The novel St Thomas' Hospital polarizing blood cardioplegia: Results in hearts with reduced ejection fraction

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Graphical Abstract: The novel St Thomas' Hospital polarizing blood cardioplegia: Results in hearts with reduced ejection fraction. Created in BioRender. Wolner, L. (2025) https://BioRender.com/d03w1mz

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Abstract

Objectives: Myocardial protection is crucial for recovery after cardiac surgery. Despite older patients with more comorbidities, most surgeons still use potassium-induced depolarized arrest with cardioplegic solutions from more than 50 years ago. However, this can cause calcium overload, mitochondrial injury, and energy depletion. We tested a new polarizing cardioplegia (STH-pol) versus traditional depolarized arrest (STH-control) in an ischemia/reperfusion model of hearts with reduced ejection fraction.

Methods: Myocardial infarction (MI) was induced by permanent ligation of the left anterior descending artery in male Sprague Dawley rats. Six weeks post-MI, the hearts were isolated and perfused on an erythrocyte-perfused working heart system. Cold ischemic arrest (4°C, 60 min) was induced by STH-pol (n=10) or STH-control (n=8), followed by reperfusion (37°C, 45 min). Hemodynamic variables were recorded throughout reperfusion, and tissue samples were taken at the end of reperfusion to analyze high-energy phosphates (HEP).

Results: Administration of STH-pol resulted in comparable hemodynamic recovery after 60 min ischemia as STH-control induced cardioplegic arrest (left ventricular systolic pressure: 109.1 ± 3.4 vs. 103.3 ± 3.6). Similarly, HEP levels did not differ between the two groups (ATP: 2.5 ± 0.4 nmol/mg protein and 2.2 ± 0.9 nmol/mg).

Conclusions: Polarizing cardioplegic arrest did not lead to a statistically significant difference in myocardial protection as compared to a clinically relevant, standard cold blood cardioplegia in rat hearts with chronic myocardial infarction.

(223 words)

Keywords: Myocardial Protection, Cardioplegia, Ischemia-Reperfusion Injury

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List of abbreviations:

ADP:	Adenosine DiPhosphate
AMP:	Adenosine MonoPhosphate
ATP:	Adenosine TriPhosphate
BW:	Body weight
Ca^{2+}:	Calcium
CF:	Coronary flow
CO:	Cardiac output
ECG:	Electrocardiogram
EF:	Ejection fraction
HEP:	High energy phosphates
HPLC:	High-performance liquid chromatography
HR:	Heart rate
HW:	Heart weight
ICS:	Intercostal space
i.p.:	Intraperitoneally
LAD:	Left anterior descending (artery)
LD:	Langendorff
LVSP:	Left ventricular systolic pressure
MVO_2:	Myocardial oxygen consumption
Na^+:	Sodium
PCr:	Phosphocreatine
SEM:	Standard error of the mean
STH:	St Thomas' Hospital
SV:	Stroke volume
SW:	Stroke work
WH:	Working Heart

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Introduction:

Patients currently undergoing cardiac surgery are usually relatively elderly with a higher prevalence of comorbidities and an elevated disease burden when compared to patients a few decades ago [1]. Except for specific surgical procedures conducted on actively beating hearts, the predominant approach in cardiac surgery involves cardioplegia to induce transient cardiac arrest. While, within the realm of intraoperative myocardial protection, there are few novel solutions like the Del-Nido cardioplegia that are used clinically, formulations developed five decades ago continue to be the established gold standard. The majority of current cardioplegic solutions contain high potassium levels, which leads to depolarized arrest [2]. Recently, in order to prevent adverse effects of potassium on the myocardium such as calcium-overload, mitochondrial damage, energy depletion, and arrhythmias, we and others presented the new concept of polarized arrest [3]. The new St Thomas' Hospital polarizing cardioplegia (STH-pol), consisting of esmolol, adenosine and magnesium appears to be the most promising polarizing solution [4]. Esmolol is an ultra-short-acting beta-blocker with a half-life of around 9 minutes that has negative chronotropic and inotropic effects and reduces myocardial oxygen consumption[5]. Adenosine acts on the SA-node pacemaker cells and inhibits them by activating A1 receptors, which open sarcolemma K_{ATP}-channels [6]. Magnesium is an endogenous calcium-channel blocker, inhibits calcium overload and induces endothelial relaxation [7]. When inducing polarized arrest, the membrane potential is kept close to the resting membrane potential of about -80 mV, thereby (a) activating fewer exchangers and membrane channels, (b) reducing transmembrane fluxes and, (c) subsequently limiting metabolic and electrical imbalances [8]. As a result, the heart utilizes less ATP and oxygen and preserves a better metabolic condition [2,9]. While individual components of polarizing cardioplegia have been examined as either solo-agents or as adjuncts to different solutions, few studies have devoted themselves to test this specific triple solution [4,10]. An extensive study investigated the effect of adenosine-lidocaine-magnesium polarizing cardioplegia in humans and found superior myocardial protection compared to Buckberg depolarized cardioplegia [11].

Recently, members of our group showed ameliorated energy metabolism in terms of increased ATP and phosphocreatine concentration during reperfusion with polarizing

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compared to depolarizing cardioplegia in a porcine model of cardiopulmonary bypass [12]. Similarly, an increased dP/dt_{max} with STH-pol as an indicator for preserved contractility has been observed [13]. Accordingly, we were able to demonstrate that LVSP, CF and external heart work parameters reveal favorable results with STH-pol[4]. We designed the present study in order to address the needs of patients with reduced ejection fraction following myocardial infarction requiring cardiac surgery. We believe that the new STH-pol cardioplegia presents itself as the most promising candidate to advance in the field of cardioplegia and myocardial protection and hence hypothesized that polarized myocardial protection will at least deliver comparable results as depolarizing arrest in an experimental study on isolated rat hearts with chronic myocardial infarction.

