Insufficient Platelet Inhibition Is Related to Silent Embolic Cerebral Infarctions After Coronary Angiography

Bum Joon Kim, MD; Seung-Whan Lee, MD; Seong-Wook Park, MD; Dong-Wha Kang, MD; Jong S. Kim, MD; Sun U. Kwon, MD, PhD

Background and Purpose—Considering that insufficient platelet inhibition is related to thrombotic complications after coronary angiography, we hypothesized that the extent of platelet inhibition by antiplatelet agents is related to the occurrence of silent embolic cerebral infarction (SECI) after coronary angiography.

Methods—Among the patients scheduled for coronary artery bypass surgery, we retrospectively analyzed the location of SECI on diffusion-weighted imaging of 272 patients, which was performed after coronary angiography, as a presurgical evaluation in Phase 1 study. In Phase 2 study, we have prospectively recruited 102 patients to compare the extent of platelet inhibition measured by the VerifyNow system among patients with and without SECI.

Results—SECI is observed in 45 patients (16.5%) in Phase 1 and 17 (16.7%) in Phase 2. The lesions were slightly more frequent in the right hemisphere. In the Phase 2 study, aspirin reaction units and P2Y12 reaction units were higher in the patients with SECI than those without (aspirin reaction units: 490±72 versus 446±53, P=0.03; P2Y12 reaction units: 352±65 versus 300±77, P=0.009). The incidence of SECI increased with the number of resistant antiplatelets; resistance to both antiplatelet agent (50%), resistance to 1 antiplatelet agent (22%), and no resistance (4%; P=0.023). From the result of logistic regression, higher aspirin reaction units, white blood cell count, low hemoglobin, and nonresponsiveness to antiplatelet agents were independent risk factors.

Conclusions—Insufficient platelet inhibition after administration of antiplatelet agents is related with SECI appearing after coronary angiography. (Stroke. 2012;43:00-00.)

Key Words: antiplatelet resistance ■ cerebral infarction ■ coronary angiography

Cerebral infarction is one of the most disabling complications of coronary angiography (CAG), which is a gold standard for the diagnosis of coronary artery disease. Therefore, during the last decade, there have been many efforts to verify the pathogenic mechanism and risk factor of cerebral infarction with or without symptoms appearing after CAG to prevent this complication.1-3

Antiplatelet agents are effective for the prevention of thrombotic complication related to CAG.4 However, routine antiplatelet therapy failed to inhibit platelet sufficiently in a significant portion of the patients.5 The resistance to antiplatelet agents is associated with the development of cardiovascular6 and cerebrovascular7 events from some clinical studies. Therefore, insufficient inhibition of platelets may be one of the pathogenic mechanisms.

We hypothesized that insufficient inhibition by antiplatelet agents may increase the risk of silent embolic cerebral infarction (SECI) appearing after CAG. To investigate this issue, we conducted a study consisting of 2 phases. The Phase 1 study was retrospectively performed to analyze the incidence and location of SECI on diffusion-weighted imaging (DWI). The Phase 2 study was performed prospectively to investigate the role of insufficient platelet inhibition on the development of SECI. This study was approved by the Institutional Review Board of our center.

Methods

Patients

Since August 2004, all patients who are scheduled for coronary artery bypass grafting in our center have routinely undergone DWI and MR angiography after CAG for the evaluation of the surgical risks related to cerebral artery stenosis.8 In the Phase 1 study, we retrospectively reviewed DWI and MR angiography, which were performed within 1 week after CAG, in patients who have received a coronary artery bypass grafting between January 2006 and July 2006. In the Phase 2 study, the patients who were recommended for coronary artery bypass grafting according to the result of CAG between January 2008 and June 2009 were prospectively recruited. To minimize the technical bias, CAG was performed by 1 experienced cardiologist (S.-W.L.), and we excluded patients who have...
received any percutaneous coronary intervention. Patients who did not take aspirin and clopidogrel according to the following protocol were also excluded.

**Antiplatelet Agent Administration and CAG**

At least 1 day before CAG, aspirin and clopidogrel were administered. Antiplatelet agents were loaded (250 mg aspirin and 300 mg clopidogrel) for patients who were naïve to antiplatelet treatment. The usual maintenance dosages of aspirin (100 mg daily) and clopidogrel (75 mg daily) were administered to previous users. During CAG, patients received heparin with a bolus dose of 8000 U and a repeat bolus of 2000 U if necessary to maintain the activated clotting time over 250 seconds. After CAG, if the patient was a candidate for coronary artery bypass grafting, the patients were enrolled. The result of CAG, access site of catheter, size and number of catheter used per patients, total procedure time, and fluoroscopy time was obtained. The left ventricular ejection fraction was obtained from the transthoracic echocardiography, which was performed on the same day CAG had been performed.

