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A COMBINED TRAUMA MODEL OF CHEST AND ABDOMINAL TRAUMA WITH HEMORRHAGIC SHOCK—DESCRIPTION OF A NEW PORCINE MODEL

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ABSTRACT—Despite the high incidence and prognostic relevance of hemorrhagic shock and abdominal and blunt chest trauma in multiply injured patients, there are no animal models combining these injuries. Therefore, we established a new porcine multiple trauma model consisting of blunt chest trauma, penetrating abdominal trauma (two incisions in the right upper liver lobe using a four-edged scalpel and subsequent liver packing), and pressure-controlled hemorrhagic shock with a mean arterial pressure of 30 ± 5 mmHg (a maximum of 45% of the total blood volume). The combined traumatic insult led to severe signs of hemorrhagic shock and impaired pulmonary function. In conclusion, a consistent, reproducible, and clinically relevant porcine model of multisystem injury with controlled (pressure-controlled blood withdrawal) and uncontrolled components of hemorrhage (liver laceration) with the potential for rebleeding was established.

KEYWORDS—Multiple trauma model, hemorrhagic shock, chest trauma, abdominal trauma, pigs

INTRODUCTION

Hemorrhagic shock due to severe abdominal trauma is one of the major causes of death within 24 h after multiple trauma (1). In about two thirds of the cases, abdominal trauma is accompanied by an additional chest trauma, which results in a further significant increase in posttraumatic complications (2). As severe bleeding is associated with a significant loss of clotting factors and often results in a severe dysfunction of the coagulation system, the reversal of the trauma-related lethal triad of coagulopathy, acidosis, and hypothermia is indispensable for a successful treatment of these bleeding trauma patients.

Diverse large animal models of hemorrhagic shock have been developed (1, 2). In these models, experiments are mainly performed in pigs as the effects of hemorrhagic shock on hemodynamic and pulmonary function are similar to the posttraumatic response in humans (1, 3). However, despite the high clinical incidence and the prognostic relevance of hemorrhagic shock combined with abdominal and chest trauma, no large animal model combining these three entities (hemorrhagic shock, liver laceration, and lung contusion) exists so far. Furthermore, the majority of previous large animal models have potential limitations due to the absence of solid organ injuries, as posttraumatic coagulopathy may complicate bleeding control from nonvascular sources such as the liver. Consequently, new large animal models of hemorrhagic shock are needed, which add an additional penetrating abdominal trauma (e.g., liver laceration) as an indicator for posttraumatic bleeding control and for clinical observation of rebleeding.

Therefore, the present study aimed to establish a new porcine trauma model, which is (i) induction of multisystem injury (lung injury, liver injury, and hemorrhagic shock), (ii) injury to a solid organ (liver) as an indicator for potential coagulation disorders and secondary bleeding, and (iii) damage of the lung as a vulnerable shock organ. Furthermore, the model should be close to the realistic preclinical emergence and cover the early hospital phase.

MATERIALS AND METHODS

Animal care

Before initiation, the study was approved by the Animal Welfare Committee of Vienna, Austria. The experiments were performed in 30 male pigs (German domestic pigs, Munichshtal) aged 12 to 16 weeks and weighing 30 ± 3 kg. Whereas water was available *ad libitum*, the animals were fasted overnight because of prophylaxis of aspiration and to prevent differences in blood sugar levels. The first 10 animals were used for adjusting the impact of the combined traumatic insults during the establishing process. The remaining 20 pigs were assigned to a sham group (n= 10), receiving only anesthesia and placement of arterial, venous, and urinary lines, as well as a trauma group, in which blunt chest trauma, liver laceration, and hemorrhagic shock were induced under normothermic conditions (n = 10).

All experimental procedures were conducted in deep anesthesia.

Premedication and anesthesia

The pigs were premedicated, and anesthesia was induced with an intramuscular application of Zoletil mixture (xylazine 146 mg, ketamine 125 mg,

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butorphanol 25 mg, tiletamine 50 mg, zolazepam 50 mg) in a dose rate of 1 mL per 15 kg in a total of 10 mL. The animals were kept in a supine position. After endotracheal intubation and during the preparation phase, anesthesia was performed using isoflurane 1.5% plus rocuronium bromide ($1\ mg \cdot kg^{-1} \cdot h^{-1}$) and sufentanil ($0.008\ mg \cdot kg^{-1} \cdot h^{-1}$) intravenously via the ear vein. From baseline (BL) on, anesthesia was maintained during the entire study period as total intravenous anesthesia with 2% midazolam plus rocuronium bromide ($1\ mg \cdot kg^{-1} \cdot h^{-1}$) and sufentanil ($0.008\ mg \cdot kg^{-1} \cdot h^{-1}$). This medication was chosen to prevent any diminution in cardiopulmonary functions (i.e., decrease in mean arterial pressure [MAP]) as effectuated by inhalative anesthetics (4).

