

## Association Between Coronary Artery Bypass Surgical Techniques and Postoperative Stroke

Roberto Lorusso, MD, PhD;\* Marco Moscarelli, MD;\* Antonino Di Franco, MD; Valentina Grazioli, MD; Francesco Nicolini, MD; Tiziano Gherli, MD; Michele De Bonis, MD; Maurizio Taramasso, MD; Emmanuel Villa, MD; Giovanni Troise, MD; Roberto Scrofani, MD; Carlo Antona, MD; Giovanni Mariscalco, MD; Cesare Beghi, MD; Antonio Miceli, MD; Mattia Glauber, MD; Marco Ranucci, MD; Carlo De Vincentiis, MD; Mario Gaudino, MD

**Background**—The impact of the coronary artery bypass grafting (CABG) technique (on- versus off-pump, single versus multiple aortic clamping) on postoperative neurological outcome remains a matter of controversy. The aim of this study was to assess the association between the incidence of postoperative stroke and the degree of aortic manipulation in one of the largest contemporary CABG series.

**Methods and Results**—A retrospective, multicenter, international study was conducted in 25 388 patients undergoing isolated CABG procedures with on-pump CABG (ONCAB) or off-pump CABG (OPCAB) technique including single or multiple aortic clamping. Postoperative stroke was defined as a postoperative neurological deficit lasting more than 24 hours and associated with evidence of a brain lesion on computed tomography. The degree of aortic manipulation was assumed to be higher for on-pump versus off-pump surgery and for multiple versus single or no aortic clamping. Logistic regression and propensity matching were used. ONCAB procedures were performed in 17 231 cases and OPCAB in 8157. The incidence of postoperative stroke was significantly lower in the OPCAB group even after propensity matching (0.4% OPCAB versus 1.2% ONCAB,  $P=0.02$ ). In the ONCAB group (but not in the OPCAB arm) the use of single aortic clamping was associated with significantly reduced postoperative stroke rate (odds ratio, 0.05; 95% CI, 0.008 to 0.07 [ $P<0.001$ ]).

**Conclusions**—OPCAB and the use of single aortic clamping in the ONCAB arm were associated with a reduced incidence of postoperative stroke. Our data confirm a strong association between aortic manipulation and neurological outcome after CABG surgery. (*J Am Heart Assoc.* 2019;8:e013650. DOI: 10.1161/JAHA.119.013650.)

**Key Words:** aortic clamp • coronary artery bypass grafting • off-pump • on-pump • stroke

Cerebrovascular injury following coronary artery bypass grafting (CABG) is associated with high morbidity and mortality rates.<sup>1–4</sup> Despite limited prevalence in patients with CABG, its repercussion on patient management, hospital resources, and early- and long-term quality of life of survivors remains important.<sup>3</sup> Furthermore, no substantial progress in

terms of reduction of neurologic adverse events has been shown in recent years despite a constant decline in global post-CABG in-hospital mortality rates.<sup>3,4</sup>

Although potentially multifactorial,<sup>1–7</sup> the cause of postoperative neurological complications has often been linked to the surgical strategy adopted for CABG, and particularly to the

From the Cardio-Thoracic Surgery Unit, Heart and Vascular Centre, Maastricht University Medical Centre (MUMC), Cardiovascular Research Institute Maastricht (CARIM), Maastricht, The Netherlands (R.L.); Cardiac Surgery Unit, Community Hospital, Brescia, Italy (R.L.); Cardiothoracic and Vascular Department, Maria Cecilia Hospital, GVM Care & Research, Cotignola (RA), Italy (M.M.); Department of Cardio-Thoracic Surgery, Weill Cornell Medicine, New York, NY (A.D.F., M. Gaudino); Cardiac Surgery Unit, Humanitas Gavazzeni, Bergamo, Italy (V.G.); Cardiac Surgery Unit, Ospedale Maggiore, University of Parma, Italy (F.N., T.G.); Cardiac Surgery Unit, San Raffaele Hospital (M.D.B., M.T.), Cardiac Surgery Unit, Ospedale Sacco (R.S., C.A.), and Cardiac Surgery and Intensive Care Units, S. Donato Hospital, IRCCS (M.R., C.D.V.), University of Milan, Italy; Cardiac Surgery Unit, Poliambulanza Hospital, Fondazione Poliambulanza, Brescia, Italy (E.V., G.T.); Cardiac Surgery Unit, Ospedale di Circolo, University of Varese, Italy (G.M., C.B.); Cardiac Surgery Unit, S. Ambrogio Hospital, Milan, Italy (A.M., M. Glauber).

