Development of a post-mortem human specimen flow model for advanced bleeding control training


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ABSTRACT

Introduction: Prompt and effective hemorrhage control is paramount to improve survival in patients with catastrophic bleeding. In the ever-expanding field of bleeding control techniques, there is a need for a realistic training model to practice these life-saving skills. This study aimed to create a realistic perfused post-mortem human specimen (PMHS) flow model that is suitable for training various bleeding control techniques.

Materials and Methods: This laboratory study was conducted in the SkillsLab & Simulation Center of Erasmus MC, University Medical Center Rotterdam, the Netherlands. One fresh frozen and five AnubiFIX® embalmed PMHS were used for the development of the model. Subsequent improvements in the exact preparation and design of the flow model were made based on model performance and challenges that occurred during this study and are described.

Results: Circulating arteriovenous flow with hypertonic saline was established throughout the entire body via inflow and outflow cannulas in the carotid artery and jugular vein of embalmed PMHS. We observed full circulation and major hemorrhage could be mimicked. Effective bleeding control was achieved by placing a resuscitative endovascular balloon occlusion of the aorta (REBOA) catheter in the model. Regional perfusion significantly reduced the development of tissue edema.

Conclusion: Our perfused PMHS model with circulating arterial and venous flow appears to be a feasible method for the training of multiple bleeding control techniques. Regional arteriovenous flow successfully reduces tissue edema and increases the durability of the model. Further research should focus on reducing edema and enhancing the durability of the model.

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Introduciton

Uncontrolled bleeding remains a leading cause of death in both military and civilian trauma patients [1–5]. Prompt and effective hemorrhage control is paramount to improve survival from catas-

trophic bleeding. In an effort to improve outcomes of severely in-

jured patients, advanced bleeding control techniques are evolving and new resources are being developed [6–11].

With this ongoing development of advanced bleeding control techniques, there is a need for a realistic training model to practice these life-saving hemorrhage control skills. These kinds of training models are especially required since procedures such as resuscitative endovascular balloon occlusion of the aorta (REBOA) can be technically challenging and require adequate and realistic training.

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Box 1

Advanced bleeding control techniques.

- Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)
- Temporary vascular shunting
- Trauma laparotomy
- (Emergency department) thoracotomy
- (Junctional) tourniquet application
- Wound clamp application
- Wound packing
- Foley catheter balloon tamponade
- Injectable hemostatic granules or sponges
- Injectable self-expanding intra-abdominal foam
- External pelvic stabilizers

Currently, hemorrhage control training curricula often use mannequins, simulators, or live tissue animal models [12–19]. One benefit of a mannequin is that it can be used repeatedly. However, it does not resemble human physiology and hence does not provide realistic feedback on the efficacy of the bleeding control intervention. On the other hand, while simulated and animal models do offer the capability of direct feedback on the success of the hemorrhage control intervention, they do not fully represent human anatomy. Furthermore, animal rights are a delicate issue in biomedical research and training.

Over the last years, the use of perfused post-mortem human specimen (PMHS) models for training surgical skills has been introduced. PMHS provide realistic anatomy and reasonable lifelike feel when compared to simulators or animal models. Previous research has described several techniques to create perfused PMHS for training surgical skills with various specifications depending on the skills that need to be practiced on the model [20–32]. However, the technique of perfusing PMHS is not yet optimized. Dead tissue and blood vessels respond differently to perfusion when compared to live tissue, and questions remain as to which perfusion technique offers not only the most realistic feel, but is also most durable. Furthermore, due to ethical considerations and because the availability of PMHS is limited, each PMHS should be used in the most optimal manner.

The primary goal of this study was to create a realistically perfused PMHS model with arteriovenous circulation that is suitable for training various advanced bleeding control techniques (Box 1), and, secondly, to examine the properties of the blood vessels of the model under pressure. We provide a description of the development of the model, the challenges encountered, and solutions for these issues.

Materials and methods

The study was conducted in the SkillsLab & Simulation Center of Erasmus MC, University Medical Center Rotterdam, the Netherlands.

Post-mortem human specimens

PMHS were obtained through the Department of Neuroscience-Anatomy, Erasmus MC, from a pool of bodies donated to science. The medical history and causes of death of these PMHS were unknown. All PMHS were tested for HIV and hepatitis B and C. Additionally, PMHS embalmed after March 2020 were tested for COVID-19. In an attempt to select PMHS with an intact vasculature, PMHS with scars indicating major vascular surgery were excluded. Furthermore, the simple fact that the PMHS could be embalmed indicated that there was an intact circulation. PMHS which could not be perfused with the embalming fluid, obviously were not used.

