During the past few years, several percutaneous systems have been introduced into clinical practice for circulatory support in hemodynamic conditions, with markedly decreased cardiac output. Currently, 3 different systems are widely available in adult human intensive cardiac care: the Impella 2.5 system (Abiomed, Germany), a catheter-based, impeller-driven, axial flow pump that pumps blood directly from the left ventricle across the aortic valve to the ascending aorta; the TandemHeart system (Cardiac Assist, USA), a left atrial-to-femoral arterial circulatory support system, driven by a continuous flow pump; and extracorporeal membrane oxygenation (ECMO), which in the heart and lung support setting is a right atrial-to-femoral arterial assist device, driven by a continuous flow pump with a membrane oxygenator included in the circuit. These 3 systems represent a powerful alternative to the currently widely used intra-aortic balloon pump. They offer a bridge to recovery, a bridge to heart transplantation, a bridge to implantation of long-term cardiac-assist devices, or a bridge to decision (in patients with acute and rapidly deteriorating heart failure where full evaluation for indication to long-term cardiac-assist devices or heart transplant has not been possible and in whom death will occur without urgent mechanical cardiac support). Their higher hemodynamic effectiveness is, however, counterbalanced by the increased size of catheters and cannulas, which are associated with a higher risk of device-related complications.

Background—Several percutaneous circulatory support systems have been recently introduced into clinical practice for the treatment of cardiogenic shock or refractory nontolerated ventricular tachycardia, in support of high-risk catheter interventions and, occasionally, cardiopulmonary resuscitation. To date, however, a direct comparison of the available systems has not been performed.

Methods and Results—Adult female pigs (weight 50–60 kg) were used throughout the experiment. Under deep anesthesia and mechanical ventilation, 3 percutaneous circulatory support systems were compared: (1) right atrium-aorta, extracorporeal membrane oxygenation (n=4); (2) left atrium-aorta, TandemHeart system (n=4); (3) left ventricle-aorta, Impella 2.5 system (n=4), and (4) left ventricle-aorta with norepinephrine at 0.1 µg/kg per minute (n=4). Hemodynamic efficacy (mean arterial pressure) was measured at 3 specific conditions: ventricular pacing at 200 and 300 beats per minute, and ventricular fibrillation. Although no or only nonsignificant differences were found among the systems at ventricular pacing of 200 and 300 beats per minute, under ventricular fibrillation, the right atrium-aorta system was significantly the most efficacious, followed by the left atrium-aorta system and the left ventricle-aorta system (∗∗∗P<0.001). However, the left ventricle-aorta system with norepinephrine still maintained mean arterial pressure comparable with the left atrium-aorta system.

Conclusions—Differences were seen in the hemodynamic efficacy of available percutaneous circulatory support systems, particularly under the most severe hemodynamic condition, ventricular fibrillation. (Circ Arrhythm Electrophysiol. 2012;5:1202-1206.)

Key Words: percutaneous circulatory support system ◼ heart-assist device ◼ cardiogenic shock ◼ ventricular tachycardia ◼ ventricular fibrillation

Direct Comparison of Percutaneous Circulatory Support Systems in Specific Hemodynamic Conditions in a Porcine Model

Petr Ostadal, MD, PhD; Mikulas Mlcek, MD, PhD; Frantisek Holy, BSc; Svatava Horakova, MSc; Stepan Kralovec; Jan Skoda, MD; Jan Petru, MD; Andreas Kruger, MD; Vladimir Hrachovina, MD, PhD; Tomas Svoboda, DVM, PhD; Otmar Kittnar, MD, PhD; Vivek Y. Reddy, MD; Petr Neuzil, MD, PhD

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Successful applications of these systems have been recently reported, not only in cases of cardiogenic shock but also as
a life-saving procedure during cardiopulmonary resuscitation or for hemodynamic support in high-risk coronary or electrophysiological interventions, particularly in patients with severe left ventricle dysfunction undergoing electrophysiological mapping and tachycardia ablation. To date, only small randomized trials comparing the safety and efficacy of these systems with intra-aortic balloon pump have been published; neither clinical nor experimental data on the direct comparison of these circulatory support systems are available. An estimation of the power of each support system is, however, essential for the selection of the most appropriate system for individual patients. The objective of our study was, therefore, to perform a head-to-head comparison of the efficacy of these systems under specific hemodynamic conditions in a porcine model.

