Off-pump versus on-pump coronary artery bypass surgery in patients with actively treated diabetes and multivessel coronary disease

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ABSTRACT

Objectives: We conducted a single-center analysis on short-term outcomes and long-term survival in actively treated diabetic patients undergoing off-pump coronary artery bypass versus on-pump coronary artery bypass surgery.

Methods: The final population consisted of 2450 patients with actively treated diabetes (mean age, 66 ± 9 years; female/male 545/1905, 22%). Of those, 1493 subjects were orally treated and 1011 subjects were taking insulin. Off-pump coronary artery bypass and on-pump coronary artery bypass were performed in 1253 and 1197 patients, respectively. Propensity score matching was used to compare the 2 matched groups.

Results: When compared with on-pump coronary artery bypass, off-pump coronary artery bypass was associated with a significant risk reduction for postoperative cerebrovascular accident (odds ratio, 0.49; 95% confidence interval [CI], 0.25-0.99; $P = .04$), need for postoperative intra-aortic balloon pump (odds ratio, 0.48; 95% CI, 0.30-0.77; $P = .002$), and reexploration for bleeding (odds ratio, 0.55; 95% CI, 0.33-0.94; $P = .02$). Off-pump coronary artery bypass did not significantly affect early (hazard ratio [HR], 1.32; 95% CI, 0.73-2.40; $P = .36$) and late (HR, 1.08; 95% CI, 0.92-1.28; $P = .32$) mortality. However, off-pump coronary artery bypass with incomplete revascularization was associated with reduced survival when compared with off-pump coronary artery bypass with complete revascularization (HR, 1.82; 95% CI, 1.34-2.46; $P = .0002$) and on-pump coronary artery bypass with complete revascularization (HR, 1.83; 95% CI, 1.36-2.47; $P < .0001$).

Conclusions: Off-pump coronary artery bypass is a safe and feasible option for diabetic patients with multivessel disease, reduces the incidence of early complications including postoperative cerebrovascular events, and provides excellent long-term survival similar to on-pump coronary artery bypass surgery in case of complete revascularization. (J Thorac Cardiovasc Surg 2016;152:1321-30)

Effect of OPCAB grafting over ONCAB grafting on outcomes of interest.

Central Message

OPCAB surgery is a safe and feasible option for diabetic patients with multivessel disease, reduces the incidence of early complications, and provides long-term survival benefit similar to ONCAB surgery.

Perspective

OPCAB surgery remains a valid option for diabetic patients with multivessel disease because it reduces the incidence of early complications and provides long-term survival benefit similar to ONCAB. Its use should not be discouraged in such a high-risk subgroup.

See Editorial Commentary page 1331.

Diabetes mellitus (DM) is a major public health and economic problem with a dramatic increase in prevalence and incidence.¹ Coronary heart disease is highly prevalent

and the major cause of morbidity and mortality among diabetic patients.² Patients with DM account for approximately one quarter of all patients who undergo coronary revascularization procedures each year.³ Coronary artery bypass grafting (CABG) when compared with percutaneous coronary intervention has been shown to be associated with better outcomes in patients with diabetes,⁴ and current clinical guidelines recommend CABG as the preferred

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CI	= confidence interval
CVA	= cerebrovascular accident
DM	= diabetes mellitus
euroSCORE	= European System for Cardiac Operative Risk Evaluation
HR	= hazard ratio
IR	= incomplete revascularization
IABP	= intra-aortic balloon pump
ONCAB	= on-pump coronary artery bypass
OPCAB	= off-pump coronary artery bypass
VIF	= variance inflation factor

revascularization strategy in diabetic patients with complex coronary artery disease.⁵ However, DM has a significant negative impact on the clinical outcome of coronary surgery in the long term and short term.⁶ The debate on the effectiveness or otherwise of off-pump coronary artery bypass (OPCAB) versus on-pump coronary artery bypass (ONCAB) surgery continues.⁷⁻⁹ In particular, the role of OPCAB in the management of diabetic patients remains controversial because comparative data are scarce and inconclusive.¹⁰⁻¹³ A recent subanalysis of the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial¹⁰ suggested that patients with diabetes had a greater risk of major cardiovascular long-term events after OPCAB than after ONCAB. However, this study presented several limitations, including a small sample size, and definitive conclusions could not be drawn.¹⁴ In this study, we used a large consecutive cohort with DM undergoing operation in a 20-year period at a single institution to perform a propensity score matching analysis of ONCAB versus OPCAB on short-term outcomes and long-term survival.

MATERIALS AND METHODS

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analyzed prospectively collected data from the National Institute for Cardiovascular Outcomes Research National Adult Cardiac Surgery Audit registry for all isolated first-time CABG procedures performed at the Bristol Heart Institute (Bristol, UK) from April 1996 to April 2015. Reproducible cleaning algorithms were applied to the database, which are regularly updated as required. Briefly, duplicate records and nonadult cardiac surgery entries were removed, transcriptional discrepancies were harmonized, and clinical conflicts and extreme values were corrected or removed. The data are returned regularly to the local units for validation.

Further details and definition of variables are available at <http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets>. From 15,119 isolated first-time CABG cases performed during the study period, we selected subjects with multivessel coronary artery disease and actively treated DM at the time of surgery. Patients with no diabetes ($n = 12,439$), single-vessel disease ($n = 121$), and no data regarding surgical strategy adopted (OPCAB vs ONCAB, $n = 109$) were excluded. The final population consisted of 2450

patients (22%; mean age, 66 ± 9 years; female/male 545/1905) with actively treated diabetes. Of those, 1493 patients were orally treated and 1011 patients were receiving insulin. OPCAB (Video 1) and ONCAB were performed in 1253 and 1197 patients, respectively (Figure 1) according to the surgeon's preference and not according to specific clinical indications. Normothermic blood cardioplegia was the standard strategy for ONCAB cases during the study period. Blood glucose level was strictly maintained at less than 11.1 mmol/L perioperatively according to unit protocol, using insulin infusion.

Pretreatment Variables and Study End Points

The effect of OPCAB over ONCAB was adjusted for the following variables: age, gender, body mass index, previous myocardial infarction within 30 days, previous percutaneous coronary intervention, diabetes mellitus (DM) on insulin, chronic obstructive pulmonary disease, Canadian Cardiovascular Society class III or IV, New York Heart Association class III or IV, current smoking, serum creatinine 200 mmol/L or greater, previous cerebrovascular accident (CVA), peripheral vascular disease, preoperative atrial fibrillation, left main disease, 3-vessel disease, left ventricle ejection fraction 49% or less and 30% or less, preoperative use of intra-aortic balloon pump (IABP), nonelective admission, emergency/salvage operation, cardiogenic shock, and year of operation. Overall risk profile was evaluated by using additive and logistic European System for Cardiac Operative Risk Evaluation (euroSCORE). Incomplete revascularization (IR) was defined as at least 1 diseased primary arterial territory not grafted.

Short-term outcomes investigated were postoperative complications, including CVA, need for IABP defined as unplanned insertion of IABP intraoperatively or postoperatively because of hemodynamic instability, reexploration for bleeding, renal replacement therapy, sternal wound reconstruction as single and combined end points, and mortality within 30 days. Long-term outcome was all-cause mortality. All-cause mortality is the most robust and unbiased index because no adjudication is required; thus, inaccurate or biased documentation or clinical assessments are avoided.¹⁵ Information about death was obtained from the institutional database and the National General Register Office for all patients. Data regarding postoperative complications and survival were available for all patients in the study.

