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ORIGINAL RESEARCH

Off-Pump Coronary Artery Bypass Grafting: Department of Veteran Affairs' Use and Outcomes

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BACKGROUND: Coronary artery bypass can be performed off pump (OPCAB) without cardiopulmonary bypass. However, trends over time for OPCAB versus on-pump (ONCAB) use and long-term outcome has not been reported, nor has their long-term outcome been compared.

METHODS AND RESULTS: We queried the national Veterans Affairs database (2005–2019) to identify isolated coronary artery bypass procedures. Procedures were classified as OPCAB on ONCAB using the as-treated basis. Trend analyses were performed to evaluate longitudinal changes in the preference for OPCAB. The median follow-up period was 6.6 (3.5–10) years. An inverse probability weighted Cox model was used to compare all-cause mortality between OPCAB and ONCAB. From 47 685 patients, 6759 (age 64±8 years) received OPCAB (14%). OPCAB usage declined from 16% (2005–2009) to 8% (2015–2019). Patients with triple vessel disease who received OPCAB received a lower mean number of grafts (2.8±0.8 versus 3.2±0.8; *P*<0.01).
The ONCAB 5-, 10-, and 15-year survival rates were 82.9% (82.5–83.3), 60.4% (59.8–61.1), and 37.2% (36.1–38.4); correspondingly, OPCAB rates were 80.7% (79.7–81.7), 57.4% (56–58.7), and 34.1% (31.7–36.6) (P<0.01). OPCAB was associated with increased risk-adjusted all-cause mortality (hazard ratio, 1.15 [1.13–1.18]; P<0.01) and myocardial infarction (incident rate ratio, 1.16 [1.05–1.28]; P<0.01).

CONCLUSIONS: Over 15 years, OPCAB use declined considerably in Veterans Affairs medical centers. In Veterans Affairs hospitals, late all-cause mortality and myocardial infarction rates were higher in the OPCAB cohort.

Key Words: coronary artery bypass grafting ■ long term survival ■ myocardial infarction ■ off-pump surgery

Coronary artery bypass grafting (CABG) is the most common adult cardiac surgical procedure performed in the United States.[1] Conventional CABG is performed with cardiopulmonary bypass (CPB) support and is known as on-pump CABG procedure (ONCAB). However, CABG without use of CPB, known as the off-pump CABG (OPCAB), became increasingly popular among surgeons in the mid-1980s.[2] CABG with CPB often triggers an inflammatory cascade that can potentially result in undesirable complications.[3] An OPCAB procedure, performed without manipulating the aorta, may lead to reduced postoperative stroke rates and possibly lower rates of postoperative atrial fibrillation.[4,5]

However, in recent years, CPB technology has improved tremendously. Inflammatory changes observed

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CLINICAL PERSPECTIVE

What Is New?

- Over a 15-year period, in Veterans Affairs medical centers nationwide, the use of off-pump coronary artery bypass surgery has declined substantially.
- Adjusted long-term mortality with off-pump surgery is higher than conventional bypass surgery in Veterans Affairs medical centers, and the patients have higher rates of myocardial infarction.

What Are the Clinical Implications?

- The limited use of off-pump coronary surgery in this large multicenter cohort may need to be addressed at the national level.

Nonstandard Abbreviations and Acronyms

CPB	cardiopulmonary bypass
ONCAB	on-pump coronary artery bypass
OPCAB	off-pump coronary artery bypass
VA	Veterans Affairs

in the postoperative period may be independent of the surgical approach.[6] A national study reported similar stroke rates with both approaches, as only a small fraction of off-pump procedures are truly anaortic.[4,7] Observational studies also consistently report lower mean number of grafts and higher incomplete revascularization rates with OPCAB.[8] The GOPCABE (German Off-Pump Coronary Artery Bypass in the Elderly) and CORONARY (CABG Off- or On-Pump Revascularization) trials report comparable results with both approaches, whereas the ROOBY (Randomized Off/On Bypass) trial, conducted at 18 Veterans Affairs (VA) medical centers, report worse results with off-pump surgery.[9–11] OPCAB surgery is also technically demanding with surgeon experience being a crucial factor in determining outcome.[12] The recent Society of Thoracic Surgeons annual report states that, nationwide, 3107 surgeons performed 156 931 isolated CABG procedures; this equates to 50 procedures per surgeon.[1] A market study from the United States projects a 0.8% annual decline in estimated CABG procedures; thus, concerns arise as to the adequacy of the average surgeon's caseload to maintain proficiency with off-pump surgery in the future.

Therefore, we queried the nationwide VA database to report temporal changes in OPCAB versus ONCAB use rates and risk-adjusted survival rates.

METHODS

Data Sharing Statement

The data that support the findings of this study are the property of the Department of Veterans Affairs ; hence, they cannot be provided on request. Codes used for statistical analyses are available for download at https://github.com/svd09 from the study repository or can be requested from the corresponding author.

Data Sources

The Veteran Health Affairs Department has the largest integrated health care system in the United States, providing care at 170 hospitals and 1025 outpatient facilities. The VA Surgical Quality Initiative Project, a central repository of patient records, was the primary data source for this study. Vital status information was obtained from linkage to the Social Security Index and the Beneficiary Identification Records Locator Subsystem.

Cohort Selection

Nationally, 52 641 patients underwent CABG (as their primary operative procedure) at 41 different VA medical centers between January 1, 2005 and September 30, 2019. After applying study exclusion criteria, 47 685 patients undergoing primary, isolated primary CABG procedures were included in this retrospective cohort analysis (Figure 1). The *International Classification of Diseases, Ninth Revision* (*ICD-9*) and *Tenth Revision* (*ICD-10*) and Current Procedural Terminology codes were used to identify patient covariates when not directly available from the VA Surgical Quality Initiative Project data (Table S1).

