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Histidine-Tryptophan-Ketoglutarate Solution versus Blood Cardioplegia in Cardiac Surgery: A Propensity-Score Matched Analysis

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ABSTRACT

Background: Choosing a cardioplegic solution is a significant issue in modern cardiac surgery. Although different options are available, the optimal strategy for myocardial protection has not been established. The aim of this study was to compare intraoperative and postoperative effects of histidine–tryptophan–ketoglutarate (HTK) solution with those of standard blood cardioplegia with St Thomas No 2 solution. The study was conducted using a large cohort of adult patients undergoing complex cardiac surgery.

Methods: This study was a single center retrospective review of prospectively collected data. Between January 2008 and December 2015, 4480 patients underwent cardiac surgery using cardiopulmonary bypass (CPB) and cardioplegic arrest. Patients were divided into a blood cardioplegia group (n = 3852) and an HTK solution group (n = 628). Propensity score matching was used to adjust for differences between the two groups, and 292 matched pairs were identified. The primary end point was Intensive Care Unit (ICU) length of stay (LOS). Secondary end points included intraoperative changes in serum sodium concentration, readmission to ICU, transfusion of blood products, 30-day hospital readmission, 30-day mortality, and the incidence of major postoperative complications.

Results: No significant differences were found between the matched groups with regard to baseline characteristics. Aortic cross-clamp and CPB times were longer for the blood cardioplegia (147.4 versus 132.8 min; $P < .001$). Administration of HTK solution was associated with acute and transient hyponatremia (141 versus 130 mmol/L; $P < .001$). ICU LOS was comparable between the groups (5.4 versus 5.4 days; $P = .585$). No significant differences were noted in any other secondary end point.

Conclusions: During complex cardiac surgery, both cardioplegia techniques were equivalent in terms of early clinical outcomes.

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INTRODUCTION

Myocardial preservation constitutes an essential adjunctive on modern cardiac surgery, in which the selection of a cardioplegic solution plays an important role. Cardioplegic solutions decrease the metabolic demands of the heart and protect the myocardium by preserving the intracellular reserves of energy, as well as avoiding osmotic, electrolytic, and pH imbalances [Yamamoto 2013].

The cardioplegic solutions currently used can be divided into two classes according to their electrolytic composition: the extracellular-type, and the intracellular-type [Chambers 2003]. Extracellular solutions are based on the normal ionic concentrations found in plasma, with moderately elevated potassium concentrations, and in some cases, increases in magnesium concentration. The moderate elevation of extracellular potassium occurring after its administration results in a change in the resting membrane potential of the myocyte, which inactivates the voltage-dependent fast sodium channels, inhibits the generation of the action potential, and produces depolarized cardiac arrest. The St. Thomas solution No 2 is one of the most widely used cardioplegic solutions (Table 1). It is commonly used with patient's blood as a vehicle and is typically infused every 20–30 minutes [Karthik 2004; Jynge 1981].

Histidine–tryptophan–ketoglutarate (HTK), or Bretschneider solution, is an example of intracellular cardioplegia characterized by a low sodium and calcium content (Table 1). The reduction in the extracellular sodium concentration minimizes the transsarcolemal gradients of this ion, hyperpolarizes the plasma membrane and produces cardiac arrest in diastole. The HTK solution also contains histidine, which acts as a buffer, tryptophan as a cell membrane stabilizer, ketoglutarate in order to improve the production of ATP, and mannitol as a free radical scavenger [Bretschneider 1980]. This solution is given as a single dose and is believed to offer adequate myocardial protection for up to three hours. In many countries, it is used not only as a cardioplegic solution, but also as an organ-preserving solution in transplant surgery [Fridell 2009].

Despite its frequent use, there are relatively few studies comparing the efficacy of the HTK solution against other common forms of cardioplegic solutions.[Edelman 2013] Most studies suffer from low sample volume or are limited to a single surgical procedure, such as coronary artery bypass

Table 1. Composition of Cardioplegia Solutions

Component	St Thomas Solution No 2	HTK Solution
Na+ (mmol/L)	110	15
Cl- (mmol/L)	160	50
K+ (mmol(L)	16	9
Mg++ (mmol/L)	32	4
Ca++ (mmol/L)	24	0.015
Ketoglutarate (mmol/L)	-	1
Tryptophan (mmol/L)	-	2
Histidine (mmol/L)	-	198
Manitol (mmol/L)	-	30
Osmolality (mOsmol/kg)	304	300

HTK indicates Histidine-Tryptophan-Ketoglutarate

grafting (CABG) or valvular surgery [De Palo 2017; Matzelle 2014; Guadino 2013; Sansone 2012; Braathen 2011; Scrascia 2011; Demmy 2008]. The aim of this study was to compare the intraoperative and postoperative effects of HTK solution administration with those obtained after the application of standard blood cardioplegia in a large cohort of adult patients undergoing complex cardiac surgery.