Statistical Analysis

For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables. Multiple imputation using bootstrapping-based expectation-maximization algorithm and including all pretreatment variables (Amelia R package, <http://www.jstatsoft.org/v45/i07/>) was used to address missing data (Table E1). To control for measured potential confounders in the data set, a propensity score was generated for each patient from a multivariable logistic regression model based on pretreatment covariates as independent variables with treatment type (OPCAB vs ONCAB) as a binary dependent variable.¹⁶ The resulting propensity score represented the probability of a patient to undergo OPCAB (area under the curve 0.63) (Figure E1). Pairs of patients receiving OPCAB and ONCAB were derived using greedy 1:1 matching with a caliper of width of 0.2 standard deviation of the logit of the propensity score (nonrandom R package, <http://CRAN.R-project.org/package=nonrandom>). The quality of the match was assessed by comparing selected pretreatment variables in propensity score-matched patients using the standardized mean difference, by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance.¹⁶ Analytic methods for the estimation of the treatment effect in the matched sample included McNemar's to compare proportions.¹⁶ Time-segmented Cox regression models (within 30 days and >30 days)¹⁷ that stratified on the matched pairs¹⁸ were used to investigate the effect of treatment (ONCAB vs OPCAB) on early and late mortality. This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets (survival R package, <http://CRAN.R-project.org/package=survival>). Last, a multivariate

VIDEO 1. OPCAB grafting technique at Bristol Heart Institute. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(16\)30668-7/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30668-7/addons).

adjustment for all baseline characteristics and intraoperative variables, such as the use of bilateral internal thoracic arteries, radial artery (RA), and the incidence of IR, was performed in the matched sample to correct the effect of OPCAB for residual imbalance (double robust) and to estimate the effect size of other covariates on all outcomes investigated. Pearson correlation coefficient and variance inflation factors (VIFs) from the covariance matrix of parameter estimates were used to assess collinearity in multivariate models (usdm R package, <http://CRAN.R-project.org/package=usdm>). Variables with VIF greater than 4 were excluded from multivariate analyses. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Distribution of pretreatment variables in the OPCAB and ONCAB groups is summarized in Table 1. Patients

undergoing ONCAB were likely to have Canadian Cardiovascular Society III/IV, 3-vessel disease, left ventricle ejection fraction of 30% or less, and cardiogenic shock. The era of surgery also was different between the 2 groups. Additive euroSCORE ($P = .02$), but not logistic euroSCORE ($P = .15$), was higher in the ONCAB group. Propensity score matching created a total of 995 pairs perfectly matched for all pretreatment variables (standardized mean difference <0.10) including era of surgery. In the matched population, additive euroSCORE ($P = .08$) and logistic euroSCORE ($P = .12$) were comparable between the 2 groups.

Intraoperative Data

Table 2 summarizes intraoperative data. When compared with ONCAB, OPCAB was associated with a lower number of grafts per patient (2.7 ± 0.7 vs 3.0 ± 0.7 , $P < .001$) (Figure 2) in the right and circumflex arteries but not the left anterior descending artery territory. The rate of bilateral internal thoracic artery was low in both groups ($P = .1$). The use of the radial artery was higher in the OPCAB group, and the saphenous vein graft was used more frequently in the ONCAB group. OPCAB conversion rate to ONCAB was 7 in 1253 (0.6%).

Effect of Off-Pump Coronary Artery Bypass on Short-Term Outcomes

Short-term outcomes are summarized in Table 3. OPCAB was associated with a higher rate of IR. When compared with ONCAB, OPCAB was significantly associated with 50% relative risk reduction for postoperative CVA ($P = .04$), need for postoperative IABP ($P = .002$), and re-exploration for bleeding ($P = .02$). Overall 30-day mortality

FIGURE 1. Number of OPCAB and ONCAB operations during the study period. ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass.

TABLE 1. Pretreatment variables distribution in the unmatched and matched off-pump coronary artery bypass and on-pump coronary artery bypass groups

	Unmatched OPCAB		Unmatched OPCAB		SMD	PS matched OPCAB		PS matched OPCAB		SMD
	n	%	n	%		n	%	n	%	
Total sample	1253	100.0	1197	100.0		995	100.0	995	100.0	
Age, y										
<60.0	307	24.5	282	23.6	4.8	242	24.3	233	23.4	2.4
60-69	449	35.8	490	40.9		360	36.2	393	39.5	
70-79	440	35.1	401	33.5		346	34.8	345	34.7	
≥8	57	4.5	24	2.0		47	4.7	24	2.4	
Female										
No	976	77.9	929	77.6	0.7	765	76.9	762	76.6	0.7
Yes	277	22.1	268	22.4		230	23.1	233	23.4	
BMI										
<30	723	57.7	726	60.7	7.5	575	57.8	575	57.8	1.1
≥30	530	42.3	471	39.3		420	42.2	420	42.2	
CCS										
No	654	52.2	526	43.9	16.5	514	51.7	491	49.3	4.6
Yes	599	47.8	671	56.1		481	48.3	504	50.7	
NYHA										
No	791	63.1	704	58.8	8.8	624	62.7	611	61.4	2.7
Yes	462	36.9	493	41.2		371	37.3	384	38.6	
MI within 30 d										
No	985	78.6	932	77.9	1.8	796	80.0	768	77.2	6.8
Yes	268	21.4	265	22.1		199	20.0	227	22.8	
PCI										
No	1157	92.3	1125	94.0	6.5	917	92.2	925	93.0	3.0
Yes	96	7.7	72	6.0		78	7.8	70	7.0	
DM on insulin										
No	733	58.5	706	59.0	0.9	583	58.6	584	58.7	0.2
Yes	520	41.5	491	41.0		412	41.4	411	41.3	
Current smoking										
No	1117	89.1	1060	88.6	1.8	889	89.3	888	89.2	0.3
Yes	136	10.9	137	11.4		106	10.7	107	10.8	
sCr >200 mmol/L										
No	1204	96.1	1147	95.8	1.3	956	96.1	958	96.3	1.0
Yes	49	3.9	50	4.2		39	3.9	37	3.7	
COPD										
No	1140	91.0	1086	90.7	0.8	903	90.8	899	90.4	1.3
Yes	113	9.0	111	9.3		92	9.2	96	9.6	
CVA										
No	1179	94.1	1131	94.5	1.6	931	93.6	940	94.5	3.8
Yes	74	5.9	66	5.5		64	6.4	55	5.5	
PVD										
No	1075	85.8	991	82.8	8.2	853	85.7	848	85.2	1.4
Yes	178	14.2	206	17.2		142	14.3	147	14.8	
AF										
No	1198	95.6	1142	95.4	0.9	949	95.4	951	95.6	0.9
Yes	55	4.4	55	4.6		46	4.6	44	4.4	
3-vessel disease										
No	346	27.6	230	19.2	19.9	298	29.9	224	22.5	9.2
Yes	907	72.4	967	80.8		697	70.1	771	77.5	
LMD										
No	964	76.9	913	76.3	1.5	770	77.4	753	75.7	4.0
Yes	289	23.1	284	23.7		225	22.6	242	24.3	