Methods and materials

Animals

We used male adult Sprague-Dawley rats (612 ± 13g, day of sacrifice, age of 16-18 weeks) (Department for Laboratory Animal Science and Genetics, Himberg, Austria). The experimental protocol was approved by the University Ethics Committee for Laboratory Animal Experiments at the Medical University of Vienna and the Austrian Ministry of Science Research and Economy (GZ 2020-0.380.434) and conforms with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996).

Surgical setup and anesthesia

For induction of MI, the rats were administered anesthesia (100 mg/kg ketamine and 5 mg/kg xylazine intraperitoneally) and maintained with 1.5-2% isoflurane. For analgesia, the animals were provided with piritramide-water (2 ampoules of piritramide + 30 ml of 5% glucose in 250 ml of water ad libitum) from 24 hours before the surgery to ensure sufficient analgesic levels prior to the surgery and to minimize postoperative pain development. After anesthetizing, the animals were intubated with a 14 G tube and ventilated with a mixture of isoflurane (1.5%) and O_2 at a rate of 80 strokes per minute, 100 mL/stroke/BW HSE (Ugo Basile, 7025 Rodent Ventilator). The rats were fixed in a supine position on a heating pad. After shaving the thorax and applying antiseptic povidone-iodine solution (Betaisodona Lösung, Mundipharma, Wien, Österreich), eye ointment (Fresenius Kabi Austria) was used and the animals were

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given piritramide (0.1ml/kg BW) intraperitoneally. ECG electrodes were then placed subcutaneously in the extremities of the rats. Importantly, before starting any operational steps, toe and tail reflexes were assessed [14].

Surgical procedure

After skin incision from the left midaxillary line at the fifth intercostal space (ICS) diagonally to the right anterior axillary line at the second ICS, a thoracotomy was performed at the fourth ICS and the LAD was occluded shortly beneath the left auricle with a 6-0 suture. Immediately, changes in color of the myocardium as well as ECG changes could be observed after successful ligation. If unethical endpoints such as edema or immobility were observed within the next few days, animals were sacrificed by an overdose of ketamine/xylazine and excluded from further experiments.

Experimental protocol and *ex-vivo* experiments

Six weeks after the MI induction, echocardiography was performed under light anesthesia prior to organ harvesting as described by Podesser et al [15]. Only animals with an ejection fraction of less than 70% were included in the present study.

For the isolated working heart experiments, the rats were deeply anaesthetized (100 mg/kg ketamine and 5 mg/kg xylazine i.p) and the hearts harvested. Hemodynamic parameters were measured in an isolated, erythrocyte-perfused working heart apparatus (Hugo Sachs Elektronik, Germany), as described by Podesser et al [15]. Pressure and temperature amplifiers with transducers and Haemosys Data Acquisition software were acquired by MDE Technologies GmbH (Germany, Münich) and used for data collection.

In short, every heart underwent 15 minutes of Langendorff mode (LD1) equilibration, followed by cannulation of the left atrium and beginning of antegrade perfusion in the working heart mode (WH1), where heart rate, left atrial pressure, aortic pressure, left ventricular systolic pressure, cardiac output (equals left atrial flow in an isolated Working Heart system) and coronary flow were continuously recorded. Afterload was set at 60 mm Hg, based on previous experiments [14]. In case of bradycardia (heart rate less than 200 bpm) the hearts were paced to 220 bpm. After 30 min of perfusion in WH1, hearts were arrested either with cold (4^{o}C) St Thomas' Hospital polarizing blood

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cardioplegia (STH-pol) or cold (4ºC) St Thomas' Hospital 2 blood cardioplegia (STH-control) at 50 mm Hg to induce cardiac arrest (7mL). Respective cardioplegia was re-administered every 20 min (5 mL). The heart remained arrested for 60 min, then reperfusion was started with oxygenated warm blood (37 ºC). During reperfusion, the heart again underwent 15 min of LD mode (LD2) and 30 min of WH mode (WH2). The hemodynamic parameters in the WH mode were continuously recorded accordingly to pre-ischemia. Stroke volume is calculated as cardiac output normalized to heart weight divided by heart rate. Stroke work is calculated as cardiac output multiplied by the left ventricular systolic pressure (LVSP).

After 45 min of reperfusion, hearts were subject to pump-function tests. Here, the afterload was increased in steps of 10 mm Hg every 30 seconds, beginning at 30 mm Hg, while hemodynamic parameters were measured. Afterwards, freeze-clamp biopsies (freeze-clamps were precooled in liquid nitrogen) of the non-infarcted interventricular septum of five animals from the STH-pol and STH-control group were quickly taken for analysis of high-energy phosphates (HEP) and stored at -80 °C prior to analysis. Five animals without myocardial infarction and without 60 minutes of ischemia served as an additional control group. Sample preparation and HPLC evaluation of high energy phosphates (HEP) were performed as previously described by Kramer et al. [16]. The energy charge (EC) was calculated according to the formula:

