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Regional Blood Flow Distribution and Oxygen Metabolism During Mesenteric Ischemia and Congestion

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Background. **Acute mesenteric ischemia is a potentially fatal vascular emergency with mortality rates ranging between 60% and 80%. Several studies have extensively examined the hemodynamic and metabolic effects of superior mesenteric artery occlusion. On the other hand, the cardiocirculatory derangement and the tissue damage induced by intestinal outflow obstruction have not been investigated systematically. For these reasons we decided to assess the initial impact of venous mesenteric occlusion on intestinal blood flow distribution, and correlate these findings with other systemic and regional perfusion markers.**

Methods. **Fourteen mongrel dogs were subjected to 45 min of superior mesenteric artery (SMAO) or vein occlusion (SMVO), and observed for 120 min after reperfusion. Systemic hemodynamics were evaluated using Swan-Ganz and arterial catheters. Regional blood flow (ultrasonic flow probes), intestinal O_2-derived variables, and mesenteric-arterial and tonometric-arterial pCO_2 gradients ($D_{mv\text{-}a}pCO_2$ and $D_{t\text{-}a}pCO_2$) were also calculated.**

Results. **SMVO was associated with hypotension and low cardiac output. A significant increase in the regional pCO_2 gradients was also observed in both groups during the ischemic period. After reperfusion, a progressive reduction in $D_{mv\text{-}a}pCO_2$ occurred in the SMVO group; however, no improvement in $D_{t\text{-}a}pCO_2$ was observed. The histopathologic injury scores were 2.7 ± 0.5 and 4.8 ± 0.2 for SMAO and SMVO, respectively.**

Conclusions. **SMV occlusion promoted early and significant hemodynamic and metabolic derangement at systemic and regional levels. Additionally, systemic pCO_2 gradient is not a reliable parameter to evaluate the local intestinal oxygenation. Finally, the $D_{t\text{-}a}pCO_2$ correlates with histologic changes during intestinal congestion or ischemia. However, minor histologic changes cannot be detected using this methodology.**

Key Words: **ischemia; reperfusion; intestinal mucosa; oxygen consumption; thrombosis; mesenteric vascular occlusion; splanchnic circulation.**

INTRODUCTION

Acute mesenteric ischemia is a potentially fatal vascular emergency with mortality rates still ranging between 60% and 80% [1, 2]. Despite the development of new diagnostic methods and the use of modern treatment modalities, the survival rate has not improved substantially during the past 70 y, and the major reason is the continued difficulty in recognizing the condition before bowel infarction occurs [2]. Mesenteric ischemia comprises a group of different pathophysiologic processes including arterial embolism, arterial thrombosis, mesenteric venous thrombosis, and nonocclusive mesenteric ischemia that has bowel necrosis as a common end point.

Due to its relatively low incidence (5% to 15% of all cases of intestinal ischemia), mesenteric venous thrombosis has attracted less attention than other forms of mesenteric ischemia. Over the past decades early systemic anticoagulation has enhanced the survival in this group of patients; however, the mortality rate can still be expected to reach 50% [2, 3].

A better understanding of the pathogenesis of mesenteric ischemia is essential to early diagnosis and prompt and effective treatment. Several experimental and clinical studies have extensively examined the hemodynamic and metabolic effects of superior mesenteric

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artery occlusion [4–7]. On the other hand, the cardiocirculatory derangement and the tissue damage induced by intestinal outflow obstruction have not been investigated systematically, despite their clear clinical importance.

For these reasons, we have decided to assess the initial impact of venous mesenteric occlusion on intestinal mucosal and serosal blood flow distribution, and to correlate these findings with other systemic and regional perfusion markers. In addition, we have compared the hemodynamic, metabolic, and histological changes induced by a temporary congestion of mesenteric territory with those occurring in a well established model of intestinal ischemia.

MATERIAL AND METHODS

The experimental protocol was approved by the Institutional Review Board, in adherence to the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for the Care and Use of Animals by the National Institutes of Health.

Animals and Surgical Procedures

Fourteen male mongrel dogs, weighing 17 ± 1.7 kg were fasted for 12 h prior to the study, with free access to water. Anesthesia was induced with an intravenous injection of 0.1 mg/kg of morphine sulfate followed by 25 mg/kg of pentobarbital sodium. Additional doses of pentobarbital, 2 mg/kg, were used as required. Atropine (0.1 mg/kg) was given intravenously to relax the bowel and facilitate the instrumentation. A cuffed endotracheal tube was placed to allow mechanical ventilation with a 1.0 fraction of oxygen inspired, at a tidal volume of 15 mL/kg (670 Takaoka ventilator). The respiratory rate was adjusted to maintain an initial arterial pCO_2 at 40 ± 5 mm Hg. A urinary bladder catheter was placed for urinary drainage. During surgical preparation, a heating pad was used to maintain normothermia. The animals received lactated Ringer solution, 10 mL/kg/h to compensate for fluid losses.

