

# Abdominal Hypertension and Decompression: The Effect on Peritoneal Metabolism in an Experimental Porcine Study

P. Skoog<sup>a,\*</sup>, T.M. Hörer<sup>a</sup>, K.F. Nilsson<sup>a</sup>, L. Norgren<sup>b</sup>, T. Larzon<sup>a</sup>, K. Jansson<sup>b</sup>

<sup>a</sup> Department of Cardio-Thoracic and Vascular Surgery, Örebro University Hospital, Örebro, Sweden

<sup>b</sup> Department of Surgery, Örebro University Hospital, Örebro, Sweden

## WHAT THIS PAPER ADDS

This experimental study explores the changes in abdominal metabolites during intra-abdominal hypertension with organ dysfunction, with focus on decompression with subsequent reperfusion. Using microdialysis early reactions in metabolite concentrations are observed, potentially useful as markers for effective abdominal compartment syndrome treatment.

**Objective:** The aim of this study was to investigate the abdominal metabolic response and circulatory changes after decompression of intra-abdominal hypertension in a porcine model.

**Methods:** This was an experimental study with controls. Three-month-old domestic pigs of both sexes were anesthetized and ventilated. Nine animals had a pneumoperitoneum-induced IAH of 30 mmHg for 6 hours. Twelve animals had the same IAH for 4 hours followed by decompression, and were monitored for another 2 hours. Hemodynamics, including laser Doppler-measured mucosal blood flow, urine output, and arterial blood samples were analyzed every hour along with glucose, glycerol, lactate and pyruvate concentrations, and lactate–pyruvate (l/p) ratio, measured by microdialysis.

**Results:** Laser Doppler-measured mucosal blood flow and urine output decreased with the induction of IAH and showed a statistically significant resolution after decompression. Both groups developed distinct metabolic changes intraperitoneally on induction of IAH, including an increased l/p ratio, as signs of organ hypoperfusion. In the decompression group the intraperitoneal l/p ratio normalized during the second decompression hour, indicating partially restored perfusion.

**Conclusion:** Decompression after 4 hours of IAH results in an improved intestinal blood flow and a normalized intraperitoneal l/p ratio.

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## INTRODUCTION

Abdominal compartment syndrome (ACS) after open repair of ruptured aortic aneurysm was described by Fietsam et al. in 1989;<sup>1</sup> over the last 15 years the role of increased abdominal pressure as a cause of postoperative complications and organ failure has become evident. ACS is now defined as sustained abdominal pressure >20 mmHg associated with new organ dysfunction or failure, while the term intra-abdominal hypertension (IAH) should be used when organ dysfunction has not occurred.<sup>2</sup>

In a recent review, Carr has pointed out that the risk of ACS can be predicted with known risk factors, and the condition prevented.<sup>3</sup> Early intervention is crucial and with limited abdominal hypertension medical therapy or minimally

invasive treatment may be sufficient;<sup>4,5</sup> in established ACS, laparotomy to reduce the high pressure and further organ-preserving measures seem to be the only effective and life-saving treatment. However, it should be noted that recurrent ACS may occur after decompressive laparotomy.<sup>6</sup>

Early diagnosis of increased intra-abdominal pressure (IAP) with organ failure is thus central, requiring pressure measurement, most commonly via the urinary bladder.<sup>7</sup> The abdominal perfusion pressure (APP) is defined as the mean arterial pressure (MAP) reduced by IAP. As the majority of diagnostic tools for ACS only indirectly reflect organ dysfunction, the decision to perform a laparotomy in a critically ill patient is sometimes delicate.

In a clinical study utilizing microdialysis, we have demonstrated that intra-abdominal metabolic derangement, measured by microdialysis, occurs in patients developing IAH after repair of ruptured abdominal aortic aneurysm (rAAA).<sup>8</sup>

Continuous monitoring may not only show deranged metabolism in IAH or ACS, but possibly also restoration of aerobic metabolism after treatment.

\* Corresponding author. P. Skoog, Department of Cardio-Thoracic and Vascular Surgery, Örebro University Hospital, SE-701 85 Örebro, Sweden.

E-mail address: [per.skoog@orebroll.se](mailto:per.skoog@orebroll.se) (P. Skoog).

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The aim of this study was to explore whether decompression of IAH reverses the metabolic derangement as evaluated by intra-abdominal microdialysis.

## MATERIALS AND METHODS

### Animals

This study was approved by the regional animal ethics committee and carried out in accordance with the European Convention for Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes,<sup>9</sup> and good practice in laboratory animal science.<sup>10</sup> Twenty-one cross-bred pigs of both sexes (Swedish country breed, Hampshire and Yorkshire, mean weight 31 kg, range 26–35 kg) were used in the study. The animals had free access to food and water until the start of the experiment.

