

## SUPPLEMENTAL MATERIAL

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## **Method 1. Description of Coronary Artery Bypass Grafting (CABG) Procedure**

### **Surgeon qualification**

In Fuwai Hospital, all surgeons should have specialized in congenital or valve heart surgery for more than 3 years before undertaking any CABG procedures. Specially for off-pump CABG, the surgeon needs to perform at least 100 on-pump CABG procedures first, so that he can get the qualification to carry out the off-pump procedure. Once qualified, the choice of off-pump CABG or on-pump CABG for a specific patient was generally decided by individual surgeons.

### **Standard surgical process**

All procedures were performed with standard bypass techniques. Anesthesia was managed by inhalation of isoflurane with the addition of fentanyl or sufentanil, and propofol was administered continuously until the end of the procedure if necessary. Surgical revascularization was performed using standard bypass techniques. For on-pump CABG, a standard cardiopulmonary bypass was established, and moderate systemic hypothermia (28°C to 32°C) and perfusion with antegrade intermittent cold crystalloid cardioplegia were used. Heparin was given to achieve activated clotting times of 480 seconds or above before institution of cardiopulmonary bypass. For off-pump CABG, stabilization devices were used to provide a motionless anastomosis site, and heparin was administered before the start of the first distal anastomosis to achieve an activated clotting time of 300 to 350 seconds. On-pump CABG involved aortic cross-clamping and cardioplegic arrest, while off-pump CABG was performed with a partial occlusion clamp. Whenever possible, complete revascularization was attempted, and the internal thoracic artery was used preferentially for revascularization

of the left anterior descending artery. The remaining vessels were to be bypassed either using another arterial conduit or the saphenous vein in the configuration decided by the surgeon. During reperfusion, the bypass grafting was completed with proximal anastomoses to the ascending aorta. The decision to switch to cardiopulmonary bypass during the procedure was based on significant hemodynamic instability or ventricular arrhythmia. After separation from cardiopulmonary bypass or on completion of all anastomoses, protamine was given to reverse the effects of heparin. Postoperatively, starting within the first 24 hours, aspirin therapy (100 mg/d) is recommended and should be continued indefinitely.

### **Role of the surgical team**

The primary surgeon was in charge of the intricate core process, including the distal and proximal anastomoses for coronary revascularization, and cardiopulmonary bypass (CPB) establishment for on-pump CABG. The surgical assistants were typically responsible for incision on the chest wall, vein and artery conduit harvesting, assisting the primary surgeon with revascularization, closing chest and suturing incision. Other assisting team members included anesthesiologists, nurses, perfusionists, and cardiac intensivists, and they usually stay in operating room or intensive care unit for all surgeries through the day.

## Method 2. Definition of the outcomes

**In-hospital mortality** was defined as death before discharge from any cause.

**Myocardial infarction (MI)** was defined as an absolute rise in cardiac troponin to over 70 times the 99th percentile upper reference limit, or an increase in CK-MB to over 10 times the 99th percentile upper reference limit.

**Stroke** was defined as brain, spinal cord, or retinal cell death attributable to focal arterial ischemia, based on:

- (1) pathological, neuroimaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or
- (2) clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution with symptoms persisting >24 h or until death, and other etiologies were excluded.

**Acute kidney injury (AKI)** was defined as (1) an increase in the serum creatinine level over 3 times the latest preoperative level or a serum creatinine level reaching 4.0 mg/dL with a minimum increase of 0.5 mg/dL relative to the last preoperative value and/or (2) a new postoperative requirement for dialysis.

**Reoperation** was defined as re-exploration for mediastinal bleeding with or without tamponade either in the intensive care unit or after returning to the operating room.