Preparation

Animals were kept in a supine position. During the whole study period, oxygenation and ventilation parameters, i.e., arterial partial pressure of oxygen and carbon dioxide (Pao_2 and $Paco_2$), inspirational oxygen fraction (Fio_2) and expirational oxygen fraction, end-tidal carbon dioxide, positive end-expiratory pressure (PEEP), respiratory frequency (RF), and tidal volume, were continuously monitored and adapted to obtain physiologic levels with a volume-controlled ventilator (Primus; Draeger, Danvers, Mass). An Fio_2 of 30%, a tidal volume of $10\ mL \cdot kg^{-1} \cdot body\ weight^{-1}$, 20 breaths $\cdot\ min^{-1}$, a PEEP of 3 mmHg, $Paco_2$ of 35 to 45 mmHg, and end-tidal CO_2 of 4.5 to 5.5% were set. Fluid management was performed during the experimental protocol with crystalloids (Ringer, 309 mOsm $\cdot\ L^{-1}$; Fresenius Kabi GmbH, Bad Homburg, Germany) $10\ mL \cdot kg^{-1} \cdot h^{-1}$. Saline-filled perfusor catheters were placed intraluminarily by preparing the following arteries and veins: left carotidal artery for arterial line (Perfusor Line; B. Braun, Melsungen, Germany), left external jugular vein for drug and medical substitution by applying a 9F central venous catheter (Arrow Int, Reading, Pa), and right external jugular vein by applying a Swan-Ganz catheter for drug and medical substitution as well as measuring hemodynamic parameters (Swan &Ganz CCombo, heparin-coated; Edwards Lifescience, Irvine, Calif); right femoral artery was provided with the arterial line for managing hemorrhagic shock (Perfusor Line; B. Braun). The urinary output was monitored after preparation of the bladder inserting a urinary catheter (Cystofix; B. Braun). Depth of anesthesia was judged according to blood pressure and heart rate during the whole experimental procedure. The entire preparation period took approximately 60 min.

Induction of multiple trauma

Baseline was defined as the time point directly before the induction of multiple trauma consisting of blunt chest trauma, penetrating abdominal injury, and hemorrhagic shock (Fig. 1). Hemorrhagic shock was maintained over a period of 1.5 h. S marked the end of the hemorrhagic shock period, R (phase of resuscitation for 1 h), and the rest of the protocol until E (end of experiment after 15.5 h). According to the previously described experiences with the isolated trauma models (5–7), the sequence of traumatic insults, described as follows, was set up (Fig. 2). Concerning sham and trauma animals, respiratory and blood gas parameters were monitored and adjusted if necessary to keep parameters on a physiologic level at BL. Fio_2 was reduced

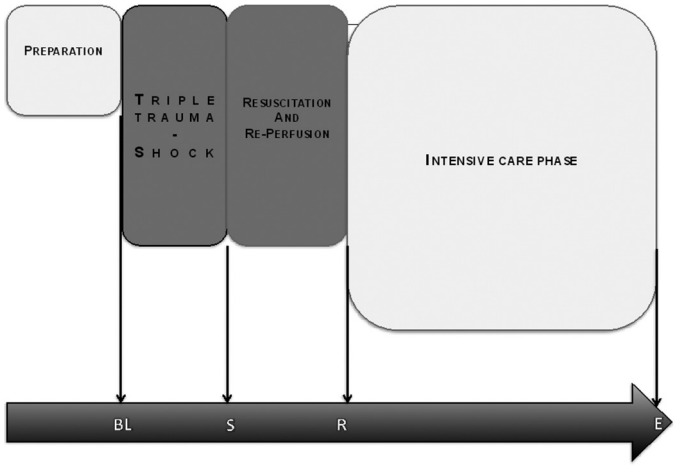

FIG. 1. **Timeline of combined porcine trauma model, 15.5 h**. Separation in four phases with several points of time, e.g., BL and S, as mentioned in the text: Preparation approximately 60 min. Baseline, just before the start of shock induction. Shock, maintained for 90 min. S displayed end of shock after 1.5 h. R (resuscitation) for 60 min. Intensive care phase for 13 h. End (E) after 15.5 h for bronchoscopy and autopsy, and finally the animals were killed.

