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Hemodynamic Indices Versus Gastric Tonometric Measurements for Prognosis of Hemorrhagic Shock: A Porcine Model

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The aim of the study reported here was to assess the prognostic value of gastric tonometry and its implications in the initial phases of hemorrhagic shock. Hemorrhagic shock was induced by use of femoral arterial bleeding in 12 hybrid swine under general anesthesia. Approximately 30% of the circulating blood volume was removed, until mean arterial pressure of 45 mmHg was reached. The shock conditions were observed over a limited period (90 min) by comparing traditional hemodynamic parameters with gastric tonometric measurements and tissue oxygenation. After a shock period of 90 min without pharmacologic treatment, blood was collected in acid-citrate dextrose-treated bags and was reinfused via the right femoral vein.

At the end of the experiment, seven animals had good hemodynamic recovery on reinfusion (group A), whereas values in five animals deceased in the same phase (group B). Hemodynamic and gastric tonometric results were compared between survivors and nonsurvivors.

Intravascular volume restoration and reduction of systemic vascular resistance (SVR) enabled the animals of group A to maintain standard ventricular kinetics and recover in terms of splanchnic regional flow. In addition, increase in intramucosal gastric pH (pHi), decrease in the pH-gap (pHa – Hi), and progressive restoration in gastric wall tissue oxygenation (PtO_2) also were observed. These results suggest that useful diagnostic and therapeutic indications can be obtained by acquisition of simple hemodynamic measurements at the beginning of the shock period. On the basis of results of statistical analysis, only mean arterial pressure and SVR were good indicators of shock development, whereas pHi was not a significant factor in this experimental model.

Clinicians caring for hemorrhagic shock patients are required to monitor and maintain the adequacy of tissue oxygenation to ensure organ function, survival, and repair. The stress response to blood loss leads to the selective redistribution of blood flow, from tissues with high ischemic tolerance to tissues with low ischemic tolerance, and the subsequent cell failure which is mainly responsible for irreversible hemorrhagic shock. Systemic markers of perfusion, such as oxygen delivery and consumption, may not accurately track shock states in certain situations.

Monitoring systems have been implemented, such as gastric tonometry for simple and non-invasive acquisition of data on gastrointestinal mucosal oxygenation. This region of the body is among the first to be affected in shock and the last to be restored to normal in resuscitation (1-8). The diversion of blood from the gut could impair the integrity of the mucosal barrier and thereby increase the translocation of endotoxins and bacteria from the gut lumen (2-5, 9-12), which is responsible for the initiation of the systemic inflammatory response and multiple organ failure (MOF). Gastric tonometry makes possible the indirect measurement of the partial pressure of carbon dioxide (PCO_2) in the internal lining of the mucosa, which extends from the gastric wall to the gastric lumen without local differences and pressure artifacts (13). Earlier studies have established that increases in PCO_2 of the stomach represent a consistent finding in the critical low-flow states of a circulatory shock as in hemorrhagic shock (14,15). Greatly increased tonometric measurement of PCO_2, and by inference, of tissue PCO_2, suggests the presence of anaerobic metabolism in tissue resulting in proton formation and titration of the bicarbonate-based buffer system. On the other hand, less severely increased tonometric measurement of PCO_2 suggests a relative imbalance between local tissue perfusion and metabolic demands. Consequently, an increase in tonometric PCO_2 measurement is clinically useful in detecting inadequate tissue perfusion, even if it has not progressed to frank anaerobic metabolism (9, 16, 17).

Gastric tonometry plays an important role in the monitoring of critically ill patients. The aim of the study reported here was to assess its prognostic implications in the initial phases of hemorrhagic shock and determine whether it can supply adequate information on the future trend of such shock. In addition, the response to alterations in peripheral circulation was evaluated during the earliest phases of the hemorrhagic shock induced. Hemodynamic and gastric tonometric parameters were monitored during shock and post-reinfusion periods in an experimental porcine model (18-26).

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Materials and Methods

This study was approved by the Ethic Animal Research Committee of the University of Bologna and the National Health Ministry, and was performed in compliance with European and Italian Laws on animal experimentation, the principles stated in the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Assurance No #A5424-01 by the National Institute of Health (NIH-Rockville Md.) (27-29).

Animals. Twelve female white swine (*Sus scrofa domestica*), body weight 37.5 ± 2.5 kg, and raised on a traditional breeding farm (Pancaldi, Budrio, Bologna, Italy), were housed singly in cages with grid floor, in a room with controlled temperature of 20 ± 2°C, 50 ± 5% humidity, and ventilation of 10 cycles/h. The animals had been allowed neither food nor water for 12 h prior to study.

