

Journal Pre-proof

Identifying and Mitigating Risk of Post-Cardiotomy Cardiogenic Shock in Patients with Ischemic and Non-Ischemic Cardiomyopathy

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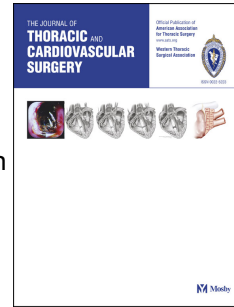
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Predictors of Post-Cardiotomy Cardiogenic Shock in Ischemic and Non-Ischemic Cardiomyopathy

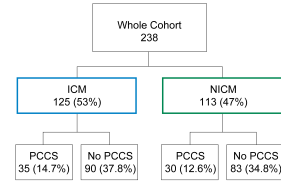
Methods & Results

January 2017 - 2020

Cohort 238 patients

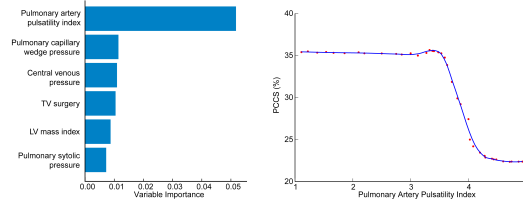
- EF <30% (209)
- EF <35% with at least moderately severe MR (32)

Primary outcome was PCCS, defined as need for Impella, extracorporeal membrane oxygenation, or vasoactive-inotropic score >25.

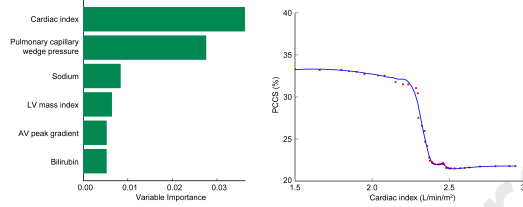


Random Forest analysis was used to identify predictors of PCCS

Ischemic Cardiomyopathy



Non-Ischemic Cardiomyopathy



Implications

Right heart function, measure by PAPI, is most predictive of PCCS in ICM, whereas degree of cardiac decompensation is most predictive of PCCS in NICM. This knowledge will help guide early use of mechanical circulatory support in high risk low ejection fraction patients.

AV: aortic valve, EF: Ejection fraction, ICM: Ischemic cardiomyopathy, LV: left ventricle, MR: Mitral regurgitation, NICM: Non-ischemic cardiomyopathy, PAPI: Pulmonary artery pulsatility index, PCCS: Post-cardiotomy cardiogenic shock, TV: Tricuspid valve

1 **Identifying and Mitigating Risk of Post-Cardiotomy Cardiogenic Shock in Patients with**
2 **Ischemic and Non-Ischemic Cardiomyopathy**

3
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26 approved 3/1/2017)

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32
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36 Glossary of Abbreviations:

37 ECMO: extracorporeal membrane oxygenation

38 EF: ejection fraction

39 IABP: intra-aortic balloon pump

40 ICM: ischemic cardiomyopathy

41 LVAD: left ventricular assist device

42 MCS: mechanical circulatory support

43 NICM: non-ischemic cardiomyopathy

44 PAPi: pulmonary artery pulsatility index

45 PCCS: post-cardiotomy cardiogenic shock

46 PCWP: pulmonary capillary wedge pressure

47

48

49

50

51 **Central Message**

52 Post-cardiotomy cardiogenic shock is predicted by right heart dysfunction in ischemic
53 cardiomyopathy and by greater cardiac decompensation in non-ischemic cardiomyopathy.

54

55 **Perspective Statement**

56 Post-cardiotomy cardiogenic shock has high morbidity and mortality. Its predictors are right
57 heart dysfunction in ischemic, and cardiac decompensation in non-ischemic cardiomyopathy.

58 Preoperative right heart catheterization in patients with low ejection fraction will help identify
59 patients at risk of post-cardiotomy cardiogenic shock and plan for possible temporary mechanical
60 circulatory support.

61

62 **Central Picture Legend:** Top 6 predictors of post-cardiotomy cardiogenic shock in ischemic
63 cardiomyopathy.

64

65

66 **Abstract:** 242/250 words

67 **Objectives:** To identify preoperative predictors of post-cardiotomy cardiogenic shock in patients
68 with ischemic and non-ischemic cardiomyopathy and evaluate trajectory of postoperative
69 ventricular function.

70 **Methods:** From 1/2017–1/2020, 238 patients with ejection fraction <30% (206/238) or 30-34%
71 with at least moderately severe mitral regurgitation (32/238) underwent conventional cardiac
72 surgery at Cleveland Clinic, 125 with ischemic and 113 with non-ischemic cardiomyopathy.
73 Preoperative ejection fraction was $25 \pm 4.5\%$. The primary outcome was post-cardiotomy
74 cardiogenic shock, defined as need for microaxial temporary left ventricular assist device,
75 extracorporeal membrane oxygenation, or vasoactive-inotropic score >25. RandomForestSRC
76 was used to identify its predictors.

77 **Results:** Post-cardiotomy cardiogenic shock occurred in 27% (65/238). Pulmonary artery
78 pulsatility index <3.5 and pulmonary capillary wedge pressure >19 mmHg were the most
79 important factors predictive of post-cardiotomy cardiogenic shock in ischemic cardiomyopathy.
80 Cardiac index < $2.2 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ and pulmonary capillary wedge pressure >21 mmHg were the
81 most important predictive factors in non-ischemic cardiomyopathy. Operative mortality was
82 1.7%. Ejection fraction at 12 months post-surgery increased to 39% (CI: 35-40) in the ischemic
83 group and 37% (CI: 35-38) in the non-ischemic cardiomyopathy group.

84 **Conclusions:** Predictors of post-cardiotomy cardiogenic shock were different in ischemic and
85 non-ischemic cardiomyopathy. Right heart dysfunction, indicated by low pulmonary artery
86 pulsatility index, was the most important predictor in ischemic cardiomyopathy, whereas greater
87 degree of cardiac decompensation was the most important in nonischemic cardiomyopathy.

88 Therefore preoperative right heart catheterization will help identify patients with low ejection
89 fraction that are at higher risk of post-cardiotomy cardiogenic shock.

90

91 **Keywords:** low ejection fraction, cardiac surgery, right heart catheterization, mechanical
92 circulatory support

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94 INTRODUCTION

95 Patients with low preoperative ejection fraction (EF) and treatable cardiac lesions have
96 the most to gain from surgery but are at high risk of death from post-cardiotomy cardiogenic
97 shock (PCCS), which carries mortality as high as 50% to 75%.¹⁻⁶ High-dose inotropic and
98 vasopressor support typically are required to separate these patients from cardiopulmonary
99 bypass and during early postoperative care; however, these drugs at high doses are toxic and lead
100 to peripheral ischemia, tissue hypoxia, acidosis, and multiorgan failure and exacerbate
101 myocardial dysfunction.⁷ Temporary mechanical circulatory support (MCS) in this setting is
102 beneficial for myocardial perfusion and recovery by unloading the left ventricle and normalizing
103 cardiac output to the body while awaiting myocardial recovery. However, deploying these
104 devices takes time and resources and may not be readily available when separating from
105 cardiopulmonary bypass. Delay in deployment increases cardiopulmonary bypass time or leaves
106 the patient in cardiogenic shock, which have deleterious effects downstream.

107 Predicting which patients are at the most risk for developing PCCS would allow earlier or
108 planned deployment of temporary MCS, and may improve outcomes; however, these risk factors
109 may be different between patients with ischemic cardiomyopathy (ICM) and non-ischemic
110 cardiomyopathy (NICM). Thus, the main objective of this study was to identify the patients most
111 at risk of PCCS in ICM and NICM so that any future MCS protocols can include these risk
112 factors. An additional objective was to evaluate these outcomes in the contemporary era of using
113 temporary MCS as rescue.

114

115 METHODS

116 *Study Population*

117 From January 1, 2017 to January 1, 2020 238 patients with left ventricular EF <30%
118 (206/238) or EF 30-34% with at least moderately severe (3+) mitral regurgitation (32/238)
119 underwent conventional cardiac surgery at Cleveland Clinic. Patients who underwent planned
120 durable left ventricular assist device implant, cardiac transplantation, or congenital operations
121 were excluded. Of the 238 patients, 125 had ICM and 113 NICM.

122 Patients were assigned to the ICM group if coronary artery disease was the primary driver
123 of their disease state. In general, patients were classified as ICM when there was a severe lesion
124 in a territory with decreased function. However, there were patients with NICM and coronary
125 artery disease, but it was not the driver of the cardiomyopathy. The majority of the reduced
126 function was not explained by the severity and territory of coronary artery disease for the
127 patients in the NICM group.

128

129 *Referral for Formal MCS Evaluation and Backup*

130 Patients felt to be at high risk for PCCS underwent a formal temporary MCS backup
131 evaluation. Patients are assessed preoperatively by the advanced heart failure team for left
132 ventricular assist device implant or transplant, and preparation is made in the operating room to
133 have the Impella equipment available. Patients that underwent this process will be described as
134 being in the MCS Backup group. Depending on surgeon preference and gestalt for the risk of
135 PCCS, intraoperatively the right axillary artery is exposed and a 10 mm woven polyester graft
136 may be sewn end to side prior to commencing cardiopulmonary bypass.⁸ Once the operation is
137 complete and the patient is being weaned from cardiopulmonary bypass, if the patient fails to
138 separate from cardiopulmonary bypass, is hemodynamically unstable after weaning, or requires
139 high dose inotropes and vasopressors, then temporary MCS is instituted at the discretion of the

140 surgeon using either extracorporeal membrane oxygenation (ECMO) or Impella. Impella 5.0/5.5
141 was the preferred device for patients with isolated left heart failure.

142 *Data*

143 Patient demographics, procedural details, and postoperative outcomes were obtained
144 from institutional registries maintained by professional abstractors for national quality reporting.
145 Preoperative hemodynamics data was obtained from right heart catheterization reports and from
146 measurements recorded closest to the date of surgery for patients who had a preoperative Swan-
147 Ganz catheter in place in the intensive care unit (ICU). Additional patient data, including results
148 of preoperative echocardiography and catheterizations, were obtained through medical records
149 review. The Institutional Review Board (IRB) of the Cleveland Clinic approved the study
150 protocol and publication of data. Patient written consent for the publication of the study data was
151 waived by the IRB given its retrospective review of data. (IRB No. 17-270, approved 3/1/2017)

152 In patients with ischemic heart disease, function, viability and quality of coronary targets
153 were collected for each of the 3 main territories: left anterior descending, circumflex, and right
154 coronary artery. Echocardiography was used to assess function with a score given based on the
155 worst segment in that territory. The scores ranged from 0 to 4: normal (0), mild/moderate
156 hypokinesis (1), moderately severe to severely hypokinetic (2), akinetic (3) and dyskinetic (4)
157 (Table 2). Viability was assessed with either cardiac positron emission tomography scans or
158 cardiac magnetic resonance imaging with gadolinium contrast. A scar score was calculated for
159 each myocardial territory, as follows: 0 no scar, 1 small scar, 2 large scar (Supplementary Table
160 1). A weighted total scar score was also calculated (Supplementary Appendix 1). Coronary artery
161 quality was assessed by coronary angiography and assigned 0 for optimal target; 1, suboptimal

162 target; 2, poor target, 3, no significant stenosis or patent bypass graft present (Table 2).