$EC = (ATP + ½\ ADP) / (ATP + ADP + AMP)$

Blood gas analysis was performed at 5 minutes after onset of WH1 and WH2. Myocardial oxygen consumption (MVO_2) was calculated according to Fick's law:

$Saturation_{(a-v)}\ O_2 \times C_{Hb} \times 1.34\ mL/g \times (CF / heart\ weight \times 100)$

Cardioplegic solutions

For the experiment, either St Thomas' Hospital polarizing cardioplegia (STH-pol) or, as control, St Thomas' Hospital 2 cardioplegia (STH-control) was used to induce cardiac arrest in the isolated working heart system. STH-pol consisted of 1 mmol/L esmolol, 0.5 mmol/L adenosine, 10 mmol/L magnesium chloride and 154 mmol/L NaCl; STH-control consisted of 16 mmol/L potassium, 110 mmol/L sodium, 1.2 mmol/L calcium, 16 mmol/L magnesium and 160 mmol/L chloride (after dilution with erythrocyte buffer). The two solutions are listed in Table 1. Both solutions (10ml) were mixed with 40 ml cold (4ºC) erythrocyte buffer immediately prior to administration.

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Statistical analysis

During *ex vivo* experiments, data was continuously recorded. Data are presented as means ± SEM. Two-way ANOVA was used when the same animal was followed up over time, providing several different p-values (time x treatment, time, treatment and for each timepoint) to identify significantly different values between the two study groups at different time points and Post-hoc test (Šídák correction). For comparisons within a group and for comparisons of individual parameters (e.g. biochemical data) between groups, a paired or unpaired t-test was used. For categorical data, Chi-square test was used. Normal distribution was checked for with the Shapiro-Wilk test. In case that a parameter did not pass the normality test, Geisser-Greenhouse correction was used. P values < 0.05 were considered significant.

MI was induced in 43 male Sprague-Dawley rats, of which eleven died immediately after LAD ligation. Six animals were excluded because of preserved ejection fraction greater than 70% (small myocardial infarctions, as measured by echocardiography). The remaining animals (n=26) were randomized to receive either treatment or control. Eight animals did not complete the experiment because preischemic cardiac output was too low (<5 ml/min) and therefore were excluded before receiving either treatment or control (5 STH-control; 3 STH-pol). The remaining 18 animals finished the protocol and were included in the analysis.

Data was recorded and saved on Sel Advance Haemosys Software and transferred into a separate Excel sheet (Microsoft Excel 2019 for MacOS, version 16.70, Microsoft Corporation, Redmond, USA). Statistical analysis and drawing of graphs were performed with GraphPad Prism (Prism 9 version 9.3.1).

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Results

Animal characteristics are described in Table 2. As noted in Table 2, left ventricular ejection fraction was comparable in both cardioplegic groups (67.4 ± 1.7 vs 63 ± 3.1 STH-pol vs STH-control; p=0.22). Previous experiments from our group have shown that healthy male Sprague Dawley rats have an ejection fraction of 80%[14]. Infarcted animals had significantly impaired LVSP and SV compared to healthy animals at baseline (Supplementary Fig S1). Therefore, the results from the present study indicate severe reduction of left ventricular function in both cardioplegic groups. No difference in time to asystole (p=0.99) was observed. One animal in the STH-pol group developed arrythmias compared to three animals in the STH-control group (p=0.21) (S2). While the total amount of arrhythmic periods (in min) in all animals was higher in the STH-control group, the difference was not significant (p=0.35) (S2). Four animals had to be paced to 220 bpm in the early phase of reperfusion in the STH-pol group in comparison to one animal in the STH-control group (p=0.15) (S2).

Hemodynamic parameters

Hemodynamic parameters were measured continuously during WH1, the last measurement before ischemia is given as *baseline,* listed in Table 3. Notably, there was no significant difference in baseline values between the two groups across all parameters.

During reperfusion, hearts recovered, and the parameters are presented as absolute values after 30 min of WH2 (WH2 30') in Table 3. Although there was no significant difference across all timepoints, STH-pol preserved hearts showed higher values in all parameters except HR, with a tendency towards better preservation of CF (WH2 5': p=0.29) and LVSP (WH2 10': p=0.33) (Fig 1)

Pump-function

At the end of the experiment (45 min of reperfusion), the hearts underwent pump-function assessment (Fig 2). Starting with an afterload of 30 mmHg, CO and LVSP were continuously recorded. At 110 mm Hg afterload, both cardioplegic groups were comparable with a mean flow of 27 ± 19 ml/min with STH-pol and 24.3 ± 8.1 ml/min with STH-control (p=0.90). There was also no statistically significant difference among the two groups regarding LVSP. At 110 mmHg afterload mean LVSP was 121.3 ± 5.9

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mmHg with STH-pol and 122.5 ± 1.5 mmHg with STH-control (p=0.89), respectively. On average, the reached afterload (value where CO has stopped) was 87.8 ± 9.1 mmHg in the STH-pol group and 100 ± 9.6 mm Hg in the STH-control group (p=0.37).

Blood gas analysis

Blood gas analysis was performed at 5 minutes after onset of WH1 and WH2 (Fig 3). The hematocrit of the buffer solution was 39.5 ± 0.8. Baseline MVO_2 was comparable in both groups (STH-pol: 12.7 ± 0.8 ml/min/100g; STH-control: 10.8 ± 0.5 ml/min/100g). After ischemia, MVO_2 fell to 9.9 ± 0.4 and 10.1 ± 0.4 ml/min/100g respectively compared to baseline; hence a reduction in the STH-pol group of 2.8 ± 0.6 ml/min/100g: 22%), which was significantly greater than the reduction in the STH-control group (of 0.7 ± 0.7 ml/min/100g: 6%) (p=0.04).
There was no significant difference between pre- and postischemic pH-values in both groups (STH-pol: 7.4 ± 0.01 vs. 7.4 ± 0.01, p=0.93; STH-control: 7.4 ± 0.01 vs. 7.4 ± 0.01, p=0.83).

