

On-pump beating heart versus conventional coronary artery bypass grafting: comparative study on early and long-term clinical outcomes

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Background: We reviewed our experience with on-pump beating (OPB) heart coronary artery bypass grafting (CABG) to evaluate the impacts of obviating aortic cross-clamping and cardioplegic arrest on clinical outcomes compared with conventional CABG (C-CABG).

Methods: Between 2006 and 2012, elective isolated cardiopulmonary bypass (CPB)-assisted CABG was consecutively performed in 645 patients (mean patient age 63.3 ± 9.1 years, 471 women) with 254 (39.4%) undergoing OPB-CABG and 391 (60.6%) undergoing C-CABG. The early and long-term clinical outcomes were compared between the two groups after adjusting for risk profiles through propensity score (PS) analyses.

Results: The OPB-CABG group presented significant morbidities more frequently than the C-CABG group, including severe chronic kidney disease (CKD) ($P=0.026$), severe chest pain ($P<0.001$), and poor left ventricular function ($P<0.001$). Early mortality occurred in 6 (2.4%) and 2 (0.5%) patients in the OPB- and C-CABG group, respectively ($P=0.087$). The number of distal anastomosis was comparable between the two groups (3.0 ± 0.9 vs. 3.0 ± 1.0 , $P=0.816$). After PS matching, the incidence of major complications such as stroke ($P>0.99$) and new-onset dialysis ($P=0.109$) was comparable. During a median follow-up of 81.0 months (quartiles 1–3, 66.6–95.0 months), 118 patients died and the PS-matched models showed no significant between-group differences in the risk of overall death [hazard ratio (HR), 1.19; 95% confidence interval (CI), 0.72–1.95; $P=0.507$] and major adverse cardiac events (MACE) (HR, 1.49; 95% CI, 0.67–3.31; $P=0.328$).

Conclusions: The OPB strategy may be as safe and effective as the conventional strategy during CABG among patients with similar risk profiles. A prospective randomized trial is warranted to better ascertain the beneficial impact of OPB-CABG as both a viable and a durable alternative strategy to C-CABG.

Keywords: Coronary artery bypass grafting (CABG); cardiopulmonary bypass (CPB); mortality

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Introduction

The optimal coronary revascularization strategy remains debated (1,2). Although conventional coronary artery bypass grafting (C-CABG) remains the gold standard, the use of

cardiopulmonary bypass (CPB), aortic cross-clamping, and cardioplegic arrest may arguably increase the risk of serious neurologic and renal complications, as well as ischemic myocardial injury (3,4). Off-pump CABG (OPCAB) has

been viewed as a potentially ideal strategy of avoiding some of the more prominent complication risks of C-CABG, by obviating the use of CPB and cardioplegic arrest altogether while achieving the surgical objectives in a qualitatively similar manner. However, recent studies have increasingly reported inferior long-term survival outcomes with OPCAB, presumably owing to the limitations associated with the inherently more challenging nature of the surgical technique (1,5,6).

On-pump beating (OPB) heart CABG (OPB-CABG) may have the potential to reap the benefits of both OPCAB and C-CABG while avoiding their major drawbacks (7,8). Unlike OPCAB, OPB-CABG provides a more stable mechanical platform for performing distal anastomosis while maintaining the beating heart status albeit on a brief period of CPB support. This dependence on CPB, however, may be argued as being a limitation that may nullify any purported advantages claimed by OPB-CABG over either OPCAB or C-CABG. Nevertheless, in certain high-risk conditions such as myocardial infarction or left ventricular dysfunction, OPB-CABG has reportedly shown greater benefits compared with C-CABG in terms of reducing the early morbidity and mortality rates (9-11). In light of these issues, we reviewed our clinical experiences with OPB-CABG and analyzed its efficacy as a viable alternative strategy for coronary revascularization by comparing the early and long-term results with those of C-CABG.

Methods

Patients

Among a total of 1,251 patients undergoing CABG with CPB support between January 2006 and December 2012, we identified 645 consecutive patients who underwent elective isolated CABG after excluding patients undergoing concomitant valvular or aortic surgery (n=544) and emergent/urgent surgeries (n=62). Of these patients, 254 (39.4%) underwent OPB-CABG (OPB-CABG group), whereas 391 (60.6%) underwent C-CABG with cardioplegic arrest and aortic cross-clamping (C-CABG group).

The decision to perform C-CABG or OPB-CABG was influenced by several factors such as the patient's demographic and clinical profiles, including left ventricular ejection fraction, site of coronary lesions, or the presence of neurological or renal dysfunction. The decision was ultimately left to the discretion of the operating surgeon

who considered all of these factors holistically. The study was approved by the institutional ethics committee/review board of Asan Medical Center (No. 2016-0225), which waived the requirement for informed consent owing to the retrospective study design.

