Physiol. Res. 71 (Suppl. 2): S163-S178, 2022 *https://doi.org/10.33549/physiolres.934999*

REVIEW

Ten Years of Our Translational Research in the Field of Veno-Arterial Extracorporeal Membrane Oxygenation

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Received May 3, 2022
Accepted October 17, 2022

Summary

Extracorporeal life support is a treatment modality that provides prolonged blood circulation, gas exchange and can substitute functions of heart and lungs to provide urgent cardio-respiratory stabilization in patients with severe but potentially reversible cardiopulmonary failure refractory to conventional therapy. Generally, the therapy targets blood pressure, volume status, and end-organs perfusion. As there are significant differences in hemodynamic efficacy among different percutaneous circulatory support systems, it should be carefully considered when selecting the most appropriate circulatory support for specific medical conditions in individual patients. Despite severe metabolic and hemodynamic deterioration during prolonged cardiac arrest, venoarterial extracorporeal membrane oxygenation (VA ECMO) can rapidly revert otherwise fatal prognosis, thus carrying a potential for improvement in survival rate, which can be even improved by introduction of mild therapeutic hypothermia. In order to allow a rapid transfer of knowledge to clinical medicine two porcine models were developed for studying efficiency of the VA ECMO in treatments of acute cardiogenic shock and progressive chronic heart failure. These models allowed also an intensive research of adverse events accompanying a clinical use of VA ECMO and their possible compensations. The results indicated that in order to weaken the negative effects of increased afterload on the left ventricular function the optimal VA ECMO flow in cardiogenic shock should be as low as possible to allow adequate tissue perfusion. The left ventricle can be also unloaded by an ECG-synchronized pulsatile flow if using a novel pulsatile ECMO system. Thus, pulsatility of VA ECMO flow may improve coronary perfusion even under conditions of high ECMO blood flows. And last but not least, also the percutaneous balloon atrial septostomy is a very perspective method how to passively decompress overloaded left heart.

Key words

Translational medicine • Extracorporeal life support • VA ECMO • Heart failure

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Introduction

Extracorporeal life support (ECLS) is a treatment modality used for urgent cardio-respiratory stabilization in patients with severe but potentially reversible cardiopulmonary failure refractory to conventional therapy. During the first decade of the XXI century many scientific articles have emphasized a usefullness of ECLS as a promising strategy that has been proven to revert otherwise fatal prognosis of refractory cardiac arrest. It was suggested particularly to 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). The crucial purpose of ECLS is thus to restore the circulation and gas exchange. Accordingly, the

primary indication is acute severe heart or/and lung failure with high mortality risk despite conventional therapy. Other elective indications are to support heart or/and lung function during temporary nonfunction (extensive bronchoalveolar lavage, operations on the trachea or mediastinum, coronary artery occlusion during procedures), massive pulmonary embolism, septic shock or severe trauma [1]. Inclusion criteria for ECLS according to guidelines [2] are: Age<70 years, witnessed arrest, arrest to first cardiopulmonary resuscitation (CPR)<5 min, initial cardiac rhythm of VF/pVT/PEA, end-tidal CO_2>10 mm Hg during CPR, intermittent restore of spontaneous circulation or recurrent VF, signs of life during conventional CPR, absence of known life limiting comorbidities and no known aortic valve incompetence. Most contraindications are relative: conditions incompatible with normal life if the patient recovers, preexisting conditions which affect the quality of life and any status not fulfilling the inclusion criteria. Regarding the outcomes of ECLS: According to the recent data from the annual international ELSO Registry the highest survival rate to discharge or transfer is steadily among neonatal ELSO population (66 %), followed by pediatric (53 %), and adult (48 %) populations [3].

However, several clinical studies reported significantly different results in terms of reduced mortality and improved neurological outcome in extracorporeal support setup [4,5,6,7,8]. This was undoubtedly a consequence of heterogeneous conditions, specifically etiology, duration of the cardiac arrest, hypothermia, etc. Moreover, there have been introduced several percutaneous systems into clinical practice for circulatory support in hemodynamic conditions with markedly decreased cardiac output but a direct comparison of these systems under defined hemodynamic conditions was missing. All these facts represented 10 years ago an impulse to start an experimental research that should provide some guides that would enable exploration and optimization of novel therapies for acute and chronical cardiac arrest. All experiments were performed on a porcine model. As experimental subjects, pigs have a number of advantages over other animal species. Primarily, pig anatomy and physiology are similar to humans, especially in cardiovascular and pulmonary systems: a comparable heart to body size ratio, spontaneous development of atherosclerosis and coronary arterial anatomy. Moreover, pigs exhibit similarity to humans being omnivores and thus have a comparable metabolism. These facts cause that pigs have been utilized as a biomedical research model particularly in cardiovascular research.

General methodology

Fully anesthetized crossbred female pigs (Sus scrofa domestica), four to five months old with body weight 50-55 kg, were used in all investigations. After 24 h of fasting, anesthesia was induced by azaperone (2 mg/kg i.m.) followed by atropine sulphate (0.02 mg/kg IM) and ketamine hydrochloride (15 to 20 mg/kg i.m.). Anesthesia was continued with initial propofol and morphine boluses, (2 mg/kg i.v. and 0.1 to 0.2 mg/kg i.v., respectively) and animals were orotracheally intubated. Continuous i.v. infusion of propofol (8 to 10 mg/kg/h) combined with morphine (0.1 to 0.2 mg/kg/h) i.v. were used to maintain anesthesia, the depth of which was regularly assessed by photoreaction and corneal reflex.

All experimental protocols were approved by the Institutional Animal Care and Use Committee in accordance with Act No 246/1992 Coll., on the protection of animals against cruelty. All research procedures were performed in accredited Animal Experimental Laboratory at the Department of Physiology, First Faculty of Medicine, Charles University in Prague.

Efficiency of the extracorporeal life support

The first study realized in our Animal Lab [9] was focused on a head-to-head comparison of the efficacy of three different widely available percutaneous circulatory support systems introduced into clinical practice for the treatment of cardiogenic shock or refractory nontolerated ventricular tachycardia: Impella 2.5 system, TandemHeart system, and extracorporeal membrane oxygenation (ECMO). The Impella 2.5 system (Abiomed, Germany) is a catheter-based, impeller-driven, axial flow pump that pumps blood directly from the left ventricle (LV) across the aortic valve to the ascending aorta; the TandemHeart system (Cardiac Assist, USA) is a left atrial-to-femoral arterial circulatory support system, driven by a continuous flow pump; and 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 (Fig. 1). Successful applications of these systems had been reported not only in cases of cardiogenic shock but

also as a life-saving procedure during cardiopulmonary resuscitation [10]. Nevertheless, only small randomized trials comparing the safety and efficacy of these systems with intra-aortic balloon pump had been published at that time [11,12]; neither clinical nor experimental data on the direct comparison of these circulatory support systems were available. That is why we have suggested an experimental protocol aimed to perform a comparison of the efficacy of these systems under specific hemodynamic conditions (Fig. 2A). Our results have shown that while there were no significant differences among three types of circulatory support in mean arterial pressure (MAP) during both levels of ventricular tachycardia, statistically significant differences were found during ventricular fibrillation (Fig. 2B): the highest MAP was maintained in the ECMO group, followed by the TandemHeart group, and the lowest efficacy was observed in the Impella group (P<0.001). In conclusion, the presented study has shown highly significant differences in hemodynamic efficacy among the three studied percutaneous circulatory support systems [9]. These data should be considered when selecting the most appropriate circulatory support for specific medical conditions in individual patients.

