Journal of Surgical Research **143,** 320–328 (2007)
doi:10.1016/j.jss.2007.02.003

L-Lactate After Embolization of the Superior Mesenteric Artery

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Submitted for publication September 11, 2006

Background. **Plasma markers for intestinal ischemia have not proven to be accurate. The value of L-lactate is unclear. Experimental models based on open surgery confound the effects of surgical trauma with that of ischemia. The aim was to create an endovascular model for acute superior mesenteric artery thromboembolism, and then to study L-lactate and lactate dehydrogenase (LD) activity in plasma and peritoneal fluid in pigs with extensive, high-grade intestinal ischemia.**

Materials and methods. **Nine pigs underwent full superior mesenteric artery embolization with 4 h of intended intestinal ischemia, whereas six were control animals. Sampling of central venous and arterial blood was performed throughout the experiment, ending with laparotomy to collect peritoneal fluid and segmental intestinal biopsies. A pathologist, blinded to the performed interventions, graded the ischemic lesions.**

Results. **There were no differences in plasma L-lactate ($P = 0.61$) or LD activity levels ($P = 0.69$), measured at different time points from baseline to end of study, between animals with extensive, high-grade intestinal ischemia and sham. Intraperitoneal L-Lactate ($P = 0.005$) and LD activity ($P = 0.018$) levels were elevated compared with sham. There were differences in grades of ischemia in the duodenum ($P = 0.003$), small intestine ($P < 0.001$), proximal ($P < 0.001$), and sigmoid ($P = 0.032$) colon between experimental animals and sham. The grade of small bowel ischemia ($n = 15$) correlated to intraperitoneal fluid L-lactate ($r = 0.80$; $P < 0.001$) and LD activity levels ($r = 0.72$; $P = 0.003$).**

Conclusions. **This endovascular study in a porcine model showed that L-lactate and LD activity levels in peritoneal fluid, not in plasma, reflect intestinal ischemia. The study suggests that plasma L-lactate not is a useful early marker in patients with suspicion of intestinal ischemia.**

Key Words: **intestinal ischemia; superior mesenteric artery; lactate; lactate dehydrogenase; endovascular study; animal model.**

INTRODUCTION

Acute thrombo-embolic occlusion of the superior mesenteric artery (SMA) is a lethal abdominal vascular emergency with an in-hospital mortality rate of 80 to 90% [1, 2]. A plasma marker with sufficient sensitivity and specificity for early detection of intestinal ischemia would have great clinical importance. Many promising potential plasma markers have been suggested through the years, but none has proven to be accurate enough. A normal D-dimer and white blood cell count [3] early in the course most likely excludes the diagnosis. On the other hand, the value of plasma L-lactate has been more unclear. It is well recognized that plasma L-lactate in mammals, the end product of anaerobic glycolysis, is an unspecific marker for acute cell hypoxemia, whereas its high sensitivity reported for intestinal ischemia [4, 5] may be related to preanalytical errors [6], timing of blood sampling, and late stage of disease [4]. Nevertheless, clinicians still use plasma L-lactate levels in their evaluation of patients with suspected intestinal ischemia. In addition, the enzymatic activity of lactate dehydrogenase (LD), which catalyzes the conversion of pyruvate to lactate, has been associated with intestinal ischemia in both experimental [7] and human [8] studies.

Extensive experimental research on intestinal ischemia using various animal models has been published, but their clinical relevance has been questioned [9]. Open surgical methods (i.e., through laparotomy) to clamp the supraceliac aorta [10], SMA [11, 12], or perform segmental mesenteric vascular occlusion [13] have been the standard approach. However, laparotomy in a porcine model has recently shown to cause

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0022-4804/07 $32.00

significant disturbances of the fibrinolytic and coagulation markers studied and thereby introducing an uncontrollable bias in the experimental model system [14]. The aim of this experimental endovascular study was to create a clinically relevant porcine model for acute SMA thromboembolism, and then to study L-lactate and LD in plasma and peritoneal fluid in pigs with extensive, high-grade intestinal ischemia.

MATERIALS AND METHODS

The study was approved by the Ethics Committee, Lund University, and the care and handling of animals were in accordance with National Institute of Health guidelines; Diary number M-110-04.

Experimental Animals

Eighteen Landrace male pigs (4 mo old; median weight 31 kg; range 27 to 37) were provided by a local breeder. The animals were housed in the laboratory facilities for 3 to 7 d before the experiment. They had free access to water, but were deprived from food 24 h before the experiment.

Anesthesia

The pigs were given premedication with ketamine (Ketalar 50 mg/mL; Pfizer, New York, NY) 500 mg and midazolam (dormicum 5 mg/mL; Roche, Basel, Switzerland) 7.5 mg intramuscularly and anesthesia was induced by tiopental (dentothal 25 mg/mL; Abbott, Lake County, IL) 375 mg intravenously, followed by oral intubation (tube 8.0 mm i.d.; Rüsch, Kernen, Germany). The tube was connected to a Servo Ventilator 900 (Elema-Schönander, Stockholm, Sweden). The pigs received approximately 6.5 l air per min (35% oxygen/65% nitrous oxide), continuously adjusted to give an arterial PCO_2 of 5.0 to 5.5 kPa. Anesthesia was delivered through a syringe pump loaded with thiopental (pentothal 25 mg/mL: 25 mg/min; Abbott), atracurium (atracurium-hameln 10 mg/mL: 2.2 mg/min; Epipharm, Stockholm, Sweden) and fentanyl (Fentanyl 50 μg/mL: 0.022 mg/min; Pharmalink, Largo, FL). The infusion rate was reduced with 25% after 1 h and 50% after 2 h until end of experiment. Ringer's acetate solution was given at the rate of 10 mL/kg body weight (BW) per h. Blood pressure and pulse frequency were measured intermittently through the femoral artery introducer with the tip of a catheter (Universal Flush, length 90 cm, 4 F (1.3 mm) in diameter with open end and five side holes; Cordis, Miami Lakes, FL) positioned in the aorta. Body temperature was measured continuously through the nostrils and a heating pad was mounted on the operating table.