Surgical procedure

All CABG procedures were performed through a median sternotomy by sufficiently experienced attending surgeons. *In situ* internal thoracic arteries (ITAs) were harvested in either a skeletonized or pedicled fashion per the operating surgeon's preference. All saphenous vein grafts (SVGs) and radial arteries were harvested by open technique. CPB was instituted by cannulating the distal ascending aorta and right atrium after systemic heparinization (300 IU/kg) with a target activated clotting time of ≥ 480 s. In the C-CABG group, the aorta was cross-clamped and myocardial protection was achieved with intermittent, antegrade tepid blood cardioplegic infusion (22–32 °C). After the first induction of cardioplegic arrest, subsequent cardioplegia was delivered every 20–30 min. The patient's body temperature was maintained between 28 and 34 °C.

In the OPB-CABG group, bypass grafting was performed on the beating heart under CPB. A vent was passed through the right superior pulmonary vein if the left ventricular was distended during cardiac manipulation. To prevent hypothermia-induced ventricular fibrillation, the body temperature was not actively cooled, but the temperature was allowed to drift between 32 and 34 °C. An Octopus stabilizer (Medtronic, Minneapolis, MN, USA) was routinely used for myocardial immobilization. When the grafts needed to be anastomosed to the ascending aorta, proximal anastomosis was performed on the arrested heart before the release of the aorta cross-clamp in the C-CABG group. During OPB-CABG, the patients underwent proximal anastomosis using either the HEARTSTRING Proximal Seal System (Guidant Corporation, Santa Clara, CA, USA) or aortic side clamping.

The left ITA was preferentially used as the first bypass graft of choice for revascularizing the left anterior descending coronary artery, whenever feasible. The determination of conduit type and configuration for bypassing the other coronary artery territories (right coronary and left circumflex territories) were based on conduit graft availability, sites of target vessels and territories, and surgeon preference (12).

Outcomes of interest

The primary early outcomes of interest were the early mortality and early major postoperative morbidities within 30 days of the operation or during hospitalization, including low cardiac output syndrome requiring mechanical circulatory support, early stroke, acute kidney injury requiring new dialysis, mediastinal bleeding, pneumonia, sternal wound infection, and new-onset atrial fibrillation. The primary long-term outcome of interest was all-cause death (13). Other long-term outcomes of interest were major adverse cardiac events (MACE) including myocardial infarction, coronary revascularization, stroke, and congestive heart failure requiring hospitalization.

Statistical analysis

The R software (version 3.4.0; R Foundation for Statistical Computing, Vienna, Austria; <http://www.r-project.org/>) was used for statistical analysis. Categorical variables, expressed as percentages or frequencies, were compared using the χ^2 test. Continuous variables, expressed as either mean \pm standard deviation (SD) or median with range (or quartiles 1–3), were compared using Student's *t*-test. Kaplan-Meier curves were made to delineate the time-related cumulative incidence of all-cause death and MACE. Intergroup comparisons were conducted with log-rank tests.

To emulate a randomized trial in which risk factors affecting the postoperative clinical outcomes are evenly distributed between the two groups, we performed adjustments with propensity scores (PSs) as a matching tool to yield comparable C-CABG and OPB-CABG groups (14). The PS, conditional on all relevant baseline variables and comorbidities, was the predicted probability of the patient to receive OPB-CABG in either of the two groups. The PSs were estimated using the logistic regression model and the log-binomial model incorporating the 27 baseline covariates listed in *Table 1*. The multicollinearity for each covariate was tested by examining the variance of inflation factors (VIFs), with a value of VIF ≥ 10 considered to indicate excessive multicollinearity. The balance between the two groups after adjustment was assessed with standardized mean differences (SMDs).

PS-matched pairs were generated by matching between the OPB-CABG and C-CABG groups on the logit of the PS with the use of calipers of width ≤ 0.2 of the SD of the logit of the PS. A conditional logistic regression model and Cox proportional hazards model were used to evaluate the impact of the OPB technique on the early and other long-

term outcomes in the PS-matched pairs. The proportional assumption in the Cox model was evaluated with Schoenfeld residuals, which yielded no evidence to suggest rejecting the assumption about the long-term outcomes. All reported P values were two-sided, and the results were considered statistically significant if $P < 0.05$.