163 Additional information on ischemia evaluation is detailed in Supplementary Appendix 1.

164 *Endpoints*

165 The primary endpoint is occurrence of PCCS, defined by fulfilling any of the following:
166 requiring placement of Impella during surgery, instituting ECMO during or after surgery, need
167 for continuation of preoperative ECMO, or vasoactive inotropic score of >25 (Supplementary
168 Appendix 2) The vasoactive inotropic score is calculated by using a formula to add up the
169 patient's vasopressor and inotropic requirements, thus describing the total amount of
170 cardiovascular support. For example, a 100 kg patient on 10 $\mu\text{g}/\text{min}$ epinephrine, 10 $\mu\text{g}/\text{min}$
171 norepinephrine and 0.5 $\mu\text{g}/\text{kg}/\text{min}$ milrinone calculates to a vasoactive inotropic score of 25.
172 (Supplementary Appendix 2) Intra-aortic balloon pump (IABP) was not included in the
173 definition of PCCS.

174 Secondary endpoints include the identification of patients most at risk of PCCS in
175 patients with ICM and NICM, evaluation of their postoperative outcomes, and longitudinal
176 follow up of their left ventricular ejection fraction.

177 *Data Analysis*

178 All statistical analyses were performed using SAS statistical software and R software
179 version 3.3.2. Categorical data are summarized by frequencies and percentages and compared
180 using the chi-squared test. Continuous variables are summarized by mean \pm standard deviation,
181 or with equivalent 15th, 50th (median), and 85th percentiles where data were skewed. For
182 continuous variables, comparisons were made using the Wilcoxon rank sum test. Parametric
183 estimates are accompanied by an asymmetric 68% confidence interval, comparable to ± 1
184 standard error.

185 **Random Forests**

186 Random forest classification (randomForestsSRC) for imbalanced data was performed to
187 assess possible nonlinear and interacting relationships between likelihood of PCCS and patient
188 characteristics.⁹ We used 5,000 trees and with 8 random variables at each split. All variables
189 listed in Supplementary Appendix 3 were included in the analysis, without variable selection.
190 Missing data were imputed using “on the fly” random forest imputation.¹⁰ Variable importance
191 was used to rank relative importance of these variables,¹¹ and their relationship with PCCS
192 visualized using risk-adjusted partial-dependency plots.¹²

193 **Longitudinal Data Analysis**

194 The continuous repeated measurements of left ventricular EF were analyzed
195 longitudinally across time. Nonlinear mixed-model regression (SAS PROC NLMIXED) was
196 used to resolve a number of time phases to form a temporal decomposition model to describe the
197 temporal trend of mean estimated left ventricular EF over time.¹³ Two time-varying temporal
198 phases were identified, an early phase and a late phase both modulating the entire longitudinal
199 curve.

200

201 **RESULTS**

202 Population Characteristics

203 Mean age in the ICM and NICM groups were 66 ± 10 and 62 ± 13 years ($P=.045$) (Table
204 1). More patients with a history of myocardial infarction were in the ICM vs NICM group (64%
205 vs 27%, $P<.0001$) as were patients with a history of peripheral artery disease (20% vs 10%,
206 $P=.027$). History of prior cardiac operation was higher in the NICM vs ICM group (29% vs
207 5.6%, $P<.0001$). Various comorbidities were similar between groups, like history of congestive

208 heart failure, renal dialysis and prior stroke. Predicted risk of operative mortality for cases for
209 which a Society of Thoracic Surgeons model is available (ICM: n=97 [78%] NICM: n=45
210 [40%]), was similar for ICM and NICM groups (median 4.0% vs 3.0%, respectively, $P=.29$)
211 (Supplementary Figure 1)

212 Preoperative echocardiographic details

213 Overall mean EF was 24.6%, which was approximately normally distributed (skewness
214 was -0.28). Mean EF in the ICM group was $24 \pm 4\%$, and $25 \pm 4\%$ in the NICM group ($P=.013$).
215 (Table 1) Mean preoperative left ventricular end diastolic inner diameter was 5.9 ± 0.79 cm in
216 the ICM group and 6.1 ± 1.0 cm in the NICM group ($P=.09$). Preoperative left ventricular end
217 diastolic inner diameter was greater than 6.5 cm in 20% (23/113) of ICM patients and 32%
218 (33/104) of NICM patients.

219 *Surgical components*

220 Of 125 patients with ICM, 72 underwent isolated CABG, 31 CABG plus mitral valve
221 surgery, 5 CABG plus tricuspid valve surgery, and 17 CABG plus mitral and tricuspid valve
222 surgery. (Table 2) In the NICM group, CABG was performed in 34% of the 113 patients,
223 however coronary artery disease was not the primary driver of their cardiomyopathy. The other
224 components of surgery in the NICM group were aortic valve surgery (69%), mitral valve surgery
225 (49%), tricuspid valve surgery (31%), aortic surgery (23%), and atrial fibrillation surgery (16%).
226 (Table 3)

227 *Surgical Details*

228 Mean myocardial ischemic time was 100 ± 36 minutes and 100 ± 48 minutes in the ICM
229 and NICM groups, respectively ($P=.56$). Mean total cardiopulmonary bypass time was 126 ± 45

230 minutes and 132 ± 63 minutes in the ICM and NICM groups, respectively ($P=.85$). There were 3
231 cases in the NICM group that underwent circulatory arrest, with a mean of 51 ± 25 minutes.

232

233 ***Post-cardiotomy cardiogenic shock***

234 PCCS occurred in 35 (28%) patients in the ICM group and 30 (27%) in the NICM group
235 (Table 4). In the ICM group, ECMO was placed in 3 patients postoperatively. In the NICM
236 group, ECMO was placed in one patient intraoperatively and in 2 patients postoperatively. An
237 Impella was placed in 30 patients, 18 in the ICM group and 12 in the NICM group. Eighteen
238 patients in the ICM group and 18 in the NICM group had a post-operative vasoactive inotropic
239 score of ≥ 25 . Of these 36 patients, 7 met multiple criteria for fulfilling our definition of PCCS.
240 (Figure 1) The distribution of the STS predicted risk of mortality score and development of
241 PCCS for ICM and NICM was similar, (ICM PCCS vs non-PCCS, $p=.34$; NICM PCCS vs non-
242 PCCS, $p=.21$) (Supplementary Figure 2).

243 ***Mechanical circulatory support***

244 Of the 30 Impella devices used, 6 were Impella 5.5, 21 were Impella 5.0, 2 were Impella
245 CP and 1 was an Impella LD. Twenty-eight were placed via the right axillary artery, 1 Impella
246 5.5 was placed via the left axillary artery, and the Impella LD was placed through a 10 mm graft
247 off the aorta. Duration of Impella support was a median of 5.9 days (15th percentile: 3.0 days,
248 85th percentile 15.0 days).

249 70 patients with ICM and 37 patients with NICM were evaluated for temporary MCS
250 backup preoperatively and Impella equipment was made available intraoperatively ahead of time
251 (MCS Backup group). For the ICM group, PCCS occurred in 22/70 (31%) of those in the MCS
252 backup group and 13/55 (24%) not in the backup group ($P=.34$). For the NICM group, PCCS

253 occurred in 20/37 (54%) patients in the backup group and 10/76 (13%) not in the backup group
254 ($P<.0001$). For those in the backup group, 18/70 patients with ICM and 12/37 with NICM
255 patients received an Impella.

256 In the operating room, when the cardiac index was $<2.0 \text{ L}^{-1}\text{m}^{-2}$ despite high doses of
257 inotropic support, Impella was used. However, when it was preserved but inotropic support was
258 still high, IABP was sometimes used, particularly in patients with poor coronary artery targets. In
259 the ICM and NICM groups, 14 patients and 7 patients had an IABP preoperatively, of which 9
260 and 5 were continued postoperatively; 30 patients (13%) had an IABP placed in surgery, 20 in
261 the ICM group and 10 in the NICM group. (Table 4) Of the 30 patients with IABP placed
262 intraoperatively, 15 met criteria for PCCS. Of the 15 patients that did not meet criteria for PCCS
263 that had an IABP placed, 11 were in ICM patients and 4 were in NICM.

264

265 *Postoperative Outcomes*

266 Median (with 15th and 85th percentile) postoperative vasoactive inotropic score was 10
267 (4.7 and 25) and 12 (4.2 and 26) in the ICM and NICM groups, respectively. Median ICU length
268 of stay was 4.2 (2.0 and 11) days in the ICM group and 4.8 (1.8 and 14) days in the NICM group.
269 Postoperative length of stay was 11 (6.9 and 21) days in the ICM group, and 12 (7 and 25) days
270 in the NICM group. Operative mortality was 1.7% (4/237); 1 patient in the ICM group and 3
271 patients in the NICM group.(Table 4) Three of the four deaths were patients who developed
272 PCCS. Other secondary outcomes and MCS characteristics are shown in Table 4.

273

274 *Predictors of Post-cardiotomy cardiogenic shock*

275 **Ischemic Cardiomyopathy Group**

276 In the ICM group, the two most important factors predictive of PCCS were lower
277 pulmonary artery pulsatility index (PAPi) particularly when less than 3.5, and higher pulmonary
278 capillary wedge pressure (PCWP) above 19 mmHg. (Figure 2) The other most important factors
279 predictive of PCCS were higher central venous pressure particularly above 8 mmHg, having
280 tricuspid valve surgery as a surgical component of the operation, greater left ventricular mass
281 index particularly when above 100, and higher pulmonary artery systolic pressure particularly
282 above 45 mmHg. (Figure 2) Scar score was the 10th highest in variable importance, and was a
283 weak negative predictor of PCCS.

284

285 **Non-Ischemic Cardiomyopathy Group**

286 In the NICM group, the two most important factors predictive of PCCS were lower
287 preoperative cardiac index particularly when less than $2.3 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, and higher pulmonary
288 capillary wedge pressure (PCWP) particularly when greater than 21 mmHg (Figure 3). The other
289 most important factors predictive of PCCS were lower sodium particularly when less than 135
290 mmol/L, greater left ventricular mass index particularly when greater than $150 \text{ g}/\text{m}^2$, lower aortic
291 valve peak gradient particularly when less than 10 mmHg, and higher bilirubin particularly when
292 greater than 1 mg/dL.