The VA Surgical Quality Initiative Project data included cardiopulmonary bypass times and aortic cross-clamp times; thus, patients who had "0" coded for their CPB time were considered to have undergone OPCAB surgery. Patients with any non-zero value coded in their CPB field were considered to have undergone ONCAB. Although patients converted from OPCAB to ONCAB were separately identified, the original intention to treat decision was not available; thus, the planned versus unplanned conversions (eg, planned conversions from ONCAB to OPCAB or from OPCAB to ONCAB) or phased procedures (eg, using both OPCAB and ONCAB) were not documented before surgery. Analyses in our study were thus classified based on any use of cardiopulmonary bypass versus no cardiopulmonary bypass being used. This methodology for identifying OPCAB from the VA Surgical Quality Initiative Project database has been applied and validated earlier.[13]

Study End Points

The *primary clinical end point* studied was time-to-death based on assessments of all-cause mortality. The last date of vital status recorded in the database

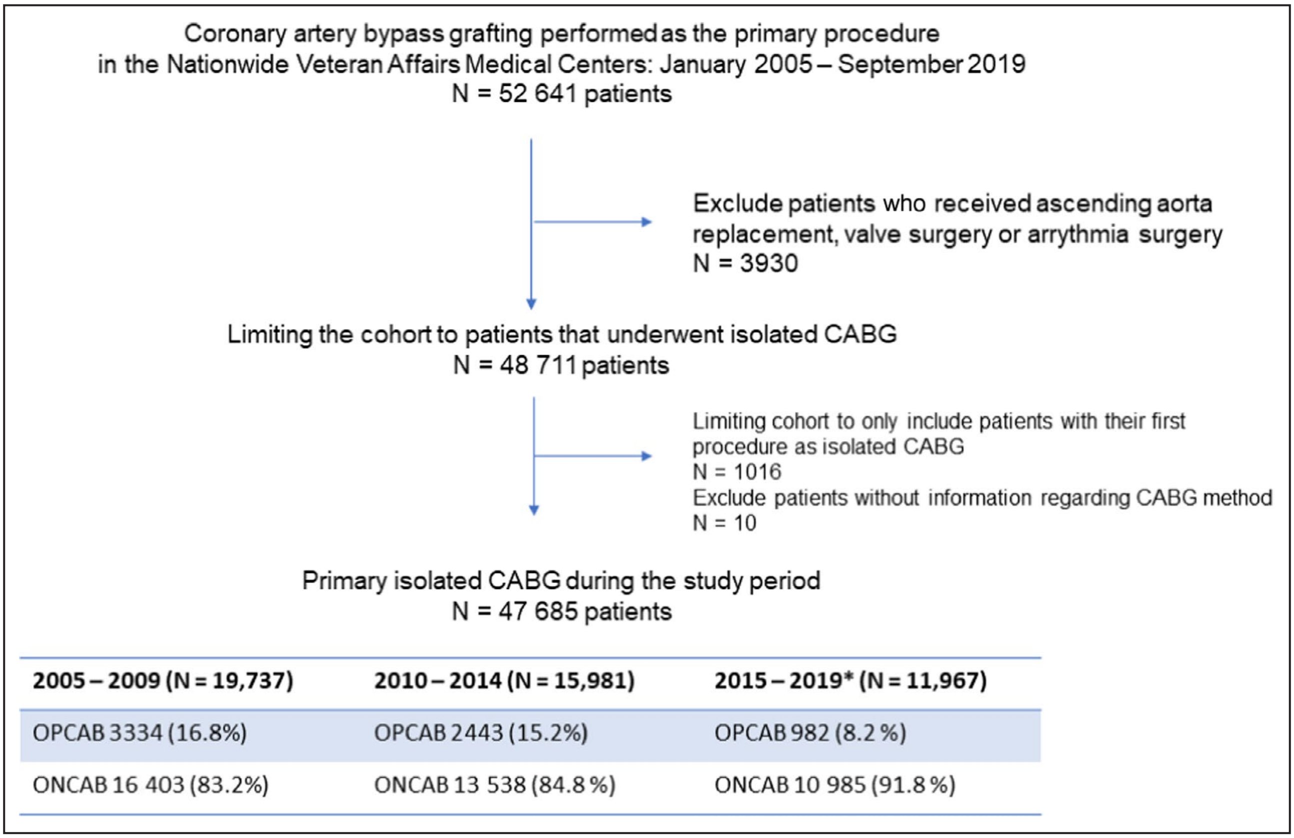

Figure 1. This flow chart presents the cohort selection process used to identify patients that receiving isolated coronary artery bypass grafting at nationwide Veteran Affairs medical centers between January 2005 and September 2019.
CABG indicates coronary artery bypass grafting; ONCAB, on-pump coronary artery bypass grafting; and OPCAB, off-pump coronary artery bypass grafting.

at the time of data abstraction was May 1, 2020. Vital status and other clinical information were last obtained from the VA Informatics and Computing Infrastructure database on October 30, 2020; thereafter, further statistical analyses were performed up to February 2021.

We hypothesized that the overall use of OPCAB among national VA medical centers would be comparable to that observed in nonfederal centers in the United States. For this same period, however, these contemporary OPCAB usage trends were not available. Hence, the other aim of our study was to report longitudinal changes in VA-based OPCAB use as well as identify clinical factors associated with OPCAB survival over the 15-year study period.

The *secondary* clinical end points studied were myocardial infarction (MI) and the time to first percutaneous coronary intervention (PCI) during follow-up.

Statistical Analysis

Descriptive Statistics

Categorical data were presented as counts (percentages). Normally distributed continuous variables were reported as means (with SDs) and skewed data were presented using medians (with interquartile ranges). Patient characteristics and early postoperative outcomes between OPCAB and ONCAB groups were tested using the χ^2 test for categorical data. For continuous data, the t test was used for normally distributed data, and for skewed data, the Wilcoxon rank-sum test was used.

Evaluating Trends Over the Study Period

The annual frequency for OPCAB use was reported. As we observed a monotonic OPCAB decline, the Cochran Armitage test was used to evaluate for statistical significance in trends over time. We further divided the overall study period into 3 equal 5-year segments (2005–2009, 2010–2014, 2015–2019). To understand the likelihood of OPCAB use in each time period and practice change over the study duration, we fit separate logistic regression models for each period. The variables included in these models were selected a priori and are patient demographics—age at surgery, sex, self-reported race, and clinical characteristics—presence of diabetes, hypertension, peripheral arterial disease, chronic obstructive pulmonary disease, heart failure, hyperlipidemia, chronic kidney disease, smoking, atrial fibrillation, prior MI, prior PCI, liver disease, left ventricular systolic dysfunction, triple vessel disease, presence of left main disease, and center OPCAB volume. Odds ratios obtained from these models provide information regarding changes in OPCAB preferences over the 15-year study period.