**Table 1. Completeness of key variables (Created by the authors)**

Variable	Completeness	Variable	Completeness
Age	100.00%	Myocardial infarction	100.00%
Angina	100.00%	NYHA score	96.32%
Aortic calcification	99.96%	Number of grafts	100.00%
Aortic regurgitation	100.00%	Number of lesions	99.85%
Aortic stenosis	100.00%	Number of other arterial grafts	100.00%
Body mass index	99.73%	Number of vein grafts	100.00%
CCS angina grade	100.00%	Operative time	99.95%
Diabetes	100.00%	Peripheral artery disease	100.00%
EuroScore	99.96%	Preoperative LVEF	99.99%
Gender	100.00%	Prior cardiac surgery	100.00%
Glomerular filtration rate	99.94%	Prior COPD	100.00%
Hyperlipidemia	100.00%	Prior myocardial infarction	100.00%
Hypertension	100.00%	Prior PCI	100.00%
Internal mammary artery	100.00%	Prior stroke	100.00%
Left main stem disease	99.83%	Smoking	100.00%
Mitral regurgitation	100.00%	Tricuspid stenosis	100.00%
Mitral stenosis	100.00%	Tricuspid regurgitation	100.00%

CCS indicates Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; EuroScore, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention

**Table 2. Covariates in the models (Created by the authors)**

Dependent variable	Statistical method	Covariates
AEC	Mixed-effects model with Poisson link function	<ul style="list-style-type: none"> <li>• Patient-level: Age, Angina, Aortic calcification, Body mass index, Gender, Glomerular filtration rate, Left main stem disease, NHYA III/IV, Number of lesions, Preoperative LVEF, Prior cardiac surgery, Prior COPD, Prior myocardial infarction, Prior PCI, Prior stroke;</li> <li>• Surgeon-level: years in practice and CABG volume before the index procedure;</li> <li>• Time (year of the surgery)</li> </ul>
Death	Mixed-effects model with Logit link function	<ul style="list-style-type: none"> <li>• Patient-level: Age, Gender, NHYA III/IV, Preoperative LVEF, Prior cardiac surgery. Because of the low event rate and limited sample size, we chose the variables with greater effect size and of clinical importance;</li> <li>• Surgeon-level: years in practice and CABG volume before the index procedure;</li> <li>• Time (year of the surgery)</li> </ul>
MI	Mixed-effects model with Logit link function	The same as covariates of AEC in the primary analysis
Stroke	Mixed-effects model with Logit link function	The same as covariates of AEC in the primary analysis
AKI	Mixed-effects model with Logit link function	The same as covariates of AEC in the primary analysis
Reoperation	Mixed-effects model with Logit link function	The same as covariates of AEC in the primary analysis, except for excluding the prior COPD. Because 0 case had prior COPD in patients with reoperation among off-pump CABG and the model couldn't converge without removing it.
Non-first procedure group	Logistic regression to calculate propensity score	All the variables listed in above online supplemental table 1 and the time variable (year of the surgery)

AEC indicates adverse events composite; AKI, acute kidney injury; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NHYA, New York Heart Association; PCI, percutaneous coronary intervention.

**Table 3. Surgeon characteristics in the CABG cohorts, by cardiopulmonary-bypass and procedure order (Created by the authors)**

	Overall	First procedure	Non-first procedure	P value‡
<b>All patients</b>				
Number of cases	21866	16759	5107	
Number of surgeons *	47	47	47	
Years in practice, median (IQR), y	24 (19, 28)	23 (19, 28)	24 (21, 29)	<0.001
CABG volume, median (IQR)	460 (252, 789)	424 (231, 731)	595 (348, 953)	<0.001
Number of surgeon-assistant pairs †	316	316	316	
Number of cases treated by pairs	19785	14838	4947	
<b>On-pump cohort</b>				
Number of cases	10109	8480	1629	
Number of surgeons *	47	47	47	
Years in practice, median (IQR), y	21 (17, 26)	21 (17, 26)	21 (16, 26)	0.09
CABG volume, median (IQR)	306 (172, 501)	297 (170, 487)	357 (190, 565)	<b>&lt;0.001</b>
Number of surgeon-assistant pairs †	285	277	250	
Number of cases treated by pairs	8600	7063	1537	
<b>Off-pump cohort</b>				
Number of cases	11757	8279	3478	
Number of surgeons *	41	40	32	
Years in practice, median (IQR), y	25 (22, 30)	25 (21, 30)	26 (23, 30)	<b>&lt;0.001</b>
CABG volume, median (IQR)	661 (388, 1006)	617 (359, 972)	757 (464, 1070)	<b>&lt;0.001</b>
Number of surgeon-assistant pairs †	243	237	181	
Number of cases treated by pairs	11185	7775	3410	

CABG indicates coronary artery bypass grafting; IQR, interquartile range.