One pilot test using a fresh frozen PMHS was conducted. The fresh frozen PMHS was stored at -20°C and thawed at room temperature two days prior to the experiment. Since, in our anatomy laboratory, PMHS are selected for freezing if it is suspected that embalming will not succeed, for instance, due to arterial disease, we decided to use AnubiFiX® [33] embalmed PMHS for the further development of the flow model. Additionally, the AnubiFiX® embalmed specimen have the advantage of reusability. In total, five AnubiFiX® embalmed PMHS were used. These PMHS were stored at room temperature in a solution of 5% phenoxy-ethanol until the experiment. Before testing, the PMHS were inspected for scars and signs of peripheral vascular disease by the investigators. A PMHS was exchanged for another PMHS if major issues with perfusion were suspected in advance.

Set-up of the flow model

The specific preparation and set-up of the flow model differed per PMHS. Improvements in the exact preparation and design of the flow model were made based on model performance and are described chronologically per PMHS in the Results section and Supplemental Digital Content 1.

In all PMHS, the perfusate consisted of a hypertonic saline solution containing 15 grams salt per liter water. In the AnubiFiX® embalmed PMHS, the first 2 liters of the perfusate contained 50,000 IE of heparin to dissolve remaining blood clots, as described by Delpech et al. [25] The perfusate was heated to 38°C to make the model more realistic and to dissolve blood clots more easily.

Testing of the flow model

To confirm perfusion throughout the PMHS and to investigate the properties of the blood vessels under pressure, the common carotid artery (CCA), internal jugular vein (IJV), brachial artery (BA), brachial vein (BV), common femoral artery (CFA), superficial femoral artery (SFA), and common femoral vein (CFV) were identified prior to and during perfusion using a SonoSite TITAN® ultrasound sound (SonoSite, Inc., Bothell, WA, USA). The blood vessels were assessed for visibility and compressibility with ultrasound, and the diameter of the arteries was measured if possible. Additionally, arterial blood pressure was measured using standard arterial pressure monitoring transducers (Safedraw™, Merit Medical, Maastricht, The Netherlands) attached to a Siemens SC 7000 patient monitor (Siemens Healthcare GmbH, Erlangen, Germany) for continuous pressure monitoring. The blood pressure measurement sites differed depending on the specific flow model set-up. Additionally, angiography was performed and wounds were assessed for bleeding. To measure the degree of fluid translocation, the circumferences of the upper arm, thigh, and abdomen were measured at baseline and every 15 minutes.

To assess whether the model is suitable for hemorrhage control training, an aortic occlusion balloon catheter was placed (ER-REBOATM, Pyritime Medical Devices, Boerne, TX, USA), a thoracotomy was performed, vascular shunts were placed, and distal flow was observed by puncturing and cannulating peripheral blood vessels.

Results

One fresh frozen pilot PMHS and five AnubiFiX® embalmed PMHS were used to develop and optimize the perfused PMHS flow model, resulting in a PMHS flow model with full arteriovenous circulation (PMHS 4) and a PMHS flow model with regional arterio-
nous circulation (PMHS 5). These two models are described below. A detailed description of the preparation, set-up, results, and improvements of the pilot study and PMHS 1, 2, and 3 is presented in Supplemental Digital Content 1. A summary of the objectives and results per PMHS, including the challenges encountered and solutions to these issues, is presented in Table 1.

**Table 1** Overview of aims, findings, and solutions to encountered challenges for each post-mortem human specimen (PMHS).

