



## Correlation of Akinesia With Graft Patency and Cardiac Enzyme After Off-Pump Coronary Artery Bypass Graft Surgery

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**Background:** The aim of the present study was to identify the clinical implications of newly developed akinesia in echocardiography after off-pump coronary artery bypass graft (CABG) surgery and its relationship with graft patency.

**Methods and Results:** A total of 512 patients underwent off-pump CABG from January 2007 to November 2008. Two hundred and thirty-nine patients, whose echocardiography and multi-slice computed tomography data were available, were included in the study. Wall motion was subdivided into 16 segments and analyzed. Patients were separated into group A with newly developed akinesia (n=20), and group B without newly developed akinesia (n=219). Morbidity and early mortality, cardiac enzyme level, and graft patency were compared. The incidence of newly developed akinesia according to the anatomical territory was as follows: anterior, 5; lateral, 3; posterior, 7; and multiple territories, 5. Significant differences in preoperative ejection fraction were observed between the 2 groups (group A, 45.0±7%; group B, 58.0±12.2%, P<0.001). There was no statistical difference in the mean number of bypassed grafts and the complete revascularization rate. Complication and early mortality rates were insignificant between the 2 groups. There was little association between graft patency, cardiac enzyme level, and newly developed akinesia (P>0.05). Multivariate analysis showed that the preoperative ejection fraction was a risk factor for newly developed akinesia.

**Conclusions:** The mechanism of development of akinesia after off-pump CABG might be attributable to intraoperative coronary malperfusion, which is probably due to cardiac manipulation rather than graft occlusion. (*Circ J* 2010; **74**: 1564–1569)

**Key Words:** Contractility; Coronary artery bypass graft; Enzyme; Graft

Coronary artery bypass graft (CABG) surgery not only prevents myocardium from ischemia or myocardial infarction,<sup>1–3</sup> but also selectively enhances myocardial contractility by adequately perfusing the hibernating myocardium.<sup>4,5</sup> In contrast, echocardiographic evidence of wall motion deterioration after CABG surgery is associated with poor patient outcome.<sup>6–9</sup> Perioperative myocardial infarction (PMI) that occurs during or after CABG surgery is a serious complication, even though the mechanism and the pathogenesis are not completely understood.<sup>10</sup>

In a small subset of patients who receive off-pump CABG, regional akinesia is newly observed on echocardiography without any apparent etiology. Wall motion deterioration could have possibly occurred due to either graft-related or non-graft-related causes. Graft occlusion attributable to graft kinking, or anastomosis site stenosis are thought to be the

reasons for graft-related akinesia, whereas intraoperative malperfusion due to long ischemic time or inappropriate manipulation might be the cause of non-graft related akinesia.

Although contractility after CABG surgery is the key to long-term survival, as mentioned above, very little is known about the pathophysiology and the consequence of newly developed akinesia. The purpose of the present study was to define the relationship between graft patency, cardiac enzyme level, and newly developed akinesia after off-pump CABG. Additionally, risk factor analysis and prognostic evaluation of patients with newly developed akinesia were done.

### Methods

#### Patients

From January 2007 to November 2008, a total of 512 patients

Received November 10, 2009; revised manuscript received April 16, 2010; accepted April 19, 2010; released online June 29, 2010  
Time for primary review: 82 days

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ISSN-1346-9843 doi:10.1253/circj.CJ-09-0857

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	Group A (n=20)	Group B (n=219)	P value
Female (%)	5 (25.0)	73 (33.3)	0.13
Mean age (years)	64.1±9.1	63.4±8.7	0.74
Mean BMI (kg/m <sup>2</sup> )	24.2±2.6	24.5±3.0	0.81
Smoker, n (%)	5 (25.0)	88 (40.2)	0.62
Diabetes, n (%)	8 (40.0)	80 (36.5)	0.62
Dyslipidemia, n (%)	9 (45.0)	115 (52.5)	0.81
Mean EuroSCORE	4.2±3.1	3.05±2.6	0.049
CVA, n (%)	2 (10.0)	14 (6.4)	0.62
Preoperative creatinine (mg/dl)	1.0±0.2	1.1±0.9	0.41
Mean EF (%)	45.0±7	58.0±12.2	<0.001
Hypertension, n (%)	14 (70.0)	140 (63.9)	0.44
PAOD, n (%)	1 (5.0)	14 (6.4)	0.49

BMI, body mass index; EuroSCORE, European System for Cardiac Operative Risk Evaluation; CVA, cerebrovascular accident; EF, ejection fraction; PAOD, peripheral artery occlusive disease.

