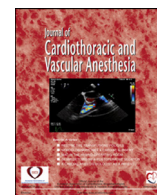




Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: [www.jcvaonline.com](http://www.jcvaonline.com)

Review Article

# Preoperative Risk Prediction Score for and In-Hospital Clinical Outcomes of Reperfusion Ventricular Fibrillation After Release of Aortic Cross-Clamps: A Retrospective Study

Ning Zhou, Jianping Gong, XiuSheng Liang, Weihua Liu,  
Heng Li, Weichao Li<sup>1</sup>

*The Sixth Affiliated Hospital of Guangzhou Medical University: Department of Anesthesiology, Qingyuan people's Hospital, Qingyuan City, Guangdong Province, People's Republic of China*



Reperfusion ventricular fibrillation (VF) is a common arrhythmia after cardiac surgery. Predictors of reperfusion VF and its relationships with the adverse prognosis are still unclear. This study aimed to identify a risk score model to predict reperfusion VF and its effect on in-hospital outcomes. The authors enrolled 1,024 consecutive patients undergoing cardiac surgery, and a total of 823 patients were included in the study. A novel risk score model was developed following logistic regression analysis of the predictors of reperfusion VF. The receiver operating characteristic curve was used to validate this model, and the effect of VF on prognosis was later identified in multivariate or Kaplan–Meier analyses. Risk factors for reperfusion VF occurrence included weight >55 kg, preoperative left ventricular ejection fraction <50%, prior stroke, hypertension, aortic valve replacement, HTK solution, and the use of  $\geq 3$  grafts in coronary artery bypass grafting. A novel risk score model was developed using the abovementioned variables, and points were assigned to each risk factor according to its odds ratio. A high score (>6) predicted greater than 65% of patients with VF occurrence. Reperfusion VF increased the risk of in-hospital cardiovascular death ( $p = 0.03$ ) and renal replacement therapy postoperatively ( $p = 0.022$ ). More attention should be given to reperfusion VF due to an adverse postoperative prognosis, and the developed risk score model may predict this risk.

© 2022 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

**Key Words:** reperfusion VF; model; predictors; outcomes; on-pump

VENTRICULAR FIBRILLATION (VF) after aortic cross-clamping most frequently occurs as a complication during cardiac surgery when the aortic cross-clamp is removed and myocardial reperfusion is initiated.<sup>1</sup> The incidence of reperfusion VF is reported to vary with the experience of the surgeon and the category of surgical procedures, ranging from 45%–to–90% in patients.<sup>2,3</sup> Besides, the VF was not included in current guidelines reporting predictors and worsened clinical outcomes.<sup>4</sup> Adverse reperfusion VF in patients may result in undesirable prognoses attributed to increased myocardial oxygen consumption, distention of the ventricle, resultant

increases in wall tension, and acidosis of the myocardial tissue.<sup>5,6</sup> Previous studies suggested that patients with VF receive defibrillator shocks, because of increased sudden cardiac death due to progressive heart failure.<sup>7</sup> Preoperative predictors of reperfusion VF and its postoperative outcomes in hospitals have not been well-characterized. Therefore, the authors sought to calculate the rate of VF by preoperatively developing a novel risk score model and later identifying the association the VF with prognosis.

## Methods

### *Design, Setting, and Ethical Statement*

Ethical approval for this retrospective cohort study (Ethical Committee approval number: IRB-202108-K4-amendment

<sup>1</sup>Address correspondence to Weichao Li, Area B24, Yinquan Road, Xincheng District, Qingyuan City, Guangdong Province  
E-mail address: [215344404@qq.com](mailto:215344404@qq.com) (W. Li).

review-01) was provided by the Ethical Committee on 12 November 2021. The authors registered the study protocol at the Chinese Clinical Trial Registration (identifier: ChiCTR2100052496).

### *Study Population, Inclusion, and Exclusion Criteria*

In this retrospective cohort study, the authors screened 1,024 consecutive patients undergoing open cardiac surgery from January 2013 to October 2021. Patients with age <18 years old, death during surgery, a loss of postoperative laboratory examination, and a deficiency of echocardiogram or color Doppler echocardiography documents before surgery were excluded.

### *Cardioplegic Solution and Deairing*

The cold blood cardioplegia was a mixture of autologous blood from the cardiopulmonary circuit and the crystalloid in a 4:1 ratio (blood/crystalloid). The crystalloid component (500 mL) consisted of Plasma-Lyte A (435 mL), mannitol 15% (20 mL), NaHCO<sub>3</sub> 8.4% (20 mL), and KCl<sub>2</sub> mEq/mL (25 mL). The potassium concentration in the entire solution was 20 mEq/L. The initial dose was 15 mL/kg, and additional doses were 5 mL/kg given every 20-to-30 minutes or when any electrical activity was observed. Solution temperature was 4°C. One liter of HTK solution (Fuzhou Haiwangfu Pharmaceutical Co., Ltd., China) contains the following components: 15 mmol/L of sodium chloride, 9 mmol/L of potassium chloride, 4 mmol/L of magnesium chloride, 18 mmol/L of histidine hydrochloride, 180 mmol/L of histidine, 2 mmol/L of tryptophan, 30 mmol/L of mannitol, 0.015 mmol/L of calcium chloride, 1 mmol/L of potassium hydrogen 2-ketoglutarate, osmolarity 310 mOsm/kg, and pH 7.02-to-7.20. This cardioplegic solution was delivered at a temperature of 4°C-to-5°C over 6-to-8 minutes. Transesophageal echocardiography was used to identify intracardiac air and deairing procedures the authors used to eliminate air before coming off pump.