MATERIALS AND METHODS

Study Population

This study was a single-center retrospective review of prospectively collected data. The institutional review board of the Fundación CardioInfantil approved the study, and because of the retrospective design and the fact that the information was collected from electronic medical records, the need for individual informed consent was waived. Using the Cardiovascular Surgical database that follows the guidelines of the Society of Thoracic Surgery database, as well as the review of electronic clinical records, we identified all adult patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) from January 1 2008 to December 31 2015. Patients placed on CPB without the use of a cardioplegic arrest were excluded.

During this time two types of cardioplegia strategies were used in our institution: standard blood cardioplegia constituted by patients' blood mixed with St Thomas No 2 solution (Plegisol® Hospira Inc., Lake Forest, IL, USA), and HTK solution (Custodiol®, Dr. Franz Kohler Chemie GMBH, Bensheim, Germany). Selection criteria for blood cardioplegia versus HTK solution were made according to the surgeon and anesthesiologist preference, as well as the characteristics of the surgical procedure. The use of blood cardioplegia was the cardioplegic strategy predominantly used throughout the study period. The general tendency was not to use HTK solution in patients with a low risk of complications (correction of atrial septal defect, atrial myxoma resection) or in patients

Table 2. Preoperative and Operative Characteristics for the Original Cohort

Variable	Blood Cardioplegia (n = 3852)	HTK Solution (n = 628)	*P*
Age (years)	62.2±12.9	57.9 ± 14.9	< .001
Male gender	2689 (69.8)	371 (59.1)	< .001
Body mass index	25.8±4.1	25.2 ± 4.1	.001
Hypertension	2343 (60.8)	325 (51.8)	< .001
Diabetes	943 (24.5)	79 (12.9)	< .001
Dyslipidemia	1464 (38.0)	110 (17.5)	< .001
Myocardial infarction	1415 (36.7)	73 (11.6)	< .001
Active endocarditis	101 (2.6)	57 (9.1)	< .001
CHF	370 (9.6)	133 (21.2)	< .001
Cerebrovascular disease	147 (3.7)	35 (5.6)	.05
COPD	272 (7.1)	39 (6.2)	.709
EF (%)	49.1 ± 12.0	50.5 ± 13.1	.023
Creatinine (mg/dL)	1.06 ± 1.3	1.19 ± 1.3	.009
Hematocrit (%)	42.4 ± 6.3	41.8 ± 7.0	.140
NYHA functional class			
I	364 (9.4)	66 (10.5)	< .001
II	2770 (71.9)	395 (62.9)	< .001
III	656 (17.0)	138 (22.0)	< .001
IV	62 (1.6)	29 (4.6)	< .001
Surgical status			
Elective	1502 (39)	301 (48)	< .001
Urgent	2157 (56)	271 (43)	< .001
Emergent	193 (5)	56 (9)	< .001
Redo operation	191 (4.9)	107 (17)	< .001
Type of surgery			
Any tipe of valve surgery	1222 (31.7)	554 (88.2)	< .001
AV surgery	576 (15.0)	288 (45.9)	< .001
MV surgery	448 (11.6)	295 (47.0)	< .001
Tricuspid surgery	122 (3.2)	85 (13.5)	< .001
Double valve surgery	140 (4)	98 (16)	< .001
Triple valve sugery	25 (0.6)	13 (2.1)	< .001
MV surgery + CABG	215 (6)	54 (9)	< .001
Maze surgery	112 (18)	170 (4)	< .001
Aorta surgery*	322 (8.4)	138 (22.0)	< .001
Aorta + CABG/valve surgery	100 (3)	54 (9)	< .001
Other	469 (12)	38 (6)	< .001

Data are presented as mean ± standard deviation or n (%). CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; NYHA, New York Heart Association; CABG, coronary artery bypass grafting; AV, aortic valve; MV, mitral valve. *Ascending aorta, aortic arch and descending aorta.

