Off-pump technique reduces surgical mortality after elective coronary artery bypass grafting in patients with preoperative renal failure

Chikara Ueki, MD,^a Hiroaki Miyata, PhD,^b Noboru Motomura, MD, PhD,^c Ryuzo Sakata, MD, PhD,^d Genichi Sakaguchi, MD, PhD,^a Takehide Akimoto, MD, PhD,^a and Shinichi Takamoto, MD, PhD,^e for the Japan Cardiovascular Surgery Database

ABSTRACT

Objectives: Most randomized controlled trials of off-pump versus on-pump coronary artery bypass grafting (CABG) have included limited numbers of patients with preoperative renal failure. This study was performed to evaluate the association between the clinical benefit of the off-pump technique and chronic kidney disease stage.

Methods: We analyzed 38,051 patients with chronic kidney disease who underwent primary nonemergent isolated CABG from 2013 to 2015 as reported in the Japan Cardiovascular Surgery Database-Adult section. These patients were stratified into 4 categories according to their estimated glomerular filtration rate (eGFR) of 60 to 90, 30 to 59, and <30 mL/min/1.73 m², and hemodialysis-dependent. The clinical outcomes were compared between patients undergoing off-pump and on-pump CABG in each stratum using inverse probability of treatment weighting.

Results: In total, 23,634 (62.1%) patients were intended for off-pump CABG. In patients with mildly reduced renal function (eGFR 60–89 mL/min/1.73 m²), there was no significant risk reduction effect of off-pump CABG for surgical mortality. Conversely, in patients with moderate or severe renal disease (eGFR <60 mL/min/1.73 m²), off-pump CABG was associated with a significantly lower incidence of surgical death (odds ratio with 95% confidence interval: eGFR 30–59 mL/min/1.73 m², 0.66 [0.51–0.84]; eGFR <30 mL/min/1.73 m², 0.51 [0.37–0.72]; and hemodialysis-dependent, 0.68 [0.51–0.90]). In addition, in patients with severe renal disease (eGFR of <30), off-pump CABG was associated with a significantly lower incidence of de novo dialysis.

Conclusions: The off-pump technique significantly reduced surgical mortality in patients with moderate or severe preoperative renal dysfunction. (J Thorac Cardiovasc Surg 2018;156:976–83)

Propensity score-adjusted odds ratio for (A) surgical mortality and (B) de novo dialysis.

Central Message

The off-pump technique improves early mortality in patients with moderate or severe preoperative renal dysfunction.

Perspective

The association between the benefit of the off-pump technique and preoperative renal function remains unclear. In this large retrospective study, the mortality benefit of the off-pump technique was manifested in patients with moderate or severe renal dysfunction. This finding will help to identify patients who would benefit from the off-pump technique.

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From the ^aDepartment of Cardiovascular Surgery, Shizuoka General Hospital, Shizuoka, Japan; ^bDepartment of Health Policy and Management, Keio University, Tokyo, Japan; ^cDepartment of Cardiovascular Surgery, Toho University, Sakura Medical Center, Sakura, Japan; ^dDepartment of Cardiovascular Surgery, Kobe City Medical Center General Hospital, Kobe, Japan; and ^eMitsui Memorial Hospital, Tokyo, Japan.

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Address for reprints: Chikara Ueki, MD, Department of Cardiovascular Surgery, Shizuoka General Hospital, 4-27-1 Kita-Ando Aoi-ku, Shizuoka 420-8527, Japan (E-mail: uekichikara@gmail.com).

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Preoperative renal disease is a well known risk factor for adverse events after coronary artery bypass grafting (CABG).^{1,2} A report from the Society of Thoracic

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CKD	= chronic kidney disease
eGFR	= estimated glomerular filtration rate
GFR	= glomerular filtration rate
IPTW	= inverse probability of treatment weighting
JCVSD	= Japan Cardiovascular Surgery Database
ONCAB	= on-pump coronary artery bypass grafting
OPCAB	= off-pump coronary artery bypass grafting
PCI	= percutaneous coronary intervention
STS	= Society of Thoracic Surgeons

Surgeons (STS) national database stated that preoperative renal disease is common in patients who undergo CABG and that early mortality and morbidity after CABG rise inversely with declining preoperative renal function.³

