Late outcomes of off-pump versus on-pump coronary bypass in patients with diabetes: A nationwide study from Taiwan

Kuan-Chih Huang, MD,^a I-Hui Wu, MD,^b Nai-Kuan Chou, MD,^b Yen-Yun Yang,^c Lung-Chun Lin, MD,^a Hsi-Yu Yu, MD,^b and Nai-Hsin Chi, MD^b

ABSTRACT

Objectives: Although the benefits and risks of on- and off-pump coronary artery bypass have been compared in several clinical trials, large-scale studies regarding long-term outcomes in patients with diabetes are lacking. We compared long-term outcomes after on- and off-pump coronary artery bypass in patients with diabetes.

Methods: We evaluated outcomes in 16,215 patients with diabetes who underwent isolated coronary artery bypass from 2000 to 2011. Clinical data validity was regulated by the single-payer, universal, and nationwide reimbursement systems. Long-term outcomes were compared using propensity score matched analyses.

Results: Off-pump surgery was associated with a greater incidence of repeat revascularization ($P = .0036$) in the long term. Propensity score matching identified 3796 patients in each group. There were no significant differences between on- and off-pump surgery regarding the long-term risks of mortality (hazard ratio [HR], 0.95; 95% confidence interval [CI], 0.87-1.02, $P = .1667$), stroke (HR, 0.97; 95% CI, 0.87-1.09, $P = .6074$), and myocardial infarction (HR, 1.05; 95% CI, 0.91-1.20, $P = .5207$). Off-pump surgery offered a survival benefit within 30 days (HR_{on vs off}, 1.52, 95% CI, 1.24-1.85, $P < .0001$). In patients with diabetes and end-stage renal disease, on-pump surgery provided a significant long-term survival benefit (HR_{on vs off}, 0.68, 95% CI, 0.51-0.91).

Conclusions: In patients with diabetes undergoing isolated coronary artery bypass, off-pump surgery provided a 30-day benefit in mortality, but both groups had similar long-term survival. In off-pump surgery, repeat revascularization was a concern in the long term. In patients with diabetes and end-stage renal disease, on-pump surgery has long-term survival benefits. (J Thorac Cardiovasc Surg 2019;157:960-9)

Off-pump and on-pump surgery had equal long-term mortality in patients with diabetes.

Central Message

In patients with diabetes, off-pump coronary artery bypass offered a survival benefit within 30 days. Off-pump and on-pump surgery had similar long-term survival.

Perspective

Long-term results of off-pump versus on-pump coronary artery bypass in patients with diabetes, especially in Asian population, are lacking. In patients with diabetes, whether off-pump or on-pump coronary artery bypass is to be performed depends not only on 30-days outcomes but also on longer-term outcomes.

See Commentaries on pages 970, 972, and 974.

In patients undergoing coronary artery bypass graft surgery (CABG), diabetes mellitus increases short-term

mortality¹ and morbidity.^{2,3} CABG when compared with percutaneous coronary intervention has superior outcomes in patients with diabetes.⁴ Diabetes itself is an adverse outcome predictor in this specific patient group. Patients with diabetes who underwent CABG had worse survival outcomes than those without diabetes (Figure E1). Morbidities such as stroke, renal failure, and infection are

From the Departments of ^aInternal Medicine and ^bSurgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei; and ^cNational Taiwan University, Health Data Research Center, Taipei, Taiwan.

Supported in part by the Ministry of Science and Technology (105-2314-B-002-128-MY2).

Received for publication Nov 2, 2017; revisions received July 31, 2018; accepted for publication Aug 1, 2018; available ahead of print Oct 25, 2018.

Address for reprints: Nai-Hsin Chi, MD, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, No. 7, Chung Shan S. Rd, Zhongzheng Dist, Taipei City 10002 (E-mail: chinaihsin@gmail.com).

0022-5223/\$36.00

Copyright © 2018 by The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2018.08.084>

Scanning this QR code will take you to the article title page to access supplementary information.

Abbreviations and Acronyms

BARI 2D	= Bypass Angioplasty Revascularization Investigation 2 Diabetes
CABG	= coronary artery bypass grafting
CI	= confidence interval
HR	= hazard ratio
NHIRD	= National Health Insurance Research Database

considered to be associated with cardiopulmonary bypass.^{3,5-10} Off-pump CABG has been proven to be beneficial in reducing such postoperative morbidities in patients with diabetes¹¹⁻¹³; however, there is a controversy regarding the long-term results of off- versus on-pump CABG,^{9,10,14-19} and the long-term all-cause mortality and repeat revascularization rate of off-pump CABG in patients with diabetes remain unclear.^{11,20} We believed that by studying the long-term outcomes of patients with diabetes who underwent CABG, we can provide surgeons with clear insights on the surgical strategy in specific patients with diabetes. The main objective of this study was to compare long-term outcomes after off- and on-pump CABG in patients with diabetes by using data from the National Health Insurance Research Database (NHIRD) in Taiwan.