### Anesthesia, ventilation, and fluid treatment

The anesthesia protocol has been published previously.<sup>11</sup> In brief, the animals were sedated at the farm at the start of the day of the experiment. Intravenous (IV) general anesthesia was induced and maintained with propofol (8 mg/kg/h IV, Diprivan; AstraZeneca, Södertälje, Sweden), and the animals were intubated. To prevent hypercapnea due to CO<sub>2</sub> absorption from the abdomen, the animals were slightly hyperventilated. Anesthetic depth was controlled throughout the day by pain provocations. Ringer-Acetate (3 mL/kg/h; Fresenius Kabi, Uppsala, Sweden) and a 2.5% glucose solution (1.5 mL/kg/h; Fresenius Kabi) were used to maintain fluid balance. The animals were maintained at a stable body temperature (data not shown). At the end of the experiments, the animals were euthanized by an IV bolus injection of propofol (200 mg) and pethidin (1 mg/kg), and a rapid IV injection of potassium chloride (40 mmol). Asystole was confirmed with electrocardiography (ECG). Throughout the experiments the animals were well anesthetized and without signs of pain.

### Surgical preparation and instrumentation

The surgical preparation and instrumentation has been described previously.<sup>11</sup> In brief, a midline laparotomy was performed together with insertion of a catheter into the carotid artery (Becton Dickinson Critical Care, Singapore) for recording arterial blood pressure and heart rate, and for arterial blood sampling. Microdialysis catheters (CMA 62; CMA Microdialysis, Stockholm, Sweden) were inserted free-floating intraperitoneally, in the jejunal wall, and in the rectal wall via the anus. A urinary catheter for measurement of urinary output and bladder pressure was inserted. A laser Doppler probe (PM15; Perimed, Stockholm, Sweden) connected to a laser Doppler device (Periflux System 5001; Perimed, Järfälla, Sweden) was placed in the jejunum facing the mucosa. Laparoscopic trocars were used to insufflate gas and to correct the position of the probes and catheters in the abdomen if required. ECG recording and pulse oximetry were performed (Datex-Ohmeda AS/3; GE Healthcare Technologies, Waukesha, WI, USA).

### Experimental protocol and measurements

After preparation, an intervention-free hour followed to obtain baseline data. Two experimental groups were created. Nine animals were planned to be in each group, but owing to catheter failure at jejunal and rectal levels in the decompression group three extra animals were added. Both groups had a CO<sub>2</sub>-pneumoperitoneum of 30 mmHg induced. The IAH group had the pressure maintained for 6 hours, while the decompression group (IAH-D) was decompressed after 4 hours and then followed for an additional 2 hours. Baseline data and data at the end of each of the 6 hours were recorded, including systemic arterial blood pressure, heart rate, body temperature, IAP, laser Doppler flux, and urine output. Arterial blood samples and microdialysis samples were also obtained at the same timings.

### Microdialysis

The microdialysis technique has been described previously.<sup>11,12</sup> In brief, the concentration of different tissue metabolites is measured by this technique. The catheters can be placed in tissues or be free-floating in the body cavities. A physiologic solution (Perfusion fluid T1; CMA, Järfälla, Sweden) perfuses slowly (0.3 µL/minute) through a double-lumen catheter with a semi-permeable dialysis membrane (cut-off: 20,000 Dalton) at the tip, and equilibration over the membrane takes place. The microdialysate is collected in microvials and analyzed by photo-spectrometry. In this study, concentrations of glucose, glycerol, lactate, and pyruvate were measured in a CMA 600 microdialysis analyser (CMA 600; CMA Microdialysis AB, Järfälla, Sweden).

### Intestinal mucosal blood flow

Mucosal blood flow was measured by a laser Doppler probe (PM15; Perimed, Järfälla, Sweden) sending a laser beam of 780-nm wavelength.<sup>13</sup> By the Doppler signal, an estimation of red blood cell flow in the jejunal mucosa was obtained as “flux”. Changes relative to baseline are presented.

### Statistics

All data are presented with the mean and 95% confidence interval (CI). A linear mixed model for repeated measurements was used for statistical analysis. Group, time, and interaction were treated as independent variables using an autoregressive correlation structure. Ninety-five percent CI was calculated for every hour, but statistical analysis was only performed at baseline, 4 hours, and 6 hours. Logarithmic transformation of laser Doppler flux, lactate, lactate–pyruvate (l/p) ratio, and glycerol was performed owing to a known skewed distribution; results are presented as geometric means with asymmetric CIs. A *p*-value of  $\leq .05$  was considered statistically significant. SPSS version 17 (SPSS, Chicago, IL, USA) was used for statistical calculations.

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