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Cardiopulmonary Effects of Hemorrhagic Shock in Splenic Autotransplanted Pigs: A New Surgical Model

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A B S T R A C T

The spleen is an important organ for hemodynamic compensation during hemorrhagic shock. The aim of the study was to compare the hemodynamic and metabolic responses of sham-operated pigs with intact spleen, splenectomized pigs, and splenic autotransplanted pigs during hemorrhagic shock. Hemorrhagic shock was induced by 30% total blood volume bleed in sham-operated, splenectomized and splenic autotransplanted pigs (n=20). Cardiopulmonary and metabolic variables were measured before, immediately after, and at 20, 60 and 100 minutes after hemorrhage. Upon hemorrhagic shock induction, body temperature, mean arterial pressure, mean pulmonary arterial pressure, cardiac output, cardiac index and oxygen delivery decreased, while lactate and shock index increased. Hemoglobin and hematocrit were significantly lower in the splenectomized and splenic autotransplant groups as compared with the control group at 60 and 100 minutes after hemorrhage ($p<0.05$). Unlike intact spleen, splenic autotransplant could not improve hemodynamic parameters in hemorrhagic shock in pigs. In comparison to mice, rats or dogs, this species could be an interesting investigation model to test new surgical procedures during splenic related hemorrhagic shock, with potential applications in human medicine.

Key words: *spleen, splenic autotransplant, hemorrhagic shock, pig*

Introduction

The functions of the spleen include erythrocyte conditioning and maintenance, extramedullary hematopoiesis, immune functions, and reservoir functions. Stress, hypoxemia and blood loss can activate splenic contraction, therefore spleen is an important organ for hemodynamic compensation during hemorrhagic shock in the dog. The spleen regulates its volume in response to an exercise-intensity-dependent signal in humans. It was observed that dogs with intact spleen had better hemodynamic parameters during hemorrhagic shock than splenectomized transfused dogs (splenectomized dogs which were given a volume of packed red blood cells simulating splenic contraction, 5 mL/kg). The conclusion was that spleen could improve cardiovascular function by a mechanism other than autotransfusion during hemorrhagic shock in dogs.

The possibility that spleen releases a humoral substance (liver-spleen factor) was first postulated by Rein et al., and the splenic cardiotonic factor named splentransin was extracted in several animal species and in human urine. The spleen releases cardioactive substances that can stimulate isolated perfused hearts.

Septic complications after splenectomy and the assumed life-long risk of fatal sepsis have changed attitudes to spleen removal. Several surgical techniques

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have been used to preserve spleen function. One of these techniques is splenic autotransplantation, which is considered when total splenectomy is required and a part of the spleen is viable and healthy. Autotransplantation results in the development of small splenic nodules that are histologically similar to normal spleen and is not indicated in animals that retain a portion of their spleen or in malignant splenic disease.

Hemorrhage leads to activation of a number of physiological mechanisms to promote the restoration of blood volume and arterial pressure. These responses to hemorrhage are associated with peripheral vasoconstriction, along with blood flow redistribution to vital organs such as the brain and heart from skin (pale mucous membrane, increased capillary refill time, cold extremities), spleen (splenic contraction), kidneys (decreased urine production), pancreas, intestine (bacterial translocation), and liver (hepatic apoptosis).

Can splenic autotransplant produce a humoral substance with a cardiostimulating effect? The aim of the present study was to compare the hemodynamic and metabolic responses of sham-operated pigs with spleens intact, splenectomized pigs and splenic autotransplanted pigs after acute blood loss of 30% of total blood volume, and to determine the role of splenic autotransplant in hemorrhagic shock.

Material and Methods

Animals

Experimental protocol was approved by the Department of Veterinary Science, Croatian Ministry of Agriculture, and was conducted in accordance with the guidelines for the treatment of laboratory animals. Emotional reassurance (gentle restraint, petting and talking) was provided by the handler. Twenty piglets of either sex, aged 3 months, weighing 19–26 kg were used in the experiment. In each animal food was withheld for 12 hours and water for 2 hours before the experiment.

