Which aortic clamp strategy is better to reduce postoperative stroke and death
Single center report and a meta-analysis
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Abstract
Background: Stroke is severe complication of coronary artery bypass grafting (CABG) which may be associated with clamp strategy, there are 2 strategies to clamp aorta including single aortic clamp (SAC) and partial aortic clamp (PAC). It is controversial that which clamping strategy is better to reduce the postoperative stroke and death, so this study aims to investigate which is better for reducing postoperative stroke and death within 30 days.

Methods: We collected 469 patients who had on-pump CABG in Fuwai Hospital during January 2014 to July 2015. The SAC group consisted of 265 patients while the PAC group included 204 patients. We compared the 2 group patient difference. At the same time, 12 studies were identified by systematic search. The odds ratio (OR) was used as effect index to compare SAC and PAC strategy by fix-effect modeling. We also tested heterogeneity and publication bias. The primary end point of study was occurrence of postoperative stroke within 30 days of operation, the second end point of study was the incidence of 30-day mortality.

Results: The single center retrospective study showed that the patients in the SAC group were older than those in the PAC group (62.5 ± 8.1 vs 60.3 ± 8.0 years, P = .01). The proportions of peripheral vascular disease and hypertension of SAC were higher than PAC (71 [26.8%] versus 36 [17.6%], P = .02; 183 [69.1%] versus 115 [56.4%], P = .01, respectively). Besides, the number of vascular anastomosis was more in the SAC group (3.29 ± 0.74 versus 2.97 ± 0.974, P < .001). The linear-regression analysis suggested that the time of cardiopulmonary bypass of SAC was shorter than the PAC group (93.2 ± 22.4 vs. 103.4 ± 26.8 minutes, P-regression < .001) and postoperative death within 30-days was similar (1.0.4% vs. 2 (1.0%), P-regression = .47). There was no stroke occurring in both the groups. And the meta-analysis suggested the postoperative stroke and death within 30-days were similar between SAC group and PAC group (OR: 0.78, 95% CI: 0.58–1.06; OR: 0.82, 95% CI: 0.61–1.10; respectively). Moreover, subgroup meta-analysis also had the same results.

Conclusion: There was no significant difference between SAC and PAC clamping strategy on postoperative stroke and death within 30-days; however, SAC can reduce the usage time of cardiopulmonary bypass.

Abbreviations: BMI = body mass index, CABG = coronary artery bypass grafting, CI = confidence interval, CPB = cardiopulmonary bypass, EF = ejection fraction, ICU = intensive care unit, OR = odds ratio, PAC = partial aortic clamp, PCI = percutaneous coronary intervention, PRISMA = preferred reporting items for systemic reviews and meta-analyses, RCT = randomized controlled trial, SAC = single aortic clamp, SD = standard-deviation.

Keywords: CABG, death, on-pump, partial aortic clamp, single aortic clamp, stroke

1. Introduction
Coronary atherosclerosis disease is a typical ischemic heart disease due to coronary stenosis or occlusion caused by atherosclerosis.[1] The patients are usually older than 40 years old, and the male patients are most common. With the lifestyle changing, the incidence of coronary atherosclerosis is increasing and affecting the human life expectancy.[2] Nowadays, the treatment strategies for coronary atherosclerosis disease include medical, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG).[3] Clinically, CABG may be performed either with cardiopulmonary bypass (on-pump) or without cardiopulmonary bypass (off-pump) for the patients with left main lesion or multivessel lesions.[4,5] As for on-pump CABG, there are 2 aortic clamping strategies: single aortic clamp (SAC) and partial aortic clamp (PAC). Patients in the SAC group all had distal and proximal bypass graft anastomoses performed during 1 crossclamp period. Patients in the PAC group all had distal bypass graft anastomoses were completed.[6,7]

Postoperative stroke is low incidence but severe complication of on-pump CABG even causing patients death, so many researchers are committed to investigate how to reducing postoperative stroke and death happening.[8] Some research showed reducing aortic manipulation would protect brain...
function from microemboli, that is SAC is better,\textsuperscript{[9]} others showed SAC did not protect against cerebrovascular accident in on-pump CABG.\textsuperscript{[10]}

This study aimed to investigate which aortic clamping strategy was better during on-pump CABG. We collected 469 patients who had on-pump CABG during January 2014 to July 2015. Among them, 263 patients had SAC clamping strategy and the rest 204 patients had PAC clamping strategy. We compared the postoperative difference between 2 groups to investigate which clamp was better for reducing postoperative stroke. At the same time, we also conducted a meta-analysis to compare which clamp strategy was better.