<table>
<thead>
<tr>
<th>PMHS</th>
<th>Aims</th>
<th>Results &amp; encountered challenges</th>
<th>Possible solutions for future PMHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot</td>
<td>- Test the perfusion set-up with inflow in the CCA and outflow from the IJV. - Test the possibility to visualize blood vessels and assess compressibility with ultrasound prior to, during, and after perfusion. - Test the possibility to cannulate peripheral blood vessels percutaneously. - Test the possibility to perform intravascular pressure measurements.</td>
<td>- Successful inflow in cannulated CCA, no venous return from IJV. - Prior to perfusion: CFA, SFA, FV, CCA, IJV, BA, and BV clearly visible with ultrasound. During and after perfusion: improved echogenicity and compressibility. - Successful percutaneous placement of arterial cannula in the BA and arterial pressure cannula in the SFA. - Successful arterial pressure measurement in the SFA.</td>
<td>- Use of AnubiFiX® embalmed PMHS since successful embalming indicates an intact circulation. Add heparin to the perfusion fluid to dissolve possible blood clots.</td>
</tr>
<tr>
<td>1</td>
<td>- Create full arteriovenous circulation via an inflow cannula in the CCA and outflow arteriotomy of the IJV. - Assess blood vessels for visibility and compressibility with ultrasound, prior to and during perfusion. - Confirm peripheral circulation by vessel cannulation. - Perform angiography of the central blood vessels. - Create bleeding wounds. - Obtain hemorrhage control by placing a REBOA catheter. - Determine possible pressure loss within the PMHS by measuring arterial pressure at 3 different sites.</td>
<td>- Successful arteriovenous circulation; venous return of perfusion fluid via IJV arteriotomy. - Prior to perfusion: CFA, SFA, FV, CCA, and BA visible and compressible. During perfusion: BV also visible. Visibility of other vessels is enhanced. - Successful cannulation of BA; successful placement of 8 French introducer sheath in CFA. Return of perfusate through needles. - Successful angiography of right subclavian artery, brachiocephalic trunk, aorta, and iliac arteries (Fig. 1). - Powerful bleeding from SFA, continuous oozing from groin, neck, and brachial incisions. - Successful placement of REBOA catheter via introducer sheath; distal hemorrhage control; proximal rise in blood pressure to 223 mmHg after balloon inflation; drop in blood pressure to 120 mmHg after balloon deflation. - Pressure loss of 10-20 mmHg between inflow at CCA and peripheral pressure canulas in BA and CFA, before REBOA.</td>
<td>- N/A</td>
</tr>
<tr>
<td>2</td>
<td>- Create full arteriovenous circulation via an inflow cannula in the CCA and outflow cannula in the IJV. - Assess blood vessels for visibility and compressibility with ultrasound, prior to and during perfusion. - Confirm peripheral circulation by vessel cannulation. - Create bleeding wounds. - Determine possible pressure loss within the PMHS by measuring arterial pressure at 3 different sites. - Limit unnecessary fluid leakage by careful preparation of the PMHS. - Request for intact groin by popliteal embalming. - Measure degree of fluid translocation. - Limit oral and rectal fluid leakage by plugging mouth and rectum.</td>
<td>- Initially no venous return from IJV due to defect in brachiocephalic trunk. Repositioning of inflow cannula to brachiocephalic trunk via thoracotomy. - Prior to perfusion: CCA, CFA, and BA visible, although difficult. During perfusion: BV and FV also visible. Visibility of other vessels is enhanced. - Successful ultrasound-guided cannulation of BA; successful cannulation of CFA. Return of perfusate through needles (Fig. 2). - Bleeding from thoracotomy wound, groin incision and FV. Significant bleeding from cardiac puncture. - Arterial pressure 150 mmHg. No pressure drop between inflow at brachiocephalic trunk and peripheral pressure canulas in BA and CFA. - Reduction of fluid loss by limiting incisional sites. - No popliteal embalmed PMHS available. - No reliable evaluation due to thoracotomy. - Successful: no fluid leakage from mouth and rectum after plugging.</td>
<td>- Careful preparation of the PMHS to prevent unnecessary leakage. - PMHS embalming via the popliteal artery. - Measurement of the degree of fluid translocation. - Plugging of mouth and rectum. - Serology blood sampling via the embalming site instead of blind sampling via subclavian artery. - N/A</td>
</tr>
</tbody>
</table>

*Other findings:* - Significant fluid loss through every incision. - Significant damage of SFA from embalming. - Translocation of fluid: peripheral edema in the legs and free intra-abdominal fluid after perfusion. - Oral and rectal fluid leakage. - PMHS embalming via the popliteal artery. - Measurement of the degree of fluid translocation. - N/A

(continued on next page)
were no other wounds and other blood vessels remained intact. Prior to perfusion, the mouth and rectum were plugged to prevent oral and rectal fluid leakage. For full arteriovenous circulation, the right CCA and IJV were cannulated with standard curved embalming cannulas which were secured with vessel loops (Fig. 3). The CCA inflow cannula was connected with a Stöckert SII heart-lung machine (Stöckert Instrumente GmbH, München, Germany) via a silicon tube (6.35 mm inner diameter). The inflow tube of the heart-lung machine was connected with a reservoir containing the perfusate. The IJV outflow cannula was connected to a standard vinyl tube (8 mm inner diameter) leading to a collection reservoir.

