# Incidence of Perioperative Stroke in Elderly Patients Undergoing Off-pump Versus On-pump Coronary Artery Bypass Grafting: A Systematic Review and Meta-analysis

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**Abstract: Objective:** To evaluate the incidence of perioperative stroke in elderly patients undergoing off- pump coronary artery bypass grafting and on-pump coronary artery bypass grafting using meta-analysis. **Methods:** Databases including Pub Med, EMbase, CNKI and Wan Fang Data were searched (1990 to 2012). **Results:** A total of 17 studies were included, involving 7257 patients including 2521 in the OPCAB group and 4754 in the CABG group. The results of meta-analysis showed that statistical difference in stroke incidence between the OPCABG and CABG. **Conclusion: OPCAB may reduce incidence of perioperative stoke in elderly patients**. However, it still needs to be confirmed by more multicenter, large-sample controlled trials in the future.
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**Key words:** Coronary artery bypass grafting; Stroke; Elderly; meta-analysis

## 1. Introduction

Coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI) and drug therapy are three main methods of treatment of coronary heart disease, and the elderly ($\geq$65 years, especially $\geq$ 70 years) is the risk factor of CABG perioperative death (Alexander et al.,2000) and complications (stroke, atrial fibrillation, renal failure, myocardial infarction, and extend the duration of mechanical ventilation, etc) (Horneffer et al.,1987; Mangano et al., 1998;Amar et al.,2002; Stamou et al.,2000), therefore, elderly patients undergoing CABG is a big challenge in this field.

In recent years, with the development of CABG technique and anesthesia level, the mortality and complication rates of elderly patients undergoing CABG were decreased significantly, especially the off-pump coronary artery bypass grafting (OPCAB) fixation and traction device improvement, so the surgeons can safely and effectively perform OPCAB in relatively still and bloodless operative field for patients with multivessel coronary artery disease (Ascione et al.,2002; Pinto et al., 2008; Lev-Ran et al., 2004). It has been found that OPCAB could significantly reduce the mortality and the incidence of stoke in elderly and high-risk patients compared with on-pump coronary artery bypass grafting (CABG), therefore, patients should preferential use OPCAB (Al-Ruzzeh et al.,2003; Akpinar et al.,2001; Ascione et al.,2001; Boyd et al.,1999; Ricci et al.,2001). However, some studies found that OPCAB had not yet shown its advantages (Fritz et al.,2004; Li et al.,2008; Kshettry et al., 2000). Therefore, we collected all clinical research of elderly patients undergoing OPCAB and CABG and occurrence of stroke in perioperative period, and perform a systematic review and meta-analysis, to explore whether OPCAB could reduce the incidence of perioperative stroke in elderly patients.

## 2. Materials and methods

### 2.1 Selection of studies

Two authors will take on the review. The search strategy described will be used to obtain titles and abstracts of studies that may be relevant to the review. Two authors will screen the search results and they will read the full text of eligible studies identified in this way. The two authors will decide on their suitability for inclusion in the review based on whether they meet the prespecified inclusion criteria. We will report disagreement and will resolve disagreement by a consensus procedure, if necessary, with a third review author.

### 2.2 Data extraction and management

Two review authors will extract the data independently to a self-developed data extraction form. Studies reported in non-English language journals will be translated before assessment. Where more than one publication of one trial exists, only the publication with the most complete data will be included. We will write to study authors for further information when necessary. Disagreements will be resolved by majority vote, if necessary, of a third review author. One author

will enter data into Review Manager software (RevMan 5.0.20), and a second author will independently check the data entry.

**2.3 Assessment of risk of bias in included studies**

Two authors will independently use the GRADE criteria to assess risk of bias for all included studies.

**2.4 Measures of treatment effect**

For dichotomous data, results will be summarised as risk ratios (RR), with 95% confidence intervals (CI). For continuous out-comes we will use weighted mean difference (WMD) (when measures are in the same unit), or standardized mean difference (SMD) (when different scales are used to evaluate the same outcome) with 95% CI as well.