(Continued)

TABLE 1. Continued

	Unmatched OPCAB		Unmatched OPCAB		SMD	PS matched OPCAB		PS matched OPCAB		SMD
	n	%	n	%		n	%	n	%	
LVEF <50%										
No	839	67.0	786	65.7	2.7	660	66.3	663	66.6	0.6
Yes	414	33.0	411	34.3		335	33.7	332	33.4	
LVEF 30%-49%										
No	923	73.7	902	75.4	2.7	729	73.3	737	74.1	
Yes	330	26.3	295	24.6		266	26.7	258	25.9	
LVEF <30%										
No	1169	93.3	1081	90.3	10.9	926	93.1	921	92.6	1.9
Yes	84	6.7	116	9.7		69	6.9	74	7.4	
Cardiogenic shock										
No	1247	99.5	1178	98.4	10.9	990	99.5	990	99.5	0.0
Yes	6	0.5	19	1.6		5	0.5	5	0.5	
Preoperative IABP										
No	1237	98.7	1167	97.5	9.0	981	98.6	981	98.6	0.3
Yes	16	1.3	30	2.5		14	1.4	14	1.4	
Nonelective										
No	644	51.4	560	46.8	9.2	520	52.3	476	47.8	8.8
Yes	609	48.6	637	53.2		475	47.7	519	52.2	
Emergency/salvage										
No	1239	98.9	1171	97.8	8.3	982	98.7	980	98.5	1.7
Yes	14	1.1	26	2.2		13	1.3	15	1.5	
Era of surgery										
1996-2004	398	31.8	306	25.6	34.6	254	25.5	256	25.7	9.8
2005-2007	267	21.3	349	29.2		273	27.4	276	27.7	
2008-2010	324	25.9	283	23.6		240	24.1	269	27.0	
2011-2015	264	21.1	259	21.6		228	22.9	194	19.5	
Additive euroSCORE	4.2 ± 2.6		4.4 ± 2.8			4.2 ± 2.7		4.2 ± 2.5		
Logistic euroSCORE	5% ± 5%		5% ± 7%			5% ± 5%		4% ± 5%		

OPCAB, Off-pump coronary artery bypass; SMD, standardized mean difference; PS, propensity score; BMI, body mass index; CCS, Canadian Cardiovascular Class; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; sCr, serum creatinine; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PVD, peripheral vascular disease; AF, atrial fibrillation; LMD, left main disease; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; euroSCORE, European System for Cardiac Operative Risk Evaluation.

was 2.4% (58 patients) with no significant difference between the 2 groups. This trend toward a benefit from OPCAB on short-term outcomes was confirmed when the results were analyzed separately for patients receiving oral or insulin treatment (Tables E2 and E3). There were no deaths in the 7 patients undergoing OPCAB who required conversion to ONCAB.

Effect of Off-Pump Coronary Artery Bypass on Long-Term Mortality

At a mean follow-up of 6.5 ± 4.5 years, there were 357 and 408 deaths in the unmatched population and 284 and 299 deaths in the matched sample in the OPCAB and ONCAB groups, respectively (Figure 2). In the matched sample, survival probability at 5 and 10 years was $82.6\% \pm 1.2\%$ and $62.6\% \pm 2.0\%$ versus $84.3\% \pm 1.3\%$ and $64.0\% \pm 1.9\%$ in the OPCAB and ONCAB groups, respectively. The 2 strategies were perfectly comparable in terms of late mortality in the overall matched sample (hazard ratio [HR], 1.08; 95% confidence

interval [CI], 0.92-1.28; $P = .32$) and among patients orally treated (HR, 1.06; 95% CI, 0.85-1.33; $P = .6$) and receiving insulin (HR, 1.12; 95% CI, 0.88-1.43) ($P = .35$) (Figure 3).

OPCAB with complete revascularization showed comparable survival when compared with ONCAB with complete revascularization ($n = 921$) (HR, 1.00; 95% CI, 0.84-1.20; $P = .96$). However, patients undergoing OPCAB with IR ($n = 139$) showed reduced survival when compared with OPCAB with complete revascularization ($n = 856$) (HR, 1.82; 95% CI, 1.34-2.46; $P = .0002$) and ONCAB with complete revascularization (HR, 1.83; 95% CI, 1.36-2.47; $P < .0001$) (Figure 4). We could not draw conclusions on the impact on IR among ONCAB cases because of the small sample size ($n = 74$).

Effect of Off-Pump Coronary Artery Bypass Versus On-Pump Coronary Artery Bypass After Full Adjustment (Double Robust)

After double robust adjustment, OPCAB was confirmed to be significantly associated with a reduced incidence of

TABLE 2. Intraoperative data

	OPCAB		ONCAB		P value
	n	%	n	%	
Overall	1253	100.0	1197	100.0	
No. of grafts					
1	36	2.9	6	0.5	<.001
2	447	35.7	253	21.1	
3	650	51.9	703	58.7	
4	119	9.5	222	18.5	
5	1	0.1	12	1.0	
6	0	0.0	1	0.1	
Mean No. of grafts/patient	2.7 ± 0.7		3.0 ± 0.7		
Graft target					
LAD					
No	35	2.8	33	2.8	1
Yes	1218	97.2	1164	97.2	
DIA					
No	1020	81.4	931	77.8	.03
Yes	233	18.6	266	22.2	
CX					
No	313	25.0	142	11.9	<.001
Yes	940	75.0	1055	88.1	
RCA					
No	398	31.8	305	25.5	<.001
Yes	855	68.2	892	74.5	
RITA					
No	1224	97.7	1160	96.9	.3
Yes	29	2.3	37	3.1	
LITA					
No	76	6.1	113	9.4	.002
Yes	1177	93.9	1084	90.6	
BITA					
No	1230	98.2	1163	97.2	.1
Yes	23	1.8	34	2.8	
RA					
No	986	78.7	1083	90.5	<.001
Yes	267	21.3	114	9.5	
SV					
No	137	10.9	58	4.8	<.001
Yes	1116	89.1	1139	95.2	
Sequential grafts					
No	1154	92.1	1150	96.1	<.001
Yes	99	7.9	47	3.9	

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; LAD, left anterior descending artery; DIA, diagonal branch; CX, circumflex artery; RCA, right coronary artery; RITA, right interior thoracic artery; LITA, left interior thoracic artery; BITA, bilateral internal thoracic artery; RA, radial artery; SV, saphenous vein.

postoperative stroke, need for postoperative IABP, sternal wound reconstruction, and reexploration for bleeding, but not dialysis. OPACB was significantly associated with a 2-fold increased risk of IR. OPCAB was not associated with increased early (within 30 days) and late mortality (Table E4).

Impact of Other Predictors of Outcomes

The impact of other predictors on outcomes of interest is reported in Tables E5-E13. In particular, diabetic patients

taking insulin were significantly associated with an increased risk of postoperative dialysis and incidence of any complication. Diabetic patients taking insulin did not significantly affect early mortality, but they were associated with an 18% relative risk increase in late mortality. IR did not significantly influence operative outcomes and early mortality, but it was associated with an approximately 50% relative risk increase in late mortality. All variables investigated showed VIF less than 4 (Table E14).

