Longitudinal Outcomes of Cardiogenic Shock Patients Undergoing Conventional Cardiac Surgery

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Abstract

Background: Cardiogenic shock is a known risk factor for early mortality following conventional cardiac surgery, however its impact on longitudinal outcomes is less established. This study evaluated longer-term outcomes of conventional cardiac surgery in patients with cardiogenic shock. Methods: This was a retrospective review of conventional cardiac operations performed in patients presenting with cardiogenic shock between 2010 and 2020. The primary outcome was survival, and secondary outcomes included postoperative complications, and rates of heart failure readmission. Multivariable Cox proportional hazards modeling was conducted to identify risk-adjusted predictors of mortality. Results: 604 patients were included, representing 4% of all cardiac cases. Median follow up was 4.3 (IQR 0.3-6.8) years. Aortic root repair/replacement (31.6%) was most commonly performed. 11.1% of patients required preoperative cardiopulmonary resuscitation. Bridging modalities included intravenous inotropes (35.4%), intra-aortic balloon pump (33.4%), Impella (0.5%), or venoarterial extracorporeal membrane oxygenation (3.3%). Operative mortality was 21.5%. Complications included reoperation (24.3%), stroke (15.9%) renal failure (19.2%), and prolonged ventilation (47.9%). Unadjusted 1- and 5-year survival were 71.7% and 62.1%. Risk-adjusted preoperative predictors for mortality included peripheral vascular disease (HR 1.75, 95% CI 1.23-2.49), dialysis dependency (HR 6.30, 95% CI 3.77–10.51) and increasing age (HR 1.02, 95% CI 1.02–1.04). Three patients eventually underwent ventricular assist device implantation and no patients underwent heart transplantation. Conclusions: Despite high initial rates of morbidity and mortality following conventional cardiac surgery in patients presenting with cardiogenic shock, 62% survive to 5 years and most do not require heart failure readmission or advanced heart failure surgical therapy.

Introduction

Cardiogenic shock is a critical state defined by decreased cardiac output and impaired end-organ perfusion[1–3]. Typically originating from an initial cardiac insult, the process often generates a systemic cascade resulting in inflammation, cardiac ischemia, and further impairment of cardiac function[4,5]. Despite years of study and advances in technology, the mortality associated with cardiogenic shock has remained remarkably high[6,7]. Most treatment options of the cardiogenic shock state focus on the support of hemodynamics with the goal of optimizing end-organ perfusion[3,8,9]. These options include invasive hemodynamic monitoring, intravenous inotropic support, and mechanical circulatory support.

Cardiogenic shock following cardiac surgery has been demonstrated to carry a very poor prognosis[10–13]. Likewise, conventional cardiac surgery in the patient presenting with cardiogenic shock is often associated with suboptimal operative outcomes. While the operation may be targeted at reversing the inciting insult, whether it be coronary ischemia or acute valvular pathology, the early-results have been dismal[14]. However, longer-term impacts following cardiac surgery in the shock state has been less established. This study aims at investigating the long-term outcomes of conventional cardiac surgical procedures in cardiogenic shock patients.

Materials and Methods

Study Population

This study was a retrospective analysis from a single academic institution. Data were extracted from the institutional Society of Thoracic Surgeons (STS) registry and supplemented with longitudinal clinical data extracted from the electronic health record. The study included adults (18 years or older) presenting in a state of cardiogenic shock that underwent conventional cardiac surgery between January 2010 and May 2020. Cardiogenic shock was defined according to the STS database as a sustained (>30 minute) episode of hypoperfusion evidenced by systolic blood pressure <90mmHg and/or, if available, cardiac index <2.2 L/min per square meter determined to be secondary to cardiac dysfunction and/or the requirement for parenteral inotropic or vasopressor agents or mechanical support to maintain blood pressure and cardiac index above those specified levels.

Patients undergoing transcatheter procedures such as transcatheter mitral or aortic valve repair or replacement, were excluded. Patients who underwent primary ventricular assist device (VAD) placement and/or heart transplantation were also excluded. This study was approved by the Institutional Review Board at the University of Pittsburgh.

Outcomes

The primary outcome of this study was overall one- and five-year survival. Secondary outcomes included postoperative complications such as renal failure, respiratory failure, reoperation, stroke, and operative mortality. Other outcomes investigated were rates of hospital readmission and need for VAD implantation or heart transplantation during follow-up.

