The correlation of akinesia with graft patency and cardiac enzyme after off-pump coronary artery bypass graft surgery

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This work is perhaps not my best but my first piece of work as a cardiac surgeon. The most important thing that I have learned is that He works for the good and I owe thanks to many people for the help that they have given me. Without my family, my professors, my colleagues and my friends, my life and my thesis would have been a failure.

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ABSTRACT

The Correlation of Akinesia with Graft patency and Cardiac Enzyme after Off-Pump Coronary Artery Bypass Graft Surgery

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The purpose of this study is to identify the clinical implications of newly developed akinesia in echocardiography after off-pump CABG and its relationship with graft patency.

512 patients underwent off-pump CABG from January 2007 to November 2008. 239 patients, whose echocardiography and multislice CT data are available, were included in this 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 two groups (A: 45.0±7%, 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 two 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.

The mechanism of akinesia developing after off-pump CABG might be attributable to intraoperative coronary malperfusion which is probably due to cardiac manipulation rather than graft occlusion.

Key words : coronary artery bypass grafting, contractility, enzyme

The Correlation of Akinesia with Graft patency and Cardiac Enzyme after Off-Pump Coronary Artery Bypass Graft Surgery

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I. Introduction

Coronary artery bypass graft (CABG) surgery not only prevents myocardium from ischemia or myocardial infarction[1, 2, 3], but also selectively enhances myocardial contractility by adequately perfusing the hibernating myocardium[4, 5]. On the other hand, echocardiographic evidence of wall motion deterioration after CABG surgery is associated with poor patient outcome[6, 7, 8, 9]. Perioperative myocardial infarction that occurs during or after coronary artery bypass graft surgery is a dreadful complication, even though the mechanism and the pathogenesis are not completely understood[10].

In a small subset of patients who received off-pump CABG, regional akinesia was newly observed in echocardiography without any apparent etiologies. 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 coronary artery bypass graft surgery is the key to long-term survival, as mentioned above, very little is known regarding the pathophysiology and the consequence of newly developed akinesia. The purpose of this study is 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 was studied.

II.Methods

1. Patients

From January 2007 to November 2008, a total of 512 patients 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. 239 patients out of 512 patients were included in the study. Patients who suffered from acute myocardial infarction (AMI) were excluded since their preoperative cardiac enzyme levels were above the normal range and most of them revealed akinesia in preoperative echocardiography. Patients, whose test results were missing, such as multislice

CT and Troponin-T, were also excluded. Patients underwent multislice computed tomography (CT) after removing chest tubes for graft patency assessment in our institution, but those who could not receive the exam due to renal failure, postoperative creatinine elevation, or other co-morbid conditions were excluded. In addition, patients who refused to take the multislice CT examination due to financial reasons were excluded. Patients with improper timing of enzyme measurement were also excluded.

Patients were divided into two 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 EuroSCORE (European System for Cardiac Operative Risk Evaluation) (A: 4.2 ± 3.1, B: 3.05 ± 2.6, p=0.049) and pre-operative mean ejection fraction (A: 45.0±7%, B: 58.0±12.2%, p<0.001) were significantly different between the two groups. There was no significant difference in gender, mean age, body mass index (BMI), incidence of smoking, hypertension, diabetes mellitus, dyslipidemia, cerebrovascular accident (CVA), peripheral artery occlusive disease (PAOD), and renal failure between the two groups.

Table 1 Patient Demographics

	A (n=20)	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^2)	24.2 ± 2.6	24.5 ± 3.0	0.81
Smoker (%)	5 (25.0)	88 (40.2)	0.62
Diabetes (%)	8 (40.0)	80 (36.5)	0.62
Dyslipidemia (%)	9 (45.0)	115 (52.5)	0.81
Mean EuroSCORE	4.2 ± 3.1	3.05 ± 2.6	0.049
CVA (%)	2 (10.0)	14 (6.4)	0.62
Pre-op Creatinine (mg/dL)	1.0 ± 0.2	1.1 ± 0.9	0.41
Mean Ejection Fraction	45.0 ± 7%	58.0 ± 12.2%	<0.001
Hypertension (%)	14 (70.0)	140 (63.9)	0.44
PAOD (%)	1 (5.0)	14 (6.4)	0.49

BMI=Body Mass Index ; CVA=Cerebro-Vascular Accident ; PAOD=Peripheral Artery Occlusive Disease

2. Wall Motion Analysis

A 16-segment model, recommended by American Society of Echocardiography[11], was utilized to analyze the 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.

3. Operative Techniques

Operations were performed by two 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 Inc, Cincinnati, OH). 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 1mg/kg and activated clotting time was maintained at 350 seconds. 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) was utilized concomitantly whenever hemodynamic instability was expected. Intracoronary shunts were used for left anterior descending 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 two groups. No significant differences in operative methods such as total arterial grafting, number of distal anastomosis, number of arterial grafts, incidence of sequential grafts, aorto-coronary grafts, composite Y grafts, and end to end extension of grafts were identified.

