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Extending REBOA: Endovascular Variable Aortic Control (EVAC) in a Lethal Model of Hemorrhagic Shock

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Abstract

Background—The duration of use and efficacy of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) is limited by distal ischemia. We developed a hybrid endovascular-extracorporeal circuit variable aortic control (VAC) device to extend REBOA duration in a lethal model of hemorrhagic shock to serve as an experimental surrogate to further development of endovascular variable aortic control (EVAC) technologies.

Methods—Nine Yorkshire-cross swine were anesthetized, instrumented, splenectomized, and subjected to 30% liver amputation. Following a short period of uncontrolled hemorrhage, REBOA was instituted for 20 minutes. Automated variable occlusion in response to changes in proximal mean arterial pressure was applied for the remaining 70 minutes of the intervention phase using the automated extracorporeal circuit. Damage control surgery and whole blood resuscitation then occurred and the animals were monitored for a total of 6 hours.

Results—Seven animals survived the initial surgical preparation. After 20 minutes of complete REBOA, regulated flow was initiated through the extracorporeal circuit to simulate VAC and

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provide perfusion to distal tissue beds during the 90-minute intervention phase. Two animals required circuit occlusion for salvage, while five animals tolerated sustained, escalating restoration of distal blood flow prior to surgical hemorrhage control. Animals tolerating distal flow had preserved renal function, maintained proximal blood pressure, and rapidly weaned from complete REBOA.

Conclusion—We combined a novel automated, extracorporeal circuit with complete REBOA to achieve endovascular variable aortic control in a swine model of uncontrolled hemorrhage. Our approach regulated proximal aortic pressure, alleviated supra-normal values above the balloon, and provided controlled distal aortic perfusion that reduced ischemia without inducing intolerable bleeding. This experimental model serves as a temporary surrogate to guide future EVAC catheter designs that may provide transformational approaches to hemorrhagic shock.

Keywords

REBOA; endovascular variable aortic control; hemorrhage control; aortic occlusion

Background

Endovascular techniques are a less invasive and more efficient way to manage vascular injury and shock(1-6), and resuscitative endovascular balloon occlusion of the aorta (REBOA) has emerged as an alternative to resuscitative thoracotomy with aortic clamping. However, despite promising reports and the development of smaller caliber REBOA devices, concerns exist including: distal ischemia, reperfusion injury, and rebound hypotension upon deflation of the balloon. (2,3,5) Additionally, the effects of prolonged supra-physiologic pressure proximal to the balloon may damage the heart, lungs, and brain. These limitations notwithstanding, the less invasive nature of REBOA makes it attractive for aortic control and the development of new approaches to this procedure provide great opportunity for therapeutic advances.

While REBOA is effective at restoring proximal perfusion, there is a time threshold beyond which the deleterious effects of aortic occlusion outweigh its initial benefit. However, for clinical scenarios in which the time interval between REBOA and definitive surgical management exceeds this threshold, a more advanced strategy is needed.(7) Variable or partial aortic occlusion that permits a controlled amount of distal perfusion while maintaining proximal aortic pressure is one strategy that may extend the window for endovascular therapies. Variable aortic control (VAC) may be particularly useful if used following an initial period of complete aortic occlusion that promotes distal hemostasis and maximizes proximal perfusion. VAC invokes the principle of permissive hypotension in an attempt to minimize hemorrhage and promote clot stabilization in the area of vascular disruption (e.g. liver, kidney, spleen, pelvis).(8) This strategy is effective not only because reduced blood pressure promotes clot stabilization, but also because regional blood flow is reduced in the face of hypovolemia. While the interaction of pressure, vascular tone, and blood flow varies with each injury scenario, it must be considered as new approaches to aortic control are explored. Regulated VAC is predicated on a new concept of “permissive regional hypoperfusion” that achieves equilibrium among: 1) reduced perfusion pressure to promote clot stabilization, 2) a low rate of of distal flow to mitigate compensatory

vasodilation and provide tissue perfusion and 3) the avoidance of undue bleeding or exsanguination.

Although not yet widely described in the management of trauma and hemorrhagic shock, VAC-like procedures are used in cardiac failure, ischemic stroke, and the deployment of aortic stent grafts.(9) Recognizing that blood flow across any REBOA device involves the interplay of hemodynamics, ongoing blood loss, and changes in aortic diameter, automation will be required to continuously adjust the degree of aortic occlusion and account for other factors associated with the patient, the injury, and the clinical setting. When developed, automated endovascular variable aortic control (EVAC) combined with judicious use of resuscitative fluid has the potential to sustain an injured patient for a longer period of time prior to definitive hemostasis when compared to existing technology.