**2.5 Unit of analysis issues**

Cross-over trials will not be included in this review. We will try to identify cluster-randomized trials; they will be included and analyzed in accordance with section 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions.

**2.6 Dealing with missing data**

The authors of papers with missing data will be contacted. We will make a note of all trials that do not use intention-to-treat (ITT) analysis; we will make every attempt to analysis our data by this principal.

**2.7 Data synthesis and Sensitivity analysis**

A ï¬xed-effects model will be used unless significant heterogeneity with $I^2$> 50% among studies. In that case a random-effects model will be used.

Subgroup analysis will be used to explore possible sources of heterogeneity. Heterogeneity among studies will be estimated by the $I^2$ statistic. Typically, values above 50% are deemed to suggest significant heterogeneity. Values of 25% to 50% are deemed to show modest heterogeneity, and values below 25% are deemed to represent low heterogeneity.

We will perform a sensitivity analysis if we find significant heterogeneity ($I^2$> 50%).

## 3. Results

**3.1 Literature search results**

We searched 190 literatures on line firstly, 41 literatures were included after reading title and abstract, and 27 articles were included after reading the full text (Ascione et al.,2002; Boyd et al.,1999; Ricci et al., 2001; Fritz et al.,2004; Li et al.,2008; Hirose et al., 2001; Demers et al.,2001; Al-Ruzzeh et al.,2001; Meharwal et al., 2002; Lin et al.,2003; Demaria et al., 2002; Hoff et al.,2002; Kilo et al.,2001; Ricci et al., 2000; Reston et al.,2003;Cheng et al.,2005; Parolari et al., 2003; Wandschneider et al.,2000; Van Dijk et al., 2002; Lev-Ran et al.,2004; Zamvar et al., 2002; Weerasinghe et al.,2005; Ramadan et al.,2010; Houlind et al.,2009; Gong et al.,2008; Geng et al., 2009; Lin et al.,2005), at last, 17 literatures met the inclusion and exclusion criteria (Ascione et al.,2002; Boyd et al.,1999; Ricci et al.,2001; Fritz et al.,2004; Li et al.,2008; Hirose et al.,2001; Demers et al.,2001; Al-Ruzzeh et al.,2001; Meharwal et al., 2002; Lin et al., 2003; Demaria et al.,2002; Hoff et al.,2002; Kilo et al., 2001; Ricci et al.,2000; Gong et al.,2008; Geng et al., 2009; Lin et al.,2005). A total of 7275 patients were included, OPCAB group was 2521 cases (34.65%) and CABG group was 4754 cases (65.35%).

**3.2 Basic characteristics of the included studies**

Five of the 17 articles were retrospective cohort study (Ascione et al.,2002; Boyd et al.,1999; Li et al., 2008; Demers et al.,2001; Al-Ruzzeh et al.,2001), the other 12 articles were case-control study (Ricci et al., 2001; Fritz et al.,2004; Meharwal et al., 2002; Lin et al., 2003; Demaria et al.,2002; Hoff et al.,2002; Kilo et al., 2001; Ricci et al.,2000; Gong et al.,2008; Geng et al., 2009; Lin et al.,2005), there were no randomized controlled trials. Except the subjects of one article were elderly patients ($\geq$65 years) (Li et al.,2008), the other studies had elderly patients who were more than 70 or 80 years old, most of the surgery were sternal thoracotomy. CABG was conducted under beating heart using heart fixator in OPCAB group, and patients underwent CABG under cardiac arrest for establishment of cardiopulmonary bypass in CABG group.

**3.3 Meta-analysis results**

The age subgroup analysis showed that the incidence of stroke of 70-75 years subgroup, 75-80 years subgroup and >80 years subgroup was significantly lower in OPCAB group than that in CABG group. The 65-70 years subgroup only included one study, and there was no significant difference in stroke between two groups [OR=0.10, 95%CI (0.01, 1.68)] (Figure 1 to 4).