Results

Baseline characteristics and operative profiles

The baseline demographics and clinical characteristics of the two groups are summarized in *Table 1*. In general, the OPB-CABG group showed higher risk profiles compared with the C-CABG group; the OPB-CABG group patients presented with hyperlipidemia ($P = 0.009$), chronic obstructive pulmonary disease ($P < 0.001$), severe chronic kidney disease (CKD) ($P = 0.026$), and severe chest pain (Canadian Cardiovascular Society class 3 or 4, $P < 0.001$) or dyspnea (New York Heart Association class 3 or 4, $P < 0.001$) more frequently than those in the C-CABG group.

With regards to the echocardiographic profiles, the patients in the OPB-CABG group presented with lower left ventricular ejection fraction ($51.5\% \pm 13.8\%$ vs. $56.0\% \pm 11.1\%$, $P < 0.001$), greater left ventricular end-systolic (36.5 ± 9.8 vs. 34.3 ± 8.0 mm, $P = 0.003$) and end-diastolic (52.6 ± 7.5 vs. 51.5 ± 6.2 mm, $P = 0.037$) dimensions, and higher peak tricuspid regurgitation pressure gradient (25.2 ± 8.5 vs. 22.5 ± 5.5 mm, $P < 0.001$) than those in the C-CABG group.

The number of distal anastomosis (3.0 ± 0.9 vs. 3.0 ± 1.0 , $P = 0.816$), CPB time (79 ± 37 vs. 77 ± 44 min, $P = 0.475$), and use of left ITA (97.7% vs. 96.9% , $P = 0.685$) were equivalent for the two groups (*Table 2*). Bilateral ITAs and SVGs were more frequently used in the OPB-CABG group.

Unadjusted outcomes

The early death rates were 2.4% ($n = 6$) in the OPB-CABG group and 0.5% ($n = 2$) in the C-CABG group ($P = 0.087$). Concerning early major morbidities, the patients in the OPB-CABG group were significantly more susceptible to acute kidney injury requiring dialysis ($P < 0.001$) than those in the C-CABG group. The incidence of other morbidities was not significantly different between the two groups (*Table 2*).

During a median follow-up of 81.0 months [quartiles 1–3, 66.6–95.0 months; 4,129.9 patient-years (PYs)], there were 52 all-cause deaths (3.7%/PY) in the OPB-CABG group and 66

Table 1 Baseline characteristics of patients in the OPB-CABG and C-CABG groups

Characteristics	Overall cohort			PS-matched cohort		
	C-CABG (n=391)	OPB-CABG (n=254)	P value	C-CABG (n=173)	OP-CABG (n=173)	SMD (%)
Age, years	62.9±9.2	63.9±9.0	0.14	62.8±9.1	62.8±8.9	0.5
Female sex	291 (74.4)	180 (70.9)	0.366	130 (75.1)	124 (71.7)	7.9
BMI, kg/m ²	24.9±2.9	24.6±3.0	0.224	24.8±2.6	24.8±3.0	1.1
Current smoker	71 (18.2)	49 (19.3)	0.797	35 (20.2)	31 (17.9)	5.9
Diabetes mellitus	180 (46.0)	129 (50.8)	0.272	93 (53.8)	84 (48.6)	10.4
Hypertension	249 (63.7)	159 (62.6)	0.845	112 (64.7)	105 (60.7)	8.4
Hyperlipidemia	54 (13.8)	56 (22.0)	0.009	37 (21.4)	33 (19.1)	5.8
Anemia	173 (44.2)	122 (48.0)	0.389	76 (43.9)	77 (44.5)	1.2
COPD	4 (1.0)	28 (11.0)	<0.001	4 (2.3)	4 (2.3)	0.1
Severe CKD (stage 4 or 5)	15 (3.8)	21 (8.3)	0.026	8 (4.6)	10 (5.8)	5.2
Dialysis	9 (2.3)	17 (6.7)	0.01	7 (4.0)	8 (4.6)	2.8
Peripheral arterial disease	26 (6.6)	24 (9.4)	0.251	15 (8.7)	13 (7.5)	4.2
Atrial fibrillation	3 (0.8)	5 (2.0)	0.326	2 (1.2)	3 (1.7)	4.8
NYHA class 3 or 4	32 (8.2)	47 (18.5)	<0.001	20 (11.6)	21 (12.1)	1.8
CCS class 3 or 4	27 (6.9)	48 (18.9)	<0.001	18 (10.4)	21 (12.1)	5.5
Previous PCI	71 (18.2)	48 (18.9)	0.895	29 (16.8)	32 (18.5)	4.6
Previous cardiac surgery	1 (0.3)	3 (1.2)	0.342	1 (0.6)	0 (0.0)	10.8
History of CVA	48 (12.3)	38 (15.0)	0.389	23 (13.3)	19 (11.0)	7.1
Recent MI (<3 months)	21 (5.4)	25 (9.8)	0.046	11 (6.4)	10 (5.8)	2.4
Multivessel disease	390 (99.7)	250 (98.4)	0.159	172 (99.4)	173 (100.0)	10.8
Left main involvement	110 (28.1)	70 (27.6)	0.945	51 (29.5)	50 (28.9)	1.3
Echocardiographic parameters						
LV ejection fraction, %	56.0±11.1	51.5±13.8	<0.001	54.7±11.7	54.4±12.9	2
LV end-systolic dimension, mm	34.3±8.0	36.5±9.8	0.003	34.9±8.9	35.4±9.7	5
LV end-diastolic dimension, mm	51.5±6.2	52.6±7.5	0.037	52.0±6.6	52.3±7.4	3.9
Peak TR pressure gradient, mmHg	22.5±5.5	25.2±8.5	<0.001	23.3±6.1	23.9±6.0	8.9
Significant TR	2 (0.5)	3 (1.2)	0.626	0 (0.0)	1 (0.6)	10.8
Significant MR	7 (1.8)	11 (4.3)	0.095	5 (2.9)	4 (2.3)	3.6