FIGURE 2. Survival curves in the unmatched and matched OPCAB and ONCAB groups. *HR*, Hazard ratio; *ONCAB*, on-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *PS*, propensity score.

TABLE 3. Short-term outcomes in the unmatched and matched off-pump coronary artery bypass and on-pump coronary artery bypass groups with relative effect size in the propensity score–matched population

	Unmatched OPCAB		Unmatched ONCAB		PS matched OPCAB		PS matched ONCAB		PS matched/ adjusted estimate (95% CI)	Adjusted <i>P</i> value
	n	%	n	%	n	%	n	%		
Sample size	1253	100.0	1197	100.0	995	100.0	995	100.0		
CVA										
No	1235	98.6	1167	97.5	983	98.8	971	97.6	0.49 (0.25-0.99)	.04
Yes	18	1.4	30	2.5	12	1.2	24	2.4		
RRT										
No	1193	95.2	1144	95.6	946	95.1	952	95.7	1.15 (0.75-1.74)	.52
Yes	60	4.8	53	4.4	49	4.9	43	4.3		
IABP										
No	1221	97.4	1136	94.9	969	97.4	942	94.7	0.48 (0.30-0.77)	.002
Yes	32	2.6	61	5.1	26	2.6	53	5.3		
SWR										
No	1240	99.0	1180	98.6	985	99.0	979	98.4	0.62 (0.28-1.38)	.24
Yes	13	1.0	17	1.4	10	1.0	16	1.6		
Reexploration										
No	1224	97.7	1155	96.5	973	97.8	956	96.1	0.55 (0.33-0.94)	.02
Yes	29	2.3	42	3.5	22	2.2	39	3.9		
Any complication										
No	1118	89.2	1028	85.9	890	89.4	849	85.3	0.69 (0.52-0.90)	.005
Yes	135	10.8	169	14.1	105	10.6	146	14.7		
30-d mortality										
No	1221	97.4	1171	97.8	970	97.5	976	98.1	1.32 (0.73-2.40)	.36
Yes	32	2.6	26	2.2	25	2.5	19	1.9		
IR										
No	1062	84.8	1102	92.1	865	86.9	921	92.6	2 (1.50-2.7)	<.001
Yes	191	15.2	95	7.9	139	14.0	74	7.4		

OPCAB, Off-pump coronary artery bypass; *ONCAB*, on-pump coronary artery bypass; *PS*, propensity score; *CI*, confidence interval; *CVA*, cerebrovascular event; *RRT*, renal replacement therapy; *IABP*, intra-aortic balloon pump; *SWR*, sternal wound reconstruction; *IR*, incomplete revascularization.

FIGURE 3. Survival curves in the matched OPCAB and ONCAB groups in patients receiving oral treatment and in patients receiving insulin. *HR*, Hazard ratio; *ONCAB*, on-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *PS*, propensity score.

DISCUSSION

To the best of our knowledge, this is the largest series with the longest follow-up reported on the impact of OPCAB in diabetic patients with multivessel coronary disease. OPCAB was associated with a trend toward a lower incidence of postoperative complications, including cardiovascular accidents, and comparable early and late survivals when compared with ONCAB. The present analysis confirmed that OPCAB was associated with an approximately 7% absolute risk increase in IR. Furthermore, OPCAB with IR showed a lower survival when compared with OPCAB and ONCAB with complete revascularization. Insulin treatment was confirmed to be an independent risk factor for postoperative complications and poorer long-term survival.

Despite several randomized controlled trials, there is still controversy with respect to the advantages and disadvantages of OPCAB versus OPCAB surgery.^{7-9,19,20} However, some evidence has suggested a potential off-pump benefit for patient subgroups with a high operative risk.²¹⁻²³ In the case of diabetic patients with multivessel disease, limited data are available with conflicting reports.¹⁰⁻¹³ A recent observational subanalysis of the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial¹⁰ concluded that patients with diabetes had a greater risk of major long-term cardiovascular events after OPCAB than after ONCAB. However, this study has been criticized¹⁴ because of the small number of patients compared (153 propensity-matched pairs), which is inadequate to draw final conclusions. Moreover, there was missing information regarding the completeness of revascularization. A subanalysis of the Randomized On/Off Bypass trial¹¹

on diabetic patients randomized to OPCAB ($n = 402$) or ONCAB ($n = 433$) concluded that 1-year graft patency rate was lower after OPCAB with no difference in the 1-year primary composite outcome. However, it is largely recognized that in the Randomized On/Off Bypass trial, surgeons were inexperienced (on average performing 8 OPCAB operations per year and with a high conversion rate of $\sim 12\%$).¹⁴ The importance of surgeon experience in OPCAB is clearly demonstrated in trials that showed no difference in hard clinical end points at 1 year or longer follow-up.^{7,8,24} Moreover, the 1% lower graft patency rate reported in the OPCAB group is clearly marginal (83.1% vs 88.4%), and it is likely not to have any clinical impact. On the other hand, Emmert and colleagues¹² compared short-term outcomes in 540 diabetic patients undergoing OPCAB and 475 diabetic patients undergoing ONCAB and showed a clear trend to reduced major complications, such as stroke, rethoracotomy for bleeding, and postoperative IABP requirement, confirming the beneficial effect of OPCAB on short-term outcomes in this subset of patients. Renner and colleagues¹³ compared 355 OPCAB and 502 ONCAB procedures and concluded that OPCAB was associated with a significantly lower 30-day mortality risk and a lower 1-year mortality risk compared with ONCAB.

In the present analysis, IR occurred in 15.2% and 7.9% of unmatched OPCAB and ONCAB groups, respectively. Although patients undergoing OPCAB with complete revascularization showed survival similar to those receiving ONCAB, OPCAB with IR was found to be significantly associated with a lower survival when compared with OPCAB and ONCAB with complete revascularization. It has

FIGURE 4. Survival curves in the matched OPCAB and ONCAB groups in patients with complete revascularization and IR. *OPCAB*, Off-pump coronary artery bypass; *ONCAB*, on-pump coronary artery bypass; *ONCR*, on pump-complete revascularization; *ONIR*, on-pump incomplete revascularization; *OPCR*, off-pump complete revascularization; *OPIR*, off-pump incomplete revascularization; *HR*, hazard ratio.