**Measurement of the Extent of Platelet Inhibition**

Within 6 hours after CAG, the extent of platelet inhibition by antiplatelet agents was measured using the VerifyNow Aspirin and VerifyNow P2Y12 (Accutecumus, Inc, San Diego, CA). Two milliliters of venous blood was collected in a 3.2% citrate vacuum collection tube. The blood samples were transferred to a dedicated cartridges containing arachidonic acid (VerifyNow Aspirin) or fibrinogen-coated beads, thrombin receptor activating peptide, adenosine di-phosphate, and prostaglandin E1 (VerifyNow P2Y12). Changes in the light transmission induced by platelet aggregation were measured. Results were expressed as aspirin reaction units (ARU), P2Y12 reaction units (PRU) and percent of platelet inhibition (percent PI).

Usually, ARU ≥550 is defined as aspirin resistance. Although PRU ≥235 was shown to be associated with clinical outcomes after percutaneous coronary intervention from previous studies, PRU ≥275 was used as defining clopidogrel resistance in this study. Because the prevalence of the CYP 2C19 variant is higher in the Korean population compared with the prevalence in Westerns,9,10 PRU ≥275 have predicted the clinical events more appropriately in this population. The patients were classified into 3 groups according to the responsiveness to antiplatelet agents; nonresponders (resistant to both aspirin and clopidogrel), partial responders (resistant to 1 of the 2 antiplatelet agents), and responders (no resistance to any antiplatelet agents).

**Clinical and Laboratory Data**

For each patient, vascular risk factor, including hypertension, diabetes mellitus, hypercholesterolemia, current smoking within 6 months, and history of ischemic stroke, were obtained. The laboratory data that were performed 1 day before CAG (on the day of admission) were used. The laboratory data includes blood cell counts, prothrombin time, activated partial thromboplastin time, fasting glucose, total cholesterol blood urea nitrogen, and creatinine.

**MRI and Analysis**

DWI and MR angiography were performed within 1 week after CAG with a 1.5-Tesla MR (GE Medical Systems, Milwaukee, WI) using a standard neurovascular coil. Interpretations of the imaging and determination of SECI were performed by a blinded investigator (B.J.K.) to the clinical data. The vascular territories of SECI were classified into right carotid circulation, left carotid circulation, or vertebrobasilar circulation. Each lesion was also dichotomized to cortical or subcortical lesion.

The degree of atherosclerosis was evaluated with respect to the severity of steno-occlusions and the number of arteries with steno-occlusions. The severity of stenosis was visually graded (0 indicating <50% stenosis; 1 indicating 50–99% stenosis, and 2 indicating occlusion) The “atherosclerosis score” was defined as the sum of the scores of steno-occlusive intracranial and extracranial arteries.12

### Table 1. General Characteristics of Patients Recruited in Phase 1

<table>
<thead>
<tr>
<th>Demographics</th>
<th>+ SECI (n=45)</th>
<th>− SECI (n=227)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±8</td>
<td>62±8</td>
<td>0.21</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>32 (71)</td>
<td>170 (75)</td>
<td>0.60</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>31 (69)</td>
<td>137 (60)</td>
<td>0.28</td>
</tr>
<tr>
<td>Diabetes mellitus, no. (%)</td>
<td>20 (44)</td>
<td>84 (37)</td>
<td>0.35</td>
</tr>
<tr>
<td>Hypercholesterolemia, no. (%)</td>
<td>16 (36)</td>
<td>97 (42)</td>
<td>0.37</td>
</tr>
<tr>
<td>Current smoking, no. (%)</td>
<td>10 (22)</td>
<td>35 (15)</td>
<td>0.20</td>
</tr>
<tr>
<td>Laboratory results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC, /mm²</td>
<td>7790±2400</td>
<td>6950±600</td>
<td>0.03</td>
</tr>
<tr>
<td>Hb, g/dL</td>
<td>13±2</td>
<td>15±2</td>
<td>0.51</td>
</tr>
<tr>
<td>Platelet, ×10⁹/mm²</td>
<td>244±62</td>
<td>227±68</td>
<td>0.12</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>168±41</td>
<td>175±45</td>
<td>0.33</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>16±7</td>
<td>18±10</td>
<td>0.17</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.0±0.4</td>
<td>1.3±1.4</td>
<td>0.60</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atherosclerosis score of cerebral arteries</td>
<td>1.6±1.9</td>
<td>1.5±1.6</td>
<td>0.83</td>
</tr>
<tr>
<td>Severity of atherosclerosis in coronary artery, 3VD: 2VD:1VD</td>
<td>35:6:3</td>
<td>65:45:13</td>
<td></td>
</tr>
</tbody>
</table>