Instrumentation. The animals were premedicated with ketamine (Ketavet 100, Gellini, Aprilia LT, Italy; 20 mg/kg of body weight, i.m.) and xylazine (Rompun, Bayer SpA, Milan, Italy; 2 mg/kg, i.m.). They were then positioned in supine manner, and ECG lead III was positioned. General anesthesia was induced with a gas mixture of O_2/N_2O (50/50%) and 2 to 3% of halothane (Halothane, Merial Italia SpA, Milan, Italy) administered by use of a mask; when swallowing reflex activity stopped, an orotracheal tube was inserted without use of muscle relaxants. Anesthesia was maintained throughout the study by use of assisted ventilation and continuous inhalation of O_2/N_2O (60/40%) and 1% isofluorane (Forane Abbott SpA, Aprilia LT, Italy). Ventilation was adjusted to maintain a respiratory rate of 12 breaths/min and an end-tidal CO_2 concentration of 30 to 35 mmHg: further changes in ventilatory settings were not made thereafter. To achieve muscular relaxation, a 20-gauge catheter was positioned in the marginal vein of the left ear with a continuous infusion of pancuronium bromide (0.03 mg/kg/h). During the study, the total amount of 500 ml of 0.9% NaCl was administered through this vein. A thermometric rectal probe was inserted to measure variations in the body temperature, and a bladder catheter was placed to monitor urine flow.

The left carotid artery and external jugular vein were exposed in the cervical region, as well as the femoral veins in the groin, and catheters were positioned and used for monitoring. After midline laparotomy, a tonometer was inserted via gastrotomy. At the end of surgery and after temporary suture of the midline laparotomy, the animals were covered with sterile blankets to ensure a constant body temperature and avoid fluid loss from the abdominal cavity. The room temperature was controlled at 23 ± 2°C during all surgical procedures and hemorrhagic shock.

Measurements. A 20-gauge catheter was positioned in the carotid artery and was used for continuous monitoring of mean arterial pressure. A 7-F fiberoptic Swan-Ganz (Opthicath 49, Abbot Laboratories, Oximetrix Division, North Chicago, Ill.) catheter was inserted through the external jugular vein into the pulmonary artery, and another two catheters were positioned into the cranial and caudal venae cavae through the femoral veins. The pressure channel of the Swan-Ganz catheters was connected via a transducer to an integrated modular system for monitoring pressure (Component Monitoring System, Hewlett Packard, Bad Homburg, Germany). The electronic channel was attached to the Oximetric III system (Abbott Laboratories, Oximetrix Division) for continuous evaluation of mixed venous oxygen saturation and determination of cardiac output (CO) and derived parameters calculated on body surface area (BSA): cardiac index (CI = CO/BSA), systemic vascular resistance (SVR = [MAP-CVP]/CO*80), oxygen delivery index ($DO_2I = CO*CaO_2/BSA$, where CaO_2 is the arterial oxygen content), and oxygen consumption index ($VO_2I = CO*CvO_2/BSA$, where CvO_2 is the mixed venous oxygen content). Cardiac output was determined by infusion of two consecutive five-milliliter boluses of 5% cold glucose solution through the Swan-Ganz catheters. The CO recorded was the average of the two measurements. During mechanical ventilation, CO and intravascular pressures were always monitored at the end of the expiratory stage.

Insertion of a tonometer (TRIP TGS Catheter Tonometrics Inc, Worchester, Mass.) into the stomach was always preceded by careful "priming" with four milliliters of 0.9% NaCl to remove air from the tonometer and obtain accurate sample. Accurate cleaning of the stomach was then performed through the tonometer to ensure precise measurement of intramucosal gastric pH (pHi). The tonometer balloon was then filled with 2.5 ml of 0.9% NaCl via a three-way tap located at its proximal end. Subsequently, PCO_2 in the solution and gastric lumen were allowed to equilibrate for 30 min. At each experimental time, the values of HCO_3 and steady-state CO_2 concentration (CO_2ss) were recorded (value of intraluminal PCO_2 in a steady state, that is corrected for temperature and equilibration time) and were used for pHi calculation, using with the Henderson-Hasselbalch equation.

$$pHi = 6.1 + \log$$

where 6.1 is the pK value and 0.03 is the coefficient of solubility of carbon dioxide (1-5, 16, 30). Values of pHi ≥ 7.35 were assumed to be normal. Arterial and venous blood samples were simultaneously collected and analysed for partial pressure of oxygen (PO_2), carbon dioxide (CO_2), pH, and bicarbonate concentration by use of a blood gas analyser.

Gastric wall pO_2 was measured, using the LICOX pO_2 monitor (GMS mbH, Kiel, Germany), consisting of two transducers to record tissue oxygen partial pressure and temperature. A flexible polarographic Clark-Type pO_2 probe (tip diameter of 500 µm, probe sensitivity of 2.5 pA/mmHg at a polarographic potential of 795 mV, temperature sensitivity 4.4%/°C) was inserted into the caudal gastric wall through the lumen of a previously inserted 20-gauge catheter for continuous monitoring of gastric oxygen partial pressure (Fig. 1). A flexible Typ-K microthermocouple was then positioned in similar manner close to the pO_2 probe to measure temperature variations.