Anesthesia and surgery

The animals were premedicated with 2 mg/kg intra-muscular (IM) of xylazine (Xylapan, Vetoquinol, Bern, Switzerland), and left auricular vein was catheterized percutaneously for continuous infusion of lactated Ringer's solution at a rate of 10 mL/kg//h during surgical procedures and for administration of drugs. Anesthesia was induced with 5 mg/kg intra-venous (IV) of ketamine (Ketaminol 10, Intervet, Boxmeer, Netherlands) and 10 μg/kg IV fentanyl (Fentanyl-Jannsen, Jannsen Pharmaceutica, Beerse, Belgium), and animals were intubated, connected to circle system and maintained on spontaneous ventilation. Anesthesia was maintained with 1.5% isoflurane (Forane, Abbott, Queenborough, UK) and continuous intravenous infusion of fentanyl in a dose of 0.8 μg/kg/min. Supplemental doses of ketamine were given during surgery to maintain sufficient anesthesia depth. Perioperative antibiotic prophylaxis was administered using 20 mg/kg IV ampicillin and sulbactam (Penactam, Krka, Novo mesto, Slovenia).

After induction of anesthesia, animals were randomly divided into three groups: control group (n=6), sham-operated pigs with spleens intact; group S (n=7), splenectomized pigs; and group A (n=7), splenectomized pigs with small fragments of 20% mass of the spleen autotransplanted in the greater omentum.

Experimental protocol

Six weeks after surgical procedure, the second phase of the experiment started. Each animal was kept *nil per os* for 12 h before the experiment, with the exception of free access to water until 2 h before the experiment.

After premedication with 2 mg/kg IM of azaperone (Stresnil, Janssen Cilag, Beerse, Belgium), auricular vein was cannulated and 5 mg/kg of thiopental sodium (Thiopental, Nycomed, Ismaning, Germany) was administered intravenously. Endotracheal intubation was done and anesthesia was maintained with 1.5% isoflurane. The pigs were maintained on spontaneous ventilation. Respiration was controlled if necessary with a ventilator (Veterinary Ventilator Model 2000, Hallowel EMC, Pittsfield, MA, USA) to maintain end-tidal CO_2 (ET-CO_2) at 35–45 mm Hg. Perioperative antibiotic prophylaxis was administered using ampicillin and sulbactam. Arterial catheter was placed in the right femoral artery for arterial blood pressure measurements, arterial lactate and arterial blood gas sampling. The catheter was connected by saline-filled tube to an electrical pressure transducer (Gabarith PMSET 1DT-XX, Becton Dickinson, Sandy, USA).

A 7.5 Fr Swan-Ganz catheter (BD Criticath SP5507H thermodilution catheter, Becton Dickinson, Sandy, USA) was introduced *via* left jugular vein into pulmonary artery for measuring pulmonary artery pressure and cardiac output (CO). Invasive arterial pressure and pulmonary artery pressure were recorded with pressure transducers and displayed on a monitor (Ultraview 1050, Spacelabs, Issaquah, USA). All transducers were zeroed to the midchest of the animal. Heart rate was measured from electrocardiogram, which was also continuously monitored. Body temperature was measured rectally. CO was measured by the thermodilution method. Five milliliters of cold, heparinized saline (4 °C) *per* measurement was used and the mean of five measurements was taken for CO.

Samples of venous blood for determination of hematocrit, hemoglobin and venous blood gases were obtained from central vein. Blood gases were measured using a blood gas analyzer (ABL5, Radiometer, Copenhagen, Denmark).

After placement of all monitoring lines, there was no further manipulation during a 30-minutes period to establish baseline condition. Thereafter, hemorrhagic shock was induced by withdrawing 30% of the estimated total blood volume (blood volume was considered to be 65 mL/kg) at a constant rate over 15 minutes from the central venous catheter. Arterial and venous blood gases as well as lactate, hemoglobin, hematocrit and hemodyna-

mic parameters were measured at baseline and at 1, 20, 60 and 100 minutes of the completion of hemorrhage.

Resuscitation was initiated after final measurements (minute 100). Success of splenic autotransplantation was confirmed after end of experiment by biopsy and pathohistological examination.

Statistical analysis

All results were expressed as mean±standard deviation. Data were analyzed using repeat measurement analysis of variance and Duncan's test for difference among means. A value of $p<0.05$ was considered statistically significant.