METHODS

Patients

The study was approved by the Research Ethics Committee of National Taiwan University Hospital (institutional review board approval: 201802001W). All patients undergoing cardiac surgery are prospectively registered in the NHIRD, which records baseline patient characteristics and surgery type (regarding usage of cardiopulmonary bypass, the amount of coronary arteries grafted) as original claim data for obligatory reimbursement under the single-payer National Health Insurance program in Taiwan. As a result, even if a patient is not followed at the same hospital in which the CABG was performed, all of the clinical data at any other hospital would still be registered after each medical service. A total of 41,155 patients who underwent CABG between 2000 and 2011 were identified (Figure 1); we excluded patients younger than 18 years of age ($n = 159$), foreigners ($n = 134$; foreigners who went back to their own country after surgery were not followed in the national health system), those who underwent emergency surgery ($n = 1484$), and those who underwent concomitant valvular surgery ($n = 6383$).

Finally, 32,995 patients who met the inclusion criteria formed the overall study population. Of these, 49.1% patients ($n = 16,215$) were diagnosed with diabetes mellitus: 4100 patients with diabetes (25.3%) underwent off-pump CABG, 9341 (57.6%) underwent on-pump CABG, and 2774 (17.1%) underwent on-pump beating-heart CABG. The on-pump beating-heart CABG group was excluded to compare the effects of cardiac pulmonary bypass under the same situation as in previous studies.^{10,16} There might be some off-pump conversion putting in this category; therefore, to examine the pure off-pump and on-pump differences, patients who underwent on-pump beating-heart CABG were excluded. The perioperative data and incidence rates of mortality and morbidity were also extracted from the NHIRD. The duration of follow-up was calculated from the date of surgery to that of death or the last medical contact.

FIGURE 1. Enrollment, grouping, and follow-up of patients. For some of the 8160 patients who were excluded, there was more than one reason for exclusion. In 15,338 patients with diabetes with isolated coronary artery bypass, those who were operated under cardiopulmonary bypass with heart beating were excluded for grouping. CABG, Coronary artery bypass grafting.

Preoperative patient data were obtained relative to age (stratified into 18-64, 65-74, and 75+ years), sex, hypertension, previous stroke, history of myocardial infarction, peripheral vascular disease, chronic obstructive pulmonary disease, pacemaker implantation, atrial fibrillation, cancer, chronic kidney disease, renal-replacement therapy, extent of coronary artery disease, and hospital volume of CABG. Diabetes mellitus treatment details were also extracted and categorized as oral medication control and insulin control. Guidelines recommend that medication such as aspirin, statins, and angiotensin II receptor be reimbursed in Taiwan; thus, we did not evaluate the prescription status in our study.

Study Endpoints

The primary endpoint of our study was mortality and the principal secondary composite endpoint included death, stroke, myocardial infarction, and repeat revascularization. Cardiovascular disease-related and cerebrovascular disease-related deaths were also documented. Hazard ratios (HRs) of the aforementioned endpoints were analyzed at 30 days and 1 year and followed up to 10 years or death/censoring.

Statistical Analysis

The basic demographic characteristics of the study subjects are shown as numbers and percentages, and the differences are presented with standardized differences. Standardized difference provides a comparison of the mean or prevalence of a baseline covariate between 2 treatment groups in the propensity score matched sample. The t -test and χ^2 test were performed to test the mean difference and the proportion between on- and

TABLE 1. Basic demographic characteristics in study subjects before and after propensity adjustment before CABG