After the monitoring devices had been calibrated, the first recordings were taken (T_0 = steady state). Hemorrhagic shock was induced by withdrawing femoral arterial blood into acid- citrate-dextrose (ACD)-treated bags. About 30% of the circulating blood volume was removed. This experimental period took about 15 min, and ended when MAP of approximately 40 mmHg was reached. Blood bags were temporarily stored at 4 to 5°C before re-infusion of their contents. The shock state was maintained for up to 90 min (shock periods: $T_1 = 30$, $T_2 = 60$, and $T_3 = 90$ min after the end of the bleeding period), after which autotransfusion (in 30 min) of the warmed blood (36 ± 2°C) was performed via the right femoral vein. Subsequently, the animals remained under observation for a further 90 min (post-reinfusion periods: $T_4 = 30$, $T_5 = 60$, and $T_6 = 90$ min after the end of the re-infusion period) until the end of the study. Throughout the study, other therapeutic interventions were not done, and measurements were taken at each experimental time. All monitoring devices were then removed and the animals were euthanized by intravenous

Table 1. Mean ± SD changes in hemodynamic standard parameters in groups A (n = 7) and B (n = 5)

Parameter		Baseline	Shock			Post-reinfusion			Friedman test
	Groups	T_0	T_1	T_2	T_3	T_4	T_5	T_6	
HR (bpm)		129 ± 25.0							
	A		182 ± 25	198 ± 26	203 ± 33	17 ± 29	170 ± 45	185 ± 28	T1 *vs* T0 $P < 0.001$ T2 *vs* T1 $P < 0.05$ T4 *vs* T3 $P < 0.001$
	B		194 ± 20.0	200 ± 40	198 ± 37	142 ± 46	-	-	T1 *vs* T0 $P < 0.001$ T4 *vs* T3 $P < 0.005$
MAP (mmHg)		76.7 ± 10.2							
	A		55.5 ± 14.0	65.0 ± 20.0	62.8 ± 21.8	78.9 ± 19.2	76.9 ± 17.3	73.3 ± 23.0	T1 *vs* T0 $P < 0.001$ T2 *vs* T1 $P < 0.05$ T4 *vs* T3 $P < 0.01$
	B		53.4 ± 5.3	53.4 ± 10.8*	50.4 ± 14.0*	67.0 ± 10.0*	-	-	T1 *vs* T0, T4 *vs* T3 $P < 0.001$
CVP (mmHg)		4.0 ± 3.7							
	A		2.8 ± 2.4	3.1 ± 3.8	2.7 ± 3.0	3.0 ± 4.0	4.0 ± 4.2	4.4 ± 4.0	
	B		2.8 ± 4.0	4.6 ± 7.4	4.0 ± 6.0	4.7 ± 5.0	-	-	

HR = heart rate; bpm = beats per minute; MAP = mean arterial pressure; CVP = central venous pressure.
T_0 = steady state; shock periods: $T_1 = 30$, $T_2 = 60$, and $T_3 = 90$ min after the end of the bleeding period; post-reinfusion periods: $T_4 = 30$, $T_5 = 60$, and $T_6 = 90$ min after the end of the reinfusion period.
Mann-Whitney U test comparing results of both groups for each parameter and at each time: *$P < 0.05$.

Table 2. Mean ± SD changes in hemodynamic parameters calculated by use of the Oximetric III system in groups A (n = 7) and B (n = 5)

Parameter		Baseline	Shock			Post-reinfusion			Friedman test
	Groups	T_0	T_1	T_2	T_3	T_4	T_5	T_6	
CI (L/min/m^2)		3.3 ± 0.77							
	A		2.24 ± 0.25	2.34 ± 0.31	2.45 ± 0.57	3.75 ± 0.43	3.79 ± 0.76	3.07 ± 0.58	T1 *vs* T0,T4 *vs* T3, T6 *vs* T5 $P < 0.001$
	B		2.97 ± 0.60§§	2.90 ± 0.86*	2.90 ± 1.15	2.80 ± 0.79§§	-	-	
SVR (dyne·s/cm^5·m^2)		2349 ± 600							
	A		2511 ± 778	2629 ± 781	2773 ± 785	2117 ± 1133	2168 ± 779	2581 ± 717	T4 *vs* T3 $P < 0.01$ T6 *vs* T5 $P < 0.05$
	B		1737 ± 421§	1772 ± 461§	1779 ± 498§§	2302 ± 850	-	-	T1 *vs* T0 $P < 0.01$ T4 *vs* T3 $P < 0.05$
DO_2I (ml/min/m^2)		388 ± 67							
	A		299 ± 37	364 ± 57	332 ± 17	507 ± 37	524 ± 98	391 ± 20	T1 *vs* T0, T2 *vs* T1, T4 *vs* 2 T3, T6 *vs* T5 $P < 0.001$ T3 *vs* T2 $P < 0.01$
	B		334 ± 37§§	332 ± 105	313 ± 12§	387 ± 138**	-	-	T1 *vs* T0 $P < 0.01$ T4 *vs* T3 $P < 0.05$
VO_2I (ml/min/m^2)		64 ± 11							
	A		83 ± 18	89 ± 28	85 ± 4	90 ± 16	100 ± 39	84 ± 21	T1 *vs* T0 $P < 0.001$ T6 *vs* T5 $P < 0.05$
	B		115 ± 21§§	118 ± 52	99 ± 11§§	81 ± 52	-	-	T1 *vs* T0 $P < 0.001$

CI = cardiac index; SVR = systemic vascular resistance; DO_2I = oxygen delivery index; VO_2 = oxygen consumption index.
Mann-Whitney U test comparing results of both groups for each parameter and at the same time: *$P < 0.05$; **$P < 0.01$; §$P < 0.005$; §§$P < 0.001$.
See Table 1 for key.

administration of 200 mg of N-[2-(m-methoxyphenil)-2-ethyl-buthyl-(1)]-γ-hydroxybutyramide, 50 mg of 4,4'-methylene-bis(ciclohexyltrimethyl-ammoniumiodide, and 5 mg of tetracaine hydrochloride solution (0.3 ml/kg; Tanax, Hoechst Roussel Vet, Milan, Italy).