### *Study Endpoint*

The primary outcomes developed a novel risk score model with predictors of reperfusion VF, and later identified the effect of VF on prognosis by multivariate analysis. After aortic unclamping, when myocardium reperfusion was initiated, the initial rhythm was defined broadly as reperfusion VF or non-VF during reperfusion period as previously described.<sup>8,9</sup> Reperfusion VF required electric defibrillation counter shocks, and was subsequently documented by surgical teams, including surgeons, anesthesiologists, and perfusionists. Postoperative arrhythmias were defined as any premature ventricular beat and any conduction disturbances requiring treatment with a pacemaker or electrical therapy in the postoperative period.

### *Development and Validation of the Risk Score Model*

Risk predictors for reperfusion VF were identified from univariate and multivariate logistic regression models. Points were assigned to each risk predictor according to its adjusted odds ratio (AOR), enabling the development of a model that predicted the rate of reperfusion VF. The Pearson chi-square test was applied to evaluate the relationship between the total score and the rate of reperfusion VF in the cohort. The receiver operating characteristic curve and area under the curve (AUC) were used to calculate the validity of the model for the total cohort.

### *Remaining Statistical Analysis*

For the purpose of this study, arrhythmic events during the procedure and their effect on the outcome of hospitalization were analyzed. Discrete variables are expressed as frequencies with their respective percentages. Continuous variables are presented as the mean ± standard deviation or median (25th, 75th percentile), and were determined by the distribution of the discrepancy variables. In appropriate patients, continuous variables were compared using Student's *t* test or Wilcoxon rank-sum test between 2 groups. The authors compared categorical variables using the Pearson chi-square test or Fisher's exact test, as appropriate.

Bivariate logistic regression analyses were conducted to identify independent predictors for reperfusion VF. Candidate variables were defined as a *p* value <0.10 in univariate analysis and the 2-group comparison of each model. The model performed well on the goodness-of-fit test. A 2-sided *p* value <0.05 was considered statistically significant. The authors conducted all analyses using SPSS 25.0 software.

## **Results**

Twenty-three patients were excluded because of electrocardiogram or color Doppler echocardiography loss. Only 3 patients who died before aortic unclamping during surgery were excluded from the analysis. In addition, 175 patients also were eliminated for age <18 years. Altogether, 823 patients were included in this analysis (Fig 1), and women accounted for 60.8% of the entire cohort, with a mean age of 54.7 years. A total of 488 patients underwent isolated valve surgery (59.3%), and 98 patients underwent isolated coronary artery bypass grafting (CABG) (11.9%). Ventricular or atrial septal defect repair was conducted in 69 or 112 patients, respectively, and 25 patients underwent cardiac myxoma removal. In total, 43 patients underwent other isolated surgeries. Reperfusion VF occurred in 226 patients (27.4%). Table 1 shows the characteristics of patients with and without reperfusion VF. Patients with reperfusion VF were heavier (weight >55 kg) (60.1% v 40.2%), had low LV ejection fraction (preoperative LVEF <50%) (24.3% v 4.2%), were more likely to have had a prior stroke (12.9% v 4.1%), had greater levels of hypertension (25.9% v 8.8%), and underwent CABG surgery with ≥3 grafts

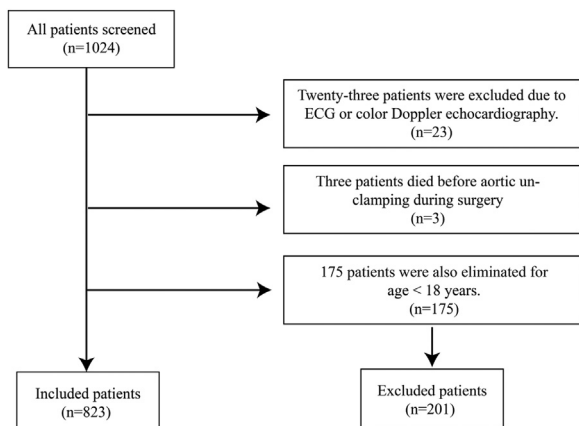


Fig 1. Flow chart of patient selection.

(12.3% v 2.0%) or aortic valve replacement (AVR) (20.6% v 5.6%).