Characteristic	Before PS matching					After PS matching				
	Off-pump CABG		On-pump CABG		Standardized difference (%)	Off-pump CABG		On-pump CABG		Standardized difference (%)
	N	%	N	%		N	%	N	%	
Patients	4104	30.38	9405	69.62		3796	50.00	3796	50.00	
Age, y (mean/SD)	65.39	10.15	65.02	9.80	3.70	65.35	10.12	65.19	10.02	1.64
18-64	1832	44.64	4279	45.50	1.72	1698	44.73	1718	45.26	1.06
65-74	1455	35.45	3473	36.93	3.07	1354	35.67	1360	35.83	0.33
75+	817	19.91	1653	17.58	5.98	744	19.60	718	18.91	1.74
Sex, female	1238	30.17	2887	30.70	1.15	1137	29.95	1133	29.85	0.23
Insulin	515	12.55	1468	15.61	8.81	481	12.67	509	13.41	2.19
Hypertension	3422	83.38	7750	82.40	2.60	3156	83.14	3177	83.69	1.49
Previous stroke	887	21.61	1969	20.94	1.66	804	21.18	754	19.86	3.26
History of myocardial infarction	1189	28.97	2664	28.33	1.43	1095	28.85	1015	26.74	4.71
Peripheral vascular disease	295	7.19	614	6.53	2.61	268	7.06	261	6.88	0.72
Chronic obstructive pulmonary disease	365	8.89	810	8.61	1.00	331	8.72	304	8.01	2.57
Implanted pacemaker	78	1.90	140	1.49	3.19	70	1.84	52	1.37	3.77
History of atrial fibrillation	133	3.24	320	3.40	0.90	120	3.16	101	2.66	2.98
Cancer	209	5.09	416	4.42	3.15	187	4.93	161	4.24	3.28
Renal-replacement therapy	25	0.61	41	0.44	2.40	22	0.58	21	0.55	0.35
Chronic kidney disease	227	5.53	373	3.97	7.36	205	5.40	204	5.37	0.12
Renal function normal	3852	93.86	8991	95.60	7.79	3569	94.02	3571	94.07	0.22
Extent of coronary artery disease										
One-vessel disease	377	9.19	172	1.83	32.68	177	4.66	145	3.82	4.18
Two-vessel disease	786	19.15	1364	14.50	12.45	684	18.02	674	17.76	0.69
Three-vessel disease	2941	71.66	7869	83.67	29.13	2935	77.32	2977	78.42	2.67
Hospital volume for CABG										
High (≥ 200 /y)	2663	64.89	4106	43.66	43.62	2423	63.83	2446	64.44	1.26
middle (100~199/y)	668	16.28	2578	27.41	27.19	642	16.91	592	15.60	3.57
Low (≤ 99 /y)	773	18.84	2721	28.93	23.85	731	19.26	758	19.97	1.79
Year of surgery										
2001	61	1.49	997	10.60	38.97	61	1.61	56	1.48	1.07
2002	304	7.41	961	10.22	9.93	296	7.80	277	7.30	1.89
2003	434	10.58	848	9.02	5.24	405	10.67	392	10.33	1.12
2004	487	11.87	913	9.71	6.96	444	11.70	425	11.20	1.57
2005	373	9.09	861	9.15	0.23	351	9.25	381	10.04	2.68
2006	414	10.09	872	9.27	2.76	379	9.98	386	10.17	0.61
2007	381	9.28	823	8.75	1.86	357	9.40	351	9.25	0.54
2008	438	10.67	838	8.91	5.93	398	10.48	394	10.38	0.34
2009	422	10.28	837	8.90	4.70	382	10.06	415	10.93	2.84
2010	419	10.21	814	8.65	5.32	380	10.01	392	10.33	1.05
2011	371	9.04	641	6.82	8.24	343	9.04	327	8.61	1.49

PS, Propensity score; CABG, coronary artery bypass grafting; SD, standard deviation.

off-pump CABG patients, respectively. Univariate and multivariate Cox proportional hazard models were used to evaluate the relationship between on- and off-pump CABG and survival. When we explored the relative hazards concerning clinical outcomes other than all-cause death, we treated death as a competing risk instead of a censoring event.

We used every variable in Table 1 as a matching variable to generate a propensity score model to adjust for selection bias in the choice of

operative approach. Logistic regression was performed with the choice of operative approach—on-pump versus off-pump—as the dependent variable. Age, sex, diabetes mellitus treated with insulin, hypertension, stroke, history of myocardial infarction, peripheral vascular disease, chronic obstructive pulmonary disease, pacemaker implantation, atrial fibrillation, cancer, renal-replacement therapy, chronic kidney disease, normal renal function, extent of coronary artery disease (1-vessel, 2-vessel, and 3-

vessel), hospital volume of CABG (high: ≥ 200 /year, medium: 100-199/year, low: ≤ 99 /year), and operation year were entered into the model. We used 0.2 as a caliber of width and 1:1 greedy matching method (propensity score matching model concordance-statistics = 0.782) (Figure E2). Cox proportional hazard models were used to estimate the HRs within the specific subgroup. Kaplan–Meier curves and log-rank tests were performed to test the difference in survival probability between the on- and off-pump CABG groups. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC), and $P < .05$ was considered statistically significant.