Analysis of data. Statistical analysis was performed by use of SPSS v.10.1 software (SPSS/PC, Inc., Chicago, Ill.). Data are expressed as mean ± SD, at a significance level of $P < 0.05$. A nonparametric Friedman test was used to compare data between experimental times, and the Mann-Whitney U test was used to compare data between groups (survived versus deceased) at the same experimental time. A nonparametric Spearman ρ correlation was calculated.

Results

Complications related to anesthesiology and surgery were not apparent. Of 12 animals studied, seven survived (group A) and reached the final experimental time (T_6), while the remaining five died (group B) within 60 min of reinfusion (T_5). Changes in hemodynamic parameters are shown in Tables 1-3. Significant differences were not observed between groups for heart rate (HR) and central venous pressure (CVP), even though CVP had a tendency to increase over time in group-B animals (Table 1). Mean arterial pressure significantly differed between groups A and B at T_2, T_3, and T_4, with group B having lower about (12 mmHg) values at each time point. The different SVR trends strongly affected hemodynamics during the shock period (from T_1 to T_3; Table 2). An early significant decrease in SVR was observed in animals of group B, and this lower value remained unchanged until the end of the shock period. Conversely, in animals of group A, SVR had an upward trend at T_2 and T_3, reaching values significantly different from those in animals of the other group. At 90 min after the end of the bleeding period (T_3), cardiac index (CI) was higher in group-B than in group-A animals and was actually lower in group-B than in group-A animals at 30 min after reinfusion (T_4). During the post-reinfusion stage, an important increase in the CI values was seen at T_4 in group-A animals while the constant reduction in CI observed during

Table 3. Mean ± SD changes in hemodynamic parameters measured and calculated by use of the Oximetric III system in groups A (n = 7) and B (n = 5)

Parameter		Baseline	Shock			Post-reinfusion			Friedman test
	Groups	T_0	T_1	T_2	T_3	T_4	T_5	T_6	
pa-SvO_2 (%)		66.3 ± 8.8							
	A		53.0 ± 13.7	54.8 ± 17.1	45.5 ± 25.0	71.3 ± 17.9	61.0 ± 15.1	53.0 ± 27.3	T1 *vs* T0, T4 *vs* T3 $P < 0.001$
	B		54.0 ± 5.7	42.5 ± 21.9	43.0 ± 11.3	-	-	-	T1 *vs* T0 $P < 0.001$, T2 *vs* T1 $P < 0.05$
crvc-SvO_2 (%)		64.0 ± 11.3							
	A		58.0 ± 26.9	57.5 ± 27.8	53.3 ± 29.7	73.8 ± 13.4	71.0 ± 15.0	58.8 ± 22.4	T4 *vs* T3 $P < 0.005$, T6 *vs* T5 $P < 0.01$
	B		49.5 ± 10.6	35.0 ± 31.1	40.5 ± 0.71	-	-	-	T1 *vs* T0 $P < 0.01$, T2 *vs* T1 $P < 0.05$
cavc-SvO_2 (%)		74.0 ± 8.7							
	A		59.3 ± 17.4	52.0 ± 16.8	44.7 ± 13.8	71.5 ± 12.6	69.0 ± 9.6	51.0 ± 15.2	T1 *vs* T0, T4 *vs* T3, T6 *vs* T5 $P < 0.001$
	B		72.0 ± 19.8	56.0 ± 39.6	50.5 ± 21.9	-	-	-	

pa-, crvc-, and cavc-SvO_2 = oxygen saturation of hemoglobin in the pulmonary artery, cranial vena cava, and caudal vena cava, respectively.
See Table 1 for key.

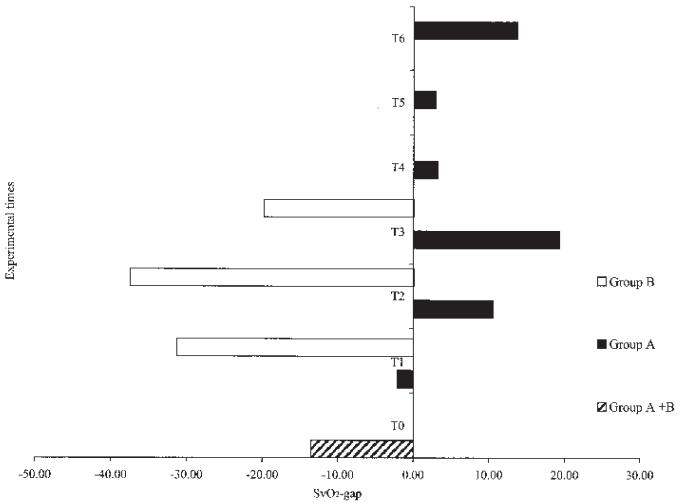

Figure 1. Mean measurement of hepatic O_2 consumption (SvO_2-gap = crvc-SvO_2 [%] – cavc-SvO_2 [%]) at each experimental time.

the shock stage, persisted in group-B animals.