Results

Lethality

Two pigs (one splenectomized and one autotransplanted pig) died during the 6-week period, so each group consisted of 6 pigs. Two animals (one splenectomized and one autotransplanted pig) died after completion of the experiment (one hour after minute 100 of the experiment).

Metabolic parameters

Data on metabolic parameters are shown in Table 1. There was no significant difference in the baseline values of metabolic parameters between the study groups.

Body temperature gradually dropped in all animals, with lowest values observed at minute 100 after hemorrhage. In group S body temperature was 33.1±1.4°C, which was significantly lower compared with 34.8±0.7°C in control group 100 minutes after hemorrhage ($p<0.05$). At minute 100 after hemorrhage, body temperature differed significantly from the baseline in all groups ($p<0.05$) (Table 1).

Arterial blood oxygen (CaO_2) and mixed venous oxygen (CvO_2) content decreased immediately after hemorrhage and 20 minutes later. Although CaO_2 and CvO_2 showed spontaneous partial recovery before resuscitation, at 60 and 100 minutes after hemorrhage these values were significantly lower in groups S and A than as compared with control group ($p<0.05$) (Table 1).

A decrease from baseline in oxygen delivery was observed in all groups at all times after hemorrhage. A significant difference in oxygen delivery was observed between control group and group A at 1.60 and 100 minutes after hemorrhage ($p<0.05$) (Figure 1).

Hyperlactatemia developed after hemorrhage in groups S and A. In control group, serum lactate concentrations decreased after hemorrhage (Figure 2). In groups S and A, arterial lactate concentration at 20, 60 and 100 minutes of removal of 30% of the blood volume differed significantly from the concentration measured in the control group in ($p<0.05$). The increase in serum lactate concentration was followed by a decrease in base excess (BE) and signs of metabolic acidosis in groups S and A. At 20, 60 and 100 minutes of hemorrhage, hemoglobin was significantly lower in groups S and A than in the control group. At 100 minutes of hemorrhage, hemoglobin and hematocrit dropped below baseline in groups S and A, but exceeded baseline level in the control group (Table 1, Figure 3).

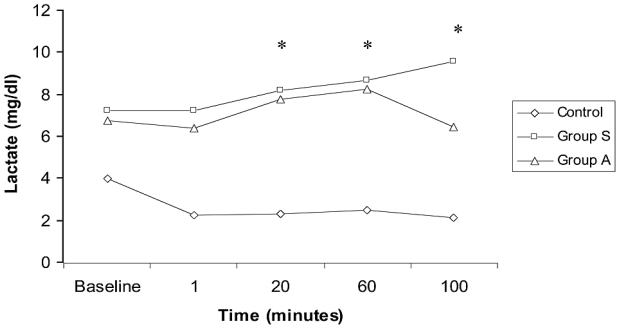

*Fig. 2. Arterial lactate concentration during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6). Groups S and A differed significantly from control group at 20, 60 and 100 minutes after removal of 30% of the blood volume (*p<0.05).*

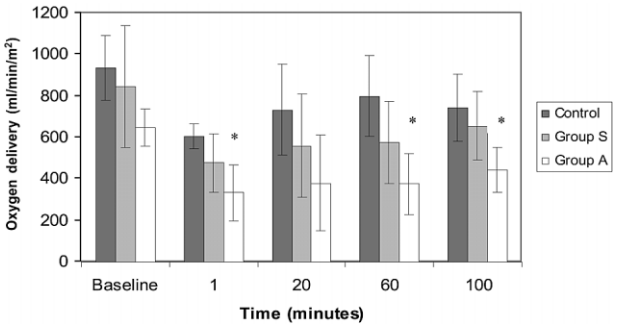

*Fig. 1. Oxygen delivery during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6). Group A differed significantly from control group at 1, 60 and 100 minutes after removal of 30% of the blood volume (*p<0.05).*

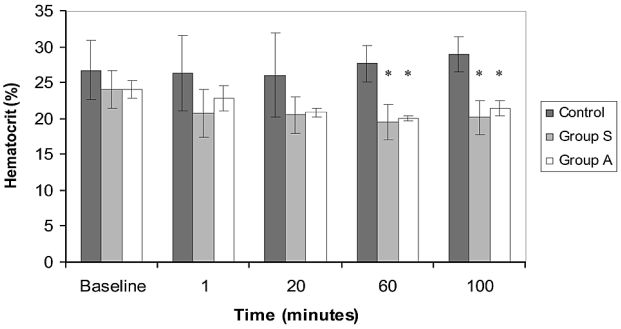

*Fig. 3. Hematocrit during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6). Groups S and A differed significantly from control group at 60 and 100 minutes after removal of 30% of the blood volume (*p<0.05).*

