ORIGINAL PAPER

DOI: https://doi.org/10.5114/kitp.2018.76473

Type of cardioplegic solution as a factor influencing the clinical outcome of open-heart congenital procedures

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Kardiochirurgia i Torakochirurgia Polska 2018; 15 (2): 86-94

Abstract

Introduction: Cardioplegia is one of the most important modalities of myocardial protection during heart surgery.

Aim: To assess the impact of blood cardioplegia on postoperative variables, in comparison with two types of crystalloid cardioplegic solutions during pediatric heart surgery.

Material and methods: One thousand one hundred and twenty-nine patients underwent surgical correction of congenital heart disease with cardioplegia administration between 2006 and 2012. Nonlinear regression models of postoperative low cardiac output syndrome (LCOS) incidence, catecholamine index and total complication count were developed using a genetic algorithm. The Akaike information criterion was applied for selection of the best model. The following explanatory variables were evaluated: cardioplegia type (ST – Saint Thomas, n = 440; FR – Fresenius, n = 432; BL – Calafiore, n = 257), congenital heart diseases (CHD) type, age, sex, genetic disorder presence, body surface area (BSA), cardiopulmonary bypass (CBP) time, aortic cross-clamp time, operation urgency, redo surgery, surgeon.

Results: Low cardiac output syndrome presence and higher than average catecholamine indexes were negatively influenced by use of crystalloid cardioplegia (ST or FR), presence of specific CHDs, redo surgery and prolonged CBP time. Increased complication count was related to: crystalloid cardioplegia, presence of specific CHDs, redo surgery, urgency of operation, operation time and CBP time. Higher BSA had a protective effect against higher catecholamine index and increased complication count. Older age was protective against LCOS.

Conclusions: Cardioplegic solutions type influences postoperative variables in children after heart surgery by the negative impact of crystalloid cardioplegia. Blood cardioplegia presents potential advantages for patients – its application may reduce the incidence of low cardiac output syndrome and related complications.

Key words: blood cardioplegia, crystalloid cardioplegia, complications.

Streszczenie

Wstęp: Kardioplegia jest jedną z najważniejszych metod ochrony mięśnia sercowego podczas operacji kardiochirurgicznych.

Cel: Analiza wpływu zastosowania podczas operacji kardiochirurgicznch u dzieci kardiopleginy krwistej na wybrane okołooperacyjne parametry kliniczne w porównaniu z dwoma rodzajami kardioplegin krystalicznych.

Materiał i metody: W latach 2006–2012 u 1129 pacjentów wykonano korekcję chirurgiczną wrodzonej wady serca z użyciem kardioplegii. Przy zastosowaniu algorytmu genetycznego utworzono nieliniowe modele regresji zachowania zmiennych [obecność zespołu niskiego rzutu serca (LCOS), indeks katecholaminowy, całkowita liczba powikłań]. Do selekcji najlepszego modelu regresji użyto kryterium informacyjnego Akaikego. Oceniano następujące zmienne objaśniające: rodzaj kardioplegii (ST – Saint Thomas, n = 440; FR – Fresenius, n = 432; BL – Calafiore, n = 257), rodzaj wrodzonej wady serca (CHD), wiek, płeć, obecność wad genetycznych, powierzchnia ciała (BSA), czas krążenia pozaustrojowego (CBP), czas zakleszczenia aorty, pilność operacji, ponowna operacja, chirurg.

Wyniki: Zespół niskiego rzutu serca oraz indeks katecholaminowy wyższy od mediany w populacji były związane z zastosowaniem kardioplegii krystalicznej (ST lub FR), obecnością specyficznej wrodzonej wady serca, ponowną operacją oraz przedłużonym czasem krążenia pozaustrojowego. Większa liczba powikłań wiązała się z zastosowaniem kardioplegii krystalicznej, obecnością specyficznej wrodzonej wady serca, ponowną operacją, pilnością operacji, czasem operacji oraz czasem krążenia pozaustrojowego. Większa powierzchnia ciała chroniła przed wystąpieniem wyższego indeksu katecholaminowego oraz większą liczbą powikłań. Starszy wiek pacjenta zabezpieczał przed wystąpieniem zespołu niskiego rzutu serca.