2. Materials and methods

2.1. Single center retrospective study

2.1.1. Consent. This study was approved by the Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College. This study complied with the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent for participation was obtained from all patients prior to enrollment in the study.

2.1.2. Patients. The patients included in this study were collected from Fuwai Hospital during January 2014 to July 2015 who met the following criterion: on-pump CABG; did not have cardiac operation before; not be cardiac shock; not emergency operation; patients did not decide which clamp is used; did not have other cardiac operations such as cardiac valve replacement. There are 469 patients involved in our study, 265 patients in SAC group and the rest 204 patients in PAC. We collected this patient information including baseline (age, sex, BMI, and other medical history), preoperative examination (creatinine, troponin, INR, ejection fraction, number of vascular anastomosis, and so on), intraoperative data (the time of clamping and cardiopulmonary bypass usage), the postoperative situation (the first 12-hours urine volume, the time of breath machine usage, hospital stay, and so on) and postoperative following-up (stroke and death). Postoperative stroke was defined according to The Society of Thoracic Surgeons (STS) criteria as any confirmed neurological deficit of abrupt onset that did not resolve within 24 hours. Delirium was not considered postoperative stroke if it resolved completely prior to discharge. An overwhelming majority of postoperative stroke was confirmed by a board-certified neurologist and/or brain imaging (computed tomography or magnetic resonance imaging).\textsuperscript{[11,12]} Pathological subtypes comprised ischaemic stroke (cerebral, retinal, and spinal infarction) and haemorrhagic stroke (intracerebral haemorrhage and subarachnoid haemorrhage) according to the findings of brain imaging.\textsuperscript{[13]}

2.1.3. Study end-point. The primary end point of study was occurrence of postoperative stroke within 30 days of operation, defined according to STS criteria as any confirmed neurological deficit of abrupt onset that did not resolve within 24 hours. The second end point of study was the incidence of 30-day mortality.

2.2. Statistical analysis

The statistical work was conducted by SPSS version 21. The continuous variables were described by means ± standard-deviation (SD) which were compared between groups by using t test or nonparametric test when appropriate. The categorical variables were described by frequency (proportions) which were compared between groups by \( \chi^2 \) test or the Fisher exact test when appropriate. The linear or logistic regression analysis was also conducted for continuous or categorical variables. Two tailed \( P < .05 \) was considered statistically significant.\textsuperscript{[12]}

2.3. Meta-analysis

2.3.1. Literature search strategy. We used 3 main medical data bases (PubMed, Web of Sciences, and Medline) to conduct literature searching up date to June 2017. The terms we used included single aortic clamp (or single crossclamp, 1 crossclamp, 1 aortic clamping), partial aortic clamp (or partial crossclamp, 2 crossclamp, 2 aortic clamp), aortic clamping strategy, and postoperative stroke. The reference lists of selected articles for relevant citations were also screened. Publication language was not restricted. A summary of the search strategy is shown in Fig. 1. This meta-analysis was performed in line with the Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) guidelines.\textsuperscript{[14]}

2.3.2. Inclusion criteria. This meta-analysis aimed to compare the effects of both SAC and PAC on postoperative stroke and death so the studies included should meet the following criteria: published in English; the study should be about on-pump CABG; comparing SAC and PAC; including the postoperative stroke and death within 30-days; retrospective study or randomized controlled trial (RCT).

2.3.3. Data extraction. The following information was extracted from the article included in meta-analysis: authors, publication year, publication journal, study design, sample size, clamping strategy, 30-days stroke, and death. The information was extracted by 2 authors independently.

2.3.4. Statistical analysis. This meta-analysis was conducted by ReviewerManager 5.3. The outcome variables were binary

![Flow chat of meta-analysis](image)

**Figure 1.** Flow chat of meta-analysis.
variables so the effect value was evaluated by using odds ratio (OR) with 95% confidence interval (CI) and P value. Literature heterogeneity was evaluated by Q-test and I²-test, the fixed effect model was used when I² < 50%, the random effects model was used when I² > 50%. Besides we conducted subgroup meta-analysis according to study design. Publication bias was shown by the funnel plot and tested by the Egger and Begg tests, and analysis according to study design. Publication bias was shown by the funnel plot and tested by the Egger and Begg tests, and analysis according to study design.

