Long-Term Outcomes of Coronary Artery Bypass Grafting in Veterans with Ischemic Cardiomyopathy

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ABSTRACT

Background: The Surgical Treatment for Ischemic Heart Failure (STICH) trial showed that surgical revascularization in ischemic cardiomyopathy (ICM) patients improves long-term mortality compared with medical treatment alone. This study examines how veterans with ICM undergoing revascularization fare against patients without ICM; it also examines the outcomes in the veteran population.

Methods: This is a retrospective review of a single-center database. From 2000 to 2018, 1,461 patients underwent isolated coronary artery bypass grafting (CABG). Two-hundred-one patients with an ejection fraction less than 35% were classified as the ICM cohort. The primary outcome was mortality. Secondary outcomes included postoperative complications. Subgroup analysis was performed within the ICM cohort comparing off-pump CABG (OPCAB) versus on-pump CABG (ONCAB).

Results: ICM patients had a higher incidence of myocardial infarction (MI), diabetes, chronic kidney disease (CKD), and preoperative intra-aortic balloon pump (IABP) use. The non-ICM cohort was more functionally independent. OPCAB was performed in 80.1% of ICM and 66.3% of non-ICM cohorts. There was no statistical difference between ICM and non-ICM cohorts in 30-day mortality (OR 1.94[0.79 – 4.75], *P* = .15). The ICM cohort had an increased 5-year mortality (OR 1.75[1.14 – 2.69], *P* = .01) and 10-year mortality (OR 1.71[1.09 - 2.67], *P* = .02). The ICM cohort showed improved, although not statistically significant, short-term mortality with OPCAB compared with ONCAB (3.1% versus 12.5%, OR 0.31[0.05 – 1.82], *P* = .20).

Conclusion: Veterans with ICM undergoing CABG demonstrated similar short-term survival compared with non-ICM veterans. The long-term survival in the ICM cohort still is inferior to patients without ICM. There is a trend toward improved short-term survival in patients with ICM undergoing OPCAB.

INTRODUCTION

Cardiovascular disease (CVD) continues to be the leading cause of death in the United States. Heart failure (HF) contributes to 9.3% of those deaths [Benjamin 2018]. The prevalence of HF in the US is rising, with a current estimate of 6.2 million Americans afflicted with the disease compared with 5.7 million in 2012 [Benjamin 2018]. Despite advances in medical therapy, HF prevalence is projected to increase to more than 8 million people by 2030; therefore more effort and research needs to be devoted to HF prevention and optimizing treatment [Benjamin 2018].

While medical therapy for ischemic cardiomyopathy (ICM) has made significant advances over the past few decades, surgical techniques and equipment have improved as well [Rezapour 2018]. A combination of medical therapy plus surgical intervention has had optimal results. The Surgical Treatment for Ischemic Heart Failure Extension Study (STICHES) trial established that coronary artery bypass grafting (CABG) is a promising treatment modality in patients with ICM [Velazquez 2016]. Long-term follow up of patients over 10 years in the STICHES trial further solidified the superior outcomes in the surgery group, particularly with regards to reduced mortality. Compared to medical therapy alone, the absolute risk reduction was 7% in patients who had a CABG along with medical therapy [Velazquez 2016].

While the STICHES trial has helped guide treatment algorithms for the general population with ICM, the outcomes of patients with ICM in the veteran population are not well established. The veteran population does not follow the same disease pattern as that of the general population. US veterans are at a significantly higher risk of developing CVD when compared with the standard US citizen [Assari 2014]. Assari et al found that veterans had a higher incidence of cardiovascular problems independent of socioeconomic disparity and comorbidities [Assari 2014]. This increased risk was thought to be owed in part to higher prevalence of comorbid psychiatric illness in the veteran population, such as post-traumatic stress disorder (PTSD).