Results are expressed as no. (column %) or mean±SD. SECI indicates silent embolic cerebral infarction; WBC, white blood cell; Hb, hemoglobin; BUN, blood urea nitrogen; 3VD, 3-vessel disease; 2VD, 2-vessel disease; 1VD, 1-vessel disease.

**Data Analysis**

We compared variables among patients with SECI (+SECI) and those without (−SECI) using the Mann-Whitney U test, y², or Fisher exact tests as appropriate. The number of lesions located at each vascular territory was compared. Also, the proportion of cortical lesions was calculated. In the Phase 2 study, multivariate analysis was used to determine the independent risk factors related to SECI. Two models were used. Model 1 included variables with P<0.15 from the univariate analysis. ARU, PRU, hemoglobin, and white blood cell (WBC) counts were entered as a continuous variable. Model 2 was performed with variables that were related to the mechanical stress (size and number of the catheter used per procedure), the variables that were significant from the previous studies (total procedure time, fluoroscopy time,1 and left ventricular ejection fraction13) and the responsiveness to antiplatelet agents. Statistical analysis was performed using SPSS for Windows (Version 16.0; SPSS Inc, Chicago, IL).

**Results**

**General Characteristics and Location of SECI**

Of the 398 patients enrolled in the Phase 1 study, CAG was performed at our center in 235 patients and 163 patients from other hospitals. Among them, 126 patients were excluded because of insufficient information of CAG (72 patients), imaging protocol violation (51 patients), and presence of symptomatic cerebral infarction before CAG (3 patients).

Finally, among the 272 patients included in this analysis, 45 (16.5%) had SECI. As shown in Table 1, the WBC counts
were higher in the +SECI group \((P=0.03)\). Analyzing by the number of lesions, 117 lesions were observed. SECIs were slightly more frequent at the right hemisphere (Table 2). The majority of the lesions (104 of 117 lesions [88.9%]) were located at the cerebral cortex. Only 10 patients of the +SECI group (10 of 45 patients [22.2%]) had significant stenosis or occlusion in the corresponding cerebral arteries which is more proximal to the vascular territory of each DWI lesion.

Figure 1 shows the representative case with SECI without any causable embolic source of atherosclerosis.

Among the 111 patients who were enrolled in the Phase 2 study, 9 patients were excluded because MRI could not be performed (8 due to patients’ refusal, 1 had a pacemaker). Seventeen of 102 patients (16.7%) had SECI. Although there was no significant difference in the WBC count between 2 groups (Table 3), dichotomizing the WBC count by patients with leukocytosis \((WBC \geq 10,000/mm^2)\) revealed a significant difference. \((P=0.03)\) Thirty-four SECIs were observed from 17 patients. SECIs were more frequently observed from the right hemisphere (Table 2) and from the cerebral cortex (21 of 34 lesions [61.8%]).

**Extent of Platelet Inhibition and SECI**

ARU was measured in all of the enrolled patients. PRU and percent PI were obtained from 95 patients. As shown in Table 3, ARU and PRU were significantly higher in the +SECI group \((P=0.03\) and \(P=0.009)\). Also, percent PI showed lesser platelet inhibition \((P=0.04)\).

Aspirin resistance and clopidogrel resistance were slightly more frequent in the +SECI group but were not statistically significant (Table 3; Figure 2). The occurrence of SECI increased as the responsiveness to antiplatelet agents decreased. Nonresponders showed the highest incidence (2 of 4 patients [50%]), partial responders the next (14 of 63 patients [22%]), and responders showed the lowest incidence (1 of 28 patients [4%]; \(P=0.023\); Figure 2).

The results of multiple logistic regression have revealed that higher ARU, WBC count, and low hemoglobin from Model 1 and the nonresponsiveness to antiplatelet agents from Model 2 were independently related with SECI (Table 4).