Wnioski: Rodzaj kardioplegii zastosowanej podczas operacji kardiochirurgicznych u dzieci wpływa na wybrane zmienne pooperacyjne. Zaznaczony jest negatywny wpływ kardioplegii krystalicznej. Zastosowanie kardioplegii krwistej może przynieść korzyści w postaci zmniejszenia częstości występowania zespołu niskiego rzutu serca oraz związanych z nim powikłań.

Słowa kluczowe: kardioplegia krwista, kardioplegia krystaliczna, powikłania.

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Received: 23.01.2018, **accepted:** 6.02.2018.

Introduction

Controlled intraoperative cardiac arrest is indispensable in the majority of pediatric cardiac surgery procedures. One of the most important myocardial protection techniques is cardioplegia – indirect or direct administration of cardioplegic solution to the coronary arteries. Both crystalloid cardioplegia and blood cardioplegia are widely used in pediatric cardiac surgery [1–3]. The choice of cardioplegic solution depends on the surgeon's preference or on the local institutional policy [4].

The advantages of crystalloid cardioplegia are the following: relatively low price, simplicity of use and myocardial protection up to 2 h after a single dose [1, 5]. Potential advantages of blood cardioplegia include: oxygen transfer by the red blood cells to the myocardium, free radical scavenging properties and physiologic osmotic pressure that protects against myocardial edema [1, 6].

The experience of many units shows clinical advantages of blood cardioplegia administration. However, the previous studies did not give an unequivocal answer as to which cardioplegic solution is the most beneficial (for all congenital cardiac malformations and all age groups of patients).

Aim

The aim of this study was to assess the impact of blood cardioplegia on postoperative clinical variables, in comparison with two types of cold crystalloid cardioplegic solutions, during open heart surgery in children.

Material and methods

Patients

One thousand one hundred and twenty-nine consecutive patients underwent surgical correction of different congenital heart diseases (CHD) with the use of cardiopulmonary bypass and cardioplegic solution administration in the Department of Pediatric Cardiac Surgery, Poznan University of Medical Sciences, between 2006 and 2012.

Medical records (surgical reports, case histories, local medical database and local data from National Cardiac Surgery Registry – "KROK") were reviewed.

The most common cardiac malformations operated on during this period are presented in Table I. Demographic data according to the type of used cardioplegic solution are presented in Table II.

This observational study has been approved by the local Ethics Committee (resolution: 75/12 from 05.01.2012).

Cardioprotection

Patients were divided into three groups according to cardioplegia type. Cold crystalloid St. Thomas cardioplegia (ST) was used from 03.01.2006 to 01.03.2008 and was administered to 440 patients. Cold crystalloid Fresenius cardioplegia (FR) was used from 02.03.2008 to 12.11.2011 and was received by 432 patients. Cold blood Calafiore cardioplegia (BL) use was initiated in our department on 25.08.2010 and was administered during 257 operations. The composition of each cardioplegic solution in given in Table III. Throughout the whole study period all types of cardioplegic solutions were administered in the indirect (via the aortic root) or direct antegrade way.

Administration of cold crystalloid cardioplegia (at 4°C) to the coronary arteries was performed by an external, pneumatic system operated by the anesthesiologist. The solution was delivered under the pressure of no more than 150 mm Hg every 30 min. The first dose was 10 ml/kg patient's body weight, and the next doses were 5 ml/kg patient's body weight.

The administration of cold blood cardioplegia (4°C) to the coronary arteries was performed by an additional pump of the heart-lung machine with a heat exchanger operated by the perfusionist. Cardioplegia infusion was under the pressure of no more than 150 mm Hg every 30 min for 3 to 3.5 min.