Propensity Score Adjustment

For propensity scoring, a logistic regression model with an a priori selection of variables, based on clinical relevance, was developed.[14] The variables included in this model were:

1. Patient demographics—age at surgery, sex, self-reported race, time period of surgery
2. Clinical characteristics—presence of diabetes, hypertension, peripheral arterial disease, New York Heart Association class, obesity, VA projected risk of mortality score, chronic obstructive pulmonary disease, heart failure, hyperlipidemia, chronic kidney disease, smoking, atrial fibrillation, prior MI, prior PCI, liver disease, left ventricular systolic dysfunction, complex coronary artery disease, elective surgery
3. Center-level characteristics: center OPCAB volume

Inverse probability treatment weights were calculated from derived propensity scores. Post-weight balance was assessed using the mean standardized difference calculated for each covariate. An absolute post-weight mean standardized difference <0.1 was considered satisfactory (Figure S1).

Long-Term Outcomes

Overall and procedure-specific survival estimates were calculated using the nonparametric Kaplan-Meier method and compared with the log-rank test. We initially tested whether the main exposure (OPCAB/ONCAB) had a time-varying association with mortality (Figure S2). Using the Grambsch-Therneau test, a time-varying relationship for OPCAB was not observed (P>0.05) and therefore a weighted Cox proportional hazards model was fit to obtain the hazard ratio (HR; and 95% CI) for mortality in the OPCAB group (reference group: ONCAB).

MI was analyzed using 2 different methods. First, a nonparametric competing risk model was constructed to evaluate the time to the first MI event during follow-up with all-cause mortality as the competing event. The cumulative incidence for MI in the OPCAB and ONCAB groups was compared using the Fine and Gray test and reported as subdistribution HRs (with 95% CIs). However, MI can also occur more than once during the follow-up. Therefore, the total number of MI events for each patient were calculated and reported as event rates per 1000 patient-years follow-up. To compare rates of MI between the OPCAB and ONCAB groups, a negative binomial generalized regression model was fit. Follow-up time was included as an offset in the model and results are presented as incidence rate ratios with 95% CIs.

The need for follow-up PCI was analyzed using a competing risk model with all-cause mortality as the competing event. The cumulative incidence for follow-up percutaneous intervention in the OPCAB and ONCAB groups were compared using the Fine and Gray test and reported as subdistribution HRs (with 95% CIs).

Imputation for Missing Data

Fewer than 5% missing data were observed in any covariate used in regression modeling; thus, 5 data sets were imputed using the method of chained equations.[15] Models were fit for each imputed data set and results pooled with the Rubin's method.

Statistical analyses were performed using R 3.6.3 (The R Foundation for Statistical Computing, Austria). Further details are provided in Data S1. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (see Table S2).[16]

This study was approved by the VA Northeast Ohio Research and Development Committee (# CY19-045). Individual patient consent was waived. Data analysis was conducted within the VA Informatics and Computing Infrastructure at the Louis Stokes Cleveland VA Medical Center. Results, figures, and article drafts were shared with all coauthors, who approved of the final version.

RESULTS

Comparison of Patients Receiving OPCAB and ONCAB

Between January 1, 2005 and September 30, 2019, 47 685 patients (mean age 64.9±8 years) underwent isolated CABG in 43 VA medical centers nationwide. Among these, 6759 (14.17%) receiving off-pump surgery compried the OPCAB cohort. The mean age of patients receiving OPCAB was lower (mean age 64.7 versus 65.0 years; P=0.01); however, the distribution appeared to be bimodal with octogenarians receiving CABG more likely to have OPCABG procedures (3.9% versus 3.2%; P=0.005). Patients receiving OPCAB were less likely to have heart failure (31.1% versus 34.2%; P<0.001) before surgery but more likely to have peripheral vascular disease (28.8% versus 24.8%; P<0.001). The prevalence of chronic kidney

Table 1. Baseline Characteristics of the Patients Receiving OPCAB and ONCAB

	OPCAB N=6759	ONCAB N=40 926	*P* value
Age, y	64.00 [59, 70]	64.00 [60, 70]	<0.001
Female sex	60 (0.9)	441 (1.1)	0.176
Diabetes			0.029
None	3756 (55.6)	22709 (55.5)	
Non-insulin-treated diabetes	1508 (22.3)	8671 (21.2)	
Insulin-treated diabetes	1495 (22.1)	9546 (23.3)	
Systemic hypertension	6384 (94.5)	38042 (93.0)	<0.001
Active smoker	1929 (28.5)	10778 (26.3)	<0.001
Chronic obstructive pulmonary disease	1656 (24.5)	9665 (23.6)	0.117
Race			0.002
Black	687 (10.2)	3761 (9.2)	
White	4595 (68.0)	28657 (70.0)	
Other*	1477 (21.9)	8508 (20.8)	
Body mass index	29.66 (5.38)	29.93 (5.35)	<0.001
Liver disease	11 (0.2)	16 (0.0)	<0.001
Peripheral artery disease	1947 (28.8)	10143 (24.8)	<0.001
Recent congestive heart failure	2113 (31.3)	13 985 (34.2)	0.016
Hyperlipidemia	3301 (48.8)	19559 (47.8)	0.113
Chronic atrial fibrillation	776 (11.5)	4836 (11.8)	0.44
Prior myocardial infarction	2935 (44.6)	16409 (42.2)	<0.001
Prior percutaneous coronary intervention	98 (1.4)	441 (1.1)	0.009
Obesity	2926 (43.3)	18475 (45.2)	0.004
Estimated glomerular filtration rate	75.01 [60.39, 91.18]	75.23 [60.95, 90.87]	0.279
Chronic kidney disease	1624 (24.0)	9434 (23.1)	0.085
Veterans Affairs projected risk of mortality score	6 (4–10) %	6 (3–10) %	0.38
Time periods observed			<0.001
2005–2009	2443 (36.1)	13538 (33.1)	
2010–2014	2443 (36.1)	13538 (33.1)	
2015–September 2019	982 (14.5)	10985 (26.8)	
Left ventricular systolic dysfunction	1327 (20.3)	8381 (21.1)	0.126
ST-segment–elevation myocardial infarction/non–ST-segment–elevation myocardial infarction at admission	110 (1.6)	1994 (3.9)	<0.001