**Methods**

**Animal Preparation**

Sixteen female pigs (Sus scrofa domestica; 50–60 kg) were used. The investigations were performed in accordance with the Guide for Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996). The animals were premedicated with azaperone (2 mg/kg IM). Fifteen minutes after premedication, the pigs were provided with 100% oxygen via a facial mask, a venous cannula was inserted into the ear vein, and anesthesia was induced by the injection of propofol (2 mg/kg IM). After intubation, the animals were connected to a volume-controlled ventilation system (Siemens Elema 900D, Germany). Anesthesia was maintained with propofol at a rate of 8 to 12 mg/kg per hour; the dose was adjusted based on physiological variables, reflexes (pupillary and corneal), lacrimation, and spontaneous movements. ECG, invasive blood pressures (femoral artery and jugular vein), pulse oximetry, capnometry, and invasive central venous oxygen saturation were continuously monitored in all animals (Monitor Life Scope TR, Nihon Kohden, Japan and Vigilance II, Edwards Lifesciences, USA). A pacing catheter was introduced into the right ventricle apex via the femoral or jugular vein. Other venous and arterial catheters and cannulas were inserted individually according to the circulatory support system used. The arterial pH, P O2, P CO2, and levels of sodium and potassium were followed throughout the study. Ventilation support, as well as oxygenated gas flow, was regularly adjusted to reach the target values (pH 7.4, P O2 12.0 kPa, and P CO2 5.0 kPa). Of note, the metabolic factors were quite well preserved after 10-minute periods of both ventricular pacing (VP) at 200 bpm and 300 bpm in healthy animals, and only mild adjustment of ventilation/oxygenation was necessary in most animals; the levels of sodium and potassium remained stable.

**Circulatory Support Systems**

**Right Atrium-to-Descending Aorta Support (RA-Ao)**

An inlet 21F cannula was inserted via the femoral vein into the right atrium, and an outlet 15F cannula was inserted into the femoral artery. Cannulas were connected to the circuit with a blood pump (Levitronix Centrimag, Levitronix, USA) and oxygenator (Quadrox, Maquet, Germany), constituting an ECMO system (Figure 1A).

**Left Atrium-to-Descending Aorta Support (LA-Ao)**

An inlet 21F cannula was inserted via the femoral vein and transseptal puncture (guided by fluoroscopy and intracardiac echocardiography) into the left atrium, and an outlet 15F cannula was inserted into the femoral artery. Cannulas were connected to the circuit with a blood pump (TandemHeart, Cardiac Assist, USA) (Figure 1B).

**Left Ventricle-to-Ascending Aorta Support (LV-Ao)**

A 13F catheter-based, impeller-driven, axial flow pump (Impella 2.5, Abiomed, USA) was inserted via the femoral artery and across the aortic valve with the inlet area placed into the left ventricle and the outlet area placed into the ascending aorta (guided by fluoroscopy and intracardiac echocardiography; Figure 1C).

**Study Design**

Three study groups were originally created according to the support system used: RA-Ao group, LA-Ao group, and LV-Ao group (4 animals per group). After hemodynamic data analysis, the fourth group was added (LV-Ao+norepinephrine [NE]), in which NE was administered together with LV-Ao support (n=4). Figure 2 shows a schematic illustration of the study design. After a 10-minute stabilization period, ventricular tachycardia (VT) at 200 bpm was simulated by right VP at 200 bpm for 10 minutes, followed by a 5-minute stabilization period, then VT at 300 bpm was simulated by VP at 300 bpm for 10 minutes, followed again by a 5-minute stabilization period, and finally ventricular fibrillation (VFib) was induced and maintained for 10 minutes. During the experiment, a target mean arterial pressure (MAP) of 70 to 80 mm Hg was maintained only by adjustment of the pump speed (rpm); no pharmacological interventions were allowed. NE was administered only in the LV-Ao+NE group, simultaneously with the induction of VFib, at a dose of 0.1 µg/kg per minute (with the exception of NE administration during VF; the animals in LV-Ao+NE group underwent the same protocol as other groups). MAP was selected as the primary end point.