With these broader differences in mind, we sought to investigate veterans with heart disease and their ability tolerate cardiac surgery. Approximately 350,000 US veterans suffer from HF, causing an annual mortality of 14.5% [Groeneveld 2018]. When evaluating surgical outcomes in

Table 1. Patient demographics

Preoperative characteristics	ICM group (N = 201) Number (%) or mean +/- SD	Non-ICM group (N = 1260) Number (%) or mean +/- SD	P
Age	64.6 +/- 9.6	65.0 +/- 9.0	.59
Sex (male)	200 (99.5)	1246 (98.9)	.42
Race – African American	45 (22.4)	282 (22.4)	.95
Race – White	76 (37.8)	506 (40.2)	.95
BMI	28.7 +/- 6.1	29.1 +/- 5.7	.39
Prior MI	152 (75.6)	632 (50.16)	<.01
Cerebrovascular disease	41 (20.4)	265 (21.0)	.84
Peripheral vascular disease	60 (30.0)	307 (24.4)	.09
Hyperlipidemia	81 (40.3)	535 (42.5)	.56
Hypertension	191 (95.0)	1210 (96.0)	.5
COPD	99 (49.3)	547 (43.4)	.12
Smoker	73 (36.3)	379 (30.1)	.08
Diabetes mellitus	105 (52.2)	518 (41.1)	<.01
Chronic kidney disease	85 (42.3)	397 (31.5)	<.01
Prior PCI	31 (22.3)	238 (25.0)	.49
ASA Classification			
III	25 (12.4)	243 (19.3)	.01
IV	175 (87.1)	1016 (80.6)	
Preoperative IABP use	93 (46.3)	70 (5.6)	<.01
Surgical priority			
Elective	184 (91.5)	1172 (93.0)	.75
Urgent/Emergent	17 (8.5)	88 (7.0)	
Mean systolic BP (mmHg)	128 +/- 24	138 +/- 25	<.01

veterans affairs (VA) patients, one meta-analysis by Matula et al showed varying results with regards to morbidity and mortality in VA patients compared with private patients, depending on the surgical field [Matula 2010]. Specific to cardiac surgery, Rosenthal et al in a retrospective review discovered an increased mortality risk in patients undergoing CABG at a VA center compared with private sector hospitals [Rosenthal 2003]. Knowing these notable differences in civilian versus veteran patients, the objective of this study is to assess the outcomes of isolated CABG in veterans with ICM and examine whether the survival benefits of surgical revascularization for ischemic cardiomyopathy, as shown in the civilian data, translate to the veteran population.

MATERIALS AND METHODS

This is a retrospective review of a prospectively collected database from a single institution. Due to the retrospective nature of the study, Institutional Review Board approval was waived. All patients who underwent isolated CABG for all indications and level of operative priority from 2000-2018 were included in the study. The age range was 36-90 years, with no age restriction or exclusion criteria. Patients were stratified into two cohorts for purposes of comparison: those with ICM and those without. ICM was defined as patients with coronary disease and an ejection fraction <35%. A subgroup analysis was performed in patients with ICM, who were further substratified based on whether cardiopulmonary bypass (CPB) was used (off-pump CABG (OPCAB) versus on-pump CABG (ONCAB). Chi-square or Fisher exact test were used for categorical variables and independent t-test or Kruskal-Wallis test for continuous variables. Clinically relevant preoperative and operative characteristics with $P < .2$ in univariate between group comparisons were considered possible confounding variables and adjusted for in multivariate logistic regression modeling. Cumulative mortality events were calculated using Kaplan-Meier survival analysis with time-to-event and censoring calculated from the date of the surgery to the date of last encounter or death. The primary outcome of interest was mortality (30-day, 5-year, and 10-year), and secondary outcomes were cardiovascular, pulmonary, and renal composite morbidity outcomes, as well as unplanned reoperation and wound complications. Descriptions of these composite

Table 1. Patient demographics [cont.]

Preoperative characteristics	ICM group (N = 201) Number (%) or mean +/- SD	Non-ICM group (N = 1260) Number (%) or mean +/- SD	P
Coronary vessel disease			
1-vessel disease	19 (9.5)	113 (9.0)	
2-vessel disease	48 (24.0)	336 (26.7)	.84
3-vessel disease	118 (58.7)	753 (59.8)	
Left main disease	59 (29.4)	386 (30.6)	.71
CCS Angina Classification			
Asymptomatic	7 (3.5)	30 (2.4)	
I	17 (8.5)	81 (6.4)	
II	33 (16.4)	226 (17.9)	
III	80 (39.8)	574 (45.6)	
IV	64 (31.8)	349 (27.7)	
NYHA Classification			
I	11 (5.5)	159 (12.6)	
II	58 (28.9)	516 (41.0)	<.01
III	78 (38.8)	445 (35.3)	
IV	48 (23.9)	79 (6.3)	
Mean FEV1 (L)	2.2 +/- 0.8	2.4 +/- 0.7	<.01
Functional independence	152 (75.6)	1055 (83.7)	.02
Prior cardiac surgery	3 (1.5)	23 (1.8)	.74

Abbreviations: ICM, ischemic cardiomyopathy; IABP, intra-aortic balloon pump; FEV1, forced expiratory volume in one second

outcomes are found in Table 2. All statistical analysis was performed using JMP Pro14 (SAS Institute, Cary, NC).