Table 3. Preoperative and Operative Characteristics for the Matched Patients

Variable	Blood Cardioplegia (n = 292)	HTK Solution (n = 292)	*P*
Age (years)	58.7 ± 14	57.7 ± 15	.906
Male gender	188 (64.4)	168 (57.5)	.090
Body mass index	26.0 ± 4	25.3 ± 4	.117
Hypertension	161 (55.1)	155 (53.1)	.619
Diabetes	28 (9.6)	32 (11)	.586
Dyslipidemia	64 (21.9)	47 (16.1)	.073
Myocardial infarction	44 (15.0)	29 (9.9)	.061
Active endocarditis	24 (8.2)	23 (7.9)	.879
CHF	57 (19.5)	62 (21.2)	.608
Cerebrovascular disease	14 (4.8)	15 (5.1)	.899
COPD	23 (7.8)	15 (5.1)	.180
EF (%)	49.0 ± 13.1	50.6 ± 12.8	.179
Creatinine (mg/dL)	1.01 ± 0.5	1.13 ± 0.9	.013
Hematocrit (%)	41.6 ± 7.4	40.9 ± 6.9	.690
NYHA functional class			
I	23 (7.9)	31 (10.5)	.254
II	185 (63.4)	196 (66.4)	.150
III	77 (26.4)	58 (19.9)	.062
IV	7 (2.4)	9 (3.1)	.613
Surgical status			
Elective	130 (44.5)	138 (47.3)	.411
Urgent	141 (48.3)	121 (41.4)	.096
Emergent	21 (7.2)	33 (11.3)	.086
Redo operation	60 (20.6)	56 (19.2)	.679
Type of surgery			
Any tipe of valve surgery	279 (96)	275(95)	.568
AV surgery	144 (49)	137 (47)	.562
MV surgery	153 (52)	149 (51)	.741
Tricuspid surgery	45 (15)	46 (16)	.909
Double valve surgery	49 (17)	47 (16)	.823
Triple valve sugery	7 (2)	10 (3)	.460
MV surgery + CABG	37 (13)	29 (10)	.296
Maze surgery	56 (19)	40 (14)	.074
Aorta surgery*	87 (30)	71 (24)	.137
Aorta + CABG/valve surgery	28 (10)	35 (12)	.350
Other	22 (8)	17 (6)	.407

Data are presented as mean ± standard deviation or n (%). CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; NYHA, New York Heart Association; CABG, coronary artery bypass grafting; AV, aortic valve; MV, mitral valve. *Ascending aorta, aortic arch and descending aorta.

who underwent isolated myocardial revascularization.

Conduct of Procedure

Anesthetic management: Balanced general anesthesia with fentanyl (10–20 µg/kg), midazolam (0.1 mg/kg), propofol (0.5-4 mg/kg), pancuronium (0.1–0.2 mg/kg) or rocuronium (0.6–0.9 mg/kg), and isoflurane (0.5–1.5%) or sevofluorane (1.5–4.5%) was employed. Patients were routinely monitored with an arterial line and central venous pressure, or pulmonary artery catheters depending on the anesthesiologist's criteria. They were selectively monitored with transesophageal echocardiography.

Surgical Procedure: A wide range of cardiac surgery procedures were performed by six surgeons during the study period. Patients were placed on CPB following standardized protocol at the Fundación CardioInfantil. After systemic anticoagulation with heparin (ACT > 400 s), CPB was established via an arterial cannula inserted in the ascending aorta/aortic arch or femoral artery, and venous drainage was obtained via a single cannula placed in the right atrium, bicaval cannulation, or femoral vein. Body temperature was maintained between 30 and 34°C. When indicated, a deep hypothermic circulatory arrest was accomplished by cooling to 18°C with or without antegrade cerebral perfusion. Surgeries were performed mostly via a median sternotomy, and only in selected cases via a minimally invasive approach.

Cardioplegia Delivery: Under CPB and after aortic-cross clamping, standard cold (4–8°C) blood cardioplegia or HTK solution was used for myocardial protection. In the blood cardioplegia group, the first dose of 10–15 mL/kg was composed of patient's blood and St Thomas No 2 solution mixed at a ratio of 4:1 (blood: St Thomas No 2 solution), which was delivered antegradely into the aorta or in the coronary ostia at a perfusion pressure (delivery line pressure) of 100 to 120 mm Hg. Subsequently, 5–8 mL/kg of the same mixture was infused antegrade/retrogradely every 20–25 minutes until aortic unclamping. HTK solution was administered following the scheme described by Arslan et al [Arslan 2005]. Patients in this group received a single dose of 1 L of HTK solution infused via the aortic root or coronary ostia. The solution was administered at a temperature of 4–8°C. Perfusion pressure was maintained at 80–100 mmHg for approximately five minutes. Thereafter, a similar amount of HTK solution was given with any evidence of electrical or mechanical activity, or after three hours of aortic cross-clamping. No specific method was used to prevent entry of the HTK solution into the cardiopulmonary bypass circuit, such as aspiration from the coronary sinus or routine ultrafiltration use.