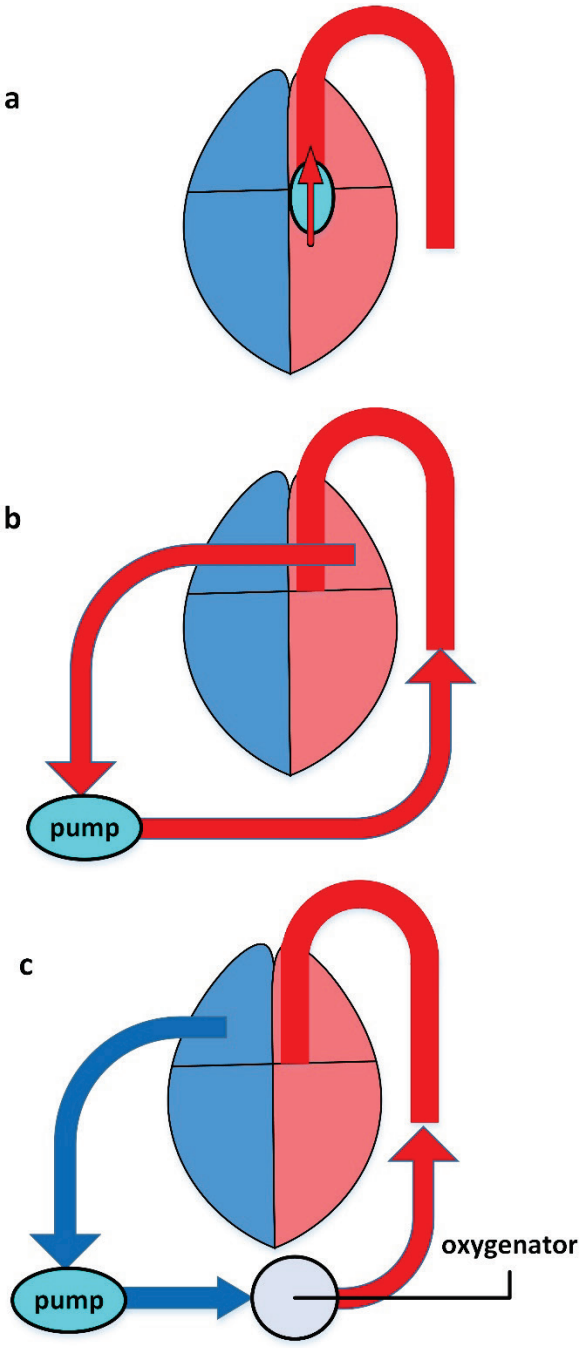

Fig. 1. The percutaneous circulatory support systems: (**a**) Impella system, (**b**) TandemHeart system, (**c**) ECMO system.

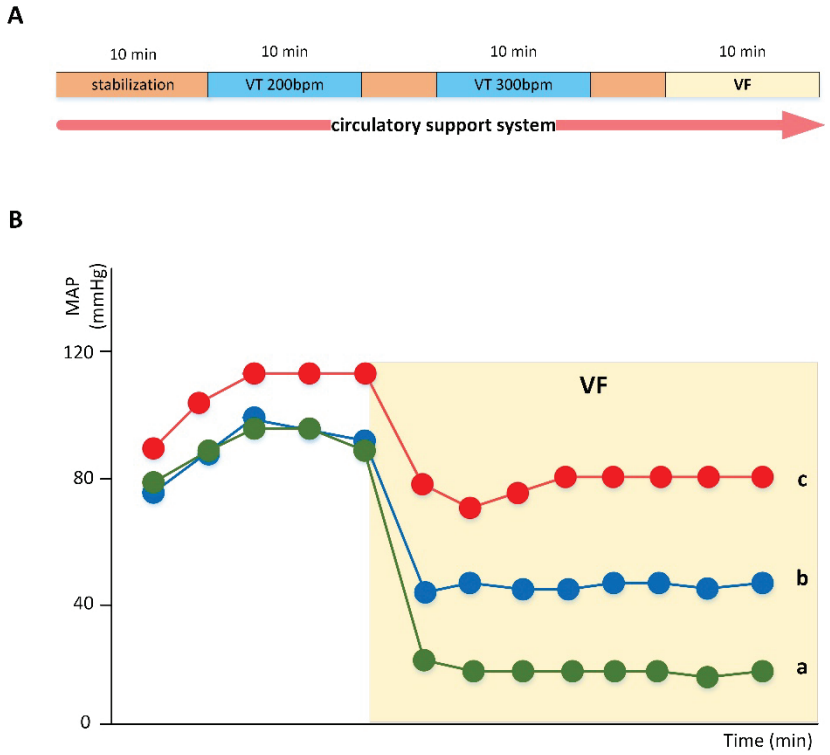

Fig. 2. (**A**) Outline of the study protocol. VT– ventricular tachycardia, VF – ventricular fibrillation. (**B**) Comparison of effects of circulatory support systems on the mean arterial pressure (MAP) at ventricular fibrillation (VF): **a** – Impella system, **b** – TandemHeart system, **c** – ECMO system.

A venoarterial ECMO (VA ECMO) allows perfusion of vital organs during cardiac arrest by oxygenated blood and provides a time span for diagnostic decision and suggestion of appropriate therapy. The most demanding vital organs are the brain and the heart, and their adequate oxygenation and perfusion are critical prerequisites for favorable clinical outcomes [13,14]. In clinical practice, a combination of a pulsatile support by intraaortic balloon counterpulsation (IABP) with VA ECMO was considered beneficial and was used both in ECMO-treated cardiogenic shock and during weaning from extracorporeal support [15]. However, it remained unclear whether coronary and carotid blood flows and coronary perfusion pressure in prolonged cardiac arrest are adequate when managed by different ECMO approaches. Therefore the aim of the next experimental study performed in our Animal Lab was to determine how efficient is femoro-femoral (FF) compares to femoro-subclavian (FS) VA ECMO in producing adequate carotid and coronary blood flow as well as cerebral and myocardial oxygenation in a pig model of prolonged cardiac arrest, and whether the contribution of IABP in these ECMO approaches is significant [16]. The protocol consisted of 15-minute intervention intervals outlined in Fig. 3A: After implementation of VA ECMO the experimental animals were divided into two arms with parallel interventions. In a pig model of prolonged cardiac arrest treated with VA ECMO, our experimental study showed several important findings (Fig. 3B): 1) the study confirmed that the increasingly used first line approach for urgent organ support in refractory arrest (FF ECMO) sufficiently assures both brain and myocardial perfusion and oxygenation, and rapidly improves the post-arrest metabolic state. 2) the FS approach, while sufficiently maintaining brain perfusion, may not be an optimal option to maintain coronary perfusion and offers worse myocardial metabolic recovery. 3) most importantly, the addition of IABP to an established VA ECMO is a controversial intervention: in the FF ECMO approach, it significantly impairs coronary perfusion and in the FS approach, coronary perfusion remains the same, still not reaching 80 % of the pre-arrest value. 4) both FF and F ECMO assure adequate coronary perfusion pressure and sustained resuscitability.

Despite advances in medical care, education and technologies, out-of-hospital cardiac arrest remains an important cause of unexpected death with a very low survival rate (cca 4-14 %) that has been unchanged for several past decades [17]. Thus, optimal deployment strategies, risk stratification and prognostic markers remained to be identified so that patients could benefit from novel technologies but also that futile efforts are avoided. Therefore, in the next ECMO study [18], the time-course of metabolic and electrophysiological changes was explored during 20 min minimal-flow

cardiac arrest and subsequent early reperfusion period (60 min) treated by extracorporeal circulation in a porcine model (Fig. 4A). We hypothesized that despite a long period of untreated arrest an early ECMO deployment could significantly improve metabolic and organ condition and thus resuscitability. Our findings proved very good efficiency of VA ECMO as all monitored parameters started to restore immediately after extracorporeal support onset. Our results indicate that despite severe metabolic and hemodynamic deterioration during prolonged cardiac arrest, restitution of adequate circulation and oxygenation can rapidly revert otherwise fatal prognosis, thus carrying a potential for dramatic improvement in survival rate (Fig. 4B). Within about 5 min of extracorporeal reperfusion, most monitored parameters returned to close-to-normal values (pH>7.3, pCO_2<50 %, MAP>40 mm Hg, K^+<5 mmol/l) and kept improving. In two-thirds of animals the return of spontaneous circulation was achieved. The only marker of a successful resuscitability to the spontaneous circulation return was the mean amplitude of intracardial electrogram (EGM) during cardiac arrest and ECMO flow.