Table 2. Surgical data

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

4. Patient Evaluation

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

5. 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 by 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. The SPSS 15.0 package (SPSS, Chicago, Illinois) was used for statistical analysis. A p-value less than 0.05 was considered significant and all odds ratios (OR) are presented with 95% confidence intervals (CI).

III. Results

1. Complications

The incidence of overall major complications did not differ between the two 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 ICU stays were all insignificant. There was no significant difference in the mortality rate between the two groups.

Table 3. Operative Outcomes and Mortality

	A (n=20)	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 Gastro-Intestinal ; ICU=Intensive Care Unit

2. Wall Motion Analysis

The overall Wall Motion Score Index (WMSI) of group A patients worsened from 1.58 ± 0.35 to 1.72 ± 0.34 (p=0.03) whereas that of group B patients improved from 1.22 ± 0.37 to 1.18 ± 0.33 (p<0.001). Preoperative WMSI among the three 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 (12 patients, 60%). A total of 37 segments were found to have new akinesia after the operation; left anterior descending (LAD) territory, 12 segments; left circumflex territory, 11 segments; and RCA territory, 14 segments.

Akinesia developed not only in territories where graft anastomosis was performed, but also in territories where graft anastomosis was not performed (figure 1). All of the LAD territories were grafted either with arterial grafts or vein grafts. 2 patients developed new akinesia in the left circumflex territory (29%), and 5 patients in the RCA territory (42%) where graft anastomosis was not performed.

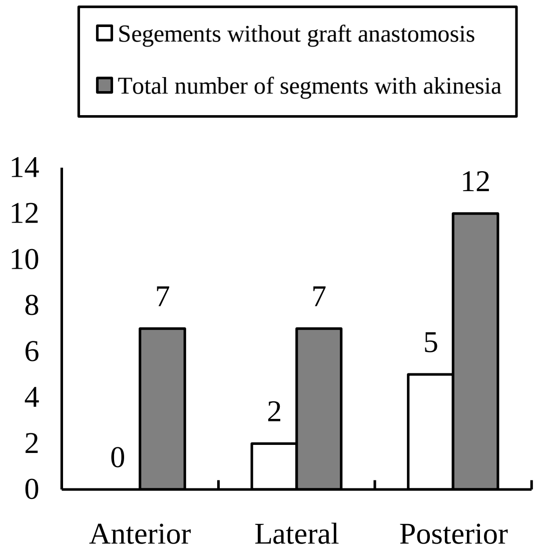

Figure 1. Number of Akinetic Segments that Graft Anastomosis was not performed

The mean ejection fraction of group A patients decreased from 45.0 ± 7% to

41.5 ± 9.1% ($p<0.001$). However, the mean ejection fraction of group B patients 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.

3. Enzyme, Graft patency, and ECG

The CK-MB level did not reveal significant difference preoperatively, immediately after the operation, day 1 or day 2 after the operation between the two 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 point of time between the two groups. Both enzyme levels peaked on day 1 after the operation and subsequently declined.

Table 4. Development of ECG findings implicating ischemia or infarct after operation

		A (20)	B (219)	p value
ECG	New Q wave (%)	2 (10)	2 (0.9)	0.04
	New ST elevation (%)	2 (10)	6 (2.7)	0.14
	Overall ECG change (%)	4 (20)	8 (3.7)	0.01
CK-MB	Preoperative	4.36 ± 4.44	4.48 ± 11.9	0.81
	Immediate postoperative	7.63 ± 4.23	6.48 ± 6.51	0.76
	POD#1	11.43 ± 8.12	12.15 ± 18.2	0.49
	POD#2	6.45 ± 3.63	7.59 ± 5.6	0.40
Troponin T	Preoperative	0.07 ± 0.15	0.08 ± 0.32	0.58
	Immediate postoperative	0.23 ± 0.31	0.17 ± 0.52	0.60
	POD#1	0.28 ± 0.48	0.23 ± 0.58	0.67
	POD#2	0.23 ± 0.33	0.20 ± 0.4	0.94

ECG=Electrocardiography, POD=Post Operative Day

Graft occlusion was observed in 3 patients in group A and 11 patients in group B. A total of 58 target vessels were revascularized in group A and 702 in group B. 4 grafts were occluded (6.9%) in group A and 14 (2.0%) in group B. However, there was no significant difference in graft patency rate (p=0.109) between the two 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 two groups was insignificant (p=0.14). Overall ECG change related to infarct was significantly higher in group A compared to group B. (table 4)

4. Multivariate analysis

The pre-operative ejection fraction was the only independent factor for newly developed akinesia (OR 0.8, CI 0.83-0.95, p=0.01). Other variables such as the method of operation, EuroSCORE, patient characteristics, and co-morbidities were not risk factors for newly developed akinesia (Table 5).