Perfusion

The pump rate was slowly increased from 0 to 50 RPM (650 mL/min). After several minutes, there was continuous venous return via the IJV cannula and some wound “bleeding” from the neck incision. We observed no other external fluid leakage.

Blood vessels, bleeding, and edema

The blood vessels were assessed with ultrasound prior to and during perfusion (Table 1). Arterial and venous cannulas were placed percutaneously in the left BA, right CFA and left FV to confirm peripheral arteriovenous circulation and measure arterial pressure. There was powerful perfusate outflow through the arterial cannulas (Fig. 2), and dripping outflow from the venous cannula. Initially, arterial blood pressure increased from 87 mmHg to 107 mmHg. The pressure decreased to 71 mmHg after 45 minutes of perfusion. At that time, there was already significant edema throughout the entire PMHS, including the head and chest, and some oral fluid leakage.

### Table 1 (continued)

<table>
<thead>
<tr>
<th>PMHS</th>
<th>Aims</th>
<th>Results &amp; encountered challenges</th>
<th>Possible solutions for future PMHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>- Create full arteriovenous circulation via an inflow cannula in the CCA and outflow cannula in the IJV.</td>
<td>- Sparse fluid return from IJV due to pre-existent ruptured aorta.</td>
<td>- Reject future PMHS if there is any doubt regarding the success of embalming.</td>
</tr>
<tr>
<td></td>
<td>- Assess blood vessels for visibility and compressibility with ultrasound, prior to and during perfusion.</td>
<td>- Prior to perfusion: CFA, SFA, FV, CCA, IJV, BA, and BV visible although difficult to identify. During perfusion: vessels easily identified.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Confirm peripheral circulation by vessel cannulation.</td>
<td>- Not performed because of pre-existent ruptured aorta.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Create bleeding wounds.</td>
<td>- Significant bleeding from neck incision, reduced by ligating arterial and venous branches.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Eliminate risk of vessel damage by blood sampling via embalming site.</td>
<td>- Not performed because of pre-existent ruptured aorta.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Request for intact groin by popliteal embalming.</td>
<td>- Intact groin. Successful placement of vascular shunts in popliteal artery and vein.</td>
<td>- Measurement of the degree of fluid translocation in future PMHS.</td>
</tr>
<tr>
<td></td>
<td>- Measure degree of fluid translocation.</td>
<td>- No fluid leakage from mouth and rectum after plugging.</td>
<td>- N/A</td>
</tr>
<tr>
<td>4</td>
<td>- Create full arteriovenous circulation via an inflow cannula in the CCA and outflow cannula in the IJV.</td>
<td>- Continuous return of fluid from IJV cannula.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Assess blood vessels for visibility and compressibility with ultrasound, prior to and during perfusion.</td>
<td>- Prior to perfusion: CCA and IJV visible but not compressible, other vessels visible and compressible. Baseline diameter (transverse/anteroposterior) of left BA was 3.9/4.2 mm and of right CFA 7.8/6.0 mm. During perfusion: diameter of left BA was 3.9/3.6 mm and of right CFA 7.4/7.4 mm. Visibility enhanced initially, but decreased with edema development.</td>
<td>- Limit tissue edema with regional perfusion.</td>
</tr>
<tr>
<td></td>
<td>- Confirm peripheral circulation by vessel cannulation.</td>
<td>- Successful ultrasound-guided cannulation of BA, CFA, and FV. Return of perfusate through cannulas.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Determine possible pressure loss within the PMHS by measuring arterial pressure at 3 different sites.</td>
<td>- No pressure drop between inflow at CCA and peripheral pressure cannulas in BA and CFA.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Measure degree of fluid translocation.</td>
<td>- Significant development of tissue edema, see Table 2.</td>
<td>- Limit tissue edema with regional perfusion.</td>
</tr>
<tr>
<td></td>
<td>- Optimize integrity of flow model and vasculature by embalming via CCA and IJV, the cannulation site.</td>
<td>- Successful, no other external fluid leakage than from neck wound.</td>
<td>- N/A</td>
</tr>
<tr>
<td>5</td>
<td>- Create bilateral and unilateral regional iliofemoral arteriovenous perfusion circuit.</td>
<td>- Successful bilateral and unilateral iliofemoral arteriovenous perfusion circuit.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Assess blood vessels for visibility and compressibility with ultrasound, prior to and during perfusion.</td>
<td>- Prior to perfusion: all vessels visible and compressible with ultrasound. Baseline diameter of left CFA was 7.0/6.0 mm (transverse/anteroposterior). During perfusion: visibility of CFA enhanced, diameter of left CFA increased to 12.0/12.0 mm.</td>
<td>- N/A</td>
</tr>
<tr>
<td></td>
<td>- Limit tissue edema with regional perfusion to enhance the durability of the flow model.</td>
<td>- Significant reduction of tissue edema, thereby increasing durability.</td>
<td>- N/A</td>
</tr>
</tbody>
</table>