In the absence of such an automated endovascular device, a translational model is required to study of the feasibility and physiologic effects of variable aortic control in the setting of hemorrhagic shock. Our experimental approach was to develop an automated extracorporeal circuit that could offload proximal aortic pressure in the setting of REBOA and deliver distal perfusion, controlling for the variables of flow and pressure. In this context, the hybrid of REBOA and the extracorporeal circuit serve as a surrogate for EVAC. This configuration will allow us to investigate dynamic partial aortic occlusion and permissive regional hypoperfusion in an experimental model. The objective of this study is to describe the experimental setup and examine the feasibility of a combined endovascular-extracorporeal approach to automated variable aortic control in a lethal model of torso hemorrhage and shock.

Methods

Overview of Experimental Design

This study was approved by the Institutional Animal Care and Use Committee at David Grant USAF Medical Center, Travis Air Force Base, California. All animal care and use was in strict compliance with the Guide for the Care and Use of Laboratory Animals in a facility accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International. Healthy adult, castrate male and non-pregnant female Yorkshire-cross swine (Sus scrofa), obtained from the University of California, Davis, were acclimated for a minimum of 7 days. At the time of experimentation, animals weighed between 72 and 90 kg, with an age between 5 and 7 months.

Following severe mixed venous and arterial liver injury and 1.5 minutes of free hemorrhage, animals underwent a 20-minute period of REBOA followed by restoration of variable, low-volume distal aortic flow using the extracorporeal circuit for the duration of the 90-minute period (Figure 1). Following this 90-minute period of REBOA with automated extra-corporeal perfusion (carotid to femoral), surgical hemostasis was performed via a laparotomy. The animal was then weaned from occlusion by gradually restoring flow through the extracorporeal circuit in response to proximal aortic pressure followed by REBOA catheter deflation. As would be the case in a real clinical scenario, these experiments were conducted in an “intention to treat” fashion. Animals unable to tolerate

VAC reverted back to standard REBOA for the duration of the 70 minutes as a salvage maneuver.

Animal Preparation

Animals were pre-medicated with 6.6 mg/kg tiletamine/zolazepam (TELAZOL, Fort Dodge Animal Health, Fort Dodge, IA) intramuscularly. Following isoflurane induction and endotracheal intubation, maintenance anesthesia consisted of 2% isoflurane in 100% oxygen. To overcome the vasodilatory effects of general anesthesia, an intravenous infusion of norepinephrine (0.01mcg/kg/hr) was initiated. Animals were mechanically ventilated with tidal volumes of 7-10 mL/kg and a respiratory rate of 10-15 breaths per minute sufficient to maintain end tidal CO2 at 40 ± 5 mm Hg. The pigs were placed on a warming blanked set at 39°C to minimize hypothermia.

Both carotid arteries were exposed through a midline neck incision, the left brachial artery was exposed through an axillary incision, and the femoral arteries were accessed through separate oblique groin incisions. Arterial access was obtained for blood collection, proximal and distal hemodynamic monitoring, and to facilitate endovascular intervention. A 4mm perivascular Doppler flow probe (Transonic Corporation, Ithaca, NY) was secured around the right CCA to monitor cerebral blood flow. Additionally, a 12F 13cm introducer sheath (Cook Incorporated, Bloomington, IN) was inserted retrograde into the left FA, through which the occlusion balloon catheter was introduced (Figure 2A). Concurrently, a splenectomy was completed to minimize hemodynamic variation from auto-transfusion. Normal saline was administered at a maintenance rate of 5 mL/kg/hr.

Development of the Variable Aortic Control Circuit

A custom extracorporeal, automated variable aortic control circuit capable of regulating distal aortic flow was constructed to experimentally replicate the desired functionality of EVAC when combined with REBOA (Figure 3A). The automation of the system was developed to facilitate a reliable and reproducible experimental design, minimizing potential for experimental bias. The hardware construct includes a commercially available flow monitor (Transonic, Ithaca, NY), a novel extracorporeal flow circuit (Figure 2A), and a custom designed control system (Figure 3B). Flow through the circuit was reliant on cardiac output and proximal blood pressure and regulated with a linear actuator that extrinsically compresses the circuit tubing (Figure 3c). In this manner, distal aortic flow was controlled across the spectrum from complete occlusion to unimpeded full flow.

The configuration of the circuit was as follows. An 18Fr cannula was inserted into the left carotid artery and advanced to the level of the aortic arch. A second cannula was inserted retrograde into the left femoral artery to the level of the infrarenal aorta (Figure 2A). These cannulas are connected with 3/8 inch internal diameter tubing. To initiate flow through the circuit, REBOA was performed by positioning and inflating a CODA balloon (Cook Medical, Bloomington, IN) at the level of the diaphragm. To achieve distal flow, pneumatic pinch valves were unclamped to allow blood flow from the proximal carotid cannula through the VAC circuit and returning to the animal through the distal trans-femoral cannula. Circuit flow rates were assessed with an inline flow meter. The flow rate was precisely regulated to

within +/- 5 mL/min of the prescribed flow rate utilizing the linear actuator. As the actuator extended and retracted, roller bearings on the opposing end of the lever arm variably compressed the tubing with a high degree of fidelity (approximately 0.01 mm step movement of the roller bearing) (Figure 2B). A complete technical description of the circuit control design is provided (Text, SDC 1).