RESULTS

Baseline Characteristics

All of the patients with diabetes who underwent isolated CABG from 2000 to 2011 in Taiwan were included in this final analysis. The median follow-up period was 5.42 years, and the longest time of survival was 15 years.

The baseline characteristics of a total of 13,441 patients with diabetes, before and after propensity score matching, are shown in Table 1. Patients who underwent off-pump CABG were older and had a greater prevalence of impaired renal function. However, the on-pump group had more severe coronary artery disease. Among the on-pump and off-pump groups, 83.67% and 71.66% of the patients, respectively, had 3-vessel disease in coronary territories (standardized difference 29.3%). Majority of the off-pump procedures were performed in high-volume centers (64.89%). After matching, we analyzed 3796 patients in each group, and both off-pump and on-pump groups shared the same distribution across all variables (Table 1).

Outcomes of CABG in All Patients With Diabetes

The survival was better in the off-pump group (HR, 1.52, 95% confidence interval [CI], 1.24–1.85, $P < .0001$ at 30 days; HR, 1.16, 95% CI, 1.01–1.32, $P = .0302$ at 1 year) (Table 2). At 1 year, the on-pump group had a greater risk of all-cause mortality and cardiovascular disease–related death (HR, 1.50, 95% CI, 1.17–1.92, $P = .0013$); however, this risk was not significant in the long-term follow-up (Table 2). The long-term event-free rate at 10 years (Figure 2, A) did not differ significantly for all-cause mortality (42.90% off-pump vs 47.91% on-pump, $P = .1635$) or death/myocardial infarction/stroke (Figure 2, B) (22.70% off-pump vs 23.44% on-pump, $P = .8274$). In the long-term follow-up, there were no differences in terms of myocardial infarction and stroke rate. The 10-year event-free rate for myocardial infarction was 75.3% in the off-pump group and 76.13% in the on-pump group ($P = .5205$) (Figure 3, B). The 10-year event-free rate for stroke was 65.23% in the off-pump group and 64.32% in the on-pump group ($P = .6077$) (Figure 3, A). Regarding repeat revascularization (Figure 4), the long-term event-free rate was significantly lower in the off-pump group than in the on-pump group (58.24% vs 65.23%, $P = .0036$).

Subgroup Analyses

Figure 5 shows the adjusted HRs for all-cause mortality and the composite endpoint (death, stroke, myocardial infarction, and repeat revascularization) in on-pump and off-pump CABG across various demographic and clinical comorbidity subgroups.

At 30 days, off-pump surgery showed superior survival outcomes in majority of subgroups: age younger than 75 years, sex, diabetes mellitus treated with insulin, hypertension, and cerebral vascular disease. At 1 year, off-pump surgery showed survival benefit only in patients younger than 75 years of age; both surgical methods had equal survival outcomes in all other subgroups.

In contrast, at the 10-year follow-up, a nonsignificant poorer survival for off-pump CABG was observed in the chronic kidney disease subgroup. There was a significant survival benefit in patients with end-stage renal disease and diabetes who underwent on-pump surgery (HR 0.68, 95% CI, 0.51–0.91).

DISCUSSION

The ROOBY (Outcomes Following Myocardial Revascularization: On and Off Cardiopulmonary Bypass) and CORONARY (CABG Off or On Pump Revascularization) studies led to the controversy regarding the selection of off-pump and on-pump bypass revascularization. The rate of repeat revascularization was predominantly emphasized by those who advocated on-pump surgery as a safer procedure.^{15,16} However, the supporters of off-pump surgery focused on perioperative complications, especially in the high-risk population.²¹ Similar issues were considered in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) study population and the results showed a greater 4-year risk of major cardiovascular events,²⁰ which was not demonstrated in our 30-day results after adjustment and propensity score matching. However, the discrepant prevalence of off-pump surgery among registry countries and the different baseline characteristics in BARI 2D were challenged.

To the best of our knowledge, the NHIRD study population is currently the largest nationwide database for CABG in patients with diabetes, with a nearly 100% national coverage. Moreover, detailed clinical follow-up data, such as cardiac death, stroke, myocardial infarction, and repeat revascularization, which were not available in the BARI 2D population, were clearly documented due to the regulation of National Health Insurance. Taiwan database is all-inclusive of patients and events and is essentially a record of every billed/paid medical event. Our study data are also linked to the death profile in the government registration; therefore, all the events including death were accurately analyzed.