Accompanying Data S1 and Figure S1 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013650>

\*Dr Lorusso and Dr Moscarelli contributed equally to this work.

**Correspondence to:** Roberto Lorusso, MD, PhD, Cardio-Thoracic Surgery Department, Heart and Vascular Centre, Maastricht University Medical Centre (MUMC), Cardiovascular Research Institute Maastricht (CARIM), P. Debyelaan 25, 6202 AZ Maastricht, The Netherlands. E-mail: roberto.lorusso@mumc.nl

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## Clinical Perspective

### What Is New?

- Off-pump coronary artery bypass and the use of single aortic clamping with on-pump coronary artery bypass are associated with a reduced incidence of postoperative stroke.

### What Are the Clinical Implications?

- Our data confirm a strong association between aortic manipulation and neurological outcome after coronary artery bypass surgery.

extent of the aortic manipulation.<sup>8</sup> Several investigations have attempted to correlate aortic manipulation with postoperative stroke rate after CABG and have almost unanimously reported a direct correlation between the 2 variables.<sup>1,2,5–18</sup> The reduction of aortic manipulation has typically been achieved by using off-pump (OPCAB) surgery and/or limited or no aortic clamping.

All of the published series, however, were limited by relatively small sample sizes and, because of the low rate of stroke after CABG, limited statistical power.

In this study, we aimed to identify the independent predictors of stroke in one of the largest contemporary nonregistry series of patients with CABG. We hypothesized that the degree of aortic manipulation is associated with postoperative stroke rate. We assumed the degree of aortic manipulation to be higher for on-pump versus off-pump surgery and for multiple versus single or no aortic clamping.

## Materials and Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request. This was a retrospective analysis of prospective collected data from 9 cardiac centers in Italy and the United States (list of centers provided in Data S1) including patients undergoing surgery between 2010 and 2018. All patients consented to surgery. The need for retrospective consent to data collection was waived by local ethical committees. A common data set, with agreed definitions and variables, was used for this study. Only in-hospital events and outcomes were assessed. Inclusion criteria were isolated elective CABG in adult patients and absence of preoperative neurological deficit.

Each data frame from each center was saved in .csv format and double-checked for consistency and possible errors (eg, extreme outliers/wrong coding). Inconsistencies were resolved after consultation with the local principal investigator. The 9 data frames were then merged and uploaded in a common data set for the analysis.

The study was approved by the ethical committee of the Community Hospital, Brescia, Italy (nr. 1434, 04/03/2014) and further released to each participating center for local approval.

## Outcomes and Analytic Plan

The primary outcome was postoperative stroke defined as a postoperative neurological deficit lasting more than 24 hours and associated with evidence of a brain lesion on computed tomography.

The main aim of the analysis was to assess whether the amount of aortic manipulation was associated with the primary outcome. We classified the degree of aortic manipulation as highest in on-pump CABG (ONCAB) with multiple aortic clamping and progressively lower for ONCAB with single aortic clamping, off-pump CABG (OPCAB) with multiple aortic clamping, and OPCAB with single or no aortic clamping.

To compare OPCAB and ONCAB, patients in the 2 groups were matched using propensity score matching. The aortic clamping strategy was included in the matching model.

To evaluate the association of the clamping strategy with postoperative stroke in the OPCAB and ONCAB groups a multivariable regression model was used in the 2 unmatched cohorts.