### 3. Results

#### 3.1. Single center retrospective study

**3.1.1. Patient baseline characteristics.** All the 469 patients’ information was shown in Table 1, which suggested that the proportion of male patients of 2 groups were similar and both were more than 80% (218 (82.3%) vs 169 (82.8%), P = .87). The patients in the SAC group were older than PAC group patients (62.5±8.1 vs 60.3±8.0 years, P = .01); the proportions of peripheral vascular disease and hypertension of SAC were higher than PAC (71 (26.8%) vs 36 (17.6%), P = .02; 183 (69.1%) vs 115 (56.4%), P = .01, respectively). Besides, the numbers of vascular anastomosis were more in the SAC group (3.29±0.74 vs 2.07±0.974, <.001). There was no significant difference on other aspects between 2 groups, and the details were shown in Table 1. According to the baseline information of 2 groups, there were confounding factors when comparing the 2 groups to investigate which clamp was better, so the linear or logistic regression analysis should be used to ensure whether clamp strategies contribute the intraoperative and postoperative difference.

#### 3.1.2. Intraoperative and postoperative difference. The 2 groups patients had on-pump CABG by using SAC or PAC respectively. First, the time of clamping of 2 groups was similar (69.8±18.0 vs 72.5±22.3 minutes, P = .38, P-regression = .03) but the time of cardiopulmonary bypass usage of SAC group was shorter than PAC group and linear regression analysis confirmed (93.2±22.4 min vs 103.4±26.8 minutes, P < .001, P-regression <.001). The first 12-hour after operation urine and chest drainage volume were similar (215.2±749.4 mL vs 2243.3±739.8 mL, P = .24, P-regression = .20; 301.6±138.8 mL vs 290.2±122.6 mL, P = .52, P-regression = .48, respectively). The time of breath machine usage was longer in the SAC group but there was no significant difference between the SAC and PAC groups after linear regression analysis (23.05±25.70 hours vs 22.61±25.62 hours, P < .001, P-regression = .97). The rest aspects were similar between 2 groups (Table 2). These results showed that SAC could reduce the usage time of cardiopulmonary bypass usage and be noninferior to PAC during hospital stay. Then we compared the 30 days stroke and death of the 2 groups.

Because the study aimed to investigate SAC and PAC which was better to reduce postoperative stroke and death happening, we had a 30-day follow-up of all patients (Table 2). Neither ischaemic stroke nor haemorrhagic stroke occurred in both the groups. One of 265 (0.37%) patients in SAC group died and 2 of 204 (0.90%) patients died during 30-day follow-up. After logistic regression analysis, SAC and PAC had same contribution to 30 days death (P-regression = .47).

#### 3.2. Meta-analysis

**3.2.1. Literature search results.** As the flow chart shown (Fig. 1), we finally collected 12 studies to conduct meta-analysis.[7,10,12,15-23] The information of the 12 studies was summarized in Table 3. These studies included 13,486 on-pump CABG patients, 5174 of them in SAC group and 10,312 of them in PAC group. Seven of 12 studies were retrospective studies, including 14,577 patients, 4701 of them having SAC and the rest having PAC.[7,10,12,15-18] Other 5 of 12 studies were RCTs, including 909 patients, among them 473 patients having SAC, and the rest 436 having PAC.[19-23]

**3.2.2. Meta-analysis results.** There was no significant difference on postoperative stroke and death within 30 days between 2 groups, after merging effect value. Comparing SAC to PAC, the OR for 30-day stroke was 0.78 (95% CI: 0.58–1.06, P = .15, I² = 0%) and the OR for 30-day death was 0.82 (95% CI: 0.61–1.10, P = .18, I² = 0%) (Fig. 2). Then, we analyzed subgroup to investigate whether different study designs had different results.

In RCTs, the ORs for 30 days stroke and death were that OR: 0.53, 95% CI: 0.19–1.45, P = .22, I² = 0%; OR: 0.46, 95% CI: 0.16–1.33, P = .15, I² = 0%, respectively (Fig. 3). In retrospective