293

294 ***Postoperative cardiac recovery***

295 For the ICM group, left ventricular EF at 1 month, 6 months and 1 year was 32%, 36%,
296 and 39%; in the NICM group it was 31%, 34% and 37%. For ICM and NICM, the left
297 ventricular EF was not significantly different in early hazard phase ($P=.74$) or late phase ($P=.77$).
298 (Figure 4). In the ICM group, for those that did and did not develop PCCS, there was a similar

299 increase in left ventricular EF after surgery ($P=.48$ early hazard phase and $P=.10$ late hazard
300 phase). (Supplementary Figure 3) . In the NICM group, for those that did and did not develop
301 PCCS, EF was higher in the late phase for the no PCCS group ($P=.14$ early hazard phase and
302 $P=.04$ late hazard phase). (Supplementary Figure 4)

303 Three patients received a durable left ventricular assist device (LVAD), at 8.9, 13 and 38
304 months from initial operation. No patient received a heart transplant after the initial operation.

306 Discussion

307 *Principal Findings*

308 Prevalence of PCCS in our cohort of patients with low ejection fraction was high;
309 however, a low operative mortality can be achieved with the use of early and planned MCS
310 deployment. In the ischemic cardiomyopathy subgroup, right heart dysfunction with lower
311 pulmonary artery pulsatility index was the most predictive of PCCS; whereas degree of heart
312 failure decompensation measured by lower cardiac index and higher pulmonary capillary wedge
313 pressure were the most predictive of PCCS in the non-ischemic cardiomyopathy subgroup.

314 *Ischemic Cardiomyopathy*

315 PAPI, an indicator of right heart function, was the most important predictor of PCCS in
316 the ICM group at a value below 3.5. PAPI has been studied in the context of inferior wall
317 myocardial infarction, postoperative LVADs requiring right ventricular assist device placement,
318 primary pulmonary hypertension, and other heart failure populations.¹⁴⁻¹⁸ In the Evaluation
319 Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness
320 (ESCAPE) trial, the authors reported that PAPI was a significant predictor of death or
321 hospitalization at 6 months, with a cutoff PAPI of 3.65.¹⁷ Another study looking at patients with

322 primary pulmonary hypertension found that patients in the lowest quartile for PAPI (PAPI <3.7)
323 had significantly lower 5 year survival.¹⁸ These cutoff values for PAPI are close to our rapid
324 change in probability for PAPI predicting increased risk of PCCS, but much higher than what is
325 described in the LVAD population (1.5-2) as a predictor of needing right ventricular assist
326 device. One reason for the difference is that in LVAD surgery, the decrease in left sided
327 pressures is immediate whereas in patients undergoing conventional surgery, the decrease in left
328 sided pressures can take many days. PAPI was a much better predictor of PCCS than the reported
329 right ventricular function on echo. As the right ventricle is thin walled, the right ventricular EF is
330 much more preload and afterload sensitive than the left ventricle. Therefore, in the setting of left
331 ventricular dysfunction and venous pulmonary hypertension, the right ventricular contraction
332 appearance on echocardiography is a poor indication of right ventricular function.

333 *Non-ischemic cardiomyopathy*

334 In the NICM group, cardiac index and PCWP were the most predictive of PCCS; right
335 heart catheterization is routinely used in our practice prior to surgery for patients with
336 cardiomyopathy. In patients with clinical evidence of decompensated heart failure, we tend to
337 delay surgery in favor of Swan-directed medical treatment with diuretics and afterload reduction
338 to optimize patients prior to surgery. In patients who would not tolerate diuretics and afterload
339 reduction yet still have decompensated heart failure, preoperative use of IABP, Impella, and
340 rarely ECMO may be useful. In patients who cannot achieve adequate fluid removal with
341 diuresis, temporary MCS may be required intra-operatively.

342 *Mechanical Circulatory Support*

343 The goal is to be able to identify patients preoperatively at highest risk of PCCS and use
344 these criteria for including patients in any future MCS protocols. We do not have a formal

345 inclusion criteria for a MCS backup protocol yet, however if a patient has the top 2 predictive
346 factors in their respective group (eg. NICM patient with high PCWP and low CI), they will be
347 highly considered for MCS backup.

348 With respect to IABP use, we do not typically place an IABP prophylactically if the
349 patient is doing well on low dose inotropic support. Patients receiving an IABP who did not meet
350 criteria for PCCS may have been on the margin for meeting criteria for PCCS or had poor
351 coronary target quality.

352 *Postoperative cardiac recovery*

353 Longitudinal evaluation of EF after cardiac surgery showed a gradual improvement in
354 function, suggesting that this group of patients can have substantial benefit when surgery is
355 offered. The majority of patients in this study had a substantial degree of myocardial viability,
356 given that 66/82 with viability studies had scar score ≤ 3 ; therefore, it would be expected to see
357 post-operative improvement in EF. Despite there being some patients with a higher scar score,
358 this was not shown to be an important predictor of PCCS. Our results suggest that the effect of
359 viability on PCCS is of lower importance among this set of factors. Similar conclusions
360 regarding the role of myocardial viability and survival were shown in a sub-study of the STICH
361 (Surgical Treatment for Ischemic Heart Failure) trial.^{19,20}

362

363 *Limitations*

364 This study is limited by its observational nature. Patients in this study underwent
365 techniques such as the Impella back up strategy that may not be available at all hospitals
366 performing cardiac surgery. Also, we used a new definition for PCCS, which limits comparison
367 to other studies utilizing a different definition (Supplementary Appendix 4). IABP support alone

368 was not used as inclusion criteria for PCCS. This study is also limited by its short- to midterm
369 follow up.

370

371 *Conclusion*

372 In patients with low ejection fraction, preoperative right heart function in ischemic
373 cardiomyopathy patients, measured by PAPI, seemed to be the most predictive of PCCS. In the
374 non-ischemic cardiomyopathy patients, high pulmonary capillary wedge pressure and low index
375 were most predictive of PCCS, suggesting that the degree of preoperative cardiac
376 decompensation is most important. Preoperative right heart catheterization should be obtained in
377 patients with low ejection fraction in order to identify patients at higher risk of PCCS and plan
378 for early use of temporary mechanical circulatory support.

379

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383 is observational and the conclusions are representative of the data and reported outcomes.

384

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443 **Tables**
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460 **Table 1: Baseline and Surgical Characteristics of the Ischemic and Non-Ischemic**
 461 **Cardiomyopathy Subgroups.**

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Patient Characteristics	ICM (n=125)		NICM (n=113)		P
	N ^a	No. (%) or Mean \pm SD	N ^a	No. (%) or Mean \pm SD	
Demography					
Patient age (years)	125	66 \pm 10	113	62 \pm 13	.045
Male	125	111 (89)	113	89 (79)	.035
Symptoms (Preop NYHA Class)					
NYHA 1	102	4(3.9)		4(4.4)	.26
NYHA 2		42(41)		25(28)	
NYHA 3		41(40)		47(52)	
NYHA 4		15(15)	90	14(16)	
Cardiac Comorbidity					
Emergency surgery	125	1(0.80)	113	1(0.88)	.94
History of Myocardial Infarction	125	80(64)	113	31(27)	<.0001
Preop Ventricular Tachycardia or Fibrillation	125	7(5.6)	113	16(14)	.026
Prior Cardiac Operation	125	7 (5.6)	113	33 (29)	<.0001
History of chronic heart failure	125	112(90)	113	101(89)	.96
Non-cardiac comorbidity					
Endocarditis	125	0(0)	113	17(15)	<.0001
Peripheral Arterial Disease	125	25(20)	113	11(9.7)	.027
Chronic obstructive pulmonary disease	125	41(33)	113	53(47)	.026
Prior Renal Dialysis	125	5(4.0)	113	10(8.8)	.12
Prior Stroke	125	11(8.8)	113	15(13)	.27
Intubated	125	3(2.4)	113	5(4.4)	.39
STS PROM (%)^c	97	1.0/4.0/8.0	45	1.0/3.0/7.0	.29
Preoperative Location					

Home	125	30(24)	113	38(34)	.1
Hospital Non-ICU	125	76(61)	113	59(52)	.18
ICU	125	19(15)	113	16(14)	.82
Preoperative vasopressors or inotropes					
On vasopressors prior to surgery (within 24 hours)	125	3(2.4)	113	3(2.7)	.9
On inotropes prior to surgery (within 24 hours)	125	0(0)	113	2(1.8)	.14
Echo data					
Preop left ventricular ejection fraction (%)	125	24 ± 4.4	113	25 ± 4.4	.013
Preop LVEDD (cm)	113	5.9 ± 0.79	104	6.1 ± 1.0	.088
Right Heart Catheterization					
Cardiac Index: Fick method (L/min/m ²) ^c	72	1.8/2.2/2.9	59	1.8/2.3/2.9	.75
Pulmonary artery Systolic Pressure (mmHg)	73	45 ± 15	62	46 ± 16	.61
Pulmonary artery Diastolic Pressure (mmHg)	73	21 ± 8.7	62	23 ± 8.6	.25
Central venous pressure (mmHg)	72	8.7 ± 5.6	62	8.5 ± 4.8	.97
Pulmonary artery pulsatility index	72	4.0 ± 3.4	62	3.8 ± 3.1	.64
Pulmonary capillary wedge pressure (mmHg)	73	19 ± 9.1	61	22 ± 7.5	.013
Surgical Characteristics					
MCS Back up Protocol	125	70(56)	113	37(33)	.00030
Impella Placed in Surgery	125	18(14)	113	12(11)	.38
Number of Surgical Components^b	125		113		<.0001
1		63(50)		26(23)	
2		40(32)		48(42)	
3		20(16)		27(24)	
4		2(1.6)		11(9.7)	
5		0(0)		1(0.88)	

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489 *Key: ICM: Ischemic cardiomyopathy, ICU: Intensive care unit, LVEDD: Left ventricular end diastolic diameter, MCS:*
490 *mechanical circulatory support; NICM: Non-Ischemic Cardiomyopathy, NYHA: New York Heart Association, PCCS:*
491 *post-cardiotomy cardiogenic shock, SD: standard deviation, STS PROM: Society of Thoracic Surgeons Predicted risk*
492 *of mortality*

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494 *a. Patients with data available.*

495 *b: Surgical Components contributing to the count: 1) atrial fibrillation surgery, 2) any major left ventricular*
496 *procedure, 3) aortic valve repair/replacement, 4) aortic root replacement/aortic root surgery, 5) coronary artery*
497 *bypass, 6) mitral valve repair/replacement, 7) tricuspid valve repair/replacement*