been suggested that patients who undergo IR have multiple comorbidities and unfavorable anatomy that could bias the data in favor of complete revascularization.²⁵ However, compelling evidence supports the hypothesis that diabetic patients are more likely to benefit from a more complete revascularization.²⁶ Raza and colleagues²⁷ recently reported a long-term survival analysis on 11,922 diabetic patients and demonstrated that complete revascularization was associated with 10% lower late mortality. Moreover, they found that OPCAB was associated with a 10% lower late mortality than ONCAB, but the difference was not statistically significant ($P = .2$). Nakano and colleagues²⁸ reported on 604 consecutive patients who underwent OPCAB during a 6-year period with 216 patients receiving IR (13%). They found that all the event-free survivals for all-cause mortality ($P < .001$), cardiac death ($P = .020$), and major adverse cardiac and cerebrovascular events ($P < .001$) were lower in the IR group. Of note, the IR rate observed in the present OPCAB series was significantly lower than that reported by others. Omer and colleagues²⁹ recently reported a 29% rate of IR in 6367 OPCAB cases compared with 11.0% in 34,772 ONCAB cases. Kleisli and colleagues³⁰ reported a 22% rate of IR in 207 OPCAB cases and 6.3% in 827 ONCAB cases. Some have

suggested that surgeon experience plays a role and emphasized the importance of surgeon volume in establishing favorable outcomes for OPCAB.²⁴ The relatively low rate of IR in the present OPCAB series is likely to be related to the high OPCAB volume in our center and supports the hypothesis that when OPCAB is routinely performed, complete revascularization can be achieved in the majority of cases. The trend toward shorter survival with OPCAB observed in some studies may be related to IR^{27,28} more likely to occur in cases with surgeons who are less experienced with this technique. Finally, although the use of additional arterial grafts has been shown to minimize the risk related to IR,³¹ the rate of bilateral internal thoracic arteries usage was low (~2%) in the present series. This may represent the concern of increased sternal wound complication in this high-risk group of patients.²⁷

Study Limitations

The main limitation of our study is that no follow-up data were available to compare the groups with respect to the cause of death (cardiac vs noncardiac), recurrence of angina, need for repeated revascularization, and graft patency. Therefore, we can only speculate about the mechanism beyond the equipoise between OPCAB and ONCAB

on long-term survival. Finally, although the data were collected prospectively, the nonspecific design for the diabetic population limits the present analysis. Propensity technique can adjust only for measurable and included variables but cannot exclude a selection bias based on nonmeasurable “eyeball.”

CONCLUSIONS

OPCAB is a safe and feasible option for diabetic patients with multivessel coronary disease. OPCAB reduces the incidence of postoperative complications and provides long-term survival comparable to ONCAB. Complete revascularization should still be the main goal while performing OPCAB surgery in diabetic patients.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: off-pump coronary artery bypass grafting, diabetes mellitus, survival

TABLE E1. Percentage of missing data

Preoperative IABP	19.776	COPD	0.635
sCr	19.518	CCS	0.622
BMI	10.424	AF	0.622
LMD	7.494	DM	0.615
MI 30 d	7.322	PCI	0.463
3-vessel disease	1.984	Shock	0.417
CVA	1.508	Nonelective	0.093
LVEF	1.27	Emergency/salvage	0.093
Current smoking	0.701	Age	0
NYHA	0.688	Female	0
PVD	0.661	Era of surgery	0

IABP, Intra-aortic balloon pump; *COPD*, chronic obstructive pulmonary disease; *sCr*, serum creatinine; *CCS*, Canadian Cardiovascular Class; *BMI*, body mass index; *AF*, atrial fibrillation; *LMD*, left main disease; *DM*, diabetes mellitus; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *CVA*, cerebrovascular accident; *LVEF*, left ventricular ejection fraction; *NYHA*, New York Heart Association; *PVD*, peripheral vascular disease.

TABLE E2. Short-term outcomes in patients with orally treated diabetes in the unmatched and matched off-pump coronary artery bypass and on-pump coronary artery bypass groups with relative effect size in the propensity score-matched population

	Unmatched OPCAB		Unmatched ONCAB		PS matched OPCAB		PS matched ONCAB		Adjusted estimate (95% CI)	Adjusted <i>P</i> value
	n	%	n	%	n	%	n	%		
Sample size	733	100.0	706	100.0	583	100.0	584	100.0		
CVA										
No	724	98.8	685	97.0	578	99.1	568	97.3	0.31 (0.11-0.84)	.02
Yes	9	1.2	21	3.0	5	0.9	16	2.7		
RRT										
No	706	96.3	683	96.7	562	96.4	565	96.7	1.11 (0.59-2.09)	.74
Yes	27	3.7	23	3.3	21	3.6	19	3.3		
IABP										
No	714	97.4	672	95.2	569	97.6	555	95.0	0.47 (0.25-0.90)	.02
Yes	19	2.6	34	4.8	14	2.4	29	5.0		
SWR										
No	728	99.3	696	98.6	579	99.3	575	98.5	0.44 (0.14-1.44)	.17
Yes	5	0.7	10	1.4	4	0.7	9	1.5		
Reexploration										
No	717	97.8	681	96.5	570	97.8	560	95.9	0.53 (0.27-1.05)	.07
Yes	16	2.2	25	3.5	13	2.2	24	4.1		
Any complication										
No	663	90.5	614	87.0	531	91.1	505	86.5	0.63 (0.43-0.90)	.01
Yes	70	9.5	92	13.0	52	8.9	79	13.5		
30-d mortality										
No	717	97.8	691	97.9	573	98.3	573	98.1	0.89 (0.38-2.09)	.78
Yes	16	2.2	15	2.1	10	1.7	11	1.9		
IR										
No	621	84.7	653	92.5	499	85.6	543	93.0	2.2 (1.51-3.3)	<.001
Yes	112	15.3	53	7.5	84	14.4	41	7.0		

OPCAB, Off-pump coronary artery bypass; *ONCAB*, on-pump coronary artery bypass; *PS*, propensity score; *CI*, confidence interval; *CVA*, cerebrovascular event; *RRT*, renal replacement therapy; *IABP*, intra-aortic balloon pump; *SWR*, sternal wound reconstruction; *IR*, incomplete revascularization.

TABLE E3. Short-term outcomes in patients receiving insulin in the unmatched and matched off-pump coronary artery bypass and on-pump coronary artery bypass groups with relative effect size in the propensity score–matched population

	Unmatched OPCAB		Unmatched ONCAB		PS matched OPCAB		PS matched ONCAB		Adjusted estimate (95% CI)	Adjusted <i>P</i> value
	n	%	n	%	n	%	n	%		
Sample size	520	100.0	491	100	412	100.0	411	100.0		
CVA										
No	511	98.3	482	98	405	98.3	403	98.1	0.87 (0.31-2.42)	.79
Yes	9	1.7	9	2	7	1.7	8	1.9		
RRT										
No	487	93.7	461	94	384	93.2	387	94.2	1.18 (0.67-2.06)	.57
Yes	33	6.3	30	6	28	6.8	24	5.8		
IABP										
No	507	97.5	464	95	400	97.1	387	94.2	0.48 (0.24-0.98)	.04
Yes	13	2.5	27	5	12	2.9	24	5.8		
SWR										
No	512	98.5	484	99	406	98.5	404	98.3	0.85 (0.28-2.56)	.77
Yes	8	1.5	7	1	6	1.5	7	1.7		
Reexploration										
No	507	97.5	474	97	403	97.8	396	96.4	0.59 (0.26-1.36)	.21
Yes	13	2.5	17	3	9	2.2	15	3.6		
Any complication										
No	455	87.5	414	84	359	87.1	344	83.7	0.77 (0.54-0.99)	.04
Yes	65	12.5	77	16	53	12.9	67	16.3		
30-d mortality										
No	504	96.9	480	98	397	96.4	403	98.1	1.81 (0.77-4.28)	.19
Yes	16	3.1	11	2	15	3.6	8	1.9		
IR										
No	441	84.8	449	91	357	86.7	378	92.0	1.76 (1.12-2.8)	.01
Yes	79	15.2	42	9	55	13.3	33	8.0		

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; PS, propensity score; CI, confidence interval; CVA, cerebrovascular event; RRT, renal replacement therapy; IABP, intra-aortic balloon pump; SWR, sternal wound reconstruction; IR, incomplete revascularization.