Previous meta-analyses of randomized trials comparing off-pump CABG (OPCAB) and on-pump CABG (ONCAB) have failed to show the mortality benefit of OPCAB.⁴⁻⁶ However, it has also been shown that the mortality benefit of OPCAB is significantly related to the risk profile of the enrolled patients.⁴ In addition, multiple retrospective studies have shown the mortality benefit of OPCAB in high-risk patient cohorts (Video 1).⁷⁻⁹ Therefore, it can be hypothesized that OPCAB is associated with a mortality benefit in patients with preoperative renal dysfunction. Most randomized trials have included limited numbers of patients with preoperative renal disease.⁵ For example, a recent large randomized trial, the Randomized On/Off Bypass (ROOBY) trial, included only a small number of patients with an elevated serum creatinine concentration (8.5% in the OPCAB group and 7.2% in the ONCAB group).¹⁰ Another recent large randomized trial, the CABG Off or On Pump Revascularization Study (CORONARY), also included only a limited number of dialysis patients (1.7% in the OPCAB group and 1.1% in the ONCAB group).¹¹ Consequently, most randomized trials could not evaluate the clinical benefit of OPCAB in patients with preoperative renal disease. A risk-adjusted retrospective study using a large data set is therefore needed to understand the association between the benefit of OPCAB and preoperative renal disease. This study was performed to determine the association between the clinical benefit of OPCAB and preoperative chronic kidney disease (CKD) stage using data from the Japan Cardiovascular Surgery Database (JCVSD).

METHODS

The JCVSD

The JCVSD was established in 2000 to evaluate surgical outcomes after cardiovascular procedures in hospitals throughout Japan. As of 2014, the

VIDEO 1. Off-pump coronary artery bypass grafting with skeletonized bilateral internal thoracic arteries for a patient with left main coronary disease. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)30934-6/fulltext](https://www.jtcvs.org/article/S0022-5223(18)30934-6/fulltext).

JCVSD-Adult section had collected clinical information from more than 538 hospitals across Japan. More than 300 variables in the data collection form are nearly identical to those of the STS National Database. The content of the JCVSD-Adult section is available online at <http://www.jacvds.umin.jp>. The methods of data collection from the JCVSD have been previously described.¹ The institutional review board at each participating hospital has approved the collection of their data for use in the JCVSD, and the Data Utilization Committee of the JCVSD approved the use of data for the present study. To date, data collection has achieved a high level of completion, with less than 3% of entries missing for overall preoperative risk factors used in risk models. In addition, the accuracy of submitted data is maintained by regular data auditing in which monthly visits are made to participating hospitals to check the reported data against clinical records. Data validity is further confirmed by independent comparison of specific hospitals' volume of cardiac surgeries entered in the JCVSD with that reported in the annual survey of the Japanese Association for Thoracic Surgery.¹² Further, from 2010 onward, the JCVSD served as part of the National Clinical Database in Japan, which includes clinician-initiated databases reflecting all surgical fields. By the end of 2013, the JCVSD had become a national database covering almost all cardiac procedures in Japan.

Study Population

The data of patients included in the JCVSD-Adult section from January 1, 2013, to December 31, 2015, were analyzed. Patients with complete data on preoperative renal function who underwent primary nonemergent isolated CABG were included. The exclusion criteria were an emergent or salvage status, redo surgery, and preoperative cardiogenic shock. Records with missing data on age (or out-of-range age), sex, or 30-day status (see "Study End Points" for an explanation) were excluded. With the exception of the body surface area and preoperative creatinine concentration, all missing or out-of-range values were imputed using the variable-specific median value. Upon completion of this data cleaning procedure, 38,804 patients were detected. After excluding 753 patients with normal renal function (estimated glomerular filtration rate [eGFR] of ≥ 90 mL/min/1.73 m²), 38,051 patients with CKD were included in the present study. These patients were stratified into 4 groups according to their most recently available preoperative eGFR, which was calculated from the Modification of Diet in Renal Disease equation: $\text{eGFR mL/min/1.73 m}^2 = 194 \times (\text{serum creatinine level [mg/dL]})^{-1.094} \times (\text{age [years]})^{-0.287} \times 0.739$ (if female).¹³ On the basis of the result, the patients were determined to have mild renal disease (eGFR = 60–90 mL/min/1.73 m²; n = 7260), moderate renal disease (eGFR = 30–59 mL/min/1.73 m²; n = 22,727), severe renal disease (eGFR <30 mL/min/1.73 m²; n = 4098), or hemodialysis dependence (n = 3966). Because an intention-to-treat principle was applied to all statistical analyses, patients intended for OPCAB were included in the OPCAB group even if they were converted intraoperatively to ONCAB and vice versa.