## Statistical Analysis

Continuous variables were tested for normality with Shapiro–Wilk test and were reported as mean and SD or median and interquartile range; *t* test or Wilcoxon–Mann–Whitney test were used to compare continuous variables. Categorical variables were reported as counts and percentages and compared with chi-square test.

Propensity score matching was used to balance the distributions of measured confounding baseline covariates between the OPCAB and ONCAB groups. Variables included in the propensity score matching model were age, sex, left ventricular function, systemic hypertension, insulin-dependent and noninsulin-dependent diabetes mellitus, chronic obstructive pulmonary disease, stroke history, transient ischemic attack history, carotid stenosis (>50%), peripheral vascular disease, renal dysfunction, previous percutaneous coronary intervention, preoperative intra-aortic balloon pump, number of vessels disease, and redo surgery. A 1:1 nearest neighbor matching model was used.

A multivariable logistic regression model was used instead to assess the effect of multiple variables on postoperative stroke in the OPCAB and ONCAB unmatched populations. Variables included in the model were all of the baseline patient characteristics, the center, and the use of single-clamp or lateral-side bite clamping (for the ONCAB) and use of single or multiple lateral-side bite clamping (for the OPCAB).

Model discrimination was evaluated by the area under the receiver operating characteristic curve. R version 3.1.2 (2014-10-31) was used for all statistical analyses and *P* value significance was set at 0.05.

## Results

From the 9 institutional databases, 25 388 patients with isolated CABG were included (17 231 with ONCAB and 8157 with

OPCAB). Two centers performed more OPCAB procedures than ONCAB (2740/1268 and 1998/944, with the OPCAB/ONCAB pump, respectively), while the others used the ONCAB strategy more frequently. One center performed OPCAB surgery only.

Table 1 reports the baseline characteristics of the overall population and the OPCAB and ONCAB groups (the baseline characteristics and postoperative outcomes in the ONCAB and OPCAB groups stratified according to the clamping technique adopted are reported in Table 2).

**Table 1.** Overall Population

	ONCAB (n=17 231)	OPCAB (n=8157)	<i>P</i> Value	SMD
Baseline characteristics				
Age, y	66.5±9.6	67.3±9.9	<0.001	0.025
Men	14 016 (81.3)	6517 (79.9)	0.007	0.037
LVEF, %	52±11.6	51.9±11.3	0.5	0.192
Systemic hypertension	6818 (39.6)	3603 (44.2)	<0.001	0.093
NIDDM	6150 (35.7)	2392 (29.3)	<0.001	0.136
IDDM	2781 (16.1)	755 (9.3)	<0.001	0.208
COPD	1531 (8.9)	2374 (29.1)	<0.001	0.533
Stroke history	79 (0.4)	42 (0.9)	0.001	0.351
TIA history	945 (5.5)	171 (2.1)	<0.001	0.432
Carotid stenosis >50%	206 (4.1)	294 (5.7)	<0.001	0.185
Peripheral vascular disease	2425 (14.1)	923 (11.3)	<0.001	0.052
Renal dysfunction*	1624 (9.4)	415 (5.1)	<0.001	0.087
Previous PCI	3089 (17.9)	3277 (40.2)	<0.001	0.138
Preoperative IABP	466 (2.7)	269 (3.3)	0.01	0.035
Left main disease	5464 (31.7)	2281 (28)	<0.001	0.082
Single-vessel disease	3002 (17.4)	950 (11.6)	<0.001	0.239
Double-vessel disease	7077 (41.1)	2822 (34.6)	<0.001	0.134
Triple-vessel disease	7152 (41.5)	4385 (53.8)	<0.001	0.247
Redo surgery	1374 (8)	180 (2.2)	<0.001	0.265
Operative details for proximal anastomosis				
Single aortic cross-clamp	10 090 (58.5)	...		
Single lateral-side bite clamp	7141 (41.4)	3731 (45.7)	<0.001	
Multiple lateral-side bite clamps	...	3973 (48.7)		
Postoperative outcomes				
Stroke	141 (0.8)	53 (0.6)	0.02	
Reoperation for bleeding	680 (3.9)	172 (2.1)	<0.001	
Patients with transfusion	7294 (42.3)	3198 (39.2)	<0.001	
Postoperative AF	3247 (18.8)	1426 (17.5)	<0.001	
Renal failure	1099 (6.4)	452 (5.5)	0.001	
In-hospital mortality	500 (2.9)	134 (1.6)	<0.001	