TABLE E4. Effect of off-pump coronary artery bypass grafting over on-pump coronary artery bypass grafting on outcomes of interest in a fully adjusted double robust analysis

	Effect size	Lower 95% CI	Upper 95% CI	<i>P</i> value
Postoperative CVA	0.47*	0.23	0.97	.04
Postoperative RRT	1.23*	0.77	1.97	.55
Sternal wound reconstruction	0.35*	0.14	0.88	.04
Reexploration for bleeding	0.57*	0.33	0.99	.04
Postoperative IABP	0.49*	0.3	0.82	.009
Any of above complications	0.7*	0.51	0.95	.02
Mortality at 30 d	1.4†	0.75	2.61	.19
IR	2.41*	1.75	3.32	<.0001
Late mortality	1.09†	0.91	1.29	.55

CI, Confidence interval; CVA, cerebrovascular event; RRT, renal replacement therapy; IABP, intra-aortic balloon pump; IR, incomplete revascularization. *Logistic regression model. †Cox regression model.

TABLE E5. Double robust analysis on postoperative cerebrovascular accident

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	0.47	0.23	0.97
Age	1.25	0.71	2.18
Female	1.17	0.51	2.67
BMI	1.43	0.82	2.51
Canadian Cardiovascular Class	0.7	0.32	1.5
NYHA class	1.29	0.59	2.8
MI within 30 d	0.81	0.33	1.97
PCI	1.26	0.39	4.01
DM on insulin	1.03	0.5	2.11
Current smoking	1.44	0.5	4.16
Creatinine > 200 mmol/L	2.3	0.62	8.48
COPD	0.33	0.07	1.52
Cerebrovascular accident	4.16	1.67	10.36
Peripheral vascular disease	2.1	0.94	4.68
Atrial fibrillation	0.65	0.08	5.02
3-vessel disease	1.37	0.57	3.32
Left main disease	1.61	0.75	3.43
Left ventricular ejection fraction 30%-49%	0.62	0.27	1.46
Left ventricular ejection fraction <30%	0.49	0.1	2.53
Cardiogenic shock	4.5	0.26	76.93
Preoperative IABP	2.75	0.47	16.09
Nonelective	1.57	0.71	3.49
Emergency/salvage	2.76	0.4	18.91
Era of surgery	1.81	1	3.28
Bilateral internal thoracic arteries	2.21	0.26	18.59
Radial artery	0.8	0.23	2.83
IR	1.01	0.33	3.06

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E6. Double robust analysis on postoperative renal replacement therapy

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	1.23	0.77	1.97
Age	1.22	0.86	1.74
Female	0.76	0.43	1.34
BMI	1.27	0.92	1.74
Canadian Cardiovascular Class	1.25	0.78	2.01
NYHA Class	0.73	0.45	1.21
MI within 30 d	0.66	0.36	1.2
PCI	0.74	0.32	1.72
DM on insulin	1.91	1.22	3
Current smoking	0.98	0.45	2.11
Creatinine >200 mmol/L	5.24	2.65	10.35
COPD	0.66	0.31	1.41
Cerebrovascular accident	2.11	1.04	4.27
Peripheral vascular disease	1.47	0.85	2.53
Atrial fibrillation	1.92	0.82	4.49
3-vessel disease	0.89	0.53	1.48
Left main disease	1.44	0.88	2.37
Left ventricular ejection fraction 30%-49%	0.94	0.56	1.57
Left ventricular ejection fraction <30%	1.26	0.56	2.86
Cardiogenic shock	4.26	0.57	31.57
Preoperative IABP	3.68	1.08	12.56
Nonelective	1.05	0.64	1.72
Emergency/salvage	1.16	0.18	7.38
Era of surgery	1.95	1.29	2.94
Bilateral internal thoracic arteries	0.94	0.12	7.34
Radial artery	0.76	0.36	1.61
IR	0.75	0.35	1.59

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E7. Double robust analysis on need for intra-aortic balloon pump

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	0.49	0.3	0.82
Age	0.97	0.65	1.43
Female	1.27	0.72	2.24
BMI	0.82	0.6	1.11
Canadian Cardiovascular Class	1.22	0.7	2.12
NYHA class	1.29	0.74	2.25
MI within 30 d	1.68	0.91	3.1
PCI	0.78	0.31	1.97
DM on insulin	1.18	0.71	1.96
Current smoking	0.24	0.07	0.84
Creatinine >200 mmol/L	2.5	1.03	6.09
COPD	0.65	0.26	1.66
Cerebrovascular accident	0.3	0.04	2.24
Peripheral vascular disease	0.77	0.38	1.55
Atrial fibrillation	1.74	0.65	4.66
3-vessel disease	0.91	0.5	1.65
Left main disease	1.31	0.75	2.29
Left ventricular ejection fraction 30%-49%	2.09	1.17	3.76
Left ventricular ejection fraction <30%	8.3	4.32	15.93
Cardiogenic shock	1.44	0.15	13.66
Preoperative IABP	0.14	0.01	2.4
Nonelective	0.87	0.48	1.57
Emergency/salvage	6.34	2.08	19.29
Era of surgery	1.75	1.15	2.66
Bilateral internal thoracic arteries	3.58	0.89	14.33
Radial artery	0.36	0.11	1.2
IR	0.92	0.42	2.03

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E8. Double robust analysis on risk of sternal wound reconstruction

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	0.35	0.14	0.88
Age	2.52	1.19	5.34
Female	0.52	0.15	1.84
BMI	2.23	0.97	5.11
Canadian Cardiovascular Class	1.07	0.44	2.59
NYHA class	0.39	0.15	1.04
MI within 30 d	0.43	0.13	1.43
PCI	2.06	0.67	6.33
DM on insulin	1.53	0.65	3.6
Current smoking	0.81	0.16	3.97
Creatinine > 200 mmol/L	4.56	1.26	16.52
COPD	3.62	1.4	9.39
Cerebrovascular accident	0.68	0.08	5.56
Peripheral vascular disease	0.61	0.17	2.18
Atrial fibrillation	1.25	0.27	5.8
3-vessel disease	0.33	0.13	1.01
Left main disease	1.12	0.44	2.87
Left ventricular ejection fraction 30%-49%	2.08	0.84	5.13
Left ventricular ejection fraction <30%	2.95	0.75	11.67
Cardiogenic shock	-	-	-
Preoperative IABP	-	-	-
Nonelective	1.3	0.51	3.34
Emergency/salvage	-	-	-
Era of surgery	2	0.7	5.72
Bilateral internal thoracic arteries	-	-	-
Radial artery	2.07	0.62	6.93
IR	1.01	0.21	4.92

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E9. Double robust analysis on risk of reexploration for bleeding