Values are n (%) or mean ± standard deviation, unless otherwise indicated. OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; PS, propensity score; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; LV, left ventricular; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; MI, myocardial infarction; MR, mitral regurgitation; TR, tricuspid regurgitation; SMD, standardized mean difference.

Table 2 Operative profiles and outcomes

Variables	C-CABG (n=391)	OPB-CABG (n=254)	P value
Operative profiles			
No. of distal anastomosis	3.0±0.9	3.0±1.0	0.816
Use of graft conduit			
Left ITA	382 (97.7)	246 (96.9)	0.685
SVG	265 (67.8)	215 (84.6)	<0.001
Radial artery	328 (83.9)	80 (31.5)	<0.001
Bilateral ITA	0 (0.0)	17 (6.7)	<0.001
Cardiopulmonary bypass time, min	79±37	77±44	0.475
Aorta cross-clamping time, min	55±26	–	–
Operative outcomes*			
Early outcomes, n (%)			
Early (<30 days) death	2 (0.5)	6 (2.4)	0.087
Early major morbidity			
LCOS requiring MCS	2 (0.5)	5 (2.0)	0.175
Early stroke	4 (1.0)	4 (1.6)	0.799
Requirement for new dialysis	3 (0.8)	15 (5.9)	<0.001
Bleeding	19 (4.9)	15 (5.9)	0.689
Pneumonia	4 (1.0)	8 (3.1)	0.098
Sternal wound infection	3 (0.8)	7 (2.8)	0.095
New-onset atrial fibrillation	23 (5.9)	23 (9.1)	0.17
Long-term outcomes, n (%/PY)			
All-cause death	66 (2.4)	52 (3.7)	0.005
MACE	21 (0.8)	22 (1.6)	0.03
Myocardial infarction	3 (0.1)	1 (0.1)	0.603
Revascularization	5 (0.2)	5 (0.4)	0.314
Late stroke	7 (0.3)	4 (0.3)	0.995
Hospitalization due to CHF	8 (0.3)	14 (1.0)	0.003
Composite of death and MACE	81 (3.0)	67 (4.8)	0.001

Values are n (%) or mean ± standard deviation, unless otherwise indicated. *, χ^2 test for early outcomes and log-rank test for late outcomes. OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; ITA, internal thoracic artery; SVG, saphenous vein graft; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; PY, patient-year; MACE, major adverse cardiac events; CHF, congestive heart failure.

(2.4%/PY) in the C-CABG group (P=0.005). The incidence of MACE (1.6%/PY vs. 0.8%/PY, P=0.030) was also higher in the OPB-CABG group, which was mainly attributable to the more frequent hospitalization for heart failure of the patients in this group (1.0%/PY vs. 0.3%/PY, P=0.003).