	Group A (n=20)	Group B (n=219)	P value
Total arterial grafting, n (%)	14 (70.0)	159 (72.6)	0.32
Distal anastomosis, mean±SD	3.1±0.8	3.3±0.8	0.69
Arterial grafts, mean±SD	2.0±0.9	2.3±0.9	0.21
Sequential graft, n (%)	9 (45.0)	117 (53.4)	0.21
Aorto-coronary grafting, n (%)	2 (10.0)	17 (7.8)	0.69
Composite Y graft, n (%)	17 (85.0)	199 (90.9)	0.52
Multiple Y composite, n (%)	5 (25.0)	52 (23.7)	0.46
End-to-end extension of graft, n (%)	3 (15.0)	49 (22.4)	0.88

underwent isolated off-pump CABG at Severance Hospital, Yonsei University College of Medicine. Cardiac enzyme level, electrocardiogram (ECG) findings, and clinical data were retrospectively studied. A total of 239 patients out of 512 were included in the study. Patients who suffered from acute myocardial infarction were excluded because their preoperative cardiac enzyme levels were above the normal range and most of them were found to have akinesia on preoperative echocardiography. Patients whose test results, such as multislice computed tomography (CT) and troponin-T, were missing, were also excluded. Patients underwent multislice CT after removal of chest tubes for graft patency assessment at Severance Hospital, but those who could not undergo the examination due to renal failure, postoperative creatinine elevation, or other comorbid conditions were excluded. In addition, patients who refused to undergo multislice CT due to financial reasons were excluded. Patients with improper timing of enzyme measurement were also excluded.

Patients were divided into 2 groups: group A with newly developed akinesia after off-pump CABG (20 patients), and group B without newly developed akinesia (219 patients). Patient characteristics are listed in **Table 1**. Mean European System for Cardiac Operative Risk Evaluation (EuroSCORE; group A, 4.2±3.1; group B, 3.05±2.6; P=0.049) and preoperative mean ejection fraction (group A, 45.0±7%; group B, 58.0±12.2%; P<0.001) were significantly different between the 2 groups. There was no significant difference in gender, mean age, body mass index, incidence of smoking, hypertension, diabetes mellitus, dyslipidemia, cerebrovascular accident, peripheral artery occlusive disease, or renal failure between the 2 groups.

### Wall Motion Analysis

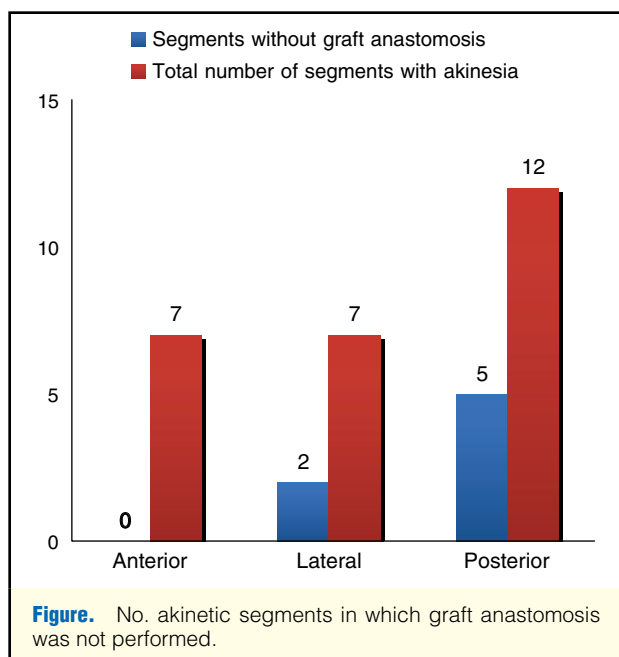
A 16-segment model, recommended by American Society of Echocardiography,<sup>11</sup> was utilized to analyze wall motion change after the operation. The left ventricle was divided into the apex, middle, and base, and each portion was subdivided into 4–6 segments and graded as follows: normal, 1; hypokinesia, 2; akinesia, 3; dyskinesia, 4; and aneurysm, 5. Wall motion score index (WMSI) was calculated by the summation of all scores from each segment divided by the number of segments visualized. Patients with newly observed akinesia in any segment regardless of the preoperative wall motion were assigned to group B.