Study End Points

The primary end-point of the study was Intensive Care Unit (ICU) length of stay (LOS). Secondary end points included aortic cross-clamp time, CPB time, changes in serum sodium concentration, readmission to ICU, 30-day hospital readmission, 30-day mortality, blood product usage, and the incidence of major postoperative complications (prolonged [> 24 h] mechanical ventilation, acute renal failure, new onset dialysis, clinical stroke, re-exploration for bleeding,

Table 4. Operative and Clinical Outcomes for the Matched Patients

Variable	Blood Cardioplegia (n = 292)	HTK Solution (n = 292)	*P*
CPB time (min)	147.5 ± 47	132.8 ± 53	.001
Aortic cross-clamp time (min)	116.1 ± 37	98.5 ± 36	< .001
Intraoperative sodium (mmol/L)			
Before CPB	140.1 ± 3.9	140.5 ± 3.7	.277
First sodium after cardioplegia	135.4 ± 3.7	130 ± 5.7	< .001
Final CPB	137.7 ± 4.3	135.6 ± 3.7	< .001
POP day 1	138.6 ± 3.3	138.4 ± 3.4	.693
Primary outcome			
ICU LOS (days)	5.39 ± 8	5.43 ± 7	.585
Secondary outcomes			
IABP use	16 (5.5)	10 (3.4)	.093
Clinical stroke	4 (1.4)	7 (2.4)	.093
Prolonged (>24 h) ventilation	10 (3.4)	16 (5.5)	.311
New onset dialysis	5 (1.7)	3 (1)	.180
Sternal wound infection	4 (1.4)	7 (2.4)	.258
Perioperative Transfusion			
Red blood cells	139 (47.7)	148 (50.7)	.456
Fresh frozen plasma	54 (18.4)	70 (24.0)	.105
Platelets	61 (20.8)	68 (23.4)	.485
Cryoprecipitate	32 (10.9)	32 (10.9)	> .999
Total	172 (58.9)	169 (57.9)	.514
Reexploration for bleeding	54 (18)	58 (20)	.569
Readmission to ICU	10 (3.4)	7 (2.4)	.688
Postoperative LOS (d)	13.7 ± 19	11.9 ± 10	.270
30 day readmission	47 (16.1)	42 (14.4)	.596
30 day mortality	16 (5.5)	27 (9.3)	.188

Data are presented as mean ± standard deviation or n (%). CPB indicates cardioplulmonary bypass time; POP, postoperative; ICU, intensive care unit; LOS, length of stay; IABP, Intraaortic ballon pump.

deep sternal wound infection or post-operative intra-aortic balloon pump [IABP] implantation). All these outcomes were defined according to the criteria of The Society of Thoracic Surgeons National Database.

Statistical Analysis

Descriptive statistics on baseline variables in the unpaired groups were presented as mean ± standard deviation (SD) or median (range) for continuous variables, and frequency (percentage) for categorical variables. Baseline differences between custodial and blood cardioplegia groups were estimated by the χ^2 test, Fisher exact test, or Wilcoxon rank sum test, as appropriate. The propensity-score matching analysis was performed to reduce confounding bias between the groups secondary to non-randomization. A propensity score representing the probability of a patient to receive HTK solution or blood cardioplegia according to preoperative characteristics was calculated using a logistic regression model. The model was based on the type of cardioplegic solution used as a dependent binary variable, and the following preoperative covariates used as independent variables: age, sex, body mass index, hypertension, diabetes, dyslipidemia, previous myocardial infarction, endocarditis, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, New York Heart Association functional class, ejection fraction, creatinine, hematocrit, type of surgery performed, redo operation, and surgical status (elective, urgent, emergent).

