

Long-term Outcomes of Coronary Artery Bypass Grafting in Veterans with Left Main Coronary Artery Disease

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ABSTRACT

Background: Studies of the civilian population with left main coronary artery disease (LMCAD) who underwent coronary artery bypass grafting (CABG) have shown 2% to 4.2% 30-day mortality. However, there is a lack of reporting from the veteran population. Here we analyze the outcomes of veterans with LMCAD who underwent CABG by a single surgeon at a single Veterans Affairs Medical Center (VAMC).

Methods: Veterans who underwent isolated CABG between 1998 to 2018 at a VAMC were further divided into a group with significant left main coronary artery disease (LMCAD) of stenosis greater than or equal to 50% and a group without left main coronary artery stenosis (non-LMCAD). The primary outcome was mortality. Secondary outcomes included postoperative complications. Multivariable regression analysis and Kaplan-Meier survival analysis were used to compare the two cohorts.

Results: The demographics and comorbidities are similar between the two cohorts except for higher average age and percentage of stroke in the LMCAD group (n = 509) compared to non-LMCAD (n = 927). Perioperative complications are comparable between the two groups except for increased length of stay (LOS) in the LMCAD group (12.9 ± 15.9 days versus 10.9 ± 9.0 days in non-LMCAD, *P* < .001). 30-day mortality in the LMCAD group is 4.1% versus 1.4% in non-LMCAD. However, Kaplan-Meier curves show no significant difference in adjusted overall survival throughout 15 years between the groups (*P* = .560).

Conclusion: Veterans with LMCAD who underwent CABG have similar postoperative complications compared to non-LMCAD group. The 30-day mortality is higher in the LMCAD group; however, there is no difference in long-term survival.

INTRODUCTION

Left main coronary artery disease (LMCAD) is the highest risk subset of coronary artery disease given the wide area of

myocardium threatened by ischemia [Cho 2019; Harskamp 2015; Lee 2016]. Accordingly, revascularization remains the standard of care for those with significant disease (>50% stenosis) regardless of the presence or absence of symptoms [Authors/Task Force members 2014; Fihn 2014; Ramadan 2018]. Historically, coronary artery bypass grafting (CABG) has been the standard of care for revascularization while percutaneous coronary interventions (PCI) is reserved for patients with high surgical risk [Harskamp 2015]. However, with advancements in percutaneous methods and efficacy over the past two decades, PCI has emerged as a viable alternative to open surgical revascularization in more instances, particularly for less complex lesions [Ramadan 2018].

At present, multiple clinical trials and pooled analysis of individual data from previous trials have not shown a clear survival benefit for either CABG or PCI with regard to LMCAD specifically [Buszman 2016; Head 2018]. Trends in the literature show improved long-term durability of revascularization and associated improved long-term morbidity outcomes with CABG as compared to PCI; however, these benefits come at the drawback of a slightly higher risk of immediate perioperative morbidity [Morice 2010; Morice 2014; Nerlekar 2016; Stone 2016]. Nevertheless, improvements in surgical techniques and technologies as well as perioperative care have made undergoing CABG progressively safer than in the past [Alexander 2016; Modolo 2019].

Appreciating the perioperative risk profile associated with CABG in contemporary surgical practice is important in guiding therapeutic decisions, particularly with strong alternative options available. Determining which strategy to undertake for revascularization of LMCAD is a complex decision-making process that requires patient personalization. Specifics of the patient's health status, their cardiovascular pathology, and additional knowledge of institution specific factors should all be taken into account. As a result of individualization of care in patients with cardiac diseases, trials in the civilian population have shown that over the past decade morbidity and mortality outcomes for CABG for LMCAD have improved. For instance, a decreased rate in major adverse cardiovascular or cerebrovascular events (MACCE) was noted in the Evaluation of Xience Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial (2010-2014) as compared to the older Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial (2005-2007) [Modolo 2019]. However, while outcomes of CABG

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Table 1. Comparison of Preoperative Variables between Non-LMCAD and LMCAD Cohort

