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Original Research

Hemodynamic Changes in Response to Hyperacute Spinal Trauma in a Swine Model

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Acute spinal cord injury (ASCI) is a devastating event that can have severe hemodynamic consequences, depending on location and severity of the lesion. Knowledge of hyperacute hemodynamic changes is important for researchers using porcine models of thoracic ASCI. The goal of this study was to determine the hyperacute hemodynamic changes observed after ASCI when using pigs as their own controls. Five Yucatan gilts were anesthetized, and a dorsal laminectomy performed at T10-T12. Standardized blunt trauma was applied for 5 consecutive min, and hemodynamic variables were collected 5 min before ASCI, and at 2, 4, 6, 8, 10, 20, 30, 60, 80 and 120 min after ASCI. Arterial blood gas samples were collected at 60 min and 10 min before, and at 30 min and between 120 and 240 min after ASCI. Parametric data were analyzed using a mixed effects model with time point as the fixed factor and subject as the random factor. We found no effect on heart rate, pulse pressure, SpO_2, $EtCO_2$, and respiratory rate between baseline and timepoints after ASCI. Diastolic arterial pressure, mean arterial pressure, and systolic arterial pressure fell significantly by 18%, 16%, and 15%, respectively, at 2 min after ASCI. However, none of the decrements in arterial pressures resulted in hypotension at any time point. Heart rate did not change significantly after ASCI. Blood glucose progressively increased to 50% above baseline between 120 and 240 minutes after ASCI. Low thoracic ASCI caused a consistent and statistically significant but clinically minor hyperacute decrease in arterial pressures (-15%) that did not produce hypotension or metabolic changes suggestive of tissue hypoperfusion. Our findings using this model suggest that mean arterial pressures should be maintained above 85 mm Hg prior to spinal trauma in order to avoid hypotensive states after ASCI.

Abbreviations and Acronyms: ASCI, acute spinal cord injury; BE, base excess; BT, core body temperature; CRI, continuous rate infusion; DAP, diastolic arterial pressure; $EtCO_2$, expired partial pressure of carbon dioxide; Et_{ISO}, end tidal isoflurane concentration; FLK, fentanyl lidocaine ketamine; Glu, glucose; HR, heart rate; Hb, hemoglobin; Lac, lactate; LRS, lactated Ringer's solution; MAP, mean arterial pressure; MLK, morphine lidocaine ketamine; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; PP, pulse pressure; RR, respiratory rate; SAP, systolic arterial pressure; SCI, spinal cord injury.

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Introduction

Spinal cord injury (SCI) is a devastating event that has an annual incidence of approximately 54 cases per million population in the U.S., which translates into 17,000 new SCI cases each year.[35] Long-term respiratory and cardiovascular consequences are the leading cause of death in SCI victims.[11] A pressor response derived from sympathetic activation[40] occurs immediately after SCI in humans shortly after injury[4,29] and in animal models of spinal injury.[1,7,13] Specifically, widened pulse pressure, tachycardia, and hypertension occur immediately after SCI, and are followed by hemodynamic conditions ranging from minor to severely unstable, depending on the location and severity of injury.[1,7,16,29] A clear correlation can be drawn between hypotensive severity and worsened neurologic outcome in animal models of SCI.[18] However, depending on the spinal segment at which SCI occurs, hemodynamic and metabolic changes can differ vastly after injury.[14] Therefore, knowledge about these potential changes may minimize the effects on the study outcomes for researchers using validated models of SCI.

Several models of acute SCI (ASCI) have been developed, primarily in rats. Differences in size, anatomy, and possibly dissimilar biologic responses compared with humans, limit the rat model in its clinical applicability.[25] However, swine provide a biomedical model for cardiovascular, metabolic,[28] gastrointestinal,[17] and transplantation[15] research among others, and have been increasingly used as a model in the neurosciences, including brain and spinal imaging and surgeries.[12,21,24,25,30,41] Swine have characteristics similar to humans and may represent an intermediary model between rats and primates. Miniature swine were specifically chosen for the current study due to their slower growth rate as compared with their commercial counterparts.[32,34] The rapid growth of conventional swine as compared with the static size of human adults could lead to differences in the physiologic and pathophysiologic response of the cardiovascular and nervous systems to ASCI.[26] A previously published porcine model of thoracic ASCI did not report the hyperacute hemodynamic response to ASCI.[25] Information on this response is important for researchers using this porcine

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model of thoracic ASCI and standard anesthetic conditions and also for acute support of swine with thoracic ASCI.

The goal of the current study was to determine the hyperacute hemodynamic and metabolic changes in an established model of porcine ASCI[25] using each pig as its own control. The tested null hypothesis was that an incomplete low thoracic ASCI in juvenile Yucatan pigs would not produce significant changes in the monitored hemodynamic and metabolic parameters. Specifically, heart rate (HR), systolic pressure (SAP), diastolic pressure (DAP), mean arterial pressure (MAP), pulse pressure (PP), core body temperature (BT), and blood gas parameters measured at baseline (5 min before induction of injury) would not differ significantly from those recorded at 2, 4, 6, 10, 20, 30, 60, 80, and 120 min after ASCI.

