Development of a Perfused Cadaver Model of Exsanguinating Hemorrhage for Procedural Training and Device Evaluation

T L Morgan, R A De Lorenzo, J A Ward, C E White, S H Husaini, J F Kragh, Jr, P E Dawson

Citation

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Abstract
Introduction: We demonstrate a novel perfused cadaver model with realistic tissue feel, true anatomy, and replicating key local physiologic parameters of acute life-threatening hemorrhage. Validation of fidelity is accomplished through measurement of hemodynamics and video confirmation of hemorrhage control.

Methods: A pulsatile pump was attached to the ascending and descending aorta of a fresh or fresh-frozen cadaver via plastic tubing. The pump provided forward flow at 60 beats per minute of water with red coloring, simulating circulation. Flow probes were attached to arteries immediately proximal to an injury/transection site, with pressure probes cannulated in a contralateral artery that indicated systemic pressure. Hemorrhage control was performed using three different devices, with cessation of hemorrhage confirmed via physiologic data as well as visually.

Results: Physiologic data confirmed that hemorrhage control was obtained under expected parameters. Flow immediately proximal to the injury site was negligible after hemorrhage control was attempted, while systemic pressure increased. When the hemorrhage control device was released, bleeding resumed and flow increased as measured proximal to the wound. Video recordings served as visual confirmation of hemorrhage control obtained using various devices.

Conclusions: Our perfused cadaver model offers realistic tissue feel and simulated blood flow with a pulse, with hemorrhage control correlating to realistic physiologic parameters. The result is an accurate representation of visual, tactile, and physiologic modeling for acute life-threatening limb hemorrhage control.

INTRODUCTION
Simulation is integral both for task training and for comprehensive training in emergency care and resuscitation, and several platforms are in widespread use including high- and low-fidelity patient simulators (e.g., mannequins), animal models and human cadavers1-3. Each of the different platforms has particular characteristics that render them more or less suitable for certain types of training and procedures2-4. Visual realism, anatomic fidelity, tissue feel, cost, durability and other factors affect a model’s realism and effectiveness. For example, a model for cricothyrotomy should have high anatomic fidelity since proper placement is heavily dependent on anatomic landmarks. In contrast, a model used for extremity hemorrhage control should provide realistic bleeding that mimics the physiologic characteristics of real hemorrhage such as brisk flow rates, pulsatile pressures, and response to appropriate interventions.

Recently, interest has focused on so-called perfused or dynamic cadavers. These are human cadavers that are prepared in such a way that fluid flows through blood vessels and vascular tissue “bleeds” realistically when traumatized. Aboud, et al have demonstrated the use of perfused cadavers in neurological, vascular, and trauma surgery5-7. They used an intra-aortic balloon pump to circulate a colored liquid, simulating blood, into the vasculature. The benefit of their model was the pulsatile
bleeding and more realistic tissue feel with oozing. Although Aboud et al examined primarily surgical procedures, the same principles could be applied for other invasive procedures in which bleeding and tissue authenticity were required5-7. For example, Garrett, et al used a fresh-frozen cadaver model for endovascular device testing and training8. In this model a pump was attached to two ends of a section of vasculature to achieve a closed circuit around the area of interest. This allowed the participant to feel pulsatile flow in a realistic anatomy to achieve arterial access via catheters and deploy stents and balloons downstream. Not previously described, however, is a perfused cadaver model specifically intended for training emergency care procedures.

We present a perfused cadaver as a training model for acute exsanguinating hemorrhage control. Our objective is to demonstrate visually and physiologically the significant hemorrhage rate this new model provides. We propose that this realism can more effectively train participants in hemorrhage control using different methods and devices. We describe the setup of the perfused cadaver model for hemorrhage control and discuss future plans for expansion to incorporate other life-saving interventions.

METHODS

The model was developed and validated in two stages. First, animal carcasses were used to prototype the model. Subsequently, the techniques were transferred to human cadavers. Approval for the work was obtained in advance from the Institutional Review Board and Animal Care and Use Committees at our institution. The study was also in compliance with Department of Defense guidelines for the use of human cadavers in research and training.

ANIMAL CARCASS PROTOTYPING

All procedures performed in the cadavers were first established in a carcass swine model. Overall, 47 swine carcasses were utilized to establish the procedures and train the study team. Carcasses were utilized immediately or frozen after being sacrificed from another study that did not harm the vascular integrity or anatomy. The descending and ascending aorta were cannulated following a thoracotomy and attached via tubing to a reservoir containing dark red fluid, simulating blood. A pulse of 60 beats/minute was established via a pump. The fluid used for perfusion was water with red coloring added.