### Table 1

|                  | SAC   | PAC   | P value |
|------------------|-------|-------|---------|
| N                | 265   | 204   |         |
| Male (n, %)      | 218 (82.3) | 169 (82.8) | .87     |
| Age, y           | 62.5±8.1 | 60.3±8.0 | .01     |
| BMI              | 26.0±3.4 | 25.6±3.1 | .21     |
| Creatinine, umol/L | 95.1±21.9 | 90.7±23.2 | .75     |
| BNP, pmol/L      | 551.7±676.6 | 473.6±378.8 | .09     |
| Triglyceride, mmol/L | 1.68±1.12 | 1.67±1.24 | .72     |
| INR              | 1.00±0.09 | 1.02±0.12 | .80     |
| Troponin, ng/mL  | 0.21±1.07 | 0.29±1.06 | .76     |
| Hyperlipidaemia (n, %) | 195 (73.6) | 142 (69.6) | .34    |
| Peripheral vascular disease (n, %) | 71 (26.8) | 36 (17.6) | .02 |
| Smoke history (n, %) | 155 (58.5) | 123 (60.3) | .69   |
| Hypertension (n, %) | 183 (69.1) | 115 (56.4) | .01  |
| Stroke history (n, %) | 12 (4.3) | 9 (4.4) | .95  |
| EF (%)           | 58.2±9.6 | 59.7±9.0 | .12     |
| Number of vascular anastomosis (n, %) | 3.29±0.74 | 2.07±0.974 | <.001 |

BMI = body mass index, EF = ejection fraction, PAC = partial aortic clamp, SAC = single aortic clamp.

### Table 2

|                  | SAC   | PAC   | P value |
|------------------|-------|-------|---------|
| N                | 265   | 204   |         |
| Clamping time, min | 60.8±18.0 | 72.5±22.3 | .58     |
| CPB usage time, min | 93.2±22.4 | 103.4±26.8 | <.001 |
| 12 h urine volume, mL | 2155.2±749.4 | 2243.3±739.8 | .25    |
| 12 h chest drainage volume, mL | 301.6±138.8 | 290.2±122.6 | .52    |
| Breath machine, h | 23.05±25.70 | 22.61±25.62 | <.001 |
| Chest tube time, h | 48.43±26.58 | 48.53±26.29 | .24    |
| ICU stay, d       | 2.48±2.01 | 2.75±2.26 | .18    |
| Respiration (n, %) | 13 (4.9) | 3 (1.5) | .04    |
| Hospital stay, d  | 17.11±8.30 | 16.05±7.26 | .06    |
| 30-d stroke (n, %) | 0     | 0     | –     |
| Ischaemic stroke (n, %) | 0     | 0     | –     |
| Haemorrhagic stroke (n, %) | 0     | 0     | –     |
| 30-d death (n, %) | 1 (0.4) | 2 (1.0) | .42    |

CPB = cardiopulmonary bypass, ICU = intensive care unit, PAC = partial aortic clamp, SAC = single aortic clamp.
studies, the merge result for 30 days stroke was that OR: 0.81, 95% CI: 0.60–1.10, \( P = 0.18, I^2 = 0\%\); the combined result for 30 days death was that OR: 0.86, 95% CI: 0.63–1.17, \( P = 0.33, I^2 = 0\%\) (Fig. 4). These results showed that SAC and PAC contributed similarly to 30 days stroke and death according to the overall meta-analysis and subgroup analysis.

### Table 3

The characteristics of included studies.

| Author-first Name | Publication year | Study design | Publication journal | Sample size (SAC/PAC) | Stroke (%) (SAC/PAC) | Death (%) (SAC/PAC) |
|-------------------|------------------|--------------|---------------------|----------------------|---------------------|---------------------|
| Danny Chu        | 2016             | Retrospective studies | JAMA Surg | 1107/712 | 1.5 vs 1.4 | 1.9 vs 1.8 |
| Juan C. Araque   | 2015             | Retrospective studies | J Thorac Cardiov Sur | 2051/6446 | 1.2 vs 1.5 | 1.0 vs 1.4 |
| Ishan Sami Uyar  | 2013             | Retrospective studies | Cardiov J Afr | 500/1500 | 1.8 vs 1.7 | 1.4 vs 1.6 |
| Mehmert Ates     | 2006             | Retrospective studies | Int Heart J | 550/550 | 1.3 vs 1.6 | 1.1 vs 1.3 |
| John W. H.       | 2006             | RCT              | J Thorac Cardiov Sur | 102/67 | 2.9 vs 4.5 | 0 vs 4.5 |
| Sinalta R        | 2004             | RCT              | Ital Heart J | 145/136 | 0.6 vs 0.7 | 1.3 vs 1.4 |
| Melih Hulusi Us  | 2003             | Retrospective studies | AnadoluKardiyolDerg. | 32/212 | 0 vs 10.4 | 3.1 vs 3.3 |
| John C. Tsang    | 2003             | RCT              | J Card Surg | 133/135 | 0 vs 1.5 | 1.5 vs 2.2 |
| Richard W. Kim   | 2001             | Retrospective studies | Eur J Cardio-Thorac | 301/306 | 1.7 vs 2.0 | 2.7 vs 1.6 |
| Francesco        | 1998             | RCT              | Eur J Cardio-Thorac | 48/43 | 2.0 vs 0 | 0 vs 0 |
| Paolo Bertolani  | 1997             | RCT              | Eur J Cardio-Thorac | 45/55 | 0 vs 5.5 | 0 vs 1.8 |
| Sary F. Aranki    | 1994             | Retrospective studies | Ann Thorac Surg | 160/150 | 0.6 vs 2.0 | 2.5 vs 5.3 |