(Continued)

Table 1. Continued

	OPCAB N=6759	ONCAB N=40 926	*P* value
Extent of coronary stenosis			<0.001
Single vessel disease	1154 (17.1)	5063 (12.4)	
Double vessel disease	1533 (22.8)	8404 (20.4)	
Triple vessel disease	3148 (46.6)	22 196 (54.2)	
Left main stenosis	524 (7.8)	3293 (8)	

ONCAB indicates on-pump coronary artery bypass grafting; and OPCAB, off-pump coronary artery bypass grafting.

*Other indicates American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, or those self-reported as from multiple categories.

disease (24% versus 23.1%; P=0.08) and chronic obstructive pulmonary disease (24.5% versus 23.6%; P=0.11) was comparable between treatment groups. The projected mortality risk was comparable in both cohorts. (Table 1).

Compared to ONCAB, OPCAB procedures were more likely to be elective (84.2% versus 83.3%; P=0.05). Patients with OPCAB received lower number of distal anastomoses (mean 2.67 versus 3.1; P<0.001) (Table 1). Even in patients with triple vessel disease, the mean number of distal anastomoses off-pump patients received were lower (2.89±0.84 versus 3.27±0.79; P<0.001); however, patients with OPCAB received more arterial grafts (1.03±0.3 versus 0.99±0.29; P<0.001). During the entire study period, 333 patients with OPCAB (4.6%) underwent an unplanned conversion to ONCAB during the procedure.

Trends in the Use of OPCAB Over Time

Overall, each center performed a median of 1002 (791–1435) procedures during the study period. The median rate of OPCAB use per center was 7.7% (interquartile range: 2.4%–22.9%). Overall, 25/43 (58%) centers used OPCAB for fewer than 10% of patients and 16/43 (37%) used it for <5% of their procedures. Although 8/25 (32%) used OPCAB surgery in <1%, 3/25 (12%) did not perform OPCAB at all. Only 8/43 (18%) centers used OPCAB for more than 30% of their patients. The median rate of OCPAB use per center declined from 10.8% (interquartile range 4%–26.6%) in 2005 to 2009 to 1.8% (interquartile range 0.7%–5.7%) in 2015 to 2019. We observed an inverse correlation between procedure year and the annual proportion of patients undergoing OPCAB (slope=−0.87, adjusted R^2=0.77). The most significant annual declines were observed in 2014 (2.4%) and 2015 (2.7%). Of the 8 centers that had >30% OPCAB use in the first time period, only 4 maintained their numbers (Figure 2). Similarly, among 13 centers that used OPCAB in 10% to 30% of patients, only 4 continued to use OPCAB at the same or a higher rate.

Overall, 6759/47 685 (14.17%) patients were operated by the OPCAB approach. However, this proportion declined from 16.8% in the first time period (2005–2009) to 15.2% (2010–2014) and then 8.2% (2015–2019) in the subsequent time period (*P*<0.001). Patients with triple vessel disease or left main disease had lower odds of OPCAB (Table 2). However, octogenarians and patients with peripheral artery disease had higher odds of receiving OPCAB in the most recent time period.

Postoperative Outcome

The 30-day mortality, acute renal failure, and stroke rates observed in the whole cohort were 640/47 685 (1.3%), 566/47 865 (1.2%), and 503/47 865 (1.1%), respectively. Postoperative event rates were comparable for 30-day mortality and postoperative stroke, whereas acute renal failure rates were lower with OPCAB (0.5% versus 1.1%; *P*<0.001). When event rates were grouped according to the time period, we observed a decline in adverse events in the ONCAB group over time (Table S3). Compared with OPCAB, from 2005 to 2008, the adverse event rates with ONCAB were significantly higher than OPCAB between 2005 and 2008; however, between 2015 and 2019, both groups reported comparable 30-day mortality, stroke and acute renal failure rates (Table 3).

In patients needing unplanned conversion from OPCAB to ONCAB, 30-day mortality, postoperative stroke, and acute renal failure rates were 4.8%, 3.3%, and 1.2%, respectively. The 30-day mortality associated with unplanned conversions reduced from 5.4% in 2005 to 2008 to 3.6% in the last time period (2015–2019).

Long-Term Survival

All-Cause Mortality

The median follow-up period was 6.6 (interquartile range 3.46–10.09) years. The survival estimates observed at 5, 10, and 15 years for the whole cohort were 82.6% (82.2%–82.9%), 60% (59.4%–60.5%), and 36.7% (35.7%–37.8%), respectively. In the ONCAB cohort, the 5-, 10-, and 15-year survival was 82.9% (82.5%–83.3%), 60.4% (59.8%–61.1%), and 37.2% (36.1%–38.4%), respectively, whereas in the OPCAB group, estimated survival at similar time points was lower: 80.7% (79.7%–81.7%), 57.4% (56%–58.7%), and 34.1% (31.7%–36.6%), respectively (log-rank test *P*<0.001) (Figure 3). On weighted analysis, patients undergoing OPCAB had a higher risk for all-cause mortality than patients who received ONCAB during the study period (HR, 1.15 [1.13–1.18]; *P*<0.001).

