (10 mL/kg) was infused to induce hypothermia. SMA was then declamped and kept in reperfusion for 6 h. Hemodynamic data and serum samples were collected during shock and resuscitation. Distal ileum was collected at the end of ischemia and reperfusion.**

Results. **All animals presented with disastrous conditions at the end of ischemia: low temperature, severe acidosis, decreased blood pressure, depressed cardiac output, and oxygen delivery. I-90 animals suffered the lowest temperature, the most severe acidosis, lowest blood pressure, and depressed cardiac output and oxygen delivery. Coagulopathy developed in I-90, whereas normal prothrombin time and thrombin time were detected in I-30 and I-60. Aspartate aminotransferase, lactate dehydrogenase, creatine kinase, and alkaline phosphatase were equally within groups ($P > 0.05$). All (6/6) of I-30, 83.3% (5/6) of I-60, and 16.7% (1/6) of I-90 pigs survived ($P < 0.01$). Base excess in I-90 was much lower than that in I-30 and I-60 animals.**

Conclusions. **We first built up an acute SMA injury animal model for DCS investigations and determined that the optimal institution time of DCS was before 60 min after SMA injury in the trauma-shock-hypothermia swine model.**

Key Words: **superior mesenteric artery; SMA injury model; damage control surgery; ischemia.**

INTRODUCTION

Injuries to the superior mesenteric artery (SMA) are rare but highly lethal. Asensio *et al.* [1] reported an incidence of less than 1%, mostly due to penetrating trauma in young males, with a mortality rate of 39–77% for those presenting with proximal mesenteric artery injuries. It is characterized by multiple associated injuries, such as small bowel, liver, colon, pancreas, duodenum, stomach, portal vein, and the inferior vena cava [2]. Because of complex anatomy, high possibility of concomitant injuries, and exsanguinating hemorrhage, the victims often present with a moribund situation and need a strategy of damage control surgery (DCS).

The strategy of DCS is usually used in the massively injured, exsanguinating patients with the triad of hypothermia, acidosis, and coagulopathy. However, most experiences are obtained from clinical or military managements, and little experimental investigations are found in literature. Establishment of austere conditions, such as hemorrhage shock-hypothermia-coagulopathy, may be not complex, but to build up a reliable, reproducible animal model and determine the right institution time of DCS is extremely difficult. Retrospective clinical analyzes [3–7] have proposed different predictive mod-

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0022-4804/09 $36.00

els to evaluate the survivals, yet the optimal institution time is still ambiguous.

Temporary intravascular shunts, pioneered by Eger [8], are now widely used as an essential approach of DCS in combined orthopedic and extremity vascular injuries during the war [9–11] and civil time [12–14]. We presumed that temporary shunts could be used as an important adjunct of DCS in SMA injuries; and as the first part of our series investigations, we aimed to build up a severe trauma-shock-hypothermia model for further study and determine the optimal time to institute DCS in this model.

MATERIALS AND METHODS

Surgical Preparation

This study was approved by the Institutional Animal Care and Use Committee of Nanjing University and followed national guidelines for the treatment of animals. Eighteen domestic female pigs (weight 28.0 ± 2.5 kg) were used for the study. After an overnight fast with water *ad libitum*, swine were premedicated with ketamine (20 mg/kg) and atropine (0.06 mg/kg). After endotracheal intubation, the animals were ventilated mechanically. Animals were maintained and anesthetized with intravenous injection of 150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ propofol (Disoprivan 2%, emulsion; Astra Zeneca, Wedel, Germany) and bolus injection of 2–5 μg/kg fentanyl (Janssen Cilag, Neuss, Germany). The ventilation was adjusted to maintain $PaCO_2$ of less than 40 mm Hg. Oxygen supplementation was given to maintain an arterial oxygen saturation of 97%. The animals were placed in a supine position. After preparation, a 5-Fr flow-directed thermodilution triple-lumen catheter (Arrow International Inc., Reading, PA) was inserted into the pulmonary artery through the right jugular vein. An angiocatheter was placed in the carotid artery, and mean arterial pressure (MAP) was transduced. All of the ends of these catheters were tunneled subcutaneously, exteriorized between scapulae, and secured. A 12-Fr Foley catheter was inserted in the urinary bladder.