Materials and Methods

The present study was approved by the Institutional Animal Care and University Committee at Louisiana State University (Protocol 19-080). Five Yucatan gilts (*Sus scrofa domestica*) weighing 44.2 ± 7.5 kg and 287 ± 4 d of age were included in the study and acclimated for approximately 4 mo. Pigs were procured from a pathogen-free facility (Sinclair Bio-Resources, Auxvasse, MO) and were free of *Brucella*, pseudorabies, porcine reproduction respiratory syndrome virus, transmissible gastroenteritis, leptospirosis, vesicular stomatitis virus, influenza, porcine epidemic diarrhea virus, and porcine circovirus type 2. Pigs were maintained under sheltered-housing conditions, in open air, with a natural light cycle, and complete rain coverage. Concrete-floored pens were approximately 9 m^2. Three pigs were housed together in one pen, while the other 2 were housed in a separate pen. Pens were located directly beside each other and were separated by vertically aligned metal bars placed 7.6 cm apart allowing social interaction between the two groups. A single heater (Model PW15R, Trustech, Hangzhou, China) was suspended above a corner of each pen to provide heat in case of low environmental temperature [<10 °C (<50 °F)]. Enrichment items included pig teethers, tire biters, and Boomer balls®. Twenty-two oz of Mazuri Mini Pig Youth feed (PMI Nutrition International LLC, Arden Hills, MN) was provided by placing feed into either feed troughs or standing feed bowls twice a day; at 2 wk before the start of the study, pigs were introduced to the same quantity of Mazuri Mini Pig Active Adult feed twice a day, based on their age requirements. Potable water was provided ad libitum via a water nipple system, procured from the city water supply (Baton Rouge Water Company, Baton Rouge, LA).

The day before surgery, the pig undergoing surgical treatment was moved to an individual pen (4.5 m^2) that allowed visual and social interaction with the other pigs. Food but not water was withheld for approximately 14 h before the surgical procedure. On the same morning, the pig received a physical examination and was excluded from the study if abnormal findings were noted. Gabapentin (Time-Cap Labs, Farmingdale, NY) was given orally by concealing the capsules into 1 or 2 marshmallows (Jet-Puffed Regular Marshmallows, Kraft Foods Group, Inc., Chicago, IL) and feeding the marshmallows to the pigs the evening before (20 mg/kg) and on the morning of (10 mg/kg) surgery. Pigs were sedated with tiletamine-zolazepam (3.3 mg/kg IM; Tiletamine–zolazepam, Zoetis, Kalamazoo, MI), morphine (1 mg/kg IM: Morphine Sulfate; Hospira, Lake Forest, IL), and atropine (0.04 mg/kg IM; Atropine Sulfate, VetOne, Boise, ID). Additional tiletamine and zolazepam (0.5 to 2 mg/kg) were administered intravenously as needed to achieve sufficient muscle relaxation to perform endotracheal intubation. The trachea was intubated with a cuffed endotracheal tube, and lungs were mechanically ventilated (Veterinary Anesthesia Ventilator 2000, Hallowell EMC, Pittsfield, MA) to maintain oxygenation (SpO_2 > 95%) and normocapnia ($EtCO_2$ = 35 to 45 mm Hg).

The start of anesthesia was defined as the time at which the vaporizer was turned into an "on" position. Isoflurane (Isoflurane, USP, Phoenix, St. Joseph, MO; or Fluriso, Vet One, Boise, ID) was administered with oxygen as the carrier gas through a circle breathing system. The caudal auricular vein was catheterized with aseptic technique with a 20-gauge 25 mm Teflon catheter (Surflash Terumo Corporation, Somerset, NJ) and Lactated Ringer's solution (Vetivex, Dechra Veterinary Products, Overland Park, KS) was administered at 5 mL/kg/h for the duration of anesthesia. Cefazolin (22 mg/kg; Cefazolin for Injection, USP, West-Ward Pharmaceutical Corp., Eaton Town, NJ; or Cefazolin for Injection, Apotex Corp. Weston, FL) was administered intravenously over a 10-min period 90 min before surgical incision, and then at 90-min intervals for the duration of surgery. Loading doses of fentanyl (5 µg/kg; Fentanyl Citrate, Hospira, Lake Forest, IL), ketamine (0.5 mg/kg; Zetamine, Vet One, Boise, ID) and lidocaine (2 mg/kg; Lidocaine, VetOne, Boise, ID) were administered over 5 min prior to initiation of a constant rate infusion (CRI) of fentanyl (25 µg/kg/h) or morphine (0.5 mg/kg/h), ketamine (20 µg/kg/min), and lidocaine (50 µg/kg/min). The start of the fentanyl or morphine, lidocaine, and ketamine (FLK or MLK) constant rate infusions (CRI) was considered the point of loading dose administration. Additional IV doses of fentanyl (5 µg/kg) and/or lidocaine (1 mg/kg) were administered as needed throughout the surgical procedure in response to signs of nociception. Cis-atracurium (0.1-0.2 mg/kg IV; Cis-atracurium Besylate Injection, manufactured in India for Gland Pharma Limited for Sandoz, Princeton, NJ) was administered 15 min prior to the start of the dorsal laminectomy to provide additional muscle relaxation, and additional doses administered as needed throughout the procedure.