**Discussion**

To the best of our knowledge, this is the first study to investigate the location of SECI and the role of platelet activation on the development of SECI occurring after CAG.

Previously, DWI examination of patients with vascular dementia implied that small clinically silent lesions may contribute to cognitive deterioration.\(^{14}\) Also, although these lesions were silent by routine neurological examination, an extensive evaluation with a neuropsychological battery shows a significant postcatheterization cognitive impairment, demonstrating the clinical relevance of SECI.\(^{1}\)

The plausible embolic sources of SECI, suggested from the previous studies, are thrombus formed from the catheter by platelet activation, dislodgement of the atheroma from the aortic arch by mechanical stress,\(^{13}\) and air embolism.\(^{15}\) Activation of the platelets by catheterization was revealed by previous studies using platelet flow cytometry,\(^{16}\) and the platelet membrane activation markers were predictive for increased risk of ischemic events after catheterization.\(^{17}\) In our study, the factors related to atherosclerotic burden (atherosclerosis score and the severity of coronary artery disease) or mechanical stress (number and size of the catheter used, total procedure time, and fluoroscopy time) did not differ by the occurrence of SECI. In contrast, several findings suggest that platelet activation takes an important role in the pathogenic mechanism. First, considering the right–left propensity

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**Table 2. Distribution of Silent Embolic Cerebral Infarction by Vascular Territories**

<table>
<thead>
<tr>
<th>Vascular Territories</th>
<th>RCC</th>
<th>LCC</th>
<th>VBC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 (%)</td>
<td>65 (56)</td>
<td>36 (31)</td>
<td>16 (14)</td>
<td>117 (100)</td>
</tr>
<tr>
<td>Phase 2 (%)</td>
<td>16 (47)</td>
<td>14 (41)</td>
<td>4 (12)</td>
<td>34 (100)</td>
</tr>
<tr>
<td>Total (%)</td>
<td>81 (54)</td>
<td>50 (33)</td>
<td>20 (13)</td>
<td>151 (100)</td>
</tr>
</tbody>
</table>

Results are expressed as no. (row %).

RCC indicates right carotid circulation; LCC, left carotid circulation; VBC, vertebrobasilar circulation.

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**Figure 1.** Silent embolic cerebral infarction occurred after coronary angiography on diffusion-weighted imaging (arrows). Multiple lesions are located at multiple vascular territories. **A**, However, there is no significant steno-occlusive lesion on the corresponding artery at the MR angiography **(B)**.
of the SECI, the majority of emboli may be originated from a more proximal source than the aortic arch.18 During CAG, the catheter is mostly located near the orifice of coronary arteries, which are at the ascending aorta. The catheter may activate platelet and cause SECI (Supplemental Figure I; http://stroke.ahajournals.org). Second, inflammation is known to be related with platelet activation.19 Therefore, the higher WBC count in the +SECI group from the Phase 1
study and the result of multivariate analysis on the Phase 2 study may also reveal the importance of platelet activation. Most of all, the values representing the resistance to antplatelet agent (ARU and PRU) were high and the extent of platelet inhibition was low in the +SECI group. Besides, the occurrence of SECI increased stepwise as the responsiveness to antplatelet agents decreased. Finally, from the multivariate analysis, high ARU and nonresponsiveness to antplatelets were independent risk factors. These findings consistently reveal the importance of platelet activation in the pathogenic mechanism of SECI.

Therefore, administering a higher dosage of antplatelet agents and sufficiently inhibiting the platelet activation can reduce the occurrence of SECI. However, loading a higher dose of antplatelet agents may increase the risk of bleeding, including intracerebral hemorrhage. Therefore, measuring resistance of antplatelet agents and selectively administering a high dose to patients with resistance may be a more logical option to reduce the occurrence of SECI after CAG.

There are several limitations in our study. First, because of the absence of DWI before CAG, the pre-existing cerebral infarction could not be excluded. However, by crudely estimating the age of the lesions by the signal intensity of apparent diffusion coefficient map, most of the lesions may be related to CAG. Additionally, considering that more than half of the patients were stable angina, the occurrence of infarction before CAG may be low. Second, neuropsychological testing before and after CAG, which may have strengthened the clinical relevance, was not performed. However, because the patients were enrolled after CAG, this may have been difficult. Third, there is no universal consensus among research groups on the validity of measuring the resistance of antplatelet agents by the VerifyNow system. Using PRU ≥275 as the clopidogrel resistance in Asians is still under investigation, and further research should be done.