TABLE 2. Hazard ratios (95% CI) of different outcomes using off-pump as reference group

Outcome	30 days								1 year			
	Event no.				Hazard ratio (On:off)				Event no.			
	On-pump		Off-pump		HR	95% CI		P value	On-pump		Off-pump	
	N	%	N	%		Low	Up		N	%	N	%
Death	248	6.53	165	4.35	1.52	1.24	1.85	<.0001	465	12.25	406	10.70
Cardiovascular-related death	101	2.66	58	1.53	1.78	1.29	2.46	.0005	156	4.11	106	2.79
Cerebrovascular disease death	5	0.13	5	0.13	1.01	0.29	3.48	.9906	12	0.32	18	0.47
Myocardial infarction	8	0.21	10	0.26	0.80	0.32	2.03	.6411	158	4.16	124	3.27
Stroke	17	0.45	17	0.45	1.00	0.51	1.96	.9960	217	5.72	209	5.51
Repeat revascularization	0	0.00	0	0.00	–				129	3.40	159	4.19

HR, Hazard ratio; CI, confidence interval.

The percentage of off-pump surgery has remained stable since 2002, accounting for approximately 30% of all isolated CABG in Taiwan (Figure E3). To avoid the influence of operation time sequence, the operation year was also matched in our study. In Western countries, the prevalence of off-pump CABG is decreasing, being approximately 20% or less. However, in Eastern countries, off-pump CABG is still a popular surgical method, with a prevalence of 65% reported in Japan.²² The off-pump technique is quite mature in Taiwan (Video 1); in comparison with the age >75 years subgroup in the German Off-Pump Coronary Artery Bypass in Elderly Study (GOPAGE), we had similar outcomes in our subgroup analysis.¹⁴

Our study has several strengths. First, we recruited the largest number of patients with diabetes. Second, all patients received health reimbursements from the government. All procedures, diagnoses, and treatments in the database were virtually followed without loss. Thus, our results reflect real-world data in Asia.

The major finding of the present study is that in patients with diabetes who underwent CABG, off-pump surgery improved all-cause mortality within 30 days, and the survival benefit persisted until 1 year. In the long-term period, there were no differences in all-cause mortality, myocardial infarction, and stroke between the on-pump and off-pump groups. Off-pump surgery provided survival benefits within 1 year probably due to avoidance of cardiopulmonary bypass. Without inflammatory response of cardiopulmonary bypass, the short-term outcomes in terms of 30-day and 1-year mortality were better for off-pump surgery. However, the survival benefit did not last in the long term probably due to the revascularization quality, which was always a concern in off-pump surgery.

Interestingly, the repeat revascularization rate was greater in off-pump surgery in the long term, which also reflected the persisting concern of revascularization quality. To reduce the influence of confounding factors of hospital experience and differences, we used hospital CABG volume as a propensity matching variable to eliminate influence of center experience. However, the single surgeon

experience and number were not allowed to be retrieved from the NHIRD, as per regulation. Although repeat revascularization was not an absolute adverse outcome but probably a benefit for patient survival, in our study, the repeat revascularization events were not scheduled or planned during operation, because these events never occurred within 30 days, and majority of these events occurred 1 year after CABG. However, in our study, the off-pump group had a greater probability of receiving repeat revascularization. Therefore, surgeons should be aware of this tendency when they perform off-pump CABG in patients with diabetes.

For patients with concomitant diabetes mellitus and end-stage renal disease, on-pump CABG provided a 32% reduction in long-term mortality rate (risk ratio = 0.68, 95% CI, 0.51-0.91). Patients with diabetes experienced diffused narrowing of the coronary arteries compared with those without diabetes. Moreover, in patients with renal failure, calcified coronary arteries would be more profound in disease.

Patients with diabetes have a greater risk of enhanced disease progression in coronary artery disease than those without diabetes, and the impact of incomplete revascularization is considered a major concern in off-pump CABG.²⁰ However, in our study, even when the off-pump group underwent more repeat revascularization, the survival rate was not reduced in the long term. However, among patients with diabetes who experienced greater short-term mortality and morbidity,² those who had single-vessel disease will require not only the protective benefit^{23,24} of the internal mammary artery whose long-term patency would not be affected by off-pump surgery²⁵ but also the short-term benefit of off-pump surgery.²⁶