Injury

The liver was marked along the planned transection plane, 2cm to the left of Cantlie's line, to provide amputation of approximately 80% of the left lateral lobe of the liver and 40% of the left medial lobe of the liver (approximately 30% of total liver volume) similar to previous descriptions.(10) At time 0, the liver was sharply transected and the abdomen rapidly closed. Complete occlusion of the aorta was achieved with REBOA 1.5 minutes following the initiation of injury (Figure 2B).

Intervention

REBOA and Restoration of Distal Aortic Flow with Automated Variable Aortic Control Circuit

Following 20 minutes of REBOA, automated variable aortic control was achieved by reintroducing oxygenated blood flow in a highly controlled fashion through the extracorporeal VAC circuit, around the inflated REBOA catheter, and into the distal aorta according to a pre-determined algorithm (Figure, SDC 2). Bypassing the inflated REBOA catheter with this circuit resulted in distal regional hypoperfusion for the remaining 70 minutes of the intervention period. During this period, the customized linear actuator on the VAC circuit continuously adjusted the degree of compression of the circuit tubing to maintain a pre-determined circuit flow rate provided MAP remained above a preset threshold of 50 mmHg (Figure, SDC 2). Below this threshold, the actuator restricted circuit blood flow to minimum flow rate of 100 mL/min to prevent death from complete cardiovascular collapse. Further, the VAC circuit was programmed to automatically clamp after 3 minutes of sustained pressure below 35 mmHg, reestablishing complete REBOA for the remainder of the 90-minute intervention period. Conversely, the VAC circuit increased the distal flow rate if a higher proximal MAP threshold was reached following 20 minutes of VAC. The flow rate was dynamic and based on proximal MAP, ranging from 100 mL/min to 300 mL/min (Figure, SDC 2). The initial flow rate of 150mL/min was determined during earlier iterations of model development, in which a flow rate of 150 mL/min after controlled hemorrhage of animals to class IV shock resulted in a proximal MAP of approximately 60 mmHg (data not shown). Two colloid boluses were allowed during VAC at T40 and T70, with administration predicated on a minimum MAP threshold and indicated by an audible alarm from the control system.

At the conclusion of the 90-minute intervention phase, the abdomen was reopened and liver hemorrhage was definitively controlled. Shed blood was quantified and fresh whole blood resuscitation was used to replenish the exact total volume of intra-abdominal shed blood.

Weaning from REBOA with Automated Variable Aortic Control Circuit and ICU Phase

Ten minutes following the start of damage control surgery, an automated weaning algorithm was initiated. When the proximal MAP exceeded the minimum threshold of 65 mmHg, the VAC circuit progressively opened to restore a full flow state. However, the circuit would also maintain or decrease flow to sustain the proximal MAP above 55 mmHg. Following a 5-minute period of full and unrestricted circuit flow, an alarm sounded to signal successful weaning from occlusion. The VAC circuit was clamped simultaneous to CODA balloon deflation to end REBOA and restore native inline aortic flow. The animal was then survived for 360 minutes from the start of the experiment. During this ICU phase, boluses were administered if the MAP dropped below 60 mmHg continuously for > 1 minute. The animals were euthanized after 360 minutes.

Data Collection

Physiologic data, including proximal and distal aortic pressures, visceral blood pressure (distal branch of the superior mesenteric artery), heart rate, core body temperature, right carotid artery blood flow, and ECG monitoring were continuously captured throughout the experiment using a multichannel data acquisition system (Biopac Systems Inc, Goleta, CA).

Results

Ex-vivo testing of the flow circuit revealed that the circuit and automated control mechanism were able to reliably achieve precise flow across all prescribed algorithms. (Figure, SDC 3A). During simulation of the weaning protocol, the circuit accurately reduced, increased or maintained the flow rate in response to the simulated proximal pressure (Figure, SDC 3B).

A total of 15 experiments were performed as part of this model validation study (6 model development and 9 model validation animals). Animal preparation, liver injury, open surgical technique, and post-hemorrhage resuscitation protocols were developed with the initial 6 model development animals. Two animals in the study group developed large air emboli from the liver injury and were excluded due to instant death after injury. The remaining 7 animals comprised the study cohort. All 7 sustained a large liver injury with intra-abdominal hemorrhage. The ACT for all animals was close to the desired target of 100 seconds. All 7 animals survived to the end of study and 2 reverted back to complete REBOA during the period of VAC due to sustained hypotension.