Pre-Op Variable	Non-LMCAD (n = 927)	LMCAD (n = 509)	P
Age	63.6 ± 9.1	66.7 ± 9.4	<.001
Sex, male	915 (98.7)	505 (99.2)	.38
COPD	384 (41.4)	210 (41.3)	.95
Current smoker	277 (29.9)	160 (31.4)	.54
Cerebral vascular disease	159 (17.2)	122 (24.0)	.002
Diabetes	385 (41.5)	207 (40.7)	.75
Prior PTCA			
0	847 (91.4)	76 (8.2)	
1	4 (0.4)	495 (97.3)	
2	13 (2.6)	1 (0.2)	
Prior cardiac surgery	14 (1.5)	12 (2.4)	.25
Preoperative IABP	85 (9.2)	86 (16.9)	<.001
Prior MI			
0	443 (47.8)	388 (41.9)	
1	96 (10.4)	256 (50.3)	.028
2 or more	182 (35.8)	71 (14.0)	
PVD	254 (27.4)	164 (32.2)	.054*
HTN	736 (79.4)	427 (83.9)	.55
BMI	29.4 ± 5.8		
28.7 (25.5, 32.5)	28.2 ± 5.3		
27.9 (24.7, 30.9)	<.001		
Albumin	3.83 ± 0.47	3.80 ± 0.47	.18*
Creatinine	1.31 ± 1.01		
1.1 (1.0, 1.3)	1.33 ± 1.33		
1.1 (0.9, 1.3)	.44		
Hemoglobin	13.40 ± 1.66	13.13 ± 1.65	.004
HDL	37.93 ± 9.04		
38 (34, 39)	39.53 ± 9.59		
38 (35, 42)	.002		
LDL	103.51 ± 29.55		
100 (96, 108)	104.18 ± 30.12		
100 (93, 110.2)	.82		
ASA Score	292 (31.5)	635 (68.5)	
2 or 3	129 (25.3)	380 (74.7)	.014
4 or 5			
LAD % stenosis	80.9 ± 17.7	64.4 ± 31.5	<.001
	85 (70, 90)	75 (50, 90)	
RCA % stenosis	67.5 ± 34.9	68.9 ± 34.0	.45
	80 (50, 99)	80 (50, 90)	
CIRC % stenosis	58.3 ± 36.5	59.5 ± 36.3	.56
	70 (30, 90)	70 (30, 90)	

Table 1. Comparison of Preoperative Variables between Non-LMCAD and LMCAD Cohort [CONTINUED]

Pre-Op Variable	Non-LMCAD (n = 927)	LMCAD (n = 509)	P
LM % stenosis	0	70.1 ± 14.6 70 (60, 80)	—

Values are reported as n (%), mean ± SD if relatively normally distributed, mean ± SD and median (IQR) if nonparametric; Bold P values <.05 are statistically significant; *P < .2 is trend-level significant. LMCAD indicates left main coronary artery disease; COPD, chronic obstructive pulmonary disease; PTCA, percutaneous transluminal coronary angioplasty; IABP, intra-aortic balloon pump; MI, myocardial infarction; PVD, peripheral vascular disease; HTN, hypertension; LDL, low density lipoprotein; ASA, American Society of Anesthesiologists; LAD, left anterior descending coronary artery; RCA, right coronary artery; CIRC, circumflex artery; LM, left main coronary artery.

procedures for LMCAD in non-governmental hospitals are well reported, little is known about the recent outcomes in veteran populations at Department of Veterans Affairs (VA) medical centers. This distinction is important because veterans experience a higher than usual burden of cardiovascular disease, and are generally presumed to be higher risk patients [Scherer 2019]. Therefore, it is unclear if results of civilian populations can be generalized to this population and used when guiding patient selection and preoperative risk counseling. The purpose of this study was to benchmark outcomes of veterans with LMCAD who underwent CABG by a single surgeon at a single VA over the past 20 years.

MATERIALS AND METHODS

This is a retrospective study of a prospectively collected database from a single cardiothoracic surgeon at a Veterans Affairs Medical Center (VAMC). All patients who underwent isolated CABG for all indications and level of operative priority between 1998 to 2018 were divided into a group with significant left main coronary artery disease (LMCAD) of stenosis greater or equal to 50% and a group without any left main coronary artery stenosis (non-LMCAD). The patients who had mild left main coronary artery stenosis were excluded from the study. There was no age restriction.