Fig 1. The age 65 to 70 years.

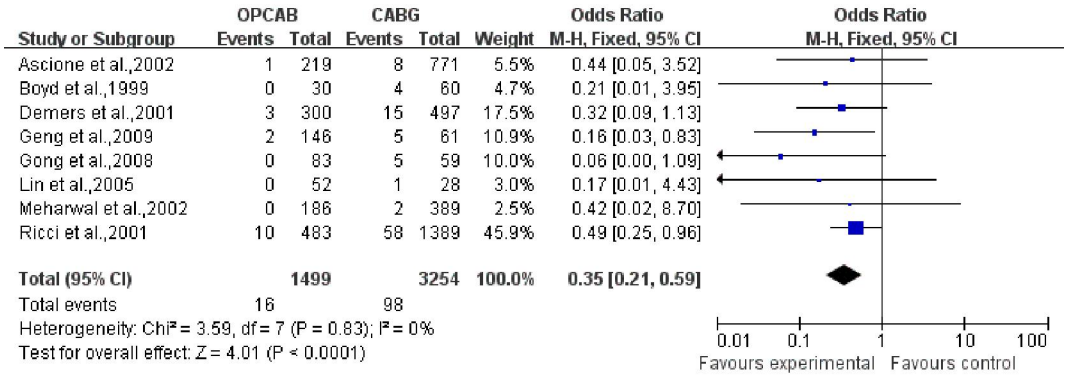


Fig 1. The age 70 to 75 years.

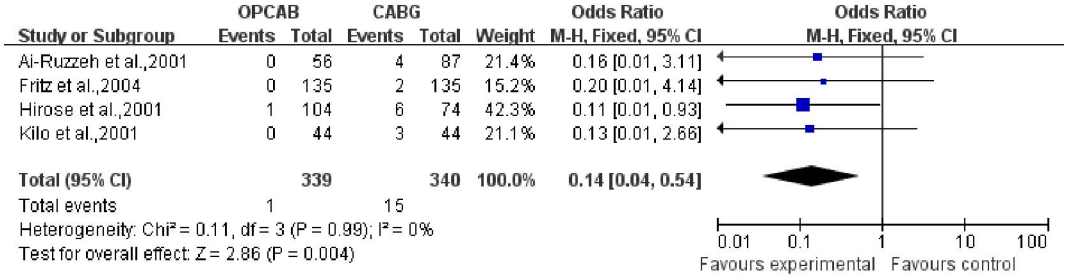


Fig 3. The age 75 to 80 years.

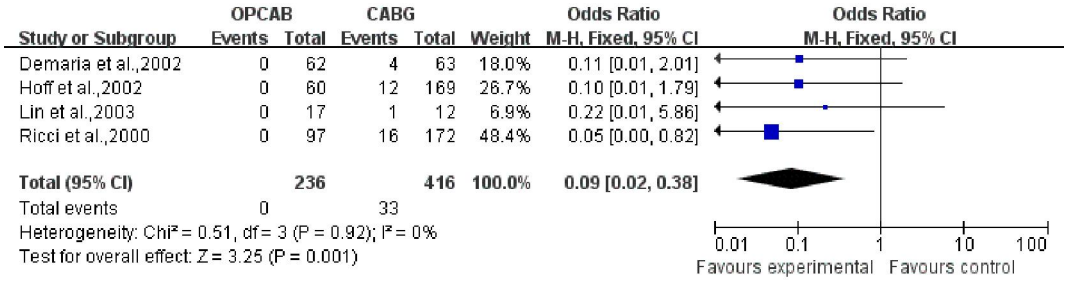


Fig 4. The age more than 80 years.