Statistical Analysis

Continuous data are presented as mean ± standard deviation for Gaussian variables or median [interquartile range (IQR)] for non-gaussian variables and all categorical data as number (percentage). Normality was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data and categorical data were compared with Pearson's Chi-squared test or Fisher's exact test when 25% of available data points had expected values <5. Non-Gaussian distributions were evaluated using Mann-Whitney U test. Kaplan Meier survival analysis was conducted to evaluate one- and five-year survival. Multivariable Cox proportional hazard models (univariate inclusion $p<0.05$) were used for modeling risk-adjusted predictors for mortality. Competing risk methods by cumulative incidence function was used to model readmissions.

Results

Patient Characteristics and Presentation

This study included 604 patients presenting with cardiogenic shock, representing 4% of patients undergoing conventional cardiac surgery within the study period. Median age was 64 years (IQR 55 to 72 years), and patients were predominantly male (63.6%) and of white race (86.9%). 48.3% and 33.1% of patients had history of previous myocardial infarction (MI) and previous cardiac intervention, respectively. The most common presentation at time of cardiogenic shock was Non-ST elevation MI (20.4%). Baseline characteristics and comorbidities are shown in **Table 1** .

Prior to cardiac surgical intervention, 214 (35.4%) of patients were supported with intravenous inotropes. 202 (33.4%) of patients were supported preoperatively with an intra-aortic balloon pump (IABP), 20 (3.31%) with veno-arterial extracorporeal membrane oxygenation (VA ECMO), and 3 (0.5%) with an Impella (Abiomed, Danvers, MA, USA) device. A total of 67 (11.1%) patients had received cardiopulmonary resuscitation prior to surgical intervention (**Table 1**).

Operative Details

The most common indication for surgery was aortic root repair or replacement (31.6%) followed by isolated coronary artery bypass grafting (CABG) (29.8%). 457 (75.7%) of cases were performed under an emergent

status, and 45 (7.5%) were performed under an emergent salvage status. 524 (86.8%) cases utilized cardiopulmonary bypass with median pump time of 171 minutes (IQR 112 to 221 minutes). Intra- or post-operative IABP was placed in 33 (5.47%) patients, with 2 (0.33%) intra-operative Impella devices, 20 (3.31%) intra-operative VA ECMO, and 8 (1.32%) post-operative VA ECMO (**Table 1**). Operative mortality was 21.5% (**Table 2**).

Postoperative Complications and Long-Term Outcomes

The most common complication following surgical intervention was respiratory insufficiency requiring prolonged mechanical ventilation (47.9%). 407 (67.4%) of patients required blood transfusion and 147 (24.3%) required reoperation. The rate of cerebrovascular accident was 15.9% (**Table 2**). Rates of overall readmission and heart failure readmission were 46.03% and 18.87%, respectively.

Median follow up was 4.28 years (IQR 0.28 to 6.80 years). One-year overall survival was 71.7%. Five-year survival was 62.1% (**Figure 1**). Multivariable analysis revealed preoperative risk-adjusted predictors of mortality consisting of increasing age (HR 1.03, 95% CI 1.02 to 1.04; P<0.001), history of peripheral vascular disease (HR 1.75, 95% CI 1.23 to 2.49; P=0.002) and renal failure requiring dialysis (HR 6.30, 95% CI 3.77 to 10.51; P<0.001). Preoperative ECMO support was not associated with increased risk-adjusted hazards for mortality, but intraoperative ECMO (HR 7.43, 95% CI 3.52 to 15.66; P<0.001) and postoperative ECMO (HR 13.67, 95% CI 5.98 to 31.25; P<0.001) were associated with increased risk-adjusted hazards. Preoperative Impella support was associated with increased hazards (HR 12.11, 95% CI 2.33 to 63.05; P=0.003). Of all cardiac procedures, aortic root repair/replacement was associated with lower risk-adjusted hazards for mortality (HR 0.41, 95% CI 0.20 to 0.83; P=0.013) (**Table 3**). During longitudinal follow-up, 3 (0.5%) patients underwent eventual VAD implantation. No patients in this study underwent heart transplantation during follow-up.

Discussion

Cardiogenic shock is a serious and often lethal manifestation following cardiac insult with extremely high rates of in-hospital mortality. Historical rates have been reported as high as 80%[15]. However, more contemporary trials such as the SHould we emergently revascularize Occluded Coronaries for cardiogenic shock (SHOCK) trial and Global Registry of Acute Coronary Events (GRACE) registries have reported rates around 60%[16,17]. Few reports have achieved mortality rates below 50%[18,19]. Considerably less data exists in the cardiac surgical population in patients with cardiogenic shock. Existing literature is limited to smaller case series and case reports. Herein, we report our experience of 604 procedures performed on patients in cardiogenic shock.