Clinically relevant preoperative, intraoperative, and operative variables with P < .2 in univariate between group comparisons were considered possible confounding variables and were adjusted for in multivariate logistic regression modeling using backwards selection of variables. 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 at 30 days, 5-year, and 10-year. Secondary outcomes were cardiovascular, pulmonary, and renal composite morbidity outcomes, as well as unplanned reoperation and wound complications. A

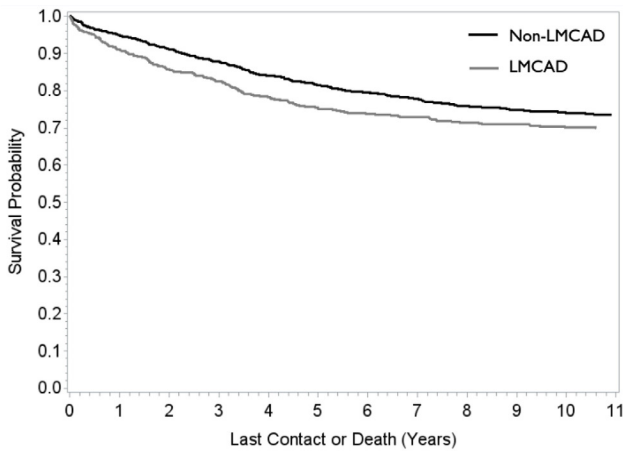


Figure 1. Kaplan-Meier survival curve for overall sample; Log-rank test $P = .084$. There is not a significant difference in unadjusted overall survival throughout the years between the groups.

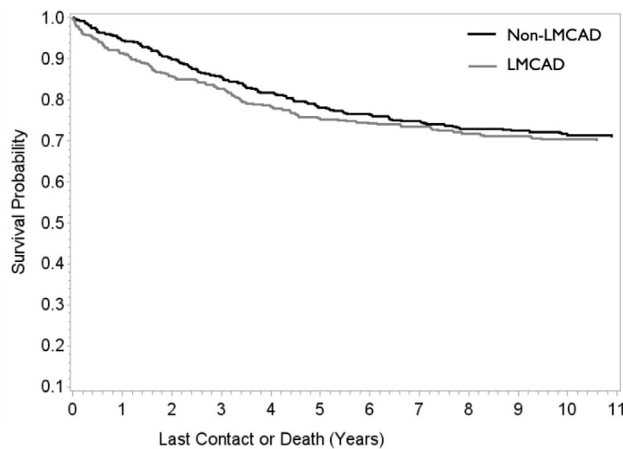


Figure 2. Kaplan-Meier survival curve; Log-rank test $P = .560$. There is not a significant difference in unadjusted overall survival throughout the years between the groups. Multivariable Cox-proportional regression model gives a hazard ratio (HR) (95% CI) of 1.13 (0.87–1.47) for overall survival throughout time for LMCAD versus non-LMCAD ($P = .352$).

subgroup analysis was performed in patients with LMCAD who were sub-stratified based on whether cardiopulmonary bypass 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. All statistical analysis was performed using JMP Pro14 (SAS Institute, Cary, NC, USA).

Of note, the CABGs are performed off-pump unless patients have active angina, LMCAD with reduced left ventricular function, diffuse CAD, non-healthy target vessel, or if the bypass needs extensive lateral wall manipulation. For perfusion, we used 4:1 blood delivered antegrade throughout the case. Our solution uses a Plegisol (Pfizer) base with 100 mg Lidocaine, 10 g mannitol, 11 mEq sodium bicarbonate, and

Table 2. Comparison of Intraoperative Variables between Non-LMCAD and LMCAD Cohort

Operative Variable	Non-LMCAD (n = 927)	LMCAD (n = 509)	P
Priority			
Elective	860 (92.8)	460 (90.4)	
Urgent	57 (6.2)	40 (7.9)	.27
Emergent	10 (1.1)	9 (1.8)	
Operative time, min	227.9 ± 70.9 219 (182, 263)	228.5 ± 73.8 218 (180, 258)	.57
ONCABG	376 (40.6) (OPCABG n = 376)	230 (45.2) (ONCABG n = 230)	.21
Bypass time, min	92.2 ± 35.2 89 (3, 264)	89.4 ± 31.0 84.5 (6, 240)	.18
Cross clamp time, min	51.9 ± 27.5 50 (0, 157)	49.1 ± 24.7 50 (0, 120)	.26

Values are reported as mean ± SD if relatively normally distributed, mean ± SD and median (IQR) if nonparametric. LMCAD indicates left main coronary artery disease; OPCAB, off-pump CABG; ONCAB, on-pump CABG.