Values are expressed as mean±SD or number (percentage). AF indicates atrial fibrillation; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IDDM, insulin-dependent diabetes mellitus; LVEF, left ventricular ejection fraction; NIDDM, noninsulin-dependent diabetes mellitus; ONCAB, on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; PCI, percutaneous coronary intervention; SMD, standardized mean difference; TIA, transient ischemic attack.

\*Creatinine >2 mg/dL.

**Table 2.** Baseline Characteristics and Postoperative Outcomes in the ONCAB and OPCAB Groups Stratified According to the Clamping Technique Adopted

	ONCAB Multi-Clamp (n=10 090)	ONCAB Single Clamp (n=7141)	OPCAB Multi- Clamp (n=3542)	OPCAB Single/ No Clamp (n=4615)
<b>Baseline characteristics</b>				
Age, y	66.5±9.6	66.3±7.8	67.3±9.9	67.1±8.7
Men	8356 (48.4)	5660 (32.8)	3474 (42.5)	3043 (37.3)
LVEF, %	51±10.5	50.6±10.4	51.7±10.3	50.3±9.9
Systemic hypertension	4886 (28.3)	1932 (11.2)	1689 (20.7)	1914 (41.4)
NIDDM	4703 (27.2)	1447 (8.3)	647 (7.9)	1745 (21.3)
IDDM	1554 (9)	1227 (7.1)	454 (5.5)	301 (3.6)
COPD	796 (4.6)	735 (4.2)	1331 (16.3)	1043 (12.7)
Stroke history	48 (0.2)	31 (0.1)	30 (0.3)	12 (0.1)
TIA history	651 (3.7)	294 (1.7)	70 (0.8)	101 (1.2)
Carotid stenosis >50%	114 (0.6)	92 (0.5)	174 (2.1)	120 (1.4)
Peripheral vascular disease	1240 (7.1)	1185 (6.8)	421 (5.1)	502 (6.1)
Renal dysfunction*	1624 (9.4)	799 (4.6)	182 (2.2)	233 (2.8)
Previous PCI	1687 (9.7)	1402 (8.1)	1253 (15.3)	2024 (24.8)
Preoperative IABP	264 (1.5)	202 (1.1)	126 (1.5)	143 (1.7)
Left main disease	3250 (18.8)	2214 (12.8)	1149 (14)	1132 (13.8)
Single-vessel disease	2494 (14.4)	507 (2.9)	651 (7.9)	299 (3.6)
Double-vessel disease	3077 (17.8)	4000 (23.2)	1366 (16.7)	1456 (17.8)
Triple-vessel disease	2967 (17.2)	4185 (24.2)	2318 (28.4)	2067 (25.3)
Redo surgery	672 (3.8)	702 (4)	124 (1.5)	56 (0.6)
<b>Postoperative outcomes</b>				
Stroke	118 (0.6)	23 (0.1)	31 (0.3)	22 (0.2)
Reoperation for bleeding	680 (1.7)	376 (2.1)	69 (0.8)	103 (1.2)
Patients with transfusion	4328 (25.1)	2966 (17.2)	1795 (22)	1403 (17.1)
Postoperative AF	2079 (12)	1168 (6.7)	723 (8.8)	703 (8.6)
Renal failure	875 (5)	224 (1.2)	248 (3)	204 (2.5)
In-hospital mortality	330 (1.9)	170 (0.9)	35 (0.4)	99 (1.2)

Values are expressed as mean±SD or number (percentage). AF indicates atrial fibrillation; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IDDM, insulin-dependent diabetes mellitus; LVEF, left ventricular ejection fraction; NIDDM, noninsulin-dependent diabetes mellitus; ONCAB, on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

\*Creatinine >2 mg/dL.