Hemodynamic stabilization and bridging of the cardiogenic shock patient population is highly debated. In our series, we utilized intravenous inotropes most frequently (35.4%), followed by the use of intra-aortic balloon pumps (33.4%). The effectiveness of intra-aortic balloon pump in cardiogenic shock, especially in the setting of acute myocardial infarction, has been argued. The IABP SHOCK II Trial has demonstrated no mortality benefit of these pumps in addition to early revascularization[2]. Early revascularization, however, has been proven to offer early and long-term survival benefit in this patient population[20]. Other methods of bridging such as venoarteroal ECMO and/or Impella device were utilized infrequently in our series, comprising less than 4% of our surgical experience. ECMO bridge to cardiac surgery other than transplant or ventricular assist device has been described in prior case series and reports. Common indications were for mechanical complications of acute myocardial infarction including ventricular septal defect or papillary muscle rupture[21–23]. Long-term outcomes of hemodynamic support with veno-arterial ECMO for cardiogenic shock have not been well studied.

Timing of surgical intervention can be as important to patient outcomes as the operation itself. No specific guidelines exist for the patient in cardiogenic shock, and often, timing is individualized according to the patient's clinical status. In our opinion, the timing of operation in these patients should be dictated by the disease process, baseline risk of the patient including comorbidity assessment, as well end-organ status. For example, a patient presenting in volume overload and marginal hemodynamics with an acute-on-chronic valvular process may benefit from intravenous diuresis, inotropic or temporary mechanical circulatory sup-

port, and improvement in end-organ status before commencing with surgery. Sometimes this is not possible such as in cases of acute valve leaflet perforation from endocarditis where the heart is not pre-conditioned to valvular insufficiency. These patients typically require emergent operations. A similar balance exists in coronary revascularization. Patients presenting with acute ST-elevation myocardial infarctions with ongoing ischemia require emergent revascularization, whether percutaneously or surgically. In a patient presenting late from an acute myocardial infarction who is in cardiogenic shock but has no ongoing signs of active ischemia, stabilizing hemodynamics and optimizing the patient for a short time period before revascularization may be appropriate in select cases.

The early mortality rates in our study were markedly lower than those described in large cardiogenic shock trials and likely a result of selection bias when deciding operative candidacy. Patients with higher comorbidity burden and perceived prohibitive surgical risk were likely turned down and not captured in this study, while previous trials investigating cardiogenic shock included all shock patients, both surgical and non-surgical candidates[16,17]. When evaluating cardiogenic shock patients for surgical intervention, we have identified several risk factors independently associated with increased hazards for mortality. This include advanced age, peripheral vascular disease, and renal failure requiring dialysis, all risk factors associated with increased morbidity and mortality in the non-shock population following cardiac surgery[24–26]. Careful patient selection for surgical intervention may help reduce short-term mortality and avoidance of futile procedures in non-salvageable patients. As observed in our study, if these high-risk patients are able to survive to hospital discharge, their longer-term outcomes are favorable. Moreover, we observed overall 1- and 5 -year survival of 71.7% and 62.1%. Additionally, heart failure readmission occurred in only 18.9% of our cohort with median readmissions per person of 0 (IQR 0-2 readmissions), and less than 1% of surviving patients required advanced heart failure surgical therapy. Such findings support efforts to perform cardiac surgical procedures in appropriately selected patients presenting with cardiogenic shock.

Each individual patient is different as is the approach that individual surgeon's and other providers may have with these patients. There are certainly multiple factors which play into the decision-making process regarding surgical candidacy. The general approach our surgical group has is to attempt to assess the patient's overall life expectancy should they survive surgery, as well as the potential reversibility of the anatomic or physiologic insults causing the shock state. For instance, a 90-year old presenting in cardiogenic shock on multiple vasoactive agents with marginal urine output will likely have poor outcomes. Similarly, a patient with significant comorbidity burden such as chronic lung disease with home oxygen dependence, dialysis, and peripheral arterial disease requiring extensive multi-component cardiac surgery may have poor outcomes and limited life expectancy even if they survive surgery.