40 mEq potassium chloride. The cardioplegia is delivered at a temperature of 4 degrees Celsius. ONCABGs are typically only vented through the aortic root.

RESULTS

Between January 1998 and December 2017, 509 patients who underwent CABG had LMCAD greater than or equal to 50% stenosis (LMCAD group) while 927 patients did not have any left main coronary artery (non-LMCAD group) at the DC VAMC. The patients were on average 64.7 years old and a majority were male (98.9%), with an average BMI of 28.97. The demographics were similar between the two cohorts except for average older age in the LMCAD group (66.7 ± 9.4 versus 63.6 ± 9.1 years old, $P < .001$). The LMCAD group also had significantly higher percentage of cerebrovascular diseases (24.0% versus 17.2%), prior percutaneous transluminal coronary angioplasty (PTCA) (97.3% versus 91.4%, $P < .001$), prior MI within 7 days of CABG (14.0% versus 10.4%, $P = .028$), higher American Society of Anesthesiologists (ASA) score (74.7% versus 68.5% ASA score 4 or 5, $P = .014$), and higher preoperative intraaortic balloon pump (IABP) (16.9% versus 9.2%, $P < .001$) (Table 1). The non-LMCAD group had significantly more patients with prior MI more than 7 days before the CABG (41.9% versus 35.8%, $P = .028$), higher BMI (29.4 ± 5.8 versus 28.2 ± 5.3 , $P < .001$), lower high-density lipoproteins (HDL) (37.93 ± 9.04 versus 39.53 ± 9.59 , $P = .002$), and higher left anterior descending (LAD) artery percent stenosis ($80.9\% \pm 17.7$ versus $64.4\% \pm 31.5$, $P < .001$) than the LMCAD group (Tables 1 and 2).

Table 3. Comparison of Postoperative Outcomes by Non-LMCAD and LMCAD Cohorts, with Multivariable Logistic Regression

Post-Op Variable	Non-LMCAD (n = 927)	LMCAD (n = 509)	P	aOR (95% CI)	Adjusted P
Perioperative MI	13 (1.4)	3 (0.6)	.16	0.33 (0.11–0.96)	.042
Renal failure	5 (0.5)	6 (1.2)	.21	1.16 (0.42–3.27)	.77
Mediastinitis	8 (0.9)	3 (0.6)	.76	0.62 (0.22–1.79)	.38
Cardiac arrest, CPR	17 (1.8)	10 (2.0)	.86	0.90 (0.42–1.92)	.78
Reop for bleeding	20 (2.2)	6 (1.2)	.18	0.63 (0.27–1.47)	.28
Ventilator > 48 hours	51 (5.5)	34 (6.7)	.37	0.69 (0.40–1.21)	.20
Stroke	3 (0.3)	1 (0.2)	.83	2.31 (0.58–9.21)	.24
30-day mortality	13 (1.4)	21 (4.1)	.001	2.32 (1.17–4.62)	.016
180-day mortality	31 (3.3)	26 (5.1)	.10	1.40 (0.77–2.55)	.27
Total mortality	254 (27.4)	154 (30.3)	.25	0.92 (0.69–1.23)	.57
MACCE	36 (3.9)	27 (5.3)	.21	1.09 (0.61–1.95)	.78
Composite					
0	839 (90.5)	454 (89.2)			
1	59 (6.4)	36 (7.1)			
2	20 (2.2)	12 (2.4)			
3	4 (0.4)	5 (1.0)	.19	—	—
4	5 (0.5)	—			
5	—	1 (0.2)			
6	—	1 (0.2)			
Binary composite	88 (9.5)	55 (10.8)	.43	0.82 (0.53–1.25)	.35
Postoperative LOS	10.9 ± 9.0 8 (6, 13)	12.9 ± 15.9 9 (7, 14)	<.001	aOR N/A PE (SE) = 0.06 (0.03)	.045
ICU LOS	2.8 ± 3.3 2 (2, 3)	3.2 ± 5.2 2 (2, 3)	.006	aOR N/A PE (SE) = 0.01 (0.03)	.92