Through a midline laparotomy, the splenectomy was performed to reduce organ contract and autotransfusion in the event of hemorrhage. To compensate the splenic blood loss, the animals were infused intravenously with warm lactated Ringer's at a volume three times the organ's weight [15]. Surgical exposure of SMA was accomplished by approaching the vessel directly at the root of the mesocolon after reflecting the transverse colon cephalad, and the whole pancreas was elevated by using a combination of blunt and sharp dissection maintaining the plane of dissection in the avascular plane [16]. After instrumentation, animals were allowed to equilibrate for a period of 15 min, and baseline measurements were obtained.

Study Design

After equilibration, ischemic insult was accomplished by clamping SMA with a nontraumatic vascular clip. The interruption of intestine blood flow without leaving any collateral branches was confirmed by immediate pallor and pulselessness of small intestine. Animals immediately underwent a standardized controlled hemorrhage to 45% estimated blood volume. Pigs were maintained for three different times: intestine ischemia for 30 min (I-30; $n = 6$), 60 min (I-60; $n = 6$), and 90 min (I-90; $n = 6$). Blood was collected in blood donation bags with citrate phosphate preservative and then placed at 4°C on an orbital shaker for later reinfusion.

Lactate Ringer's (4°C, 10 mL/kg) was gradually infused through the jugular vein catheter with abdomen cavity open to induce hypothermia while in hemorrhage shock. The infusion rate was constrained to be slow, avoiding acute cardiac dysrhythmia or cardiac arrest. If core temperature did not reach 34–35°C, abdominal lavage using 500 mL of 4°C Ringer's was performed. Temporary abdominal closing of the skin with bowel clips was then performed in all pigs to avoid abdominal compartment syndrome.

After maintenance of intestine ischemia for three previous durations, SMA was declamped and maintained reperfusion for 6 h. All animals were closely monitored in the animal intensive care unit, and the propofol micropump was disconnected. Vital signs, urine output, and systemic hemodynamic parameters were periodically recorded. Warmed lactate Ringer's (38°C) was infused to increase MAP and reverse hypothermia. The shed blood was reinfused. Sodium bicarbonate was indicated if arterial base excess (BE) decreased below −5. Hypothermia was carefully corrected by airway heating and humidification, rising ambient temperature above 28°C, using these warmed fluids for abdominal lavage, covering the skin with surgical drapes, and placing a warming blanket (Augustine Medical, Eden Prairie, MN) on the operating table. Survivals were killed for necropsies at the end of resuscitation under the influence of anesthetic.

Blood Samples

Blood was sampled serially during the experiment at the following time points: at baseline, end of ischemia, and hourly during resuscitation. Samples were drawn from the jugular artery and pulmonary artery for blood gas analysis. Blood was drawn for measurement of electrolytes, liver enzymes, renal function tests, and markers of cell damage. Blood gas analysis was performed on GEM premier 3000 (Instrumentation Laboratory, Lexington, MA). Serum chemistry measures were made on a Roche Modular System P (Hitachi, San Jose, CA). Coagulation times were measured on an Automated Blood Coagulation Analyzer (CA-6000; Sysmex, Kakogawa, Japan).

Hemodynamic Parameter

MAP was measured hourly using a transducer (P231D; Statham Gould, Oxnard, CA) that was connected to an Electronic Medicine Honeywell Recorder (Honeywell Inc., Pleasantville, NY) for electronic calculation of mean pressures. Cardiac output (CO) was determined hourly by the thermal dilution technique, using a Swan-Ganz catheter and a CO computer (Arrow International Inc., Reading, PA). Systemic oxygen delivery (DO_2) and oxygen consumption (VO_2) were calculated as previously described [17].

Intestinal Light Microscope Study

Biopsies of antimesenteric wedge of the distal ileum (10 cm from the ileocecal valve) were taken at the end of ischemia and resuscitation with care for preservation of the intestinal lumen continuity. The tissues were immersed in 10% formalin for at least 24 h and then embedded in paraffin wax, cut into 5-μm sections, and stained with hematoxylin and eosin. Three slices obtained from the same section were examined under light microscopy by a blinded, experienced pathologist and scored using the grading scale described by Chiu [18].

Statistics

All data are presented as group means ± SEM. Statistical analysis was performed by using SPSS software (SPSS/Windows; SPSS Inc., Chicago, IL). Within-group analysis was performed by the analysis of variance for repeated measurements with the Dunnet post hoc test. Between-groups analysis was performed by analysis of variance for factorial analysis with the Bonferroni post hoc test. χ^2 and Fisher exact tests were used to compare the survival rates. Significance was defined as $P < 0.05$.