498 *c: 15th/50th/85th percentiles.*

Surgical Components	N^a	#(% of n)
Ischemic Cardiomyopathy group	125	
CABG only		72 (58)
CABG+MV surgery		31 (25)
CABG+TV surgery		5 (4.0)
CABG+MV+TV surgery		17 (14)
Echocardiography Evaluation	125	
Myocardial Function in LAD Territory	122	# (% of N)
Mild-moderate hypokinesia		4(3.3)
Moderately severe – severe hypokinesia		54(44)
Akinetic		61(50)
Dyskinetic		3(2.5)
Myocardial Function in LCX Territory	122	
Mild-moderate hypokinesia		11(9)
Moderately severe – severe hypokinesia		58(48)
Akinetic		51(42)
Dyskinetic		2(1.6)
Myocardial Function in RCA Territory	122	
Mild-moderate hypokinesia		7(5.7)
Moderately severe – severe hypokinesia		50(41)
Akinetic		63(52)
Dyskinetic		2(1.6)
Right heart dysfunction	124	
None		47(38)
Low Normal		15(12)
Mild		34(27)
Moderate		18(15)
Moderate-severe		8(6.5)
Severe		1(0.81)
Not documented		1(0.81)
Scar Score	125	#(% of n)
Availability of Preop MRI with Gadolinium		13 (10)

Availability of Preop cardiac PET		71 (57)
Total patients in the CABG primary procedure group with a viability study		82 (66)
Total Scar Score ^b	82	
0		25(30)
1		10(12)
2		23(28)
3		8(9.8)
4		6(7.3)
5		7(8.5)
6		3(3.7)
Coronary Angiography Data	125	#(% of n)
Coronary Dominance	123	
Right		104(85)
Left		12(9.8)
Co-dominant		7(5.7)
Target Vessel Evaluation in LAD Territory	123	
Optimal		77(63)
Suboptimal		36(29)
Poor		6(4.9)
Territory without significant stenosis (or patent bypass graft present)		4(3.3)
Target Vessel Evaluation in LCX Territory	123	
Optimal		75(61)
Suboptimal		28(23)
Poor		7(5.7)
Territory without significant stenosis (or patent bypass graft present)		13(11)
Target Vessel Evaluation in RCA Territory	123	
Optimal		56(46)
Suboptimal		42(34)
Poor		18(15)
Territory without significant stenosis (or patent bypass graft present)	122	7(5.7)
Complete Revascularization (all significant stenotic territories have been revascularized)		112(92)

499
500 **Table 2: Surgical Components and preoperative evaluation of the Ischemic Cardiomyopathy**
501 **Group**

502 Demonstrates the main surgical components of the Ischemic Cardiomyopathy group. Also
503 shows the evaluation of the Ischemic Cardiomyopathy group, which includes echocardiography,
504 scar score, and coronary angiography.

505

506 Key: AV: aortic valve, CABG: coronary artery bypass graft, MV: mitral valve, TV: tricuspid valve

507 *a: Patients with data available.*

508 *b: Total Scar score = (LAD scar score*2) + LCX Scar score + RCA Scar score*

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Table 3: Surgical Components of Non-Ischemic Cardiomyopathy Group.

Surgical Components of NICM group	113	#(% of n)
AV Surgery + CABG		17(15)
AV Surgery + Aortic		14(12)
AV Surgery		14(12)
MV surgery		11(10)
MV surgery + TV Surgery		10(8.8)
AV Surgery + MV surgery + TV surgery		7(6.2)
AV Surgery + MV surgery		6(5.3)
CABG + MV surgery +TV surgery		5(4.4)
CABG + aortic		4(3.5)
CABG + AV Surgery + MV surgery		4(3.5)
CABG + AV Surgery + MV surgery + TV surgery		4(3.5)
AV Surgery + Aortic + MV surgery		4(3.5)
AV Surgery + MV surgery + TV surgery + Aortic		4(3.5)
TV Surgery		2(1.8)
AV surgery + TV surgery		1(0.9)
AV surgery + TV surgery + Aortic		1(0.9)
AV surgery + CABG + Aortic		1(0.9)
Pericardiectomy + AV surgery + CABG		1(0.9)
Reconstruction of LV free wall rupture		1(0.9)
AV Surgery + CABG + LV aneurysm repair		1(0.9)
AV Surgery + CABG + VSD closure		1(0.9)
CABG only		0
CABG + MV surgery		0
CABG + TV surgery		0

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Demonstrates the main surgical components of the Non-Ischemic Cardiomyopathy group. Surgical components that may have been performed but are not included in this list are: surgical ablation, epicardial lead placement, closure of patent foramen ovale, left atrial appendage ligation, and reoperative sternotomy

- 520 Key: AV: Aortic valve, CABG: coronary artery bypass grafting, LV: left ventricle, MV: mitral valve, NICM: Non-
521 Ischemic Cardiomyopathy, TV: tricuspid valve, VSD: ventricular septal defect

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Table 4: Primary and Secondary Outcomes, Complications, and Mechanical Circulatory

Support Characteristics

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	ICM		NICM		
Complications and Outcomes	N	NO. (%)	N	NO. (%)	P
Primary Outcome	125		113		
Post cardiectomy cardiogenic shock (PCCS)		35(28)		30(27)	.80
VIS (Vasoactive Inotropic Score) greater than 25		18(14)		18(16)	.74
Placement of ECMO in surgery		0(0)		1(0.88)	.29
Placement of ECMO after surgery		3(2.4)		2(1.8)	.74
Placement of Impella in surgery		18(14)		12(11)	.38
Need for durable LVAD within 30 days from surgery		0 (0)		0 (0)	
Secondary Outcomes					
Stroke permanent	125	2(1.6)	113	5(4.4)	.20
Reop for bleed/tamponade	125	10(8)	113	4(3.5)	.14
Other non-cardiac reop	125	23(18)	113	18(16)	.61
Cardiac reop excluding Valve dysfunction/graft occlusion	125	2(1.6)	113	2(1.8)	.92
Renal failure requiring dialysis	120	4(3.3)	103	5(4.9)	.57
Prolonged ventilation >24 hour	125	30(24)	113	40(35)	.054
Hospital Death	125	1(0.8)	113	3(2.7)	.27
Operative mortality (in-hospital or <=30 days since procedure)	124	1(0.81)	113	3(2.7)	.27
MCS Characteristics	N^a	No. (%)	N^a	No. (%)	P
IABP					
Preop IABP Support	125	14(11)	113	7(6.2)	.17
Preop IABP continued postoperatively	14	9(64)	7	5(71)	.74
Placement of IABP in surgery	125	20(16)	113	10(8.8)	.097
ECMO					
Preop ECMO support	125	1(0.8)	113	1(0.88)	.94
Preop ECMO continued postoperatively	1	0(0)	1	0(0)	
Placement of ECMO in surgery	125	0(0)	113	1(0.88)	.29
Placement of ECMO after initial surgery	125	3(2.4)	113	2(1.8)	.74
Impella					
Preop Impella support	125	1(0.8)	113	0(0)	.34
Placement of Impella in surgery	125	18(14)	113	12(11)	.38
Placement of Impella after surgery	125	0 (0)	113	0 (0)	
Durable LVAD or Transplant					
Need for durable LVAD <6 months after index operation	125	0 (0)	113	0 (0)	

Need for durable LVAD >6 months after index operation?	125	1(0.8)	113	2(1.8)	.50
Heart Transplant after index operation?	125	0(0)	113	0 (0)	

a: Patients with data available.

Key: ECMO: extracorporeal membrane oxygenation, IABP: intra-aortic balloon pump, ICM: ischemic

cardiomyopathy, LVAD: left ventricular assist device, NICM: non-ischemic cardiomyopathy, PCCS: post-cardiotomy

cardiogenic shock, VIS: vasoactive inotropic score

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Figure Legends

Figure 1: Predictors of Post-Cardiotomy Cardiogenic Shock in Ischemic and Non-Ischemic Cardiomyopathy. In this cohort of low ejection fraction patients, the primary outcome was post-cardiotomy cardiogenic shock (PCCS). Predictors of PCCS in ischemic and non-ischemic cardiomyopathy were found based on random forest analysis. Pulmonary artery pulsatility index was the most significant predictor of post-cardiotomy cardiogenic shock (PCCS) in the ischemic cardiomyopathy group, whereas cardiac index was the most significant predictor in the non-ischemic cardiomyopathy group.

Key: AV: aortic valve, EF: ejection fraction, ICM: Ischemic Cardiomyopathy, LV: left ventricle, LVEDD: left ventricular end diastolic diameter, NICM: Non-ischemic cardiomyopathy, PCCS: post-cardiotomy cardiogenic shock, TV: tricuspid valve

Figure 2: Predictors of Post-Cardiotomy Cardiogenic Shock in Patients with Ischemic Cardiomyopathy. Panel A shows the variable importance from random forest analysis of predictive factors, with pulmonary artery pulsatility index (PAPi) and pulmonary capillary wedge pressure (PCWP) as the most predictive. The random forest partial dependency plots for this analysis is shown for the top variables: B) PAPi, C) PCWP, D) central venous pressure, E) tricuspid valve (TV) surgery, F) left ventricle (LV) mass index, and G) pulmonary systolic pressure. Right heart function, as indicated by PAPi, seems to be most predictive of post-cardiotomy cardiogenic shock in patients with ischemic cardiomyopathy.

Figure 3: Predictors of Post-Cardiotomy Cardiogenic Shock in Patients with Non-Ischemic Cardiomyopathy. Panel A shows the variable importance from random forest analysis of predictive factors, with cardiac index and pulmonary capillary wedge pressure (PCWP) as the most predictive. The random forest partial dependency plots of this analysis are shown for the

top variables: B) cardiac index, C) PCWP, D) sodium, E) left ventricle (LV) mass index, F) aortic valve (AV) peak gradient, and G) bilirubin. Variables showing decompensated heart failure seem to be most predictive of post-cardiotomy cardiogenic shock in patients with non-ischemic cardiomyopathy.

Figure 4: Progression of Ejection Fraction in Patients with Ischemic and Non-Ischemic Cardiomyopathy. The lines represent unadjusted estimates of temporal trend of postoperative LV EF from available echocardiography in the ICM (blue) and NICM (green) groups, with vertical bars showing 68% confidence interval. Number of EF records and patients at risk is reported below. Ejection fraction in the ICM group at preoperative, 3 months, 6 months, 12 months, and 24 months was 24%, 34%, 36%, 39%, and 39%, respectively. Ejection fraction in the NICM group at pre-surgery, 3 months, 6 months, 12 months, and 24 months was 25%, 32%, 34%, 37%, and 40%, respectively. For both ICM and NICM, there is no overlap of the upper confidence interval of preoperative LVEF with the lower confidence interval of the postoperative LVEF, therefore we can say LVEF significantly increased ($p < .05$).

Key: EF: Ejection fraction, ICM: Ischemic cardiomyopathy, LV: Left ventricle, NICM: Non-ischemic cardiomyopathy

Supplementary Figure 1: Society of Thoracic Surgeons Predicted Risk of Mortality for Ischemic and Non-ischemic cardiomyopathy groups. This shows the cumulative distribution function of the Society of Thoracic Surgeons predicted risk of mortality stratified by ischemic cardiomyopathy (ICM) in blue and non-ischemic cardiomyopathy (NICM) in green. In the ICM group, 50% had lower than a 3.5% score. In the NICM group, 50% had lower than a 3.4% score.