High energy phosphates

As depicted in Fig 4, mean PCr values were not significantly different between treatment groups and significantly reduced as compared to sham animals without MI and ischemia (28.9 ± 4.9 nmol/mg protein, $p < 0.0001$). Similar, ATP values and energy charge did not differ significantly between treatment groups. These values were significantly reduced compared to sham (Fig. 4: panel A and D). Xanthine and hypoxanthine showed increased values in both cardioplegic treatment groups compared to sham, but only hypoxanthine reached the level of significance (panel C). The protein/wet weight ratio revealed no significant difference between the two treated groups (STH-pol: 9.5 ± 0.5 %; STH-control: 8.8 ± 0.4 %) (panel B). However, the sham group showed a significantly higher protein/wet weight ratio compared to the STH-control group (control: 10.8 ± 0.6, p=0.02).

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Discussion

This current experimental study is the first to investigate the efficacy of the novel STH-pol cardioplegia in a setting of cardioplegic arrest in rat hearts with chronic MI, thereby mimicking a patient with ischemic cardiomyopathy undergoing elective cardiac surgery. Our results indicate that there was no statistically significant difference in myocardial protection between the novel STH-pol cardioplegia and a clinically relevant, standard cold blood cardioplegia (STH-control).

This is important novel information, as so far, both small and large animal experiments were only performed on healthy myocardium without prior ischemic damage. It is important to stress that left ventricular dysfunction of the two groups was comparable prior to cardioplegic arrest. Healthy adult rats have an ejection fraction of about 80% [14]. In our study the hearts had a reduced ejection fraction (less than 70%) due to preceding MI. Of note, we did not observe any significant difference between the two cardioplegic solutions at any timepoint during the reperfusion period or in pump function. This is in contrast to our previously published study on healthy pigs, where we found superior protection of systolic and diastolic function and improved protection of the metabolic status of the heart in STH-pol protected hearts [4]. Similarly, another large animal study demonstrated increased LV-dP/dtmax with STH-pol after reperfusion [13]. However, Aass *et al* also used healthy animals and it has to be mentioned that significant changes were only seen at a later time point of reperfusion, namely after 165-180 minutes.

Kramer et al. have recently investigated the effect of normothermic (34°C) STH-pol in healthy pig hearts and found a decreased metabolic and hemodynamic efficacy in comparison to depolarizing cardioplegic arrest [16]. Based on this study the temperature of 4°C was chosen.

In the present study, CF showed a tendency towards a faster recovery in the STH-pol group during early reperfusion without reaching statistical significance (p=0.29) and may indicate an ameliorated flow reserve with STH-pol. This finding may be due to the well-known vasodilative effect of adenosine on the coronary arteries. This was also seen in a previous experimental study, where adenosine cardioplegia increased cardiac output during early reperfusion [17]. Our surrogate end-point parameter LVSP also showed a tendency towards a better recovery with STH-pol during early reperfusion (p=0.33). Potentially this is a result of improved coronary perfusion, also

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caused by the vasodilative effect of adenosine. During early reperfusion, we observed more arrhythmias in the STH-control compared to the STH-pol group (S1). This can be attributed to the high potassium concentration of the STH cardioplegia [18]. Another explanation are the well-known antiarrhythmic and negative chronotropic effects of esmolol, which have been observed in the STH-pol group as well as by others [19]. Conversely, we found that more hearts in the STH-pol group required pacing.

Another interesting finding was the significantly higher MVO_2 reduction in the STH-pol group compared with the STH-group. This may be due to a reduced energy demand during ischemia in the STH-pol group which is reflected by a slightly better preservation of LV hemodynamics at the early phase of reperfusion. Depolarized arrest is associated with increased energy demand due to Ca^{2+}-overload with resulting hypercontractility [3]. This has been observed clinically in patients with myocardial stunning [20].

Freeze-clamp biopsies of the non-infarcted septum were taken at the end of the protocol for analysis of high energy phosphates. In our study, we could not observe a significant difference of HEP between the two study groups. One can speculate that due to the chronic myocardial infarction, the 60 minutes ischemia and the cardiac stress at pump-function evaluation, the PCr and ATP levels in the terminal state of this model are too low to observe any protective effect of the polarizing cardioplegia. Comparing the HEPs sham animals, the reduction of PCr and ATP was significant. The energy charge reveals the unfavorable overall metabolism in the STH-pol and STH-control at the termination of the experiment compared to sham animals. This underlines the severity of this animal model and is in line with the substantial decrease of most hemodynamic parameters during reperfusion. Taken together, our findings provide important translational insights, as they suggest that the use of STH-pol cardioplegia may offer comparable myocardial protection even in hearts with pre-existing ischemic injury — a condition frequently encountered in clinical cardiac surgery. This is of particular relevance for patients with ischemic cardiomyopathy undergoing procedures such as coronary artery bypass grafting, where optimal myocardial protection remains a key challenge. Future studies in large animal models with chronic myocardial injury and ultimately clinical trials will be essential to confirm these results and to establish the safety and efficacy of STH-pol cardioplegia in the human surgical setting.