Study End Points

The study end points were surgical mortality, postoperative renal failure with newly required dialysis, and a composite outcome consisting of surgical mortality and major morbidity. Surgical mortality was defined as death within 30 days after surgery and death during the index hospitalization. Major morbidity was defined as any of the following postoperative complications during hospitalization or within 30 days postoperatively: stroke, reoperation for bleeding, mechanical ventilation required for >24 hours postoperatively, renal failure with newly required dialysis, or deep sternal wound infection.

Statistical Analysis

Continuous variables are expressed as mean $\pm$ SD, and the unpaired *t* test or Wilcoxon rank sum test was used for comparisons. Categorical variables are expressed as percentages and were compared using the χ^2 test. Two risk-adjustment methods were used to adjust for differences in baseline characteristics because the patients were not randomly assigned to receive either ONCAB or OPCAB. First, the risk-adjusted effect of OPCAB on each clinical outcome was estimated within a simultaneous multivariable logistic regression model that included 29 preoperative variables: age, sex, body mass index, presence of unstable angina, peripheral vascular disease, cerebrovascular disease (presence of stroke or a history of transient ischemic attack), hypertension, hyperlipidemia, diabetes, smoking history, chronic lung disease (mild, moderate, or severe), immunosuppressive therapy, arrhythmia, preoperative intra-aortic balloon pump counterpulsation, preoperative inotropic agents, grade ≥ 1 aortic stenosis, grade ≥ 2 aortic regurgitation, grade ≥ 1 mitral stenosis, grade ≥ 2 mitral regurgitation, grade ≥ 2 tricuspid regurgitation, previous percutaneous coronary intervention (PCI), history of myocardial infarction, left ventricular dysfunction (left ventricular ejection fraction of <30%), congestive heart failure, New York Heart Association class III or IV, triple-vessel disease, left main coronary artery disease, urgent surgery, and hospital annual CABG volume. All of these variables except hospital annual CABG volume are the known risk factors comprising the STS risk model for isolated CABG.² Second, inverse probability of treatment weighting (IPTW) was performed to verify the estimated prognostic effect.¹⁴ Each patient's estimated propensity score (the probability of being intended to undergo OPCAB) was calculated in a simultaneous multivariable logistic regression model including the 29 previously mentioned preoperative variables as covariates. Propensity scores were created within the whole cohort and each of the 4 renal disease categories (c-statistic with 95% confidence interval: whole cohort, 0.588 [0.583–0.594]; mild renal disease, 0.628 [0.615–0.641]; moderate renal disease, 0.632 [0.625–0.639]; severe renal disease, 0.642 [0.624–0.659]; hemodialysis dependence, 0.633 [0.616–0.651]). The inverse probability weights calculated using the propensity score were applied to a logistic regression model to obtain the propensity-weighted odds ratio of OPCAB. The same propensity scores were used for every outcome. All reported *P* values are 2-sided, and *P* < .05 was considered statistically significant. Statistical analysis was performed using SPSS version 20.0 (IBM Corp, Armonk, NY).

RESULTS

Patient Characteristics and Surgical Data

Among the 38,051 patients analyzed, 23,634 (62.1%) were planned for OPCAB. Among these patients, unplanned conversion from OPCAB to ONCAB occurred in 734 patients (3.1%). The patient characteristics in the overall cohort are presented in Table 1. Patients in the OPCAB group were significantly older and had more comorbidities such as cerebrovascular disease, chronic

lung disease, peripheral vascular disease, a history of PCI, and aortic valve insufficiency. The ONCAB group contained significantly more patients with diabetes and had a significantly higher prevalence of previous myocardial infarction, left ventricular dysfunction, unstable angina, congestive heart failure, New York Heart Association class III or IV, left main coronary artery disease, and triple-vessel disease. Moderate to severe renal disease (eGFR <60 mL/min/1.73 m²) was observed in most patients (79.1% in the ONCAB group, 79.5% in the OPCAB group). Although the preoperative eGFR was slightly lower in the OPCAB than ONCAB group, the distribution of renal disease stages was almost identical between the 2 groups.