Initially, the blood vessels were better visible with ultrasound during perfusion than before. However, due to increasing edema, it became more difficult to visualize the vessels. The circumferences of the upper arm, thigh, and abdomen were measured at baseline and every 15 minutes during perfusion to measure the development of edema and are presented in Table 2.

Considerations

By selecting a properly embalmed PMHS without signs of significant vascular disease, we have successfully created a PMHS circulating flow model through cannulation of the CCA and IJV, with realistic “bleeding” feedback. We minimized external leakage by...
making only one necessary wound and by plugging human cavities. However, after 45 minutes of perfusion at a low flow of 650 ml/min, there was already significant tissue edema, complicating the visualization and puncturing of blood vessels. Next, we have created a flow model with selective iliofemoral circulation in an attempt to reduce tissue edema and increase the durability of the PMHS.

Regional circulation flow model – AnubiFiX® embalmed (PMHS 5)

Set-up 1: bilateral iliofemoral perfusion

The PMHS for regional iliofemoral circulation was embalmed via the right SFA and FV, which was also the perfusion cannulation site. To create a regional bilateral iliofemoral perfusion circuit, the right SFA was cannulated with a standard curved embalming cannula and the right FV with a straight embalming cannula (Fig. 4). Both cannulas were connected to the pump system as described before. The contralateral CFA and FV were exposed and a Javid™ shunt (Bard® Peripheral Vascular, Inc., Tempe, AZ, USA) was constructed between these vessels (Fig. 4). Subsequently, the aorta and inferior vena cava (IVC) were exposed and clamped via median laparotomy (Fig. 4).

Perfusion

The pump rate was slowly increased from 0 to 50 RPM (650 ml/min). Instantly, there was continuous venous return via the FV cannula and “bleeding” from a SFA branch that was subsequently ligated.

Blood vessels and edema

All vessels were visible and compressible with ultrasound (Table 1). The arterial pressure was 45 mmHg with a flow of 650 ml/min. Baseline circumferences of the left upper arm and thigh were 26.1 and 35.7 cm respectively. After 30 minutes of perfusion, mild edema was observed in the left thigh, possibly due to perfusion of the deep femoral artery on that side. The circumferences of the left upper arm and thigh were 25.9 and 36.7 cm respectively. No other edema was observed.

Set-up 2: unilateral iliofemoral perfusion

To create unilateral iliofemoral perfusion, we clamped the right common iliac artery and vein just below the aortic bifurcation and constructed a Javid™ shunt (Bard™ Peripheral Vascular, Inc., Tempe, AZ, USA) between these vessels (Fig. 4). There was successful circulation of perfusate within this unilateral iliofemoral circuit.

Considerations

It was feasible to create both bilateral and unilateral iliofemoral circuits with arteriovenous circulation. This kind of flow models can be used to practice hemorrhage control skills for iliac and groin injuries. With this set-up, there was only mild edema, thereby significantly increasing the durability of the PMHS.

By adapting and optimizing each successive PMHS flow model, we have established a reproducible PMHS flow model with full and regional arteriovenous circulation that is suitable for training various advanced bleeding control techniques.

Costs

Generally, the embalming process with AnubiFiX® takes 45 minutes preparation time and 165 minutes waiting time to allow the embalming fluid to take effect. However, the PMHS, including the embalming, are fully managed by the Department of Neuroscience and Anatomy. The price for an AnubiFiX® embalmed PMHS at our institution was 1500 euro. There is no price difference between AnubiFiX® embalmed or fresh frozen PMHS. The costs for the set-up of the perfusion model are low, since cannulas and tubing are reusable. The costs for disposables such as vessel loops, sutures, gauzes, and heparin depend on local price agreements, but should not exceed 100 euro. Preparation of the perfusion model was done by one vascular/trauma surgeon, one surgical resident, and one medical student and takes about 45 minutes.