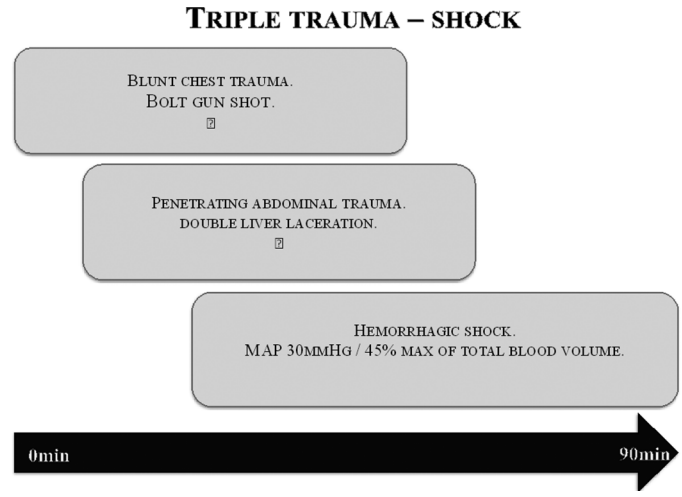

FIG. 2. **After preparation, trauma was induced with a 3-fold impact**. (i) Blunt chest trauma caused by a single bolt gunshot to the right chest. (ii) Laparotomy and laceration of liver by double stab. (iii) Hemorrhagic shock by withdrawing arterial blood from the right femoral artery down to 30 mmHg and/or 45% of total blood volume. Entire duration of shock was 90 min. Subsequent reperfusion followed.

to 21% in sham as well as in trauma animals for 10 min to mimic realistic clinical and equal conditions in both groups at BL. Respiratory frequency was maintained at 22.8 ± 3.0 per minute in sham and 22.1 ± 3.8 per minute in trauma animals at BL.

Blunt thoracic trauma was induced by applying a panel of 1-cm thickness to the right dorsal, lower chest. A bolt was shot onto this panel using cattle killing cartridges (9 × 17; Dynamit Nobel AG, Troisdorf, Germany) simulating blunt lung contusion. The shot was applied while the lungs of the animals were deflated.

Afterward, laparotomy was performed with exploration of the right upper liver lobe. Penetrating abdominal injury was induced by two incisions made to the right upper liver lobe using a sharp, custom-made, four-edged scalpel. After a short period of uncontrolled bleeding (approximately 30 s), liver packing was carried out with five sterile packs of the same size. Laceration-associated bleeding was assessed macroscopically every 30 min. The evaluation and documentation were performed by photodocumentation (Fig. 3).

Pressure-controlled hemorrhagic shock was induced by withdrawing blood (a maximum of 45% of the total blood volume) from the right femoral artery to reach an MAP of 30 ± 5 mmHg. Hemorrhagic shock was maintained for 90 min. The shed blood was abolished.

General treatment

The animals were constantly evaluated, monitored, and, if required, treated according to current standards of emergency medicine and trauma surgery, such as protocols of ATLS (Acute Trauma Life Support) as well as recommendations made in the latest update of the European Resuscitation Council from 2010 (8, 9). These protocols allow standard techniques such as inserting chest tubes in case of pneumothoraces and draining blood from cardiac tamponade by needle punctures. Further emergency medicine drugs were applied intravenously (i.e., epinephrine, amiodarone) as required for life-threatening events (i.e., ventricular fibrillation, cardiac arrest). Liquids were given for all animals during the whole protocol in the form of crystalloids (Ringer, 309 mOsm $\cdot\ L^{-1}$; Fresenius Kabi GmbH, Graz, Austria) in a rate of $10\ mL \cdot kg^{-1} \cdot body\ weight^{-1} \cdot h^{-1}$.

Resuscitation, protocol and euthanasia

At point of time S (1.5 h after BL), fluid resuscitation was performed for the next 60 min representing the early phase in the hospital ("golden hour of shock"). With four times the shed blood volume, colloids (HES 130/4, 6%; Voluven, 308 mOsm $\cdot\ L^{-1}$; Fresenius Kabi GmbH) and crystalloids (Ringer, 309 mOsm $\cdot\ L^{-1}$; Fresenius Kabi GmbH) were used for fluid resuscitation in a relation of 1:8 (12.5% HES and 87.5% Ringer) meeting current standards of emergency medicine (10). For fluid balance, application of crystalloids, colloids, and drugs and urinary output were monitored and analyzed.

The sham animals received only crystalloids in a rate of $10\ mL \cdot kg^{-1} \cdot body\ weight^{-1} \cdot h^{-1}$. After resuscitation, normothermia was maintained over the entire study period. The animals were killed 15.5 h after the preparation of arterial, venous, and urinary lines (sham groups) or trauma induction, and autopsy was performed obtaining organ samples.

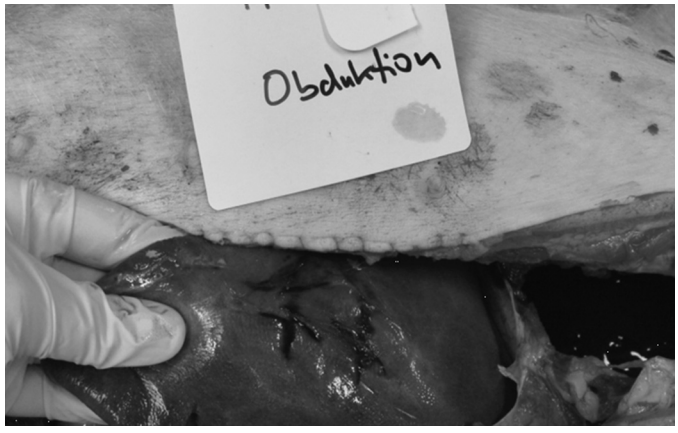

FIG. 3. **Photodocumentation**. Liver. Penetrating abdominal trauma was induced by laparotomy and preparation of the right upper liver lobe. Two stitches were performed as double stab by a self-made four-edged scalpel. Thirty seconds of bleeding and immediate liver packing with five sterile pads.