Limitations

The current study has several limitations. First, this was a retrospective, observational study. It does not compare or contrast potential treatment strategies for the patient in cardiogenic shock, but is rather aimed at describing a single center experience with conventional cardiac surgery in this patient population. Therefore, the scope of this study was not to create any inferences with regard to the utility of cardiac surgical procedures versus other non-surgical or medical treatments in these patients. Furthermore, the database utilized for this study captures only patients with cardiogenic shock that underwent cardiac surgery within our institution. As a result, we are unable to comment on rates of overall survival of cardiogenic shock within our institution. There exists potential for selection bias, as it is likely that a significant portion of patients presenting with cardiogenic shock were turned down for surgical intervention. As a result, patients who were less ill and/or had decreased comorbidity burden were likely selected for surgery. Finally, the granularity of decision-making in these complex patients could not be fully captured.

Conclusions

In our review of 604 patients with cardiogenic shock undergoing conventional cardiac surgery, we describe high rates of early morbidity and mortality. However, despite this, 62% of patients survive to 5 years and most do not require heart failure readmission or advanced heart failure surgical therapy during follow-up. These

data are therefore supportive of conventional cardiac surgery in appropriately selected patients presenting in cardiogenic shock.

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Disclosures

Arman Kilic, MD is on the medical advisory board for Medtronic, Inc. This affiliation does not create direct conflicts with the content of this manuscript.

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Table 1. Baseline characteristics, preoperative comorbidities, and operative details of patients in cardiogenic shock who underwent conventional cardiac surgical procedures

	Number (%)
	604
Age, years	64.00 (55.00-72.00)
Body mass index	28.76 (25.47-33.09)
Female	220 (36.42%)
Race	
White	525 (86.92%)
Black	62 (10.26%)
Other	17 (2.81%)
Diabetes mellitus	161 (26.66%)
Dialysis dependency	28 (4.64%)

	Number (%)
Chronic obstructive pulmonary disease	137 (22.68%)
Hypertension	446 (73.84%)
History of immunosuppression	41 (6.79%)
Family history of coronary artery disease	82 (13.58%)
History of cancer	35 (5.79%)
Cardiovascular disease	110 (18.21%)
Peripheral vascular disease	160 (26.49%)
Previous cardiac intervention	200 (33.11%)
Previous myocardial infarction	292 (48.34%)
History of heart failure	193 (31.95%)
History of mediastinal radiation	5 (0.83%)
Serum creatinine, mg/dL	1.10 (0.90- 1.50)
Total serum albumin, g/dL	3.60 (3.10- 3.70)
Total serum bilirubin, mg/dL	0.60 (0.60- 0.90)
Cardiac presentation	65 (10.76%)
Asymptomatic	
Symptoms unlikely ischemia	120 (19.87%)
Stable angina	3 (0.50%)
Unstable angina	33 (5.46%)
Non-ST elevation MI	123 (20.36%)
ST elevation MI	117 (19.37%)
Angina equivalent	1 (0.17%)
Other	142 (23.51%)
NYHA class symptoms	
Class 1	410 (67.88%)
Class 2	5 (0.83%)
Class 3	27 (4.47%)
Class 4	162 (26.82%)
Preoperative cardiopulmonary resuscitation (CPR)	67 (11.09%)
Cardiac arrhythmia at presentation	177 (29.30%)
Number of diseased coronary vessels	
0	301 (49.83%)
1	48 (7.95%)
2	63 (10.43%)
3	192 (31.79%)
Left ventricular ejection fraction, %	50.00 (33.00-58.00)
Preoperative antiplatelet therapy	364 (60.26%)
Preoperative anticoagulation	283 (46.85%)
Bridging support	
Intravenous inotropes	214 (35.43%)
Intra-aortic balloon pump	
None	369 (61.09%)
Preoperative	202 (33.44%)
Intraoperative	30 (4.97%)
Postoperative	3 (0.50%)
Impella device	
None	599 (99.17%)
Preoperative	3 (0.50%)
Intraoperative	2 (0.33%)
Extracorporeal membrane oxygenation	

	Number (%)
None	556 (92.05%)
Preoperative	20 (3.31%)
Intraoperative	20 (3.31%)
Postoperative	8 (1.32%)
Operation performed	
Aortic Root	191 (31.62%)
CABG and AVR	19 (3.15%)
CABG and MVr/MVR	36 (5.96%)
Double Valve	25 (4.14%)
Isolated AV	30 (4.97%)
Isolated CABG	180 (29.80%)
Isolated MVr/MVR	21 (3.48%)
Isolated TV	1 (0.17%)
Triple Valve	4 (0.66%)
Other	97 (16.06%)
Operative status	
Urgent	102 (16.89%)
Emergent	457 (75.66%)
Emergent salvage	45 (7.45%)
Operative details	
Cardiopulmonary bypass utilization	524 (86.75%)
Perfusion time, minutes	171.0 (112.0-221.0)
Cross-clamp time, minutes	112.0 (81.00-153.0)