In this model the right lower extremity vessels were the target of injury. The left common iliac or left femoral artery was cannulated with a pressure probe to allow monitoring of the systemic pressure during the procedure. A circumferential flow probe was placed around either the right iliac or right femoral artery proximal to the injury/transection site to measure actual flow immediately proximal to the injury and the hemorrhage control site.

After the above system was prepared, the right femoral artery, right external iliac artery, or the right common iliac artery was transected using a scalpel under direct visualization to simulate severe injury to the extremity. Pressure was measured in the contralateral artery to the injury while flow was measured in the ipsilateral artery. Maintenance or increase of pressure in the contralateral artery signified the pump was indeed still delivering blood to the descending aorta for distribution. Flow was measured in the ipsilateral artery to determine if flow decreased when hemorrhage control was visually observed.

HUMAN CADAVER

The cadavers were obtained from a willed body program. All cadavers were either fresh or fresh-frozen. The selection criteria for the cadavers are provided in Table 1. Eight cadavers were utilized in total.

Table 1

<table>
<thead>
<tr>
<th>Cadaver selection criteria.</th>
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<tr>
<td>Selection Criteria for Cadavers</td>
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<tr>
<td>1. Under 75 years of age (established after the first specimen was received)</td>
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<tr>
<td>2. Uncompromised vascular system</td>
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<tr>
<td>3. No heart bypass surgery</td>
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<td>4. No recent extensive chemotherapy radiation treatment</td>
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The setup for the experiments was similar to the swine model. Specimens were prepared for the studies by performing a left lateral thoracotomy, a transverse surgical incision of the aorta and insertion of tubing (7mm diameter) into the aorta to allow perfusion of the lower and upper body (Figure 1). Incisions were made in the left upper thigh to locate the femoral artery so that a pressure transducer could be placed in order to capture data on the blood pressure in the perfusion system during testing. Additionally, an incision was made on the right upper thigh or inguinal area to locate the right femoral or iliac artery and a transonic flow probe was attached to assess simulated blood flow rates through the vessel. The flow probe was attached to the vessel...
proximal to the transection site but distal to the hemorrhage control site. This allowed for measurement of the flow rate immediately proximal to the hemorrhage area. This method was chosen instead of measuring bleeding from the wound directly as quantifying spurting blood is problematic and less efficacious. The tubing in the aorta was attached to a pulsatile pump, which pushed fluid through the body to simulate normal blood flow. The overall design of the experiment is illustrated in Figure 2.

**Figure 1**
A view of the tubing (7mm diameter) inserting into the aorta to allow perfusion of the lower and upper body.

**Figure 2**
Diagram of the overall design.

The Harvard Apparatus (Holliston, MA) Pulsatile Blood Pump Model 1423 is a piston pump with directional flow valves. Stroke rate is adjustable from 0 to 100 per minute, volume from 15 to 100 ml, and duty cycle from 25 to 50% systolic in steps of 5%. Inflow comes from a 5 to 10 L supply reservoir. At the pump head we used Tygon 2001 tubing, 0.5 inch ID, 0.75 inch OD. Outflow goes to the vessel being perfused, stepped down through connectors and tubing as needed. The pump is afterload sensitive. Excessive resistance will compromise stroke rate and duty cycle. If the rate slows, the pump should be stopped to prevent overheating. The tubing should be secured well, with hose clamps and tape. To prevent spills there should always be a bypass tube from the outflow back to the reservoir. The bypass can be regulated with a valve, but should never be completely closed.

The system was assessed for assurance that the transducers were properly placed and functional. For the hemorrhage control studies, a deep incision was made in either the mid thigh or mid humerus area to simulate critical bleeding. The hemorrhage control device was then applied to a targeted area. Simulated blood flow and blood pressure data were then collected for each iteration of hemorrhage control. In most cases, the experiments were performed over a two-day period, with specimen preparation occurring on the first day and testing on the second day.

Overall, three different devices were used to provide hemorrhage control, depending on the location of hemorrhage. The combat application tourniquet (CAT; Composite Resources, Rock Hill, SC) was used for thigh hemorrhage via placement of the tourniquet on the limb proximal to the wound. The Combat Ready Clamp (CRoC; Combat Medical Systems, Fayetteville, NC) was used for lower limb hemorrhage by placement in inguinal area or abdominal area. The CRoC was used for upper limb hemorrhage when applied to clavicular area. The Abdominal Aortic Tourniquet (AAT; Speer Operational Technologies, Greenville, SC) was used for lower body hemorrhage with placement over the abdominal aorta. These are recently developed devices intended to treat life-threatening exsanguinating hemorrhage from combat wounds on the extremities and extremity-trunk junction areas9. Hemorrhage control was assessed by visual control and data from the flow probe proximal to transection of vessel. Not all procedures and devices were used with each cadaver. The equipment utilized is described in Table 2.
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Table 2
The major equipment used and estimated cost. It is notable that only the pump is needed to re-create the model for training purposes. The other equipment is for model validation and medical device testing.