## 4. Discussion

Previous meta-analysis (Demers et al.,2001; Reston et al.,2003) showed that OPCAB could reduce the perioperative mortality, the incidence of stroke, atrial fibrillation and myocardial infarction in elderly patients compared with CABG, which could shorten the duration of hospitalization and reduce costs. However, other meta-analysis (Cheng et al.,2005) showed that OPCAB couldn't reduce the mortality, incidence of perioperative stroke and acute myocardial infarction; it also couldn't reduce the mortality and incidence of stroke of 1-2 years after operation. Another meta-analysis (Parolari et al., 2003) showed that OPCAB couldn't reduce the incidence trends of adverse events (death, stroke, myocardial infarction) [OR=0.48, 95%CI (0.21, 1.09), *P*=0.08]. The reasons for different meta-analysis results are as followings: 1) the characteristics of patients are different, such as, age, gender, preoperative comorbidities and non-selective surgical ratio, etc; 2) the different study type, such as, randomized controlled trials, or non-randomized controlled trials; 3) the sample size of included study is not large enough; 4) OPCAB needs excellent operative procedure and the learning curve is longer, which may reduce the efficacy of OPCAB. In our study, the meta-analysis included elderly patients (≥65 years); while the subjects of two meta-analyses (Cheng et al.,2005; Parolari et al., 2003) were general population, and most patients were younger than 70 years old.

In this study, the meta-analysis suggested that the incidence of perioperative stroke of elderly patients was decreased in OPCAB group, and >80 years subgroup showed more differences, but there was no significant difference in incidence of stroke between different age subgroups; after exclusion of low-quality study, the incidence of stroke was lower in OPCAB

group, which was consistent with the results of Weerasinghe *et al* （2005）. CABG use cardiopulmonary bypass to form non-pulsatile blood flow and microemboli, and it needs aortic cannulation, which could cause perioperative cerebral hypoperfusion, microemboli embolism, partial brain damage, or massive cerebral infarction in CABG group; and these complications may be the reason for incidence of perioperative stroke（Wandschneider et al.,2000; Van Dijk et al., 2002). However, OPCAB technology avoid the use of cardiopulmonary bypass, thus maintaining pulsatile blood flow, and avoid operating aorta with non-contact technology (Lev-Ran et al.,2004；Ramadan et al.,2010), which could be effective to guarantee the perioperative brain perfusion, reduce the aortic plaque shedding and reduce the incidence of stroke (Zamvar et al.,2002). The exactly mechanism still needs to explore.

The average number of vascular graft was significantly lower in OPCAB group than that in CABG group, suggesting the degree of revascularization was more fully in CABG group than that in OPCAB group. It has also been reported (Kilo et al.,2001) that the surgical results of OPCAB group with inadequate revascularization were better than that of CABG group with fully revascularization in elderly patients (>75 years). The life expectancy of was shorter in elderly patients, OPCAB didn't focus on the degree of revascularization, but solving the culprit artery causing angina and heart failure, to relieve symptoms, improve quality of life, shorten operative time and reduce the incidence of perioperative adverse events. It still needs further research to discuss.

In our study, the meta-analysis showed that the incidence of OPCAB perioperative stoke in elderly patients was lower than CABG group, the older, the more benefit; this results need multi-center, large sample, randomized controlled double-blind trials to confirm (Houlind et al.,2009). Firstly, the included studies of our meta-analysis were retrospective observational studies, which lacked of randomness and existed selection bias; secondly, the included studies may affect the baseline factors of our results, there was confounding factors; thirdly, the funnel plot showed the presence of publication bias, the reason is that literatures with positive results is easy to publish than negative results; at last, the sensitivity analysis showed that meta-analysis of retrospective cohort study had two opposite results after exclusion of three low-quality studies (Ascione et al.,2002; Li et al.,2008). The comparable score of baseline data of two groups was 0 points in the three studies, there were significant confounding factor, thus affecting the comparability of incidence of perioperative stroke between OPCAB group and CABG group. Therefore, our findings need to be carefully explained.

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