Management of body temperature

The animals' body temperature was continuously measured by anal application of wire thermometers (Infinity Delta; Draeger).

Measurement of hemodynamics, blood gas parameters, and acid-base excess

Basic hemodynamic parameters were continuously monitored. Documentation was done at points of time BL and S. A standard electrocardiogram was used to monitor cardiac rhythm and heart rate (HR in 1 breath · min^{-1}); mean arterial blood pressure (in mmHg) was monitored. In addition, central venous pressure (in mmHg), cardiac output (in L · min^{-1}), and mixed venous oxygenation saturation were obtained and analyzed (Vigilance; Edwards Lifescience). The oxygenation and ventilation parameters FIO_2, expirational oxygen fraction, end-tidal carbon dioxide, PEEP, RF, and tidal volume were continuously monitored. Intermediate maneuvers were performed to support pulmonary functions by increasing inspirational FIO_2 (>30%) and boosting lungs (PEEP > 8 mmHg). This procedure was implemented according to the standard respiratory management on intensive care units. Arterial blood gases were taken: arterial pH, PaO_2, and $PaCO_2$; base excess and lactate were analyzed with a gas analyzer (ABL 800 Flex; Drott, Wiener Neudorf, Austria). FIO_2 was adapted to the peripheral oxygen saturation as well as to the PaO_2. FIO_2 was increased by 5% in case of peripheral oxygen saturation less than 92% or PaO_2 less than 80 mmHg. FIO_2 was reduced again, when PaO_2 exceeded the value of 110 mmHg. To prevent pulmonary atelectasis, recruitment maneuvers were regularly performed before the different study time points. If adequate PaO_2 levels (80–110 mmHg) could not be maintained and a remarkable reduction of pulmonary compliance (<16 mL/mbar) occurred in the absence of pneumothorax, the PEEP was increased gradually. To prevent negative hemodynamic adverse effects (e.g., decrease in MAP), long-term PEEP values never exceeded 10 mmHg.

In general, all measurements in sham and trauma animals were made at BL and at the end of shock (S) (1.5 h after BL).

Liver, renal, and coagulation disorders

The evaluation and documentation of liver laceration were performed by photodocumentation (Fig. 7). Liver damage was monitored by measuring liver enzymes AST (U · L^{-1}) and ALT (U · L^{-1}). The renal function was monitored by serum creatinine concentration (μmol · L^{-1}) as well as the urinary output (mL · h^{-1}) (11) at the points of time BL and S. Coagulation parameters were obtained for prothrombin time.

Statistical analysis

The statistical evaluation was carried out with Prism, version 5.0a (Graph Pad Software, Inc, La Jolla, Calif). Measurements are presented as means, SEM, and maximum and minimum in box plots. Unpaired *t* test was calculated when comparing two values between sham and trauma animals. Wilcoxon matched paired tests were performed. There were 10 animals in the sham and trauma groups. The significance was calculated as $P < 0.05$.

RESULTS

Survival and outcome

All sham animals survived (n = 10). Ten animals were needed for the implementation of the new multiple trauma model as it was necessary to determine the feasible maximum stress induced in the experimental groups. These animals had a mortality rate of 100% and were no longer taken into account in the study. Among them, nine pigs suffered from sudden death within the first 5 h after BL mainly because of circulatory failure, tension pneumothoraces, and severe blood loss (e.g., perforation of the liver during laparotomy). One animal suffered from late death close to the end point after 14 h because of cardiac arrest. The establishing process was necessary for team members to learn handling and manual techniques starting at preparation, inducing trauma, and sustaining stable conditions of the animals from start to end. Once the multiple trauma model had been established, mortality was 0% (n = 10). It was reproducible to detect any potential benefit of a therapeutic approach (e.g., induction of therapeutic hypothermia) (1).