During the shock period, progressive and significant decreases in oxygen delivery index (DO_2I) were recorded and followed a similar pattern in the two groups. However, on reinfusion**,** DO_2I returned to or slightly exceeded baseline values in group-A animals, while high values observed in group-B animals at T_1 decreased significantly at T_2 and T_3. Oxygen consumption index (VO_2I) remained unchanged in group-A animals, while a progressive increase in oxygen consumption peaking at T_2 and a subsequent decrease at the pre-terminal period were recorded in group-B animals (Table 2).

Hemoglobin oxygen saturation measured in the pulmonary artery (pa-SvO_2) was not significantly different between groups. Since standard deviations of hemoglobin oxygen saturation measured in the cranial vena cava (crvc-SvO_2) and in the caudal vena cava (cavc-SvO_2) were high, there was significant difference (Table 3). However, comparison of mean values of crvc-SvO_2 and cava-SvO_2 for both groups at the different experimental times revealed important increase in the hepatic O_2 consumption of group-B animals (Fig. 1) and, conversely, an extremely low extraction coefficient for group-A animals.

Regarding arterial bicarbonate concentration, both groups maintained stable values, with no significant differences (Fig. 2a). Lactic acid concentration constantly increased from T_0 to T_4 in group-A animals, whereas it peaked at T_2, then decreased again at T_3 and T_4 in group-B animals (Fig. 2b). In group-A animals, lactic acid values tended to decrease only during final experimental times, but always remained higher than baseline. The highest ammonium value was registered at T_3, when it was about 1.5 times that recorded at T_0 (Fig. 2c). In group-B animals, ammonemia increased and, at T_3, it was 3 times greater than the value at T_0. Consequently, a sharp decrease was observed in ammonemia data from group-B animals; a significant peak at T_3 was followed by a return to baseline at T_4.

Rectal temperature of the pigs remained stable at 37 ± 1.6°C during the study. Oliguria quickly developed in both groups after bleeding, which resulted in a significant ($P < 0.0005$) decrease in urine output by about 80 to 90%, from T0 to T1 that persisted until the end of the shock period. A modest increase in urine flow (approx. 50%) was observed in both groups at 30 to 60 min after reinfusion.

Monitoring of local-regional perfusion confirmed previous results (19), in terms of pHi trend and gastric tonometric CO_2 pressure (tCO_2) modifications (Table 4). In both groups, pHi decreased at each time point between T_0 and T_3, but the only significant reduction was seen between T_1 and T_0. In both groups, tCO_2 increased from T_0 and T_3, and decreased at T_4 only for group-A animals. At 30 min after reinfusion (T_4), ptO_2 was significantly lower in group-B animals (–63%, $P < 0.0005$), compared with that in group-A animals.

The pHi had significant ($P < 0.001$) correlation with pH measured at various vascular sites (pulmonary artery pH, $\rho = 0.74$; crvc pH, $\rho = 0.73$; cavc pH, $\rho = 0.70$) and arterial base excess D = 0.77).

During the shock period, the values of the pH-gap = (pHa – pHi)**,** where pHa is the blood pH collected from the carotid artery, were markedly higher in group-A animals due to regional hypoperfusion that regressed at T_4, during the post-reinfusion stage; reverse trend was observed in group-B animals, with slow, progressive increase in the pH-gap that peaked at T_4, (Fig. 3a). In similar manner, altered tissue oxygenation was confirmed through verification of the following statement: the more the pH-gap approaches zero, the more the CO_2-gap (tCO_2–PCO_2) tends toward the same limit (Fig. 3b; pH-gap – CO_2-gap, $\rho = 0.90$, $P < 0.001$).