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	0.57	0.33	0.99
Age	0.98	0.64	1.5
Female	1.1	0.59	2.06
BMI	0.91	0.64	1.31
Canadian Cardiovascular Class	1.35	0.74	2.44
NYHA class	0.55	0.29	1.03
MI within 30 d	1.37	0.71	2.65
PCI	0.33	0.08	1.44
DM on insulin	0.93	0.53	1.64
Current smoking	0.68	0.25	1.84
Creatinine >200 mmol/L	2.77	1.03	7.47
COPD	1.39	0.59	3.29
Cerebrovascular accident	0.54	0.13	2.3
Peripheral vascular disease	0.72	0.32	1.65
Atrial fibrillation	2.18	0.8	5.94
3-vessel disease	1.11	0.58	2.13
Left main disease	0.7	0.37	1.33
Left ventricular ejection fraction 30%-49%	0.72	0.37	1.4
Left ventricular ejection fraction <30%	1.66	0.71	3.9
Cardiogenic shock	13.13	1.66	104.09
Preoperative IABP	-	-	-
Nonelective	2.54	1.31	4.93
Emergency/salvage	4.85	1.21	19.39
Era of surgery	1.08	0.67	1.75
Bilateral internal thoracic arteries	1.81	0.37	8.83
Radial artery	0.36	0.11	1.2
IR	0.85	0.33	2.14

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E10. Double robust analysis on incidence of any complication among cerebrovascular accident, renal replacement therapy, need for intra-aortic balloon pump, sternal wound reconstruction, and reexploration for bleeding

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	0.7	0.51	0.95
Age	1.03	1.01	1.05
Female	0.82	0.56	1.20
BMI	1.03	1	1.06
Diabetes mellitus on insulin	1.43	1.05	1.96
Canadian Cardiovascular Class	1.08	0.77	1.50
NYHA class	0.84	0.6	1.19
MI within 30 d	1.06	0.72	1.54
PCI	1.11	0.64	1.85
Current smoking	0.77	0.42	1.31
Creatinine >200 mmol/L	5.15	2.98	8.75
COPD	0.85	0.5	1.38
Cerebrovascular accident	1.65	0.92	2.81
Peripheral vascular disease	1.11	0.73	1.64
Atrial fibrillation	1.27	0.63	2.34
3-vessel disease	0.75	0.52	1.08
Left main disease	1.47	1.05	2.06
Left ventricular ejection fraction 30%-49%	1.3	0.91	1.83
Left ventricular ejection fraction <30%	3.04	1.85	4.90
Cardiogenic shock	0.85	0.13	4.38
Preoperative IABP	1.43	0.44	3.88
Nonelective	1.07	0.75	1.52
Emergency/salvage	4.72	1.8	11.81
Era of surgery	1.65	1.14	2.41
Bilateral internal thoracic arteries	1.27	0.72	2.37
Radial artery	0.71	0.41	1.18
IR	1.05	0.62	1.71

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E11. Double robust analysis on mortality within 30 days

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	1.4	0.75	2.61
Age	1.05	1.005	1.09
Female	1.64	0.86	3.14
BMI	0.81	0.55	1.2
Canadian Cardiovascular Class	1.65	0.81	3.36
NYHA class	1.17	0.59	2.29
MI within 30 d	1.01	0.48	2.13
PCI	1.49	0.49	4.54
DM on insulin	1.49	0.79	2.8
Current smoking	0.24	0.03	1.78
Creatinine >200 mmol/L	1.03	0.23	4.54
COPD	0.59	0.17	1.99
Cerebrovascular accident	1.5	0.52	4.32
Peripheral vascular disease	1.54	0.74	3.18
Atrial fibrillation	2.16	0.83	5.66
3-vessel disease	1.39	0.62	3.14
Left main disease	0.83	0.42	1.66
Left ventricular ejection fraction 30%-49%	2.59	1.3	5.17
Left ventricular ejection fraction <30%	3.79	1.54	9.32
Cardiogenic shock	1.24	0.06	25.92
Preoperative IABP	0.54	0.03	10.61
Nonelective	2.25	1.04	4.86
Emergency/salvage	1.55	0.27	9
Era of surgery	0.76	0.4	1.46
Bilateral internal thoracic arteries	4.01	0.49	33.02
Radial artery	0.35	0.08	1.51
IR	0.79	0.3	2.11

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E12. Double robust analysis on incomplete revascularization

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	2.41	1.75	3.32
Age	1.17	0.92	1.49
Female	1.4	1	1.96
BMI	0.94	0.78	1.14
Canadian Cardiovascular Class	0.87	0.63	1.2
NYHA class	1.18	0.85	1.65
MI within 30 d	0.79	0.53	1.19
PCI	0.66	0.35	1.21
DM on insulin	0.99	0.73	1.35
Current smoking	0.87	0.52	1.46
Creatinine >200 mmol/L	1.07	0.52	2.17
COPD	1.16	0.72	1.86
Cerebrovascular accident	1.01	0.55	1.87
Peripheral vascular disease	1.01	0.67	1.53
Atrial fibrillation	0.95	0.48	1.91
3-vessel disease	1.21	0.86	1.71
Left main disease	1.19	0.85	1.67
Left ventricular ejection fraction 30%-49%	0.99	0.55	1.77
Left ventricular ejection fraction <30%	0.52	0.05	5.47
Cardiogenic shock	1.14	0.35	3.68
Preoperative IABP	1.18	0.84	1.64
Nonelective	1.4	0.43	4.54
Emergency/salvage	1.48	1.13	1.93
Era of surgery	1.48	0.5	4.41
Bilateral internal thoracic arteries	0.21	0.13	0.35
Radial artery	0.56	0.33	0.91

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E13. Double robust analysis on late mortality

	Effect	Lower 95% CI	Upper 95% CI
OPCAB	1.09	0.91	1.29
Age	1.06	1.04	1.07
Female	0.92	0.76	1.12
BMI	1.13	1.01	1.27
Canadian Cardiovascular Class	1.02	0.84	1.23
NYHA class	1.06	0.87	1.28
MI within 30 d	0.72	0.54	0.95
PCI	1.02	0.66	1.59
DM on insulin	1.18	1	1.4
Current smoking	1.27	0.93	1.72
Creatinine >200 mmol/L	2.5	1.68	3.72
COPD	1.38	1.03	1.83
Cerebrovascular accident	1.8	1.34	2.42
Peripheral vascular disease	1.72	1.39	2.14
Atrial fibrillation	1.82	1.32	2.52
3-vessel disease	0.87	0.71	1.07
Left main disease	1.1	0.9	1.35
Left ventricular ejection fraction 30%-49%	1.31	1.08	1.59
Left ventricular ejection fraction <30%	2.28	1.71	3.03
Cardiogenic shock	0.48	0.09	2.44
Preoperative IABP	1.2	0.39	3.7
Nonelective	1.18	0.97	1.42
Emergency/salvage	1.13	0.53	2.41
Era of surgery	0.91	0.66	1.23
Bilateral internal thoracic arteries	0.87	0.43	1.77
Radial artery	1.07	0.84	1.36
IR	1.49	1.15	1.92

CI, Confidence interval; OPCAB, off-pump coronary artery bypass; BMI, body mass index; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IR, incomplete revascularization.