\* Number of surgeons indicates the number of surgeons who had experience performing both first and non-first CABG procedures.

† Number of surgeon-assistant pair indicates the number of surgeon and assistant pairs who had ever performed CABG as both first and non-first CABG procedures, as well as had performed as least 5 CABG cases.

‡ The Kruskal-Wallis test was used to compare the surgeon characteristics between first and non-first procedure group in specific CABG cohorts. Significant differences (<0.05) are in bold. The years in practice and CABG volumes were calculated at patient level.

**Table 4. Patient demographic and clinical characteristics in propensity score matched cohorts (Created by the authors)**

	Overall	Matched on-pump CABG cohort (n=3084)			Matched off-pump CABG cohort (n=6882)		
		First procedure (n=1542)	Non-first procedure (n=1542)	Absolute standardized difference <sup>‡</sup>	First procedure (n=3441)	Non-first procedure (n=3441)	Absolute standardized difference <sup>‡</sup>
Age, mean (SD), y	61.1 (8.7)	60.3 (8.7)	60.5 (8.5)	0.0178	61.7 (8.9)	61.2 (8.5)	0.0587
Female, No. (%)	2319 (23.3)	346 (22.4)	365 (23.7)	0.0293	807 (23.5)	801 (23.3)	0.0041
BMI, mean (SD), kg/m <sup>2</sup> *	25.7 (3.1)	25.7 (3.1)	25.8 (3.1)	0.0155	25.7 (3)	25.6 (3.1)	0.0143
Smoking, No. (%)	5569 (55.9)	823 (53.4)	824 (53.4)	0.0013	1957 (56.9)	1965 (57.1)	0.0047
Diabetes, No. (%)	2219 (22.3)	344 (22.3)	335 (21.7)	0.0141	786 (22.8)	754 (21.9)	0.0223
Hypertension, No. (%)	6393 (64.1)	1000 (64.9)	1016 (65.9)	0.0218	2215 (64.4)	2162 (62.8)	0.032
Hyperlipidemia, No. (%)	7409 (74.3)	1126 (73.0)	1116 (72.4)	0.0146	2592 (75.3)	2575 (74.8)	0.0114
Prior COPD, No. (%)	73 (0.7)	7 (0.5)	9 (0.6)	0.0181	29 (0.8)	28 (0.8)	0.0032
Prior MI, No. (%)	3693 (37.1)	557 (36.1)	594 (38.5)	0.0496	1296 (37.7)	1246 (36.2)	0.0301
Prior stroke, No. (%)	782 (7.8)	121 (7.8)	112 (7.3)	0.0221	269 (7.8)	280 (8.1)	0.0118
Prior PCI, No. (%)	533 (5.3)	70 (4.5)	85 (5.5)	0.0445	198 (5.8)	180 (5.2)	0.023
Prior cardiac surgery, No. (%)	363 (3.6)	45 (2.9)	56 (3.6)	0.0401	126 (3.7)	136 (4.0)	0.0152
Angina, No. (%)	8591 (86.2)	1271 (82.4)	1281 (83.1)	0.0172	3023 (87.9)	3016 (87.6)	0.0062
NYHA III/IV, No. (%)	3391 (34.0)	474 (30.7)	450 (29.2)	0.034	1242 (36.1)	1225 (35.6)	0.0103
eGFR, median (IQR), mL/min/1.73 m <sup>2</sup> †	94 (23.9)	94.1 (23.6)	93.8 (23.6)	0.012	93.9 (24.1)	94.2 (23.9)	0.0113
PAD, No. (%)	1366 (13.7)	137 (8.9)	135 (8.8)	0.0046	535 (15.5)	559 (16.2)	0.0191
LM disease, No. (%)	1784 (17.9)	262 (17.0)	258 (16.7)	0.0064	620 (18.0)	644 (18.7)	0.0186
Three-vessel disease, No. (%)	6174 (62.0)	1092 (70.8)	1052 (68.2)	0.0564	2072 (60.2)	1958 (56.9)	0.0673
Preoperative LVEF, mean (SD)	61.2 (7.4)	60.8 (8.0)	60.7 (7.7)	0.018	61.3 (7.3)	61.5 (6.9)	0.0282
Aortic calcification, No. (%)	941 (9.4)	87 (5.6)	97 (6.3)	0.0275	394 (11.5)	363 (10.5)	0.0287
EuroSCORE>3, No. (%)	2384 (23.9)	308 (20.0)	285 (18.5)	0.0379	919 (26.7)	872 (25.3)	0.0311