In the unmatched population, the incidence of postoperative stroke was significantly lower in the off-pump group (53 versus 141 strokes, 0.6% versus 0.8% with OPCAB versus ONCAB, respectively;  $P=0.02$ ). OPCAB was also associated with significantly lower in-hospital mortality rates (134 versus 500 deaths, 1.6% versus 2.9% death rates in OPCAB versus ONCAB, respectively;  $P<0.001$ ) and significantly lower re-exploration for bleeding, need for blood transfusion, and incidence of atrial fibrillation and renal failure (Table 1).

### Propensity Matched Comparison

After propensity matching, 4131 matched pairs with limited heterogeneity were generated, for a total sample size of 8262 patients, or 32.5% of the original cohort (Table 3, Figure S1A and S1B).

Fifty patients had postoperative stroke in the ONCAB group and 18 in the OPCAB group (1.2% versus 0.4%, respectively;  $P=0.02$ ). Other relevant postoperative outcomes are reported in Table 3.

**Table 3.** Propensity Score–Matched Cohorts

	ONCAB (n=4131)	OPCAB (n=4131)	P Value	SMD
Baseline characteristics				
Age, y	67.2±10	67.1±9.9	0.4	0.031
Men	3361 (81.4)	3354 (81.2)	0.8	0.023
LVEF, %	50.9±11.2	51±11.3	0.7	0.011
Systemic hypertension	1688 (40.9)	1676 (40.6)	0.8	0.022
NIDDM	1223 (29.6)	1264 (30.6)	0.3	0.001
IDDM	384 (9.3)	412 (10)	0.3	0.001
COPD	1024 (24.8)	962 (23.3)	0.1	0.043
Stroke history	1090 (26.4)	1100 (26.2)	0.8	0.055
TIA history	134 (3.2)	118 (2.9)	0.3	0.041
Carotid stenosis >50%	909 (22)	911 (22.1)	0.9	0.002
Peripheral vascular disease	426 (10.3)	468 (11.3)	0.1	0.023
Renal dysfunction*	242 (5.9)	265 (6.4)	0.3	0.002
Previous PCI	1779 (43.5)	1734 (42)	0.1	0.001
Preoperative IABP	141 (3.4)	122 (3)	0.2	0.020
Left main disease	1153 (27.9)	1214 (29.4)	0.1	0.024
Single-vessel disease	568 (13.7)	544 (13.1)	0.4	0.039
Double-vessel disease	1504 (36.4)	1566 (37.9)	0.1	0.030
Triple-vessel disease	2059 (49.8)	2021 (48.9)	0.1	0.033
Redo surgery	175 (4.2)	163 (3.9)	0.5	0.030
Operative details for proximal anastomosis				
Single aortic cross-clamp	2120 (51.3)	...		
Single lateral-side bite clamp	2011 (48.6)	1976 (47.8)	0.6	
Multiple lateral-side bite clamps	...	1498 (36.2)		
Postoperative outcomes				
Stroke	50 (1.2)	18 (0.4)	0.02	
Reoperation for bleeding	168 (4.1)	99 (2.4)	<0.001	
Patients with transfusion	1566 (37.9)	1401 (33.9)	0.001	
Postoperative AF	3142 (18.9)	634 (11.9)	<0.001	
Renal failure	257 (6.2)	242 (5.8)	0.5	
In-hospital mortality	120 (2.9)	80 (1.9)	0.005	

Values are expressed as mean±SD or number (percentage). AF indicates atrial fibrillation; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; IDDM, insulin-dependent diabetes mellitus; LVEF, left ventricular ejection fraction; ONCAB, on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; NIDDM, noninsulin-dependent diabetes mellitus; PCI, percutaneous coronary intervention; SMD, standardized mean differences; TIA, transient ischemic attack.

\*Creatinine >2 mg/dL.

