

# Stroke in Off-Pump Coronary Artery Bypass Grafting

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Stroke is a devastating complication after coronary artery bypass grafting (CABG). The incidence of stroke after CABG has been reported to be 2%–5% in previous literatures.<sup>1–4)</sup> In addition, stroke has been included as one of the major cardiovascular events after revascularization in studies comparing short- and long-term outcomes between percutaneous coronary intervention (PCI) and CABG.<sup>5, 6)</sup> Most studies have shown a greater incidence of stroke after CABG than after PCI.

The causes of stroke during the perioperative period are embolism, hypoperfusion, hypoxia, bleeding, and metabolic abnormality. Among them, the release of emboli from the ascending aorta during surgical maneuvers is the most probable cause. Although great effort is taken to avoid the release of emboli, i.e., the single cross-clamp method, preoperative evaluation of atheromas in the ascending aorta by an epiaortic echo,<sup>7)</sup> etc., it is difficult to eliminate this ominous complication as long as a cardiopulmonary bypass is performed with clamping of the ascending aorta.

In the mid-1990s, great attention was paid to off-pump CABG (OPCAB) to avoid the adverse effects of cardiopulmonary bypass and to reduce the mortality and morbidity of CABG. By using the OPCAB technique, we have found it possible to avoid using cardiopulmonary bypass and manipulating the ascending aorta. Thus we consider that there is a possibility for eliminating perioperative stroke by using the OPCAB technique.

## Incidence of Stroke in OPCAB

Several studies have compared the surgical results of conventional CABG and OPCAB.<sup>8–10)</sup> In institutions with surgeons experienced in OPCAB, better operative outcomes,

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including the incidence of stroke, have been noted while maintaining long-term outcomes comparable to those of on-pump CABG. Brizzio et al.<sup>8)</sup> reported a 58% reduction in the incidence of stroke and an 84% decrease in the risk of death after stroke after OPCAB as compared to that after on-pump CABG. The actual rate of stroke after OPCAB was as low as 1.0% in this series. However, Chu et al.<sup>9)</sup> found no difference between in-hospital mortality and the rate of postoperative stroke in a cohort of 63,000 patients using a nonvoluntary national database, and they expressed their concern regarding interinstitutional differences in the surgical outcomes of OPCAB. Sedrakyan et al.<sup>10)</sup> reported a meta-analysis of 41 randomized clinical trials comparing surgical outcomes between OPCAB and on-pump CABG. They demonstrated that perioperative stroke was reduced by 50% using the OPCAB technique as compared to conventional CABG, though the incidence of stroke was not completely eliminated.

## Timing of Clinical Manifestation of Stroke in OPCAB

Peel et al.<sup>11)</sup> sought to evaluate the chronological distribution of the onset of stroke in a cohort of cardiac surgery patients undergoing on-pump CABG versus OPCAB. They noted that the majority of the strokes associated with OPCAB occurred after an initially uncomplicated neurological recovery following cardiac surgery. The median time for the onset of stroke after OPCAB was 4 d (range, 0–14 d), and 2 d (range, 0–11 d) after on-pump CABG. On-pump CABG was associated with a higher risk of stroke (odds ratio [OR], 5.3; a 95% confidence interval (CI), 2.6–10.9;  $p < 0.01$ ) as compared to OPCAB. Nishiyama et al.<sup>12)</sup> studied the temporal pattern of stroke after OPCAB and on-pump CABG from a registry in Japan. They found that the incidence of stroke after OPCAB (1.0%) was lower than that of on-pump CABG (2.5%) ( $p = 0.0043$ ) and that most of the strokes (90%) in OPCAB occurred after first awakening from surgery without a neurological deficit (defined as a delayed stroke), while almost half of the strokes after

on-pump CABG were early strokes. In our single institution registry of OPCAB,<sup>13</sup> we noted no incidence of early stroke, but 1.3% of the patients developed delayed strokes. According to the results of those studies, strokes associated with OPCAB are quite likely to occur after full recovery from anesthesia without any neurological deficit generally beyond 24 h after surgery.