TABLE 1

Variables (Units)	Time (min)	Control	Group S	Group A
Body temperature (°C)	Baseline	36.8 (0.8)	35.1 (1.4)	35.4 (0.9)
	Shock 1	36.3 (0.7)	34.9 (1.3)	35.3 (1.0)
	Shock 20	35.9 (0.7)	34.3 (1.3)	34.8 (0.9)
	Shock 60	35.3 (0.6)	33.5 (1.5)	34.2 (0.8)
	Shock 100	34.8 (0.7)	33.1 (1.4)*	33.5 (0.8)
CaO_2 (vol %)	Baseline	12.3 (2,2)	11.1 (1.2)	10.9 (1.4)
	Shock 1	12.1 (2,1)	10.3 (1.1)	10.3 (1.3)
	Shock 20	12.2 (2,3)	9.7 (1.3)	9.8 (0.6)
	Shock 60	13.0 (1,3)	10.1 (1.6)*	10.0 (1.1)*
	Shock 100	13.3 (1,5)	10.3 (1.8)*	9.8 (0.7)*
CvO_2 (vol %)	Baseline	10.6 (2.1)	9.9 (1.5)	10.1 (1.8)
	Shock 1	9.7 (2.1)	8.1 (1.3)	9.2 (1.7)
	Shock 20	10.5 (2.4)	8.3 (1.3)	9.0 (0.8)
	Shock 60	11.3 (1.6)	8.8 (1.2)*	9.1 (1.2)*
	Shock 100	12.0 (1.5)	9.0 (1.7)*	9.1 (0.8)*
Hemoglobin (g/L)	Baseline	88 (14)	76 (9)	73 (10)
	Shock 1	85 (17)	70 (8)	67 (10)
	Shock 20	86 (18)	66 (8)*	64 (5)*
	Shock 60	91 (8)	69 (12)*	66 (8)*
	Shock 100	95 (8)	70 (13)*	66 (6)*
Base excess (mEq/L)	Baseline	3.4 (11.0)	–1.8 (10.1)	2.7 (9.3)
	Shock 1	3.2 (6.5)	–1.6 (10.0)	–1.7 (6.8)
	Shock 20	2.8 (3.2)	–2.0 (10.9)	–2.5 (5.2)
	Shock 60	3.2 (1.6)	–2.0 (12.2)	–4.7 (6.8)
	Shock 100	2.4 (2.9)	–4.4 (14.2)	–3.5 (8.1)

Metabolic parameters: CaO_2, arterial oxygen content (vol %); CvO_2, venous oxygen content (vol %). Values expressed as mean (standard deviation). Shock 1, 20, 60 and 100, measured 1, 20, 60 and 100 minutes after completion of hemorrhage (*: $p<0.05$ *vs*. control)

Hemodynamic parameters

Data on hemodynamic measurements are shown in Table 2. Baseline values of the hemodynamic parameters were not significantly different in any of the experimental groups.

The values of arterial pressure, cardiac output, cardiac index and cardiac work decreased upon induction of hemorrhagic shock and increased after 20, 60 and 100 minutes of hemorrhage (Table 2, Figures 4 and 5). Hemorrhage caused a non significant fall in heart rate in all groups immediately after hemorrhage. At 100 minutes after hemorrhage heart rate values were non significantly higher than baseline values in all groups (Table 2).

There was no statistically significant difference between groups in systolic blood pressure. Immediately after hemorrhage, systolic blood pressure decreased in all groups and began to increase after 20 minutes (Figure 4). The values of diastolic blood pressure were statistically significantly higher in the control group than in groups S and A at 1, 20, 60 and 100 minutes after hemorrhage ($p<0.05$). The mean blood pressure values were statistically significantly higher in the control group than in groups S and A at 1 minute after hemorrhage; at 60 minutes of hemorrhage only group S showed a statistically significantly lower mean arterial pressure (MAP) than the control group ($p<0.05$) (Table 2). In all groups, baseline blood pressure values differed significantly from the post-hemorrhagic values ($p<0.01$).