**Statistical Analysis**

The results are expressed as means±SEM. A 2-way ANOVA repeated measures test with subsequent Bonferroni test was used for comparison of differences between groups. Differences were considered to be statistically significant at P<0.05.

**Results**

No difference in MAP was found among the systems at VP 200 bpm (Figure 3A). At VP 300 bpm, the differences did not achieve statistical significance, but the target MAP was reached only in the RA-Ao group (Figure 3B). Statistically significant differences were found during VFib: the highest MAP was maintained in the RA-Ao group, followed by the LA-Ao group, and the lowest efficacy was observed in the LV-Ao group, P<0.001 (Figure 4A, Table). Administration of NE to the LV-Ao support (LV-Ao+NE group) increased the MAP to levels comparable with the LA-Ao group (Figure 4B, Table).

**Discussion**

The major finding of the present study was the significant difference in the hemodynamic efficacy of the currently available percutaneous circulatory support systems, favoring the RA-Ao system (ECMO), followed by the LA-Ao system (TandemHeart). The least efficacious appeared to be LV-Ao system (Impella 2.5). However, even the LV-Ao system allowed short-time blood pressure support during VFib when NE at 0.1 µg/kg per minute was added.

A substantial number of articles describing the use of different circulatory support systems in patients with cardiogenic shock and high-risk coronary intervention have been published. Three randomized trials and their meta-analysis compared the Impella or TandemHeart support with intra-aortic balloon pump in the treatment of cardiogenic shock, showing increased cardiac index at the cost of higher incidence of bleeding; there was no difference in mortality. There are, however, clinical conditions in which intra-aortic...
balloon pump is clearly insufficient for life support, such as recurrent nontolerated VT, electrical storm, serious mechanical complications of acute myocardial infarction, or cardiac arrest, that does not respond to conventional resuscitation approaches. Similarly, electrophysiological activation and entrainment mapping and catheter ablation of nontolerated VT, particularly in patients with severe left ventricular dysfunction, are often not feasible without hemodynamic support. Several articles have already been published with case reports or small series of patients undergoing electrophysiological mapping and catheter ablation on circulatory support: the successful use of the Impella system was described by Fishberger et al,6 and Abuissa et al,7 support with the TandemHeart system was reported by Friedman et al,8 and the efficacy of ECMO was shown by Carbucicchio et al9 and Thomas et al.14 The largest series during VT ablation has been with the use of the Impella 2.5 system (used with intravenous vasoactive agent support).15

Table. Comparison of the Effect of Circulatory Support Systems on the Mean Arterial Pressure at Ventricular Fibrillation: Bonferroni Post Test

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<tbody>
<tr>
<td>RA-Ao vs LA-Ao Mean difference</td>
<td>32.00</td>
<td>23.25</td>
<td>25.25</td>
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<td>28.25</td>
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<td>29.00</td>
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<tr>
<td>P value</td>
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<td>0.0045*</td>
<td>0.0075*</td>
<td>0.0077*</td>
<td>0.0041*</td>
<td>0.0021*</td>
<td>0.0002**</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
<td>0.0002**</td>
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<tr>
<td>RA-Ao vs LV-Ao Mean difference</td>
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<td>48.75</td>
<td>48.25</td>
<td>49.00</td>
<td>50.00</td>
<td>51.25</td>
<td>54.25</td>
<td>55.00</td>
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<td>56.50</td>
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<td>0.0005**</td>
<td>0.0007**</td>
<td>0.0003**</td>
<td>0.0001***</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>RA-Ao vs LV-Ao+NE Mean difference</td>
<td>36.50</td>
<td>28.75</td>
<td>30.50</td>
<td>27.25</td>
<td>29.50</td>
<td>33.00</td>
<td>38.00</td>
<td>32.75</td>
<td>27.25</td>
<td>22.25</td>
</tr>
<tr>
<td>P value</td>
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<td>0.0015**</td>
<td>0.0031*</td>
<td>0.0073*</td>
<td>0.0051*</td>
<td>0.0021*</td>
<td>0.0002**</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LA-Ao vs LV-Ao Mean difference</td>
<td>21.00</td>
<td>25.50</td>
<td>23.00</td>
<td>22.25</td>
<td>21.75</td>
<td>24.25</td>
<td>25.00</td>
<td>24.75</td>
<td>23.25</td>
<td>27.50</td>
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<tr>
<td>P value</td>
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<td>0.0025*</td>
<td>0.0063*</td>
<td>0.0059*</td>
<td>0.0083*</td>
<td>0.0079*</td>
<td>0.0032*</td>
<td>0.0020*</td>
<td>0.0016**</td>
<td>0.0009***</td>
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<td>5.25</td>
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<td>1.25</td>
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<tr>
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<tr>
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<td>−20.00</td>
<td>−17.75</td>
<td>−21.75</td>
<td>−20.50</td>
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<td>−16.25</td>
<td>−22.25</td>
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<td>−34.25</td>
</tr>
<tr>
<td>P value</td>
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<td>0.0194</td>
<td>0.0089*</td>
<td>0.0170</td>
<td>0.0445</td>
<td>0.0371</td>
<td>0.0016**</td>
<td>&lt;0.0001***</td>
<td>&lt;0.0001***</td>
</tr>
</tbody>
</table>