Temperature

The physiologic body temperature in pigs is reported to be between 38.0°C and 39.5°C (12). Sham pigs showed a mean body temperature of 37.7°C ± 0.2°C at BL and of 38.0°C ± 0.3°C at S (Fig. 4A). At point of time R, the temperature was 38.1°C ± 0.3°C. Trauma pigs displayed a mean body temperature of 37.4°C ± 0.3°C at BL; it increased up to 38.1°C ± 0.3°C at S with no significant differences to the sham group at S (Fig. 4A). Afterward, the trauma animals showed a slight decrease in temperature down to 37.2°C ± 0.3°C at R (Fig. 4, B and C). Comparing that with BL, the mean body

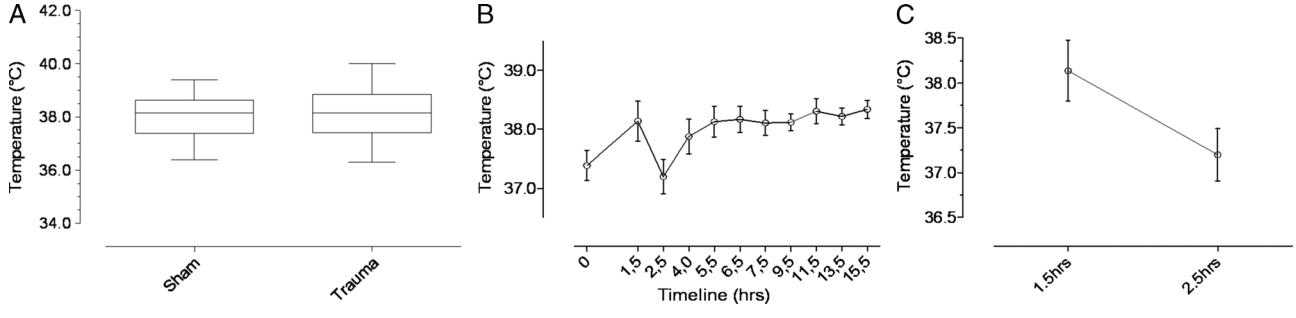

FIG. 4. **A, Temperature in normothermic sham and trauma animals**. Measurements performed at the end of shock. Box plots with results in mean and SEM with maximum and minimum. B, Temperature in normothermic trauma animals, n = 10. Measurements gained over 15.5 h. Results in mean and SEM with minimum and maximum. C, Comparison of temperature measurement in normothermic trauma animals, n = 10. S versus R. Results displayed in mean and SEM with minimum and maximum.

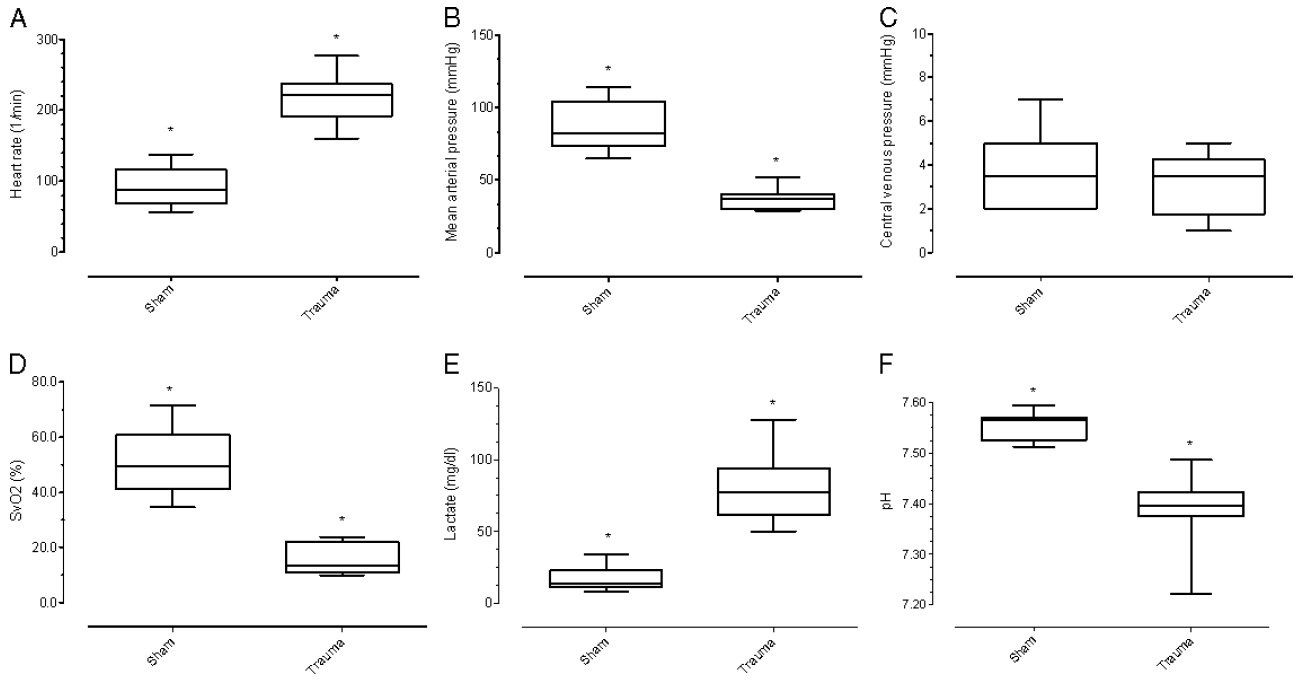

FIG. 5. **Results of basic hemodynamics and blood gases**. Sham versus trauma animals. Results shown in box plots with mean and SD with maximum and minimum. *x* Axis represents sham and trauma. *y* Axis represents different hemodynamic parameters, n = 10. **P* < 0.05. A, Heart rate, (B) MAP, (C) central venous pressure, (D) mixed venous oxygenation saturation (Svo_2), (E) lactate levels, and (F) pH.