Discussion

In the evolving field of advanced bleeding control techniques, realistic training is of outmost importance to help improve the outcome of severely injured patients. A perfused PMHS training model offers both feedback and the most realistic anatomy and feel for practicing these techniques. This study showed that it is feasible to create a fully perfused PMHS model with circulating flow for the training of multiple advanced bleeding control options. The model can be used in trauma scenario training for surgeons, surgical residents, military medical personnel, and other first responders who are being exposed to severely bleeding trauma patients. We have demonstrated that it is possible to create both arterial and venous flow with realistic pressures via a single arterial inflow cannula in the common carotid artery and outflow via the internal jugular vein, eliminating the need for separate arterial and venous inflow cannulas. Additionally, we have demonstrated that it is possible to create regional arteriovenous flow.

Previous studies have described models with only arterial or venous perfusion [21,26-28,30,32,34,35], or with separate venous and arterial perfusion [23,29,31,36]. These models are often pressurized without circulation [22,23,29,31,36]. Naturally, injuries in trauma patients are not limited to exclusively the arterial vascular system or the venous vascular system, but often involve both vascular systems. A training model with both arterial and venous flow is therefore essential for realistic bleeding control training. Although using a separate arterial and venous circuit is a successful technique to establish flow or pressure in both vascular systems, it generally results in retrograde flow in one of the systems. This may compromise the realism of the model for percutaneous and endovascular procedures. Furthermore, perfusion cannulas are often placed in the femoral artery and vein, excluding an entire leg.

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<table>
<thead>
<tr>
<th>Time of perfusion [minutes]</th>
<th>Ø Upper arm [cm]</th>
<th>Ø Thigh [cm]</th>
<th>Ø Abdomen [cm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (baseline)</td>
<td>29.0</td>
<td>43.5</td>
<td>91.5</td>
</tr>
<tr>
<td>15</td>
<td>30.5</td>
<td>44.0</td>
<td>95.5</td>
</tr>
<tr>
<td>30</td>
<td>29.0</td>
<td>45.0</td>
<td>94.5</td>
</tr>
<tr>
<td>45</td>
<td>29.0</td>
<td>46.0</td>
<td>95.8</td>
</tr>
<tr>
<td>60a</td>
<td>29.0</td>
<td>46.0</td>
<td>98.0</td>
</tr>
<tr>
<td>30 min after perfusion</td>
<td>28.5</td>
<td>45.5 (Δ 104.6±4)</td>
<td>101.5 (Δ 110.9±6)</td>
</tr>
</tbody>
</table>

* The pump was paused for 8 minutes.
  b Increase from baseline.
from perfusion. In addition, separate arterial and venous perfusion generally requires two pump systems to achieve a lower pressure in the venous system than in the arterial system, thereby increasing the complexity and costs of the system.

To our knowledge, this is the first perfusion model using AnubiFiX® embalmed PMHS. Previously described models have mainly used fresh (frozen) PMHS [20-23,25,26,28-32,34-36]. While fresh PMHS are the most realistic in terms of color and stiffness, they only last for a limited time because of the decomposition process. Furthermore, using these PMHS at our institution was considered unfeasible due to their limited availability, unknown medical history, and an unfavorable preselection for fresh frozen PMHS with regard to the vascular system. Other authors have described the use of Thiel or formalin embalmed PMHS [20,24,27,28]. A successful embalming process suggests that the PMHS has an intact vascular system, which is essential for the flow model. Furthermore, the advantage of embalmed specimen is that they are reusable. Of course, the reusability of a particular specimen depends on the techniques practiced on it. Used PMHS can also be preserved and used for other educational purposes, for instance anatomy education for medical students. However, the main disadvantage of using traditional formalin embalmed PMHS is that it increases tissue stiffness and changes tissue colors, resulting in a less realistic model and in impediment of perfusion. On the other hand, the AnubiFiX® embalming technique preserves the color, flexibility, and suppleness of the tissues, thereby allowing realistic training of all kinds of surgical procedures. Although we did not perform endovascular techniques other than REBOA in the present study, we did demonstrate that it was possible to perform angiography and to cannulate blood vessels using the Seldinger technique. Therefore, it should be possible to perform other endovascular procedures on the flow model.