In our study, the NHIRD recorded all events, diagnosis, and treatment based on the final surgical procedure; therefore, it was difficult to know about the off-pump to on-pump conversion. To eliminate the influence of conversion, we selected only cases of off-pump surgery without any usage of cardiopulmonary bypass circuit in the payment system and on-pump surgery without any usage of off-pump equipment such as stabilizers. Indeed, we cannot completely eliminate the influence of conversion; therefore,

TABLE 2. Continued

1 year				10 years							
Hazard ratio (On:off)				Event no.				Hazard ratio (On:off)			
95% CI				On-pump		Off-pump		95% CI			
HR	Low	Up	P value	N	%	N	%	HR	Low	Up	P value
1.16	1.01	1.32	.0302	1142	30.08	1214	31.98	0.95	0.87	1.02	.1667
1.50	1.17	1.92	.0013	219	5.77	166	4.37	1.14	0.89	1.44	.0946
0.68	0.33	1.40	.2931	23	0.61	32	0.84	0.73	0.43	1.24	.2424
1.18	0.93	1.65	.0713	417	10.99	403	10.62	1.04	0.91	1.20	.5332
1.04	0.86	1.26	.0668	612	16.12	634	16.70	0.97	0.87	1.08	.5586
0.82	0.64	1.02	.0648	526	13.86	617	16.25	0.84	0.75	0.95	.0036

FIGURE 2. Kaplan–Meier curves of patients with diabetes after CABG. A, All-cause mortality survival curve of off-pump and on-pump groups. B, MACC (death, myocardial infarction, and stroke). CABG, Coronary artery bypass grafting; CI, confidence interval; MACC, major cardiovascular and cerebral events.

FIGURE 3. Freedom from myocardial infarction and stroke after CABG. A, Freedom from stroke. B, Freedom from myocardial infarction. CABG, Coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction.

the outcomes of off-pump surgery may have been overestimated.

The status of chronic kidney disease has been reported to have a strong influence on long-term outcomes after CABG in patients with diabetes,²⁷ and the benefit of on-pump CABG was significant in the end-stage renal disease subgroup in our study. On-pump CABG is known to have a greater number of bypasses^{15,28} and superior graft patency,²⁹⁻³¹ and its renaissance was accompanied by

many criticisms of off-pump CABG such as fewer distal anastomoses on inferior and lateral aspects, incomplete revascularization, and poor vein graft patency. However, in the era of aggressive percutaneous coronary intervention and new-generation medications that ameliorate disease progression in patients with diabetes to some degree, the shortcoming of off-pump CABG might be overcome. Moreover, for patients with extremely high atherosclerosis burdens due to the lack of effective medication, the benefit of

FIGURE 4. Freedom from repeat revascularization. CI, Confidence interval; CABG, coronary artery bypass grafting.

on-pump CABG remains evident; the patients with diabetes mellitus and concomitant end-stage renal disease in our study support this notion.

Study Limitations

Because the study analysis was retrospective and only clinical events and services regulated by reimbursements

were recorded, factors such as effectively controlled diabetes mellitus; HbA1c; the completeness of revascularization; left ventricular ejection fraction or patients' functional capacity; choices of conduits (percentage of bilateral internal mammary arteries or total arterial grafting); and surgeon experience were not evaluated. The single surgeon experience cannot be retrieved from the NHIRD;

FIGURE 5. Subgroup analyses. HR, Hazard ratio; CI, confidence interval; HTN, hypertension; CVD, cardiovascular disease; ESRD, end-stage renal disease; CKD, chronic kidney disease.

VIDEO 1. Total arterial graft bypass surgery. We describe the total arterial graft coronary artery bypass in National Taiwan University Hospital. The patient was a 64-year-old man with diabetes who had moderate mitral regurgitation and left ventricular ejection fraction 45%. Total arterial graft using T-shape graft, right internal thoracic artery as a free graft attached to the side arm of left internal thoracic artery. The left internal thoracic artery was anastomosed to the left anterior descending artery, and right internal thoracic artery was used to bypass the obtuse marginal branch and posterior descending artery. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32478-4/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32478-4/fulltext).

therefore, we studied hospital CABG volume and entered this variable into propensity score matching to eliminate the influence of surgeon experience. The decision to perform off- versus on-pump CABG was dependent on the patients' clinical characteristics and surgeons' preferences. Although we attempted to reduce selection bias using statistical methods such as propensity score matching, unmeasured confounders or detection bias may have affected our results.