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Limitations

Apart from species differences, this study has certain limitations. First, the hemodynamic parameters were measured in an isolated working heart that allows perfusion but does not replace *in vivo* conditions. The model used is artificial and therefore may limit the translational potential of the findings. However, the isolated heart is one of the most widely used ex-vivo model to describe the function of the heart independently of the rest of the organism. Our system could not directly measure the Dp/Dt and contractility therefore lacks interpretation. Further, we used only male rats, sex-differences cannot be ruled out.

Moreover, we were using rat hearts with significantly impaired LV ejection fraction. For this reason, we were unable to extend ischemia for more than one hour; preliminary studies on 120 min of global ischemia failed in our experimental model.

Conclusion

In conclusion, we demonstrated for the first time that there is no statistically significant difference in myocardial protection between St Thomas' Hospital polarizing cold blood cardioplegia and a clinically relevant, standard cold blood cardioplegia (St Thomas' Hospital No. 2 cardioplegia) in rat hearts with chronic ischemic heart disease. Further studies are needed to show the impact and efficacy of St Thomas' Hospital polarizing cold blood cardioplegia in preservation of ultrastructure or in pressure-overloaded hearts.

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Authors contribution statement

L.W., A.K. and B.K.P. conceived and designed research; L.W., M.I., P.L.S. and S.H. performed experiments; L.W. and A.K. analyzed data; L.W., P.L.S., M.I., L.W., S.H., A.K., D.J.C and B.K.P interpreted results of experiments; L.W. and P.L.S prepared figures, S.H., A.K., D.J.C and B.K.P edited and revised manuscript; L.W., P.L.S., M.I., L.W., S.H., A.K., D.J.C and B.K.P approved final version of manuscript.

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Conflict of Interest:

David J. Chambers is co-inventor of the STH-Pol solution. All other authors have nothing to disclose with regard to commercial support.

Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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Figure legend

Figure 1: Hemodynamics

Stroke volume (panel A) (p-value: time x treatment: 0.99; time: <0.0001; treatment: 0.03)

Left ventricular systolic pressure (panel B) (p-value: time x treatment: 0.68; time: <0.0001; treatment: 0.15)

Heart rate (panel C) (p-value: time x treatment: 0.99; time: 0.93; treatment: 0.18)

Coronary flow per heart weight (panel D) (p-value: time x treatment: 0.76; time: <0.0001; treatment: 0.03)

Data are given as mean ± SEM; mmHg= millimeter mercury; mL=milliliter; bpm= beats per minute; mL/min/HW= milliliter per minute per heart weight (in g)

Figure 2: Pump-function curves

Cardiac Output with afterload (CO - panel A), reached afterload in mmHg (panel B) and the left ventricular systolic pressure with afterload (LVSP - panel C)

Data are presented as mean ± SEM

Figure 3: Blood gas analysis

Reduction of Myocardial oxygen consumption (MVO_2 - panel A) and pH (panel B)

*Data are presented as mean ± SEM; *p =0.04*

Figure 4: Biochemical evaluation

High-energy phosphates (panel A), protein/wet weight ratio (panel B), xanthine and hypoxanthine levels (panel C)), energy charge (panel D)

*PCr= phosphocreatine, AMP= adenosine monophosphate, ADP= adenosine diphosphate, ATP= adenosine triphosphate. Data are presented as mean ± SEM; * p < 0.05; ** p < 0.01, *** p < 0.001, **** p < 0.0001*

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Table 1: Composition of STH-pol and STH-2 cardioplegia solution after mixing with erythrocyte buffer

components	STH-pol (mmol/L)	STH-control (mmol/L)
potassium	-	16
sodium	154	110
calcium	-	1.2
esmolol	1	-
adenosine	0.5	-
magnesium	10	16
chloride	154	160

STH-pol group and STH-control group

Table 2: Animal characteristics

	STH-pol (n=10)	STH-control (n=8)	p-value
Body weight (g)	627.3 ± 20	594.2 ± 15	0.21
Heart weight (g)	2.6 ± 0.1	2.6 ± 0.1	0.88
Time to asystole (sec)	62.9 ± 10.0	63.1 ± 7.0	0.99
Arrhythmias	1	3	0.21
Pacing	4	1	0.15
Ejection fraction (%)	67.4 ± 1.7	63 ± 3.1	0.22

STH-pol group vs. STH-control group, given as mean ± SEM;

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Table 3: Hemodynamic parameters before cardioplegic arrest (baseline) and after 30 min of WH2

Variable	STH-pol vs STH-control (baseline)	p-value	STH-pol vs STH-control (WH2 30')	p-value
CO (ml/min)	92.6 ± 10.7 vs. 80.9 ± 6.5	0.95	33.8 ± 10.7 vs. 37.2 ± 7.5	> 0.99
CF/HW (ml/min/HW)	4.7 ± 0.2 vs. 4.1 ± 0.2	0.82	2.8 ± 0.4 vs. 2.8 ± 0.4	> 0.99
HR (beats/min)	297 ± 22 vs. 287 ± 19	>0.99	260 ± 22 vs. 275 ± 20	>0.99
LVSP (mmHg)	109.1 ± 3.4 vs. 103.3 ± 3.6	0.94	91.2 ± 3.7 vs. 82.8 ± 5.5	0.7
SV (ml)	0.137 ± 0.009 vs. 0.123 ± 0.01	0.98	0.07 ± 0.02 vs. 0.06 ± 0.01	> 0.99
SW (LVSP x CO, mmHg/ml)	4423 ± 362 vs. 3650 ± 462	0.77	1440 ± 367 vs. 1500 ± 494	>0.99
CO/HW (ml/min/HW)	40.3 ± 2.7 vs. 35.4 ± 2.6	0.86	15.2 ± 3.3 vs. 16.2 ± 3.2	>0.99