BMI indicates body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, interquartile range; LVEF, left ventricular ejection fraction; LM, left main stem; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; SMD, standardized mean difference; SD, standard deviation.

\*  $\text{BMI (kg/m}^2\text{)} = \text{weight (kg)} / (\text{height [m]})^2$ .

†  $\text{eGFR (mL/min/1.73 m}^2\text{)} = 186 \times (\text{serum creatinine level [mg/dL]})^{-1.154} \times (\text{age [y]})^{-0.203}$ .

‡ Absolute standardized difference was calculated to measure the difference between first and non-first procedure groups in specific CABG cohorts. The standardized difference being less than 0.1 shows the matched groups were well-balanced.

**Table 5. Outcome difference associated with non-first versus first procedure groups in propensity score weighted and matched cohorts**  
(Created by the authors)

	IPTW method*		1:1 propensity matching method†			
	RR <sub>adj</sub> /OR <sub>adj</sub> ‡ (95% CI)	P value	First procedure	Non-first procedure	RR <sub>adj</sub> /OR <sub>adj</sub> ‡ (95% CI)	P value
<b>On-pump CABG cohort</b>						
<b>Total patients</b>			1542	1542		
AEC, total number	0.92 (0.81-1.03)	0.15	221	192	0.87 (0.71-1.06)	0.17
one event, n (%)			184 (11.9)	155 (10.1)		
two events, n (%)			14 (0.9)	14 (0.9)		
three events, n (%)			3 (0.2)	3 (0.2)		
four events, n (%)			/	/		
Death, n (%)	1.47 (0.85-2.54)	0.17	4 (0.3)	7 (0.45)	1.75 (0.51-5.98)	0.37
MI, n (%)	0.84 (0.69-1.03)	0.09	60 (3.9)	66 (4.3)	1.12 (0.77-1.63)	0.56
Stroke, n (%)	0.63 (0.42-0.96)	<b>0.03</b>	26 (1.7)	11 (0.7)	0.42 (0.21-0.86)	<b>0.02</b>
AKI, n (%)	0.98 (0.83-1.16)	0.81	120 (7.8)	94 (6.1)	0.77 (0.58-1.02)	0.06
Reoperation, n (%)	0.73 (0.50-1.05)	0.09	11 (0.7)	14 (0.9)	1.27 (0.58-2.80)	0.55
<b>Off-pump CABG cohort</b>						
<b>Total patients</b>			3441	3441		
AEC*, total number	1.28 (1.14-1.45)	<b>&lt;0.001</b>	291	384	1.32 (1.13-1.54)	<b>&lt;0.001</b>
one event, n (%)			263 (7.6)	315 (9.2)		
two events, n (%)			14 (0.4)	27 (0.8)		
three events, n (%)			/	5 (0.15)		
four events, n (%)			/	/		
Death, n (%)	2.04 (1.04-4.01)	<b>0.04</b>	5 (0.15)	12 (0.35)	2.40 (0.85-6.81)	0.10
MI, n (%)	1.46 (1.18-1.82)	<b>0.001</b>	66 (1.9)	112 (3.3)	1.74 (1.27-2.38)	<b>&lt;0.001</b>

Stroke, n (%)	1.69 (1.15-2.47)	<b>0.007</b>	22 (0.6)	39 (1.1)	1.77 (1.05-2.99)	<b>0.03</b>
AKI, n (%)	1.20 (1.01-1.43)	<b>0.04</b>	157 (4.6)	175 (5.1)	1.12 (0.90-1.39)	0.31
Reoperation, n (%)	0.94 (0.69-1.28)	0.68	41 (1.2)	46 (1.3)	1.12 (0.73-1.72)	0.59