Notably, the prognosis after stroke depends greatly on the type of stroke. A higher mortality rate has been reported for early stroke as compared to that after delayed stroke.<sup>14,15</sup> Long-term results have been found to be worse after early stroke than those after delayed stroke.<sup>14</sup>

### Mechanisms of Occurrence of Strokes in OPCAB

What are the mechanisms that cause strokes after OPCAB? Nishiyama et al.<sup>12</sup> have reported that a history of stroke and postoperative atrial fibrillation were independent risk factors for delayed stroke. Toumpoulis et al.<sup>14</sup> reported female gender, white race, preoperative renal failure, respiratory failure, and postoperative renal failure as independent risk factors for delayed stroke. Filsoufi et al.<sup>15</sup> found female gender and extensive aortic lesions to be independent predictors of delayed stroke. We have found that most patients with delayed stroke after OPCAB developed thrombo-embolism in diseased carotid and intracranial arteries and have accordingly advocated the importance of preoperative assessment of the carotid arteries.<sup>13</sup>

Careful attention needs to be paid to the coagulation status of patients after OPCAB. In their OPCAB series, Mariani et al.<sup>16</sup> found a postoperative increase in procoagulant activity, represented by prothrombin factors 1 and 2, which was also accompanied by an increase in the levels of von Willebrand factor and fibrinolysis. They recommended the institution of an aggressive perioperative anticoagulant regimen in all OPCAB cases in order to avoid acute graft failure. Kurlansky<sup>17</sup> also raised concerns regarding a hypercoagulable state following OPCAB in relation to acute graft failure and thus the long-term incidence of cardiac events. From the results of our study,<sup>13</sup> where we noted that the majority of delayed strokes were caused by thrombo-embolism, the hypercoagulable state immediately after OPCAB may adversely affect the occurrence of stroke.

According to the results of previous studies, the major causes of stroke are postoperative atrial fibrillation in the hypercoagulable state or thrombo-embolism in the diseased carotid and intracranial arteries, particularly in female patients

with previous histories of stroke.

### Prevention of Stroke in OPCAB

After OPCAB, patients who developed delayed stroke inevitably showed a previous hypercoagulable state; therefore we consider it essential to immediately neutralize the hypercoagulable state after OPCAB. The administration of aspirin should not be stopped before surgery; further, the anticoagulation protocol needs to be more aggressive, using subcutaneous heparin or even intravenous heparin particularly for patients with severe stenosis in the carotid and intracranial arteries detected by preoperative assessment, combined with two types of antiplatelet drugs, i.e., aspirin and thienopyridines.

Further, the incidence of postoperative atrial fibrillation should be aggressively prevented. Atrial fibrillation has been reported to occur in 20%–40% of patients after CABG.<sup>10</sup> The incidence of postoperative atrial fibrillation may be reduced by the prophylactic administration of beta-blockers or amiodarone.

There are several controversies regarding the management of CABG patients with coexistent carotid disease. Previous studies have suggested combined carotid endarterectomy (CEA) with CABG; however, a recent systematic review of 97 studies found an incidence of 10%–12% of death, stroke, and myocardial infarction after staged or combined procedures.<sup>18</sup> Since OPCAB reduces the incidence of perioperative stroke, we question whether the strategy of combined procedures would work in the OPCAB era. Further, many patients with a carotid disease are recently most likely to be treated with carotid artery stenting (CAS). Thus the strategy for the treatment of CABG patients with carotid diseases may need to be reconsidered.

Fareed et al.<sup>19</sup> reviewed 12 studies of combined CEA and OPCAB. The operative mortality therein was 1.5%, the risk of death or ipsilateral stroke was 1.6% (0.4–2.8%), and the risk of death or any stroke was 2.2%, which indicates better early outcomes than those following combined CEA and on-pump CABG. Another systematic review of early outcomes of staged CAS and on-pump CABG has shown that the overall mortality was 5.5%, the risk of suffering an ipsilateral stroke was 3.3%, and the risk of suffering any stroke was 4.2%.<sup>20</sup> According to these studies, the risk of stroke may not be reduced following combined procedures as compared to that following OPCAB for such high-risk patients. In patients with significant carotid stenosis, some intervention for the carotid disease after CABG may be needed, because the long-term outcomes of such patients

with respect to the incidence of stroke were worse than those of patients without carotid disease.<sup>13</sup> Further clinical studies are needed to clarify these issues.

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