Adjusted outcomes

In multivariate Cox proportional hazard models, increased age, severe CKD, atrial fibrillation, and reduced left ventricular ejection fraction were found to be associated with an increased risk for all-cause death or the composite

Table 3 Operative outcomes in the propensity score-matched cohort

Clinical outcomes	C-CABG (n=173)	OPB-CABG (n=173)	P value
Early outcomes, n (%)			
Early (<30 days) death	0 (0.0)	2 (1.2)	0.478
Early major morbidity			
LCOS requiring MCS	0 (0.0)	1 (0.6)	>0.99
Early stroke	1 (0.6)	1 (0.6)	>0.99
Requirement for new dialysis	2 (1.2)	8 (4.6)	0.109
Bleeding	9 (5.2)	5 (2.9)	0.413
Pneumonia	0 (0.0)	2 (1.2)	0.478
Sternal wound infection	1 (0.6)	4 (2.3)	0.368
New-onset atrial fibrillation	14 (8.1)	14 (8.1)	>0.99
Long-term outcomes, n (%/PY)			
All-cause death	34 (2.8)	30 (3.0)	0.506
MACE	11 (0.9)	14 (1.4)	0.325
Myocardial infarction	2 (0.2)	1 (0.1)	0.585
Revascularization	3 (0.2)	4 (0.4)	0.551
Late CVA	3 (0.2)	2 (0.2)	0.792
Hospitalization due to CHF	5 (0.4)	9 (0.9)	0.148
Composite of death and MACE	42 (3.5)	40 (4.0)	0.382

Values are n (%) or mean \pm standard deviation, unless otherwise indicated. χ^2 test for early outcomes and log-rank test for late outcomes. OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; CVA, cerebrovascular accident; PY, patient-year; MACE, major adverse cardiac events; CHF, congestive heart failure.

of death and MACE. The CPB strategy (OPB *vs.* conventional), however, did not significantly influence the risk of all-cause death (P=0.333) or the composite of adverse outcomes (P=0.098; *Table S1*).

The baseline profiles were well balanced between the two groups with SMDs <10% for most covariates after PS matching (*Table 1*). In the PS-matched pairs, the incidence of early mortality and early major morbidities were comparable between the two groups (*Table 3*).

The results of risk analyses for the early and long-term clinical outcomes of the OPB strategy are summarized in *Table 4*. Patients in the OPB-CABG group showed an increased risk of acute kidney injury requiring new dialysis (P=0.001), all-cause death (P=0.006), and MACE (P=0.033) in the overall cohort. After PS matching, however, the OPB strategy did not significantly influence the risk of early complications including the need for new dialysis (P=0.074)

and early stroke (P>0.99).

With regards to the long-term outcomes, the risks of all-cause death [hazard ratio (HR), 1.19; 95% confidence interval (CI), 0.72–1.95; P=0.507], MACE (HR, 1.49; 95% CI, 0.67–3.31; P=0.328), and the composite of death and MACE (HR, 1.21; 95% CI, 0.78–1.89; P=0.381) were similar for the two groups in the PS-matched pairs (*Table 4, Figure 1*).

Likewise, when PS matching from the log-binomial method was performed (*Table S2*), the incidence of early and long-term outcomes between the two groups was comparable (*Table S3*). The risk of early and long-term outcomes was not significantly affected by the OPB strategy (*Table S4*).

Discussion

This article describes our institutional experiences with OPB-CABG and its clinical outcomes compared with

Table 4 Comparative outcomes of OPB-CABG versus conventional CABG

Outcomes	Overall cohort			PS-matched cohort		
	OR/HR	95% CI	P value	OR/HR	95% CI	P value
Early outcomes						
Early death	4.71	1.07–32.29	0.059	NA	NA	NA
LCOS requiring MCS	3.91	0.83–27.42	0.105	NA	NA	NA
Early stroke	1.55	0.36–6.60	0.539	1.00	0.04–25.42	>0.99
New dialysis	8.12	2.64–35.31	0.001	4.15	1.02–27.74	0.074
Bleeding	1.23	0.60–2.46	0.562	0.54	0.16–1.60	0.282
Pneumonia	3.15	0.98–11.89	0.064	NA	NA	NA
Sternal wound infection	3.67	1.01–17.13	0.062	4.07	0.59–80.08	0.211
New-onset atrial fibrillation	1.59	0.87–2.92	0.129	1.00	0.46–2.18	>0.99
Long-term outcomes						
All-cause death	1.69	1.16–2.45	0.006	1.19	0.72–1.95	0.507
MACE	1.93	1.05–3.53	0.033	1.49	0.67–3.31	0.328
Death + MACE	1.73	1.25–2.41	0.001	1.21	0.78–1.89	0.381

Early outcomes are given as odds ratio; long-term outcomes are given as hazard ratio. Cox proportional hazard assumption (by scaled Schoenfeld residuals): death ($P=0.917$), MACE ($P=0.790$), composite outcome ($P=0.974$). OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; PS, propensity score; OR, odds ratio; HR, hazard ratio; CI, confidence interval; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; MACE, major adverse cardiac events; NA, not applicable.