AEC indicates adverse events composite, which is defined as the number of any adverse events occurred, including death, myocardial infarction, stroke, acute kidney injury or reoperation; AKI indicates acute kidney injury; CABG, coronary artery bypass grafting; CI, confidence interval; EuroSCORE, European System for Cardiac Operative Risk Evaluation; MI, myocardial infarction; OR<sub>adj</sub>, adjusted odds ratio; RR<sub>adj</sub>, adjusted risk ratio.

\* The propensity score is calculated by establishing a multivariable logistic regression model with all patient characteristics (online supplemental table 1) included to estimate the propensity for patients to undergo a non-first procedure. The inverse probability of treatment weighting (IPTW) is used based on the inverse of the propensity score and the mixed-effects model analyses repeated.

† The 1:1 propensity score matching method is used to form matched CABG cohorts by matching first vs non-first patients treated by the same surgeon with similar propensity score using the greedy nearest neighbor matching algorithm without replacement, with a caliper width at 0.01 according to the absolute value of the difference between propensity scores.

‡ For the adverse events composite, the adjusted rate ratio (non-first vs first) is estimated from the model with a Poisson link function; For every individual event (binary variable, i.e., death, MI, stroke, AKI and reoperation), the adjusted odds ratio (non-first vs first) for each outcome is estimated from the model with a logit link function. Significant differences (<0.05) are in bold.

**Table 6. Outcome difference associated with non-first versus first procedure in patients performed by the same surgeon-assistant pairs (Created by the authors)**

Outcome	On-pump CABG cohort (n=8600)				Off-pump CABG cohort (n=11185)			
	First procedure (n=7063)	Non-first procedure (n=1537)	RR <sub>adj</sub> */OR <sub>adj</sub> † (95% CI)	P value	First procedure (n=7775)	Non-first procedure (n=3410)	RR <sub>adj</sub> */OR <sub>adj</sub> † (95% CI)	P value
AEC*, total number	982	193	0.89 (0.76-1.05)	0.17	720	385	1.29 (1.14-1.47)	<b>&lt;0.001</b>
one event, n (%)	817 (11.6)	153 (10.0)			621 (8.0)	314 (9.2)		
two events, n (%)	62 (0.9)	17 (1.1)			43 (0.6)	28 (0.8)		
three events, n (%)	11 (0.2)	2 (0.1)			3 (0.0)	5 (0.1)		
four events, n (%)	2 (0.0)	0 (0.0)			1 (0.0)	0 (0.0)		
Death, n (%)	25 (0.4)	8 (0.5)	1.51 (0.98-2.33)	0.06	16 (0.2)	12 (0.4)	2.31 (1.49-3.57)	<b>&lt;0.001</b>
MI, n (%)	311 (4.4)	68 (4.4)	0.95 (0.74-1.22)	0.70	194 (2.5)	112 (3.3)	1.40 (1.12-1.75)	<b>0.003</b>
Stroke, n (%)	87 (1.2)	10 (0.7)	0.54 (0.30-0.97)	<b>0.04</b>	53 (0.7)	39 (1.1)	1.82 (1.30-2.57)	<b>0.001</b>
AKI, n (%)	469 (6.6)	91 (5.9)	0.91 (0.69-1.20)	0.52	343 (4.4)	176 (5.2)	1.23 (1.00-1.52)	0.05
Reoperation, n (%)	90 (1.3)	16 (1.0)	0.73 (0.46-1.16)	0.18	114 (1.5)	46 (1.3)	0.98 (0.69-1.39)	0.93

AEC, adverse event composite; AKI indicates acute kidney injury; CABG, coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction; OR<sub>adj</sub>, adjusted odds ratio; RR<sub>adj</sub>, adjusted risk ratio.

\*For the adverse events composite (AEC, count variable, the “n (%)” presents the number of patients with given number of events and the percentage of those patients among specific procedure group. A mixed-effects model with a Poisson link function and surgeon-specific random intercepts is fitted. The risk-adjusted rate ratio (non-first vs first) is estimated, and when it achieves a statistically significant level of 0.05, the P value is in bold.