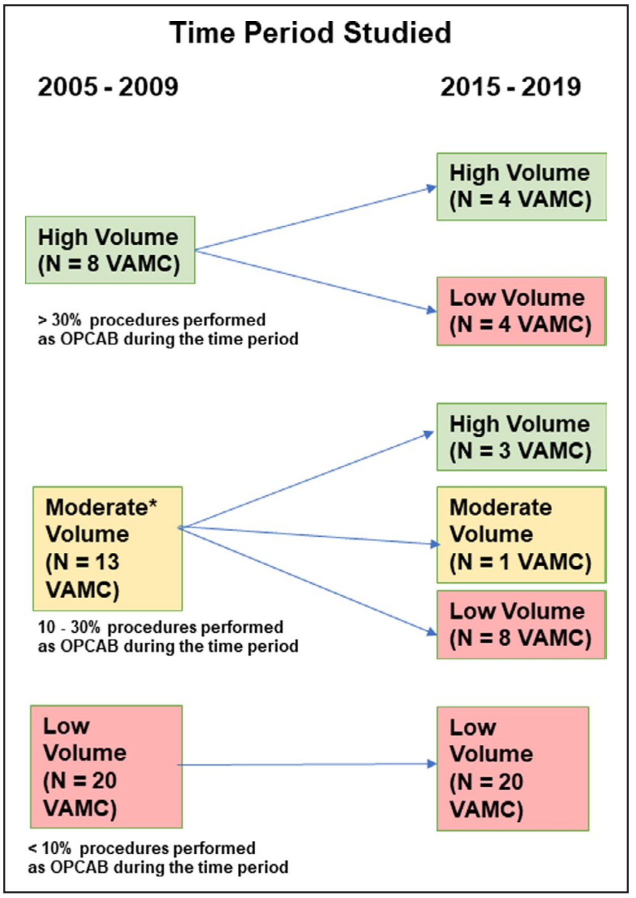

Figure 2. VA medical centers were stratified depending upon the OPCAB volume in each time period (2005–2009 and 2015–2019) into low volume (<10% of total procedures performed OPCAB), moderate volume (10%–30% of total procedures performed OPCAB), and high volume (>30% total procedures performed OPCAB).
As depicted in the figure, we observed a decline in high and moderate volume centers between the first (2005–2009) and last (2015–2019) time periods. *-1 center that reported data in 2005 to 2009 did not report data between 2015 and 2019. OPCAB indicates off-pump coronary artery bypass grafting; and VAMC, Veterans Affairs Medical Center.

Myocardial Infarction

The 5- and 10-year cumulative incidence for MI was 5.9% and 5.1% in the OPCAB group and 10.4% and 9.5% in the ONCAB group. The likelihood of suffering from MI was higher in patients receiving OPCAB (sub-HR, 1.09 [1.01–1.19]; *P*=0.03).

In 327 772 patient-years of follow-up, 6000 MI events were observed (18.3 events per 1000 patient-years follow-up). MI was more common in the OPCAB group (19.4 events per 1000 patient-years follow-up) than the ONCAB group (18 events per 1000 patient-years follow-up) (incidence rate ratio, 1.16 [1.05–1.28]; *P*<0.001).

Follow-Up PCI

The 10-year cumulative incidence for follow-up PCI was 1.2% and 0.6% in the OPCAB and ONCAB

Table 2. Results of the Logistic Regression Model Fit to Determine the Odds of Patients With Specific Clinical Covariates to Receive an Off-Pump Surgery in Each Time Period

Patient covariates	Time period			
	2005–2009		2015–2019	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age at surgery*	1.09 (1.04–1.15)	0.001	0.98 (0.88–1.09)	0.73
Triple vessel disease	0.65 (0.6–0.71)	<0.001	0.73 (0.62–0.85)	<0.001
Left ventricular ejection fraction <30%	0.92 (0.83–1.02)	0.1	0.99 (0.8–1.2)	0.92
Chronic obstructive pulmonary disease	0.97 (0.88–1.06)	0.45	1.02 (0.83–1.23)	0.87
Female sex	0.53 (0.3–0.86)	0.01	0.91 (0.42–1.71)	0.78
Current smoking	1.08 (0.98–1.19)	0.10	0.92 (0.75–1.12)	0.41
Diabetes	1 (0.95–1.06)	0.92	1.02 (0.92–1.11)	0.75
Elective surgery	1.11 (1–1.24)	0.06	0.99 (0.79–1.26)	0.94
Left main coronary artery disease	0.87 (0.79–0.96)	0.005	0.83 (0.69–0.99)	0.05
Peripheral artery disease	1 (0.92–1.09)	0.91	1.55 (1.27–1.88)	<0.001
Heart failure	0.88 (0.81–0.96)	0.005	0.82 (0.68–0.98)	0.03
Chronic kidney disease	1.1 (0.99–1.210)	0.06	1.04 (0.86–1.25)	0.67
Chronic atrial fibrillation	0.86 (0.77–0.97)	0.01	1.06 (0.65–1.65)	0.8
Hypertension	1.36 (1.15–1.62)	<0.01	1.48 (1.08–2.09)	0.02
Self-reported race				
White	0.87 (0.75–1)	0.05	0.81 (0.65–1.02)	0.06
Other†	0.8 (0.69–0.94)	0.005	0.84 (0.6–1.16)	0.28
Prior myocardial infarction	1.06 (.97–1.15)	0.18	0.83 (0.69–0.99)	0.04
Prior percutaneous coronary intervention	0.87 (0.57–1.29)	0.5	0.95 (0.28–2.37)	0.92
Obesity	0.94 (0.86–1.02)	0.13	0.95 (0.81–1.11)	0.51

OR indicates odds ratio.
*Coefficient for age at surgery presented for every 10-year increase.
†Other indicates American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, or those self-reported as from multiple categories.

groups, respectively. Compared with patients receiving ONCAB, those operated with OPCAB were more likely to need follow-up PCI (sub-HR, 1.75 [1.35–2.26]; *P*<0.001).

Results in the Octogenarian Subgroup

Overall, 2040/47685 (4.2%) octogenarian patients were operated during the 15-year study period. OPCAB was performed in 329 patients (16%). Among octogenarians, 30-day mortality (OPCAB: 4% versus ONCAB: 3.2%; *P*=0.6), stroke (OPCAB: 1.5% versus ONCAB: 2.2%; *P*=0.5) and acute renal failure (OPCAB: 1.8% versus ONCAB: 2.5%; *P*=0.6) were comparable. Survival at 5 (OPCAB: 63% versus ONCAB: 59%) and 10 years (OPCAB: 24% versus ONCAB: 23%) was comparable (log-rank test *P*=0.4).