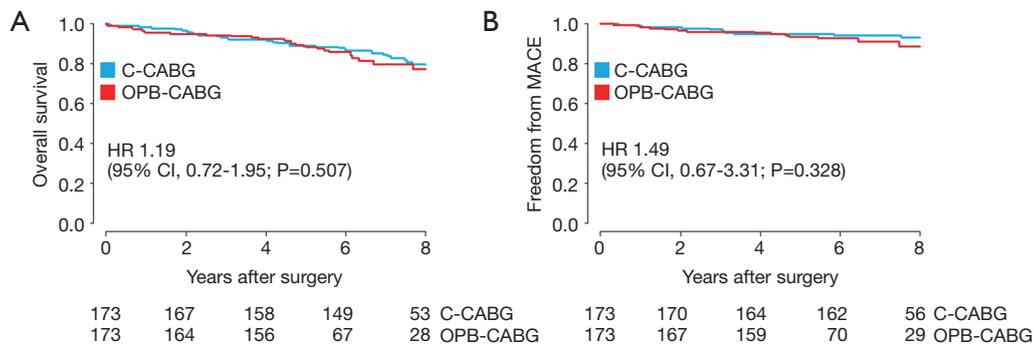


Figure 1 Kaplan-Meier curves for (A) overall survival and (B) freedom from MACE in the propensity score-matched cohorts. MACE, major adverse cardiac event; OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting.

those of C-CABG. As suggested by previous studies demonstrating the clinical advantages of the OPB strategy in high-risk patients (7-11), patients who underwent OPB-CABG had more morbidities than those who underwent C-CABG in this study. The OPB strategy provided comparable early and long-term clinical outcomes to

those of C-CABG in a selected set of patients with similar morbidities. To our knowledge, the present cohort represents one of the largest volume in which the two strategies were compared. A PS method was used to adequately balance the risk profiles between the two groups.

Since its introduction in the 1990s, OPCAB has

gradually gained acceptance as a potentially ideal method which may allow the major complication risks of C-CABG, including but not limited to embolic stroke, renal dysfunction, and the physiologic derangements of systemic inflammatory response to be avoided (3,4,15). By obviating aortic cross-clamping and the use of CPB, OPCAB was believed to be particularly advantageous for treating high-risk patients with low cardiac reserves (4,15-17). Despite the promising early outcomes reported with OPCAB, extensive meta-analyses, randomized controlled trials, and rigorously adjusted retrospective studies have increasingly reported less favorable long-term survival outcomes after OPCAB compared with C-CABG (1,2,5,6). Furthermore, situations requiring urgent unexpected conversion to on-pump surgery have been reported to significantly increase the risk of mortality and postoperative complications (18-20). In this respect, the OPB-CABG strategy has presented as a reasonable method of providing stable hemodynamic support and coronary blood flow while avoiding aortic manipulations and cardioplegic arrest (7). Despite its postulated physiological advantages, the OPB strategy has generated less interest than the other two strategies due to the uncertainty regarding any differential benefits with this technique. Consequently, relatively few separate in-depth analyses were conducted and no large volume studies have been performed. Thus, the present study analyzing and comparing the 2 strategies may provide useful insights regarding this less commonly adopted method of coronary bypass surgery.

In the present study, crude intergroup comparison showed a higher incidence of early and long-term adverse clinical events in the OPB-CABG group patients (*Table 2*). This may be attributable in part to the greater proportion of patients with prominent high-risk profiles in the OPB-CABG group such as severe CKD or recent myocardial infarction (*Table 1*). Due to intergroup disparities in some of the important risk factors, the two groups were analyzed and compared after PS matching. The results showed no significant differences in the early and long-term clinical outcomes; the two groups showed similar early outcomes such as mortality ($P=0.478$), low cardiac output syndrome ($P>0.99$), stroke ($P>0.99$), and new postoperative dialysis requirements ($P=0.109$; *Table 3*). Furthermore, risk analyses in the PS-matched pairs showed no significant intergroup differences in all-cause death ($P=0.507$), MACE ($P=0.328$), and the composite of adverse outcomes ($P=0.381$) (*Table 4*). Of note, the number of distal anastomosis was also comparable between the two groups (3.0 ± 0.9 vs. 3.0 ± 1.0 ,

$P=0.816$; *Table 2*), indicating that OPB-CABG was not a limitation to achieving a similar degree of completeness of revascularization to C-CABG. These finding showed that the OPB strategy may be comparable in safety level and efficacy compared to C-CABG in performing surgical coronary revascularization.