†For every individual event (binary variable, i.e., death, MI, stroke, AKI and reoperation), a mixed-effects model with a logit link function and surgeon-specific random intercepts is fitted. The risk-adjusted odds ratio (non-first vs first) for each outcome is estimated, and when it achieves a statistically significant level of 0.05, the P value is in bold.

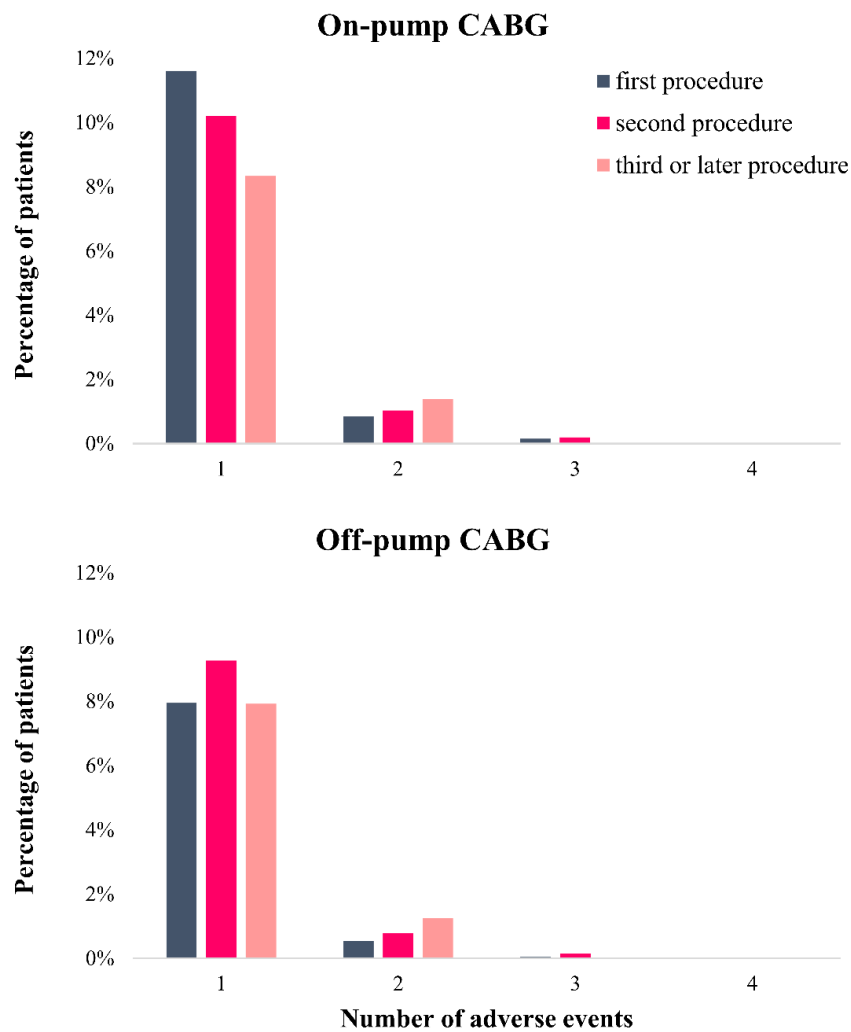
**Table 7. Outcome difference associated with non-first versus first procedure in patients undergoing CABG after 11:00 am (Created by the authors)**