### Operative Technique

Operations were performed by 2 surgeons and surgical strategy remained substantially unchanged during the study period. The operation was performed through a full sternotomy incision. The left internal thoracic artery was harvested in a skeletonized fashion and they were used in all of the patients. The radial artery was harvested using a Harmonic scalpel (Ethicon Endosurgery, Cincinnati, OH, USA). The right internal thoracic artery and saphenous vein were harvested if necessary. Heparin-mixed papaverine was used to avoid vasospasm of the left internal thoracic artery. Heparin was given at a dose of 1 mg/kg and activated clotting time was maintained at 350 s. Calcium channel blocker (Diltiazem) was continuously given to prevent radial artery spasm. Cardiac stabilization was achieved by using an Octopus tissue stabilizer and Starfish heart positioner (Medtronic, Minneapolis, MN, USA) was utilized concomitantly whenever hemodynamic instability was expected. Intracoronary shunts were used

	Group A (n=20)	Group B (n=219)	P value
Major complications (%)	1/20 (5)	16/219 (7.3)	0.61
TIA (%)	0	1 (0.5)	0.76
Pneumonia (%)	0	3 (1)	0.60
Postoperative bleeding (%)	1 (5)	1 (0.4)	0.03
UGI bleeding (%)	0	4 (2)	0.54
Ventricular arrhythmia (%)	0	3 (1)	0.60
CK-MB >50 ng/ml (%)	0	4 (2)	0.54
Superficial wound infection (%)	0	2 (1)	0.76
Atrial fibrillation (%)	1 (5)	18 (9)	0.80
Hospital stay (days)	9.8±4.8	9.8±3.4	0.95
ICU stay (days)	2.3±0.4	2.5±0.5	0.74
Mortality (%)	0	1 (0.5)	0.76

TIA, transient ischemic attack; UGI, upper gastrointestinal; CK-MB, creatine kinase isoenzyme MB; ICU, intensive care unit.



for left anterior descending (LAD) coronary artery anastomosis in most cases and proximal silicone elastomer snares were used for anastomosis of other coronary arteries.

Surgical features are listed in [Table 2](#). Operative parameters were compared between the 2 groups. No significant differences in operative methods such as total arterial grafting, number of distal anastomoses, number of arterial grafts, incidence of sequential grafts, aorto-coronary grafts, composite Y grafts, and end-to-end extension of grafts were identified.

### Patient Evaluation

Creatine kinase isoenzyme MB (CK-MB) and troponin-T sampling were obtained the day before the operation and on day 1 and day 2 after the operation. Electrocardiography was recorded on the same day as cardiac enzymes. Electrocardiography was done 1–5 days prior to the operation and 1 week after the operation. Multislice CT was done 7–10 days after the operation whenever feasible and delayed if the patient suffered any complications after the operation.

### Statistical Analysis

Data were collected prospectively and studied retrospectively supported by our database for off-pump CABG. Complications were defined in accordance with the guidelines established by the Society of Thoracic Surgeons Adult Cardiac Database Definition of Terms Version 2.52.1. Patient characteristics, operation method, and surgical outcome were compared using t-test. The comparison of preoperative and postoperative ejection fraction was done using paired t-test. Univariate analysis was performed with Fisher's exact test for categorical variables and Student's t-test for continuous variables. Multivariate logistic regression analysis was performed for risk factor analysis of newly developed akinesia. SPSS 15.0 (SPSS, Chicago, IL, USA) was used for statistical analysis.  $P < 0.05$  was considered significant and all odds ratios (OR) are presented with 95% confidence intervals (CI).

## Results

### Complications

The incidence of overall major complications did not differ between the 2 groups, even though the incidence of postoperative bleeding was significantly higher in group A ([Table 3](#)). The other comparisons of complications such as atrial fibrillation, superficial wound infection, and the number of hospital stays and intensive care unit stays were all insignificant. There was no significant difference in the mortality rate between the 2 groups.

### Wall Motion Analysis

The overall WMSI of group A patients worsened from  $1.58 \pm 0.35$  to  $1.72 \pm 0.34$  ( $P = 0.03$ ), whereas that of group B patients improved from  $1.22 \pm 0.37$  to  $1.18 \pm 0.33$  ( $P < 0.001$ ). Preoperative WMSI among the 3 anatomical territories (anterior, lateral, and posterior wall) were insignificant in both group A and B ( $P = 0.085$ ,  $P = 0.160$ ; respectively). Newly developed akinesia was detected in 20 patients (group A). The incidence of newly developed akinesia was as follows: anterior wall, 5; lateral wall, 3; posterior wall, 7; and multiple territories, 5. The right coronary artery (RCA) territory (posterior wall) was the region where akinesia was observed the most frequently (12 patients, 60%). A total of 37 segments were found to have new akinesia after the operation: LAD territory, 12 segments; left circumflex territory, 11 segments; and RCA territory, 14 segments.