RESULTS

CABG was performed in 1,461 consecutive patients, of which 201 patients had ICM. The mean follow up was 9.9 years. The vast majority of patients were male (99.0%), and there was no statistical difference in gender between ICM and non-ICM patients (P = .42). Patients in the ICM group were more likely to have a history of diabetes (P < .01), myocardial infarction (MI) (P < .01), chronic kidney disease (CKD) (P < .01), higher New York Heart Association (NYHA) classification (P = .01), and intra-aortic balloon pump (IABP) use (P < .01). OPCAB was performed in 80.1% of ICM group and 66.3% of the non-ICM group (P < 0.01) (Table 1).

Table 2 outlines the postoperative risk-adjusted outcomes. (Table 2) Our data did not show a statistically significant difference on multivariate analysis in 30-day mortality between patients with and without ICM (5.0% versus 2.1%, P = .15). However, in the 10-year follow up, mortality significantly was higher for the ICM group (54.1% versus 34.9%; aOR 1.71; Log-rank P < .001). ICM group also had higher rates of pulmonary complications (12.4% versus 5.2%, P < .01), which included ventilator >48 hours, reintubation events,

tracheostomy, and pneumonia. The ICM group also had a higher rate of return to the operating room (OR) for bleeding (3.5% versus 1.2%, P = .02).

In the secondary analysis of OPCAB versus ONCAB in patients with ICM, there was no statistically significant difference in mortality over 10 years (53.8% versus 55.2%; Log-rank P = .7019, Table 1). Patients with ICM undergoing OPCAB had less pulmonary complications (9.3% versus 25.0%, P < .01). The OPCAB group also had a lower incidence of return to the operating room for bleeding (.6% versus 15%, P < .01).

DISCUSSION

Our data present a valuable insight into long-term outcomes of US veterans undergoing CABG for ICM, with results that mirror those seen in the civilian population. Our cohort showed a significant difference in 10-year mortality, with ICM patients having worse outcomes than their non-ICM counterparts (Figure 1). This is not surprising given that patients suffering from ICM generally are sicker, often have a history of MI, have a decreased physiologic reserve, and have other comorbidities that lead to their demise, as seen in our study sample [Trachiotis 1998]. Overall, however, our 10-year mortality of ICM patients who had CABG was at

54.1%, which is lower than the civilian data in the STICHES trial, which had their 10-year mortality at 58.9% [Velazquez [Puskas 2009]. Dewey et al also demonstrated that patients with reduced ventricular function fared better during CABG
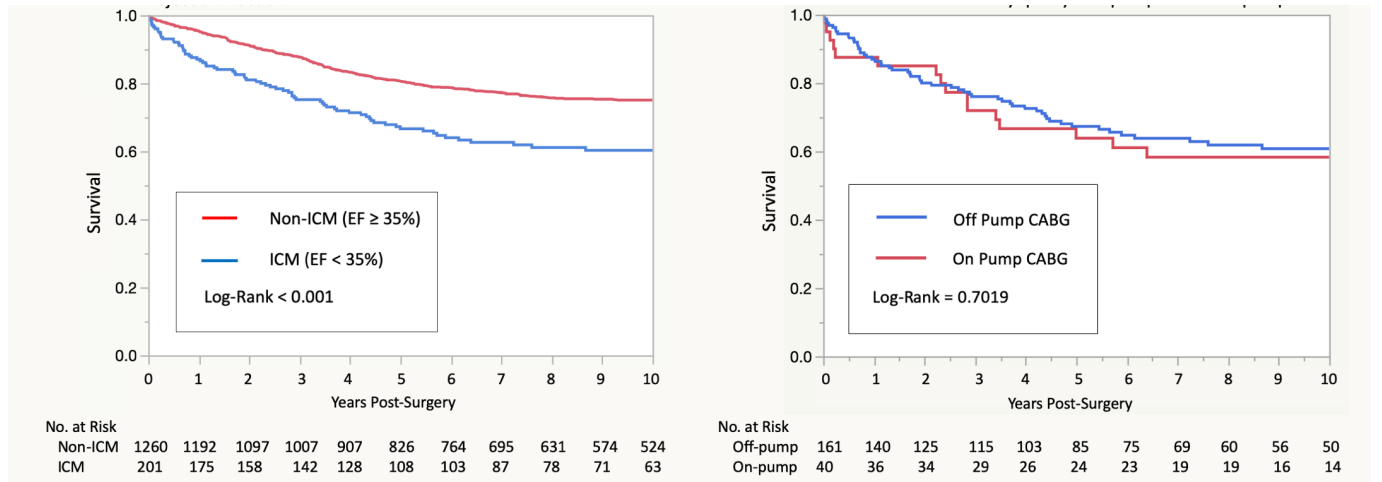
A) Survival after coronary artery bypass grafting in patients with ischemic cardiomyopathy versus patients with preserved ejection fraction; B) Survival after coronary artery bypass grafting in patients with ischemic cardiomyopathy: Off-pump versus on-pump.