The right carotid artery was dissected and a polyethylene cannula (P240) was placed to measure mean arterial pressure and to collect arterial blood samples for blood gas, pH, bicarbonate, base deficit, hematocrit, and hemoglobin analysis. A 7.5 Fr flow-directed thermodilution fiberoptic pulmonary artery catheter with thermal filament (CCOmbo 744H7.5F Edwards Swan-Ganz; Baxter Edwards Critical Care, Irvine, CA) was introduced through the right external jugular vein and its tip placed in the pulmonary artery, guided by the pressure wave tracings. This catheter was connected to a cardiac computer (Vigilance; Baxter Edwards Critical Care, Irvine, CA), to measure cardiac output, using 3-mL bolus injections of isotonic saline at 20°C every 15 min. The same catheter was also used to collect mixed venous blood samples for gas analysis.

All pressure-measuring catheters were connected to disposable pressure transducers (Transpac Transducer; Abbott, Chicago, IL) and then to a Biopac Data Acquisition System (model MP100; Biopac Systems, Goleta, CA) for continuous recording of systemic and pulmonary artery pressures.

The abdomen was opened via a median celiotomy. The proximal jejunum and the distal ileum were transected; all connections to the small bowel were then transected and ligated at the base of the mesentery except the superior mesenteric artery and vein. A complete isolation of the small bowel was performed in order to avoid interferences of possible collateral blood flow through the intestinal wall or mesentery.

A transit time ultrasonic flow probe (Transonic System Inc., Ithaca, NY) was placed around the superior mesenteric vein and connected to a flowmeter (T206 transonic volume flowmeter; Transonic Systems, Inc., Ithaca, NY). Ileal serosal blood flow was measured by a laser-Doppler angle probe (type R) attached to the ileal serosal with double adhesive cyanoacrylate glue, and connected to a BLF-21D perfusion monitor (Transonic Systems, Inc., Ithaca, NY).

A small incision was made in the terminal ileum; a 16F-TRIP tonometry catheter was introduced proximally and fixed by a purse-string suture. This catheter was connected to a gas capnometer (Tonocap model TC-200; Tonometrics, Datex-Egstrom, Finland) for intestinal pCO_2 measurement. A fluid-filled polyethylene catheter was placed in the mesenteric vein to collect mesenteric blood samples.

Blood samples from arterial, venous, and mesenteric territories were analyzed immediately after their collection with a Stat Profile Ultra Analyzer (Nova Biomedical, Waltham, MA).

Experimental Design

After completion of the surgical preparation, the animals were allowed to recover for 60 min and baseline measurements were obtained (BL). The animals were then randomly assigned into two experimental groups: SMAO (superior mesenteric artery occlusion, $n = 7$) and SMVO (superior mesenteric vein occlusion, $n = 7$). The superior mesenteric artery or vein was occluded with a non-crushing vascular clamp for 45 min (II-45). After reperfusion, the animals were observed for an additional 120 min (II-45 to R120). At the end of the experiment, the animals were euthanized via anesthesia overdose, followed by an intravenous injection of saturated potassium chloride.

Measured Variables

Mean systemic and pulmonary arterial pressures (MAP and MPAP, respectively), as well as superior mesentery vein and intestinal serosal blood flows (SMVBF and SBF, respectively), were continuously recorded. Intermittent cardiac output and intestinal mucosal pCO_2 were measured every 15 min. Arterial, mesenteric and mixed venous base deficit, pH, pCO_2, pO_2, oxygen saturation, hemoglobin, hematocrit, bicarbonate, and lactate were measured at baseline (BL), 45 min after intestinal ischemia (II-45), and 30, 60, and 120 min after reperfusion (R30, R60 and R120, respectively).

Three pCO_2 gradients were analyzed during the experimental protocol: the pulmonary artery-arterial, superior mesenteric vein-arterial and intestinal mucosal (tonometric)-arterial gradients ($D_{pa\text{-}a}pCO_2$, $D_{mv\text{-}a}pCO_2$, and $D_{t\text{-}a}pCO_2$, respectively). Intestinal oxygen delivery, consumption, and extraction (DO_2intest, VO_2intest and O_2ERintest) were calculated using standard formulae. The regional lactate gradient, (mv-a)-lactate, was calculated as the difference of mesenteric vein and arterial lactate.

Histological Analysis

Whole-thickness specimens from distal ileum for histopathologic study were obtained at baseline (three animals of each group) and at the end of the reperfusion period (R120). The formalin-fixed tissue was sectioned and then stained with hematoxylin and eosin. An investigator (CMFR), blinded to the experimental group, examined the slides under light microscopy at magnifications of ×50, ×100, and ×400. Mucosal injury was scored on a scale from 0 to 5 as described by Chiu *et al.* [8]. The grading system was as follows: grade 0, normal mucosal villi; grade 1, subepithelial Gruenhagen's space, capillary congestion; grade 2, extension of subepithelial space with moderate lifting of epithelial layer from lamina propria; grade 3, massive epithelial lifting down sides of villa, few tips denuded; grade 4, denuded villi with lamina propria and dilated capillaries exposed; and grade 5, digestion and disintegration of lamina propria, hemorrhage, and ulceration. A scoring system to grade the congestion of intestinal