Baseline injury characteristics, resuscitation metrics, and outcomes are shown in Table 1. The 2 animals that did not tolerate distal flow required re-occlusion of the circuit after only 2 and 15 minutes, respectively. An averaged hemodynamic profile for all animals is shown in Figure 4A. The liver injury created a consistent and rapid decrease in the proximal MAP over the 1.5 minutes of free hemorrhage prior to intervention with a subsequent increase during the initial 20-minute period of complete REBOA. Animals that tolerated distal flow via the VAC circuit during the remaining 70 minutes consistently maintained a proximal MAP > 60mmHg, (Table 2). Furthermore, animals that tolerated sustained flow through the VAC circuit organ demonstrated continued distal organ function following the intervention with sustained urine production and lactate clearance. Animals that tolerated VAC were able

to wean from partial flow to full native aortic flow without large fluctuations in proximal MAP (Figure 4B).

Discussion

The objective of this study was to demonstrate the feasibility of REBOA coupled with a novel automated extracorporeal circuit in order to establish a predicate model with which to study the emerging concept of automated EVAC. Findings demonstrate that initiation of this circuit in conjunction with complete REBOA effectively regulates proximal aortic pressure within desirable and pre-determined parameters while providing a variable degree of distal aortic perfusion that mitigates ischemia without leading to exsanguination. Observations from this study show complete survival from what is an otherwise uniformly fatal injury with a preserved distal organ function after 90 minutes of intervention and before definitive surgical control of hemorrhage. This study supports the principle of “permissive regional hypoperfusion” in the setting of non-compressible torso hemorrhage, provides a model to study it, and suggests a transforming potential for automated, endovascular variable aortic control (EVAC) in the setting of shock.

The advancement of endovascular technologies in response to ongoing clinical and translational research has resulted in the development of REBOA as a viable alternative to traditional thoracotomy and aortic cross clamping. However, REBOA still results in a significant ischemic insult to distal tissue beds and is only tolerated in short intervals.(3, 11) Extended periods of complete aortic occlusion can result in irreversible ischemic injury, permanent organ failure, limb ischemia, and death.(3, 4) Unfortunately, these consequences restrict the application of REBOA in many clinical scenarios to a technique of last resort. However, EVAC may offer new therapeutic options for non-compressible truncal injury. Similar to REBOA, EVAC would lessen the physiologic impact of aortic occlusion compared to traditional thoracotomy and aortic cross clamping. Additionally, EVAC maneuvers would likely require an abbreviated period of complete aortic occlusion to provide for early hemodynamic recovery and clot stabilization. What distinguishes EVAC from current resuscitative strategies is the early restoration of low volume distal flow to minimize the ischemic burden of sustained complete aortic occlusion. Furthermore, control of an EVAC device with smart technology is conceivable to regulate distal flow based on the patient's physiology. Moreover, the expanded capability of future low-profile endovascular devices would allow EVAC to be applied more liberally and earlier in the patient's care. The results of our current study highlight that this approach is rational and feasible.

The model in this series of experiments was constructed to be a temporary surrogate of automated variable aortic control and not the end solution. While examples exist in cardiovascular surgery of the use of extra-corporeal circuits to offload the left ventricle during aortic cross clamp and to deliver distal aortic perfusion during an aortic repair, none are automated to regulate a desired range of proximal aortic pressure or distal flow and are too cumbersome to be used in settings of trauma.(12, 13) This model confirms the effectiveness of the general approach to left ventricular off-loading and extends the concept to the setting of trauma and shock. Additionally, the model in this study, including the pressure-responsive computer algorithm of the circuit, provides a means by which to study

the principles of automated, variable aortic control and permissive regional hypoperfusion in the setting of torso hemorrhage. The design of this model should also allow for the more efficient development of catheter-based devices including ones to accomplish regulated endovascular variable aortic occlusion (EVAC).

Our previous attempts to mitigate the deleterious effects of REBOA with existing endovascular technology utilized a similar porcine liver injury model.(10) A significant limitation of this prior experimental model of partial REBOA with balloon catheters was an inability to quantify or control the amount of blood flow being delivered to the distal aorta. Instead of measuring direct flow, the degree of occlusion was based on the pressure gradient proximal and distal to the balloon. Our current experience suggests an uncoupling of the relationship between pressure gradient and flow particularly during periods when circulating blood volume and/or cardiac output are changing (Figure, SDC 4). This finding led us to surmise that flow rates in prior studies may have exceeded what was physiologically tolerable in the face of an uncontrolled vascular injury. Thus, the lack of current balloon catheter technology to measure and precisely regulate distal aortic flow was the impetus for redesigning the experimental setup and creating an automated computer-controlled model of variable aortic control.