Statistical methods

Multivariable regression models were created to assess the co-influence of specific types of cardioplegia on selected clinical variables (with the binominal function or Poisson function). The dependent outcome variables were the following parameters:

– 30-day mortality – "Death_30d",
– the low cardiac output syndrome (defined as acidosis and oliguria occurrence accompanied by the necessity of inotropic drug support and vasodilatation drug administration) – "LCOS",
– delayed sternal closure – "DSC",
– mechanical ventilation time longer than the median value of the entire cohort (18 h) – "INTUB_time",
– intensive care unit stay longer than the median value for all patients (4 days) – "ICU_LOS",

Table I. List of operated cardiac malformations during 2006–2012

Cardiac disease	Number of patients (% of occurrence)
ASD II	260 (23)
VSD	230 (20)
AVSD	148 (13.1)
ToF	111 (9.8)
TGA	81 (7.2)
AS/AI	81 (7.2)
UVH	58 (5.1)
AVVI	46 (4.1)
TAPVR	20 (1.8)
MIX	94 (8.7)

ASD II – atrial septal defect, VSD – ventricular septal defect, AVSD – atrioventricular septal defect, ToF – tetralogy of Fallot, TGA – all spectrum of transposition of great arteries, AS/AI – aortic valve malformations (complex and simple), UVH – all spectrum of single ventricle disease, including hypoplastic left heart syndrome, AVVI – isolated atrioventricular valve malformations, TAPVR – all spectrum of total anomalous pulmonary venous return, MIX – other, less frequent cardiac malformations.

Table II. Demographic data according to type of used cardioplegic solution

Parameter	FR	ST	BL
Demographic variables:			
N	432	440	257
Gender (female/male)	204/228	207/233	103/154
Age [days]	295 (77–741)	313 (82–967)	366 (116–999)
Body weight [kg]	7.2 (4.1–11.5)	7.5 (4.1–13)	8.6 (4.9–13.5)
Body surface area [m^2]	0.37 (0.25–0.52)	0.38 (0.24–0.57)	0.41 (0.28–0.59)
Down's syndrome	53	49	31
Intraoperative variables:			
CBP [min]	83 (52–123)	89 (60–126)	81 (50–118)
Ao-x-clamp [min]	42 (24–66)	45 (27–62)	43 (24–61)
Postoperative variables:			
ICU time [days]	4 (3–9)	4 (3–8)	4 (3–8)
Mechanical ventilation [h]	18 (7–73)	22 (8–75)	12 (7–39)
30-day mortality (%)	14.9	14.9	8.9

FR – Fresenius crystalloid cardioplegic solution, ST – St. Thomas crystalloid cardioplegic solution, BL – Calafiore cold blood cardioplegic solution, CBP – cardiopulmonary bypass time, Ao-x-clamp – aortic cross-clamp time, ICU time – intensive care unit stay time. Data presented as median and ranges.

Table III. Chemical composition of crystalloid component of cardioplegic solutions

Component [mM/dm^3]	ST	FR	BL
K^+	16.37	5	670.74
Cl^-	2.28	60.92	475.5
Na^+	93.94	19.61	154
Ca^+	16.66	0.97	–
SO_4^{2-}	1.21	–	–
$H_2PO_4^-$	1.28	–	–
Mannitol	200.03	200.03	–
Magnesium DL-hydrogen aspartate	–	1.6	57.71
6-Methylprednisolone	–	0.67	–
Sodium bicarbonate	25	25	–
Gentamycin	–	0.042	–
pH	4–6	5–7	7.35–7.45

FR – Fresenius crystalloid cardioplegic solution, ST – St. Thomas crystalloid cardioplegic solution, BL – Calafiore cold blood cardioplegic solution.

– hospitalization time longer than the median value for all patients (12 days) – "HOSP_time",
– vasoactive-inotropic score value higher than the median value of all patients (4.7) – "VIS" (vasoactive-inotropic score mcg/kg/min = DPA + DBX + 100 × ISO + 100 × ADR (where: DPA = dopamine, DBX = dobutamine, ISO = isoprenaline, ADR = adrenaline, score modified according to a local catecholamine administration policy) [7, 8]),
– the total amount of complications (including: acute renal failure requiring hemodiafiltration, pneumonia, cardiac arrhythmia, bleeding requiring reoperation, neurological complications, metabolic acidosis, pulmonary hypertension crisis and mediastinitis) – "Compl_count".