Pigs were placed in sternal recumbency for the procedure. HR and cardiac rhythm were monitored using electrocardiography and a multiparameter monitor (Spectrum, Datascope Corp, Mahawah, NJ), hemoglobin oxygen saturation was monitored using pulse oximetry (SpO_2, Masimo Technology, Irvine, CA), and BT was monitored using a thermistor probe placed in the lower third of the esophagus. SAP, DAP, and MAP were monitored by connecting a calibrated blood pressure transducer (DTXPlus, BD Medical Systems, Sandy, UT) zeroed and leveled to the sternum of the pig to an arterial catheter aseptically placed in the coccygeal artery. A gas analyzer (Gas Module SE, Datascope, Mindray North America, Mahwah, NJ) was used to monitor expired partial pressure of carbon dioxide ($EtCO_2$), and anesthetic agent (Et_{ISO}). Blood gas analysis (EPOC Blood Analysis System, Siemens Medical Solutions USA, Malverne, PA) was performed on arterial blood samples collected anaerobically to monitor plasma electrolytes, gases, and metabolic parameters. Blood gas results were obtained 1 h before, 10 min before, 30 min after, and 2 to 4 h after ASCI. An 8F or a 10F Foley urinary catheter (Female Canine Guidewire Inserted Foley Catheter Kit; Foley Catheter with Wire Stylet in a Procedure Kit, MILA International, Florence, KY) was used to catheterize the urethra, and urine production was monitored during and after the surgical procedure. While under general anesthesia, BT was supported via the use of a warm-air blowing device (Bair Hugger, Arizant, Eden Prairie, MN) and a circulating water blanket (T/Pump TP500, Gaymar Industries, Orchard Park, NY) as needed, with a target temperature between 36.6 and

38.3 °C (97.9 and 100.9 °F). Active warming was discontinued if BT reached 38.3 °C (100.9 °F).

Acute spinal cord injury was produced as described in a previous study.[25] In brief, after exposing the spinal cord of the 10th through the 12th thoracic vertebrae via dorsal laminectomy, the blunt injury to the spinal cord was induced using a flat circular impactor tip (100 g weight; 9.53 mm diameter; 20 cm height drop). After dropping the rod, it was left in place for 5 consecutive min before being removed.

Triggers for treatment of tachycardia and bradycardia were the presence of a sustained (lasting more than 10 min) HR higher than 200 bpm and lower than 100 bpm, respectively, by the intravenous administration of analgesic drugs (fentanyl 5 µg/kg, lidocaine 1 mg/kg, or morphine 0.5 mg/kg) or the anticholinergic drug atropine (0.02 mg/kg IV). Hypotension was defined as a sustained MAP below 65 mm Hg or a SAP below 90 mm Hg.[33] Treatment of hypotension was tailored to each pig using the following general parameters: 1) if PP variation observed on the arterial waveform under a fixed tidal volume delivered by a mechanical ventilator was less than 15%, intravenous dobutamine (0.5 to 5 µg/kg/min IV; Dobutamine Injection USP, Hospira, Lake Forrest, IL) was administered to achieve normotension; 2) if PP variation exceeded 15%, either a fluid bolus of Lactated Ringers solution (LRS, 5 mL/kg IV) or colloid boluses (3 mL/kg; Hetastarch 6%, Hospira, Lake Forest, IL) were administered over 5 min as needed depending on packed cell volume and total solids measured at that time; and 3) if the bolus did not resolve the hypotension, intravenous dobutamine was administered (0.5 to 2 µg/kg/min IV). Hypertension was defined as an SAP higher than 130 mm Hg that was sustained for longer than 10 min.[38] The same treatment used for tachycardia was used to treat hypertension.

After the rod was removed, dura, muscle planes, and the skin were sutured and pigs recovered in a quiet room sternally recumbent in a custom-made U-shaped padded positioner (Dandy Products, Goshen, OH). Recovery was defined as the time between the end of anesthesia to extubation, at which time data collection for this study was concluded. After recovery from anesthesia, pigs were transferred to a long-term study on postoperative care that was part of the same protocol (19-080).

All perianesthetic events and monitored values were recorded every 5 min for the duration of the anesthetic episode, with the exception of a 30-min period after ASCI during which readings were recorded every 2 min, by using a digital anesthetic record (VetDAR, Dimple Hill Software LLC, Corvallis, OR). For statistical analysis, baseline was set at 5 min before ASCI, and postinjury timepoints were 2, 4, 6, 10, 20, 30, 60, 80, and 120 min after ASCI. Monitored parameters included HR, PP, SpO_2, $EtCO_2$, respiratory rate (RR), Et_{ISO}, DAP, SAP, MAP, and BT. Measured arterial blood gas parameters were PCV, pH, arterial partial pressure of carbon dioxide (PaO_2), arterial partial pressure of oxygen (PaO_2), Na^+, K^+, iCa, Cl^-, glucose (Glu), lactate (Lac), BUN, and creatinine. Calculated parameters included HCO_3^-, base excess (BE), and hemoglobin (Hb). A generalized timeline including the main events on this experiment is provided in Figure 1.