Our bench-top testing has validated the feasibility of tightly regulating flow with computer-controlled algorithms in an ex-vivo flow circuit (Figures, SDC 3 and SDC 4). Additionally, we have been able to replicate this precise control in our large animal model. Utilizing the described EVAC resuscitation paradigm, we have noted significant improvement in immediate survival for animals undergoing EVAC as compared to previous work with a similar liver injury model.(10) In this present study, all animals survived to the end of the experiment. This suggests that even in critically injured animals, attempts to reinstate partial distal flow did not ultimately compromise short-term salvage of the animal.

Current technologies in endovascular aortic occlusion are dependent on manual inflation of a REBOA balloon.(6, 14, 15) Small changes in the diameter of an occlusion balloon result in large changes in flow (based on the Poiseuille's Law), making control of distal flow by manual adjustment of balloon diameter extremely difficult. While waiting for the technological advances that will make endovascular graded occlusion of the aorta possible, we have utilized our extracorporeal circuit as a stepping stone to demonstrate the utility of automated computer control of variable aortic occlusion. The development of catheters capable of EVAC with computer-controlled automation promises a more efficient and responsive system during resuscitation. Furthermore, the creation of an automated endovascular aortic occlusive device will help “cognitively offload” healthcare providers and free them to focus efforts on key manual resuscitative interventions, from the preparation of a patient for transport to providing definitive surgical hemorrhage control, while automated aortic control maximizes a patient's physiology.

Automated computer-controlled variable aortic control offers new advances in weaning patients from aortic occlusion. Current methods of weaning a patient from complete aortic occlusion are imprecise and poorly studied. Upon reintroduction of aortic flow, the redistribution of blood with accumulated ischemic metabolites results in ischemia

reperfusion injury, systemic inflammatory response, and often hemodynamic collapse.(16, 17) As many as 50% of patients treated with traditional REBOA require re-occlusion of the aorta, adding to the existing ischemic burden.(3, 4) Besides minimizing distal ischemia through partial aortic flow, an automated-computer controlled model of EVAC provides an alternative to the dichotomous open or occluded paradigm provided by REBOA. These initial experiments have demonstrated that our weaning protocol is able to rapidly transition from complete occlusion to open flow automatically in under 20 minutes. The weaning in both animals that required re-occlusion of the aorta occurred successfully without hemodynamic collapse utilizing this algorithm despite significant ischemic burden at the time of initiation of weaning. Moreover, the sustained distal aortic flow for the 5 other animals facilitated immediate weaning from occlusion, presumably due to decreased distal ischemic burden. This rapid return of full aortic flow further underscores how EVAC might minimize the physiologic impact of aortic occlusion.

Beyond translational experiments for hemorrhage, the variable aortic control afforded by this experimental model could be utilized in polytrauma models to evaluate effects of supraphysiologic blood flow on proximal vascular beds. In particular, this model is ideally suited to evaluate effects of partial and complete aortic occlusion on patients with concomitant traumatic brain injury (TBI), a patient group that has faired poorly with traditional REBOA techniques.(3, 4) This expanded capability may even limit the inherent physiologic variation in large animal experiments by providing precise regulation of proximal or distal arterial blood pressure or flow for extended periods of time. Such applications could accelerate the transition toward more clinically relevant models of traumatic brain injury and ischemia-reperfusion injury.

The present proof-of-concept study is limited by a lack of a comparison group receiving only REBOA for the entire 90-minute intervention phase and prevents broader interpretation of the results. Likewise, these experiments did not include a group in which no intervention was performed after injury. However, the author's previous experience utilizing a similar liver injury model suggests a uniformly, rapidly fatal injury in the absence of expeditious application of complete REBOA.(10) Additionally, the use of large diameter aortic cannulas in the femoral artery likely resulted in flow restriction to the hindlimb of the animal and may have artificially increased the ischemic burden. Limitations notwithstanding, this study provides an important first step toward novel resuscitation paradigms and experimental methodology.

Conclusion

This study demonstrates the life-saving potential of a novel, automated, extracorporeal circuit used in conjunction with complete resuscitative endovascular balloon occlusion of the aorta. Initiation of the extracorporeal circuit in this study regulated proximal aortic pressure within a pre-determined range, alleviating supra-normal values above the balloon occlusion. This approach also provided controlled distal aortic perfusion that reduced end-organ ischemia without inducing intolerable bleeding, confirming the principle of permissive regional hypoperfusion. The endovascular-extracorporeal approach in this study serves as a temporary surrogate for future automated variable aortic control designs – including the