*Independent Predictors of Reperfusion VF*

The authors conducted multivariate logistic regression models to analyze the clinical markers of this VF (Table 2). Weight >55 kg increases the risk of VF by 2.78-fold compared with lighter individuals (AOR: 1.98; 95% confidence interval [CI] 1.42-2.77, p < 0.001). Lower preoperative LVEF acted as a contributor, and LVEF <50% increased the risk of VF by 4.86-fold (AOR: 4.86; 95% CI 2.85-8.31, p < 0.001). Patients with hypertension showed a 2.78-fold increased risk of VF occurrence (AOR: 2.78; 95% CI 1.74-4.46, p < 0.001) compared with other patients. Prior stroke was associated with a

Table 1  
Baseline Characteristics in Patients with VF and VF-Free

	VF(n = 228), % (n)	VF-Free (n = 595), % (n)	p Value
Age, y	52.7 ± 12.3	49.4 ± 12.0	0.001
Male	53.6% (124)	38.8% (232)	<0.001
Weight > 55 kg	60.1% (136)	40.2% (240)	<0.001
NYHA class ≥ III	50.2% (116)	63.9% (382)	0.001
Smoker	24.2% (56)	9.5% (57)	<0.001
Drinker	17.3% (40)	4.8% (29)	<0.001
Medical history			
Dyslipidemia	9.5% (22)	5.6% (34)	0.037
Hypertension	25.9% (60)	8.8% (53)	<0.001
Diabetes	6.9% (16)	4.6% (28)	0.165
COPD	4.3% (10)	5.6% (34)	0.470
Prior stroke	12.9% (30)	4.1% (25)	<0.001
Previous MI	7.7% (18)	6.1% (37)	0.365
Atrial fibrillation	23.8% (54)	32.9%(197)	0.01
Preoperative LVEF <50%	24.3% (55)	4.1% (25)	<0.001
Antegrade cardiac cardioplegia			
HTK solution	92 (40.7%)	128 (21.4%)	<0.001
Cold blood cardioplegia	134 (59.3%)	469 (78.6%)	<0.001
Surgery variables			
CABG			
Number of grafts ≥3	12.3% (32)	2.0% (12)	<0.001
Number of grafts ≤2	3.5% (12)	6.3% (42)	0.372
Heart valve surgery			
Aortic valve replacement	20.6% (48)	5.6% (34)	<0.001
Mitral valve replacement	20.6% (48)	37.8% (226)	<0.001
Mitral and aortic valve replacement	16.3% (38)	13.7% (82)	0.264
Valve repairs	5.1% (12)	5.8% (35)	0.760
Ventricular septal defect repair	1.7% (8)	3.5% (61)	0.192
Auricular septal defect repair	3.4% (12)	10.2% (100)	0.002
Cardiac myxoma removal	3.4% (8)	2.8% (17)	0.606
Others	6.8% (16)	4.5% (27)	0.141
Cardiopulmonary bypass time (min)	125 ± 22.3	123 ± 21.4	0.087
Cross-clamp time (min)	90 ± 10.4	87 ± 9.7	0.067
Duration of the operation (min)	139 ± 22.3	136 ± 23.4	0.089
Postoperative pro-BNP (pg/mL)	2034.9 ± 302.2	2104.9 ± 404.7	0.123
Postoperative troponin I	20.2 ± 3.5	21.7 ± 4.5	0.073
Complications			
Major cardiovascular events	13.2% (30)	4.8% (29)	0.021
All-cause death	11.5% (26)	2.8% (17)	<0.001
Cardiovascular	9.2% (21)	1.1% (7)	<0.001
Noncardiovascular	2.2% (5)	1.6% (10)	0.607

(continued)

**Table 1** (continued)

	VF(n = 228), % (n)	VF-Free (n = 595), % (n)	p Value
New MI	2.6% (6)	0.3% (2)	0.002
Stroke	1.7% (4)	1.6% (10)	0.925
Bleeding requiring to operation	15.5% (36)	2.3% (14)	<0.001
Pneumonia	9.5% (22)	7.7% (46)	0.345
Postprocedure ventricular arrhythmia	19.0% (44)	23.9% (143)	0.171
Postoperative ARF	11.2% (26)	7.0% (42)	0.038
Renal replacement therapy	10.3% (24)	2.3% (14)	<0.001
Pacemaker	13.8% (32)	8.2% (49)	0.011
Length of stay (d)	25.5 ± 10.1	24.1 ± 9.9	0.079
Intubation >96 h	7.7% (18)	3.6% (22)	0.011

Abbreviations: ARF, acute renal failure; BNP, Brain Natriuretic Peptide; CABG, coronary artery bypass grafting; COPD, Chronic obstructive pulmonary disease; HTK, histidine-tryptophan-ketoglutarate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; VF, ventricular fibrillation.

3.66-fold increase in the risk of VF (AOR: 3.66; CI 1.92-6.96,  $p < 0.001$ ). Aortic valve replacement (AOR: 3.85; 95% CI: 2.28 -6.51,  $p < 0.001$ ) and the use of  $\geq 3$  grafts in CABG (AOR: 3.79; 95% CI: 1.81-7.95,  $p < 0.001$ ) were associated with an increased risk of VF. HTK solution (AOR: 2.03; 95% CI 1.37-2.98,  $p < 0.001$ ) also increases risk of reperfusion VF.