Values are reported as n (%), mean ± SD if relatively normally distributed, mean ± SD and median (IQR) if nonparametric; bold P values <.05 are statistically significant. LMCAD indicates left main coronary artery disease; MI, myocardial infarction; MACCE, major adverse cardiovascular or cerebrovascular events; LOS, length of stay.

DISCUSSION

Some of the first randomized trials that showed CABG to be superior to medical treatment for patients with greater than 75% left main stenosis and left ventricular dysfunction were studies done in the VA system in the 1980s and 1990s [Takaro 1982; Vaughan Sarrazin 2007]. However, subsequent literature on LMCAD outcomes since the 90s has almost exclusively come from the civilian population. The outcomes of LMCAD patients who underwent CABG after 1995 showed that the 30-day mortality ranged between 3% and 4.2% and the survival at two years was approximately 95% [VA Coronary Artery Bypass Surgery Cooperative Study Group 1992]. 30-day mortality of LMCAD patients who underwent CABG continued to decrease in the civilian population. Given that previous studies have shown the veteran population to be a much higher risk cohort with a more severe comorbidity

profile as compared to civilians, it is unclear whether the surgical care of veterans undergoing CABG for LMCAD has made the same strides as have been shown in the civilian setting [Morice 2014; Nerlekar 2016; Taggart 2008]. In this study, we evaluated 30-day morbidity and mortality outcomes as well as long-term mortality outcomes of veterans undergoing CABG for LMCAD. Through a retrospective review of prospectively collected records of veterans undergoing CABG for LMCAD at a single VA medical center over a 20-year period, we found that veterans with LMCAD who underwent CABG have similar postoperative complications and long-term mortality compared to non-LMCAD patients.

The 30-day mortality was significantly higher in the LMCAD group compared to the non-LMCAD group in this study (4.1% versus 1.4%, $P = .016$), (Table 3) however, the long-term mortality in both the unadjusted survival and multivariable Cox-proportional regression model Kaplan-Meier survival

Table 4. Overall Survival with Time

Time	Survival % (95% CI)	
	Non-LMCAD (n = 927)	LMCAD (n = 509)
1 year	94.8% (93.4%–96.3%)	91.0% (88.4%–93.5%)
2 year	91.1% (89.2%–92.9%)	85.7% (82.6%–88.8%)
5 year	81.3% (78.8%–83.9%)	75.1% (71.2%–78.9%)
10 year	73.9% (71.0%–76.8%)	69.9% (65.9%–74.0%)

LMCAD indicates left main coronary artery disease.

Table 5. Outcomes by Off- versus On-Pump in LMCAD Cohort, with Multivariable Logistic Regression

Post-Op Variable	Off-Pump (n = 279)	On-Pump (n = 230)	P	aOR On versus Off (95% CI)	Adjusted P
30-day mortality	7 (2.5)	4 (1.7)	.76	0.77 (0.21 – 2.78)	.69
180-day mortality	18 (6.5)	8 (3.5)	.13	0.65 (0.27 – 1.56)	.34
Total mortality	84 (30.1)	70 (30.4)	.94	1.60 (0.96 – 2.67)	.07
Postoperative LOS	12.7 ± 18.7 8 (6, 14)	13.2 ± 11.7 10 (7, 14)	.012		.0002
ICU LOS	3.2 ± 6.1 2 (2, 3)	3.1 ± 3.3 2 (2, 3)	.16		.23

LOS indicates length of stay. Bold P values <.05 are statistically significant

curve showed no difference in survival in 10 years (Figures 1 and 2). LMCAD patients have had better results over the years as the perioperative care for CABG improved with preoperative IABP use, increased use of transesophageal ultrasonography, better imaging quality, and optimized postoperative ICU care (Table 4) [Deppe 2017; Lee 2016; Taggart 2008].