The degree of collinearity of the covariates was estimated by calculating the inflation factor of variance, tolerance, and condition indexes. After obtaining propensity scores, the patients were paired in a 1:1 ratio using a greedy matching algorithm. The quality of the propensity-score matching in balancing the two groups was assessed by the Savage score test. The treatment effect in the matched sample was evaluated using logistic models or analysis of covariance (ANCOVA) according to the type of variable. The Kaplan-Meier survival analysis was used for time variables censoring the records in case of patient death. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA) with statistical significance set at the alpha level of 0.05.

RESULTS

Characteristics and Clinical Outcome for the Unmatched Cohort

During the study period, a total of 4480 patients underwent cardiac surgery using CPB and cardioplegic arrest. Of this population, 3852 patients (86%) received standard blood cardioplegia in a 4: 1 ratio and 628 patients (14%) received HTK solution. The preoperative clinical characteristics in both groups are shown in Table 2. Before matching, significant differences in demographic characteristics and comorbid diseases between the two groups were noted. The blood cardioplegia group was significantly older, and consisted of a greater number of men with a higher prevalence of hypertension, diabetes, dyslipidemia, history of myocardial infarction, and slightly lower values of ejection fraction. Active endocarditis, congestive heart failure, and higher values of creatinine were more prevalent in the HTK solution group. The unmatched blood cardioplegia cohort included more urgent/emergent operations (62% versus 52%; $P < .001$) and a lower percentage of redo procedures (4.9% versus 17%; $P < .001$). Regarding the procedures performed, valvular surgery of any kind (aortic, mitral or tricuspid) was more common in the HTK solution group (88.2% versus 31.7%, $P < .001$), whereas CABG surgery was more common in the blood cardioplegia group (20.9% versus 65.3%, $P < .001$).

Characteristics and Clinical Outcomes of Propensity Score-Matched Patients

After propensity score matching, 292 patients in the blood cardioplegia group and 292 patients in the HTK solution group were included in the study. No significant differences were found between the matched groups with regard to demographic characteristics or type of procedures performed (Table 3). Regarding intraoperative variables (Table 4), the HTK group had shorter aortic cross-clamp times (98.5 ± 39 versus 116.1 ± 38 min; $P < .001$) and shorter CPB times (132.8 ± 53 versus 147 ± 47 min; $P = .001$). Following cardioplegia delivery, patients in the HTK group showed a significant decrease in serum sodium concentration during CPB compared to patients who received blood cardioplegia. The serum sodium concentration returned to normal values on the first postoperative day. In the HTK solution group 87 (30%) patients required a second dose of cardioplegia due to return of electrical activity. No patients required a third dose of HTK solution. Regarding the primary study endpoint, the ICU LOS did not differ between groups matched by propensity score (Table 4). Furthermore, no significant differences were found in any secondary outcome variables.

DISCUSSION

The use of cardioplegia is one of the most important measures of myocardial protection in cardiac surgery. Although there are multiple types and forms of cardioplegia administration, the optimal strategy for achieving adequate myocardial protection is still debated. The present study compared standard blood cardioplegia and HTK solution in a wide range of cardiac patients undergoing diverse surgical procedures and demonstrated that both strategies of myocardial protection were equivalent in terms of early clinical outcomes and mortality.

Intermittent blood cardioplegia has been the conventional form of myocardial protection in many countries, reaching a significant margin of safety. However, the increasing interest in minimally invasive procedures, as well as in other technically complex surgeries, makes the use of a single administration cardioplegia, such as the HTK solution, attractive [Garbade 2013]. Although the HTK solution has been used for many years, it is surprising that relatively few studies have compared this solution with other usual forms of myocardial protection [Edelman 2013]. When such studies have been performed, they have tended to focus on specific surgical procedures (CABG or mitral valve surgery), and have mostly included a relatively limited number of patients.

Experimental studies comparing single dose administration of HTK solution with intermittent application of blood cardioplegia or St Thomas solution suggest reduced myocardial protection with the HTK solution [Aarsaether 2009; Fannelop 2009]. Fannelop et al reported that the application of multidose cold blood cardioplegia was superior to a single administration of HTK solution with respect to the preservation of left ventricular systolic function in an experimental pig model. This improved function was associated with a lower release of troponin T, suggesting better protection against ischemia [Fannelop 2009]. Similar findings were reported by Aaersaeth et al [Aarsaether 2009]. However, the superiority observed in experimental studies has not been corroborated by clinical studies.