The mean differences are expressed in mmHg. The P values represent the actual values, and the levels of significance corrected for 6 comparisons are shown as *P<0.05, **P<0.01, and ***P<0.001. RA-Ao indicates right atrium-aorta (extracorporeal membrane oxygenation); LA-Ao, left atrium-aorta (TandemHeart); LV-Ao, left ventricle-aorta (Impella 2.5); LV-Ao+NE, left ventricle-aorta system with norepinephrine.
submaximal pump rate. But it should also be noted that the decision as to which mechanical support device to use must take into account factors beyond their efficacy in maintaining blood pressure and blood flow. That is, the ease of use of a particular device must also be taken into consideration. For example, although the Impella 2.5 device provided the least level of support, given the fact that it is quicker and easier to place and use, it may be appropriate for many patients with reasonable ventricular function. However, for the patient with a mechanical aortic valve or severe systolic dysfunction and recurrent polymorphic VT/VF, the TandemHeart device may be preferable. Or for the patient with concomitant lung dysfunction or cyanotic congenital heart disease, the peripheral ECHO device may be better suited for use. The choice of device should be tailored to the individual patient and clinical requirement.

Limitations
A limitation of this study was the selection of MAP as the primary end point for the evaluation of hemodynamic efficacy. The comparison of systems with different principles of support, however, makes it impossible to use the conventional techniques for cardiac index measurement based on standard flow in pulmonary artery or aorta, that is, the RA-Ao system decreases flow in the pulmonary artery, and both the RA-Ao and LA-Ao systems change the direction of flow in the aorta. An alternative to the measurement of MAP as a hemodynamic efficacy end point could be the assessment of flow rate in the major aortic arch branches (eg, the carotid artery), which is, however, associated with other measurement errors. Nevertheless, MAP in our experiment was not affected by any vasoressor therapy (with exclusion of NE during the VFib study in LV-Ao+NE group). Other monitoring options that were not assessed in this study include: (1) central venous oxygen saturation, and (2) evaluating end-organ perfusion using cerebral oximetry; these should be considered in future studies. Our results may be also influenced by the limited number of animals used (4 per group). Only NE at 0.1 μg/kg per minute was used in this study; however, it is likely that other vasoactive agents would provide similar benefits. Future studies should also evaluate these devices in animal models of pathological disease states such as in postmyocardial infarction or heart failure models.

In conclusion, the present study has clearly shown highly significant differences in hemodynamic efficacy among the currently available percutaneous circulatory support systems. These data should be considered when selecting the most appropriate circulatory support for specific medical conditions in individual patients.

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Disclosures
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**Figure 3.** Comparison of the effect of circulatory support systems on the mean arterial pressure (MAP). A, Ventricular pacing at 200 beats per minute (bpm); B, ventricular pacing at 300 bpm. Data are expressed as means±SEM.

**Figure 4.** A, Comparison of the effect of circulatory support systems on the mean arterial pressure (MAP) at ventricular fibrillation (VFib). B, Comparison of the effect of circulatory support systems on the MAP at VFib, including the LV-Ao+norepinephrine (NE) group (with NE administered at the induction of VFib). Data are expressed as means±SEM. RA-Ao indicates right atrium-aorta; LA-Ao, left atrium-aorta; LV-Ao, left ventricle-aorta; LV-Ao+NE, left ventricle-aorta system with NE.


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