STH-pol group vs. STH-control group; given as mean ± SEM; CO=p; CF/HW= coronary flow per heart weight; HR= heart rate; LVSP= left ventricular systolic pressure; SV= stroke volume; SW= stroke work; CO= cardiac output

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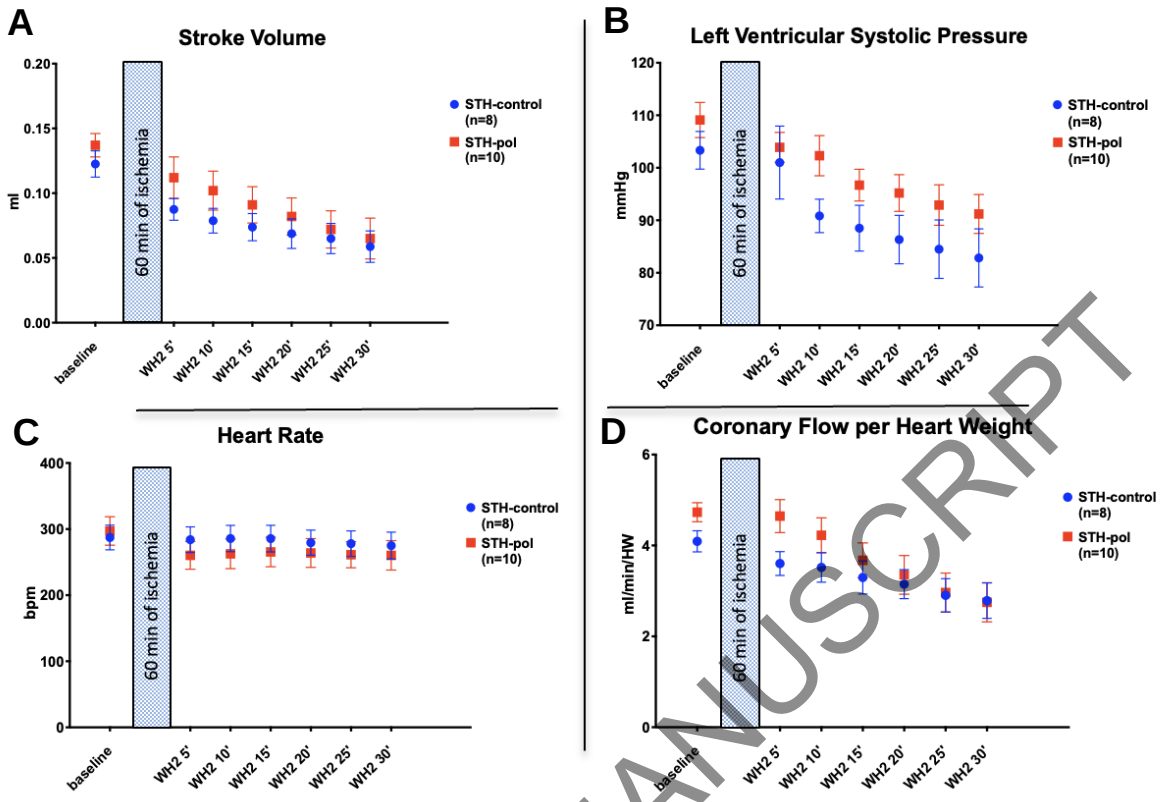

Figure 1: Hemodynamics

Stroke volume (panel A) (p-value: time x treatment: 0.99; time: <0.0001; treatment: 0.03)

Left ventricular systolic pressure (panel B) (p-value: time x treatment: 0.68; time: <0.0001; treatment: 0.15)

Heart rate (panel C) (p-value: time x treatment: 0.99; time: 0.93; treatment: 0.18)

Coronary flow per heart weight (panel D) (p-value: time x treatment: 0.76; time: <0.0001; treatment: 0.03)

Data are given as mean ± SEM; mmHg= millimeter mercury; mL=milliliter; bpm= beats per minute; mL/min/HW= milliliter per minute per heart weight (in g)