Statistical analysis was performed using R (Version 3.6.1, The R Foundation, Vienna, Austria, www.r-project.org). Hemodynamic and metabolic variables were analyzed with a mixed effect model for repeated measures adjusted for pig (random factor) and time point (fixed factor) and reported a mean ± SD. Significance was set at $P < 0.05$, and if detected, a posthoc pairwise Tukey test was used to test differences among time points.

Results

All 5 pigs completed the study. Mean anesthesia duration was 480 ± 61 min. The time from start of anesthesia to ASCI was 309 ± 70 min, and the time from the end of ASCI to the end of anesthesia was 171 ± 20 min. Mean Et_{ISO} was 1.4% ± 0.2% for the majority of the procedure but fell significantly to 1.2% ± 0.1% (-20%; $P < 0.001$) at 120 min after ASCI. Mean urine output during general anesthesia was 1.3 ± 0.6 mL/kg/h. Initial mean BT was 35.8 ± 0.7 °C (96.4 ± 1.4 °F). BT rose 2% above baseline (36.8 ± 0.6 °C [98.2 ± 1.2 °F]; $P = 0.003$) at 20

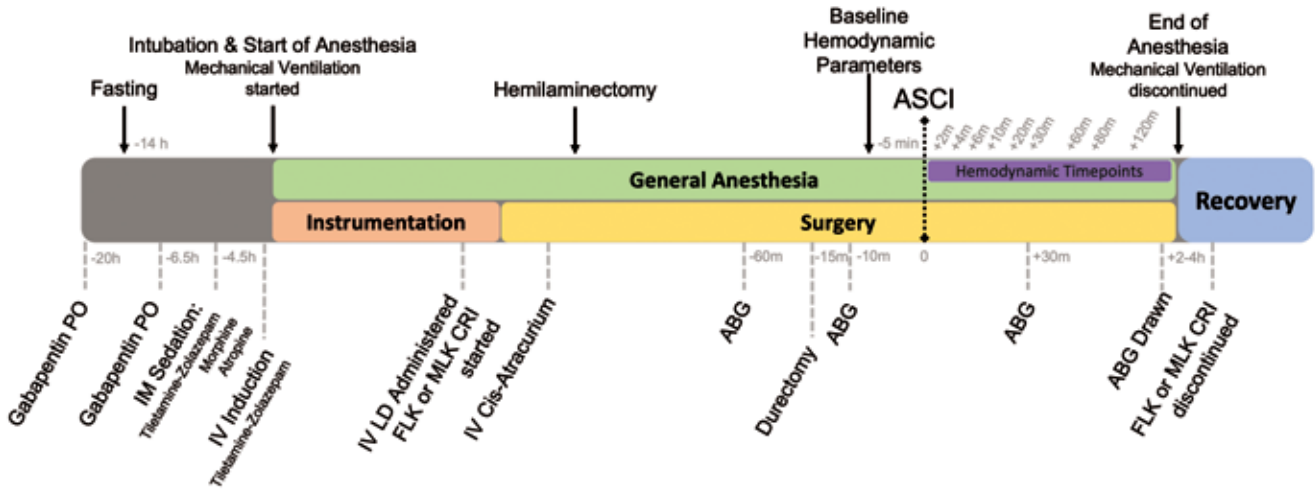

Figure 1. Generalized visual timeline of the main events and drugs administered to 5 Yucatan gilts in an experimental model of low thoracic acute spinal trauma (ASCI). Baseline hemodynamic parameters were collected 5 min before ASCI and at 2, 4, 6, 10, 20, 30, 60, 80, and 120 min after ASCI. Monitored parameters throughout anesthesia included heart rate, pulse pressure, peripheral hemoglobin oxygen saturation, end-tidal partial pressure of carbon dioxide, respiratory rate, end-tidal isoflurane concentrations, systolic, diastolic, and mean arterial pressures, and body temperature. Analyzed arterial blood gas parameters were packed cell volume, pH, arterial partial pressure of carbon dioxide, arterial partial pressure of oxygen, bicarbonate, base excess, hemoglobin, sodium, potassium, ionized calcium, chloride, glucose, lactate, blood urea nitrogen, and creatinine. CRI = constant rate infusion; D/C = discontinued; FLK = fentanyl, lidocaine, and ketamine infusion; h = hour; IM = intramuscular; IV = intravenous; LD = loading dose; m = minute; MLK = morphine, lidocaine, and ketamine infusion; PO = orally; TZ = tiletamine-zolazepam.

Table 1. Variables measured at baseline (-5 min) and 2, 4, 6, 10, 20, 30, 60, 80, and 120 min after ASCI.