Discussion

The physiologic response of the patient to stress or disease

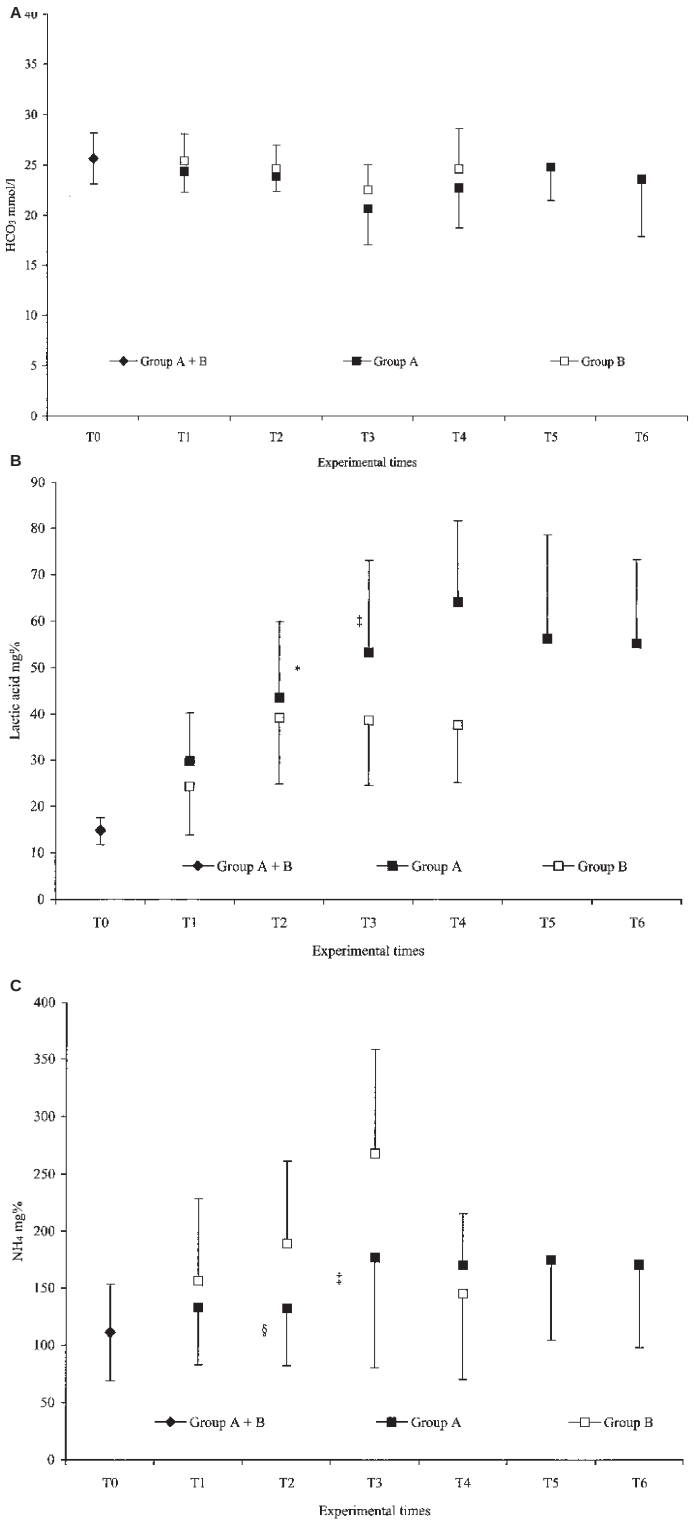

Figure 2. Mean (SD) arterial bicarbonate (A), lactic acid (B) and ammonium (C) concentrations of both groups at the experimental times. Mann-Whitney U test: $^{*}P < 0.05$; $^{\S}P < 0.005$; $^{\ddagger}P < 0.0005$.

process has long been recognized to greatly affect outcome according to the extent of injury and shock. Monitoring of the patient's physiologic responses is, therefore, important not only because it enables the assessment of the physiologic reserve but also since it provides a reliable baseline with which to judge the effectiveness of any treatment applied. Tonometry provides clinicians with a minimally invasive method of monitoring the gastrointestinal tract. This specific and important organ system, an early indicator of organ hypoperfusion, poorly tolerates reductions in oxygenation. Moreover, gastric tonometry has been used as a predictor of organ dysfunction and mortality in critically ill patients and has proven to be a better predictor of mortality than are base deficit, lactate concentration, oxygen delivery, and oxygen consumption (9, 14-17).

The aim of the study reported here was to assess the prognostic value of gastric tonometry, compared with standard hemodynamics, and to measure pre- and posthepatic hemoglobin oxygen saturation in a porcine model of hemorrhagic shock. To investigate whether gastric tonometry can supply additional and more accurate information in the initial phases of the hemorrhagic shock, when rescue procedures have not yet been started, animals did not receive pharmacologic treatment during shock. Although a control group (not reinfused group) was not included in this experiment and, thus, the percentage of recovery in terms of improvement secondary to reinfusion alone could not be calculated, the current model already induces appreciable physiologic stress in the opinion of the authors. Consequently, it was not advisable to extend the observation time of acute shock to 90 min without therapeutic intervention, this being a situation that does not occur under normal clinical conditions. Moreover, the authors believe that the experimental evidence is not affected by lack of a control group, and have, therefore, tried to minimize the number of animal used for experimental purposes.

Results of this study suggest that, at the beginning of the shock period, useful diagnostic and therapeutic indications can be acquired by simple measurement of hemodynamics, such as MAP, CI, and SVR. Although the current findings indicate that the SvO_2-gap, which presented an early, marked increase in group-B animals, may be a better indicator of shock development than some other hemodynamic parameters, MAP, CI, SVR, DO_2I, and VO_2I, that are are highly predictive of shock development. These parameters, in fact, become meaningful only after reinfusion, when the situation gets more complicated, and use of more sophisticated techniques is important to acquire information that traditional and invasive hemodynamics cannot supply. Comparison of data indicates that classic hemodynamic parameters behave differently; the incapacity to centralize circulation and increase systemic vascular resistances to survive during reinfusion appears to be highly predictive.