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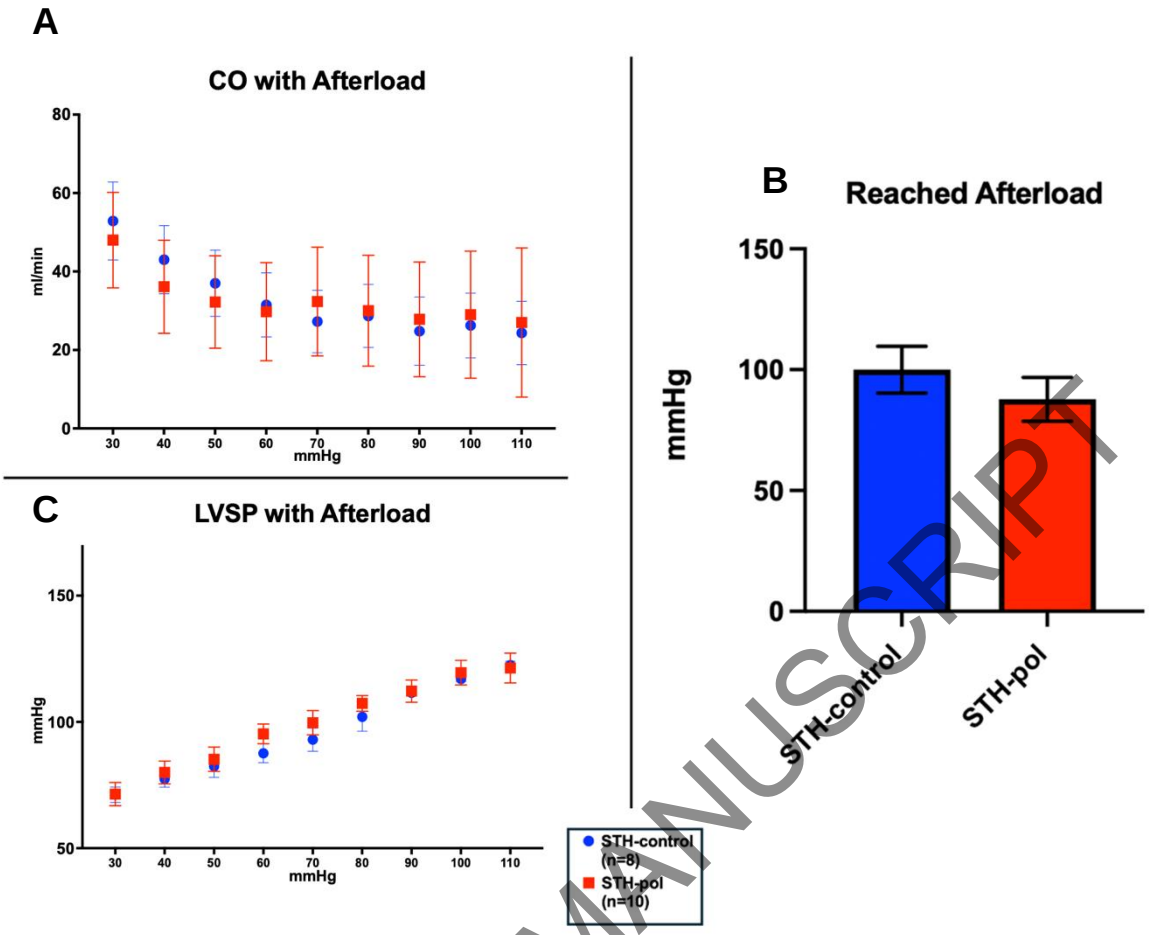

Figure 2: Pump-function curves

Cardiac Output with afterload (CO - panel A), reached afterload in mmHg (panel B) and the left ventricular systolic pressure with afterload (LVSP - panel C)

Data are presented as mean ± SEM

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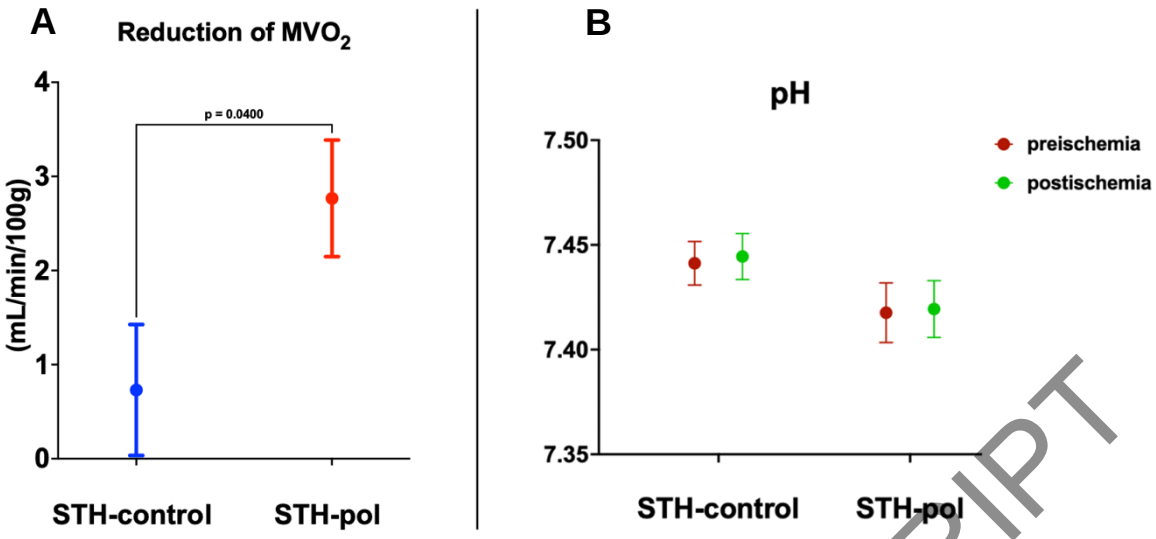

Figure 3: Blood gas analysis

Reduction of Myocardial oxygen consumption (MVO_2 - panel A) and pH (panel B)