temperature significantly increased up to 38.3°C ± 0.2°C at E (Fig. 4B) ($P < 0.05$).

Hemodynamics

In trauma animals (n = 10), the mean shed blood volume was 919.2 ± 115.9 mL. Trauma animals showed a significantly increased heart rate compared with sham animals ($P < 0.0001$) at S (Fig. 5A). Accordingly, MAP was significantly decreased in trauma animals compared with sham animals ($P < 0.0001$) at S (Fig. 5B). Cardiac output was significantly lower in trauma animals (2.1 ± 0.2 L · min^{-1}) compared with sham animals (3.7 ± 0.3 L · min^{-1}) at S ($P = 0.0002$). Cardiac output in trauma animals declined significantly from 4.7 ± 0.2 L · min^{-1} at BL to 2.1 ± 0.2 L · min^{-1} at S ($P < 0.0001$). Central venous pressure of sham and trauma pigs at S is demonstrated in Figure 5C. Mixed venous oxygenation saturation at S was significantly higher in sham (50.9% ± 3.7%) than in trauma pigs (15.6% ± 1.7%) ($P <$ 0.0001; Fig. 5D).

Blood gas parameters and acid-base excess

According to the Institute of Veterinary Medicine at University of Vienna (VetMedUNI Vienna, personal communication), the physiologic arterial pH in pigs is between 7.39 and 7.45 (2, 13). The mean arterial pH in sham pigs was 7.45 ± 0.01 at BL and rose significantly up to 7.55 ± 0.01 at S ($P < 0.0001$), which was partially due to a slightly higher RF in sham than in trauma animals at S (sham RF: 29.6 ± 3.0/min vs. trauma RF: 26.5 ± 5.3/min at S).

The mean arterial pH in trauma pigs started with 7.44 ± 0.01 at BL and declined to 7.37 ± 0.02 at S ($P = 0.0049$). The results of the mean arterial pH in sham and trauma animals were significantly different at S ($P < 0.0001$; Fig. 5F). Lactate was 17.0 ± 2.6 mg · dL^{-1} in sham animals at S, which was significantly lower than that in trauma animals with 79.4 ± 7.6 mg · dL^{-1} at S. The base excess in sham animals started with 5.4 ± 0.5 mmol · L^{-1} at BL, which represents no significant change with 6.1 ± 0.5 mmol · L^{-1} at S. The base excess in trauma animals was 6.0 ± 0.4 mmol · L^{-1} at BL and decreased significantly to −3.6 ± 0.9 mmol · L^{-1} at S. At S, sham and trauma animals differed significantly from each other ($P < 0.0001$; Fig. 6).

Pulmonary function

Pao_2 and $Paco_2$ in sham pigs were 110.2 ± 3.2 mmHg and 38.6 ± 0.7 mmHg ($P < 0.0001$) over the entire study period. In the trauma group, blunt chest trauma resulted in severe hemorrhagic contusion of the affected lung and also partly of the contralateral side (Fig. 7). Accordingly, Pao_2 was significantly decreased in trauma animals (78.5 ± 4.7 mmHg) compared with sham animals (92.8 ± 3.9 mmHg) ($P = 0.03$) at S. $Paco_2$ in trauma pigs did not differ significantly from sham animals at S (35.0 ± 1.3 mmHg vs. 32.9 ± 0.7 mmHg) ($P > 0.05$).

Liver, renal, and coagulation disorders

At S, the liver enzyme aspartate aminotransferase was 31.3 ± 2.7 U · L^{-1} in sham pigs, significantly different to trauma

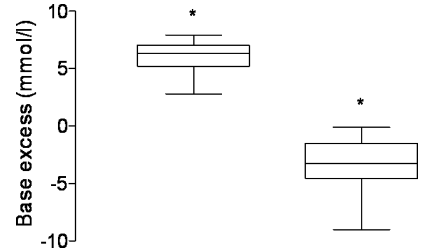

FIG. 6. **Base excess in mmol · L^{-1}**. Sham versus trauma animals. Results shown in box plots with mean and SD with maximum and minimum. *x* Axis represents sham and trauma. *y* Axis represents values of base excess, n = 10. **P* < 0.05.