CO and cardiac index decreased from baseline in all three groups, however, never reaching statistical significance. The lowest values of cardiac index were recorded immediately after hemorrhage. There were no statistically significant differences among the three groups in CO or cardiac index either (Table 2, Figure 5). A significant stroke index decrease from 82.8±24.3 to 51.7±6.5 mL/beat/m^2 was recorded upon hemorrhagic shock induction in group S ($p=0.039$) (Table 2).

Pulmonary arterial mean pressure was statistically significantly higher in sham-operated pigs than in splenectomized pigs at 1 minute after hemorrhage (Table 2).

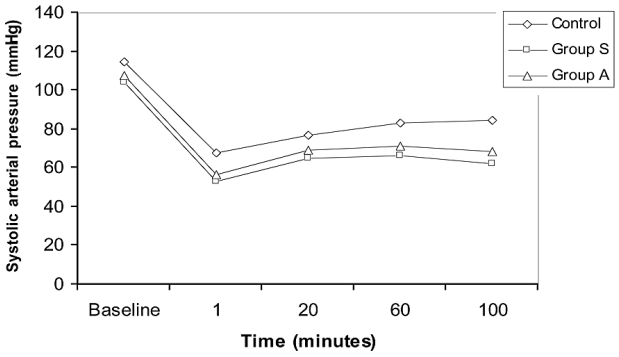

Fig. 4. Systolic arterial pressure during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6).

TABLE 2

	Time (min)	Control	Group S	Group A
Heart rate (beats/min)	Baseline	106 (31)	93 (21)	116 (13)
	Shock 1	96 (21)	88 (14)	105 (33)
	Shock 20	86 (29)	93 (24)	110 (33)
	Shock 60	122 (33)	98 (6)	118 (32)
	Shock 100	116 (34)	94 (20)	140(19)
DAP (mm Hg)	Baseline	75 (12)	66 (22)	69 (9)
	Shock 1	44 (6)	33 (6)*	32 (4)*
	Shock 20	50 (8)	36 (8)*	40 (6)
	Shock 60	53 (8)	38 (8)*	41 (2)*
	Shock 100	52 (6)	36 (8)*	40 (6)*
MAP (mm Hg)	Baseline	92 (12)	82 (21)	83 (14)
	Shock 1	53 (5)	41 (8)*	42 (6)*
	Shock 20	61 (7)	47 (11)	53 (10)
	Shock 60	65 (8)	50 (12)*	52 (5)
	Shock 100	65 (8)	47 (14)	54 (11)
CO (l/min)	Baseline	6.3 (1.4)	5.1 (2.1)	4.2 (0.8)
	Shock 1	4.3 (1.6)	3.1 (1.0)	2.5 (1.4)
	Shock 20	4.9 (1.3)	3.9 (1.9)	2.8 (1.8)
	Shock 60	5.0 (1.3)	3.9 (1.7)	2.7 (1.3)
	Shock 100	4.5 (0.8)	4.3 (1.5)	3.2 (1.0)
SI (mL/beat/m^2)	Baseline	77 (24)	83 (24)	52 (10)
	Shock 1	56 (18)	52 (7)	36 (20)
	Shock 20	81 (36)	62 (21)	39 (25)
	Shock 60	57 (31)	58 (16)	36 (21)
	Shock 100	52 (20)	73 (27)	34 (13)
PAMP (mm Hg)	Baseline	27 (12)	24 (7)	26 (4)
	Shock 1	23 (5)	13 (6)*	18 (3)
	Shock 20	18 (7)	15 (7)	19 (4)
	Shock 60	18 (5)	16 (6)	20 (6)
	Shock 100	18 (7)	19 (6)	22 (7)
Cardiac work	Baseline	709 (126)	546 (294)	450 (79)
	Shock 1	284 (87)	173 (92)	143 (82)
	Shock 20	375 (79)	264 (183)	210 (162)
	Shock 60	412 (91)	223 (185)	201 (106)
	Shock 100	378 (75)	239 (189)	223 (88)

Hemodynamic parameters: DAP, diastolic arterial pressure (mm Hg); MAP, mean arterial pressure (mm Hg); CO, CO (L/min); SI, stroke index (mL/beat/m^2); PAMP, pulmonary arterial mean pressure (mm Hg); Shock 1, 20, 60 and 100, measured 1, 20, 60 and 100 minutes after completion of hemorrhage (*:$p<0.05$ *vs.* control). Values expressed as mean (standard deviation).