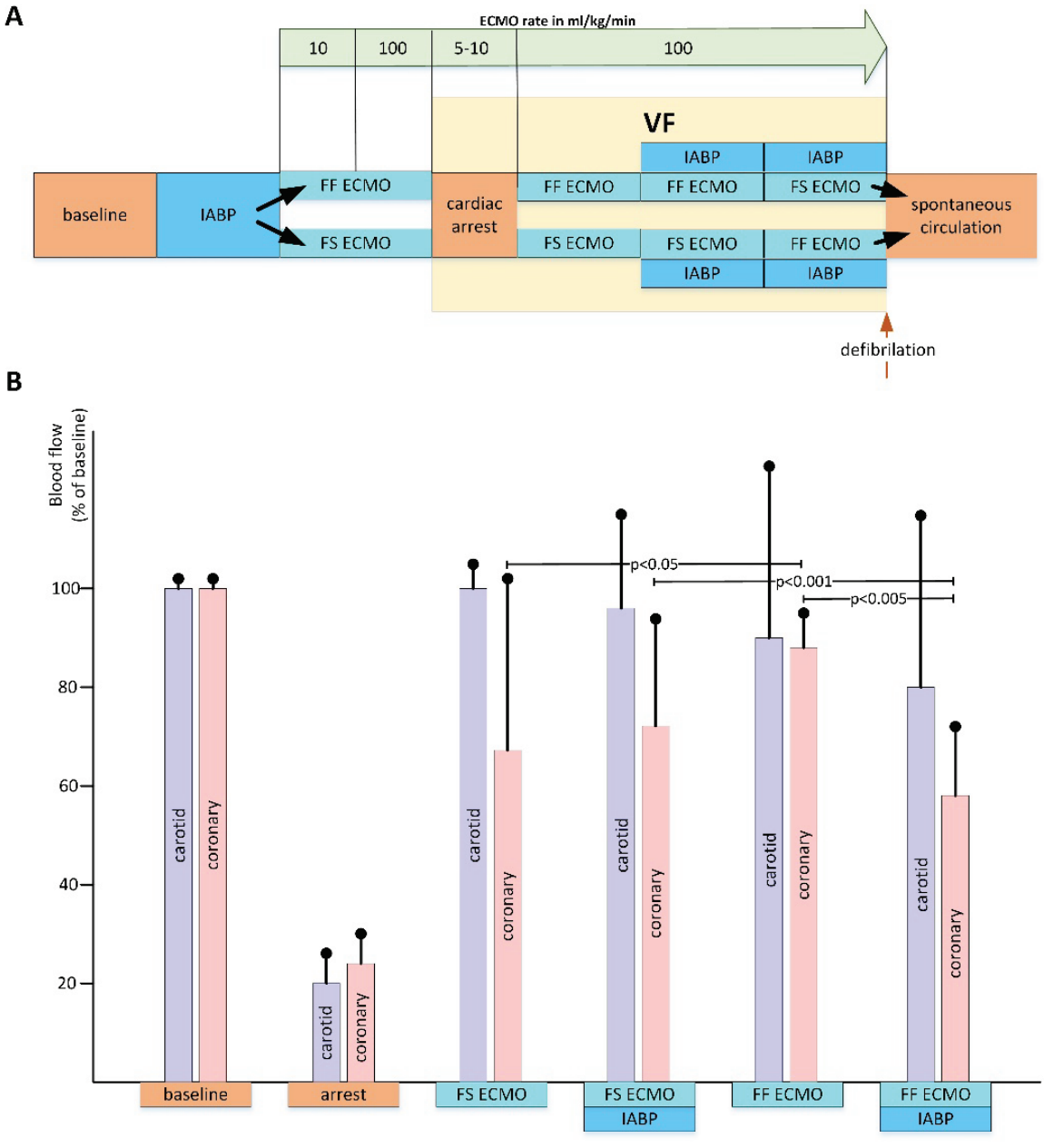

Fig. 3. (**A**) Outline of the study protocol. IABP – intraaortic balloon countepulsation, FF – femoro-femoral, FS – femoro-subclavian. (**B**) Carotid and coronary blood flow velocities relative to baseline. VF – ventricular fibrillation.

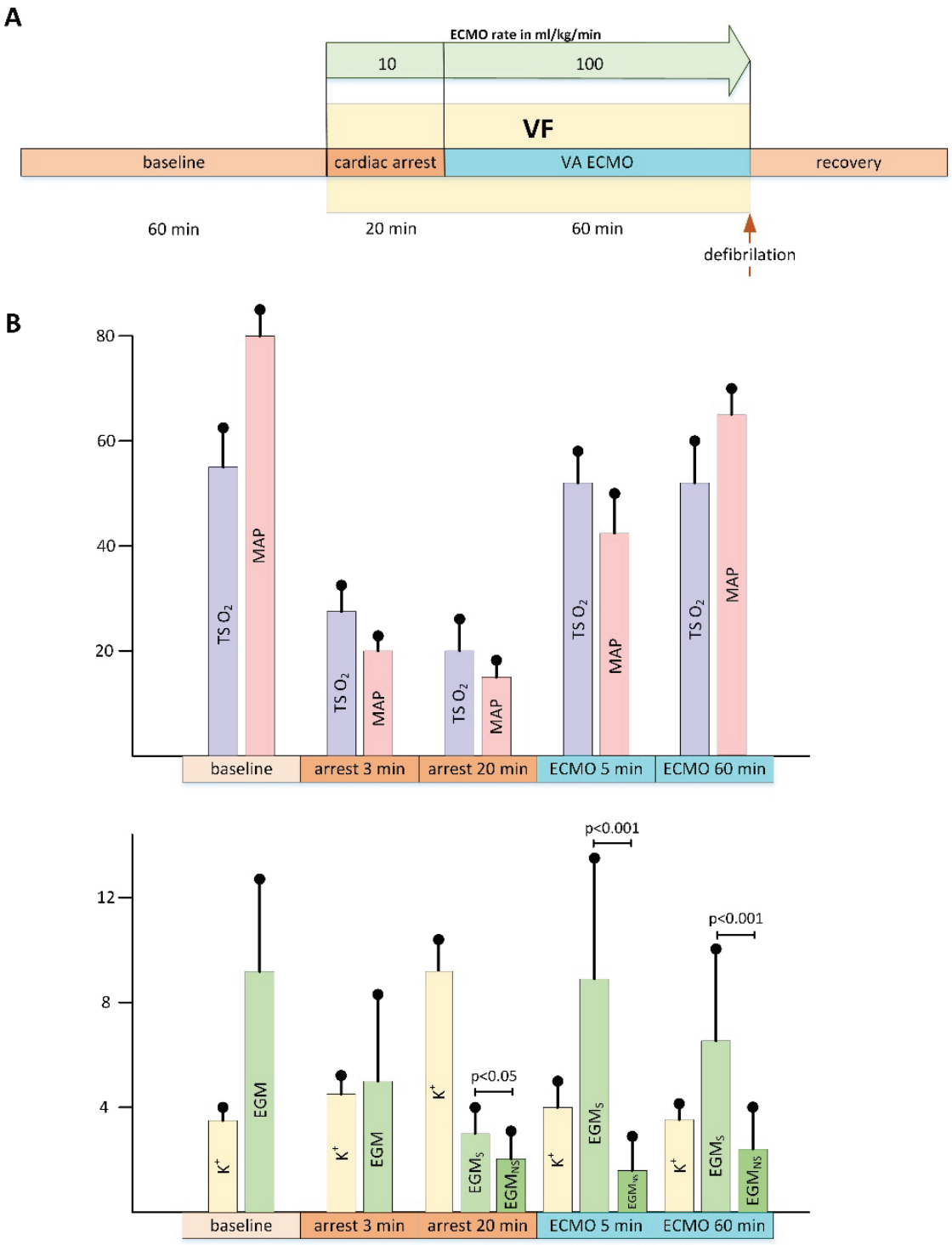

Fig. 4. (**A**) Outline of the study protocol. VF – ventricular fibrillation. (**B**) Effect of cardiac arrest and VA ECMO on selected parameters. TS O_2 – tissue oxygenation (%), MAP – mean arterial pressure (mm Hg), EGM – intracardiac electrograms amplitude (arb), K^+ – plasma potassium (mmol/l), EGMs – intracardiac electrograms amplitude in successfully resuscitated animals, EGMn – intracardiac electrograms amplitude in non-successfully resuscitated animals.