The aforementioned models were developed using the following explanatory variables:
– type of cardioplegia – blood cardioplegia (BL) vs. crystalloid cardioplegia (CR = St. Thomas cardioplegia + Fresenius cardioplegia) = "Cardiopl_double"; or blood cardioplegia vs. St. Thomas cardioplegia (ST) vs. Fresenius cardioplegia (FR) = "Cardiopl_triple"; both options were used interchangeably,
– patient's sex – "Sex",
– patient's age (in days) – "Age",
– type of congenital cardiac disease "CHD" (following cardiac diseases were considered: "AS/AI" – aortic valve diseases – complex and simple; "ASDII" – atrial septal defect, "VSD" – ventricular septal defect, "AVSD" – all types

of atrioventricular septal defect (unbalanced forms were excluded), "ToF" – tetralogy of Fallot, "AVVI" – isolated atrioventricular valves diseases, "TGA" – transposition of great arteries excluding single ventricle, "UVH" – all spectrum of single ventricle heart, including hypoplastic left heart syndrome (HLHS), "MIX" – other, less frequent cardiac malformations),
– patient's body surface area (m^2) – "BSA",
– presence of concomitant genetic diseases – "Genetic" – mainly Down's syndrome,
– surgeon performing the operation – "Surgeon",
– redo surgery – "REDO",
– urgent surgery – "Urgency",
– total operation time (min) – "OP_time",
– cardiopulmonary bypass time (min) – "CBP_time",
– aortic cross-clamp time (min) – "Ao-X-clamp_time",
– use of deep hypothermic circulatory arrest – "DHCA".

Continuous variables: BSA, Age, OP_time, CBP_time and Ao-X-clamp_time were discretized to quartiles in the majority of models.

Development of statistical models

For each dependent outcome variable a nonlinear multivariable regression model was created (Poisson version for "Compl_count" variable, binominal logistic version for the rest of variables). All independent variables entered the preliminary model. A genetic algorithm was used to search for the best model [9] by application of the Akaike information criterion [10]. A genetic algorithm is one of the best alternatives to the strategy of fitting all possible models, which definitely makes the computational time prohibitive even for recent computers. Conversely, a genetic algorithm explores only a subset of all possible models, randomly but with the preponderance towards the best model. This is achieved by simulation of biological processes: generation of the model's offspring with a mutation, recombination with another model and finally model selection. This makes genetic algorithms computationally fast. The leave-one-out cross-validation (LOOCV) method was used to validate the best model by its comparison to the preliminary model using a cross-validation estimate of prediction er-

Table IV. Model of vasoactive-inotropic score value. Model type: binomial

Variable	*P*-value	Odds ratio	95% CI	
Intercept	0.0033	0.2435	0.0932	0.6149
Cardioplegia: FR	0.0416	1.5198	1.0165	2.2765
Cardioplegia: ST	0.0140	1.6503	1.1078	2.4648
Age: 90–319 days	0.0537	0.5785	0.3300	1.0058
Age: 319–860 days	0.6587	0.8406	0.3900	1.8262
Age: 860–999 days	0.5105	1.4862	0.4652	4.9541
CHD type: ASDII	0.4268	0.7333	0.3431	1.5910
CHD type: AVSD	0.3386	1.4717	0.6686	3.2680
CHD type: AVVI	0.0495	2.3700	1.0090	5.6761
CHD type: MIX	0.1619	1.7387	0.8051	3.8086
CHD type: TGA	0.8591	1.0910	0.4207	2.8950
CHD type: ToF	< 0.0001	6.0350	2.6233	14.3336
CHD type: UVH	0.2662	1.6706	0.6804	4.1770
CHD type: VSD	0.6426	0.8423	0.4094	1.7523
BSA: 0.25–0.38 m^2	0.8534	0.9514	0.5616	1.6192
BSA: 0.38–0.54 m^2	0.0041	0.3245	0.1493	0.6951
BSA: 0.54–0.59 m^2	0.0002	0.0986	0.0287	0.3228
Genetic	0.1002	1.5265	0.9235	2.5360
Redo surgery	0.0320	1.7736	1.0564	3.0173
CBP time: 54–86 min	< 0.0001	4.6875	2.6491	8.5421
CBP time: 86–110 min	< 0.0001	7.1750	3.9919	13.2737
CBP time: 110–126 min	< 0.0001	13.0896	6.9434	25.4268