## Determinants of Postoperative Stroke

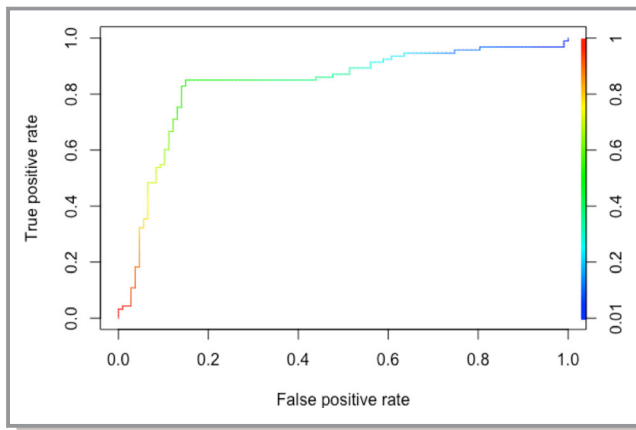
### ONCAB group

The use of single aortic clamping was associated with a lower incidence of postoperative stroke (odds ratio [OR], 0.05; 95% CI, 0.008 to 0.07 [ $P<0.001$ ]). Age (OR, 1.3; 95% CI, 1.1 to 1.55 [ $P<0.001$ ]) and the use of an intra-aortic balloon pump (OR, 1.3; 95% CI, 1.1 to 1.6 [ $P=0.02$ ]) were the other independent predictors of postoperative stroke. The

area under the receiver operating characteristic curve was 0.83 (Figure 1).

### OPCAB group

Age (OR, 1.4, 95% CI, 1.1 to 1.6 [ $P=0.001$ ]), use of a preoperative intra-aortic balloon pump (OR, 1.8; 95% CI, 1–2.5 [ $P=0.02$ ]), and chronic obstructive pulmonary disease (OR, 1.2, 95% CI, 1 to 1.4 [ $P=0.05$ ]) were associated with an increased incidence of



**Figure 1.** Receiving operating characteristic curve and area under the curve (AUC) in the on-pump coronary artery bypass grafting overall population. AUC: 0.83.

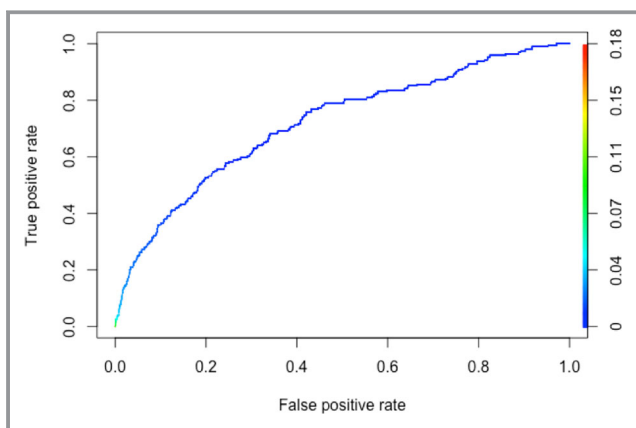
postoperative stroke. The use of single or multiple lateral side bite clamping was not associated with the incidence of postoperative stroke (OR, 1.1; 95% CI, 0.8 to 1.66 [ $P=0.11$ ]). The area under the receiver operating characteristic curve was 0.81 (Figure 2).

When the single-clamp technique was used the incidence of stroke in the matched population was 0.1% for ONCAB versus 0.3% for OPCAB ( $P=0.1$ ).

A sensitivity analysis was performed in the overall unmatched populations (ONCAB and OPCAB) by excluding the ONCAB group with multiple aortic clamping. The use of single aortic clamping was associated with a lower incidence of postoperative stroke (OR, 0.06; 95% CI, 0.009 to 0.08 [ $P<0.001$ ]).

## Discussion

This series is one of the largest contemporary nonregistry CABG cohorts. Our results suggest that the extent of



**Figure 2.** Receiving operating characteristic curve and area under the curve (AUC), off-pump coronary artery bypass grafting overall population. AUC: 0.81.

ascending aortic manipulation during CABG is associated with postoperative stroke rate. In fact, the use of OPCAB and the single-clamp technique during ONCAB were associated with significantly lower postoperative stroke rates.