*Construction of a Model for Predicting Reperfusion VF*

Points were assigned to each risk predictor according to its AOR, enabling the development of a model that predicted the rate of reperfusion VF. The presence of preoperative LVEF  $< 50\%$  (odds ratio: 4.86) was assigned 4 points, the presence of hypertension (AOR: 2.78) was assigned 2 points, the presence of aortic valve replacement (AOR: 3.85) was assigned 3 points, the presence of number of grafts  $\geq 3$  in CABG (AOR: 3.79) was assigned 3 points, the presence of prior stroke (AOR: 3.66) was assigned 3 points, and the presence of weight  $> 55$  kg (AOR: 1.98) was assigned 1 point. In addition, the presence of HTK solution (AOR: 2.03) was assigned 2 points (Fig 2A). The novel model score was developed with a range of 0-to-10 points based on this calculation (Fig 2B).

**Table 2**  
Independent Predictors of Reperfusion Ventricular Fibrillation

Covariate	Incidence of Reperfusion VF	Adjusted OR (95% CI)	p Value
Weight $> 55$ kg	136 (36.2%)	1.98 (1.42-2.77)	$< 0.001$
Preoperative LVEF $< 50\%$	55 (68.7%)	4.86 (2.85-8.31)	$< 0.001$
Hypertension	60 (56%)	2.78 (1.74-4.46)	$< 0.001$
Prior stroke	30 (57.6%)	3.66 (1.92-6.96)	$< 0.001$
Aortic valve replacement	34 (40.4%)	3.85 (2.28-6.51)	$< 0.001$
CABG with number of grafts $\geq 3$	32 (72.7%)	3.79 (1.81-7.95)	$< 0.001$
HTK solution (versus cold blood cardioplegia)	92 (41.8%)	2.03 (1.37-2.98)	$< 0.001$

Abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; HTK, histidine-tryptophan-ketoglutarate; LVEF, left ventricular ejection fraction; OR, odds ratio.

*Validation for Predicting Reperfusion VF Risk Score*

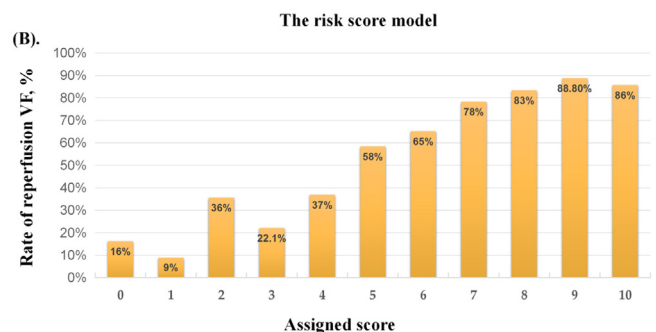
The rates of reperfusion VF and its risk scores in the cohorts are shown in Fig 2, A and B. The Pearson chi-square test was applied to evaluate the relationship between the total score and the rate of reperfusion VF in the cohort ( $p < 0.001$ ). In addition, the established receiver operating characteristic curves and AUC were validated in the model for the total cohort. The AUC for this model was 0.746 ( $p < 0.0001$ ).

*Clinical Outcomes*

Compared with patients without reperfusion VF, patients with VF exhibit an increased risk of in-hospital cardiovascular death and postprocedure renal replacement therapy.

(A).

Risk factor for reperfusion VF	Assigned score
Preoperative LVEF $< 50\%$	4
Number of grafts $\geq 3$ in CABG	3
Aortic valve replacement	3
Prior stroke	3
Hypertension	2
HTK solution (vs.Cold blood cardioplegia)	2
Weight $> 55$ kg	1



**Fig 2.** (A) Predictive factors for reperfusion VF and development of the risk score model for reperfusion VF. (B) Reperfusion VF rate and the risk score model.

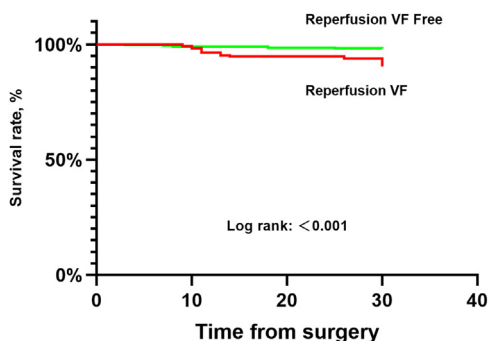


Fig 3. Kaplan–Meier survival curve for patients with reperfusion VF versus without VF. Kaplan–Meier survival curves suggested that patients with reperfusion VF after aortic unclamping had worse survival than patients without VF ( $p < 0.001$ ).

Kaplan–Meier survival curves suggested that patients with reperfusion VF after aortic unclamping had worse survival than patients without VF (Fig 3). Multivariate logistic regression analysis suggested that VF increased the risk of cardiovascular death 2.4-fold (9.2% v 1.1%,  $p = 0.03$ ) (Table 3) and the risk of postprocedure renal replacement therapy 2.84-fold (10.3% v 2.3%,  $p = 0.022$ ) (Table 4).