development of low profile, endovascular devices – that should be pursued as potentially transformational approaches to non-compressible torso hemorrhage and shock.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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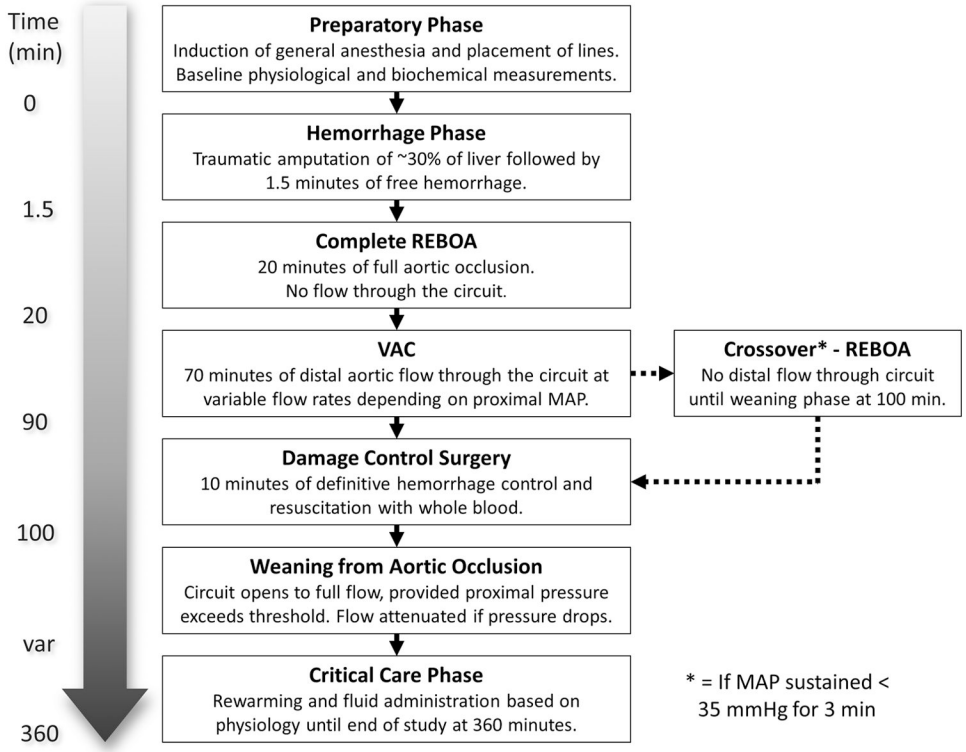

Figure 1. Study Flow

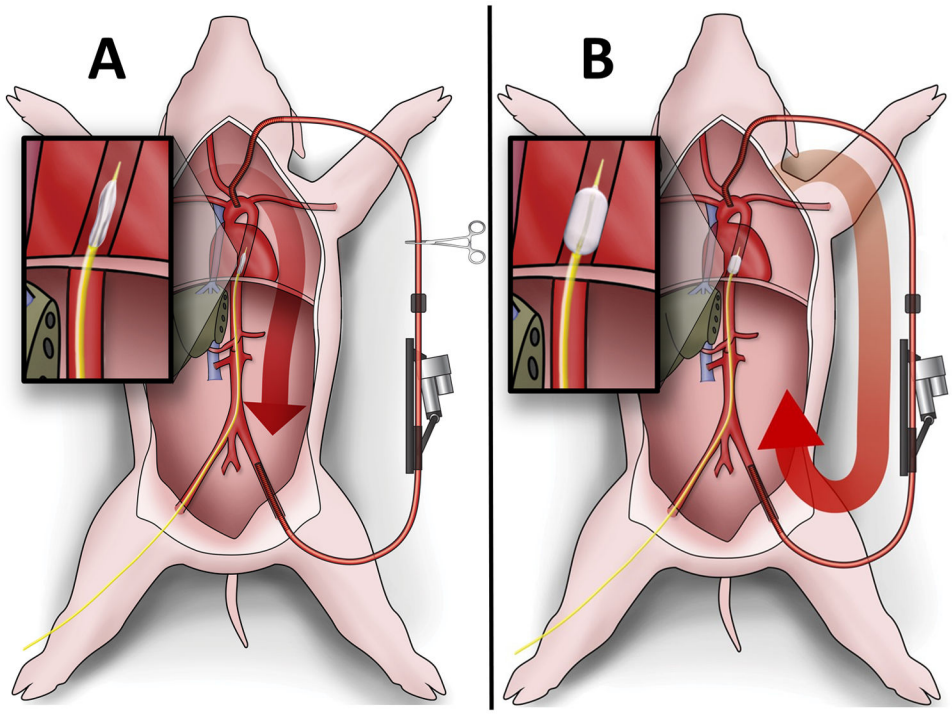

Figure 2.

Schematic of Experimental Setup: ***A)*** Aortic cannulas placed in the carotid and femoral arteries are connected to the clamped circuit. ***B)*** Occlusion of the aorta with a CODA balloon and unclamping of the circuit diverted blood flow through the circuit. Data from the proximal pressure and inline flow monitors is relayed in real time back to the data acquisition system and on to the control box, which regulates flow in the circuit based on a prescribed algorithm.