Cross-validation estimate of prediction error: preliminary model: 0.179, the best model: 0.157.
CHD – type of congenital cardiac disease, CBP time – cardiopulmonary bypass time, FR – Fresenius crystalloid cardioplegic solution, ST – St. Thomas crystalloid cardioplegic solution, BSA – patient's body surface area, ASD II – atrial septal defect, AVSD – atrioventricular septal defect, AVVI – isolated atrioventricular valve malformations, MIX – other, less frequent cardiac malformations, TGA – all spectrum of transposition of great arteries, ToF – tetralogy of Fallot, UVH – all spectrum of single ventricle disease, including HLHS, VSD – ventricular septal defect, CI – confidence interval.

ror. The smaller estimate of prediction error in the developed model than in the preliminary one signified the better performance of the former. The impact of an independent variable on an outcome variable (associated with the regression coefficient) was described by the odds ratio (OR) with 95% confidence interval (CI). Thus, the lower and upper confidence limits yielded an interval estimate of OR at 0.05 α. Predicting variables were considered significant at $p < 0.05$.

Statistical software

The R Project (R: A Language and Environment for Statistical Computing, version 3.0.1) with the glmulti library implementing a genetic algorithm for the model search was used for statistical analysis [11]. Leave-one-out cross-validation was performed using a boot library [12]. Because of time-consuming calculations, R batch scripts were created for automatic execution.

Results

The variable "Type of cardioplegia" entered into 3 out of 8 created models and with other explanatory variables had a statistically significant impact on the following dependent variables: vasoactive-inotropic score, low cardiac output syndrome presence, total amount of complications.

The model of vasoactive-inotropic score value in studied cohort was explained by the following predictors (Table IV):

- Increasing risk for vasoactive-inotropic score value higher than the cohort median:
  - Type of cardioplegia – use of crystalloid Fresenius ($p = 0.0416$) and St. Thomas cardioplegia ($p = 0.014$),
  - Atrioventricular valve defect ($p = 0.0495$), and tetralogy of Fallot presence ($p < 0.001$),
  - Reoperation ($p = 0.032$),
  - Cardiopulmonary bypass time longer than first quartile for studied population (CBP_time: in the second quartile: $p < 0.001$; CBP_time: in the third quartile: $p < 0.001$; CBP_time: in the fourth quartile: $p < 0.001$),
- Decreasing risk for vasoactive-inotropic score value higher than the cohort median:
  - Patient's body surface area greater than the median value (BSA in the third quartile: $p = 0.0041$; BSA in the fourth quartile: $p = 0.0002$),

The low cardiac output syndrome occurrence model was explained by the following predictors (Table V):

Table V. Model of low cardiac output syndrome occurrence. Model type: binomial

Variable	*P*-value	Odds ratio	95% CI	
Intercept	< 0.0001	0.0015	0.0001	0.0118
Cardioplegia: FR	0.0015	3.3730	1.6436	7.4629
Cardioplegia: ST	< 0.0001	5.0853	2.4728	11.3444
Age: 90–319 days	0.1729	0.6369	0.3333	1.2250
Age: 319–860 days	0.2640	0.6440	0.2958	1.3932
Age: 860–999 days	0.0017	0.2023	0.0720	0.5339
CHD type: ASDII	0.1209	4.0899	0.7822	31.8598
CHD type: AVSD	0.1684	3.1425	0.7327	22.1247
CHD type: AVVI	0.0421	6.1369	1.2219	46.9253
CHD type: MIX	0.0336	5.6853	1.3674	39.2556
CHD type: TGA	0.1144	0.2409	0.0462	1.8487
CHD type: ToF	0.1165	3.7052	0.8569	26.1832
CHD type: UVH	0.0532	5.2252	1.1440	37.9075
CHD type: VSD	0.1506	3.3172	0.7696	23.4585
Redo surgery	0.0172	2.3611	1.1520	4.7631
Urgency	0.0242	2.2657	1.1079	4.6131
Operation time: 150–205 min	0.5381	0.7135	0.2461	2.1706
Operation time: 205–265 min	0.0831	2.4927	0.9216	7.4218
Operation time: 265–960 min	0.1600	2.2686	0.7442	7.4485
CBP time: 54–86 min	0.0360	4.3529	1.2307	20.8097
CBP time: 86–110 min	0.0348	4.6372	1.2494	23.1424
CBP time: 110–126 min	0.0004	14.2120	3.6971	73.0373