CONCLUSIONS

In patients with diabetes, off-pump CABG offered a survival benefit within 30 days. There was no significant difference in myocardial infarction, stroke, and repeat revascularization between the on-pump and off-pump groups during long-term follow-up. However, the off-pump group experienced more repeat revascularization in the long term. For patients with concomitant diabetes mellitus and end-stage renal disease, on-pump CABG provided a significant survival benefit.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The authors thank the staff at the Seventh Core Laboratory, Department of Medical Research, National Taiwan University Hospital, for their technical support. The authors acknowledge the statistical assistance provided by the Taiwan Clinical Trial

Statistical Center, Training Center, and Pharmacogenomics Laboratory. We would especially like to thank Yi-Jia Liou for figure preparation.

References

1. Nalysnyk L, Fahrbach K, Reynolds MW, Zhao SZ, Ross S. Adverse events in coronary artery bypass graft (CABG) trials: a systematic review and analysis. *Heart*. 2003;89:767-72.
2. Carson JL, Scholz PM, Chen AY, Peterson ED, Gold J, Schneider SH. Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. *J Am Coll Cardiol*. 2002;40:418-23.
3. Hertzberg D, Sartipy U, Holzmann MJ. Type 1 and type 2 diabetes mellitus and risk of acute kidney injury after coronary artery bypass grafting. *Am Heart J*. 2015;170:895-902.
4. Hammoud T, Tanguay JF, Bourassa MG. Management of coronary artery disease: therapeutic options in patients with diabetes. *J Am Coll Cardiol*. 2000;36:355-65.
5. Pintar T, Collard CD. The systemic inflammatory response to cardiopulmonary bypass. *Anesthesiol Clin North Am*. 2003;21:453-64.
6. Stroobant N, Van Nooten G, Van Belleghem Y, Vingerhoets G. Relation between neurocognitive impairment, embolic load, and cerebrovascular reactivity following on- and off-pump coronary artery bypass grafting. *Chest*. 2005;127:1967-76.
7. Wynne R, Botti M. Postoperative pulmonary dysfunction in adults after cardiac surgery with cardiopulmonary bypass: clinical significance and implications for practice. *Am J Crit Care*. 2004;13:384-93.
8. Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Flather M, et al. Off-pump versus on-pump coronary artery bypass grafting: insights from the Arterial Revascularization Trial. *J Thorac Cardiovasc Surg*. 2018;155:1545-53.e7.
9. Filardo G, Hamman BL, da Graca B, Sass DM, Machala NJ, Ismail S, et al. Efficacy and effectiveness of on- versus off-pump coronary artery bypass grafting: a meta-analysis of mortality and survival. *J Thorac Cardiovasc Surg*. 2018;155:172-9.e175.
10. A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease. *N Engl J Med*. 2009;360:2503-15.
11. Magee MJ, Dewey TM, Acuff T, Edgerton JR, Hebel JF, Prince SL, et al. Influence of diabetes on mortality and morbidity: off-pump coronary artery bypass grafting versus coronary artery bypass grafting with cardiopulmonary bypass. *Ann Thorac Surg*. 2001;72:776-80; discussion 780-1.
12. Renner A, Zittermann A, Aboud A, Pühler T, Hakim-Meibodi K, Quester W, et al. Coronary revascularization in diabetic patients: off-pump versus on-pump surgery. *Ann Thorac Surg*. 2013;96:528-34.
13. Srinivasan AK, Grayson AD, Fabri BM. On-pump versus off-pump coronary artery bypass grafting in diabetic patients: a propensity score analysis. *Ann Thorac Surg*. 2004;78:1604-9.
14. Diegeler A, Börgermann J, Kappert U, Breuer M, Böning A, Ursulescu A, et al. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. *N Engl J Med*. 2013;368:1189-98.
15. Kim JB, Yun SC, Lim JW, Hwang SK, Jung SH, Song H, et al. Long-term survival following coronary artery bypass grafting: off-pump versus on-pump strategies. *J Am Coll Cardiol*. 2014;63:2280-8.
16. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med*. 2009;361:1827-37.
17. Shroyer AL, Hattler B, Wagner TH, Baltz JH, Collins JF, Carr BM, et al. Comparing off-pump and on-pump clinical outcomes and costs for diabetic cardiac surgery patients. *Ann Thorac Surg*. 2014;98:38-44; discussion 44-5.
18. Takagi H, Yamamoto H, Iwata K, Goto S-N, Umemoto T. Ask not which can impair early morbidity—ask which can improve late survival: a meta-analysis of randomized trials of off-pump versus on-pump coronary artery bypass. *Int J Cardiol*. 2012;158:435-8.
19. Halkos ME, Anderson A, Binongo JNG, Stringer A, Lasanajak Y, Thourani VH, et al. Operative strategies to reduce cerebral embolic events during on- and off-pump coronary artery bypass surgery: a stratified, prospective randomized trial. *J Thorac Cardiovasc Surg*. 2017;154:1278-85.e1271.
20. Singh A, Schaff HV, Mori Brooks M, Hlatky MA, Wisniewski SR, Frye RL, et al. On-pump versus off-pump coronary artery bypass graft surgery among patients with type 2 diabetes in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. *Eur J Cardiothorac Surg*. 2016;49:406-16.