In conclusion, our study demonstrated that platelet activation has an important role in SECI occurring after CAG. Measurement of platelet inhibition may predict SECI occurring after CAG, and increasing the dose of antplatelet agents in the patients with insufficient platelet inhibition may be helpful in prevention.

### Sources of Funding

This study was supported by grants from the Korea Health 21 Research and Development Project (A102065) and the Korea Healthcare technology R&D Project (A070001), Ministry of Health, Welfare and Family Affairs, Republic of Korea.

### Disclosures

None.

### References


### Table 4. Result of Multivariate Analysis of SECI Occurrence After CAG

| Entered variables are: Model 1: ARU, PRU, WBC, and Hb; Model 2: size and no. of the catheter used, total procedure time, fluoroscopy time, left ventricular ejection fraction, and the responsiveness to antplatelet agents. OR indicates odds ratio; CI, confidence interval; SECI, silent embolic cerebral infarction; CAG, coronary angiography; ARU, aspirin reaction unit; Hb, hemoglobin; WBC, white blood cell. The definition of responsiveness to antplatelet agent is; responder: no resistance to aspirin and clopidogrel; partial responder: resistant to one antplatelet agent; nonresponder: resistance to both aspirin and clopidogrel. |
| --- | --- | --- |
| **Model 1** | OR (95% CI) | P |
| **ARU** | 1.011 (1.001–1.021) | 0.029 |
| **Hb** | 0.701 (0.502–0.980) | 0.038 |
| **WBC** | 1.406 (1.106–1.787) | 0.005 |
| **Model 2** |  |  |
| Responsiveness to antplatelet agent** |  |  |
| Responder | 1 |  |
| Partial responder | 7.459 (0.905–61.483) | 0.061 |
| Nonresponder | 30.567 (1.764–529.729) | 0.019 |

*The definition of responsiveness to antplatelet agent is; responder: no resistance to aspirin and clopidogrel; partial responder: resistant to one antplatelet agent; nonresponder: resistance to both aspirin and clopidogrel.


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Insufficient Platelet Inhibition is related with Silent Embolic Infarctions after Coronary Angiography
**Supplemental Methods**

The sample size of phase 2 was calculated as the following description. First, according to the previous studies, the aspirin resistance and clopidogrel resistance in patients receiving per-cutaneous coronary intervention was 12~15%\(^1,2\) and 13%~29%\(^1,3\). However, because the higher rate of CYP variant in Koreans, and because catheterization itself may activate platelets, we assumed the immediate post-procedural resistance to aspirin and clopidogrel as 20% and 30% of the enrolled patients.\(^1\) (Allocation ratio; aspirin responder / resistance = 4, clopidogrel responder / resistance = 2.3)

Second, the incidence of silent embolic infarction (SECI) after coronary angiography (CAG) was 15% from the result of phase 1 study. From the previous study thrombotic events were more frequent in anti-platelet resistance patients 2~4 times.\(^1,3\)

Therefore we have assumed that the incidence of SECI may be 35% in anti-platelet resistance group and 10% in the non-resistance group. (The overall incidence is 15% assuming that the incidence of anti-platelet resistance is 20%)

The statistical power (1 - beta) was 0.80, and the alpha error probability was 0.05. The calculated sample size for aspirin resistance patients were 26 and for aspirin responder 104. (Total 130) The sample size for clopidogrel resistance patients were 32 and for clopidogrel responder 74. (Total 106)

**Supplemental Results**

Among the 102 patients in phase 2 study, thirty-three patients were approached by right femoral artery, 68 patients by right radial artery and 1 patient by left radial artery. The lesion occurrence of SECI in right and left hemisphere was not related to the access site of the catheter. The number of lesions according to the vascular territory is on supplemental table 1.

Though the three types of contrast used for the CAG (Iopamidol, Ioxaglate and Iodixanol) were nephrotropic and low osmolar, they may differ in ionic/non-ionic, density and viscosity. And this difference may have influenced the systemic hemodynamics\(^4\), platelet inhibition\(^5\) and finally the occurrence of SECI. However, there was no difference. Supplemental table 2 shows the type of contrast used for CAG.