Cross-validation estimate of prediction error: preliminary model: 0.09, the best model: 0.087.
CHD – type of congenital cardiac disease, CBP time – cardiopulmonary bypass time, FR – Fresenius crystalloid cardioplegic solution, ST – St. Thomas crystalloid cardioplegic solution, ASD II – atrial septal defect, AVSD – atrioventricular septal defect, AVVI – isolated atrioventricular valve malformations, MIX – other, less frequent cardiac malformations, TGA – all spectrum of transposition of great arteries, ToF – tetralogy of Fallot, UVH – all spectrum of single ventricle disease, including HLHS, VSD – ventricular septal defect, CI – confidence interval.

- Increasing risk for LCOS in studied population:
  - Type of cardioplegia – use of crystalloid Fresenius (p = 0.0015) and St. Thomas cardioplegia (p < 0.001),
  - Presence of atrioventricular valve defect (p = 0.0421) and other less frequent cardiac malformations (p = 0.0336),
  - Reoperation (p = 0.0172),
  - Urgent operation (p = 0.0242),
  - Cardiopulmonary bypass time longer than first quartile of the cohort (CBP_time: second quartile: p = 0.036; CBP_time: third quartile: p = 0.0348; CBP_time in the fourth quartile: p < 0.001),
- Decreasing risk for LCOS appearance in studied population:
  - Patient's age in 4th quartile of the cohort (p = 0.0017).

The model of the total amount of complications was explained by the following predictors (Table VI):

- Increasing the amount of complications:
  - Type of cardioplegia – use of crystalloid St. Thomas cardioplegia (p = 0.0002),
  - Complex cardiac malformations presence (AVSD: p = 0.0099; AVVI: p < 0.001; MIX: p = 0.0034; ToF: p < 0.001; UVH: p = 0.003),
  - Reoperation (p < 0.001),
  - Urgent operation (p = 0.0126),
  - Operation time, cardiopulmonary bypass time and patient's age – odds ratios not exceeding more than 1.0011 (OR and CI – Table V),
- Decreasing the total amount of complications:
  - Patient's body surface (p < 0.001).

The variable "Type of cardioplegia" entered into another two models explaining 30-day mortality and hospitalization time. However, the impact of used cardioplegia type was not statistically significant for these models (Tables VII and VIII).

Models of delayed sternal closure, mechanical ventilation time and intensive care unit stay time were created. However, the variable "Type of cardioplegia" did not enter into the mentioned models.

Discussion

This study shows that the type of cardioplegic solution, as well as the method of its administration, has a significant co-influence on selected postoperative clinical parameters such as vasoactive-inotropic score, low cardiac output syndrome presence and total amount of complications. These variables reflect postcardiotomy heart failure in children after CHD correction in a complementary way. The impact of cardioplegia type on these parameters described as the odds ratio ranges between 1.44 and 5.09 and is never dominant in relation to other explanatory variables in spe-