Compared to the randomized EXCEL and SYNTAX trials, which had 75–77% male patients, veterans in our study were similar in age and BMI but had significantly higher percentage of male (98.9%) than the LMCAD patients who underwent CABG [Lee 2016; Morice 2014]. Notably, veterans had significantly higher comorbidities than the civilian population reported in the EXCEL and SYNTAX trials; LMCAD patients in our study were 49.7% with prior MI (versus 16.9% and 25.4%, respectively in EXCEL and SYNTAX), 31.4% current smoker (versus 20.8% and 24.0%), 40.7% diabetic (versus 28.0% and 25.6%), 83.9% hypertensive (versus 62.4% and 66.9%), 41.3% with COPD (versus 8.5%), and 32.2% with PVD (versus 8.8%) (Table 1) [Lee 2016; Morice 2014]. Despite having significantly higher comorbidities, the veterans in our study had fewer 30-day postoperative complications such as perioperative MI (0.6%) and stroke (0.2%) when compared to patients in the EXCEL trial (n = 957, 6.2% and 1.3%, respectively) [Lee 2016]. Our patients also had similar postoperative LOS to that in SYNTAX (12.9 ± 15.9 versus 13.6 ± 9.6 days) [Morice 2014].

In the subanalysis between ONCAB and OPCAB in our LMCAD cohort, 30-day postoperative outcomes were similar except that OPCAB had statistically significantly shorter LOS (12.7 ± 18.7 days versus 13.2 ± 11.7 days, adjusted P < .01) (Table 5). The 30-day, 180-day, and all-time mortality were no different between ONCAB and OPCAB groups, contrary to the finding in ROOBY trial (Table 5) [Deppe 2017]. The ROOBY trial reported that OPCAB in general had higher mortality and more adverse events than ONCAB patients at five-year follow up [Deppe 2017]. The use of OPCAB has decreased in the United States in the past decade likely due to multiple studies that associated OPCAB with less complete revascularization that resulted in worse long-term graft patency than ONCAB [Deppe 2017; Shroyer 2017]. The ROOBY trial was carried out in the VA system with average surgeon experience of 120 cases of OPCAB prior to the trial [Deppe 2017]. However, the primary surgeons were a mix of attending surgeons and residents in multiple different VAMCs [Deppe 2017]. Our study was free of surgeon and cardiac team variability, and our subanalysis results would support performing OPCAB in LMCAD patients in the care of an experienced surgeon and cardiac team that is proficient in OPCAB.

The success of our cardiothoracic surgery team lies in the consistency of the surgery team and optimization of the perioperative management in collaboration with the cardiology

department. The veterans were receiving optimized medical treatment based on guidelines from the Cardiac Surgery Enhancement Program for VAMCs that started in 1991. Dual antiplatelet therapy with aspirin and Plavix was instituted in 2008. Additionally, our cardiothoracic surgery team has been experienced in OPCAB since 1998 due to the surgeon's preference, and the ancillary staff have been experienced in the perioperative process for patients. In addition, the Heart Center was established in 2015 to provide veterans comprehensive medical management, interventions, and follow-up care by coordinators, perfusionists, physician assistants, cardiologists, and cardiac surgeons. Therefore, the outcomes of the LMCAD patients did not differ significantly between the first and the second decades in this study (Table 4).

There are several limitations of this study. First, this study is a retrospective database study and therefore limited by the biases inherent to such a design. This study is also limited by the fact it reviews data from CABG surgeries performed at a single institution by a single surgeon experienced at OPCAB, and therefore it is unclear how generalizable these results are to the broader veteran population.

In conclusion, veterans with LMCAD who underwent CABG have similar postoperative complications compared to the non-LMCAD group except for increased length of hospital stay. The 30-day mortality is higher in the LMCAD group, as seen in the private sector. However, there is no difference in long-term survival between the two cohorts. Despite a higher comorbidity profile, veterans have similar outcomes when undergoing CABG for LMCAD when compared to the civilian population.

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