Key: ICM: ischemic cardiomyopathy, NICM: non-ischemic cardiomyopathy, STS PROM: Society of Thoracic Surgeons predicted risk of mortality

Supplementary Figure 2: Society of Thoracic Surgeons Predicted risk of Mortality and Development of Post-cardiotomy Cardiogenic Shock. This is a scatter plot of the available STS PROM scores and whether the patients developed post-cardiotomy cardiogenic shock.

Panel A shows the data for the ischemic cardiomyopathy patients, and panel B shows the data for the non-ischemic cardiomyopathy patients.

Key: ICM: ischemic cardiomyopathy, NICM: non-ischemic cardiomyopathy, PCCS: Post-cardiotomy cardiogenic shock, STS PROM: Society of Thoracic Surgeons predicted risk of mortality

Supplementary Figure 3: Progression of Ejection Fraction in patients with Ischemic Cardiomyopathy in setting of PCCS. The lines represent unadjusted estimates of temporal trend of postoperative LV EF from available echocardiography in ICM patients with no PCCS (black) and with PCCS (red) groups, with vertical bars showing 68% confidence interval.

Number of EF records and patients at risk is reported below. In the ICM patients that did have PCCS, ejection fraction at pre-surgery, 3 months, 6 months, 12 months, and 24 months was 23%, 33%, 34%, 36%, and 42%, respectively. In the ICM patients that did not have PCCS, ejection fraction at pre-surgery, 3 months, 6 months, 12 months, and 24 months was 24%, 34%, 37%, 39%, and 40%, respectively. For both ICM with and without PCCS, there is no overlap of the upper confidence interval of preoperative LVEF with the lower confidence interval of the postoperative LVEF, therefore we can say LVEF significantly increased ($p < .05$).

Key: EF: Ejection fraction, ICM: Ischemic cardiomyopathy, LV: Left ventricle, PCCS: Post-cardiotomy cardiogenic shock

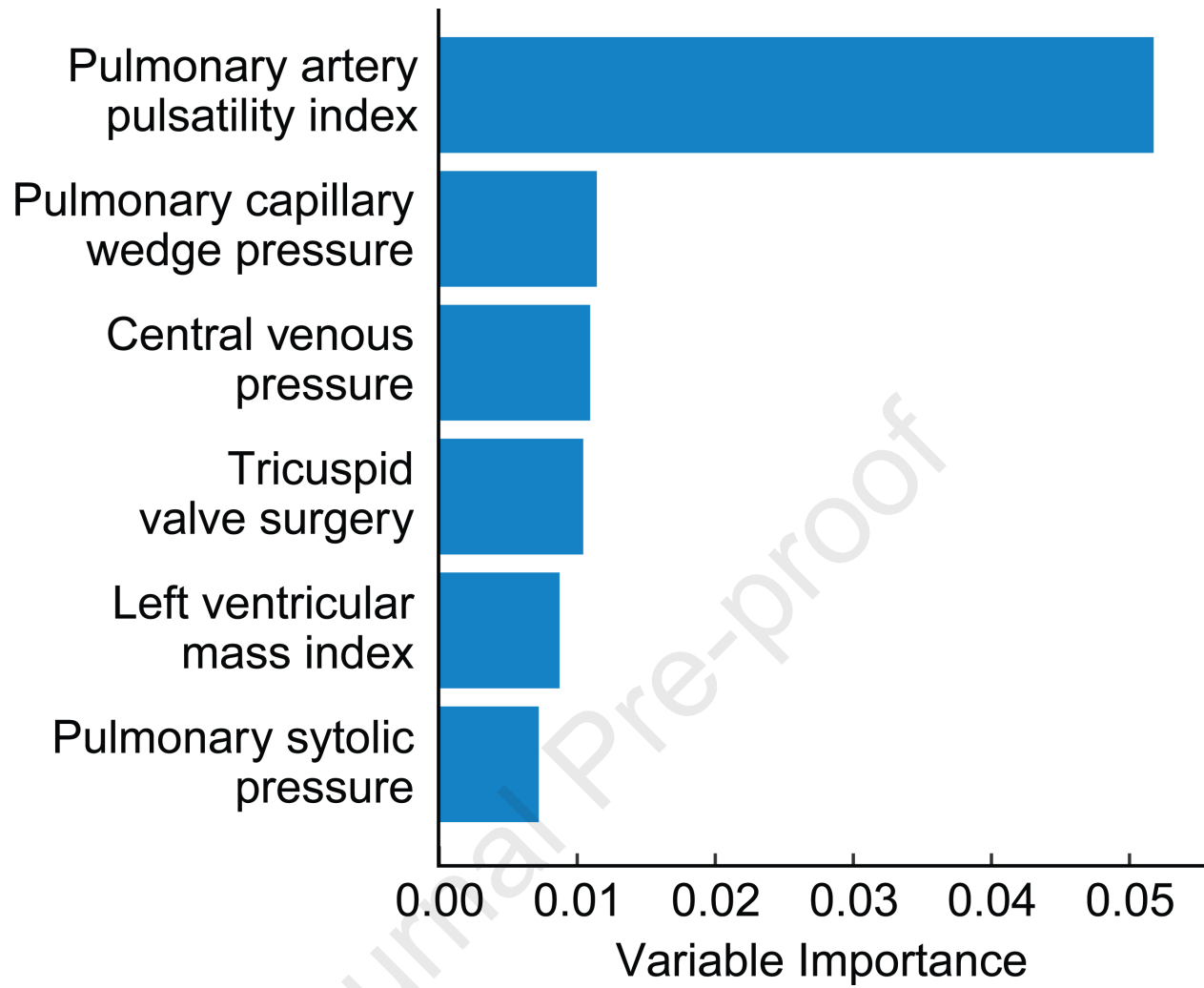
Supplementary Figure 4: Progression of Ejection Fraction in patients with Non-ischemic

Cardiomyopathy in setting of PCCS. The lines represent unadjusted estimates of temporal trend of postoperative LV EF from available echocardiography in NICM patients with no PCCS (black) and with PCCS (red) groups, with vertical bars showing 68% confidence interval.

Number of EF records and patients at risk is reported below. In the NICM patients that did have PCCS, ejection fraction at pre-surgery, 3 months, 6 months, 12 months, and 24 months was 24%, 28%, 30%, 34%, and 35%, respectively. In the NICM patients that did not have PCCS, ejection fraction at pre-surgery, 3 months, 6 months, 12 months, and 24 months was 25%, 34%, 35%, 38%, and 41%, respectively. For both NICM with and without PCCS, there is no overlap of the upper confidence interval of preoperative LVEF with the lower confidence interval of the postoperative LVEF, therefore we can say LVEF significantly increased ($p < .05$).

Key: EF: Ejection fraction, LV: Left ventricle, NICM: Non-ischemic cardiomyopathy, PCCS: Post-cardiotomy cardiogenic shock

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Predictors of Post-Cardiotomy Cardiogenic Shock in Ischemic and Non-Ischemic Cardiomyopathy

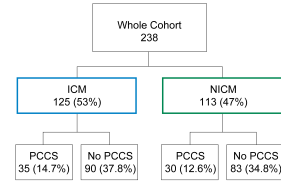
Methods & Results

January 2017 - 2020

Cohort 238 patients

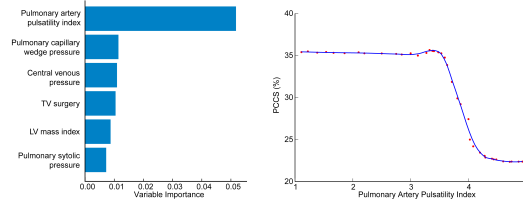
- EF <30% (209)
- EF <35% with at least moderately severe MR (32)

Primary outcome was PCCS, defined as need for Impella, extracorporeal membrane oxygenation, or vasoactive-inotropic score >25.