The behavior of the traditional hemodynamic parameters observed during post-reinfusion for the two groups justifies the assumption that the effects of anemia and local hypoxemia alone cannot account for the different outcomes. Results are, in fact, likely to be influenced by the SVR trend and local hypovolemia. Monitoring of local-regional perfusion followed a similar pattern and the findings confirmed previous results (19), in terms of pHi trend and gastric tonometric CO_2 pressure (tCO_2) modifications. None of the conventional markers of resuscitation (lactate concentrations, base acid deficit and DO_2I) correlated strongly with pHi, thus confirming that the regional flow may not be evaluated with certainty from global parameters (13). Animals of group A had greater percentage increase in pH-gap at the end of shock period and this could be ascribed to the

Table 4. Mean ± SD changes in tonometric parameters measured in groups A (n = 7) and B (n = 5)

Parameter	Groups	Baseline	Shock			Post-reinfusion			Friedman test
		T_0	T_1	T_2	T_3	T_4	T_5	T_6	
pHi		7.22 ± 0.14							
	A		7.11 ± 0.16	7.10 ± 0.19	7.02 ± 0.18	7.12 ± 0.21	7.16 ± 0.17	7.09 ± 0.28	T1 *vs* T0 $P < 0.01$, T4 *vs* T3 $P < 0.05$
	B		7.17 ± 0.13	7.14 ± 0.12	7.07 ± 0.12	7.09 ± 0.14	-	-	T1 *vs* T0 $P < 0.01$
tCO_2 (mmHg)		54.0 ± 15.0							
	A		66.0 ± 19.4	68.9 ± 28.5	72.4 ± 32.5	59.7 ± 17.9	58.3 ± 16.5	66.1 ± 26.0	T1 *vs* T0 $P < 0.01$, T4 *vs* T5 $P < 0.05$
	B		59.5 ± 14.7	60.7 ± 12.3	65.5 ± 13.7	67.7 ± 13.4	-	-	
PtO_2 (mmHg)		59.0 ± 29.7							
	A		37.7 ± 18.1	36.6 ± 19.3	37.9 ± 22.4	65.5 ± 35.1	50.7 ± 16.1	49.2 ± 30.2	T1 *vs* T0 $P < 0.01$, T4 *vs* T3 $P < 0.001$ T5 *vs* T4 $P < 0.05$
	B		36.5 ± 23.7	32.1 ± 20.6	26.5 ± 15.8	24.1 ± 2.2*	-	-	T1 *vs* T0 $P < 0.01$

pHi = intramucosal gastric pH; tCO_2 = gastric tonometric CO_2 pressure not corrected by use of the correction factor; $PtCO_2$ = gastric wall tissue oxygenation. Mann-Whitney U test comparing results of both groups for each parameter and at each time: $^*P < 0.000$.
See Table 1 for key.

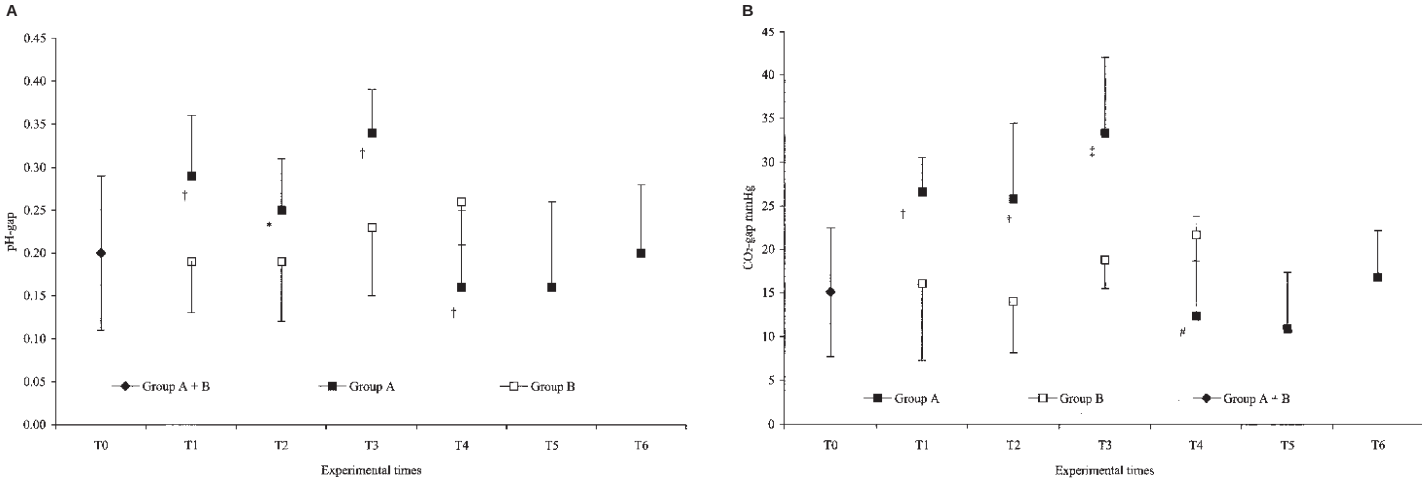

Figure 3. Mean (SD) pH-gap = pHa – pHi (a) and CO_2-gap = tCO_2 – PCO_2 (b) values for both groups at the experimental times. For group B, both values were significantly lower than those for group A during the shock period and until T_3 (Mann-Whitney U test: $^*P < 0.05$; $^\#P < 0.01$; $^\dagger P < 0.001$; $^\ddagger P < 0.0005$). At T_4, the pH-gap value for group A decreased and reached a value at T_6 similar to that at T_0.