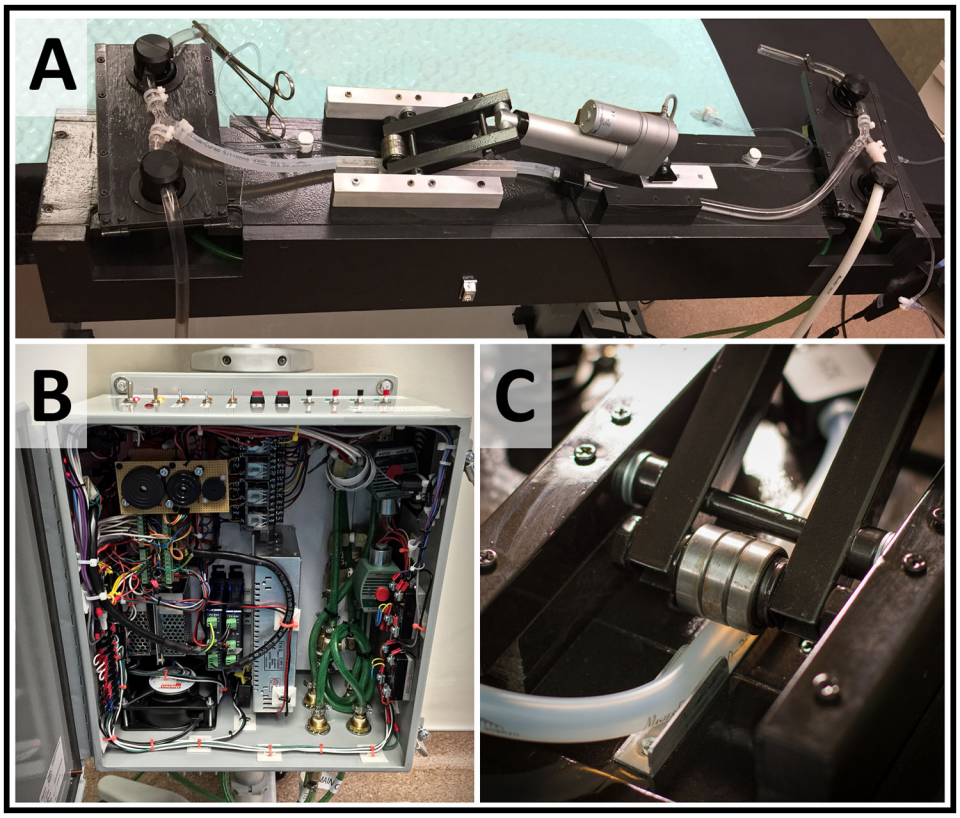

Figure 3.

Components of the Variable Aortic Control Device: Transonic® TS410 Flowmeter receives input from an inline flow probe Custom control system utilizing an Arduino® microcontroller Flow circuit consists of a linear actuator, pneumatic, and electric pinch valves Close-up view of the linear actuator demonstrates the roller bearing/tubing interface