As shown in Table 2, the surgical duration was significantly shorter in the OPCAB than ONCAB group (307.3 vs 354.7 minutes, respectively). In the ONCAB group, cardioplegic heart arrest was used in 8190 patients (56.8%), and cold blood cardioplegia was used in most of these patients. The number of distal anastomoses was significantly lower in the OPCAB than ONCAB group (3.02 vs 3.17, respectively).

Clinical Outcomes

Surgical mortality. In the whole cohort, the surgical mortality rate was significantly lower in the OPCAB than ONCAB group (1.5% vs 2.4%, respectively; *P* < .001). When stratified according to preoperative renal function, worsening preoperative renal dysfunction was associated with increasing surgical mortality (Table 3).

Although the risk reduction effect of OPCAB was not statistically significant in the mild renal disease group, the risk reduction effect of OPCAB was significant in patients with moderate or severe renal disease (Tables 3 and 4). The risk adjustment in the multivariable logistic regression model as well as the IPTW analyses confirmed these results (Table 4).

Renal failure with newly required dialysis. In the whole cohort, the incidence of newly required dialysis was significantly lower in the OPCAB than ONCAB group (1.5% vs 2.1%, respectively; *P* < .001). In patients with normal renal function or mild to moderate renal disease, the incidence of newly required dialysis was $\leq 1\%$. Conversely, in patients with severe renal disease, the incidence of newly required dialysis was quite high (12.9% in the ONCAB group, 7.8% in the OPCAB group; Table 3).

The renoprotective effect of OPCAB was significant in patients with severe renal disease (Tables 3 and 4). The risk adjustment in the multivariable logistic regression model as well as the IPTW analyses confirmed these results (Table 4).

Composite outcome. In the whole cohort, the incidence of the composite outcome was significantly lower in the

TABLE 1. Patient characteristics

Variable	% Missing	ONCAB (n = 14,417)	OPCAB (n = 23,634)	P value
Age, y	0.0	68.5 ± 10.0	69.8 ± 9.7	.001
Male sex	0.0	11,636 (80.7)	18,976 (80.3)	.249
Body mass index	0.0	23.8 ± 3.7	23.7 ± 3.5	<.001
Smoking history	0.0	7696 (53.4)	12,541 (53.0)	.427
Diabetes	0.0	8066 (55.9)	12,526 (53.0)	<.001
Hyperlipidemia	0.0	9221 (64.0)	15,240 (64.5)	.421
Hypertension	0.0	11,220 (77.8)	18,670 (79.0)	.004
Serum creatinine, mg/dL	0.0	1.70 ± 2.33	1.72 ± 2.39	.246
eGFR, mL/min/1.73 m ²	0.0	45.2 ± 21.4	45.0 ± 25.3	.294
60 to 90 (mild)		2789 (19.0)	4471 (18.5)	.295
30 to 59 (moderate)		8620 (58.6)	14,107 (58.5)	.807
<30 (severe)		1498 (10.2)	2600 (10.8)	.066
Preoperative dialysis	0.0	1510 (10.3)	2456 (10.2)	.788
Cerebrovascular disease	0.0	1595 (11.1)	2956 (12.5)	<.001
Chronic lung disease	0.0	1730 (12.0)	3462 (14.6)	<.001
Peripheral vascular disease	0.0	2303 (16.0)	4418 (18.7)	<.001
Previous PCI	0.0	3376 (23.4)	6134 (26.0)	<.001
Previous myocardial infarction	0.0	5255 (36.5)	7307 (30.9)	<.001
Congestive heart failure	0.0	3470 (24.1)	5111 (21.6)	<.001
Unstable angina	0.0	4676 (32.4)	6621 (28.0)	<.001
Preoperative arrhythmia	0.0	872 (6.0)	1396 (5.9)	.036
NYHA class III or IV	0.0	2561 (17.8)	3130 (13.2)	<.001
LVEF of <30%	0.0	1178 (8.2)	978 (4.1)	<.001
Preoperative IABP	0.0	1852 (12.8)	2676 (11.3)	<.001
Preoperative inotropic agents	0.0	153 (1.0)	176 (0.7)	.001
Left main disease ≥50%	3.5	5879 (40.8)	9147 (38.7)	<.001
Triple-vessel disease	3.5	11,048 (76.6)	16,930 (71.6)	<.001
Aortic stenosis grade ≥1	0.0	477 (3.3)	812 (3.4)	.387
Aortic insufficiency grade ≥2	0.0	927 (6.4)	1994 (8.4)	<.001
Mitral stenosis grade ≥1	0.0	158 (1.1)	218 (0.9)	.152
Mitral insufficiency grade ≥2	0.0	2318 (16.1)	3944 (16.7)	.109
Tricuspid insufficiency grade ≥2	0.0	1095 (7.6)	2222 (9.4)	<.001
Steroids	0.0	206 (1.4)	414 (1.8)	.009
Urgent status	0.0	1676 (11.6)	2259 (9.6)	<.001