Endovascular Procedure

A minimal right groin incision was made to expose the femoral vessels. After puncture (needle length 70 mm; Cordis) of the femoral artery, a guide wire (Radiofocus: length 150 cm, flexible tip 3 cm, 0.89 mm in diameter; Terumo, Somerset, NJ) was advanced up to the thoracic aorta under X-ray illumination, followed by placement of an introducer (Medikit Super Sheath: length 11 cm, 5 F (1.7 mm) in diameter; Boston Scientific, Natick, MA). The guide wire was then withdrawn. The femoral vein was catheterized similarly; the guide wire was followed up to the inferior vena cava before a second introducer (Check-Flo, length 13 cm, 10 F (3.3 mm) in diameter; Cook, Bloomington, IN) was placed. The end of the femoral introducers reached the aorta and vena cava inferior, respectively. A "Cobra" catheter (Super Torque, length 65 cm, 5 F (1.7 mm) in diameter; Cordis) was inserted into the femoral artery introducer and advanced to the L1 vertebrae. Digital subtraction aortogram with lateral projections was performed to facilitate catheterization of the

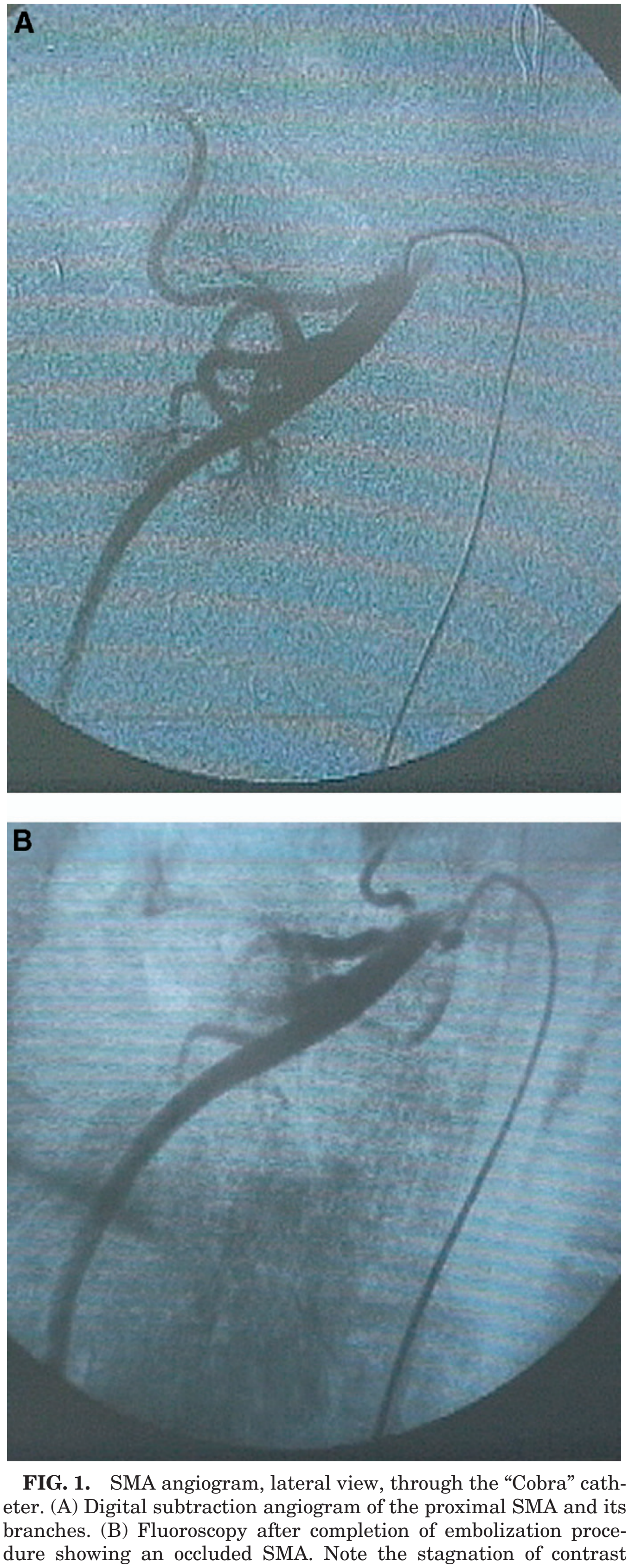

FIG. 1. SMA angiogram, lateral view, through the "Cobra" catheter. (A) Digital subtraction angiogram of the proximal SMA and its branches. (B) Fluoroscopy after completion of embolization procedure showing an occluded SMA. Note the stagnation of contrast within the proximal SMA and its branches indicating no flow.