DISCUSSION

Salient Findings in Our Study

Nationally, we observed a significant decline in the use of OPCAB procedures among VA medical centers. A substantial proportion of centers that were using OPCAB more frequently in the initial part of the study changed their practice with OPCAB surgery being seldom used in the more recent time period. With a median follow-up of 6.6 years, OPCAB was associated with increased long-term mortality in our patient cohort. We also observed higher rates of MI and PCI in patients undergoing off-pump surgery.

Usage Trends of OPCAB

In patients operated at VA medical centers, 14% of isolated CABG procedures were performed off pump. However, the use of OPCAB was reduced to almost half of the initial rate over this 15-year period. A study using data from the Society of Thoracic Surgeons reported that 196 576/1 016 543 (19.3%) patients nationwide underwent off-pump surgery between January 2007 and December 2014.[17] As approximately 15.2% of veterans received OPCAB during that time period, it is fair to assume that our findings may be mirrored nationwide. The use of OPCAB in Japan (66%) and South Korea (61%) is, however, much higher.[18,19] The German Heart Surgery registry, which compiles data from 78 centers, reported that 20.6% of 33 999 isolated CABG procedures in 2018 were performed off pump. Contrary to the trends in the United States, OPCAB

Table 3. Intraoperative Details and Early Postoperative Outcome in Both Study Groups

	OPCAB N=6759	ONCAB N=40 926	*P* value
Number of distal anastomoses*	2.67 (0.88)	3.1 (0.84)	<0.001
Distal anastomoses with an arterial conduit†	0.99 (0.29)	1.03 (0.3)	<0.001
Cardiopulmonary bypass time		98 (70 126)	
Aortic cross-clamp time		65 (4089)	
Grafting details‡			<0.001
Complete revascularization	3833 (68.2)	23 321 (78.3)	
Incomplete revascularization	1799 (31.9)	6433 (21.7)	
30-d mortality	73 (1.1)	567 (1.4)	0.049
Postoperative stroke	65 (1.0)	501 (1.2)	0.074
Postoperative mediastinitis	39 (0.6)	284 (0.7)	0.315
Postoperative acute kidney failure	43 (0.6)	460 (1.1)	<0.001

ONCAB indicates on-pump coronary artery bypass grafting; and OPCAB, off-pump coronary artery bypass grafting.
*Based on information from 35 464/47 865 (74.1%) patients.
†Based on information from 35 386/47 865 (73.9%) patients.
‡Data presented as mean and SD.

use in Germany has actually gradually increased from 13.1% (5914/45 171) in 2009 to 20.6% (7019/33 999) in 2018.[20,21] In Brazil, 11% of 226 697 CABG procedures between 2008 and 2017 were operated off pump.[22] Therefore, a wide variation in the use of OPCAB exists globally. Over time, changes in the preference for OPCAB in specific patient cohorts were also observed. Most important, octogenarians were more likely to receive OPCAB. Literature demonstrates that octogenarians, women, and patients with severe left ventricular dysfunction or prior stroke may fare better if cardiopulmonary bypass is avoided.[8,23] Although a meta-analysis reports lower stroke rates after OPCAB among octogenarians, a recent study demonstrates that true benefit is derived only with an anaortic approach.[4,8] However, among studies included in this

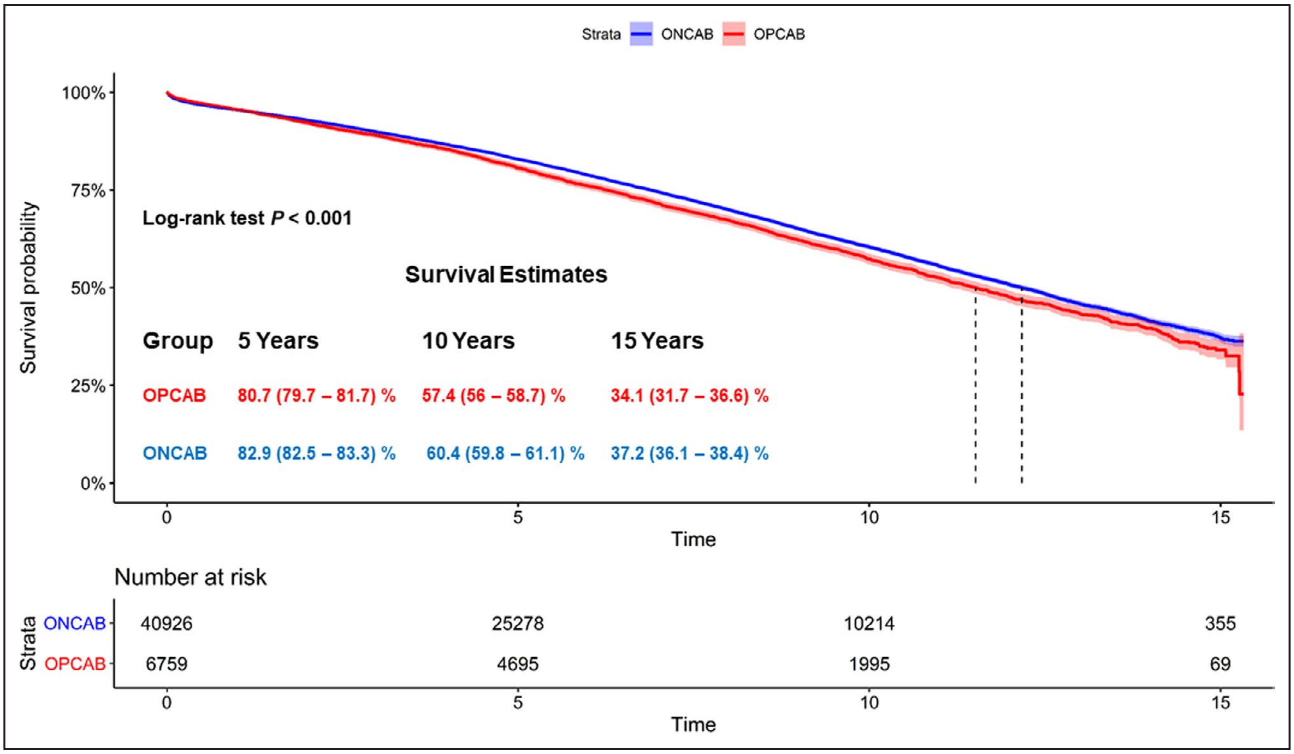

Figure 3. This graph presents the unadjusted survival estimates calculated by the Kaplan-Meier method for the patients undergoing on-pump and off-pump isolated coronary artery bypass grafting during the study period.
ONCAB indicates on-pump coronary artery bypass grafting; and OPCAB, off-pump coronary artery bypass grafting.

meta-analysis, the use of anaortic surgery varied between 6.5% and 78.6%, and the use of off-pump surgery ranged between 30% and 81%.[4] Therefore, few surgeons appear to adopt the appropriate technique of OPCAB surgery that could confer a lower stroke risk. As our cohort was primarily men, we were unable to evaluate the differential effect of OPCAB on women.