Mild therapeutic hypothermia (HT) was introduced into the clinical management of cardiac arrest survivors after the publication of the results of clinical trials showing a benefit compared with standard treatment [19]. Recently, however, several authors presented a critical view of the current evidence for the protective role of HT in post-cardiac arrest syndrome. In analyses of the available randomized data, they showed that the evidence for the benefits of HT in cardiac arrest survivors remains inconclusive [20]. Therefore, the aim of the next

study realized in our experimental lab was to compare the effects of mild therapeutic HT and controlled normothermia (NT) on several clinically relevant outcomes in an animal model of cardiac arrest and thus to test the hypothesis that mild HT can increase the efficiency of an extracorporeal life support [21].

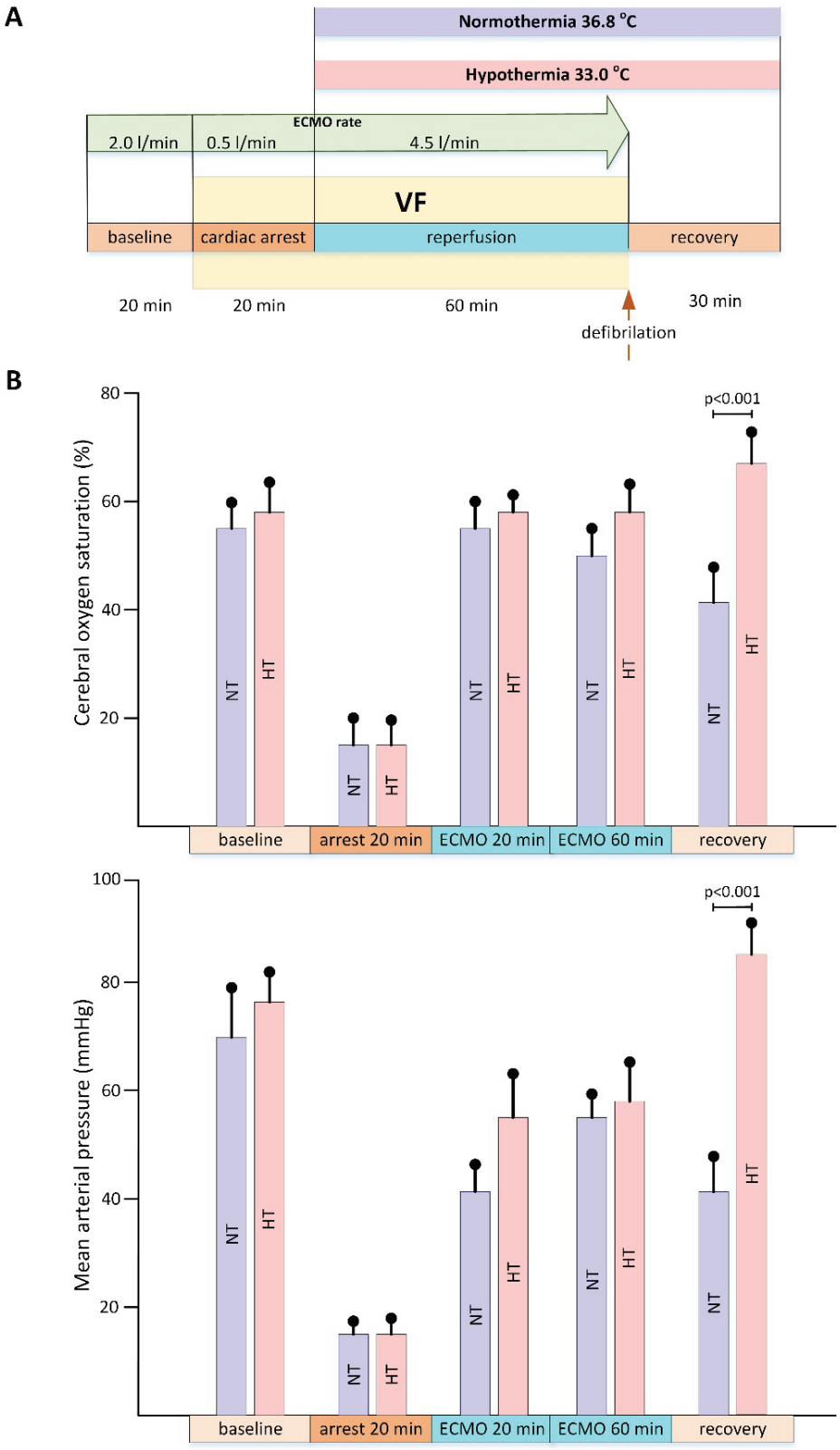

Fig. 5. (**A**) Outline of the study protocol. VF – ventricular fibrillation. (**B**) Comparison of effects of mild hypothermia (HT) and normothermia (NT) on brain oxygen saturation and mean arterial pressure during the study protocol.

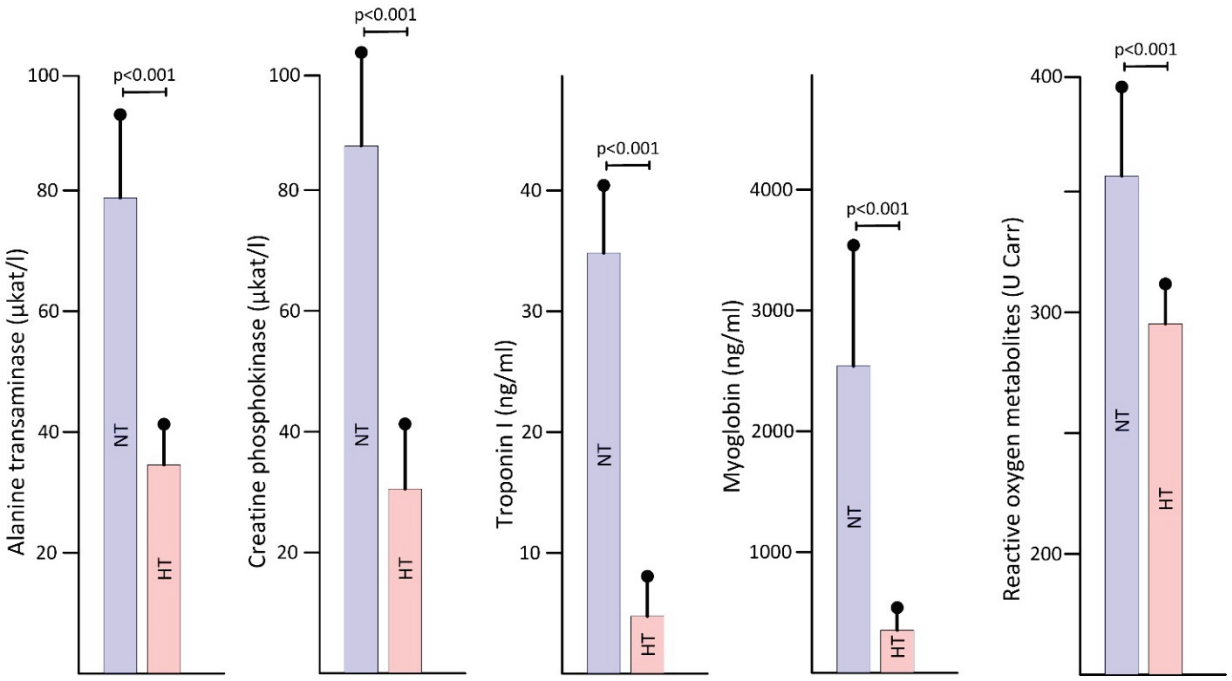

Fig. 6. Comparison of effects of mild hypothermia (HT) and normothermia (NT) on biomarkers of tissue injury at 90th min of reperfusion.