## Discussion

This research presents an up-to-date cohort investigation of the predictors and outcomes of reperfusion VF in cardiac surgeries. The main findings were as follows: (1) there were 7 predictors; mainly weight  $>55$  kg, preoperative LVEF  $< 50\%$ , hypertension, prior stroke, AVR, HTK solution, and CABG with  $\geq 3$  grafts, for predicting intraoperative VF; (2) the present retrospective cohort survey developed a novel risk score model for preoperatively predicting reperfusion VF according to these predictors; and (3) VF was associated with an increased rate of postoperative cardiovascular death and renal replacement therapy.

### Predictors of Reperfusion VF

Prior stroke plays an important role in predicting the risks of reperfusion VF because of a possible cause-and-effect association for cerebrocardiac syndrome.<sup>10</sup> Prior studies have suggested that significant cardiac arrhythmias occur in more than 50% of all patients with acute cerebrovascular events,<sup>11</sup> and sudden death after ischemic stroke is common in 19% of patients.<sup>12</sup> Consistent with previous studies, this VF appeared

in nearly 57.6% (30/52) of the prior stroke patients in the current study. The catecholamine surge, a sympathetic and parasympathetic disorder of hypothalamus stimulation,<sup>10,13</sup> likely explains potential mechanisms in arrhythmias after stroke diagnosis.<sup>14</sup>

Hypertension and weight  $>55$  kg are clinical markers of reperfusion VF, increasing the risk of VF occurrence. The preoperative stage of cardiac remodeling, considered an arrhythmogenic substrate,<sup>15</sup> is correlated with VF occurrence during the procedure. Obesity and hypertension both lead to cardiac remodeling through various mechanisms, including the inflammatory response, neurohormonal activation, and metabolic derangements.<sup>16</sup> Paulus and Tschöpe reported that obesity and hypertension lead to chronic systemic inflammation, and the release of circulating proinflammatory cytokines correlates with arrhythmogenesis.<sup>17</sup> Alan J et al. reported that obesity and hypertension synergistically impair cardiac mitochondrial biogenesis and function.<sup>18</sup>

Preoperative LVEF  $< 50\%$  increases the risk occurrence of reperfusion VF, implying that systolic dysfunction already exists preoperatively. In the background of surgery, LVEF may further deteriorate because of myocardial injury from myocardial ischemia and surgical procedures.<sup>19</sup> Systolic dysfunction is also an intense predictor of sudden cardiac death in VF.<sup>20</sup> The underlying mechanisms were associated with ventricular electrical and mechanical instability and electrical remodeling.<sup>21</sup>

A total of  $\geq 3$  bypass conduits in CABG as an independent risk predictor of reperfusion VF signifies preoperatively large myocardial infarction, which may increase the risk of ventricular fibrillation storm significantly.<sup>22</sup> In the setting of ischemic isolation of the heart and previous myocardial electrical remodeling, this factor increased the susceptibility and risk of VF occurrence. Migratory re-entrant activity at the Purkinje-muscle junction may become a latent mechanism.<sup>23</sup> Aortic valve replacement appears to be an independent marker of reperfusion VF. Aortic valve replacement itself may not increase the risk of VF, but preoperative left ventricular hypertrophy or hemodynamically severe valve obstruction from severe aortic stenosis or insufficiency commonly exists in patients with aortic valve replacement.<sup>24</sup> Previous evidence suggested that significant left ventricular hypertrophy is a risk factor for ventricular fibrillation during surgery<sup>1</sup> and has an intense predictive effect for ventricular arrhythmias. Preoperative cardiac dysfunction induced by valve obstruction was also a triggering

Table 3  
Analyses of Independent Predictors of In-hospital Cardiovascular Death Using Logistic Regression Models

Variables	Univariate		Multivariable	
	Adjusted OR(95% CI)	p Value	Adjusted OR(95% CI)	p Value
Reperfusion VF	6.24 (3.00-12.97)	$<0.001$	2.40 (1.09-5.32)	0.03
Renal replacement therapy	0.02 (0.01-0.06)	$<0.001$	4.35 (1.78-10.6)	$<0.001$
Prior stroke	3.33 (1.31-8.44)	0.011	3.94 (1.31-11.88)	0.015
Postoperative VA	3.10 (1.07-8.92)	0.036	4.33 (1.35-13.8)	0.014

Abbreviations: CI, confidence interval; OR, odds ratio; VA, ventricular arrhythmia; VF, ventricular fibrillation.



Table 4  
Analyses of Independent Predictors of Renal Replacement Therapy Using Logistic Regression Models

Variables	Univariate		Multivariable	
	Adjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Reperfusion VF	6.88 (3.23-14.63)	<0.001	2.84 (1.16-6.97)	0.022
Preoperative LVEF <50%	5.54 (2.74-11.19)	<0.001	3.07 (1.35-7.00)	0.008

Abbreviations: CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio; VF, ventricular fibrillation

factor according to a previous predictor for preoperative LVEF <50% in the study. The VF in the background of concomitant ventricular hypertrophy and cardiopulmonary bypass likely is associated with several mechanisms, subendocardial ischemia, sensitivity to proarrhythmias with wall stress, and imbalance between oxygen supply and demand.<sup>25</sup>

HTK solution and cold-blood cardioplegia are used widely for on-pump cardiac surgeries. Abundant studies have suggested that HTK solution significantly increased the high risks associated with reperfusion VF compared with cold-blood cardioplegia, and reperfusion VF incidence for some studies was the highest at 71% in the populations with perfusing HTK solution and at 13% of patients with cold blood cardioplegia.<sup>26</sup> Reperfusion VF induced by HTK solution is linked with inadequate intraoperative myocardial protection caused by heterogeneous reperfusion, oxidative stress, and the alteration of electrolyte concentration across the cell membranes and low adenosine-triphosphate levels.