Data are presented as n (%) or mean ± SD. ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump counterpulsation.

OPCAB than ONCAB group (6.8% vs 10.3%, respectively; $P < .001$). The incidence of the composite outcome tended to rise as the preoperative renal function worsened. In all renal function strata except patients with normal renal function, the incidence of the composite outcome was significantly lower in the OPCAB group (Table 3). These results were confirmed in the multivariable logistic regression model as well as in the IPTW analyses (Table 4).

DISCUSSION

The mortality benefit of OPCAB has not been confirmed in previous randomized trials.^{4,6} However, most randomized trials that compared OPCAB versus ONCAB did not report the proportion of enrolled patients with preoperative renal disease.⁵ In addition, among the randomized trials that did report the proportion of patients with renal disease, the prevalence of chronic renal failure

TABLE 2. Surgical data for overall cohort

Variable	ONCAB (n = 14,417)	OPCAB (n = 23,634)	P value
Surgery duration, min	354.7 ± 102.9	307.3 ± 100.2	<.001
CPB time, min	144.8 ± 55.8	—	—
Cardioplegia-arrested heart	8190 (56.8)	—	—
Blood cardioplegia	6372 (77.8)	—	—
Cold cardioplegia	6390 (78.0)	—	—
Distal anastomoses, n	3.17 ± 1.11	3.02 ± 1.23	<.001
ITA use			
Left	13,605 (94.4)	22,375 (94.7)	.108
Right	4387 (30.4)	10,461 (44.3)	<.001
Bilateral	4081 (28.3)	9795 (41.4)	<.001
None	500 (3.5)	594 (2.5)	<.001
Missing	6 (0.0)	0 (0.0)	

Data are presented as n (%) or mean ± SD. *ONCAB*, On-Pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *CPB*, cardiopulmonary bypass; *ITA*, internal thoracic artery.

was only 4.1%.⁵ Considering that renal function is an important risk factor in the reported risk models for CABG,^{1,2} this insufficient evaluation of preoperative renal function is a serious problem when interpreting the results of randomized trials. In this context, large retrospective studies focusing on preoperative renal function are still required to evaluate the clinical benefit of OPCAB. In the present study, we evaluated the association between the prognostic effect of OPCAB and preoperative renal function using a large data set from the JCVSD. The results showed that the risk reduction effect of OPCAB for surgical mortality was significant in patients with moderate or severe preoperative renal dysfunction.