The study protocol has consisted of 20 min minimal-flow cardiac arrest and subsequent reperfusion by increasing the ECMO flow to 4.5 l/min (100 ml/kg/min). Simultaneously with onset of the reperfusion period the animals were randomly assigned to one of the two groups: NT or HT (Fig. 5A). To simulate clinical conditions, norepinephrine was administered when the mean arterial blood pressure remained below 60 mm Hg at 10 min after the restoration of circulation. During recovery period, the mean arterial blood pressures and brain oxygen saturations were significantly higher in the HT group, despite the fact that the norepinephrine doses administered to this group were significantly lower compared with the NT group (Fig. 5B). The study has also proved by analyzed laboratory parameters of organ injury that in porcine model of cardiac arrest mild HT (33 °C) was superior to controlled NT (36.8 °C) for prevention of organ damage and oxidative stress suppression during recovery period after cardiac arrest and VA ECMO reperfusion (Fig. 6). Moreover, our other study proved that when combined with normokalemia mild HT exerts an antiarrhythmic effect [22].

Appropriate biomodels for translational research

The rapid adoption of extracorporeal circulatory support in acute medicine was logically linked with the need for further experimental research into these devices what was manifested in increasing demand for development of appropriate biomodels. For the rapid transfer of knowledge to clinical medicine a porcine model is the most appropriate, in particular when taking into consideration its reasonable physiological and anatomical similarities with human being as well as the size of the instrumentation (catheters and cannulas) and extracorporeal support [23,24]. Therefore, the aim of another our study was to develop and prepare a biomodel for acute cardiogenic shock that would be suitable for further experimental research of extracorporeal methods supporting the failing circulation, specifically in our case for further study of pathophysiological mechanisms of adverse events that could accompany a clinical use of VA ECMO [25]. In order to achieve these aims two types of models of acute heart failure were examined (Fig. 7): a) a hypoxic model with continuous perfusion of the coronary arteries by deoxygenated blood; and b) an ischemic model of controlled hypoperfusion of one of the main branches of the left coronary artery: left anterior descending artery (LAD) or left circumflex artery (LCx). The ischemic model was superior to the hypoxic one (Fig. 8) as it offered a pathophysiologically accurate, technically simple and reproducible method of the heart failure induction with minimal mortality. Episodes of ventricular fibrillation did not occur during slow progressive ischemization, which is otherwise regularly accompanied by complete coronary closure with a significant increase in mortality.

The already mentioned growing worldwide use of mechanical circulatory supports and extracorporeal membrane oxygenation in clinical practice, was reflecting in preclinical experimental testing. A stable and reliable model of a chronic heart failure (HF) was required for many experiments to understand hemodynamics or to test effects of new treatment methods. In our experimental laboratory we have suggested such a model by tachycardia-induced cardiomyopathy, which can be produced by rapid cardiac pacing in pigs. This biomodel represents potent means to study decompensated dilated cardiomyopathy, hemodynamics of progressive chronic HF with low cardiac output, and effects of applied treatment. The pacing protocol (Fig. 9) was accompanied by daily auscultation of heart beat, ECG, and pacemaker interrogation in order to verify the heart rate and constant pacing parameters, including battery life. Moreover the echocardiographic assessments were used to reveal the structural and functional heart changes. Physical examination revealed severe clinical signs of decompensated chronic HF in all animals after 4-8 weeks of pacing protocol (Table 1). A model of progressive chronic heart failure can be produced by the suggested methodology. The technique presented in the study is easy to perform with widely available equipment, and the results are robust and reproducible [26]. This tachycardia-induced cardiomyopathy offers a valuable object for further experimental studies on hemodynamics, investigation of disease mechanisms and effects of applied treatments.

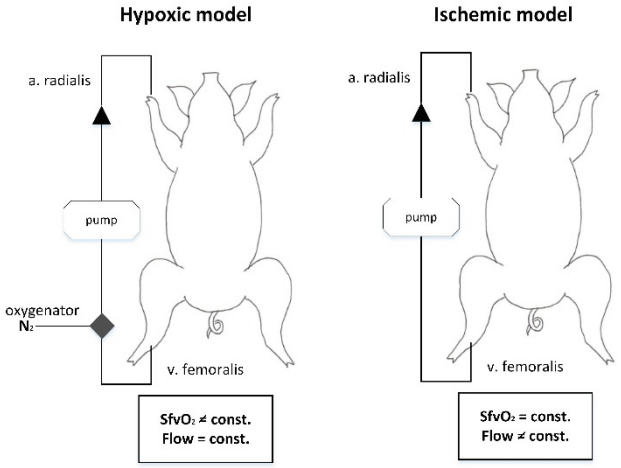

Fig. 7. Comparison of hypoxic and ischemic model of the acute cardiogenic shock. $SfvO_2$ – blood oxygen saturation of femoral vein.

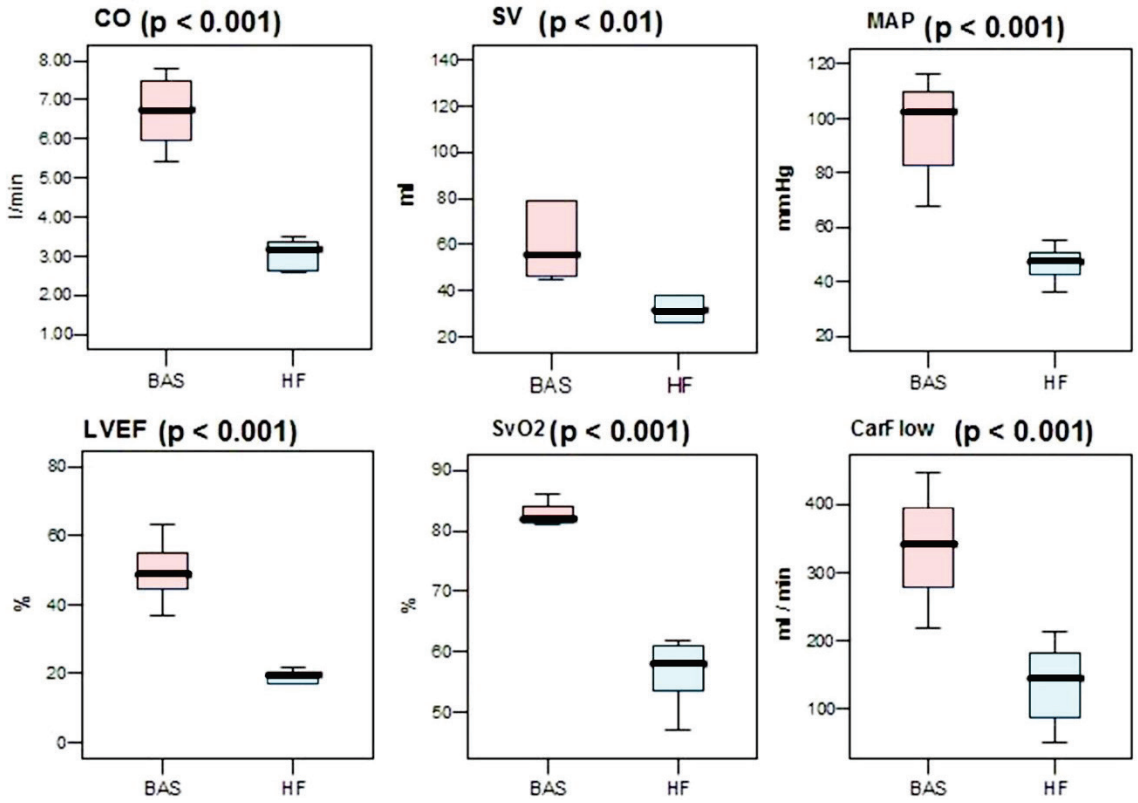

Fig. 8. Significant decreases in all hemodynamic parameters after development of heart failure in the ischemic model. BAS – baseline, HF – heart failure, CO – cardiac output, MAP – mean arterial pressure, LVEF – left ventricular ejection fraction, SvO2 – mixed venous blood saturation, CarFlow – flow in the right carotid artery, SV – stroke volume.