The supplemental results of laboratory tests in phase 2 study, which were not statistically significant, are also presented on supplemental table 2.
**Supplemental table 1.** Number of SECI in each vascular territory after CAG by access site

<table>
<thead>
<tr>
<th></th>
<th>RCC</th>
<th>LCC</th>
<th>VBC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial artery access</td>
<td>7 (47%)</td>
<td>7 (47%)</td>
<td>1 (7%)</td>
<td>15 (100%)</td>
</tr>
<tr>
<td>Femoral artery access</td>
<td>9 (47%)</td>
<td>7 (37%)</td>
<td>3 (16%)</td>
<td>19 (100%)</td>
</tr>
</tbody>
</table>

Results are expressed as number of lesions (Raw %)
RCC: Right carotid circulation; LCC: Left carotid circulation VBC: Vertebro-basilar circulation
**Supplemental table 2.** Type of contrast and supplemental laboratory results in phase 2 study

<table>
<thead>
<tr>
<th></th>
<th>+SECI (N=17)</th>
<th>-SECI (N=85)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of contrast (P:H:V)</strong></td>
<td>0:8:9</td>
<td>8:36:41</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>Laboratory results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>43±53</td>
<td>36±52</td>
<td>0.64</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>24±17</td>
<td>25±16</td>
<td>0.69</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>101±32</td>
<td>111±32</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Results are expressed as number or mean (range).

*P=Pharmoray® (Iopamidol), H=Hexabrix® (Ioxaglate) V=Visipaque ® (Iodixanol),
AST=aspartate aminotransferase, ALT=alanine aminotransferase
LDL=low density lipoprotein
**Supplemental Figure**

**Figure.** Diagram showing anatomy of the aorta. The tip of cardiac catheter (red line) is located at the ascending aorta. (a) The Aortic plaques are more common and severe on the distal aortic arch. Considering the blood flow and anatomy of the aorta, emboli originated from the tip (a) may flow through right carotid artery (A) and left carotid artery (B). However, emboli originated from the aortic plaque (b) may prefer to flow to the left carotid artery (B) than the right (A).
Supplemental References


5. D'Anglemont De Tassigny A, IDéE JM, Corot AC. Comparative effects of ionic and nonionic iodinated low-osmolar contrast media on platelet function with the PFA-100 (platelet function analyzer). Invest Radiol. 2001; 36 :276-82.
불완전한 혈소판 억제는 관상동맥조영술 후 발생하는 무증상 색전뇌경색과 관련이 있다

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(Stroke. 2012;43:727-732.)

Key Words: antiplatelet resistance ■ cerebral infarction ■ coronary angiography

배경과 목적
불완전한 혈소판 활성 억제가 관상동맥조영술 후 혈전 합병증 발생과 관련이 있다는 점을 고려하여, 저자들은 혈액소관계에 의한 혈소판 억제 정도가 관상동맥조영술 후 무증상 색전뇌경색(silent embolic cerebral infarction, SECI) 발생과 관련 있을 것이라는 가설을 세웠다.

방법
관상동맥우회술(coronary artery bypass surgery)이 예정된 환자 중 관상동맥조영술 후 시행한 1272명의 환자들의 환산장조영상에서 SECI의 위치를 후향적으로 분석하는 1차 연구를 시행하였다. 2차 연구에서 저자들은 전방적으로 모집한 102명의 환자들에서 VerifyNow로 평가한 혈소판 억제 정도와 SECI 발생 여부를 비교하였다.

결과
SECI는 1차 연구 환자 중 45명(16.5%)에서 발견되었고 2차 연구 환자 중 17명(16.7%)에서 발견되었다. 2차 연구에서 아스피린 반응 유무(aspirin reaction unit) 및 P2Y12 반응 유무는 SECI가 발생한 환자에서 그렇지 않은 환자에 비하여 유의하게 높았다(aspirin reaction units: 490±72 vs 446±53, P=0.03; P2Y12 reaction units: 352±65 vs 300±77, P=0.009). SECI의 발생은 저항성을 보이는 혈소판 억제의 차이에 비례하여 증가하는 경향을 보였다. 두 가지 혈소판 및 항혈소판제에 대한 저항성(50%), 한 가지 항혈소판제에 대한 저항성(22%) 및 저항성이 없는 경우(4%: P=0.023)로 지식체화질환의 결과, 낮은 아스피린 반응 유무, 복합구 수치, 낮은 혈소판수 등 항혈소판제 비반응성이 유의한 위험 인자로 확인되었다.

결론
혈액소관계 투여 이후 불완전한 혈소판 활성 억제는 관상동맥조영술 후 발생하는 SECI와 관련이 있다.