Variable	-5 min	2 min	4 min	6 min	10 min	20 min	30 min	60 min	80 min	120 min
$EtCO_2$ (mm Hg)	43 ± 5.8	41.2 ± 4.5	40.2 ± 4.6	42.2 ± 5.9	42.4 ± 5.5	42.2 ± 4.5	43.4 ± 5	45 ± 4.9	42.6 ± 7.2	44.7 ± 14
Et_{ISO} (%)	1.5 ± 0.2	1.5 ± 0.1	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.1	1.4 ± 0.2	1.2 ± 0.1*
% change from baseline	-	-	-	-	-	-	-	-	-	*-4%**
HR (beat/minute)	151 ± 17	136 ± 16	150 ± 23	156 ± 24	158 ± 23	166 ± 21	168 ± 23	163 ± 26	164 ± 24	149 ± 22
% change from baseline	-	*-9.9%*	*-0.8%*	*3%*	*4.1%*	*9.3%*	*11.1%*	*7.5%*	*8.5%*	*-1.6%*
DAP (mm Hg)	90 ± 14	74 ± 12*	77 ± 11	78± 13	77 ± 9	77 ± 9	76 ± 6	75 ± 11	71 ± 9*	51 ± 6*
% change from baseline	-	*-18.2%**	*-15.1%*	*-14%*	*-15.1%*	*-14.2%*	*-16%*	*-17.3%*	*-21.5%**	*-36.2%**
MAP (mm Hg)	103 ± 15	87 ± 15*	89 ± 13	89 ± 13	89 ± 10	91± 10	90 ± 8	89 ± 10	85 ± 9*	66 ± 8*
% change from baseline	-	*-16.1%**	*-13.8%*	*-14%*	*-13.6%*	*-11.8%*	*-13%*	*-13.6%*	*-17.1%**	*-15%**
SAP (mm Hg)	120 ± 15	102 ± 17*	105 ± 13	105 ± 12*	105 ± 11*	108 ± 10	106 ± 11	108 ± 9	102 ± 8*	88 ± 9*
% change from baseline	-	*-14.7%**	*-12.2%*	*-12.5%**	*-12.8%**	*-9.7%*	*-11.7%*	*-10%*	*-15%**	*-26.7%**
PP (mm Hg)	29.8 ± 1.9	28.6 ± 7.9	28.8 ± 6.5	27.4 ± 7.5	27.8 ± 9.4	31 ± 4.9	30.2 ± 6.6	33.4 ± 9.3	31.6 ± 7.3	37 ± 5
SpO_2 (%)	96.2 ± 3	97.8 ± 1.6	97.6 ± 1.6	97 ± 2.4	97 ± 2.4	97.6 ± 1.9	98 ± 2.1	97.4 ± 2.1	97.2 ± 1.7	98 ± 0.8
RR (breath/min)	11 ± 1.6	12 ± 1.9	12 ± 1.7	12 ± 1.7	12 ± 1.7	12 ± 1.7	12 ± 1.7	12 ± 1.5	12 ± 1.5	10 ± 1.7
BT (°C)	35.8 ± 0.7	36.4 ± 0.5	36.4 ± 0.5	36.4 ± 0.5	36.4 ± 0.5	36.8 ± 0.6*	36.9 ± 0.6*	37.6 ± 0.8*	37.9 ± 1*	37.7 ± 0.8*
% change from baseline	-	*1.7%*	*1.7%*	*1.8%*	*1.8%*	*2.9%**	*3.2%**	*5.2%**	*5.9%**	*5.5%**

Data are presented as mean ± SD.
*Within a row: values differ significantly ($P < 0.05$) from the value for baseline (-5 min).

min after ASCI and continued to increase throughout anesthesia, peaking at 120 min after ASCI (+4%; $P < 0.0001$). Blood glucose was significantly higher (+50%; $P = 0.003$) between 120 min to 240 min after ASCI (123 ± 13 mg/dL) as compared with values at 60 min (82 ± 7 mg/dL) before ASCI. Values of monitored hemodynamic parameters are summarized in Table 1 and time courses of selected parameters are shown in Figure 2. Arterial blood gas parameters are summarized in Table 2.

The expired fraction of anesthetic gas did not significantly affect the dependent parameters that were tested in the mixed model. HR, PP, SpO_2, $EtCO_2$, and RR did not change significantly from baseline to timepoints after ASCI. DAP, MAP, and SAP fell significantly by 18% ($P = 0.047$), 16% ($P = 0.02$), and 15% ($P = 0.01$) respectively at 2 min after ASCI. SAP, but not DAP or MAP, was also significantly lower at 6 ($P = 0.04$) and 10 min ($P = 0.03$) after ASCI, but not at 4 min after ASCI. All arterial pressures were also significantly below baseline at 80 (DAP and MAP, $P = 0.01$; SAP, $P = 0.007$) and 120 min (DAP, MAP, SAP; $P < 0.0001$) after ASCI. However, none of these decrements in arterial pressures caused hypotension at any timepoint, and pressures did not return to baseline for the remainder of anesthesia. To correct hypotension, one pig was given dobutamine before, during, and after ASCI; for the same reason, another 2 pigs also received dobutamine, one 3 h before ASCI and the other nearly 2 h after ASCI.

Blood gas results from 10 min before ASCI were not available for 2 pigs, and results for 2 to 4 h after ASCI were not available for one pig. Two data points for hemodynamic values were not available for 120 min after ASCI in 2 pigs that were recovering from anesthesia, as anesthetic monitoring had been discontinued at that time.