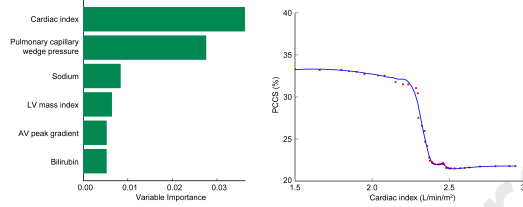


Random Forest analysis was used to identify predictors of PCCS

Ischemic Cardiomyopathy



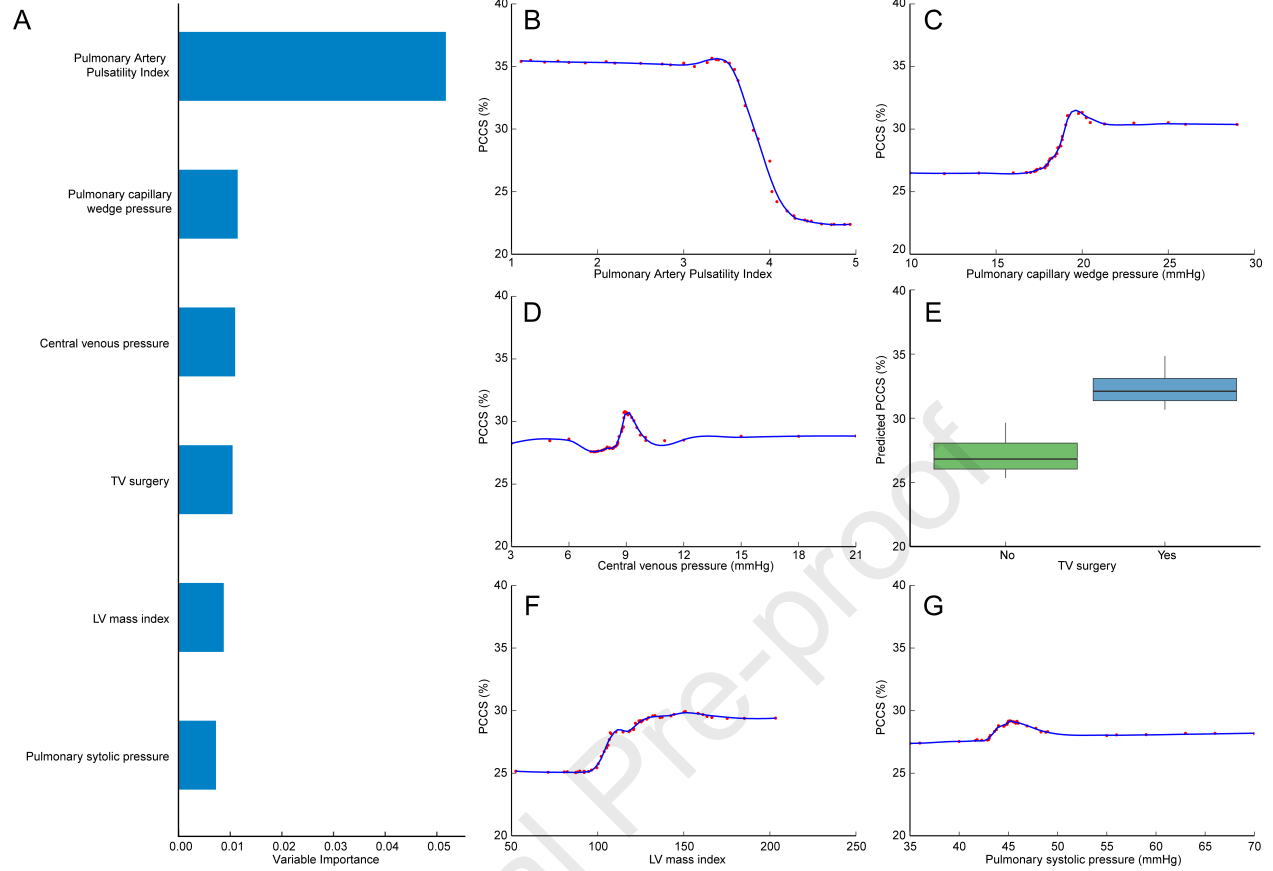
Non-Ischemic Cardiomyopathy

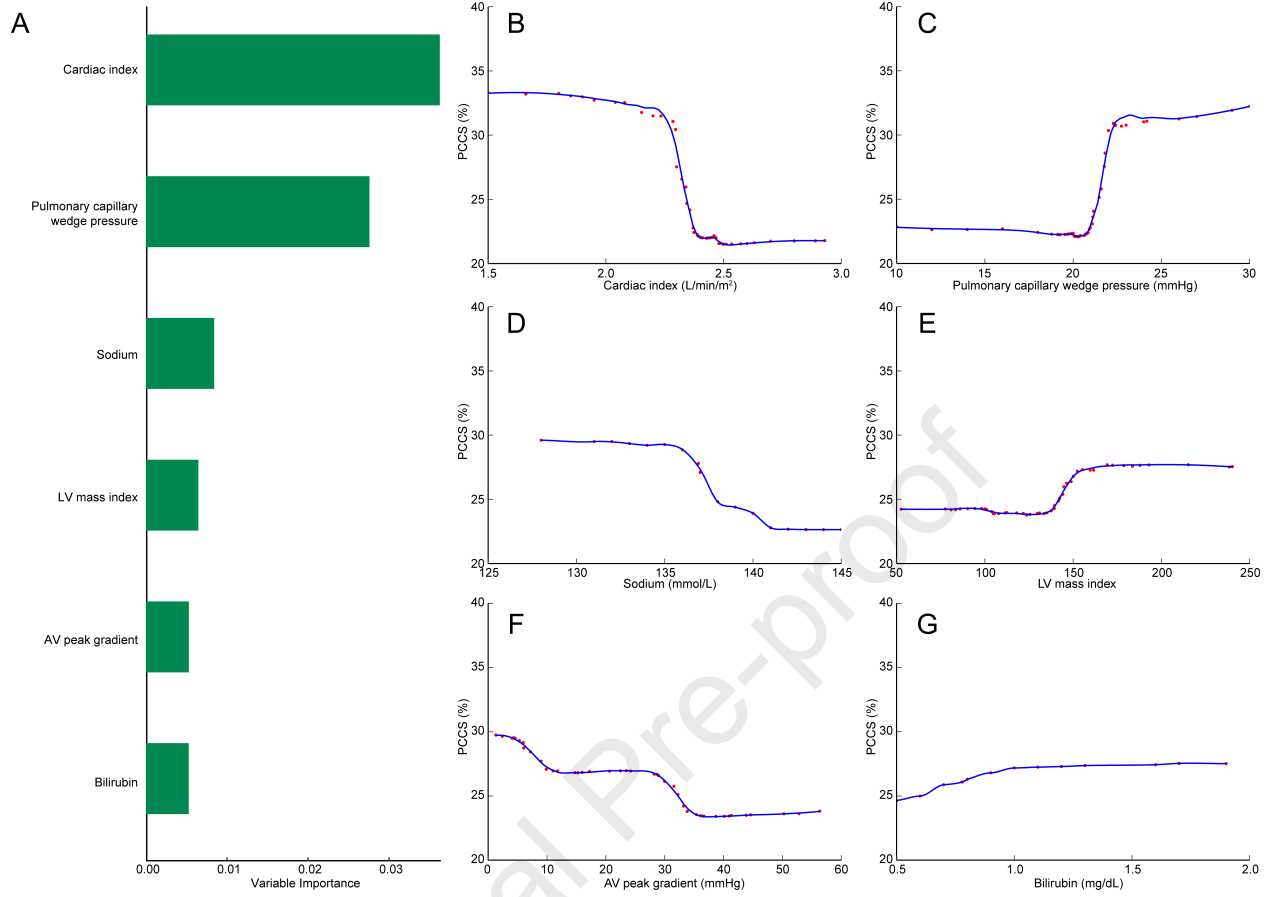


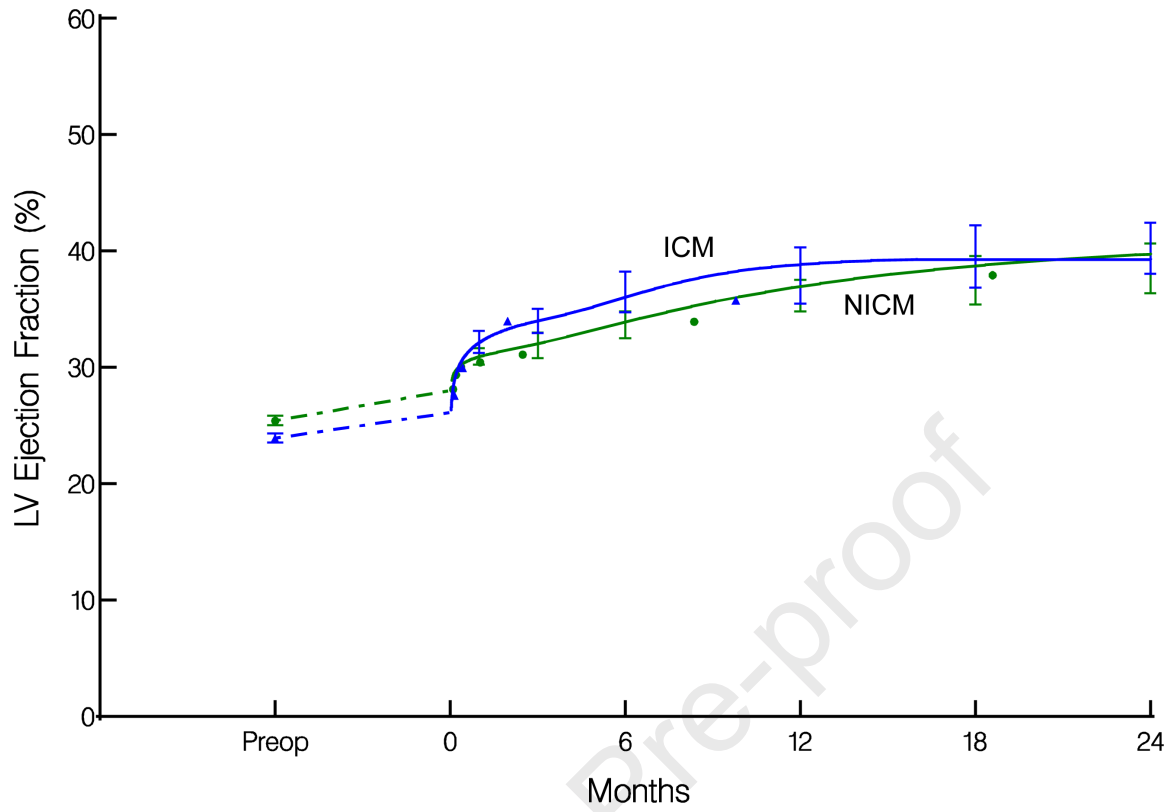
Implications

Right heart function, measure by PAPI, is most predictive of PCCS in ICM, whereas degree of cardiac decompensation is most predictive of PCCS in NICM. This knowledge will help guide early use of mechanical circulatory support in high risk low ejection fraction patients.

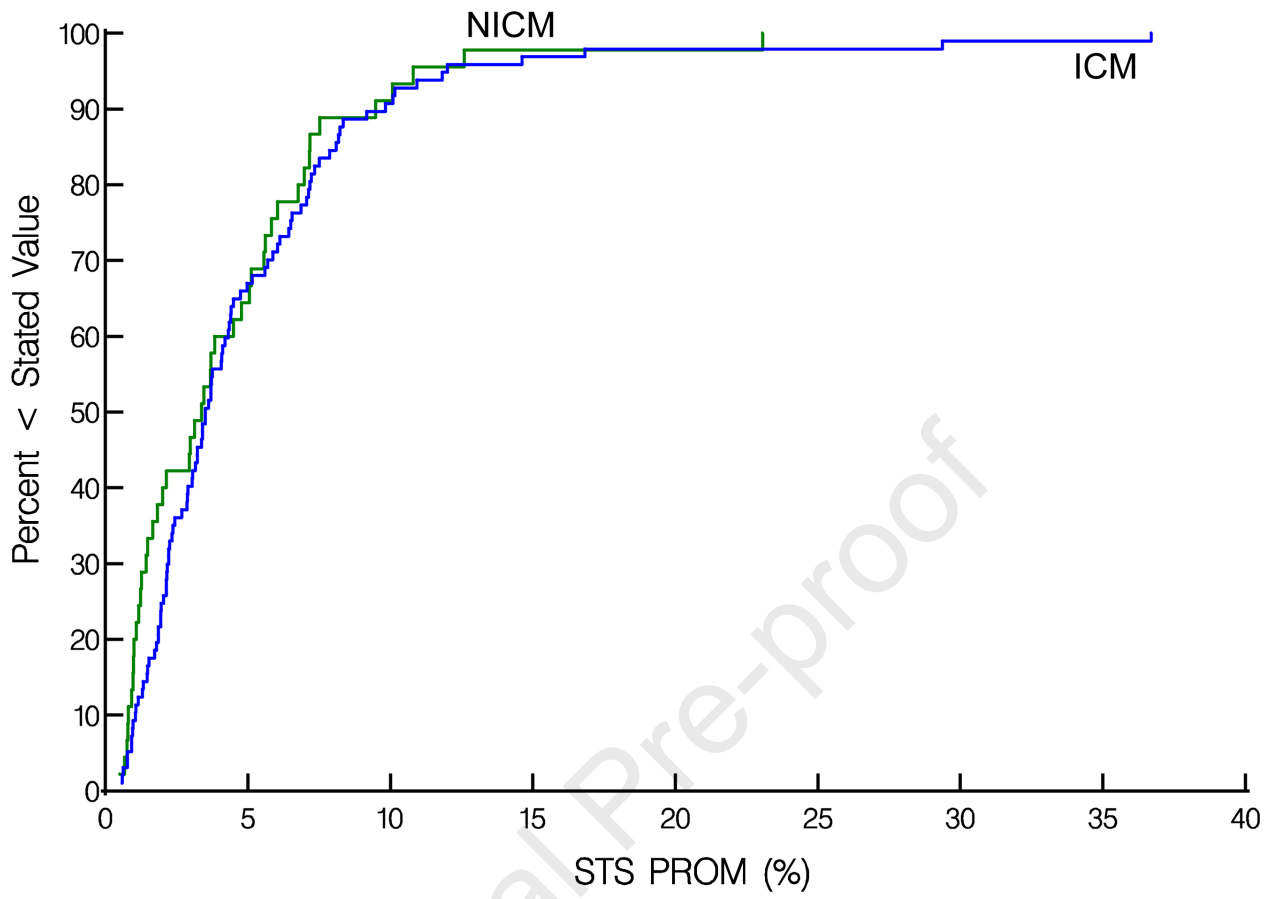
AV: aortic valve, EF: Ejection fraction, ICM: Ischemic cardiomyopathy, LV: left ventricle, MR: Mitral regurgitation, NICM: Non-ischemic cardiomyopathy, PAPI: Pulmonary artery pulsatility index, PCCS: Post-cardiotomy cardiogenic shock, TV: Tricuspid valve