Table 1. Numerical results of the animal model after cessation of pacing protocol. All values expressed as mean ± standard deviation.

Parameter		Value
Heart rate	HR	100 ± 38 bpm
Mean arterial pressure	MAP	47 ± 38 mm Hg
Cardiac output	CO	2.9 ± 0.8 l/min
Mixed venous hemoglobin saturation	SvO_2	62 ± 18 %
LV ejection fraction	EF	25 ± 16 %
Central venous pressure	CVP	14 ± 4 mm Hg
LV end-diastolic volume	LV EDV	189 ± 59 ml

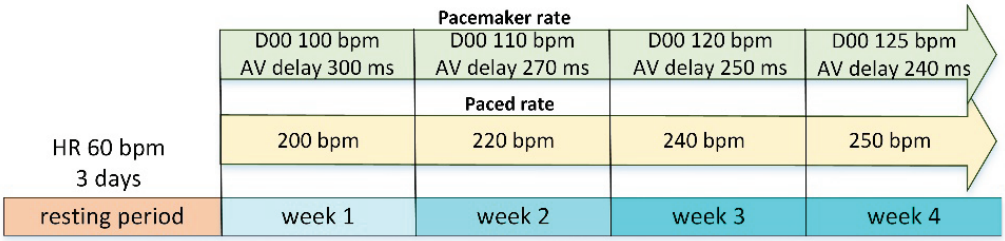

Fig. 9. Outline of the pacing protocol. HR – heart rate, AV – atrioventricular, D00 – operation mode, bpm – beats per minute.

Adverse events accompanying a clinical use of VA ECMO

The occurrence of a myocardial dysfunction as a result of VA ECMO has been acknowledged for many years [27]. During peripheral VA ECMO therapy, an inflow is realized from the right atrium into the extracorporeal blood pump. Oxygenated blood is then returned into the femoral artery. This VA ECMO setting offers partial or full circulatory support; however, it could be associated with specific consequences for the failing heart. The inflow component of the VA ECMO circuit decreases preload of the right heart, whereas the outflow component increases LV afterload [28]. In cases of extremely compromised LV systolic function combined with increased afterload the failing LV becomes overloaded, although the right ventricle may be fully unloaded [29]. Progressive distension of the overloaded LV with subsequent severe pulmonary edema is a critical condition that often requires urgent intervention. As data regarding the relationship among extracorporeal blood flow (EBF), central hemodynamics and LV performance were insufficient, our study planned to describe hemodynamic and LV performance changes resulting from a gradual increase in EBF during VA ECMO in a porcine model of cardiogenic shock. The cardiogenic shock was induced by myocardial hypoxia (Fig. 10A) leading to extensive myocardial injury. Our results demonstrated that increasing EBF in cardiogenic shock during VA ECMO may cause impairment of LV performance in a flow-dependent manner (Fig. 10B). These data indicate that the optimal VA ECMO flow in cardiogenic shock should be as low as possible to allow adequate tissue perfusion.

Negative effects of increased afterload on the LV function may lead not only to LV distension, a rise in the end-diastolic volume, and end-diastolic pressure, but also progression into pulmonary edema can consequently occur [25]. Furthermore, clinical work by Kim *et al.* [30] has described how excessive cumulative fluid balance during early phases of VA ECMO increases the risk of mortality. Therefore, the purpose of the next study was to evaluate the acute fluid changes in the lungs during VA ECMO support [31]. Lung impedance changes were registered during incremental increases in EBF under both healthy and failing heart conditions using a new, computational analysis of the raw electrical impedance tomography (EIT) data (Fig. 11A). The results have shown that in the heart failure conditions, the reduction of lung tissue electrical impedance was observed when VA ECMO flow was increased. This was significantly different from a healthy heart with identical ECMO support (Fig. 11B). Under constant ventilation and fluid infusion in a failing circulation supported by increased EBF, this can be interpreted as a fluid accumulation in the lungs.

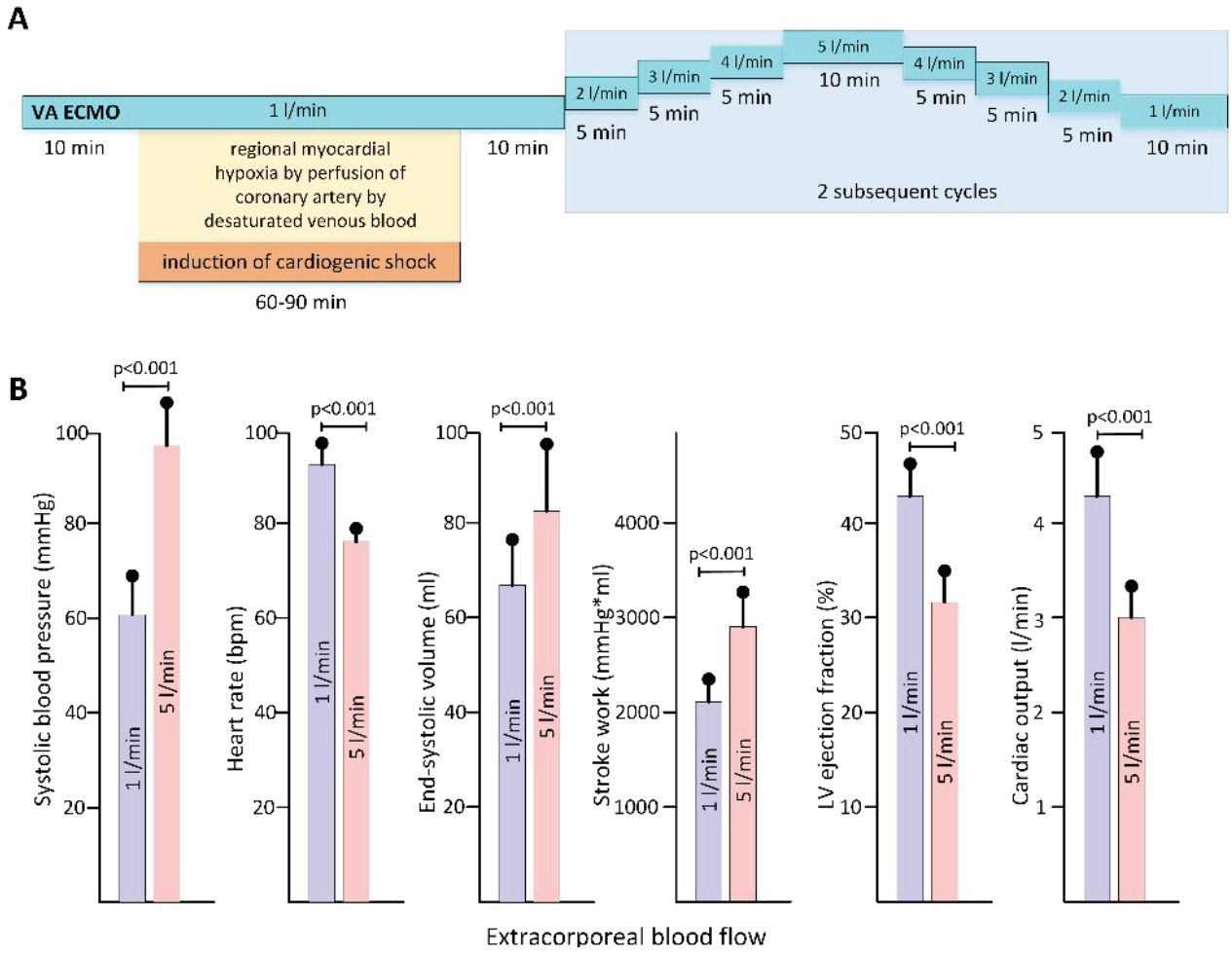

Fig. 10. (**A**) Outline of the study protocol. (**B**) Comparison of effects of the venoatrial extracorporeal blood flow on selected hemodynamic parameters and parameters of the left ventricular performance.