#### A Novel Risk Score Model Reflecting Reperfusion VF

The authors used 7 predictors to develop a risk score model reflecting reperfusion VF: weight >55 kg, preoperative LVEF <50%, hypertension, prior stroke, AVR, HTK solution, and the use of  $\geq 3$  grafts in CABG. This model is simple but sufficiently accurate to show that the AUC for the prediction score was 0.746 in the cohort. This model allowed the authors to critically estimate reperfusion VF for the preoperative stage. If a coexisting stroke was noted in the patient, the use of HTK solution, LVEF <50%, or hypertension, reperfusion VF reached the highest risk in the patient undergoing AVR or CABG with  $\geq 3$  grafts. This highest risk was indicated by a score of 7-to-10 in the present study. Alternative surgery protocols, including transcatheter aortic valve replacement, CABG with off-pump, or percutaneous coronary intervention, should be carefully considered in the preoperative stage. If the patient has coexisting stroke, LVEF <50%, or hypertension, reperfusion VF has reached a relatively higher risk in patients undergoing mitral and aortic valve replacement, cardiac myxoma removal, CABG with  $\leq 2$  grafts, or other cardiac surgery. This risk level was indicated by a score of 4-to-6 in the present study. A prophylactic therapeutic schedule also should be considered in this relatively higher-risk patient, and prior

controversial studies have suggested that prophylactic treatment with amiodarone before aortic unclamping may decrease the rate of reperfusion VF.<sup>27</sup>

#### Clinical Outcomes

VF was a powerful predictor of adverse outcomes after cardiac surgery, particularly cardiovascular death and postprocedure dialysis. The authors found that patients with reperfusion VF had higher cardiovascular death and postprocedure dialysis than those without VF. Evidence on the relationship between reperfusion VF and postoperative cardiovascular death in hospitals may be lacking. Previous studies have suggested that electric defibrillation is associated with an increased risk of cardiovascular death.<sup>28</sup> In addition, El-Chami et al. reported that prior stroke, postoperative renal failure, and postoperative VA increased cardiovascular death in a Cox proportional hazards model.<sup>29</sup> In accordance with the authors' findings, reperfusion VF, postoperative renal replacement therapy (RRT), prior stroke, and postoperative ventricular arrhythmia as predictors also may have caused an increase in cardiovascular death in the study.

Reperfusion VF and preoperative LVEF <50% are independent risk factors for postprocedure dialysis. Prior studies have suggested that perioperative hemodynamic instability is associated with the need for RRT after cardiac surgery.<sup>30</sup> Haase-Fielitz et al. reported that reduced reperfusion mean arterial pressure increased the rate of RRT after cardiac procedures.<sup>31</sup> Reperfusion VF is accompanied commonly by hemodynamic instability, needing more vasoactive drugs that are a marker of postoperative RRT.<sup>32,33</sup> Any further disturbance of hypotension may lead to ischemia and cellular damage in renal organs.<sup>34</sup> Some studies have suggested that preoperative LVEF dysfunction plays a risk factor in acute renal failure. An imbalance between renal oxygen delivery and renal oxygen consumption generally is assumed to play a pivotal role in RRT resulting from perioperative hemodynamic instability.

#### Reperfusion VF After Release of Aortic Cross-Clamp

Reperfusion VF is a major concern in patients undergoing cardiac valve surgeries, off-pump or on-pump CABGs, aortic root surgeries, cardiac transplantations, and other needed cardiac procedures. Despite the improvement in myocardial protection strategies, reperfusion VF is reported to occur in 45%-to-90% of patients.<sup>35</sup> After release of the aortic cross-clamping, the heterogeneous recovery of myocardial cells and the subsequent increase in reentry and automaticity, as well as the possibility of reperfusion-induced injury, can result in a high incidence of reperfusion VF. The VF was caused by the redistribution of coronary blood flow away from the subendocardium, resulting in myocardial ischemia and impairing ventricular performance.<sup>36,37</sup> With increased myocardial oxygen consumption, this will result in intramyocardial acidosis and release of creatine kinase MB postoperatively.<sup>38,6</sup> Reperfusion VF also may result in increased myocardial wall

tension, and defibrillation with direct-current countershock will result in myocardial injury.<sup>39</sup> A variety of antiarrhythmic drugs may affect the incidence of the VF. Amiodarone is more effective than a placebo in preventing reperfusion VF after aortic cross-clamping release in cardiac surgery. However, the amiodarone group required the same number of electrical direct-current countershocks to terminate reperfusion VF as the lidocaine or placebo groups.<sup>40</sup> Cardiac cardioplegia prevents myocardial ischemic injury and also affects VF. The del Nido cardioplegia protocol showed lower incidence of reperfusion VF than cold-blood cardioplegia in patients undergoing aortic valve replacement.<sup>32</sup> There was significantly more spontaneous ventricular fibrillation after release of cross-clamping in the HTK group, compared with the cold-blood cardioplegia group.<sup>26</sup> In addition, preoperative cardiac electrophysiologic changes also play a crucial role in the occurrence of VF.<sup>41</sup>