Outcome	On-pump CABG cohort (n=4604)				Off-pump CABG cohort (n=4992)			
	First procedure (n=3061)	Non-first procedure (n=1543)	RR <sub>adj</sub> <sup>*</sup> /OR <sub>adj</sub> <sup>†</sup> (95% CI)	P value	First procedure (n=1619)	Non-first procedure (n=3303)	RR <sub>adj</sub> <sup>*</sup> /OR <sub>adj</sub> <sup>†</sup> (95% CI)	P value
AEC <sup>*</sup> , total number	406	191	0.91 (0.74-1.12)	0.39	149	303	1.30 (1.04-1.64)	<b>0.02</b>
one event, n (%)	342 (11.2)	150 (9.7)			133 (8.2)	303 (9.2)		
two events, n (%)	26 (0.8)	16 (1.0)			8 (0.5)	28 (0.8)		
three events, n (%)	4 (0.1)	3 (0.2)			0 (0.0)	5 (0.2)		
Death, n (%)	9 (0.3)	9 (0.6)	1.06 (0.54-2.07)	0.87	4 (0.2)	12 (0.4)	2.04 (0.74-5.66)	0.17
MI, n (%)	131 (4.3)	66 (4.3)	0.93 (0.64-1.34)	0.69	39 (2.4)	107 (3.2)	1.59 (1.05-2.40)	<b>0.03</b>
Stroke, n (%)	39 (1.3)	10 (0.6)	0.50 (0.25-1.01)	0.05	11 (0.7)	39 (1.2)	1.58 (0.78-3.19)	0.20
AKI, n (%)	190 (6.2)	88 (5.7)	0.91 (0.66-1.27)	0.59	74 (4.6)	171 (5.2)	1.09 (0.75-1.57)	0.65
Reoperation, n (%)	37 (1.2)	18 (1.2)	0.86 (0.45-1.64)	0.65	21 (1.3)	45 (1.4)	1.10 (0.61-1.98)	0.76

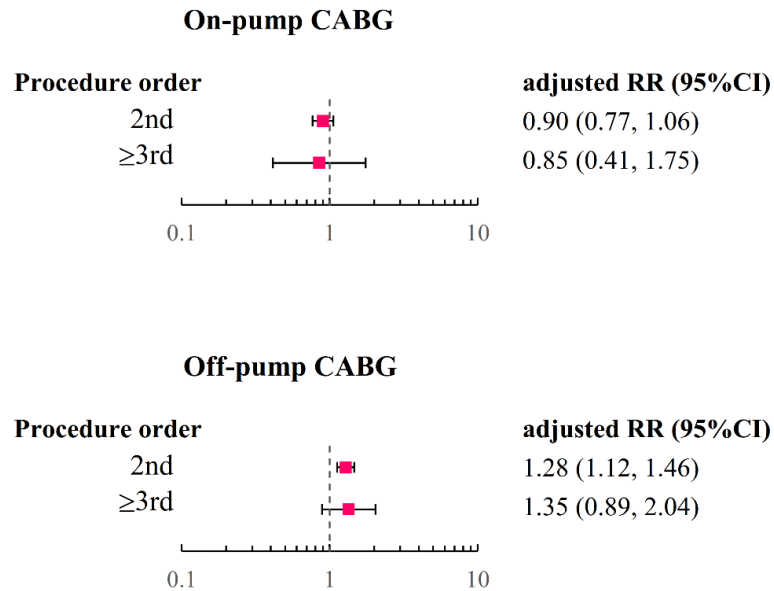
AEC, adverse event composite; AKI indicates acute kidney injury; CABG, coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction; OR<sub>adj</sub>, adjusted odds ratio; RR<sub>adj</sub>, adjusted risk ratio.

\*For the adverse events composite (AEC, count variable, the “n (%)” presents the number of patients with given number of events and the percentage of those patients among specific procedure group. A mixed-effects model with a Poisson link function and surgeon-specific random intercepts is fitted. The risk-adjusted rate ratio (non-first vs first) is estimated, and when it achieves a statistically significant level of 0.05, the P value is in bold.

†For every individual event (binary variable, i.e., death, MI, stroke, AKI and reoperation), a mixed-effects model with a logit link function and surgeon-specific random intercepts is fitted. The risk-adjusted odds ratio (non-first vs first) for each outcome is estimated, and when it achieves a statistically significant level of 0.05, the P value is in bold.



**Figure 1. Distribution of number of adverse events (Created by the authors)**  
CABG, coronary artery bypass grafting.



**Figure 2. Association between later procedure order and adverse events composite compared to the first procedure in the on-pump and off-pump CABG cohorts (Created by the authors)**

CABG, coronary artery bypass grafting; CI, confidence interval; RR, rate ratio.