A novel electrocardiogram (ECG)-synchronized, pulsatile ECLS system has recently been introduced, enabling decreased EBF during systole and increased EBF during diastole, which, ideally should decreaseafterload and improve LV function in the setting of VA ECMO [32]. The aim of another our study was to compare the effects of synchronized pulsatile and standard continuous ECMO flow on cardiac performance and coronary blood flow [33]. The pressure-volume loop of the LV was analyzed, hemodynamic parameters and coronary blood flow were measured during experimental protocol (Fig. 12 A). The study had the crossover design, the animals were randomly assigned to start at each EBF rate in continuous mode for 5 min, followed by pulsatile mode for 5 min, or vice versa. Synchronized pulsatile flow was present at all EBF rates, apparent as an increase in the diastolic pressure wave form immediately after the diacrotic notch, and was associated with a significant reduction in LV end-systolic pressure and significantly increased LV ejection fraction and mean arterial pressure compared with continuous EBF across all flow rates. Compared with continuous flow, ECG-synchronized pulsatile flow was also associated with significantly increased coronary flow velocity across all EBF values (Fig. 12B). Our results suggested that ECG-synchronized pulsatile flow preserves LV function (and may actually unload the LV) and increases coronary flow, CO, and MAP compared with standard ECMO continuous-flow in a porcine model of severe acute cardiogenic shock.

Recently published case reports and small studies [34,35] have documented the feasibility and efficacy of percutaneous balloon atrial septostomy (BAS) in patients on VA ECMO. But as the real impact on LV unloading and performance was still not well understood in detail, our research team designed an experimental study of cardiogenic shock managed by VA ECMO in which BAS was performed to assess the effects of this technique on LV decompression and work load, together with the impact on overall end-organ oxygen delivery [36]. The experimental protocol is presented in

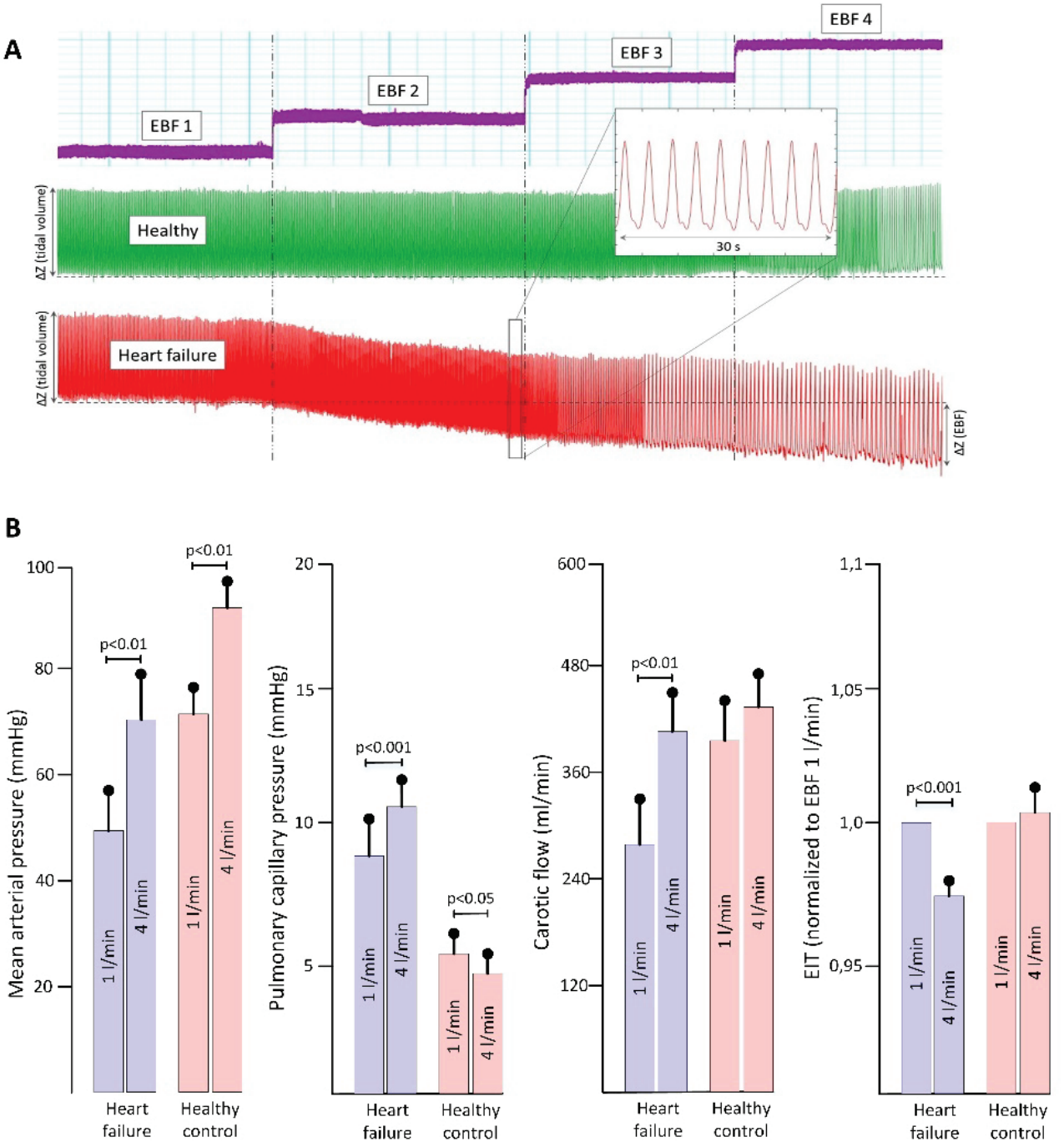

Fig. 11. (**A**) Outline of the study protocol with representative example of EIT waveforms from one animal. Stepwise changes with increasing extracorporeal blood flow (EBF) are aligned with electrical impedance for both healthy (green) and heart failure (red) conditions. Electrical impedance waveforms represent impedance of lung regions during breathing cycles. (**B**) Comparison of effects of the venoatrial extracorporeal blood flow on selected hemodynamic parameters and EIT.

Figure 13A. Immediately after BAS had been performed, significant decrease to 66 % of no-BAS value in the stroke work (SW) was observed (Fig. 13B). The most extensive available experience with BAS during VA ECMO comes from a retrospective investigation of pediatric and adult patients. Our results in an acute ischemic heart failure animal model support the idea that BAS is a powerful unloading tool. In acute cardiogenic shock supported by peripheral VA ECMO, BAS provided immediate and significant LV work reduction by reducing both preload (end-diastolic volume) and afterload (end-systolic pressure) (Fig. 13B).