Table VI. Model of total amount of complications. Model: Poisson

Variable	*P*-value	Odds ratio	95% CI	
Intercept	0.0902	0.4630	0.1791	1.0803
Cardioplegia: FR	0.0555	1.2647	0.9984	1.6154
Cardioplegia: ST	0.0002	1.5507	1.2338	1.9680
CHD type: ASDII	0.9947	1.0027	0.4765	2.3668
CHD type: AVSD	0.0099	2.6279	1.3431	5.9410
CHD type: AVVI	0.0005	3.8997	1.9005	9.0694
CHD type: MIX	0.0034	2.9466	1.5253	6.6075
CHD type: TGA	0.9714	1.0139	0.5058	2.3294
CHD type: ToF	0.0004	3.7040	1.9026	8.3398
CHD type: UVH	0.0030	3.0527	1.5540	6.9189
CHD type: VSD	0.0611	2.0139	1.0309	4.5478
Redo surgery	< 0.0001	1.6633	1.3156	2.0846
Urgency	0.0126	1.3473	1.0652	1.7014
Age	< 0.0001	1.0011	1.0008	1.0014
BSA	< 0.0001	0.0011	0.0003	0.0043
Operation time	< 0.0001	1.0043	1.0034	1.0051
CBP time	0.0324	1.0002	1.0000	1.0003

Cross-validation estimate of prediction errors: preliminary model: 2.01, the best model: 1.96.
CHD – type of congenital cardiac disease, CBP time – cardiopulmonary bypass time, FR – Fresenius crystalloid cardioplegic solution, ST – St. Thomas crystalloid cardioplegic solution, BSA – patient's body surface area, ASD II – atrial septal defect, AVSD – atrioventricular septal defect, AVVI – isolated atrioventricular valve malformations, MIX – other, less frequent cardiac malformations, TGA – all spectrum of transposition of great arteries, ToF – tetralogy of Fallot, UVH – all spectrum of single ventricle disease, including HLHS, VSD – ventricular septal defect, CI – confidence interval.

Table VII. Model of 30-day mortality. Model: binomial

Variable	*P*-value	Odds ratio	95% CI	
Intercept	< 0.0001	0.0114	0.0023	0.0432
Cardioplegia: CR	0.1920	1.4502	0.8443	2.5917
CHD type: ASDII	0.3584	0.5035	0.1097	2.2077
CHD type: AVSD	0.2404	1.9116	0.6924	6.2581
CHD type: AVVI	0.7547	1.2537	0.2934	5.3051
CHD type: MIX	0.5689	1.3914	0.4716	4.7490
CHD type: TGA	0.0039	0.1542	0.0446	0.5864
CHD type: ToF	0.7357	1.2201	0.4026	4.2233
CHD type: UVH	0.0231	4.0588	1.2741	14.7541
CHD type: VSD	0.9720	0.9795	0.3233	3.3931
Urgency	< 0.0001	5.4288	3.0082	9.8320
CBP time: 54–86 min	0.2592	2.0555	0.6322	8.1218
CBP time: 86–110 min	0.0681	3.1152	1.0011	12.0565
CBP time: 110–126 min	< 0.0001	13.5062	4.5520	50.8774
DHCA	0.7079	1.1532	0.5405	2.4160

Cross-validation estimate of prediction errors: preliminary model: 0.093, the best model: 0.082.
CHD – type of congenital cardiac disease, CBP time – cardiopulmonary bypass time, DHCA – use of deep hypothermic circulatory arrest, CR – crystalloid cardioplegia, ASD II – atrial septal defect, AVSD – atrioventricular septal defect, AVVI – isolated atrioventricular valve malformations, MIX – other, less frequent cardiac malformations, TGA – all spectrum of transposition of great arteries, ToF – tetralogy of Fallot, UVH – all spectrum of single ventricle disease, including HLHS, VSD – ventricular septal defect, CI – confidence interval.

Table VIII. Model of hospitalization time. Model: binomial continuous

Variable	*P*-value	Odds ratio	95% CI	
Intercept	0.7933	0.9292	0.5364	1.6130
Cardioplegia: CR	0.1194	0.7892	0.5856	1.0633
CHD type: ASDII	0.0001	0.3252	0.1879	0.5594
CHD type: AVSD	0.0011	0.3468	0.1825	0.6503
CHD type: AVVI	0.7515	0.8865	0.4206	1.8787
CHD type: MIX	0.0262	0.4906	0.2604	0.9160
CHD type: TGA	0.2248	0.6002	0.2621	1.3662
CHD type: ToF	0.8247	1.0695	0.5891	1.9398
CHD type: UVH	0.1486	0.5763	0.2708	1.2131
CHD type: VSD	0.1346	0.6728	0.3989	1.1289
Genetic	0.0004	2.1924	1.4221	3.4082
Urgency	0.0595	1.5593	0.9849	2.4866
Ao_X_clamp time	0.0006	1.0099	1.0043	1.0157
DHCA	0.1262	0.9773	0.9473	1.0052