First, the risk reduction effect of OPCAB for surgical mortality was significant in patients with moderate or severe preoperative renal dysfunction. This risk reduction effect of OPCAB was not shown in patients with normal renal function or mild preoperative renal dysfunction. This result is consistent with the findings reported by Chawla et al,¹⁵ who compared OPCAB versus ONCAB among various patient strata of preoperative renal function using a large data set (n = 742,909) from the STS national database. In the propensity analysis, the authors reported that patients with CKD (eGFR <90 mL/min/1.73 m²) experienced an associated mortality benefit of OPCAB but that patients with normal renal function did not (risk difference with

TABLE 3. Postoperative outcomes among various stages of renal disease

Outcome	ONCAB (n = 14,417)	OPCAB (n = 23,634)	P value
Overall cohort	14,417	23,634	
Surgical mortality	354 (2.5)	344 (1.5)	<.001
Newly required dialysis	308 (2.1)	357 (1.5)	<.001
Composite outcome	1501 (10.4)	1600 (6.8)	<.001
Mild renal disease (eGFR 60-90)	2789	4471	
Surgical mortality	34 (1.2)	30 (0.7)	.015
Newly required dialysis	16 (0.6)	22 (0.5)	.639
Composite outcome	182 (6.5)	193 (4.3)	<.001
Moderate renal disease (eGFR 30-59)	8620	14,107	
Surgical mortality	133 (1.5)	131 (0.9)	<.001
Newly required dialysis	81 (0.9)	102 (0.7)	<.001
Composite outcome	726 (8.4)	749 (5.3)	<.001
Severe renal disease (eGFR <30)	1498	2600	
Surgical mortality	82 (5.5)	72 (2.8)	<.001
Newly required dialysis	193 (12.9)	203 (7.8)	<.001
Composite outcome	339 (22.6)	369 (14.2)	<.001
Preoperative dialysis	1510	2456	
Surgical mortality	105 (7.0)	111 (4.5)	.001
Composite outcome	254 (16.8)	289 (11.8)	<.001

Data are presented as number (%). eGFR is expressed in mL/min/1.73 m². *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *eGFR*, estimated glomerular filtration rate.

TABLE 4. Effect of off-pump technique on outcomes in patients with various stages of renal disease

Outcome	OR (95% CI)		
	Unadjusted	Risk-adjusted (multivariable logistic regression)	IPTW
Overall cohort			
Surgical mortality	0.59 (0.51-0.68)*	0.65 (0.56-0.76)*	0.66 (0.56-0.77)*
Newly required dialysis	0.70 (0.60-0.82)*	0.76 (0.65-0.89)†	0.75 (0.64-0.88)†
Composite outcome	0.62 (0.58-0.67)*	0.67 (0.62-0.72)*	0.67 (0.62-0.73)*
Mild renal disease (eGFR 60-90)			
Surgical mortality	0.55 (0.33-0.90)‡	0.68 (0.40-1.14)	0.67 (0.41-1.11)
Newly required dialysis	0.86 (0.45-1.63)	1.22 (0.62-2.41)	1.15 (0.59-2.21)
Composite outcome	0.65 (0.52-0.80)*	0.73 (0.59-0.91)†	0.73 (0.59-0.90)†
Moderate renal disease (eGFR 30-59)			
Surgical mortality	0.60 (0.47-0.76)*	0.64 (0.50-0.83)*	0.66 (0.51-0.84)†
Newly required dialysis	0.77 (0.57-1.03)	0.83 (0.61-1.13)	0.84 (0.62-1.14)
Composite outcome	0.61 (0.55-0.68)*	0.65 (0.58-0.72)*	0.66 (0.59-0.73)*
Severe renal disease (eGFR <30)			
Surgical mortality	0.49 (0.36-0.68)*	0.51 (0.36-0.73)*	0.51 (0.37-0.72)*
Newly required dialysis	0.57 (0.46-0.71)*	0.62 (0.49-0.77)*	0.61 (0.49-0.75)*
Composite outcome	0.57 (0.48-0.67)*	0.59 (0.50-0.71)*	0.59 (0.50-0.70)*
Preoperative dialysis			
Surgical mortality	0.63 (0.48-0.83)†	0.67 (0.50-0.90)†	0.68 (0.51-0.90)†
Composite outcome	0.66 (0.55-0.79)*	0.64 (0.53-0.78)*	0.66 (0.55-0.80)*

eGFR is expressed in mL/min/1.73 m². OR, Odds ratio; CI, confidence interval; IPTW, inverse probability of treatment weighting; eGFR, estimated glomerular filtration rate. **P* < .001. †*P* < .01. ‡*P* < .05.