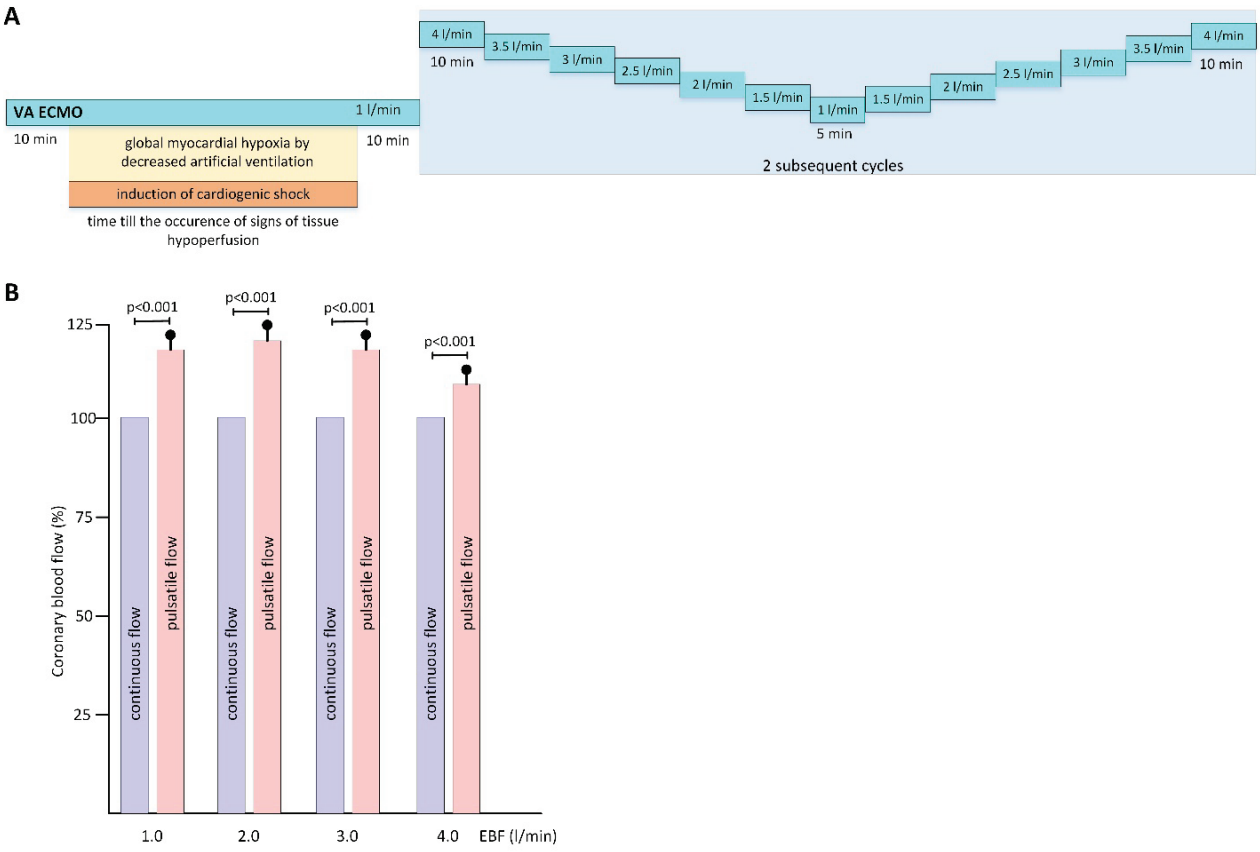

Fig. 12. (**A**) Outline of the study protocol. (**B**) Comparison of effects of continuous and pulsatile extracorporeal blood flow (EBF) on the coronary blood flow.

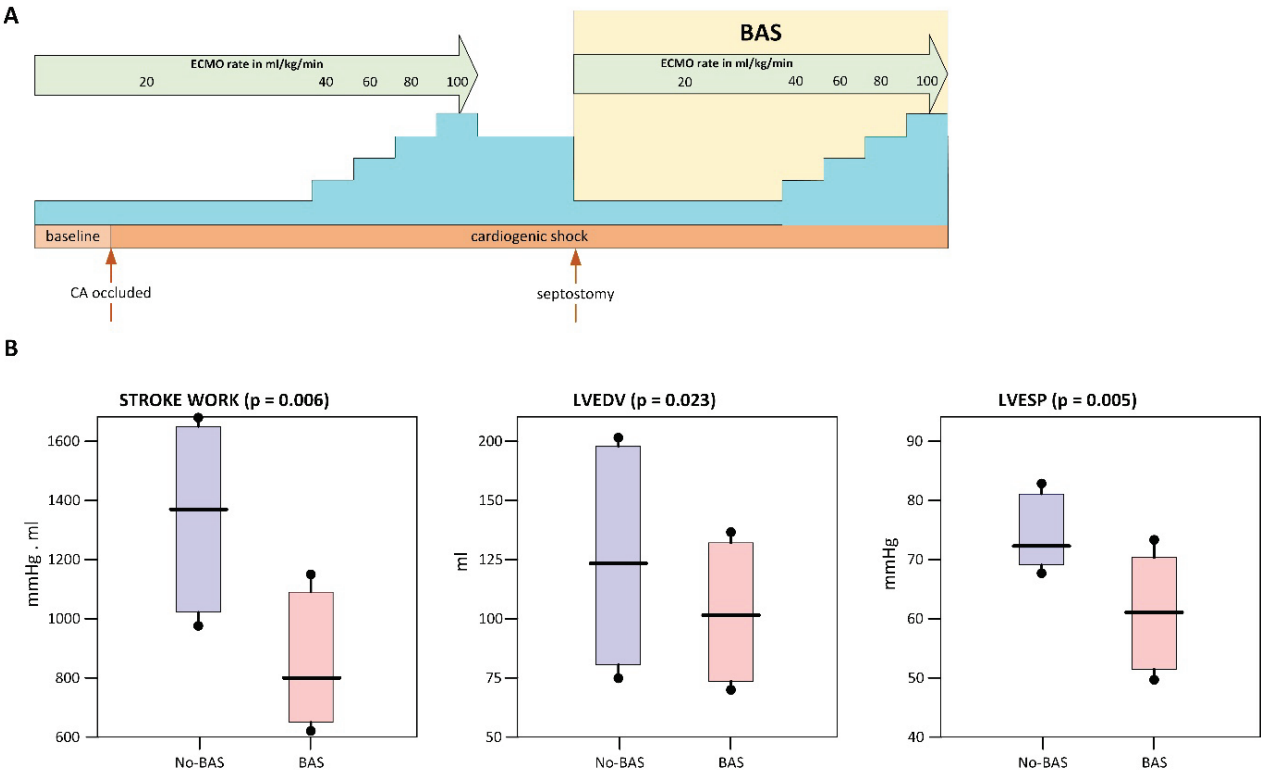

Fig. 13. (**A**) Outline of the study protocol. BAS – balloon atrial septostomy. (**B**) Comparison of effects of percutaneous balloon atrial septostomy (BAS) on stroke work, left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic pressure (LVESP).

Conclusions

Circulatory decompensation developed on grounds of heart failure represents a severe condition that requires intensive treatment. When the physiological compensatory mechanisms with conventional therapy approaches are insufficient to revert failing hemodynamics, ECMO systems can serve as extracorporeal circulatory support [1]. VA ECMO flow increases perfusion of all systemic tissues. Studies mentioned in this review proved supporting effects of VA ECMO on myocardial perfusion and carotic blood flow. On the other hand, the VA ECMO circuit is set in parallel with the native cardiac output and the reinfusion flow is increasing LV afterload. The interactions of these two circulations are defined by changes in pressures, flows, and overall impact on the hemodynamics [37]. Aortic reinfusion increases the LV afterload associated with higher arterial blood pressure, and thus it impacts myocardial work. Nevertheless there are promising approaches that are able to compensate negative effect of excessive ECMO blood flow on the failing heart. First of all, decreasing the VA ECMO support to the minimal EBF rate necessary for tissue perfusion is advised in situations of decompensated HF. Pulsatility of VA ECMO flow improved coronary perfusion even under conditions of high ECMO blood flows. And last but not least, the BAS is a very perspective method how to passively decompress overloaded left heart.

Conflict of Interest

There is no conflict of interest.

Acknowledgements

This work was supported by Grant No. GA ČR 22-34020S.

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