Discussion

In the present study we reported the hemodynamic and metabolic changes observed after induction of ASCI based on a previously published domestic porcine model[25] using a combined intravenous and inhalational anesthetic regimen. Hyperacute hemodynamic changes consisted of a statistically significant decrease in arterial pressures by roughly 15% at 2 min after ASCI, which subsided after approximately 10 min, returning to values similar to baseline. Hypotension and hyperlactatemia did not occur. Since systemic lactate can be used as a marker of systemic tissue perfusion,[8,23] it can be inferred that adequate tissue perfusion was maintained even after ASCI in this model of low thoracic ASCI. As such, we reject the tested null hypothesis because significant changes were observed in systemic arterial pressures and glucose after low thoracic ASCI. As such, we reject the tested null hypothesis because significant changes did occur in systemic arterial pressures and glucose after low thoracic ASCI. Furthermore, even though significant changes were observed, pigs did not experience the expected adverse effects that could potentially be caused by ASCI such as hypotension and/or bradycardia.

The location of SCI can greatly affect hemodynamic changes that occur after ASCI. For example, the loss of supraspinal sympathetic control observed with lesions above T2-T6 does not occur in low thoracic (T6 and below) SCI.[9,11,14,36] Hypotension, bradycardia, and dysrhythmias are frequently observed in human patients with cervical lesions because the lesion interrupts the descending pathways responsible for the activation of preganglionic sympathetic neurons, with consequent loss of sympathetic activity, leaving unopposed parasympathetic tone.[7,14,29,36] Myocardial injury due to massive catecholamine surge immediately after SCI is considered the primary mechanism of decreased cardiac output seen in patients with brain and/or with high spinal trauma.[36] However, previous studies have reported little to no change in HR and BP immediately after low thoracic SCI,[1,16,24,37] as lesions at this level preserve the integrity of the sympathetic preganglionic neurons innervating cardiac nodes and muscle, and lungs.[16]

The lack of change in HR after ASCI found in our model is consistent with previously published data.[37] A study employing a similar model of ASCI in swine with a lighter impactor (50 g), but with additional weight (total of 150 g) applied after the impact for the same length of time (5 min).[37] ASCI was tested at T2 and T10, and hemodynamic variables compared. In swine with T2 ASCI, HR and BP showed an immediate spike right after impact and returned to near baseline after 2 min, whereas in swine with T10 ASCI, HR and MAP were unchanged.[37] This finding is