### Study Limitations

This study had limitations, mainly because of the limited population range and single-center origin, nonrandomized study. Incidences of reperfusion VF were undervalued because of patients' hearts that were exposed to natural cardioversion, and attributed to recording methods that alone called for intrathoracic and extrathoracic defibrillation. In addition, some additional limitations would be (1) the retrospective nature of the study, (2) the likely confounding of older sicker patients having both VF and poor outcome, (3) the lack of a validation population, and (4) the accuracy of chart review for determining types of arrhythmia.

### Conclusions

The rate of reperfusion VF was predicted based on the development of a novel risk score model according to several established preoperative predictors: weight >55 kg, preoperative LVEF <50%, prior stroke, hypertension, AVR, HTK solution perfused, and CABG with  $\geq 3$  grafts. Reperfusion VF presents significant risk factors for cardiovascular death and renal replacement therapy after cardiac surgery.

### Conflicts of Interest

All the authors of this manuscript declare no conflicts of interest.

### References

- 1 Mauermann WJ, Pulido JN, Barbara DW, et al. Amiodarone versus lidocaine and placebo for the prevention of ventricular fibrillation after aortic crossclamping: A randomized, double-blind, placebo-controlled trial. *J Thorac Cardiovasc Surg* 2012;144:1229–34.
- 2 Leeuwenburgh BP, Versteegh MI, Maas JJ, et al. Should amiodarone or lidocaine be given to patients who arrest after cardiac surgery and fail to cardiovert from ventricular fibrillation? *Interact Cardiovasc Thorac Surg* 2008;7:1148–51.

- 3 Baravelli M, Cattaneo P, Rossi A, et al. Low-risk profile for malignant ventricular arrhythmias and sudden cardiac death after surgical ventricular reconstruction. *Pacing Clin Electrophysiol* 2010;33:1054–62.
- 4 Members Writing Committee, CM Otto, Nishimura RA, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in *J Am Coll Cardiol* 2021;77:1276]. *J Am Coll Cardiol* 2021;77:450–500.
- 5 Buckberg GD, Hottenrott CE. Ventricular fibrillation. Its effect on myocardial flow, distribution, and performance. *Ann Thorac Surg* 1975;20:76–85.
- 6 Lockerman ZS, Rose DM, Cunningham JN Jr, et al. Reperfusion ventricular fibrillation during coronary artery bypass operations and its association with postoperative enzyme release. *J Thorac Cardiovasc Surg* 1987;93:247–52.
- 7 Poole JE, Johnson GW, Hellkamp AS, et al. Prognostic importance of defibrillator shocks in patients with heart failure. *N Engl J Med* 2008;359:1009–17.
- 8 Ayoub CM, Sfeir PM, Bou-Khalil P, et al. Prophylactic amiodarone versus lidocaine for prevention of reperfusion ventricular fibrillation after release of aortic cross-clamp. *Eur J Anaesthesiol* 2009;26:1056–60.
- 9 Almdahl SM, Veel T, Eide M, et al. Postcardioplegia ventricular fibrillation: No impact on subsequent survival. *Scand Cardiovasc J* 2014;48:249–54.
- 10 Chen Z, Venkat P, Seyfried D, et al. Brain-heart interaction: Cardiac complications after stroke. *Circ Res* 2017;121:451–68.
- 11 Koppikar S, Baranchuk A, Guzmán JC, et al. Stroke and ventricular arrhythmias. *Int J Cardiol* 2013;168:653–9.
- 12 Sörös P, Hachinski V. Cardiovascular and neurological causes of sudden death after ischaemic stroke. *Lancet Neurol* 2012;11:179–88.
- 13 Hachinski V. Post-stroke depression, not to be underestimated. *Lancet* 1999;353:1728.
- 14 Loubinoux I, Kronenberg G, Endres M, et al. Post-stroke depression: Mechanisms, translation and therapy. *J Cell Mol Med* 2012;16:1961–9.
- 15 Yamada C, Kuwahara K, Yamazaki M, et al. The renin-angiotensin system promotes arrhythmogenic substrates and lethal arrhythmias in mice with non-ischaemic cardiomyopathy. *Cardiovasc Res* 2016;109:162–73.
- 16 Mouton AJ, Li X, Hall ME, et al. Obesity, hypertension, and cardiac dysfunction: Novel roles of immunometabolism in macrophage activation and inflammation. *Circ Res* 2020;126:789–806.
- 17 Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: Comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *J Am Coll Cardiol* 2013;62:263–71.
- 18 Zhang X, Li ZL, Eirin A, et al. Cardiac metabolic alterations in hypertensive obese pigs. *Hypertension* 2015;66:430–6.
- 19 Anselmi A, Abbate A, Girola F, et al. Myocardial ischemia, stunning, inflammation, and apoptosis during cardiac surgery: A review of evidence. *Eur J Cardiothorac Surg* 2004;25:304–11.
- 20 Tung P, Albert CM. Causes and prevention of sudden cardiac death in the elderly. *Nat Rev Cardiol* 2013;10:135–42.
- 21 Kusumoto FM, Bailey KR, Chaouki AS, et al. Systematic review for the 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society [published correction appears in *J Am Coll Cardiol* 2018;72:1756]. *J Am Coll Cardiol* 2018;72:1653–76.
- 22 Nademanee K, Taylor R, Bailey WE, et al. Treating electrical storm: Symptomatic blockade versus advanced cardiac life support-guided therapy. *Circulation* 2000;102:742–7.
- 23 Berenfeld O, Jalife J. Purkinje-muscle reentry as a mechanism of polymorphic ventricular arrhythmias in a 3-dimensional model of the ventricles. *Circ Res* 1998;82:1063–77.
- 24 Bavry AA, Arnaoutakis GJ. Perspective to 2020 American College of Cardiology/American Heart Association (ACC/AHA) guideline for the management of patients with valvular heart disease. *Circulation* 2021;143:407–9.