2016]. Perhaps more importantly, the 30-day outcomes after CABG did not significantly differ between ICM and non-ICM patients, which suggests that HF patients can tolerate the physiologic stressors of CABG and should thus be considered for this operation, as the STICHES trial has shown it to be beneficial for that patient population [Velazquez 2016].

Although 30-day mortality was not significantly different between ICM and non-ICM groups, there were some differences in complication rates. The ICM cohort was found to have a significantly higher incidence of pulmonary complications when compared with the non-ICM group. This can be explained in part by the fact that patients in the ICM group had a lower forced expiratory volume in one second (FEV1) and worse functional independence when compared with the non-ICM group (Table 1). Frailty has been shown to be a risk for postoperative complications including mortality, thus posing another explanation as to why patients in our cohort with ICM had higher long-term mortality [Lee 2010]. Furthermore, although not statistically significant, there was a 6% higher proportion of smokers in the ICM group. Smoking is a risk factor for the development of ICM as well as CVD in general, as well as myriad other complications. Previous studies have shown that with respect to CABG, smoking increases the risk of pulmonary complications and death [Saxena 2013; Sørensen 2012]. When comparing outcomes between ONCAB and OPCAB in patients with ICM, there was a strong trend toward improved 30-day survival in the OPCAB group, although not statistically significant (P = .07). The failure to reach significance likely is due to low power in our secondary analysis with only 201 patients. These results are consistent with the findings by Puskas et al, who found in a retrospective analysis that high risk patients have a greater mortality benefit from OPCAB as compared to ONCAB

when CPB was not used [Dewey 2004]. On the contrary, our OPCAB outcomes in patients with ICM are not congruent with the outcomes of the ROOBY trial, which showed that OPCAB had worse survival and more adverse events at 5-year follow up [Shroyer 2017]. A major difference, however, was that in our study, patients were not randomized to off-pump versus on-pump prior to the operation, so selection bias likely was present. Furthermore, a criticism of the ROOBY trial was that their surgeons were inexperienced in the OPCAB approach, whereas the surgeons in our study are facile with OPCAB.

What was statistically significant in our secondary analysis was that there were fewer pulmonary complications and fewer returns to OR for bleeding with OPCAB. The benefits of OPCAB that have been explained in literature previously in civilian patients can likely be applied to our cohort as well. A recent meta-analysis by Sepehripour et al highlighted the reasons why OPCAB offers end organ protection. There is less manipulation of the aorta, thus reducing the risk of cerebral embolization during surgery. There also is an inherent inflammatory reaction to CPB itself, which can lead to pulmonary and renal injury [Sepehripour 2013]. Furthermore, the frequent use of anticoagulation in CPB is not a necessity in the off-pump approach, which likely reduces the incidence of reoperation for bleeding in OPCAB [Sepehripour 2014]. These findings provide an explanation for the findings of fewer pulmonary complications and returns to the OR that we saw in our cohort.