Cardiac work dropped upon induction of hemorrhagic shock, and baseline values of cardiac work were significantly different from post-hemorrhagic values in all groups ($p<0.05$).

Shock index differed between groups, however, without statistical significance. Shock index increased from 0.92±0.16 at baseline to 1.37±0.39 after 100 minutes in the control group ($p=0.042$), from 0.93±0.35 to 1.86±0.93 in group S ($p>0.05$), and from 1.10±0.24 to 2.23±0.89 in group A ($p>0.05$) (Figure 6).

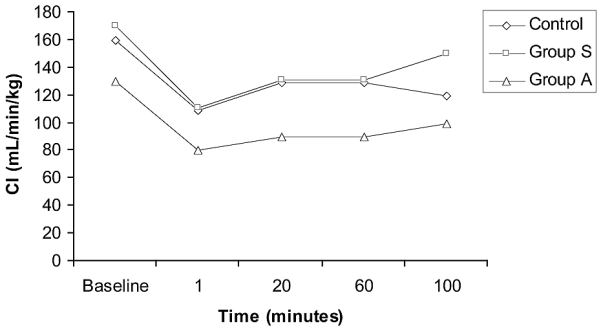

Fig. 5. Cardiac index during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6).

Discussion

The rise in serum lactate in clinical shock is the result of a combination of increased lactate production and decreased lactate clearance by the liver because of diminished blood flow to the liver. The occurrence of high lactate in any clinical shock syndrome carries a poor prognosis. It is reported that 25% human patients died within the first 24 hours of septic shock, and these early fatalities had a higher blood lactate (12.2±3.0 *vs.* 4.6±1.3 mg/dL) concentration. The duration of lactic acidosis is associated with the development of multiple organ failure and death. High lactate levels due to hemorrhagic shock appear to be associated with better outcomes than increases in lactate due to either cardiogenic or septic shock states.

The lactate level increase (2- to 3.5-fold baseline) is commonly seen in pigs during hemorrhagic shock in a volume dependent, pressure dependent and oxygen debt model. In splenectomized dogs, serum lactate concentration was two- to fourfold that in spleen intact dogs. In this study, each splenectomized dog died during the post-hemorrhagic period. The post-shock elevation of lactate

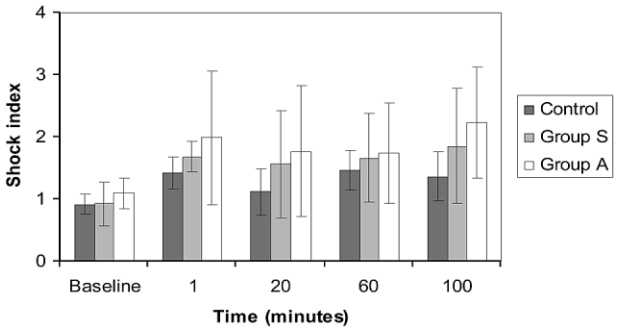

Fig. 6. Shock index during hemorrhagic shock in control group (n=6), splenectomized group (group S; n=6), and splenic autotransplanted group (group A; n=6).

concentration in splenectomized dogs was associated with anaerobic metabolism as the result of cellular hypoxia.

During our experiment, serum lactate concentration 100 minutes after hemorrhage in animals that died immediately upon completion of the experiment was above 10 mg/dL. It is concluded that high serum lactate concentration could be an indicator of lethal outcome. Splenectomized and autotransplanted pigs had statistically higher values of arterial lactate than sham-operated pigs because these two groups sustained a more severe shock syndrome.

Base excess (BE) has been used as an indirect measure of serum lactate. Both BE and lactate, or their combination can be used to predict outcome in patients admitted to ICU. Patients who had either BE more negative than –4 mmol/L or arterial lactate greater than 1.5 mmol/L had a mortality rate of 50.6%. A BE decrease from baseline positive values to posthemorrhagic negative values was recorded in the experiments with pressure dependent model and volume dependent model of hemorrhagic shock in anesthetized pigs.