TABLE E14. Person correlation coefficient and variance inflation factors from the covariance matrix

	Pearson correlation between predictors																								
	VIF	Age	Female	CCS	NYHA	MI	PCI	DM on insulin	Current smoking	sCr >200 mmol/L	COPD	CVA	PVD	AF	LMD	LVEF	Cardiogenic shock	IABP	Nonelective	Emergency/salvage	BMI	Era of surgery	3-vessel disease	IR	OPCAB
Age	1.24	1.00	0.01	-0.00	0.09	0.01	-0.02	-0.16	-0.24	-0.02	0.07	0.04	0.03	0.10	0.09	0.04	0.04	0.00	0.09	-0.02	-0.14	0.16	0.09	0.05	0.01
Female	1.06	0.01	1.00	0.15	0.12	0.02	0.03	0.08	0.00	-0.00	-0.04	-0.02	0.01	-0.02	0.00	-0.05	0.04	-0.01	0.06	0.01	0.06	-0.09	-0.04	0.05	-0.00
CCS	1.25	-0.00	0.15	1.00	0.34	0.04	0.03	0.03	-0.02	0.00	0.01	-0.01	0.02	-0.01	0.03	0.03	0.03	0.03	0.23	0.11	0.08	-0.15	-0.01	-0.00	-0.02
NYHA	1.24	0.09	0.12	0.34	1.00	-0.01	0.03	0.08	-0.01	0.04	0.15	0.02	0.08	0.04	-0.01	0.12	0.05	0.03	0.07	0.12	0.13	-0.06	0.02	0.03	-0.01
MI	1.34	0.01	0.02	0.04	-0.01	1.00	0.07	0.02	0.14	0.04	0.02	-0.01	-0.01	0.00	0.10	0.11	0.08	0.05	0.38	0.11	0.01	0.30	0.06	-0.00	-0.03
PCI	1.06	-0.02	0.03	0.03	0.03	0.07	1.00	0.03	0.06	0.05	0.04	-0.02	-0.02	-0.02	0.01	0.01	0.03	0.06	0.04	0.08	0.03	0.19	-0.06	-0.02	0.02
DM on insulin	1.07	-0.16	0.08	0.03	0.08	0.02	0.03	1.00	-0.00	0.09	0.02	0.04	0.07	-0.02	-0.04	0.07	-0.02	0.00	0.03	-0.01	0.09	-0.05	0.01	-0.00	0.00
Current smoking	1.12	-0.24	0.00	-0.02	-0.01	0.14	0.06	-0.00	1.00	0.02	0.08	0.02	0.03	-0.02	-0.01	0.02	-0.02	0.00	0.06	-0.03	0.01	0.07	0.00	-0.01	-0.00
sCr >200 mmol/L	1.03	-0.02	-0.00	0.00	0.04	0.04	0.05	0.09	0.02	1.00	0.08	0.01	0.04	-0.03	-0.02	0.05	0.02	-0.02	0.01	-0.02	-0.03	0.05	0.04	0.02	0.01
COPD	1.07	0.07	-0.04	0.01	0.15	0.02	0.04	0.02	0.08	0.08	1.00	0.03	0.07	0.03	0.04	0.04	-0.02	0.01	0.04	-0.02	0.06	0.14	0.04	0.03	-0.01
CVA	1.02	0.04	-0.02	-0.01	0.02	-0.01	-0.02	0.04	0.02	0.01	0.03	1.00	0.08	0.03	-0.02	-0.01	-0.02	0.01	0.02	-0.01	-0.00	-0.00	0.05	0.00	0.02
PVD	1.03	0.03	0.01	0.02	0.08	-0.01	-0.02	0.07	0.03	0.04	0.07	0.08	1.00	0.01	0.03	0.06	-0.03	-0.04	0.03	-0.01	-0.01	0.04	0.01	0.01	-0.01
AF	1.03	0.10	-0.02	-0.01	0.04	0.00	-0.02	-0.02	-0.02	-0.03	0.03	0.03	0.01	1.00	0.01	0.09	0.02	-0.03	0.03	-0.03	0.03	-0.01	-0.02	0.00	0.00
LMD	1.08	0.09	0.00	0.03	-0.01	0.10	0.01	-0.04	-0.01	-0.02	0.04	-0.02	0.03	0.01	1.00	0.04	0.03	0.01	0.23	0.06	0.00	0.09	0.06	0.03	-0.02
LVEF	1.08	0.04	-0.05	0.03	0.12	0.11	0.01	0.07	0.02	0.05	0.04	-0.01	0.06	0.09	0.04	1.00	0.09	0.07	0.13	0.08	-0.03	-0.01	0.09	0.03	0.00
Cardiogenic shock	1.19	0.04	0.04	0.03	0.05	0.08	0.03	-0.02	-0.02	0.02	-0.02	-0.02	-0.03	0.02	0.03	0.09	1.00	0.29	0.04	0.29	-0.04	-0.00	-0.01	-0.00	0.00
IABP	1.13	0.00	-0.01	0.03	0.03	0.05	0.06	0.00	0.00	-0.02	0.01	0.01	-0.04	-0.03	0.01	0.07	0.29	1.00	0.03	0.17	-0.00	0.11	0.01	0.01	-0.00
Nonelective	1.33	0.09	0.06	0.23	0.07	0.38	0.04	0.03	0.06	0.01	0.04	0.02	0.03	0.03	0.23	0.13	0.04	0.03	1.00	0.12	-0.03	0.06	0.08	0.02	-0.04
Emergency/salvage	1.15	-0.02	0.01	0.11	0.12	0.11	0.08	-0.01	-0.03	-0.02	-0.02	-0.01	-0.01	-0.03	0.06	0.08	0.29	0.17	0.12	1.00	0.00	0.00	0.01	0.01	-0.01
BMI	1.11	-0.14	0.06	0.08	0.13	0.01	0.03	0.09	0.01	-0.03	0.06	-0.00	-0.01	0.03	0.00	-0.03	-0.04	-0.00	-0.03	0.00	1.00	0.15	-0.02	0.01	-0.01
Era of surgery	1.34	0.16	-0.09	-0.15	-0.06	0.30	0.19	-0.05	0.07	0.05	0.14	-0.00	0.04	-0.01	0.09	-0.01	-0.00	0.11	0.06	0.00	0.15	1.00	0.02	0.06	0.06
3-vessel disease	1.09	0.09	-0.04	-0.01	0.02	0.06	-0.06	0.01	0.00	0.04	0.04	0.05	0.01	-0.02	0.06	0.09	-0.01	0.01	0.08	0.01	-0.02	0.02	1.00	0.21	-0.08
IR	1.07	0.05	0.05	-0.00	0.03	-0.00	-0.02	-0.00	-0.01	0.02	0.03	0.00	0.01	0.00	0.03	0.03	-0.00	0.01	0.02	0.01	0.01	0.06	0.21	1.00	0.11
OPCAB	1.03	0.01	-0.00	-0.02	-0.01	-0.03	0.02	0.00	-0.00	0.01	-0.01	0.02	-0.01	0.00	-0.02	0.00	0.00	-0.00	-0.04	-0.01	-0.01	0.06	-0.08	0.11	1.00

VIF, Variance inflation factor; CCS, Canadian Cardiovascular Class; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; DM, diabetes mellitus; sCr, serum creatinine; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PVD, peripheral vascular disease; AF, atrial fibrillation; LMD, left main disease; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; BMI, body mass index; IR, incomplete revascularization; OPCAB, off-pump coronary artery bypass.