Data are presented as mean ± SEM

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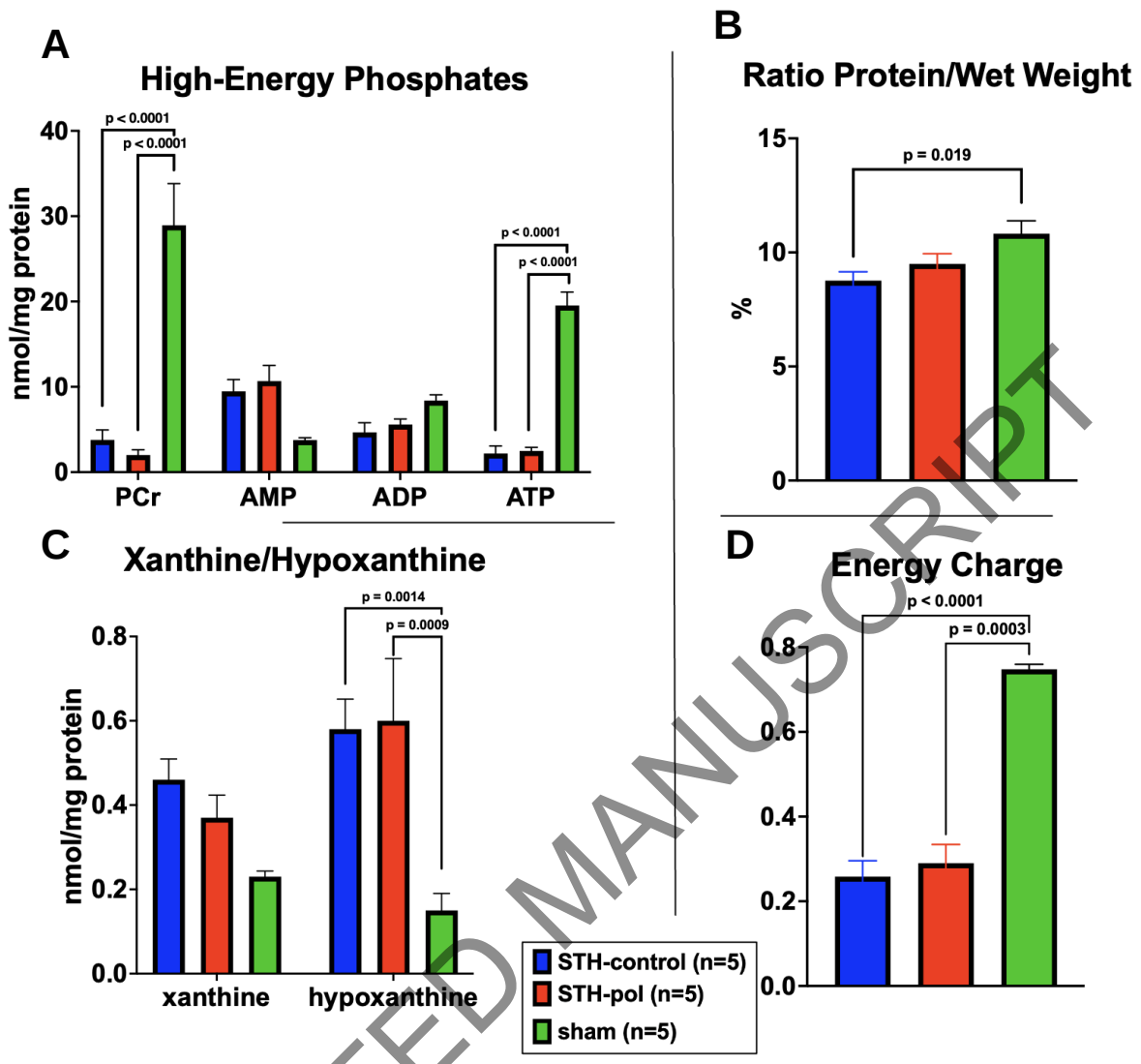

Figure 4: Biochemical evaluation

High-energy phosphates (panel A), protein/wet weight ratio (panel B), xanthine and hypoxanthine levels (panel C)), energy charge (panel D)

PCr= phosphocreatine, AMP= adenosine monophosphate, ADP= adenosine diphosphate, ATP= adenosine triphosphate. Data are presented as mean ± SEM

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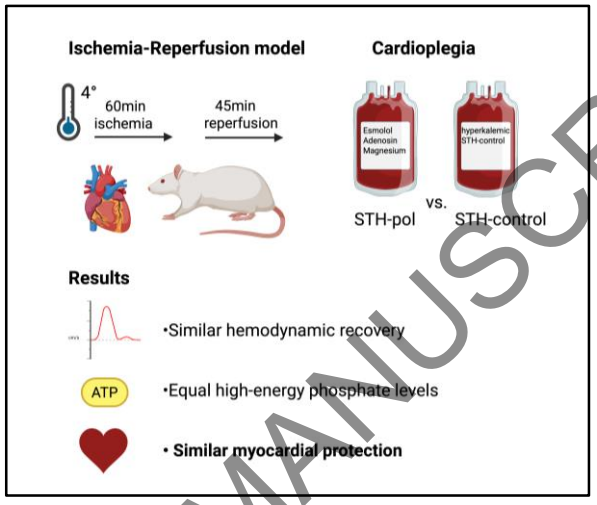
The novel St Thomas' Hospital polarizing blood cardioplegia: Results in hearts with reduced ejection fraction

Summary

In an experimental study we investigated the effect of a novel polarizing cold blood cardioplegia in rats with ischemic heart disease and compared it to a standard depolarizing cardioplegia. We looked at the effects on the hemodynamics and energy metabolism. In cocnlusion, the two solutions provided similar myocardial protection.



Legend: LVSP: adenosine diphosphate; ATP: Adenosine triphosphate STH: St Thomas' Hospital

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