Several studies have shown stroke rates after CABG ranging from 0.5% to 3%.<sup>1–19</sup> The occurrence of such adverse events in patients with CABG indicates a poor prognosis with regards to morbidity and mortality.<sup>1–4</sup> In a study analyzing almost 670 000 patients from the Nationwide Inpatient Sample from 1999 to 2011, stroke rate was 1.9%, with 2.1% and 4.9% of mortality and morbidity, respectively, leading to a 5-fold increased risk of operative death and complications.<sup>4</sup> Of note, while mortality steadily decreased over the years (from 2.7% to 1.6%), the event rate of neurological complications steadily increased during the study period.<sup>4</sup>

Our findings are in accordance with published data, showing a relatively low rate of stroke after isolated CABG (<1%) and significantly higher in-hospital mortality rate in patients who experienced postoperative stroke (32.4% versus 2.2% nonstroke patients,  $P<0.001$ ).

Age, chronic renal failure, recent myocardial infarction, previous cerebrovascular accident, hypertension, diabetes mellitus, left ventricular dysfunction, low cardiac output syndrome, atrial fibrillation, cerebrovascular disease, and use of intra-aortic balloon pump have all been shown to increase the risk of postoperative neurologic events.<sup>1,2,5–7</sup>

The effect of aortic clamping strategy on postoperative neurological complications was addressed by Calafiore et al<sup>13</sup> in 2002 and subsequently by several other authors.<sup>8–12,14</sup> Daniel et al<sup>12</sup> showed that the single-clamp technique was significantly associated with reduced neurological events as compared with multiple aortic clamping. In a series of 12 000 patients with CABG, the use of an aortic facilitating device to perform the proximal anastomosis significantly reduced the rate of stroke after CABG, but was inferior to the no-aortic touch technique.<sup>10</sup>

Of note, the use of the single-clamp technique in ONCAB allows the user to choose the most optimal site to perform the anastomosis. It also provides faster delivery of antegrade cardioplegia to the more ischemic, vulnerable areas of the myocardium during the cross-clamp period when saphenous vein grafts are used, and makes measuring the length of the needed graft material easier (therefore optimizing the quantity of conduit needed). On the other hand, cross-clamp times may be longer (especially when training residents).

The absolute absence of aortic manipulation (so-called “anaortic” technique) seems to provide even additional neurological protection. Valley et al.<sup>11</sup> reported that the anaortic strategy resulted in 0.25% of neurologic adverse events as compared with 1.1% in the groups with side-clamping for proximal anastomoses. Other studies reported postoperative stroke in the 0.2% to 0.3% range using the anaortic technique.<sup>14–16,20</sup>

A randomized study comparing ONCAB versus OPCAB in a limited patient population showed a reduced cerebral embolism in patients with OPCAB who had a better neurocognitive score at discharge.<sup>18</sup> The difference in neurocognitive impairment between the 2 groups, however, was not significant at 6 weeks or 6 months after surgery.<sup>18</sup> Marui et al<sup>17</sup> showed that, despite no difference in terms of 30-day mortality between patients with ONCAB and OPCAB, the OR of postoperative stroke in ONCAB versus OPCAB for high-risk patients (Euroscore >6%) was 8.30 (95% CI, 2.25–30.7;  $P<0.01$ ). Hammon and associates,<sup>8</sup> however, reported that the use of the single cross-clamp ONCAB technique achieved similar stroke rates than OPCAB as well as similar postoperative neurocognitive dysfunction. In a small randomized trial comparing single and multiple aortic clamps, the single-clamp group showed a 9% rate of persistent neurocognitive deficits as assessed by clinical examination and computed tomography imaging, as compared with 26% and 27% in the multiple-aortic manipulation and OPCAB groups, respectively.<sup>18</sup>

It must be emphasized, however, that most of the published literature on the correlation between aortic manipulation and postoperative stroke is likely to be underpowered for clinical events. Assuming an incidence of postoperative stroke after CABG of 1%, 9300 patients are required to detect a 50% risk difference with 80% power, while the majority of the published series are less than half of this sample size.