The HTK solution has been compared with other forms of cardioplegia in patients undergoing CABG surgery. Wiesenack et al compared 485 patients undergoing CABG surgery using a miniaturized extracorporeal circulation circuit plus anterograde blood cardioplegia with a control group of 485 patients using a conventional circuit plus HTK solution. No significant differences were reported regarding the duration of intubation, hospital and ICU LOS, and mortality at 30 days. Although the incidence of postoperative complications was lower in the blood cardioplegia group, these results can also be attributed to the use of a miniaturized circuit [Wiesenack 2004].

Other studies comparing the HTK solution with conventional cardioplegia solutions in patients undergoing CABG surgery have found no significant difference in most clinical outcomes [Prathanee 2015; Aarsaether 2009; Demmy 2008]. In recent years, several small studies have shown equivalent or superior myocardial protection using HTK solution as a cardioplegic strategy versus traditional hot or cold blood cardioplegia in the mitral valve, aortic valve, and thoracic aortic surgery [Hummel 2016; Braathen 2011; Scrascia 2011].

A few studies have evaluated the use of HTK solution versus standard cardioplegia in cardiac surgery performed with minimally invasive techniques. Similar clinical results and inferior protection of the right ventricle with HTK solution were found [De Palo 2017; Guadino 2013; Sansone 2012]. Despite these divergent results, all of the reports highlight the ease and convenience of a single administration of HTK solution when using the minimally invasive approach. The present study did not evaluate clinical outcomes considering whether the surgery was performed through a traditional median sternotomy or minimally invasive techniques due to the relatively few cases accomplished with this latter strategy.

In the propensity-matched analysis, there were significant longer CPB and cross-clamping times in the blood cardioplegia group. This finding can be explained by the frequent interruptions necessary for the repetitive administration of blood cardioplegia in contrast to a single initial dose of HTK solution. In addition, we adopted the low-dose regime proposed by Arslan et al [Arslan 2005]. With this strategy, the initial amount of HTK solution (approximately 15 mL/kg) is less than the 20 to 25 mL/kg conventionally reported in the literature, and the administration time is two to three minutes shorter. Although we did not routinely evaluate myocardial injury markers such as troponin I or creatine kinase MB, the finding of comparable clinical outcomes with both cardioplegic strategies suggests that there is no increased deleterious cellular effect or elevated cardiac injury with this HTK solution delivery protocol.

In some studies, hyponatremia has been reported following administration of HTK solution for myocardial protection, and there is some concern about its potential deleterious effect, as well as the hazards of its acute correction [Luek 2013; Kim 2011]. In the current study, we found that acute and transient hyponatremia frequently occurred after HTK administration, but this hyponatremia probably has minimal clinical relevance as the serum sodium increases to a normal level at the end of CPB without a specific treatment [Lindner 2012].

The current study is in accordance with the findings of two recent reports that used propensity-score matching methodology. Viana et al concluded that the use of HTK solution is as safe as blood cardioplegia for myocardial protection in complex cardiac surgery, and Hoyer et al reported that HTK solution is safe and effective in aortic valve surgery [Hoyer 2017; Viana 2013]. Our study differs from their investigations because it involves a larger number of high-risk patients who underwent a wide range of surgical procedures. Furthermore, information about intraoperative sodium concentration was added.

There are certain limitations in our investigation that need to be highlighted. First, this is a retrospective, single-center study, with the inherent limitations of this type of design. Although we use a propensity score analysis in order to minimize potential biases, we cannot completely exclude the possibility that unknown confounding factors contributed to our results. Second, the comparison of endpoints such as the incidence of ventricular fibrillation after removal of the cross clamp, postoperative ejection fraction and cardiac enzyme levels could not be performed because those variables are not routinely collected in our database. In our center, postoperative investigations of markers of myocardial injury are not performed unless clinically indicated. Finally, our study excluded patients undergoing surgical procedures considered to be low-risk, as well as patients undergoing isolated CABG, in whom the protocol of the service uses blood cardioplegia as a measure of myocardial protection. The relatively high mortality found in both groups is characteristic of this high-risk cohort, and therefore, these results might not be applicable to other types of patients.

CONCLUSION

In conclusion, in a large cohort of patients undergoing diverse high-risk cardiac procedures, HTK solution and blood cardioplegia were equivalent in terms of early clinical outcomes. Even though blood cardioplegia was associated with higher CPB and aortic cross-clamp times, comparable postoperative course regarding ICU LOS, hospital stay, 30-day mortality, and incidence of postoperative complications was found with both strategies.

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