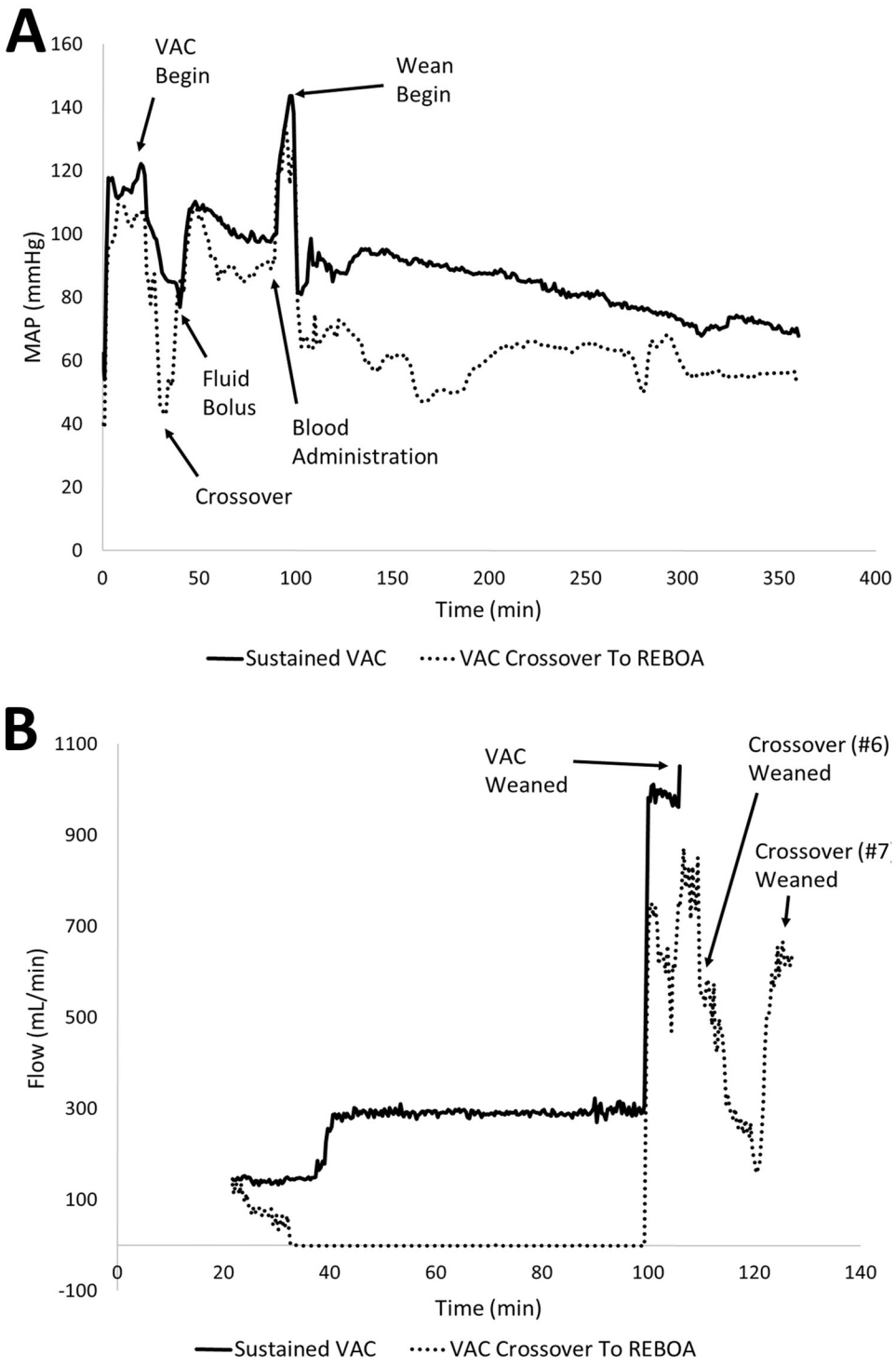

Figure 4.

Hemodynamic Data: ***A)*** Proximal MAP throughout the experiment. Note animals requiring crossover sustained precipitous drop upon EVAC, however rebounded upon re-occlusion. Following damage control, animals that tolerating sustained EVAC maintained a MAP near baseline for the remainder of the study. ***B)*** Circuit flow during EVAC phase. Averaged

continuous MAP for five animals that tolerated EVAC showed sustained initial flow at 150 mL/min, with flow rate of 300 mL/min beyond T40 and immediately weaned from REBOA.

Table 1

Injury Characteristics, Resuscitation Metrics, and Outcomes

ID	Pre-Injury ACT	% Liver Resected	% EBL	Transfusion Volume	Crystalloids	Total UOP	Time to Wean (min)
1	130	21	14.4	607	2800	NA	5.7
2	78	24	32.8	1358	2600	682	6.0
3	90	27	22.4	1354	4460	380	6.3
4	119	31	31.9	2004	4236	50	6.0
5	98	29	26.2	1618	4460	152	6.0
6*	106	26	57.1	2709	4800	59	10.3
7*	91	23	41.7	3104	5000	41	34.4
Average	101	25	32.5	1832	4050	227	10.7
Std Dev	16	3	12.8	794	886	234	9.8

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Table 2

Hemodynamic and Laboratory Analysis

ID	Init MAP	Min Free-Bleed MAP	Max Occlusion MAP	Min VAC MAP	Δ Hgb	Min pH	Max BE	Max K^+	Max Lactate	Lactate T360	Max Creat
1	78	57	171	104	1.3	7.36	0.1	4.8	5.4	5.1	2.7
2	83	52	154	33	5.3	7.14	-10.3	6.7	14.5	5.0	2.9
3	82	45	116	63	3.7	7.21	-7	6.2	12.1	7.2	3.1
4	77	39	116	72	5.8	7.25	-7.3	6.3	9.2	7.5	2.9
5	67	41	117	58	4.3	7.30	-5.1	6.4	9.2	4.2	3.8
6*	76	32	67	17	5.7	7.01	-12.2	6.8	13.3	6.7	2.6
7*	71	47	162	29	6	7.03	-14.7	6.8	13.4	10.1	2.9
Average	76	44	129	53	4.6	7.18	-8.1	6.3	11.1	6.5	2.98
Std Dev	5	7	33	27	1.5	0.12	4.9	0.6	2.9	1.8	0.36