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Estimated Cost</th>
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<tr>
<td>1. Harvard Apparatus pulsatile blood pump</td>
<td>$0,000</td>
</tr>
<tr>
<td>2. Grass PI22.3C DC strain gauge amplifier</td>
<td>$2,750</td>
</tr>
<tr>
<td>3. PC for data capture/analysis</td>
<td>$500</td>
</tr>
<tr>
<td>4. Transonic Transit time flow probe</td>
<td>$1,750</td>
</tr>
<tr>
<td>5. Blood pressure transducers</td>
<td>$100</td>
</tr>
<tr>
<td>6. Flow Meter</td>
<td>$12,600</td>
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</table>

RESULTS
The CRoC was used for hemorrhage control in all eight cadavers, with six experiments performed in the inguinal region for lower extremity bleeding and two experiments in the upper arm/clavicular area for upper extremity bleeding. Multiple iterations were performed on each cadaver. Flow was reduced to the area of the wound when the CRoC was applied, with the systemic pressure increasing. When the CRoC was released, the flow to the wound resumed, with a concomitant decrease in systemic pressure. Mean pressure in the system was increased to 176% of baseline (standard deviation (SD) of 50%) when the CRoC was applied to inguinal area. Pressure then normalized to 101.9% (SD of 24.3%) after release of the CRoC. Flow decreased from 100% at baseline to -2.4% with CRoC applied. When hemorrhage control was released, flow increased to 96.2 % (SD of 13%) (Table 3).

Table 3
Percentage change (standard deviation) of baseline for pressure and flow using the CRoC for control of a proximal femoral artery hemorrhage.

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>CRoC</th>
<th>Release</th>
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<tbody>
<tr>
<td>Pressure</td>
<td>100.0 (0.0)</td>
<td>176.4 (50.3)</td>
<td>101.9 (24.3)</td>
</tr>
<tr>
<td>Flow</td>
<td>100.0 (0.0)</td>
<td>-2.40 (10.2)</td>
<td>96.2 (13.0)</td>
</tr>
</tbody>
</table>

Figure 3A depicts uncontrolled hemorrhage from the femoral artery with the CRoC in place but not tightened. Hemorrhage control is demonstrated in Figure 3B upon tightening of the CRoC.

DISCUSSION
The data show that a pulsatile large animal blood pump delivers sufficient volume to simulate uncontrolled hemorrhage. Blood pressure and flow measurements obtained in this study indicate that the expected inverse relationship between pressure and flow was achieved. We obtained the data for validation of the model for hemorrhage control.
Figure 4 graphically demonstrates the inverse relationship between flow to the damaged extremity and systemic pressure once hemorrhage control is achieved via the CRoC. Essentially, in uncontrolled hemorrhage, flow from the wound is high and systemic pressure is low. When hemorrhage is controlled by the tourniquet, flow from the wound drops and systemic pressure rises. (See Video 1, Supplemental Digital Content, which shows hemorrhage control in our model using a CRoC) The blood flow measurement also served to establish achievement of hemorrhage control, as visual assessment is sometimes difficult to confirm.

We focused our model on the leading cause of preventable battlefield death: exsanguinating external hemorrhage. There is a pressing need to address this issue and no one model has emerged as clearly superior for this purpose. Of course, the perfused cadaver model has potential for use in a variety of other emergency care conditions beyond combat casualty care. For example, Aboud and Garrett identify the advantage of realistic tissue feel and pulsatile flow for neurosurgical, trauma surgical and endovascular device training.

Studies of non-perfused cadavers have also demonstrated the utility of the model in the training arena. Proano et al showed that using a cadaver model to teach new emergency medicine residents to perform a tube thoracostomy reduced the time needed to complete the procedure on the first and subsequent attempt. Custalow et al showed that using an animal model for simulating resuscitative procedures improves competency and speed. In their model, the time to perform saphenous vein cut down, thoracotomy, and cricothyrotomy were reduced after training on a pig model. Also, the same study found that more critical steps were accomplished in the group that had previous animal simulation.

In simulation for training purposes, the objective is outcome performance and confidence/perception of competence of the trainee. In contrast, device and technique evaluation requires high model fidelity. Quantitative measurements of key characteristics determine the level of fidelity with physiologic (or pathophysiologic) states. In these cases fidelity must extend beyond content and face validity (“realism”) and embrace the physiologic characteristics that are relevant to the procedure being evaluated.