21. Ueki C, Miyata H, Motomura N, Sakaguchi G, Akimoto T, Takamoto S. Off-pump versus on-pump coronary artery bypass grafting in patients with left ventricular dysfunction. *J Thorac Cardiovasc Surg.* 2016;151:1092-8.
22. Japanese Associate for Coronary Artery Surgery (JACAS). Coronary artery surgery results 2013, in Japan. *Ann Thorac Cardiovasc Surg.* 2014;20:332-4.
23. Dimitrova KR, Hoffman DM, Geller CM, Dincheva G, Ko W, Tranbaugh RF. Arterial grafts protect the native coronary vessels from atherosclerotic disease progression. *Ann Thorac Surg.* 2012;94:475-81.
24. Endo M, Tomizawa Y, Nishida H. Bilateral versus unilateral internal mammary revascularization in patients with diabetes. *Circulation.* 2003;108:1343-9.
25. Zhang B, Zhou J, Li H, Liu Z, Chen A, Zhao Q. Comparison of graft patency between off-pump and on-pump coronary artery bypass grafting: an updated meta-analysis. *Ann Thorac Surg.* 2014;97:1335-41.
26. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, et al. Off-pump or on-pump coronary-artery bypass grafting at 30 days. *N Engl J Med.* 2012;366:1489-97.
27. Ohira S, Doi K, Numata S, Yamazaki S, Kawajiri H, Yaku H. Impact of chronic kidney disease on long-term outcome of coronary artery bypass grafting in patients with diabetes mellitus. *Circ J.* 2016;80:110-7.
28. Bakaeen FG, Chu D, Kelly RF, Ward HB, Jessen ME, Chen GJ, et al. Performing coronary artery bypass grafting off-pump may compromise long-term survival in a veteran population. *Ann Thorac Surg.* 2013;95:1952-8; discussion 1959-60.
29. Angelini GD, Culliford L, Smith DK, Hamilton MC, Murphy GJ, Ascione R, et al. Effects of on- and off-pump coronary artery surgery on graft patency, survival, and health-related quality of life: long-term follow-up of 2 randomized controlled trials. *J Thorac Cardiovasc Surg.* 2009;137:295-303.
30. Khan NE, De Souza A, Mister R, Flather M, Clague J, Davies S, et al. A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. *N Engl J Med.* 2004;350:21-8.
31. Widimsky P, Straka Z, Stros P, Jirasek K, Dvorak J, Votava J, et al. One-year coronary bypass graft patency: a randomized comparison between off-pump and on-pump surgery angiographic results of the PRAGUE-4 trial. *Circulation.* 2004;110:3418-23.

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

Readers who found these articles interesting may also like to read the following papers found in recent and future issues of our sister publications, *Seminars in Thoracic and Cardiovascular Surgery* and *Operative Techniques in Thoracic and Cardiovascular Surgery*!

Adult: Coronary

ORIGINAL SUBMISSION: Frozen Apex Repair of a Dilated Cardiomyopathy. Masashi Komeda. *Semin Thorac Surg* 2018: Volume 30, Issue 4.

Editorial Commentary: The Frozen Apex: A Useful Addition to the Surgeons Armamentarium? James Kirklin. *Semin Thorac Surg* 2018: Volume 30, Issue 4.

ORIGINAL SUBMISSION: Remote Ischemic Preconditioning in High Risk Cardiovascular Surgery Patients: a Randomized-Controlled Trial. Nicole S. Coverdale. *Semin Thorac Surg* 2018: 26-33.

Editorial Commentary: Remote Ischemic Preconditioning: a Complex Question with an Even More Complex Answer. Sarah A. Schubert. *Semin Thorac Surg* 2018: 34-35.

FIGURE E1. All-cause mortality of DM and non-DM after CABG. *CABG*, Coronary artery bypass grafting; *DM*, diabetes mellitus; *non-DM*, no diabetes mellitus.

FIGURE E2. PS matching model. *PS*, Propensity score.

FIGURE E3. Trend of CABG in Taiwan. CABG, Coronary artery bypass grafting.