### Study Limitations and Strengths

This investigation is a retrospective study from a multicenter international group. The lack of prospective systematic analysis, as well as institutional differences in myocardial revascularization strategy, may have hampered the quality of the data and information. The surgical strategies varied across the participating centers, and selection biases regarding patient allocation to specific surgical strategy may be present.

Data included only elective procedures. The use of the intra-aortic balloon pump increased the incidence of strokes in all patients; therefore, the results might have been different if unstable and emergent patients were also included. Thus, the data and study findings should be interpreted with caution. Also, we have no information as to when the strokes occurred postoperatively, since a stroke noted immediately after surgery as opposed to >24 hours would more likely be attributable to intraoperative techniques.

Transient neurological deficits may not have resulted in computed tomography scans. Since patients with lesions documented on computed tomography only were reported, the overall incidence of neurological events attributable to aortic manipulation may have been underestimated. Moreover, the involvement of a neurologist in the diagnosis of stroke was not systematically reported. Furthermore, this study focused on in-hospital outcomes: postdischarge

outcome was not addressed, but it may have played an additional role with respect to patient morbidity and mortality. Also, the rate of postoperative strokes resulting in transient versus permanent deficits or death was not consistently reported, as well as data on the use of antiplatelet agents, the incidence of calcified or atheromatous ascending aortas, and the use of epiaortic ultrasound.

We also did not detect significant differences between OPCAB and ONCAB when the single-clamp technique was used; hence, it may be speculated that OPCAB is as safe as ONCAB when there is less aortic manipulation.

Patient heterogeneity was addressed by employing propensity score matching and regression analysis, but this can account only for known and measured confounders. On the other hand, this study represents the largest study to date on the association between neurologic complications and CABG surgical strategy. The reported data represent a “real-life” scenario, and, as such, provide a reliable portrait of daily practice according to variable surgical preference.

### Conclusions

The results of this analysis of more than 25 000 patients from 9 centers strongly suggest that the postoperative stroke rate and the degree of aortic manipulation are closely associated. OPCAB and the use of single aortic clamping in patients with ONCAB are both associated with a reduced incidence of postoperative strokes. When the single-clamp technique is used in patients with ONCAB, there is no difference in the incidence of strokes between patients undergoing CABG on or off cardiopulmonary bypass.

### Disclosures

Professor Lorusso has consulted with Medtronic and LivaNova (honoraria for presentation, paid at the institution/university) and is an advisory board member for Eurosets and PulseCath (fee for attendance, paid at the institution/university). The remaining authors have no disclosures to report.

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# **Supplemental Material**

## **Data S1.**

### **List of participating centers for patient enrollment**

Cardiac Surgery Unit, Community Hospital, Brescia, Italy;  
Cardiac Surgery Unit, Ospedale Maggiore, University of Parma, Parma, Italy;  
Cardiac Surgery Unit, San Raffaele Hospital, University of Milan, Milan, Italy;  
Cardiac Surgery Unit, Poliambulanza Hospital, Fondazione Poliambulanza, Brescia, Italy;  
Cardiac Surgery Unit, Ospedale Sacco, University of Milan, Milan, Italy;  
Cardiac Surgery Unit, Ospedale di Circolo, University of Varese, Varese, Italy;  
Cardiac Surgery Unit, S. Ambrogio Hospital, Milan, Italy;  
Cardiac Surgery and Intensive Care Units, S. Donato Hospital, IRCCS, University of Milan, Milan, Italy;  
Department of Cardio-Thoracic Surgery, Weill Cornell Medicine, New York, NY, USA.

**Figure S1.** A: histogram of the raw treated (ON-PUMP) versus raw control (OFF-PUMP) variables before (left) and after (right) propensity matching. B: visual distribution of propensity scores.