	Group A (n=20)	Group B (n=219)	P value
<b>ECG</b>			
New Q wave, n (%)	2 (10)	2 (0.9)	0.04
New ST elevation, n (%)	2 (10)	6 (2.7)	0.14
Overall ECG change, n (%)	4 (20)	8 (3.7)	0.01
<b>CK-MB (ng/ml)</b>			
Preoperative	4.36±4.44	4.48±11.9	0.80
Immediate postoperative	7.63±4.23	6.48±6.51	0.76
POD1	11.43±8.12	12.15±18.2	0.49
POD2	6.45±3.63	7.59±5.6	0.39
<b>Troponin T (ng/ml)</b>			
Preoperative	0.07±0.15	0.08±0.32	0.57
Immediate postoperative	0.23±0.31	0.17±0.52	0.59
POD1	0.28±0.48	0.23±0.58	0.66
POD2	0.23±0.33	0.20±0.4	0.94

ECG, electrocardiography; POD, postoperative day. Other abbreviation see in Table 3.

Akinesia developed not only in territories where graft anastomosis was performed, but also in territories where graft anastomosis was not performed (Figure). All of the LAD territories were grafted either with arterial grafts or vein grafts. Two patients developed new akinesia in the left circumflex territory (29%), and 5 patients in the RCA territory (42%) where graft anastomosis was not performed.

The mean ejection fraction of group A patients decreased from 45.0±7% to 41.5±9.1% (P<0.001). The mean ejection fraction of group B patients, however, remained unchanged (58.0±12.2%, 58.7±11%, P>0.05). The preoperative ejection fraction was significantly lower in group A, as mentioned above.

### Enzyme, Graft Patency, and ECG

The CK-MB level was not significantly different before the operation, immediately after the operation, on day 1 or day 2 after the operation between the 2 groups (Table 4). Although there was a trend of a higher troponin-T level after the operation in group A, statistical analysis showed no significant difference in troponin-T levels at any time between the 2 groups. Both enzyme levels peaked on day 1 after the operation and subsequently decreased.

Graft occlusion was observed in 3 patients in group A and in 11 patients in group B. A total of 58 target vessels were revascularized in group A and 702 in group B. Four grafts were occluded (6.9%) in group A and 14 (2.0%) in group B. There was no significant difference in graft patency rate (P=0.109), however, between the 2 groups.

An increased incidence of new Q wave was observed in group A patients (P=0.04), but the incidence of new ST elevation between the 2 groups was insignificant (P=0.14). Overall ECG change related to infarct was significantly higher in group A compared to group B (Table 4).

### Multivariate Analysis

The preoperative ejection fraction was the only independent factor for newly developed akinesia (OR=0.8, 95%CI=0.83–0.95, P=0.01). Other variables such as the method of operation, EuroSCORE, patient characteristics, and comorbidity were not risk factors for newly developed akinesia (Table 5).

	OR	95%CI	P value
Diabetes mellitus	2.2	0.5–10.9	0.33
Dyslipidemia	2.9	0.6–14.1	0.19
PAOD	13.0	0.5–360.1	0.13
Total arterial graft	0.6	0.2–2.4	0.46
Age (>70 years)	0.7	0.1–4.2	0.76
Preoperative EF	0.9	0.8–1.0	0.001
EuroSCORE	1.3	0.8–2.0	0.3

OR, odds ratio; CI, confidence interval. Other abbreviations see in Table 1.

## Discussion

CABG surgery, if successfully performed, improves ischemia in patients with coronary artery occlusive disease and prevents the development of myocardial infarction.<sup>12</sup> Despite the advance in surgical techniques and diagnostic modalities, wall motion change after CABG surgery is not fully understood and hence conflicts exist. The difficulty in studying this area is attributable to varying preoperative myocardial contractility status, irregularly performed examinations such as contrast echocardiography or magnetic resonance imaging, and lack of knowledge in perioperative myocardial pathophysiology. Voci et al reported that 66% of the segments, which were subnormal before CABG, showed improvement immediately after the operation in their study involving 32 patients.<sup>13</sup> The wall motion score was applied in the study of Rubenson et al,<sup>6</sup> and no significant change in mean overall segmental wall motion score was seen, but significant worsening was noted in the septal motion of the apical and basal segment.