We believe that the part of achieving success after revascularization in patients with ICM is the multidisciplinary patient assessment. All veterans with ICM undergo assessment of myocardial viability of left anterior descending artery territory and evaluation of right ventricular function. This

Table 2. Postoperative outcomes after coronary artery bypass grafting

Postoperative outcomes	ICM group (N = 201)	Non-ICM group (N = 1260)	ICM versus Non-ICM aOR with 95% CI	Adjusted P
30-day mortality, N (%)	10 (5.0)	26 (2.1)	1.94 [0.79 - 4.75]	.15
5-year mortality, N (%)	64 (37.4)	229 (21.7)	1.75 [1.14 – 2.69]	.01
10-year mortality, N (%)	73 (54.1)	280 (34.9)	1.71 [1.09 – 2.67]	.02
aCardiovascular, N (%)	6 (3.0)	27 (2.1)	0.98 [0.33 - 2.93]	.97
bPulmonary, N (%)	25 (12.4)	66 (5.2)	1.88 [1.07 - 3.30]	.03
Renal failure, N (%)	2 (1.0)	6 (0.5)	0.66 [0.07 - 6.53]	.72
cReturn to OR, N (%)	7 (3.5)	15 (1.2)	3.10 [1.19 - 8.06]	.02
dWound complications, N (%)	2 (1.0)	12 (1.0)	0.57 [0.07 - 4.61]	.60
All complications, N (%)	40 (19.9)	155 (12.3)	1.50 [0.96 - 2.34]	.07
Postoperative outcomes	ICM with Off Pump CABG (N = 161)	ICM with On Pump CABG (N = 40)	Off versus On Pump CABG aOR with 95% CI	Adjusted P
30-day mortality, N (%)	5 (3.1)	5 (12.5)	0.19 [0.07 - 1.16]	.07
5-year mortality, N (%)	50 (37.3)	14 (37.8)	0.60 [0.22 – 1.69]	.34
10-year mortality, N (%)	57 (53.8)	16 (55.2)	0.59 [0.22 -1.58]	.29
aCardiovascular, N (%)	3 (1.9)	3 (7.5)	0.01 [0.01 - 3.54]	.10
bPulmonary, N (%)	15 (9.3)	10 (25.0)	0.18 [0.06 - 0.55]	<.01
Renal failure, N (%)	2 (1.2)	0 (0)	NA	NA
cReturn to OR, N (%)	1 (0.6)	6 (15)	0.03 [0.01 - 0.30]	<.01
dWound complications, N (%)	1 (0.6)	1 (2.5)	NA	NA
All complications, N (%)	26 (16.2)	14 (35.0)	0.31 [0.12 - 0.79]	.02

Abbreviations: ICM, ischemic cardiomyopathy; CABG, coronary artery bypass grafting; aOR, adjusted odds ratio; NA, Not applicable due to low N; OR, operating room; aCardiovascular = composite outcome of postoperative myocardial infarction, cardiac arrest, and stroke; bPulmonary = composite outcome of failure to wean from ventilator > 48 hours, reintubation, tracheostomy, and pneumonia; cReturn to OR = postoperative bleeding requiring return to the operating room. dWound complications = includes superficial and deep wound infections

process has allowed us to identify patients who will benefit the most following revascularization. The same deliberation in patient selection is applied with regard to performing ONCAB versus OPCAB. Ultimately, the decision of whether to do CABG with or without CPB should be personalized to each individual patient, and this study should give surgeons further comfort in knowing that short-term outcomes are improved in the off-pump approach, when applied to the appropriate patient population.

There are several limitations to this study. The inherent weaknesses of a retrospective analysis are present. In addition, the outcomes largely belong to a single operator in the patient population involved in this analysis, which may limit the generalizability of the study. It is important to note that the primary operator for our series is very experienced in the off-pump approach. OPCAB technically is more challenging, and prior literature – including the CORONARY and GOPCABE trials – have shown that more experienced operators achieve better outcomes, including less bleeding, less renal dysfunction, and shorter hospital stay [Diegeler 2019; Lamy 2016; Sellke 2005]. Furthermore, our patient population was almost entirely male. Females actually have been shown to have worse short-term outcomes when undergoing CABG, and inclusion of more females might have altered our results [Saxena 2012].

In conclusion, veterans with ICM undergoing CABG demonstrated comparable short-term survival compared to non-ICM veterans. However, the long-term survival in ICM cohort still is inferior to patients without ICM. Veterans had comparable outcomes to the civilian population, despite a higher risk profile. There is a strong trend of improved short-term survival and less short-term complications in patients with ICM undergoing OPCAB compared with ONCAB, and multidisciplinary assessment should be employed when deciding which approach to use.

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