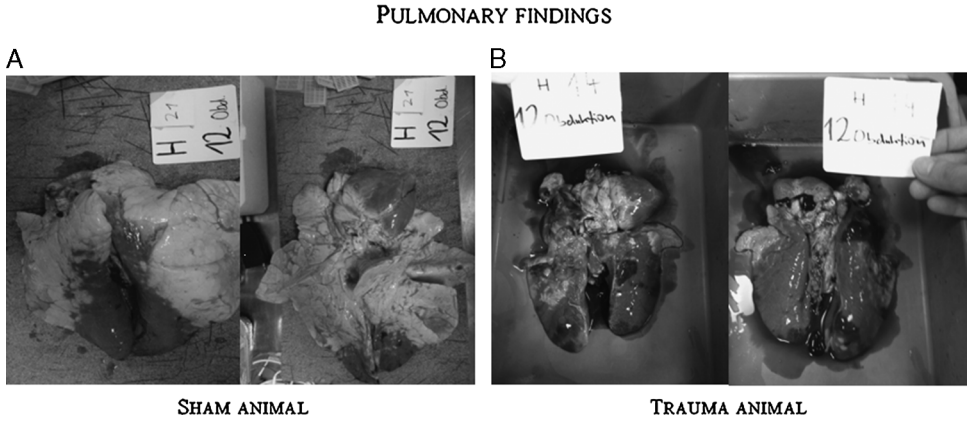

FIG. 7. **Photodocumentation**. Lungs. Pathological findings are shown after autopsy at end of study period. A, Sham group. B, Trauma group.

pigs with 112.4 ± 27.9 U · L^{-1} ($P < 0.0001$). No significant differences in ALT between sham and trauma pigs (49.1 ± 4.4 vs. 47.3 ± 4.4 U · L^{-1}) were observed at S. No significant differences in urinary output (mL · h^{-1}) were found in sham animals comparing results at BL and S. The induction of trauma resulted in a significantly decreased urinary output at S (69.2 ± 23.2 mL · h^{-1}) compared with values at BL (237.7 ± 54.1 mL · h^{-1}) ($P < 0.02$) and compared with sham animals at S (227.5 ± 43.3 mL · h^{-1}) ($P < 0.004$). No differences could be observed concerning serum creatinine concentrations (μmol · L^{-1}) in sham animals over the observation period. Serum creatinine concentrations in trauma animals increased after shock from 69.1 ± 1.2 μmol · L^{-1} at BL up to 104.7 ± 2.2 μmol · L^{-1} at S ($P < 0.0001$). Furthermore, serum creatinine levels were significantly increased at S compared with sham animals (77.7 ± 4.1 μmol · L^{-1}) ($P < 0.0001$). Prothrombin time displayed no significant differences between sham (12.7 ± 0.5 s) and trauma animals (12.4 ± 0.3 s) at point of time S. Neither sham nor trauma animals showed significant changes of prothrombin time comparing BL and S.

DISCUSSION

According to epidemiologic data of the German Trauma Registry, there is a high coincidence of chest trauma (60%), abdominal trauma (25%), and hemorrhagic shock in multiple trauma patients. Abdominal trauma represents one of the leading causes for early mortality due to hemorrhagic shock within the first 24 h after trauma. In the further clinical course, abdominal trauma predisposes for the development of sepsis and multiple organ dysfunction syndrome (2, 14). In about 66% of the cases, abdominal trauma is accompanied by an additional chest trauma, which is found in 60% of multiple trauma patients. Severe chest trauma and especially lung contusions are associated with a higher incidence of respiratory insufficiency and hemodynamic failure as well as a mortality rate of 10%. In those patients with an abbreviated injury scale of the chest of 5 points, mortality increases to 30% (15). Besides the direct consequences of lung contusions on pulmonary function, the lung represents a primary target organ for secondary damage due to the inflammatory response after hemorrhagic shock and multiple trauma. Therefore, there seems to be a further significant relationship between abdominal trauma and pulmonary function (14).

Despite this close relationship between chest and abdominal trauma and the significant clinical relevance of this combined trauma there is—to the best of our knowledge—no large animal model addressing this issue (3, 16–23). So far, large animal models focus either on isolated insults, such as hemorrhagic shock or chest trauma, or on a combination of hemorrhagic shock and either pulmonary contusion or abdominal trauma (liver and/or spleen laceration). Only in a recently published pig model a combination of a single rib fracture with abdominal trauma and hemorrhagic shock has been established (24). However, the rib fracture was mainly used to create a soft tissue trauma and not to induce a significant chest trauma. Therefore, this model cannot be regarded as a combined chest and abdominal trauma model. The "bleeding multiple trauma" model established in this study combines three isolated traumatic insults, each reflecting single aspects of severe multiple trauma. The model resulted in significant hemodynamic and metabolic disorders as well as in significant organ dysfunction (e.g., kidney). All these changes prove that a suitable setup of our established porcine trauma model was chosen. Furthermore, this model allows to analyze the effects of therapeutic interventions (e.g., induced hypothermia) in the multiple trauma setting and to observe possible complications (e.g., coagulopathy, secondary organ dysfunction).