PAC = partial aortic clamp, RCT = randomized controlled trial, SAC = single aortic clamp.

3.2.3. Publication bias. The publication bias of the studies included in this meta-analysis was shown as Fig. 5. The funnel plot suggested that there was no publication bias, besides that the Begg and Egger tests supported there was no publication bias (Begg test: \( P = .24 > .05 \), Egger test: \( P = .11 > .05 \), respectively).

### 4. Discussion

At present, surgical treatment is still preferred one for left main coronary artery and multiple vessel disease.[24] There are 2 surgery ways to conduct CABG including on-pump and off-pump CABG. The outcome of CABG is very well, but very few patients will have stroke after operation which is severe complication and...
The stroke is mainly caused by microthrombus, it is thought that reducing aortic manipulation can reduce the microthrombus and protesting from stroke. Moreover, it is reported that inflammation not only contributes to stroke pathogenesis but also has a possible association with outcome in acute ischemic cerebrovascular syndromes. Clamping strategy may contribute to postoperative stroke by promoting inflammation, but the relationship between stroke and clamping strategy remains further investigated.

After comparing the 2 group baseline characteristics, confounding factors exist such as age, peripheral vascular disease, hypertension, and number of vessel anastomose; it suggests the patients in the SAC group are at high risk (Table 1). To compare clamping strategy effect on outcomes of patients, we conduct regression analysis (Table 2). It indicates that different clamping strategies have similar effect on postoperative situations and 30-day stroke and death, but SAC has advantage on shorter usage of cardiopulmonary bypass (69.8 ± 18.0 min vs 72.5 ± 22.3 minutes, P-regression = .05). As reported, the usage cardiopulmonary bypass would bring side effect on body such as acute kidney injury, brain injury, blood loss, transfusion, and other organ dysfunction.

![Figure 3](image1.png)

*Figure 3.* The merge effect of 5 RCTs: the ORs for 30 days stroke and death were that OR: 0.53, 95% CI: 0.19 to 1.45, P = .22, I² = 0%; OR: 0.46, 95% CI: 0.16 to 1.33, P = .15, I² = 0%, respectively. OR = odds ratio, CI = confidence interval. RCT = randomized controlled trial.

![Figure 4](image2.png)

*Figure 4.* The merge effect of 7 retrospective studies: the merge result for 30 days stroke was that OR: 0.81, 95% CI: 0.60 to 1.10, P = .22, I² = 0%. The combined result for 30 days death was that OR: 0.86, 95% CI: 0.63 to 1.17, P = .33, I² = 0%. OR = odds ratio, CI = confidence interval.
Since 1990, there were only 12 studies about comparing the different clamping strategy effects on postoperative stroke and death and different studies had different conclusions. And we conducted a meta-analysis to investigate which clamp is better. This meta-analysis shows different clamp strategies contribute similarly to postoperative stroke and death. The ORs for stroke and death are that OR: 0.78, 95% CI: 0.58–1.05, \(P = .10\); OR: 0.82, 95% CI: 0.61–1.10, \(P = .18\), respectively (Fig. 2). Meanwhile, we analyze subgroup according to study design and the results are consistent with the overall results. Because ORs are less than 1 (\(P > .05\)), it is inferred that SAC may have tendency to protect patients from stroke and death but without significant difference. We think that some reasons can explain the phenomenon: 2 clamp strategies are the same in fact; lack of middle and long-term following-up results; the sample size of RCT is small.

In summary, according to the Fuwai hospital retrospective study, it suggested that SAC and PAC group patients have same outcomes including postoperative stroke and death but SAC could reduce the usage of cardiopulmonary bypass which was good for patients. Besides, the meta-analysis confirms the single center study. The meta-analysis indicates that there is no difference on postoperative stroke and death within 30 days comparing SAC with PAC.

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- **Writing – original draft**: L. Chen, X. Hua.
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