95% confidence interval: eGFR of 60–89: 0.09, 0.02–0.17; eGFR of 30–59: 0.30, 0.12–0.47; and eGFR of 15–29: 1.92, 1.06–2.78).¹⁵ There are 2 major differences between the data from the national database of the United States and Japan. The first is the prevalence of renal dysfunction in patients who underwent CABG. In the report from the STS national database, CKD (eGFR <60 mL/min/1.73 m²) was present in 24.1% of the overall cohort.¹⁵ In the present study, however, CKD (eGFR <60 mL/min/1.73 m²) was present in as high as 79.4% of the overall cohort. In the report from the National Cardiovascular Data Registry Cath-PCI registry, CKD was present in 29.2% of the overall patients who underwent PCI in the United States,¹⁶ which is comparable with that of patients who underwent CABG (24.1%). In contrast, the Japanese multicenter PCI registries reported that the prevalence of CKD in patients who underwent PCI was 28.3% to 38.5%,^{17,18} which is comparable with that of patients in the United States and is extremely low compared with patients who underwent CABG in the present study. Therefore, the high prevalence of CKD in the present study cohort seems to have been affected by the differences in the coronary revascularization strategy (PCI/CABG ratio) between the 2 countries rather than the differences in the prevalence of CKD among different ethnic groups. The second is the frequency of OPCAB. In the report from the STS national database, 21.3% of patients were intended to undergo OPCAB.¹⁵ However, in the present study, up to 62.1% of patients were intended to undergo OPCAB. Despite these 2 large differences, the

mortality benefit of OPCAB in patients with preoperative renal disease was confirmed in both of the studies from the United States and Japan. This seems to support the validity of the results in the present study. This mortality benefit of OPCAB, which has been shown in patients with preoperative renal disease, would explain why the previous randomized trials could not show the mortality benefit of OPCAB.

Second, the renoprotective effect of OPCAB was significant in patients with severe preoperative renal dysfunction. This is consistent with the previously mentioned study that analyzed data from the STS national database.¹⁵ In their propensity-weighted analysis, Chawla et al¹⁵ showed that the renoprotective effect of OPCAB was significant in patients with moderate or severe renal disease (risk difference per 100 patients with 95% confidence interval: eGFR of 30–59: 0.47, 0.31–0.62; eGFR of 15–29: 2.79, 1.37–4.20). However, in their center-level analysis, the renoprotective effect of OPCAB was confirmed only in patients with severe renal disease.¹⁵ Other studies have also reported the renoprotective effect of OPCAB in patients with preoperative renal disease.^{19,20} In their study of patients with non-dialysis renal insufficiency (serum creatinine concentration of >150 μmol/L), Ascione et al¹⁹ reported that the postoperative serum creatinine concentration was significantly higher in the ONCAB than OPCAB group at 12 hours postoperatively and that the incidence of postoperative dialysis was higher in the ONCAB than OPCAB group (15.8% vs 5.9%,

respectively; $P = .06$). Furthermore, Sajja et al²⁰ performed the first randomized trial to compare OPCAB versus ONCAB in patients with non-dialysis renal insufficiency and reported worsening of renal function (serum creatinine concentration, glomerular filtration rate [GFR]) in the ONCAB than OPCAB group. In contrast, a meta-analysis of randomized trials did not show a risk reduction effect of OPCAB in patients with newly required dialysis.⁵ Moreover, some other studies have denied the renoprotective effect of OPCAB.²¹⁻²³ In their case-matched study of 5589 patients who underwent CABG, Elmistekawy et al²¹ showed that the requirements of postoperative newly required dialysis were equivalent at 2.6% in the OPCAB group and 2.1% in the ONCAB group. In a propensity score analysis of patients with preoperative renal dysfunction, Chukwuemeka et al²² reported that OPCAB was not associated with a reduced risk of renal dysfunction. In addition, a study of acute kidney injury after CABG in elderly patients did not show a renoprotective effect of OPCAB.²³ However, these studies might lack statistical power because of the limited number of enrolled patients with moderate or severe renal dysfunction. In the previously mentioned study using the STS national database, the risk difference of newly required dialysis per 100 patients was 0.47 in patients with moderate renal disease and 2.79 in patients with severe renal disease.¹⁵ This means that the “number needed to treat” was 213 patients with moderate renal disease and 36 patients with severe renal disease. The previously mentioned study by Elmistekawy et al²¹ included up to 1368 patients with moderate or severe renal dysfunction (GFR of 30–59, $n = 1244$ patients; GFR of 15–29, $n = 124$ patients), but the number of patients who underwent OPCAB was limited because of the low frequency of OPCAB (9.8%). Another study by Reents et al²³ included only 299 patients with moderate or severe renal dysfunction in the OPCAB group (GFR of 30–59, $n = 268$; GFR of 15–29, $n = 31$ patients). The study by Chukwuemeka et al,²² which focused on patients with preoperative renal dysfunction, included only 146 patients in the OPCAB group. Considering the number needed to treat, enrollment of quite a large number of OPCAB patients with moderate or severe renal dysfunction is required to prove the renoprotective effect of OPCAB. This also explains why the renoprotective effect of OPCAB was not shown in previous randomized trials.