- 25 Stevens SM, Reinier K, Chugh SS. Increased left ventricular mass as a predictor of sudden cardiac death: is it time to put it to the test? *Circ Arrhythm Electrophysiol* 2013;6:212–7.
- 26 Braathen B, Jeppsson A, Scherstén H, et al. One single dose of histidine-tryptophan-ketoglutarate solution gives equally good myocardial protection in elective mitral valve surgery as repetitive cold blood cardioplegia: A prospective randomized study. *J Thorac Cardiovasc Surg* 2011;141:995–1001.
- 27 Zheng Y, Gu Q, Chen HW, et al. Efficacy of amiodarone and lidocaine for preventing ventricular fibrillation after aortic cross-clamp release in open heart surgery: A meta-analysis of randomized controlled trials. *J Zhejiang Univ Sci B* 2017;18:1113–22.
- 28 Biton Y, Daimee UA, Baman JR, et al. Prognostic importance of defibrillator-appropriate shocks and antitachycardia pacing in patients with mild heart failure. *J Am Heart Assoc* 2019;8:e010346.
- 29 El-Chami MF, Sawaya FJ, Kilgo P, et al. Ventricular arrhythmia after cardiac surgery: Incidence, predictors, and outcomes. *J Am Coll Cardiol* 2012;60:2664–71.
- 30 Haase-Fielitz A, Haase M, Bellomo R, et al. Perioperative hemodynamic instability and fluid overload are associated with increasing acute kidney injury severity and worse outcome after cardiac surgery. *Blood Purif* 2017;43:298–308.
- 31 Haase M, Bellomo R, Story D, et al. Effect of mean arterial pressure, haemoglobin and blood transfusion during cardiopulmonary bypass on post-operative acute kidney injury. *Nephrol Dial Transplant* 2012;27:153–60.
- 32 Sanetra K, Gerber W, Shrestha R, et al. The del Nido versus cold blood cardioplegia in aortic valve replacement: A randomized trial. *J Thorac Cardiovasc Surg* 2020;159:2275–83:e1.
- 33 Kantathut N, Cherntanomwong P, Khajareern S, et al. Lactated Ringer's as a base solution for del Nido cardioplegia. *J Extra Corpor Technol* 2019;51:153–9.
- 34 Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. *Clin J Am Soc Nephrol* 2006;1:19–32.
- 35 Fiore AC, Naunheim KS, Taub J, et al. Myocardial preservation using lidocaine blood cardioplegia. *Ann Thorac Surg* 1990;50:771–5.
- 36 Vaillant F, Dehina L, Mazzadi A, et al. Heart rate reduction with ivabradine increases ischaemia-induced ventricular fibrillation threshold: Role of myocyte structure and myocardial perfusion. *Resuscitation* 2011;82:1092–9.
- 37 Vaillant F, Dehina L, Dizerens N, et al. Ivabradine but not propranolol delays the time to onset of ischaemia-induced ventricular fibrillation by preserving myocardial metabolic energy status. *Resuscitation* 2013;84:384–90.
- 38 Wongtanarasarin W, Siri-Angkul N, Wittayachamnankul B, et al. Mitochondrial dysfunction in fatal ventricular arrhythmias. *Acta Physiol (Oxf)* 2021;231:e13624.
- 39 Dahl CF, Ewy GA, Warner ED, et al. Myocardial necrosis from direct current countershock. Effect of paddle electrode size and time interval between discharges. *Circulation* 1974;50:956–61.
- 40 He LM, Zhang A, Xiong B. Effectiveness of amiodarone in preventing the occurrence of reperfusion ventricular fibrillation after the release of aortic cross-clamp in open-heart surgery patients: A meta-analysis. *Front Cardiovasc Med* 2022;9:821938.
- 41 Li W, Liu W, Li H. Electrocardiography is useful to predict postoperative ventricular arrhythmia in patients undergoing cardiac surgery: A retrospective study. *Front Physiol* 2022;13:873821.