To mimic the pathophysiological alterations after major trauma, relevant animal trauma models need to fulfill diverse criteria. First, we certainly assume that the use of a pig model is most adequate, as these animals show a response to hemorrhagic shock similar to humans (25). Further criteria for a relevant trauma model have been summarized by Cho et al. (26) and by the recommendations of the 2000 Military Medicine Workshop on Animals Models in Hemorrhage and Resuscitation Research (27). Key points are the need of volume-controlled models that have the potential for uncon trolled bleeding, surgical manipulation coincident with hemorrhage as in clinical situations, significant soft tissue injury to better approximate the postinjury inflammatory state, and the severity of trauma with lethality that closely mimics clinical situations. Finally, duration of hypotension before resuscitation should be comparable to the clinical situation. Majde et al. (27) underlined these findings by indicating that the induction of a defined and reproducible trauma with sufficient hemorrhage is a key factor in the development of a

relevant animal trauma model. Regarding the pulmonary contusions, Davis and Kaups (28) stated that it is not possible to detect a benefit of a therapeutic modality in a pulmonary contusion model if the inciting injury is not severe enough to cause hypoxia. According to our results, our model fulfills all the requirements mentioned above such as the refractory hypoxemia characteristic for victims of severe pulmonary contusions. One possible therapeutic intervention that can be investigated in the established model is the posttraumatic use of induced hypothermia. In this context, this model allows investigating whether the liver laceration or the lung contusion starts to rebleed after induction of hypothermia, which represents a significant adverse effect of a decreased body core temperature (29).

During the establishing process of our model, we observed that chest trauma was associated with hemorrhagic infarction, pneumothoraces, contusions, and bleedings. At the beginning of the implementation process, the lungs were inflated during the induction of blunt chest trauma, and six pigs died because of tension pneumothoraces consecutively leading to cardiac arrest and sudden decline in oxygenation (Pa_{O_2}). Deflated lungs and the use of chest tubes as required by emergency medicine protocols (ATLS) prevented such critical events during the further protocol. Furthermore, abdominal trauma with liver laceration and hemorrhagic shock were induced. While establishing the abdominal penetrating trauma, one animal died because of severe blood loss caused by the accidental laceration of a huge liver vein. The amount and the velocity of blood withdrawal for induction of hemorrhagic shock caused another two fatalities. Therefore, the induction of hemorrhagic shock had to be adjusted in our model. Once both the impact of liver laceration and the amount of blood for hemorrhagic shock had been established, all pigs survived. Above all, the hemorrhagic shock in our model displays the clinical situation straight after accidents in a realistic way. The blood volume was drained down to approximately 45% of total blood volume (30 ± 5 mmHg). In contrast to other studies, no fluids were restored during shock to extend the hemorrhagic situation.

There are also some limitations of the established model that have to be considered. First, the whole protocol (sham and trauma) was conducted under anesthesia/narcosis, even though no actual trauma occurs under such circumstances. Animal ethics do not permit any other procedure. Thus, sham animals serve as control group and reflect any differences induced by our shock protocol. Furthermore, the complexity of our experimental model, although providing clinical realism, adds many variables that might influence the results. First, the species-specific differences need further investigations before adapting a therapeutic approach to the clinical setting despite the similarities between humans and pigs in response to hemorrhagic shock. In our model, induction of hemorrhagic shock with a withdrawal of 30% of the total blood volume and chest and abdominal trauma did not result in a significant reduction of coagulation activity. Therefore, we had to intensify the hemorrhagic shock with the induction of a loss of up to 45% of the total blood volume. This is in line with results of previous studies in which simple moderate hemorrhage and resuscitation with lactated Ringer's solution did not seem to deplete coagulation substances low enough to change clotting time (30). Furthermore, diverse drugs (e.g., catecholamines) and infusions (e.g., crystalloids, colloids) were applied, which might have the potential to modulate cellular injury and influence survival. However, the therapeutic application of these substances mimics the clinical situation. Furthermore, organ function and pathohistology of organ damage have to be studied more deeply in this model in further studies using therapeutic interventions.

CONCLUSIONS

We developed a new, clinically relevant porcine model of multisystem injury (pulmonary contusion, liver laceration) with both controlled as well as uncontrolled components of hemorrhage and the potential for rebleeding. The use of this large animal model therefore allows the assessment of the effects therapeutic interventions (e.g., induced hypothermia) and to examine possible complications (e.g., risk of bleeding) in the posttraumatic setting.

The newly described model is consistent and reproducible, as evidenced by low variance and uniform mean values of interindividual responses of blood loss and coagulation parameters.

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