Consistent with the results of previous large randomized trials,^{10,11} fewer distal anastomoses were placed per patient who underwent OPCAB than ONCAB in the present study. Therefore, we performed an additional analysis on postoperative myocardial infarction. However, the risk of perioperative myocardial infarction was not higher in the OPCAB group as shown by the odds ratio (OPCAB vs ONCAB) for perioperative myocardial infarction with

95% confidence interval: overall cohort (0.7% vs 0.9%), 0.82 (0.65–1.03); mild renal disease (0.8% vs 0.8%), 1.02 (0.59–1.76); moderate renal disease (0.7% vs 1.1%), 0.67 (0.51–0.90); severe renal disease (0.5% vs 0.6%), 0.90 (0.39–2.10); and preoperative dialysis (0.8% vs 0.4%), 2.47 (0.95–6.43) (estimated using the IPTW method). However, we could not estimate the long-term prognostic effect of fewer distal anastomoses in the OPCAB cohort because of the lack of long-term follow-up data in our database.

The present study has several limitations. First, because of the retrospective nature of this study, multivariable logistic regression and propensity score analysis could not completely adjust for potential selection bias. However, the confirmation of the clinical advantage of OPCAB using 2 different risk adjustment methods reinforces the validity of our results. Second, this study included only Japanese patients. Considering the differences in the prevalence of CKD among different ethnic groups,²⁴ it is necessary to verify whether the findings of the present study can be applied to other ethnic groups. However, as mentioned previously, the report from the STS national database¹⁵ and the present study show similar results despite the large difference in the prevalence of CKD. Third, a relatively small number of adverse events occurred in patients with mild renal disease. This raises concern that the comparative analyses in this stratum might lack sufficient statistical power to detect the clinical effect of OPCAB. Therefore, we cannot make a definitive conclusion about the clinical benefit of OPCAB in patients with mild renal disease. Additionally, patients with CKD in the present study showed a high incidence of other preoperative risk factors such as diabetes mellitus (ONCAB, 55.9%; OPCAB, 53.0%), New York Heart Association class III or IV heart failure (ONCAB, 17.8%; OPCAB, 13.2%), and left main coronary artery disease (ONCAB, 40.8%; OPCAB, 38.7%). With this high-risk profile of the present cohort, the external validity of our findings for the general CABG population might be controversial. Finally, because of the lack of long-term data in the present study, our analysis of the clinical benefit of OPCAB is limited to short-term outcomes. Boulton et al²⁵ reported that among patients with moderate to severe renal disease, long-term survival was worse in those who underwent OPCAB than ONCAB. The association between OPCAB and long-term survival in patients with preoperative renal dysfunction requires further study.

CONCLUSIONS

Among patients who undergo elective CABG, OPCAB significantly reduces surgical mortality in patients with moderate or severe preoperative renal dysfunction. It is essential to consider the preoperative renal function of enrolled patients when interpreting the results of

randomized trials that evaluated the risk reduction effect of OPCAB. Further comparison of OPCAB versus ONCAB with a particular focus on this high-risk patient cohort is needed.

Webcast

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Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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