Increased Long-Term Adverse Event Rates

We observed increased long-term mortality and higher MI rates with off-pump surgery. As reported earlier, in our cohort, the number of grafts were lower, and rates of incomplete revascularization were higher in the patients receiving OPCAB. A contemporary meta-analysis of 51 randomized trials supports our observation.[24] This meta-analysis also reported increased reintervention rates in patients receiving OPCAB. Although our findings are similar to the ROOBY trial,[9] the CORONARY trial reported similar results in both groups. In this trial, patients were operated by a more selected group of surgeons skilled in OPCAB surgery.[25] These results may underline the importance of center and surgeon experience in performing these complicated procedures. However, we believe that our observational cohort mirrors current practice.

Clinical Implications

In the VA system, OPCAB procedures significantly declined between 2005 and 2018. In this study, OPCAB was associated with a higher incidence of incomplete revascularization which may have contributed to decreased long-term survival and increased rates of MI and follow-up PCIs.

Strengths and Limitations

As with any observational, retrospective, cohort database analysis, our study should be interpreted with certain limitations. When covariates were not directly reported, *ICD* and Current Procedural Terminology codes, which are subject to coding errors, were used. We did not have access to individual operative notes, therefore, could not report conversions from on- to off-pump approach. Therefore, we performed an as-treated analysis. Surgeon-specific identifiers were not released by the VA Central Office's administration staff. We, therefore, adjusted for center-based volume but not surgeon-specific technical experience. We were unable to identify cardiovascular specific mortality and hence, modeled all-cause mortality. However, in lieu of cardiovascular mortality, we have provided information regarding MI rates and follow-up PCI in both groups. Lastly, in spite of propensity weighting methods, residual confounding and unobserved factors may have influenced observed differences in outcome rather than the type of surgical strategy itself.

CONCLUSIONS

In VA medical centers, OPCAB use has reduced substantially. In our cohort, the risk-adjusted ONCAB long-term outcomes were better than those for OPCAB. MI and follow-up PCI rates were also higher in patients undergoing off-pump surgery.

ARTICLE INFORMATION

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Disclosures

Authors do not have any disclosures related to this article.

Supplemental Material

Data S1
Tables S1–S3
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Data S1. Statistical Analyses

Treatment of missing data

Missing data was observed in the following variables: complex coronary anatomy – 4.96%, prior myocardial infarction 4.65%, left ventricular dysfunction 3.17%, chronic kidney disease 0.07%, obesity 0.06% and COPD 0.002%. As the maximum missing information in any variable was < 5%, 5 imputed datasets were derived using the chained equations approach. Propensity scores and inverse probability weights were obtained for each imputed dataset. Weighted Cox model were fit for each dataset and the 5 coefficients and standard errors were pooled together according to Rubin's rule.

Pre- and post-weighting balance

Improvement in covariate balance was assessed by comparing the standardized differences pre- and post-weighting. For each covariate included in the model, after weighting, an absolute standardized difference < 0.1 was considered adequate balance (S-Figure 1).

OPCAB as a time-varying coefficient

From the Kaplan and Meier curve of estimated survival, the lines for ONCAB and OPCAB appear to diverge beyond 5 years of follow-up. Hence, the benefit of using OPCAB as a time-varying covariate in the Cox proportional hazard model (CPH) was evaluated. The OPCAB variable was tested in a CPH model using the Grambsch-Therneau test and was found not to satisfy criteria for being a time varying covariate (p = 0.2) (S-Figure 2). Therefore, a weighted CPH model without a time-varying coefficient was fit to model all-cause mortality.

Table S1.

This table provides the list of ICD or CPT codes used for identifying procedures and some clinical conditions.

Condition/Procedure	ICD Code 9th version	ICD Code 10th version	CPT code
Coronary artery bypass grafting			'33521','33522','33523','33517','33518','33519', '33510','33511','33512','33513','33514','33515','33516','33533','33534','33535','33536'
Valve repair/ replacement			'33364','33427','33426','33405','33420','33411','33425','33426','33430','33460','33463','33464','33465', '33858','33859','33254','33257','33258','33259'
Acute myocardial infarction	410.01, 410.21, 410.31, 410.41, 410.51, 410.61, 410.71, 410.81, 410.91, 410.1, 410.2, 410.3, 410.4, 410.5, 410.6, 410.7, 410.8, 410.9	I21.9	
Chronic liver disease	"456.0","456.1","456.2","572.2","572.3","572.4", "572.5","572.6","572.7","572.8"	"I85.0","I85.9","I86.4",'I98.2', "K70.4","K71.1","K72.1","K72.9","K76.5","K76.6","K76.7"	
ST Elevation myocardial infarction	'410.00',"410.10","410.20","410.30", "410.40","410.40","410.50","410.60", "410.70","410.80","410.90","I21.3"	I21.3	
Congestive heart failure	'428.0'	I50.2	
Hyperlipidemia	'272.4'	E78.5	
Chronic Atrial fibrillation	I48.20	427.31	
Prior percutaneous intervention	V45.82	Z98.61	

Table S2.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any pre-specified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	9
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8 – 9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10 – 11
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental section
		(c) Summarise follow-up time (eg, average and total amount)	13
Outcome data	15*	Report numbers of outcome events or summary measures over time	13

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	None

*Give information separately for exposed and unexposed group.