Dependence on CPB support is a limitation that may argue for the OPB strategy as being qualitatively similar to C-CABG. However, the obviating of aortic cross-clamping and the need for cardioplegic arrest may provide cardio-protection against the obligate global intraoperative myocardial ischemia in C-CABG (7,8). This may be particularly advantageous in acute myocardial infarction or poor left ventricular function with low cardiac reserve as these patients may be unable to tolerate the extreme myocardial manipulation of OPCAB or the controlled ischemia of C-CABG (9,10,21,22). Compared with OPCAB, CPB-assisted beating heart surgery may afford a stable surgical platform for ensuring optimal anastomosis quality that would otherwise not be possible with OPCAB as the heart is continuously perfused while being protected from distention injury and the anastomosis site is securely stabilized (23-25).

Despite these postulated benefits of the OPB strategy, additional significant advantages of obviating aortic cross-clamping and cardioplegic arrest with the OPB-CABG group were not clearly apparent in either the early or long-term comparisons with C-CABG. This may be attributable to the limited sample size which may not have been sufficiently powered to show an actual inter-group difference with respect to the primary hard endpoints, particularly in the subgroup of patients with high-risk profiles. In this regard, our study results should be interpreted accordingly, and warranting further randomized controlled trials over a larger volume of patients to confirm and objectively validate the benefits of the OPB strategy and to identify the patient subgroup most likely to benefit from this therapeutic approach.

Limitations

This study has limitations inherent to retrospective and observational single-center studies. Because our study included coronary procedures performed by five different well-seasoned surgeons having different CPB and revascularization strategies, the possibility of surgical bias remains at issue. In addition, despite the similarity in surgeon skill levels, unmeasured confounders outside the

range of adjustments made with PS matching may have influenced the study outcomes. We could not systematically evaluate and compare the completeness of revascularization and long-term graft patency between the two groups due to the limited availability of data for these assessments. Although the present study was focused on the clinical outcomes relating to the CPB strategy, the question of how the specific factors relating to each may influence the long-term clinical outcomes remain at issue that needs to be clarified through further randomized trials.

Conclusions

The OPB strategy was preferred over the conventional strategy during surgical revascularization in patients with significant morbidities in a real-world practice setting. The OPB strategy showed safety and efficacy comparable to the conventional strategy during CABG in selected patients that were matched for similar risk profiles. Although obviating aortic cross-clamping and cardioplegic arrest did not show a significantly greater clinical benefit compared to the conventional strategy as expected, a prospective randomized trial over a larger volume of patients may be warranted to better validate the beneficial impact of OPB-CABG as both a viable and a durable alternative strategy to C-CABG.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the institutional ethics committee/review board of Asan Medical Center (No. 2016-0225), which waived the requirement for informed consent owing to the retrospective study design.

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Supplementary

Table S1 Multivariate predictors of all-cause death and the composite of death and MACE (Cox regression)

Risk factors	All-cause death			Composite of death and MACE		
	OR	95% CI	P value	OR	95% CI	P value
Age (by 1-year increment)	1.07	1.05–1.09	<0.001	1.05	1.03–1.07	<0.001
Severe CKD (stage 4 or 5)	5.03	3.03–8.35	<0.001	4.09	2.57–6.51	<0.001
Atrial fibrillation	6.99	2.82–17.35	<0.001	8.62	3.75–19.77	<0.001
LVEF (by 1% increment)	0.97	0.95–0.99	0.004	0.97	0.96–0.98	<0.001
LVEDD (by 1-mm increment)	0.94	0.89–0.995	0.033	–	–	–
OPB vs. conventional strategy	1.23	0.81–1.87	0.333	1.34	0.95–1.89	0.098

Only variables with $P \leq 0.10$ in univariate analysis were included in the multivariate analysis. MACE, major adverse cardiac events; OR, odds ratio; CI, confidence interval; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; OPB, on-pump beating.

Table S2 Baseline characteristics in the PS-matched cohort (log-binomial method)