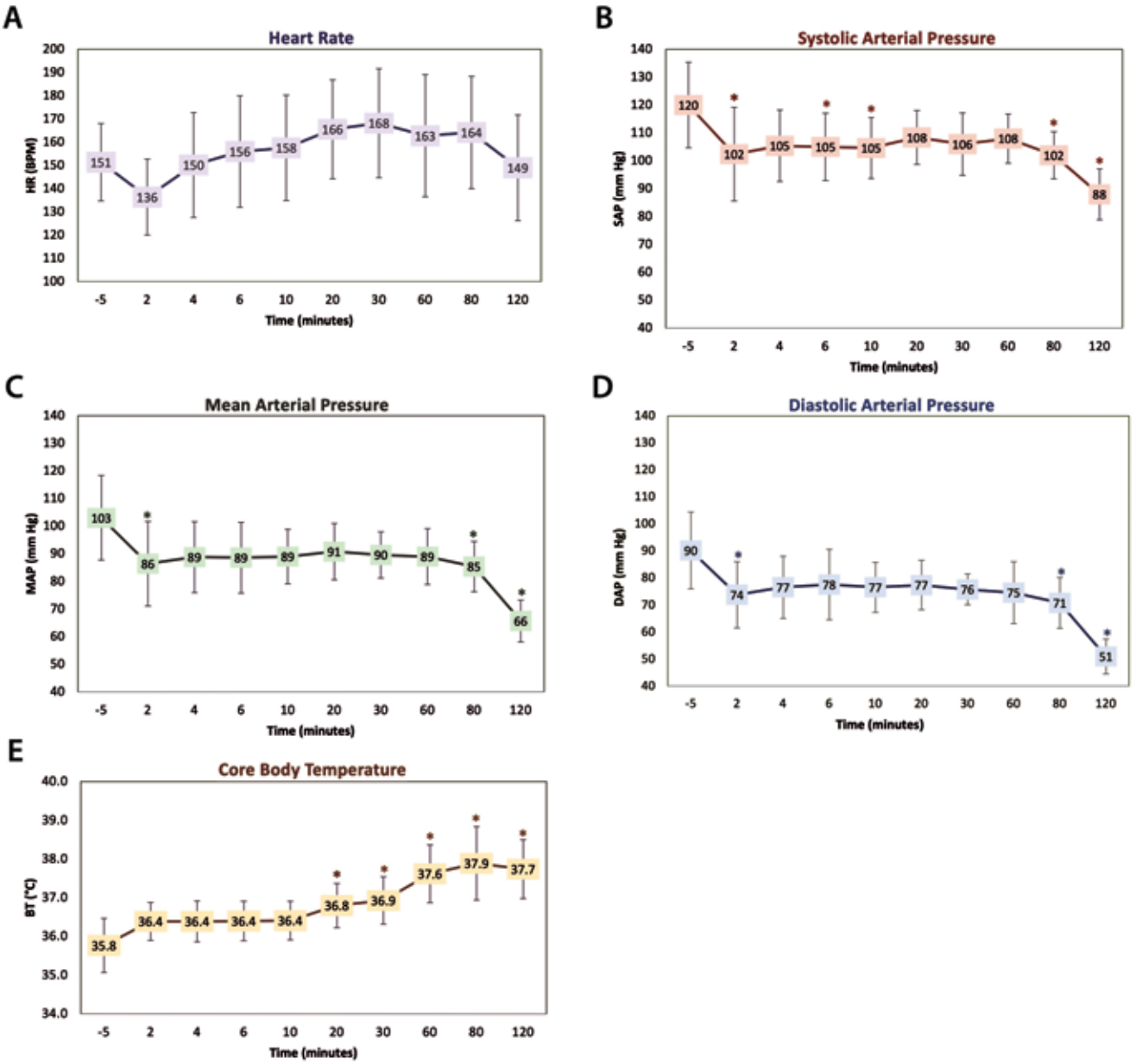

Figure 2. Changes in mean ± SD values of selected variables [DAP (2A), MAP (2B), SAP (2C), HR (2D), and BT (2E)] at selected time points (5 min before ASCI, 2, 4, 6, 10, 20, 30, 60, 80, and 120 min after ASCI). *values differ significantly ($P < 0.05$) from the baseline value (-5 min).

also consistent with another study on the hemodynamic effects of balloon compression of the spinal cord at specific segments in domestic cats, where compression of the spinal cord at T9 and T11 elicited negligible changes in BP.[1]

Findings from the aforementioned study[37] are in contrast with ours, as we observed a significant decrease in mean arterial pressures from 103 ± 15 to 87 ± 15 mm Hg at 2 min after ASCI. In our study, baseline MAP was 103 ± 15, whereas values ranged from 76 ± 9 to 134 ± 34 in previous studies.[1,24,37] We speculate that this difference could be due to 3 potential factors. First, the anesthetic maintenance regimens used in one model[37] differed from that used in the present study, as the former used a completely intravenous anesthetic protocol (ketamine 5 to 11 mg/kg/h; propofol 10 to 20 mg/kg/h; and fentanyl 10 to 20 µg/kg/h IV) whereas the latter combined intravenous anesthesia and inhalational maintenance as described in the methods. Propofol is known to better preserve aortic pressures and increase aortic compliance in dogs as compared with isoflurane,[3] and to decrease tonic sympathetic nerve activity in people.[5] Differences in sympathetic tone and baroreflex activity related to the different anesthetic regimens may be responsible for the dissimilarities in mean arterial pressures observed immediately after ASCI. Second, the timing of baseline hemodynamic data collection differed between studies, as the present study used values from 5 min before ASCI as baseline, whereas the previous study used values collected 60 min before ASCI as the baseline.[37] This relatively long time period between baseline and ASCI could lead to questions about differences in anesthetic depth and/or surgical manipulation (or lack of thereof), which may have altered hemodynamic parameters closer to the time of ASCI. Third, our impactor may have generated a greater force of impact, resulting in an accentuated decrement in MAP due to a greater degree of spinal tissue trauma. Nonetheless, both studies showed that minimal hemodynamic changes developed

Table 2. Arterial blood gas parameters (not temperature adjusted) observed at selected time points.

Variable	-60 min	-10 min	30 min	120-240 min
FiO_2 (%)	94.2 ± 1.8	94.3 ± 1.3	94 ± 1.1	97.8 ± 2.9
PCV (%)	24.6 ± 1.9	28.3 ± 3.4	24.2 ± 4.1	28 ± 5.8
pH	7.5 ± 0.1	7.5 ± 0.1	7.5 ± 0.1	7.4 ± 0.2
$PaCO_2$ (mm Hg)	44.5 ± 6.3	44.1 ± 6.2	45.2 ± 4.6	60.1 ± 34
PaO_2 (mm Hg)	554 ± 47	553 ± 10	481 ± 59	394 ± 185
HCO_3 (mmol/L)	31.5 ± 1.6	32 ± 2.6	31.7 ± 1.6	33.3 ± 2.6
BE (mmol/L)	7.5 ± 1.8	8.3 ± 2.8	7.7 ± 1.9	8.6 ± 2.2
Hemoglobin (g/dL)	8.4 ± 0.6	9.5 ± 1.2	7.6 ± 0.7	9.5 ± 2
Na^+ (mmol/L)	138 ± 2	138 ± 1	136 ± 2	138 ± 3
K^+ (mmol/L)	3.8 ± 0.3	4 ± 0.2	4 ± 0.2	4 ± 0.3
iCa (mmol/L)	1.3 ± 0	1.3 ± 0	1.3 ± 0.1	1.3 ± 0.1
Cl^- (mmol/L)	80 ± 37	100 ± 5	99 ± 3	97 ± 2
Anion Gap (mmol/L)	13.8 ± 0.8	12 ± 0	10.5 ± 2.3	13.7 ± 1.7
Glu (mg/dL)	82 ± 7	90 ± 10	99 ± 11	123 ± 13*
% change from baseline	-	*9.4%*	*20.7%*	*50.3%*
Lac^- (mmol/L)	2.2 ± 0.3	2.5 ± 0.5	1.9 ± 0.7	1.8 ± 0.6
BUN (mg/dL)	12.2 ± 1	12 ± 1.4	11.8 ± 1.3	12.8 ± 1.3
Creatinine (mg/dL)	1 ± 0.4	1.1 ± 0.1	1.1 ± 0.1	1.4 ± 0.6