AVR, aortic valve replacement

CABG, coronary artery bypass grafting

MI, myocardial infarction

MVr, mitral valve repair

MVR, mitral valve replacement

TV, tricuspid valve

Table 2 . Postoperative complications following conventional cardiac surgery performed in patients in cardiogenic shock

Complications	**Number (%)**
Operative mortality	130 (21.52%)
Sepsis	25 (4.14%)
Prolonged mechanical ventilation	289 (47.85%)
Stroke	96 (15.89%)
Renal failure	116 (19.21%)
Reoperation	147 (24.34%)
Blood transfusion	407 (67.38%)

Table 3. Cox proportional hazards multivariable model for risk-adjusted predictors of mortality following conventional cardiac surgery in patients presenting with cardiogenic shock

	Hazard Ratio	**95% Hazard Ratio Confidence Limits**	**95% Hazard Ratio Confidence Limits**	**P-Value**
Age, increasing	1.028	1.015	1.041	<.001
Body mass index, increasing, per kg/m^2	0.980	0.956	1.004	0.106
Dialysis dependency	6.296	3.770	10.514	<.001
Peripheral vascular disease	1.749	1.231	2.486	0.002
ECMO utilization				
No ECMO	Reference	Reference	Reference	Reference
Preoperative usage	0.961	0.346	2.665	0.939
Intraoperative usage	7.426	3.521	15.662	<.001
Postoperative usage	13.674	5.984	31.249	<.001
Impella utilization				
No Impella	Reference	Reference	Reference	Reference
Preoperative usage	12.108	2.325	63.053	0.003
Postoperative usage	0.581	0.070	4.807	0.614
Operation performed				
Isolated CABG	Reference	Reference	Reference	Reference
Isolated valve	0.469	0.214	1.028	0.059
Double valve	1.050	0.424	2.597	0.916
CABG + valve	1.015	0.618	1.667	0.953
Triple valve	1.369	0.680	2.754	0.379
Aortic root repair/replacement	0.408	0.201	0.828	0.013

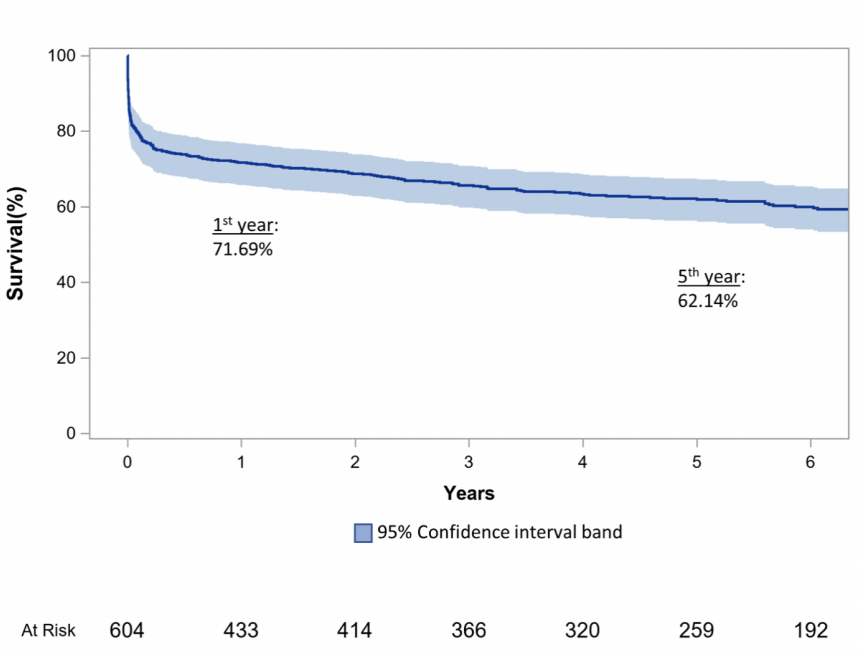
*Variables adjusted also adjusted for in this model: usage of intravenous inotropes, history of cancer and previous myocardial infarction, NYHA Class, cardiac presentation, number of diseased coronary vessels,

CABG, coronary artery bypass grafting

ECMO, extracorporeal membrane oxygenation

Figure Legend

Figure 1. Overall unadjusted survival of patients who underwent conventional cardiac surgical procedures with initial presentation of cardiogenic shock



At Risk	604	433	414	366	320	259	192