In our experiment, BE followed lactate concentration in splenectomized and autotransplanted groups of pigs, and decreased from baseline –1.8 and 2.8 mEq/L to –4.4 and –3.5 mEq/L at 100 minutes of hemorrhage. Pigs that died after 100 minutes of the experiment had BE below –10 mEq/L. Data from the present study indicate that BE may be of value as an indicator of shock severity in the swine model of hemorrhagic shock.

Cardiac performance was evaluated during hemorrhagic shock in splenectomized transfused dogs given a volume of packed red blood cells simulating splenic contraction (5 mL/kg). It was observed that 4–8 mL/kg of blood were displaced by splenic contraction during a 40% hemorrhage. During hemorrhage, CO and stroke volume decreased to a significantly greater extent in the splenectomized and splenectomized transfused groups than in the spleen intact group. One reason was splenic contraction in the spleen intact dogs. Splenic contraction began at 3 minutes after hemorrhage and total splenic volume decreased by 55%. After hemorrhage, there was a progressive increase in CO and stroke volume in all groups. At 120 minutes after hemorrhage, the change in CO and stroke volume from control values was less in the spleen intact (27%) than in the splenectomized and splenectomized transfused animals (50% and 60%, respectively). There was no significant between-group difference in CO and stroke volume 300 minutes after hemorrhage.

In one study, hemorrhagic shock was induced by bleeding 28% of the total blood volume in pigs and the shock state was maintained for one hour. A 25% CO decrease was observed immediately after completion of bleeding and a 12% CO decrease 60 minutes after completion of bleeding. Cardiac index decreased by about 33% after removal of 20% of total blood volume in anesthetized piglets. In a porcine pressure-dependent model of hemorrhagic shock, pigs were also bled but maintained mean arterial pressure (MAP) at 35 mm Hg for 90 minutes. A >80% drop in cardiac index and stroke volume was recorded at 30 minutes. This drastic fall could be the consequence of using the pressure dependent model (*versus* volume dependent model used in our study) and different anesthetic protocols (ketamine and halothane *versus* azaperone, thiopental and isoflurane in our study).

In our study, CO in splenectomized pigs was reduced by 39% immediately after completion of hemorrhage and by 24% 60 minutes after completion of hemorrhage. CO decreased immediately after blood withdrawal in each group. At 100 minutes after hemorrhage, control group had a higher CO than splenectomized and splenic autotransplanted pigs, however, the difference did not reach statistical significance ($p>0.05$). Cardiac index had a minimal value upon induction of hemorrhagic shock to increase thereafter, yet not exceeding the baseline value measured before blood withdrawal. CO increases in proportion to the heart rate, myocardial contractility and preload, and in inverse proportion to afterload value.

In the current study, a statistically significant fall of blood pressure was observed in all groups after hemorrhage. Upon completion of the 15-minute period of hemorrhage, the mean arterial blood pressure decreased by 50% in splenectomized pigs, by 49% in splenic autotransplanted pigs, and by 42% in the control group. Arterial blood pressure depends on CO, blood vessel capacity and blood volume. Changes of CO are discussed above. Blood vessel capacity was not changed immediately after hemorrhage, but vasoconstriction began soon as a compensatory mechanism for hemorrhagic shock. The most significant between group differences were observed in diastolic blood pressure. Sham-operated pigs compensated hypovolemia with splenic contraction and blood autotransfusion, which increased total blood volume.

Our findings are in line with a previous study using a porcine model. The mean arterial pressure (MAP) of splenectomized, anesthetized pigs decreased by 45–48% from baseline at 30 minutes of hemorrhagic shock induction (35% of total blood volume withdrawn); at 90 minutes of hemorrhagic shock induction no MAP increase was observed. MAP decreased by 25% after removal of 20% of total blood volume in anesthetized piglets.

Blood pressure was significantly more depressed in splenectomized groups than in spleen intact dogs. While blood pressure progressively increased in all animals during early shock, it failed to reach prehemorrhage values in any group. During late shock, arterial blood pressure returned closer to baseline values in splenectomized transfused and spleen intact dogs than in splenectomized dogs. At 15 minutes of hemorrhage (41% of total blood volume over a 15-minute period), systolic blood pressure decreased in spleen intact dogs by only 34% and in splenectomized dogs by 59%.