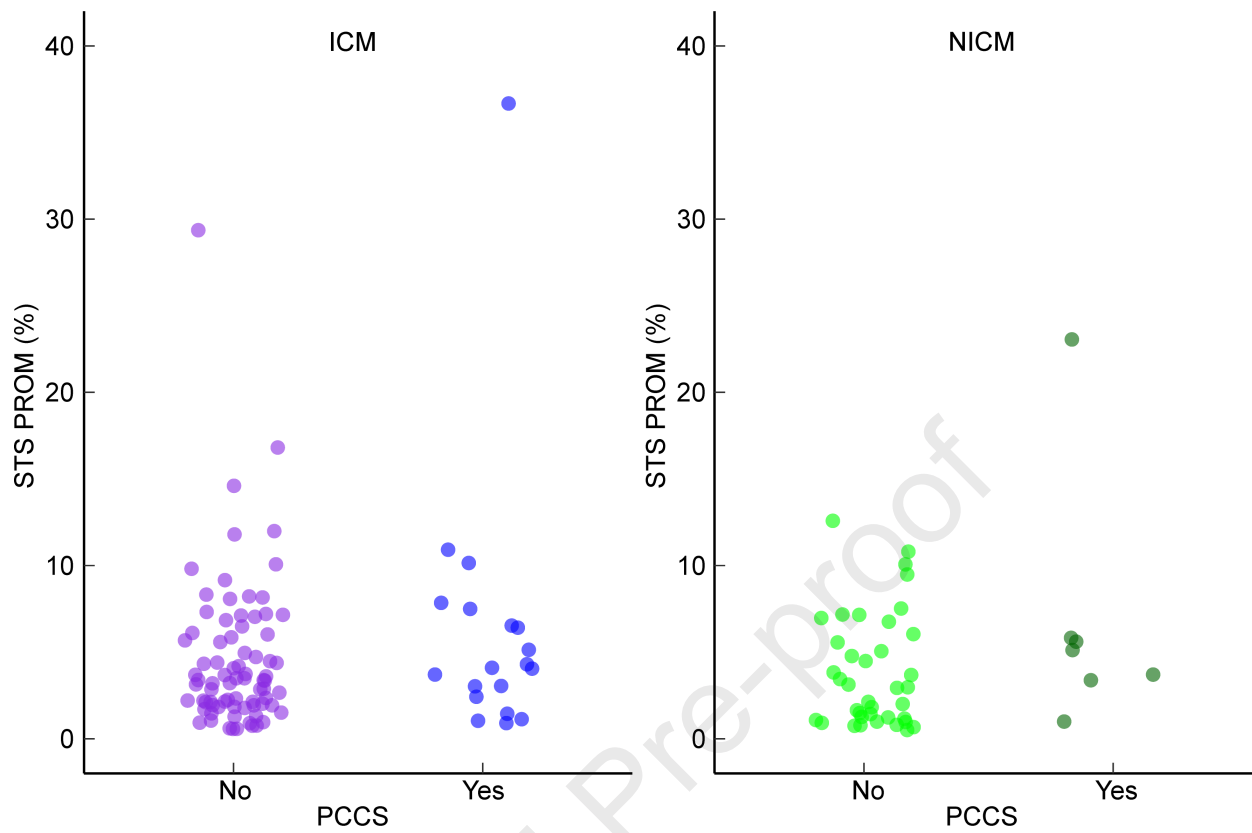


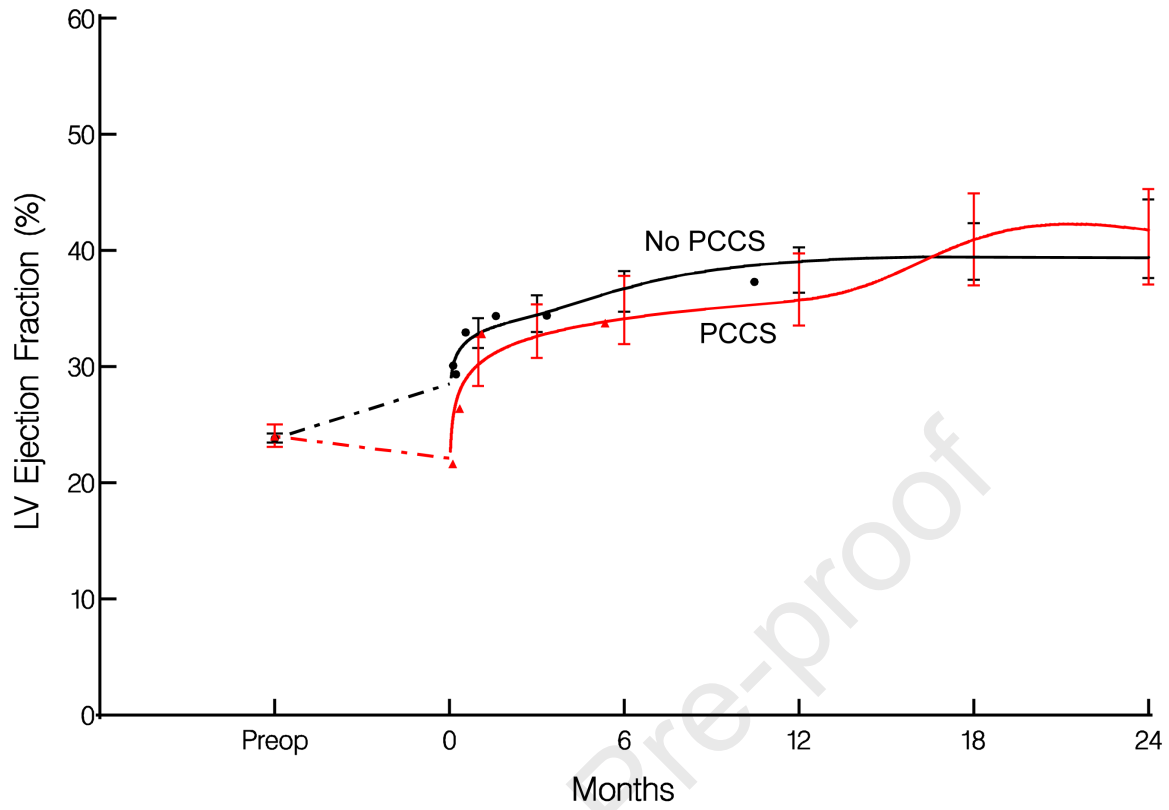




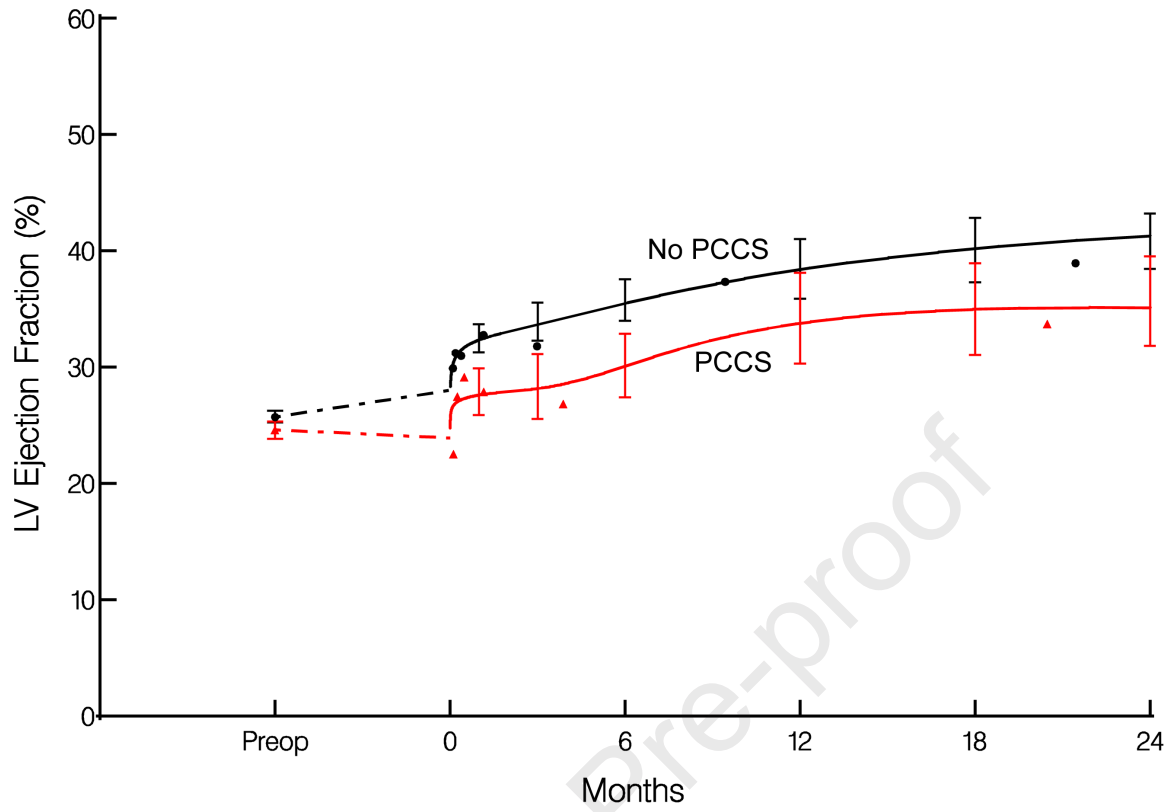
		Months							
ICM	LVEF records	279	31	22	21	72			
	Patients	125	60	53	47	40			
NICM	LVEF records	225	36	18	20	50			
	Patients	113	52	44	40	31			







PCCS	LVEF records	90	9	7	6	13			
	Patients	35	18	17	13	9			
No PCCS	LVEF records	189	22	15	15	31			
	Patients	90	42	36	34	31			



		Months							
PCCS	LVEF records	71	14	5	6	10			
	Patients	30	17	14	12	8			
No PCCS	LVEF records	154	22	13	14	14	8	40	
	Patients	83	35	30	28	23			

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Appendix 1: Preoperative Heart disease Evaluation

Right heart catheterization

Cardiac index (Fick method), pulmonary artery systolic and diastolic pressure, central venous pressure, and pulmonary capillary wedge pressure (PCWP) were collected if available.