Characteristics	PS-matched cohort		
	C-CABG (n=180)	OPB-CABG (n=180)	SMD (%)
Age, years	63.6±9.3	62.6±9.0	10.1
Female sex	130 (72.2)	135 (75.0)	6.3
BMI, kg/m ²	24.6±2.8	24.7±3.0	4.4
Current smoker	31 (17.2)	37 (20.6)	8.5
Diabetes mellitus	95 (52.8)	85 (47.2)	11.1
Hypertension	114 (63.3)	109 (60.6)	5.7
Hyperlipidemia	40 (22.2)	33 (18.3)	9.7
Anemia	85 (47.2)	78 (43.3)	7.8
COPD	4 (2.2)	7 (3.9)	9.7
Severe CKD (stage 4 or 5)	9 (5.0)	7 (3.9)	5.4
Dialysis	6 (3.3)	4 (2.2)	6.8
Peripheral arterial disease	16 (8.9)	11 (6.1)	10.6
Atrial fibrillation	1 (0.6)	3 (1.7)	10.6
NYHA class 3 or 4	22 (12.2)	22 (12.2)	<0.1
CCS class 3 or 4	20 (11.1)	20 (11.1)	<0.1
Previous PCI	35 (19.4)	34 (18.9)	1.4
Previous cardiac surgery	1 (0.6)	2 (1.1)	6.1
History of CVA	28 (15.6)	23 (12.8)	8
Recent MI (<3 months)	15 (8.3)	13 (7.2)	4.1
Multivessel disease	179 (99.4)	180 (100.0)	10.6
Left main involvement	57 (31.7)	57 (31.7)	<0.1
Echocardiographic parameters			
LV ejection fraction, %	54.4±12.1	53.2±13.2	9.5
LV end-systolic dimension, mm	35.1±9.1	36.1±9.6	11.4
LV end-diastolic dimension, mm	51.6±6.7	52.5±7.4	12
Peak TR pressure gradient, mmHg	23.5±6.0	23.5±5.1	0.5
Significant TR	0 (0.0)	1 (0.6)	10.6
Significant MR	5 (2.8)	5 (2.8)	<0.1

Values are n (%) or mean ± standard deviation, unless otherwise indicated. OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; PS, propensity score; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; LV, left ventricular; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; MI, myocardial infarction; MR, mitral regurgitation; TR, tricuspid regurgitation; SMD, standardized mean difference.

Table S3 Operative outcomes in the PS-matched cohort (log-binomial method)

Clinical outcomes	C-CABG (n=180)	OPB-CABG (n=180)	P value
Early outcomes, n (%)			
Early (<30 days) death	0 (0.0)	3 (1.7)	0.246
Early major morbidity			
LCOS requiring MCS	0 (0.0)	2 (1.1)	0.478
Early stroke	1 (0.6)	3 (1.7)	0.615
Requirement for new dialysis	2 (1.1)	9 (5.0)	0.066
Bleeding	9 (5.0)	7 (3.9)	0.798
Pneumonia	2 (1.1)	4 (2.2)	0.681
Sternal wound infection	1 (0.6)	5 (2.8)	0.217
New-onset atrial fibrillation	11 (6.1)	15 (8.3)	0.541
Long-term outcomes, n (%/PY)			
All-cause death	34 (2.5)	30 (2.4)	0.46
MACE	13 (0.9)	12 (0.9)	0.779
Myocardial infarction	1 (0.1)	1 (0.1)	0.946
Revascularization	2 (0.1)	4 (0.3)	0.288
Late CVA	5 (0.4)	1 (0.1)	0.142
Hospitalization for CHF	6 (0.4)	8 (0.6)	0.301
Composite of death and MACE	44 (3.3)	39 (3.3)	0.487

Values are n (%) or mean \pm standard deviation, unless otherwise indicated. χ^2 test for early outcomes and log-rank test for late outcomes. OPB-CABG, on-pump beating heart coronary artery bypass grafting; C-CABG, conventional coronary artery bypass grafting; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; CVA, cerebrovascular accident; PY, patient-year; MACE, major adverse cardiac events; CHF, congestive heart failure.

Table S4 Comparative outcomes of OPB-CABG versus conventional CABG in the PS-matched cohort (log-binomial method)

Outcomes	PS-matched cohort		
	OR/HR	95% CI	P value
Early outcomes			
Early death	NA	NA	NA
LCOS requiring MCS	NA	NA	NA
Early stroke	3.03	0.38–61.65	0.339
New dialysis	4.68	1.19–31.01	0.051
Bleeding	0.77	0.27–2.11	0.61
Pneumonia	2.02	0.39–14.72	0.419
Sternal wound infection	5.11	0.81–98.51	0.138
New-onset atrial fibrillation	1.4	0.63–3.21	0.417
Long-term outcomes			
All-cause death	1.21	0.73–1.99	0.46
MACE	1.12	0.51–2.48	0.779
Death + MACE	1.17	0.75–1.81	0.487

Early outcomes are given as odds ratios; long-term outcomes are given as hazard ratios. Cox proportional hazard assumption (by scaled Schoenfeld residuals): death ($P=0.873$), MACE ($P=0.997$), composite outcome ($P=0.885$). PS, propensity score; OR, odds ratio; HR, hazard ratio; CI, confidence interval; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; MACE, major cardiac adverse event; NA, not applicable.