Shock index (heart rate/systolic blood pressure) has a normal range between 0.5 and 0.7 in humans. Shock index elevation to more than 0.9 should be treated immediately at an intensive care unit. Elevation of shock index to more than 1.5 may be life-threatening. In our study, the splenectomized and autotransplanted animals had a shock index of more than 1.5 during hemorrhagic shock.

Two animals (splenectomized and autotransplanted) with a shock index of >2.2 during hemorrhagic shock died after the experiment. It is concluded that shock index could serve as a prognosis indicator during hemorrhagic shock.

In human medicine, unstable patients suspected of splenic injury and intra-abdominal hemorrhage should undergo exploratory laparotomy and splenic repair or removal. Prognosis is usually excellent, but those patients left asplenic by their injuries and surgery increase the risk of fatal and debilitating infection for the remainder of their lives. Conservative approach of this surgery (like partial splenectomy or autotransplantation of the repaired spleen) is thus very often proposed. Autotransplantation is a technically simple and relatively rapid procedure. The imunologic effect and the possibility of phagocytosis of splenic autotransplant were investigated in a number of experiments, concluding that the imune function of splenic autotransplant was comparable to that of intact spleen.

In this study on pigs, our results suggest that spleen autotransplantation may partially restore hemorheological functions following splenectomy but splenic autotransplant is not able to improve hemodynamic parameters during hemorrhagic shock. Anyway, this swine model can be useful for evaluation of hemodynamic and metabolic parameters in experimental induced hypovolemic shock. Further investigations could be interesting to correlate this model to human physiology; however, these first data are still concordant with the actual knowledge about human physiology during spleen autotransplantation. This surgical model could be useful for evaluation of new surgical procedures during human splenic autotransplantation or for the treatment of traumatic spleen rupture, and give more relevant data than studies on mice, rats or rabbits.

Conclusion

Sham-operated animals were hemodynamically more stable than splenectomized and autotransplanted animals. Therefore, we conclude that splenic autotransplant cannot improve hemodynamic parameters during hemorrhagic shock in pigs. This report can serve as a basis for additional research into the role of the spleen and splenic autotransplant in the pathophysiologic events during hemorrhagic shock in pigs. Moreover, these data confirm the relevance of the swine model for testing new treatment of hemorrhagic shock during splenic autotransplantation or after traumatic spleen rupture, and perhaps for further investigation with applications in the human clinical field.

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KARDIOPLUMONARNI EFEKTI HEMORAGIJSKOG ŠOKA U SVINJA S TRANSPLANTIRANOM SLEZENOM: NOVI KIRURŠKI MODEL

S A Ž E T A K

Slezena je organ koji ima važnu ulogu pri hemodinamskoj kompenzaciji hemoragijskog šoka. Cilj ovog istraživanja bio je usporediti hemodinamske i metaboličke odgovore za vrijeme hemoragijskog šoka u kontrolne skupine svinje, u splenektomiranih svinja i u svinja u kojih je učinjena autotransplantacija slezene. Hemoragijski šok je izazvan iskrvarenjem 30% ukupnog volumena krvi u sve tri skupine životinja (n=20). Kardiopulmonarni i metabolički parametri su mjereni prije iskrvarenja, neposredno nakon iskrvarenja, te 20, 60 i 100 minuta nakon iskrvarenja. Nakon nastanka hemoragijskog šoka došlo je do smanjenja tjelesne temperature, srednjeg arterijskog krvnog tlaka, srčanog minutnog volumena, srčanog indeksa i dostave kisika, dok su se vrijednosti laktata i indeksa šoka povećale. Vrijednosti hemoglobina i hematokrita bile su značajno niže u splenektomiranih svinja i u svinja u kojih je učinjena autotransplantacija slezene nego u kontrolne skupine svinja 60 i 100 minuta nakon iskrvarenja ($p<0,05$). Za razliku od slezene, autotransplantat slezene nije mogao poboljšati hemodinamske parametre za vrijeme hemoragijskog šoka u svinja. Miševi, štakori i psi bili bi zanimljiv animalni model za provođenje novih istraživanja o ulozi slezene za vrijeme hemoragijskog šoka, koja bi bila primjenjiva i u humanoj medicini.