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Association Between Coronary Artery Bypass Surgical Techniques and Postoperative Stroke

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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.1–4 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.3 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.3,4

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

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

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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 8,157 with OPCAB). Two centers performed more OPCAB procedures than ONCAB (2,740/1,268 and 1,998/944, 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=8,157) | $P$ Value | SMD  |
|--------------------------------|------------------|-----------------|-----------|------|
| **Baseline characteristics**   |                  |                 |           |      |
| Age, y                         | 66.5±9.6         | 67.3±9.9        | <0.001    | 0.025|
| Men                            | 14,016 (81.3)    | 6,517 (79.9)    | 0.007     | 0.037|
| LVEF, %                        | 52±11.6          | 51.9±11.3       | 0.5       | 0.192|
| Systemic hypertension          | 6818 (39.6)      | 3,603 (44.2)    | <0.001    | 0.093|
| NIDDM                          | 6150 (35.7)      | 2,392 (29.3)    | <0.001    | 0.136|
| IDDM                           | 2,781 (16.1)     | 755 (9.3)       | <0.001    | 0.208|
| COPD                           | 1,531 (8.9)      | 2,374 (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    | 2,425 (14.1)     | 923 (11.3)      | <0.001    | 0.052|
| Renal dysfunction*             | 1,624 (9.4)      | 415 (5.1)       | <0.001    | 0.087|
| Previous PCI                   | 3,089 (17.9)     | 3,277 (40.2)    | <0.001    | 0.138|
| Preoperative IABP              | 466 (2.7)        | 269 (3.3)       | 0.01      | 0.035|
| Left main disease              | 5,464 (31.7)     | 2,281 (28)      | <0.001    | 0.082|
| Single-vessel disease          | 3,002 (17.4)     | 950 (11.6)      | <0.001    | 0.239|
| Double-vessel disease          | 7,077 (41.1)     | 2,822 (34.6)    | <0.001    | 0.134|
| Triple-vessel disease          | 7,152 (41.5)     | 4,385 (53.8)    | <0.001    | 0.247|
| Redo surgery                   | 1,374 (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 | 7,141 (41.4)     | 3,731 (45.7)    | <0.001    | ...  |
| Multiple lateral-side bite clamps | ...             | 3,973 (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      | 7,294 (42.3)     | 3,198 (39.2)    | <0.001    |      |
| Postoperative AF               | 3,247 (18.8)     | 1,426 (17.5)    | <0.001    |      |
| Renal failure                  | 1,099 (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, non-insulin-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.
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).

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

| Baseline characteristics | ONCAB Multi-Clamp (n=10 090) | ONCAB Single Clamp (n=7141) | OPCAB Multi-Clamp (n=3542) | OPCAB Single/No Clamp (n=4615) |
|--------------------------|-------------------------------|-----------------------------|---------------------------|-------------------------------|
| **Baseline characteristics** |                              |                             |                           |                               |
| 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, %                  | 51.0±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)                     |
| **Postoperative outcomes** |                             |                             |                           |                               |
| 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, non-insulin-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.

### 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.
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

### Table 3. Propensity Score–Matched Cohorts

| Baseline characteristics | ONCAB \( (n=4131) \) | OPCAB \( (n=4131) \) | \( P \) Value | SMD |
|--------------------------|-----------------|-----------------|-------------|-----|
| 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.
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 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%. The occurrence of such adverse events in patients with CABG indicates a poor prognosis with regards to morbidity and mortality. 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 49% of mortality and morbidity, respectively, leading to a 5-fold increased risk of operative death and complications. 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.

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.

The effect of aortic clamping strategy on postoperative neurological complications was addressed by Calafiore et al in 2002 and subsequently by several other authors. Daniel et al 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.

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. Vallely et al 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.

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.

Figure 2. Receiving operating characteristic curve and area under the curve (AUC), off-pump coronary artery bypass grafting overall population. AUC: 0.81.
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.\(^\text{18}\) The difference in neurocognitive impairment between the 2 groups, however, was not significant at 6 weeks or 6 months after surgery.\(^\text{18}\) Marui et al\(^\text{17}\) 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,\(^\text{8}\) 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.\(^\text{18}\)

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 antplatelet 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.