Fresh and fresh-frozen cadavers have been hypothesized to provide a better model for procedure skills training because they have not been embalmed, which distorts tissue planes and may cause increased stiffness. In the future we plan to compare fresh vs. fresh-frozen cadavers to determine if the mild decrease in the tissue compliance of fresh-frozen results in decreased efficacy in simulation of hemorrhage and hemorrhage control.

In addition to training students to perform a procedure, the perfused cadaver model that we present has been used in our institution to validate various medical devices. We show that using pressure and flow probes on vasculature in the perfused cadaver model will quantitatively demonstrate that cessation of blood flow to the area of interest has indeed been achieved.

This model will be refined and standardized in order to provide a more reliable model for teaching and evaluation. Our future work includes developing a model for junctional (groin and axilla) and neck hemorrhage, and the development of a pneumothorax model. This latter endeavor will incorporate thoracic ventilation and perfusion to recreate the anatomy and physiology for training and evaluation of needle decompression, tube thoracostomy, chest seals, and resuscitative thoracotomy. As cricothyrotomy is one of the major emergent procedures in the emergency department, we have already performed this procedure under perfusion using video confirmation of hemorrhage. (See Video 2, Supplemental Digital Content, which demonstrates simulated hemorrhage while a cricothyrotomy is performed). We plan to standardize and validate this procedure because mannequin or animal models do not provide the realistic tissue feel or hemorrhage present when performing the procedure on a patient. Work in the surgical field suggests that tissue compliance is important for model fidelity and we plan to measure this objectively.

LIMITATIONS

Although overall the model is novel and effective, there are several less desirable aspects, such as the condition of the cadavers, setup and laboratory cost, and inability to perform certain procedures more than once. The cadavers were primarily from recently deceased donors in their sixties, with an age range from 54 to over 90 years. The maximum age for the study was reduced to 75 years after an early specimen was found to be unusable due to increased arteriosclerosis with age. This made work with the arteries difficult. However, significantly younger cadavers are seldom available. The costs of procuring cadavers, performing the
setup, and disposing of the cadavers are potentially greater than other simulation models, but this model is not intended to be used in all training circumstances. It may be used optimally in situations necessitating the most realistic conditions to ensure the participant is truly proficient at a procedure, e.g., credentialing.

Also, this is only the first study performed in this model. While we believe this model would be beneficial in medical simulation and education, this study only attempted to recreate the physiological parameters of exsanguination. Further studies will be needed to systematically determine the extent to which learners find the model useful, learn the procedure better than using other methods such as manikins, and improve their retention and behavioral transfer. This is best described in the four steps of reaction, learning, behavior and results by Kirkpatrick, D. and Kirkpatrick, J. in Evaluating Training Programs: The four levels.

The incisions made to induce hemorrhage were not standardized, as the investigators chose a body area to make the incision based on the device being tested. In order to use the model to evaluate procedural training efficiency, the incisions must be standardized to limit variability between cadavers.

The two different types of cadavers utilized in this study were fresh and fresh-frozen. Both are considered “fresh,” as they are not embalmed, and are used or frozen within two weeks of death. The data in our study for the fresh and fresh-frozen cadavers were similar in terms of increase of pressure in the system with hemorrhage control and decrease of flow to damaged extremity. Subjectively, however, the tissue feel of the fresh cadavers was more realistic than in the fresh-frozen cadavers. Allowing the fresh-frozen cadavers to thaw several days in advance of utilization increased the realism and tissue compliance. Future efforts will be needed to quantify this effect and determine its significance.

CONCLUSIONS

Our model of a perfused cadaver can simulate exsanguinating bleeding for evaluating hemorrhage control devices, and may have additional benefit for training purposes. The model provides realistic anatomic landmarks as well as improved tissue feel not found in mannequin models currently available. Physiologic data and video recording validate the model’s fidelity.

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Author Information

Trent L. Morgan, MD
Emergency Services, United States Air Force
Wright-Patterson AFB, OH
trlmorga@gmail.com

Robert A. De Lorenzo, MD, MSM
Department of Emergency Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA;
US Army Institute of Surgical Research
Fort Sam Houston, Texas, USA

John A. Ward, PhD
Department of Clinical Investigation, San Antonio Military Medical Center
Fort Sam Houston, Texas, USA

Chris E. White, MD, MSM
Department of Clinical Investigation, San Antonio Military Medical Center
Fort Sam Houston, Texas, USA

Syed H. Husaini, MD
Department of Clinical Investigation, San Antonio Military Medical Center
Fort Sam Houston, Texas, USA

John F. Kragh, Jr, MD
US Army Institute of Surgical Research
Fort Sam Houston, Texas, USA

Patti E. Dawson, BS
Department of Clinical Investigation, San Antonio Military Medical Center
Fort Sam Houston, Texas, USA