higher SVR values, which are responsible for the marked splanchnic hypoperfusion. Experimental evidence suggests that the decrease in systemic DO_2I involves a progressive deterioration of the PtO_2 values, whereas at the end of shock period, the pH-gap results probably reflect the different pattern followed by the systemic resistances and the intravascular volume redistribution. This observation is also supported by the stability of the bicarbonate values in the two groups and the exclusive modification of the tCO_2 values. Nevertheless, the percentage reduction in pHi observed in group-A animals was not significantly different from that of group-B animals.

On the other hand, pHi behaved differently during post-reinfusion; animals of group A rapidly recovered from shock and, consequently, the parameter nearly returned to baseline, whereas recovery was not registered for group-B animals. Intravascular volume restoration and SVR reduction enabled the animals of group A to maintain standard ventricular kinetics and recover in terms of regional flow. Increase in pHi, decrease in pH-gap, and progressive restoration of the PtO_2 values were observed in group-A animals at T_4. Conversely, the increase in SVR and the impossibility of restoring a satisfactory intravascular volume affected the progressive failure of CI and worsening of the local-regional tension in group-B animals at T_4. The status of local hypoxia in group-B animals was confirmed by the PtO_2 trend, whereas the upward trend of the pH-gap highlighted a persistently altered tissue oxygenation due to blood volume redistribution with subsequent severe local hypovolemia. Nevertheless, the pHi in group-A animals at T_6 was exactly the same as that recorded in group-B animals at T_4, and, thus, it is hard to relate changes in SVR and restoration of vascular volume to this pHi value. Regarding the tCO_2 increase observed at T_4, it may depend on the persisting tissue hypoxia, and the source of increased tissue CO_2 is the intracellular buffering of excess hydrogen ions by bicarbonate (14, 15).

In the opinion of the authors, the difference between the two groups in terms of ammonemia may be related to the difference in renal perfusion secondary to the different SVR trend. Group-B animals, in particular, appeared to have the highest renal perfusion, leading to hyperproduction of NH_4^+ during shock. The sharp decrease observed in group-B animals on reinfusion may not depend on renal flow modification since this event should been seen in both groups. In reality, a relationship between such a measurement and the systemic data may not be hypothesized on account of the onset of irreversible shock.

Regarding the animal model selected, swine have been widely used to study the pathophysiologic mechanism(s) of hemorrhagic shock and to evaluate not only the widely used technological approaches, but also techniques that are not routine

procedures (9, 18-26, 31, 32). The porcine model has proven reliable when applied to the study of the cardiovascular and gastrointestinal systems (18-20). The increasing number of physiopathologic and anesthesiologic studies on swine has involved wider use of this animal and allowed researchers to determine the mean values of the hemodynamic, hematologic, and biochemical variables and blood gas parameters (32-37).

Although administration of H_2 antagonists is recommended to reduce intraluminal CO_2 production and increase the accuracy of gastric tonometry (38, 39), the authors did not use these drugs for this experimental study, since their routine administration was required neither to reduce gastric acid and its reaction with duodenal bicarbonate nor to obtain adequate pHi measurement (16, 17). The systemic factors inherent in measurement of intramucosal PCO_2, such as respiratory acidosis or alkalosis, may also limit the use of gastric tonometry. Even though some authors have stated that the stomach is not the most appropriate organ for monitoring splanchnic circulation and have suggested that comparison between jejunal pHi and gastric tonometric values should be mandatory, the authors decided to measure pHi only in the stomach and make a comparison focusing on gastric wall tissue oxygenation (40-42).

In conclusion, even though the relevance of this study may be limited by the fact that only gastric hypoperfusion was considered, whereas the other viscera were disregarded, the aim of this work was to assess the effectiveness of such monitoring technique in the evaluation of hemorrhagic shock-related clinical conditions. Additionally, researchers evaluated gastrointestinal tract ischemia during all the phases of circulatory shock, and reactions of the gastric wall to hypoperfusion and lower oxygenation also were assessed. Without taking into consideration hepatic DO_2 and VO_2, which would require a more complicated monitoring system, traditional measurement of hemodynamics seems to be adequate for monitoring the development and possible therapeutic response (not investigated in this study) in the initial phases of hemorrhagic shock. Although a minimally invasive assessment of the adequacy of perfusion of the gastrointestinal tract has become clinically feasible with the gastric tonometer, pHi does not appear to supply any additional prognostic information at the beginning of hemorrhagic shock according to the findings of this study. Nevertheless, this reliable and easily accessible technique can provide excellent opportunities for monitoring gastrointestinal tract ischemia in the recovery phase after shock and critical illness.

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