Recently, Minneti et al. described a ventilated perfusion model for the training of acute care and vascular surgical procedures [37]. In this technique, the femoral artery and vein are cannulated and connected to a ventilator circuit. The main advantage of using air perfusion instead of fluid perfusion is that it reduces tissue edema and extends the durability of the model. However, since our main purpose of the model was to train hemorrhage control skills with realistic bleeding feedback, we opted for a fluid perfusion model. Moreover, the training of endovascular techniques, such as REBOA, has not yet been investigated in the ventilated model, nor has
the feasibility of ventilated perfusion been described in embalmed PMHS. One of the constraining factors of our model is the necessity for an intact vasculature. In the Netherlands, there is a limited availability of bodies donated to science, and in general, donated bodies are of the ageing population. Consequently, there is a high prevalence of arterial disease, which negatively influences the success rate of the flow model. To make the best possible use of each donated body, the embalmers attempt to select bodies with an intact vasculature for embalming and preserve the other bodies as fresh frozen specimens. We therefore chose to use embalmed PMHS for the development of our flow model. However, even after this selection, the embalming process does not completely succeed in approximately 10% of the cases due to a compromised vascular system, in our study leading to a dismissal of the PMHS.

Another limitation of our fully perfused flow model was the rapid development of tissue edema and accumulation of fluid in the abdomen. To reduce this abdominal fluid accumulation, Minneti et al. described the ligation of the branch pulmonary arteries prior to perfusion [29]. Another option would be to place an abdominal catheter to drain the fluid. This preserves the integrity of the vascular tree and requires less preparation time than performing artery ligation. With regard to tissue edema, we used a hypertonic perfusate in an attempt to hinder the translocation of intravascular fluid. Despite this attempt, tissue edema developed quickly. Another option to minimize edema is to reduce the perfusion pressure. Alternatively, we demonstrated unilateral and bilateral iliofemoral perfusion in our last model. The advantage of using regional perfusion is that it limits tissue edema, thereby significantly prolonging the usability of the model. Regional perfusion allows the training of several bleeding control techniques, and it can also be applied to other body regions [20, 26, 27, 34]. In our bilateral model, the aortic and IVC clamps can be temporarily removed to allow the training of advanced bleeding control techniques for thoracoabdominal hemorrhage, such as REBOA or resuscitative thoracotomy. Using a PMHS in the most optimal manner with regional perfusion requires a tailored scenario sequence training plan. However, ideally, a PMHS model for realistic trauma scenario training is (1) fully perfused, (2) has both arterial and venous flow that is pulsatile, warmed and red-colored, (3) will last at least one full day, and (4) requires limited preparation time. Therefore, options to reduce the development of tissue edema, for instance, using an oily perfusate, have to be explored [24]. Incorporating a perfused PMHS model as a technical training component in a multistep bleeding control training curriculum has the potential to reduce the use of animals for live tissue training, allowing the live tissue component to focus on physiological modeling and integral team training.

Conclusions

We have described the development and optimization of a fully perfused PMHS model with circulating arterial and venous flow via a single arterial inflow cannula and venous outflow cannula. The present study demonstrated that it is feasible to create a flow model for the realistic training of multiple bleeding control techniques. Regional arteriovenous flow successfully reduces tissue edema and increases the durability of the model. Further research should focus on reducing edema, enhancing the durability of the model, and the aspect of optimizing the perfusion fluid.

Disclaimer

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Dutch, German or U.S. Department of Defense, or Dutch, German or U.S. governments. Several authors are employees of the Dutch, German, or U.S. government.

Author contributions

SV, BBB, JD, EB, AL, MV, GK, and RH prepared the study set-up. SV, BBB, PS, OW, and RH performed the study and collected the data. SV, BBB, PS, OW, JD, EB, AL, MV, GK, and RH prepared the manuscript. SV prepared the tables and figures. SV, BBB, PS, OW, JD, EB, AL, MV, GK, and RH contributed to the final version of the paper.

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Data availability

Upon request.

Declaration of interest statement

The authors declare that there are no conflicts of interest that could inappropriately influence (bias) their work. We confirm that this submission has not been published elsewhere and is not under consideration by another journal. All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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Supplementary materials

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References