Data are presented as mean ± SD (SD) values.
*Within a row value differs significantly ($P < 0.05$) from the value for -60 min.

after ASCI at T10 and did not produce hypotension in the studied model of blunt spinal trauma, regardless of anesthetic regimen. This finding is also important in humans, given that avoiding hypotension (SAP < 90 mm Hg) is considered a key factor in providing neuroprotection, as ischemia of the injured spinal cord is one of the most relevant contributors to neuronal injury after ASCI.[19] A recent retrospective study on patients who had experienced SCI found that recovery of motor function was positively correlated with the amount of intraoperative time spent in the range of MAP between 70 and 94 mm Hg.[6]

A similar but not identical ASCI model in infant piglets found no significant difference in HR, MAP, BT, $PaCO_2$, PaO_2, Lac, and blood glucose when either complete or incomplete SCI was applied at T7.[24] These findings are mostly consistent with ours, with the exception of MAP changes. The timing of data collection also differed from ours in their study, as baseline was obtained 60 min before ASCI, and after ASCI, data were collected at 15, 30, and 60 min.[24] We suspect that this study[24] may have not found significant changes in arterial pressures after ASCI due to the choice of time points, as the 15-min window from ASCI to the first data collection may have failed to capture hyperacute changes such as the loss of significance in SAP difference at 10 min after ASCI found in the current study.

In the present study, arterial pressures were significantly decreased by 80 min and 120 min after ASCI as compared with values before ASCI. We speculate that this effect may have been produced by either the lack of surgical stimulation, as at this point in time surgical procedures had ended and pigs were recovering, or by secondary damage to the spinal cord caused by build-up of inflammatory substances and hemorrhage at the site of trauma. In addition, chronic hypotension after ASCI has been previously reported in humans.[11,20] Long term data collection was beyond the scope of the current study. Therefore, we cannot infer that decreased arterial pressures seen at 80 and 120 min after ASCI represented the start of a chronic hypotensive state due to altered regional sympathetic tone below T10.

During this study, one pig received dobutamine before, during, and after ASCI. However, use of dobutamine did not affect hemodynamic values based on our statistical analysis. Two other pigs also received dobutamine, but due to dobutamine's short half-life[2] and the elapsed time between discontinuation and ASCI, we can exclude any effect of dobutamine on measured hemodynamic variables. In addition, RR, $EtCO_2$, and Et_{ISO} were unchanged by ASCI which may be due to the provision of mechanical ventilation during the surgical procedure.

Glucose was the only metabolic parameter to significantly increase by 120 min after ASCI, but did not meet the threshold for hyperglycemia in *Sus scrofa domestica*.[22] We speculate that this rise in glucose can be attributed to a stress response and/or a systemic inflammatory response. Both situations promote hyperglycemia and transient insulin resistance.[10] Surgical stimulation[27] and ASCI[10] both cause stress and systemic inflammation that increase blood glucose levels perioperatively. A previous study did not find a significant change in glucose levels after ASCI in their model.[24] The anesthetic regiment used in that study[24] was fentanyl and propofol, which suppress the stress response to surgery in piglets.[31] Differences in age and anesthetic regimens may have contributed to the differences observed in the current and the previous study.[24]

Pigs were hypothermic (35.8 °C; 96.4 °F) at the beginning of the surgical procedure. The increase in body temperature [to 37.7 °C (99.9 °F) by the end of monitoring] observed in this study throughout the anesthetic episode is to be attributed to the provided artificial active warming. Phenomena like neurogenic fever and malignant hyperthermia were ruled out due to absence of the characteristic presentations.

Finally, some limitations should be considered when interpreting these data. Although our sample size was low (only 5), we did detect significant changes in some parameters. More invasive hemodynamic measures such as cardiac output and spinal cord perfusion pressure were not included in our design due to logistical constraints.

In conclusion, minor hemodynamic changes and stable metabolic parameters indicate that adequate tissue perfusion was maintained in this cohort of pigs undergoing blunt spinal trauma of T10-T12. A drop in arterial blood pressure of 15% to 20% is expected after ASCI at this site in the spinal cord and with this anesthetic regimen. Given the positive correlation between motor function outcome and the amount of intraoperative time spent with MAP between 70 and 94 mm Hg in people,[6] we recommend maintaining MAP above 85 mm Hg before inducing ASCI. This practice should maintain adequate tissue perfusion pressures in pigs used for this model of ASCI, and potentially improve their neurological outcome.

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