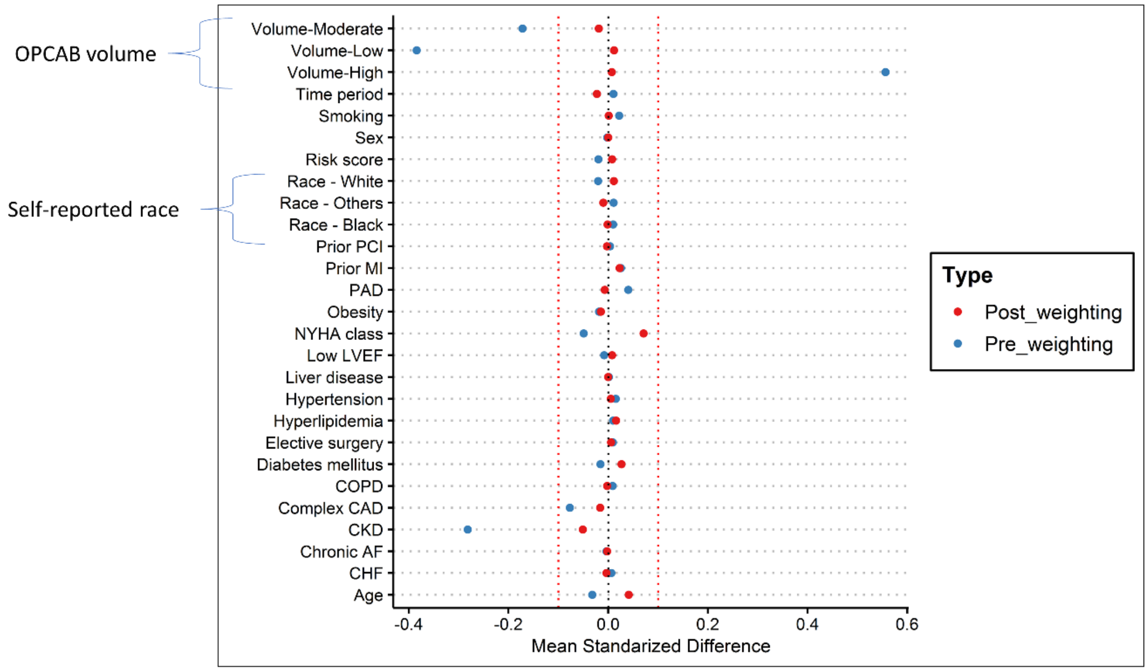
Table S3.

This table presents a comparison of the crude post-operative events in both groups for each time period included in the study.

Time Period	Endpoint	OPCAB	ONCAB	p-value
2005 – 2009	Patients operated	N = 3,334	N = 16,403	
	30-day mortality	32 (1.0)	269 (1.6)	0.004
	Stroke	31 (0.9)	222 (1.4)	0.058
	Acute renal failure	23 (0.7)	219 (1.3)	0.003
2010 - 2014	Patients operated	N = 2,443	N = 13,538	
	30-day mortality	32 (1.3)	167 (1.2)	0.831
	Stroke	25 (1.0)	152 (1.1)	0.744
	Acute renal failure	12 (0.5)	111 (0.8)	0.113
2015 – September 2019	Patients operated	N = 982	N = 10,985	
	30-day mortality	9 (0.9)	131 (1.2)	0.538
	Stroke	9 (0.9)	127 (1.2)	0.602
	Acute renal failure	8 (0.8)	130 (1.2)	0.378

Figure S1.

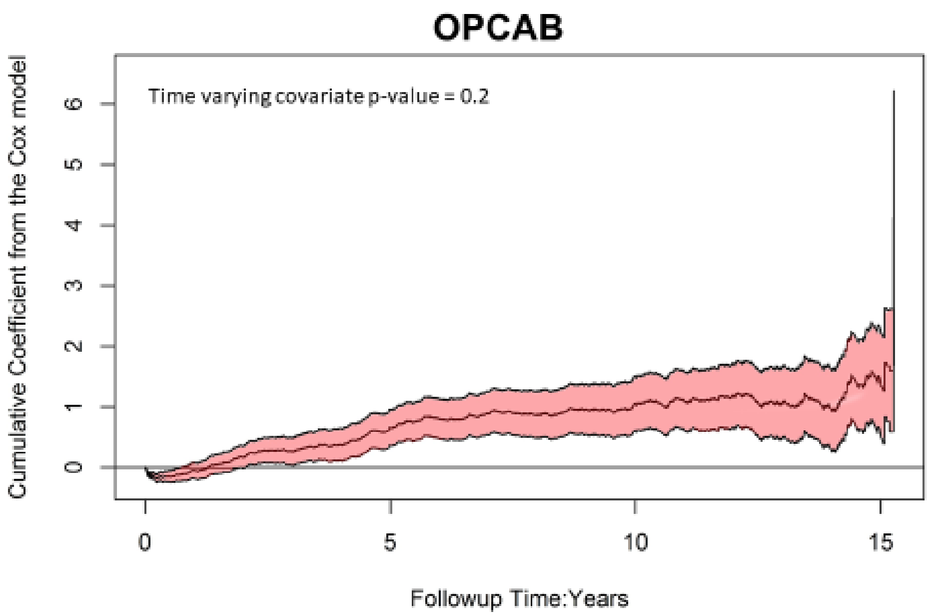
This plot presents the absolute standardized mean difference (SMD) for all levels of the covariates included in the logistic regression model fit to derive the propensity score. As demonstrated, in the figure, the absolute SMD pre-weighing (blue dots) is improved post-weight (red dots). The post-weighted SMD for each covariate is < 0.1 (dotted red line).



Abbreviations: AF – atrial fibrillation, CAD – coronary artery disease, CHF – Congestive heart failure, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, LVEF – left ventricular ejection fraction, MI – myocardial infarction, PAD – peripheral arterial disease, PCI – percutaneous intervention.

Figure S2.

This graph demonstrates the time varying effect of OPCAB as a covariate in the Cox proportional hazards model. As reported, OPCAB failed to demonstrate a statistical significant time-varying effect in the model (Grambsch-Therneau p-value = 0.2).



Abbreviations: OPCAB – off-pump coronary artery bypass grafting