Pulmonary artery pulsatility index (PAPi) was calculated from the following equation:

Pulmonary pulsatility index (PAPi) = (pulmonary artery systolic pressure – pulmonary artery diastolic pressure) / Central venous pressure

Ischemic Heart Disease Evaluation

Echocardiography was used to assess the regional function of the heart. We defined the territories according to the coronary anatomy of majority of patients – right dominant circulation. The left anterior descending (LAD) territory included all anterior, anteroseptal and apex segments. The circumflex territory included all anterolateral and inferolateral segments. The right coronary artery (RCA) territory included all inferior and inferoseptal segments. The scores were as follows: 0 for normal function, 1 for mild or moderate hypokinetic, 2 for moderately severe to severely hypokinetic, 3 for akinetic, and 4 for dyskinetic. The scores were taken from the echo reports of staff cardiologist interpretations.

Coronary angiography was also examined for each patient that underwent a coronary artery bypass procedure. These studies were interpreted retrospectively by cardiothoracic surgery residents in order to assess the quality of targets for coronary artery bypass.

Again, we used the 3 main coronary artery territories (LAD, circumflex, and RCA) to break down the scores of the target vessel evaluation. For those patients that were left dominant, we designated the left posterior descending artery to correlate to the RCA territory grade, in order to keep consistency with the echo territory grading. The grades were as follows: 0 for optimal target, 1 for suboptimal target, 2 for poor target, and 3 for a territory without significant stenosis or that has a patent bypass graft present. An optimal target was a target that was adequate size with adequate runoff. A suboptimal target was defined as either a small target or a target with small area of myocardial distribution, but could still be grafted. A poor target was defined as a target that was likely not graftable – due to a combination of being a small target and poor runoff. Complete revascularization was also noted for each case. This

was defined as all diseased territories with an artery >75% stenosis (left main >50%) having at least 1 bypass graft placed to that territory.

Viability testing

Viability testing consisted of cardiac positron emission tomography (PET) scans and cardiac magnetic resonance imaging (MRI) with gadolinium contrast. We did not include single photon emission computed tomography (SPECT), since this test cannot differentiate fixed perfusion defect from scar and hibernating myocardium. Significant scar was defined according to how the results were reported. Similar to the echocardiographic evaluation, viability was assessed according to the 3 main coronary territories – LAD, circumflex, and RCA. The scores were as follows: 0 for no scar, 1 for some scar but small, 2 for significant scar. Significant scar was defined as greater than 50% wall thickness seen on MRI, or greater than 20% scar in a territory on cardiac PET scan. Our grading system from 0-2 was used for both MRI and PET so that the data could be combined. When patients had both a PET scan and an MRI, we chose the MRI data over the PET data since MRI has better spatial resolution.^{1,2} From the viability data in the 3 territories, we calculated a weighted total scar score that gave more importance to the LAD territory. The total scar score is as follows:

total scar score = (scar score in LAD territory x 2) + (scar score in the circumflex territory) + (scar score in the RCA territory).

LAD Scar Score	82	
No Scar (0)		51(62)
Small scar (1)		20(24)
Large scar (2)		11(13)
LCX Scar Score	82	
No Scar (0)		60(73)
Small scar (1)		17(21)
Large scar (2)		5(6.1)
RCA Scar Score	82	
No Scar (0)		51(62)
Small scar (1)		16(20)
Large scar (2)		15(18)

Supplementary Table 1: Scar Score by territory

Key: LAD: left anterior descending, LCx: left circumflex, RCA: right coronary artery

Appendix 2: Vasoactive inotropic score (VIS)

The VIS has been used in other studies, and it has been shown to predict morbidity and mortality after cardiac surgery.³ The VIS formula used by many of these studies does not include phenylephrine, and so we used an expanded version of the formula that has been previously described.³⁻⁵

Vasoactive-Inotropic Score = dopamine dose ($\mu\text{g}/\text{kg}/\text{min}$) + dobutamine dose ($\mu\text{g}/\text{kg}/\text{min}$) + 100 x epinephrine dose ($\mu\text{g}/\text{kg}/\text{min}$) + 100 x norepinephrine dose ($\mu\text{g}/\text{kg}/\text{min}$) + 10 x milrinone dose ($\mu\text{g}/\text{kg}/\text{min}$) + 10,000 x vasopressin dose ($\text{U}/\text{kg}/\text{min}$) + 10 x phenylephrine dose ($\text{mcg}/\text{kg}/\text{min}$)

VIS was calculated preoperatively and immediately postoperatively. The preoperative VIS was calculated from the inotropic and vasopressor doses required in the hours before surgery. The postoperative VIS score was calculated from the vasopressor and inotropic doses during the first hour upon arrival to the cardiovascular intensive care unit.

A VIS of equal to or greater than 25 was used as the threshold for PCCS. This threshold was created after analyzing what value of VIS correctly portrayed the use of multiple moderate - high dose inotropes and vasopressors.

Appendix 3: Variables included in Random Forest analysis of imbalanced data.

Demographics

Age (years), Sex, Race (white, black, other), Body mass index (BMI, $\text{kg}\cdot\text{m}^{-2}$).

Symptoms

NYHA functional class, Myocardial infarction.

Ventricular Function.

Right ventricular systolic pressure (mmHg), LV systolic function, LV ejection fraction (%).

Valve Pathology

Presence of pulmonary regurgitation

Regurgitation grade in aortic, mitral, and tricuspid valve.

Presence of stenosis of aortic valve.

Aortic valve area (cm^2)

TV regurgitation velocity (cm/s)

LV structure

LV inner diameter in diastole (cm), LV end diastolic volume (mL).

LV Mass

Posterior wall thickness (cm), Intraventricular septal thickness (cm), LV relative wall thickness (cm), LV Mass Index (BSA) (g/m^2).

Cardiac Comorbidity

Atrial fibrillation/flutter, Ventricular tachycardia or fibrillation, Number of cardiac operations, Congestive heart failure.

Laboratory chemistries

Bilirubin (mg/dL), Creatinine (mg/dL), Blood urea nitrogen (mg/dL), Hematocrit (%), Sodium (mmol/L).

Hemodynamics

Cardiac Index ($L \cdot \text{min}^{-1} \cdot \text{m}^{-2}$) Fick method, Pulmonary diastolic pressure (mmHg), Pulmonary systolic pressure (mmHg), Central venous pressure (mmHg), Pulmonary artery pulsatility index (PAPi), Pulmonary capillary wedge pressure (mmHg).

Non-Cardiac Comorbidity

Peripheral artery disease, Hypertension, Diabetes (types-pharmacologically treated, insulin treated, non-insulin/diet treated), Chronic obstructive pulmonary disease, Smoking, Stroke.

Coronary Artery Disease

Coronary artery stenosis (left main trunk [LMT] >50%, left anterior descending system [LAD] > 50%, left circumflex system [LCX] > 50%, right coronary artery system [RCA] >50%), Total number of systems diseased greater than 50%.

Coronary Perfusion Territories

Myocardial function territory (LAD, LCX, RCA)

Target vessel evaluation territory (LAD, LCX, RCA)

Scar score

Scar score= (viab_lad*2) + viab_lcx + viab_rca

Where-

Maximum mri_lad or pet_lad, if both available take mri_lad (viab_lad)

Maximum mri_lcx or pet_lcx, if both available take mri_lcx (viab_lcx)

Maximum mri_rca or pet_rca, if both available take mri_rca (viab_rca)

Etiology (cardiomyopathy)

Ischemic cardiomyopathy

Concomitant Procedure

CABG only, Any ITA graft.

Aortic valve surgery, Mitral valve repair, Mitral valve replacement, Tricuspid valve surgery,

Atrial fibrillation surgery.

Number of surgical components, created with the following procedures:

1. Coronary artery bypass
2. Aortic valve repair or aortic valve replacement
3. Aortic root replacement/aortic root surgery
4. Mitral valve repair/replacement
5. Tricuspid valve repair/ Tricuspid valve replacement
6. Atrial fibrillation surgery
7. Any major left ventricular procedure

Preoperative support

No support, Intra-aortic balloon pump (IABP)

Preoperative location

Home, hospital floor, intensive care unit (ICU).

Experience

Date of Surgery

Appendix 4: Post-cardiotomy Cardiogenic Shock Definition

The definition of post-cardiotomy cardiogenic shock (PCCS) in the literature is quite variable, and terms such as low cardiac output syndrome and PCCS seem to be used interchangeably. Cardiogenic shock is traditionally defined as hypotension (systolic blood pressure <90 mmHg) despite adequate cardiac filling, with signs of hypoperfusion.⁶⁻⁸ Studies have used this definition in defining post-cardiotomy cardiogenic shock (PCCS), with additional inclusion criteria such as the inability to wean from cardiopulmonary bypass despite maximal pharmacologic and IABP support.⁹ Another definition of PCCS is the need for any mechanical circulatory support or inotropic support for greater than 30 minutes in the ICU.¹⁰ Furthermore, refractory PCCS has been defined as hypoperfusion despite optimal volume loading, vasoactive medical support, and IABP.⁶ Given the ambiguity of the definition of PCCS, we chose to define PCCS in a way that reflected the level of intensity of the pharmacologic and mechanical support. We chose to have one of the criteria for PCCS to be insertion of an Impella or ECMO since these are 2 of the highest levels of mechanical support, with the ability to either fully support the LV (Impella) or give biventricular support (ECMO). We did not include placement of an IABP in our definition of PCCS, as it only provides about 0.5 L/min of support, a fraction of what is provided by Impella and ECMO devices.¹¹ We also chose to use a vasoactive inotropic score threshold as an additional inclusion criteria for PCCS, which has not been described before to the authors' knowledge. We sought influence from prior definitions of PCCS that were characterized by the use of multiple high dose inotropes, or maximal pharmacologic support. We sought to quantify these prior definitions with a score that reflects the clinical situation appropriately. After analyzing the different vasoactive inotropic scores, we decided a

threshold of 25 properly reflected patients on multiple vasopressors and inotropes at moderate to high doses. 65 of the 66 patients that developed PCCS were on inotropic support; therefore, we felt that a high VIS was more likely to be reflective of a low cardiac output state rather than a vasoplegic state, especially in the context of this population's low preoperative ejection fraction.

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