Nevertheless, the reason for this study was because while we were searching for patients who developed PMI after off-pump CABG, we realized that there was a subset of patients with new akinesia on postoperative echocardiography whose preoperative echocardiography indicated normal or hypokinetic wall motion. Most of their cardiac enzyme levels were below the diagnostic criteria for PMI. We were not certain about the clinical implication and prognostic value of this group of patients. Hence, we started studying the data of the patients with newly developed akinesia after off-pump CABG

and compared them with others in order to identify the risk factors, cause, and clinical outcome of patients with newly developed akinesia.

Analyzing wall motion by subdividing the apical, middle, and basal layers into 16 segments according to the model proposed by the American Society of Echocardiography distinguishes this research from many previous studies that used ejection fraction as the only parameter for contractility. This is a more precise way of assessing regional wall motion than using global ejection fraction. Another unique feature of the present study is that compared to most contractility studies, which are mainly performed under cardiopulmonary bypass, the present study consisted solely of off-pump CABG patients. Ribeiro et al<sup>14</sup> reported that most new echocardiographic septal wall motion abnormalities after CABG were not caused by perioperative infarction or generalized cell necrosis, but they studied only on-pump CABG patients and the effect of cardiopulmonary bypass could not be eliminated. Stunning phenomenon is an important factor in studying contractility after open heart surgery, but it can also be a confounding factor.<sup>15</sup> Off-pump CABG eliminates the influence of cardiopulmonary bypass on postoperative contractility, which can possibly aggravate wall motion.

We concluded that newly developed akinesia after off-pump CABG was not related to graft patency. Only 3 patients were found to have their grafts occluded out of 20 patients who developed akinesia postoperatively. Second, newly developed akinesia is not equivalent to PMI. In other words, new akinesia that occurs after bypass graft surgery does not always result in permanent myocardial cell necrosis. Cardiac enzyme levels did not differ significantly between the 2 groups and none of the patients in group A met the diagnostic criteria for PMI.<sup>16</sup>

One of the surprising findings was that akinesia developed in territories where no graft anastomosis had been performed. This is an important finding because this could be a clue to the hypothesis that graft patency was not related to newly developed akinesia after off-pump CABG. Twenty-nine percent of the patients were non-graft patients who developed akinesia in the left circumflex territory and 42% were non-graft patients who developed akinesia in the RCA territory. Additionally, the incidence of newly developed akinesia was greatest in the posterior wall (RCA territory) and the ratio between new akinesia in the LAD territory to the non-LAD territory was 5:13, if we exclude the number of occurrences of akinesia in combined segments. The LAD territory is where least elevation and manipulation of the heart is needed for anastomosis of the graft, whereas the RCA territory and the left circumflex territory require more effort and manipulation of the heart.

The preoperative ejection fraction was significantly lower in group A and it was found to be the independent risk factor for newly developed akinesia on multiple logistic regression analysis. Patients with lower ejection fraction might have a lower threshold for ischemia because most of them have experienced ischemic episodes sometime in the past and have subnormal contractility.

Complication rate and mortality rate were not significantly different between the 2 groups. This could imply that akinesia that is observed in a short period of time after the operation has less clinical significance and physicians should distinguish it from PMI because many reports have proven that the prognosis of PMI is much worse than that of the comparison group.<sup>17,18</sup> Use of troponin-I or troponin-T as a marker for infarction is suggested because they are sensitive and related

to adverse outcomes after off-pump CABG.<sup>19–21</sup>

The present results were based on observations in a small series of patients and hence there were a limited number of segments with newly developed akinesia. In addition, coronary angiography was not routinely performed after the operation despite the fact that conventional coronary angiography has a higher diagnostic yield compared to multislice CT, unless PMI is highly suspected. Although we previously published a report on the usefulness and accuracy of multislice coronary CT in the diagnosis of graft patency and stenosis,<sup>22</sup> the fact that multislice coronary CT rather than coronary angiography was used to measure the graft patency in the present study remains a limitation. Some patients were excluded due to incomplete results such as missing multislice CT, echocardiography, or cardiac enzyme level data because of expense, patient refusal, or inappropriate medical status. Short follow up remains a limitation and echocardiography was not repeated in every patient for the same reason. Long-term clinical status should be monitored in order to conclusively define the clinical implication of newly developed akinesia, and serial echocardiography should be done.

In conclusion, new akinesia that develops after off-pump CABG is irrelevant to graft patency, and cardiac enzyme level. Because there was little association between newly developed akinesia and a bad prognosis, short-term echocardiographic assessment is suggested rather than coronary angiography or reoperation. The cardiac enzyme level could be a good diagnostic marker for differentiation of patients with myocardial necrosis among those with newly developed akinesia.

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