Cross-validation estimate of prediction errors: preliminary model: 0.272, the best model: 0.229.
CHD – type of congenital cardiac disease, Ao_X_clamp time – aortic cross-clamp time, DHCA – use of deep hypothermic circulatory arrest, CR – crystalloid cardioplegia, ASD II – atrial septal defect, AVSD – atrioventricular septal defect, AVVI – isolated atrioventricular valve malformations, MIX – other, less frequent cardiac malformations, TGA – all spectrum of transposition of great arteries, ToF – tetralogy of Fallot, UVH – all spectrum of single ventricle disease, including HLHS, VSD – ventricular septal defect, CI – confidence interval.

cific models. This indicates the presence of more influential factors playing roles in aforementioned models as seen in a clinical context. However, cardioplegia type together with negative composition of other clinical variables (prolonged cardiopulmonary bypass time, low patient's body surface area, urgency of operation and complex CHD) can have a significant impact on postoperative course. In contrast to blood cardioplegia, crystalloid cardioplegic solutions have

a significantly negative influence on postoperative course in presented regression models. This may suggest a similar, if not better, clinical result of cold blood cardioplegia administration. This observation corresponds with other reports [13, 14]. Similarly, the influence of cardioplegia type was not dominant relatively to other clinical variables examined in this study.

Contrary to our findings, Young *et al.* [15] described less frequent inotropic drug administration in patients who received crystalloid cardioplegia. Similarly, Sinha *et al.* [16] reported shorter mechanical ventilation time and shorter hospital stay time in patients receiving crystalloid cardioplegia.

The cardioplegia type variable entered into the model of 30-day mortality, but without statistical significance. This observation is similar to other studies where type of used cardioplegia did not impact in-hospital mortality [13, 15].

Cardioplegia type was not a predictor in mechanical ventilation time and intensive care unit stay time models. It can be explained by a stronger influence of other non-cardiac variables. They may affect the long ICU stay time due to prolonged mechanical ventilation (e.g. caused by pulmonary hypertension or pneumonia). It corresponds with other observations [17, 18] where type of cardioprotection has no influence on respiratory time, ICU stay time or hospitalization time. Similarly, the presence of delayed sternal closure (DSC) was not related to the type of used cardioplegia. It is comparable to other reports where the following variables may have a prevalent influence on DSC usage: cardiopulmonary bypass time, aortic cross clamp time, postoperative massive bleeding, severe preoperative patient's condition [19–21].

This study has several limitations. It is a retrospective observational study concerning a 6-year period. Intraoperative and postoperative procedures, quality of ICU care and surgeons' technique have evolved during that time. It could have affected the results of statistical analyses. The analysis of surgeon's influence on the studied variables showing a lack of impact may mitigate the bias connected with the operator's learning curve and the era of operation.

A certain drawback of the study may be connected with the multiplicity – creation of different models of clinical outcome based on the same set of independent variables. However, from the data-mining perspective this study tried to verify whether there is any influence of the most interesting variable – cardioplegia type – on our dependent variables that were not completely isolated one from another and were different manifestations of potentially inadequate cardioprotection.

The next limitation is the absence of a myocardial injury biomarker, whose postoperative blood levels could be correlated with type of used cardioplegia. These markers were not examined due to the retrospective character of the study. Moreover, myocardial injury biomarker release after operations with cardiopulmonary bypass and heart arrest makes their routine use difficult and confined to selected cases only [22, 23].

Better postoperative myocardial contractility was reported after blood cardioplegia administration [24, 25]. Due to the incompleteness of echocardiographic data this parameter was not included in the study.

Conclusions

Cardioprotection together with other factors influences postoperative clinical results in children with CHD. Contrary to crystalloid cardioplegia, blood cardioplegia does not adversely affect the outcome. Moreover, its application may have a protective effect by decreasing low cardiac output incidence and related complications.

Disclosure

Authors report no conflict of interest.

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