Table 5. Multivariate analysis for newly developed akinesia

	Odds Ratio	C.I.	p Value
Diabetes Mellitus	2.2	0.5-10.9	0.33
Dyslipidemia	2.9	0.6-14.1	0.19
PAOD	13	0.5-360.1	0.13
Total Arterial Graft	0.6	0.2-2.4	0.46
Age (>70)	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

PAOD = Peripheral Arterial Occlusive Disease; EF=Ejection Fraction

IV. Discussion

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

Nevertheless, the reason that began this study was because while we were searching for patients who developed perioperative myocardial infarction after off-pump CABG, we realized that there was a subset of patients with new akinesia in post-operative echocardiography whose pre-operative echocardiography revealed normal or hypokinetic wall motion. Most of their cardiac enzyme levels were below the diagnostic criteria for perioperative myocardial infarction. 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 which used the ejection fraction as the only parameter for contractility. This is more precise way of assessing regional wall motion than using global ejection fraction. Another unique feature of this study is that compared to most contractility studies, which are mainly performed under cardiopulmonary bypass, this study is comprised of solely off-pump CABG patients. Ribiero et al. [14] reported that most new echocardiographic septal wall motion abnormalities after CABG were not caused by perioperative infarction or generalized cell nerosis, but patients included were all 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 also can be a confounding factor[15]. 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. Secondly, newly developed akinesia is not equivalent to perioperative myocardial infarction (PMI). In other words, new akinesia that occurs after bypass graft surgery does not always implicate permanent myocardial cell necrosis. Cardiac enzyme levels did not differ significantly between the two groups and none of the patients in group A met the diagnostic criteria for PMI[16].

One of the surprising findings was that akinesia developed in territories where no graft anastomosis was performed. This is an important finding because this could be a clue to our hypothesis that graft patency was not related to newly developed akinesia after off-pump CABG. 29% of the patients were non-grafted patients who developed akinesia in the left circumflex territory and 42% for 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 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 in multiple logistic regression analysis. Patients with lower ejection fraction might have a lower threshold for ischemia because most of them experienced ischemic episodes sometime in the past and have subnormal contractility.

Complication rate and mortality rate did not reveal any significant difference between the two 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 them from PMI since many reports have proven that the prognosis of PMI is much worse than that of the comparison group[17, 18]. Using 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[19, 20, 21].

Our 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 conventional coronary angiography had more diagnostic yield compared to the multislice CT scan, unless PMI was highly suspected. Although we previously published the usefulness and the accuracy of multislice coronary CT diagnosing graft patency and stenosis[22], the fact that the multislice coronary CT rather than the coronary angiography was used to measure the graft patency in this study remains a limitation. Some patients were excluded due to incomplete examination results such as multislice CT, echocardiography, or cardiac enzyme level because of expense, patient refusal, or inappropriate medical status. A short follow-up duration remains a limitation and echocardiography was not repeated in every patient for the same reason. The long-term clinical status should be monitored in order to conclusively define the clinical implication of newly developed akinesia and serial echocardiography should be compared.

V. Conclusion

In conclusion, new akinesia that develops after off-pump CABG is irrelevant to graft patency and cardiac enzyme level. Since there was little association between newly developed akinesia and a bad prognosis, short-term echocardiographic assessment is suggested rather than performing a coronary angiography or a re-operation. The cardiac enzyme level could be a good diagnostic marker for making decisions in patients with newly developed akinesia to distinguish them from having myocardial necrosis.

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ABSTRACT(In Korean)

무심폐기 관상동맥우회술을 시행 받은 환자에서 새롭게 발생한 심근 무운동성(akinesia)과 도관 폐쇄 및 심근 효소와의 관계 분석

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양 홍 석

무심폐기 관상동맥우회술 후 심초음파 검사에서 이전에 관찰되지 않았던 분절에서 새롭게 발생한 심근 무운동성(akinesia)과 도관 폐쇄 여부 및 심근 효소와의 관계를 분석하고자 하였다.

2007년1월부터 2008년 11월까지 무체외순환 관상동맥우회술을 시행한 512명의 환자 가운데 수술 전후 심초음파와 수술 후 multislice CT를 이용하여 도관의 개존 여부를 평가한 239명의 환자들을 대상으로 하였다. 심근 운동 능력을 16분절로 세분화하여 이전에 관찰되지 않던 무운동성이 새롭게 발생한(newly developed akinesia) 환자군(A군 : 20명)과 발생하지 않은 환자군(B군 : 219명)을 대상으로 두 군간의 합병증 및 조기사망, 수술 후 심근효소 최고치(peak cardiac enzyme level), 심전도 변화양상(new Q wave, new ST elevation), 도관 개존 여부의 차이를 분석하였다. 또한 무운동성(akinesia) 발생에 영향을 미치는 위험인자에 대하여 조사하였다.

심근 무운동성은 전벽에서 5명, 측벽에서 3명, 후벽에서 7명 발생하였으며 복합 분절에서 발생한 환자가 5명이었다. 양군간의 수술전

심실 구출률은 통계적으로 유의한 차이가 있었다 (A군 45±7%, B군 58±12.2%, p<0.001). 이식된 도관의 평균 개수(A군 : 3.1±0.8, B군 3.3±0.8)와 완전 재혈관화(complete revascularization)는 통계적으로 차이가 없었다. 양군간의 합병증 발생과 조기사망은 통계적으로 차이가 없었으며 수술 후 심근효소(CK-MB, Troponin-T), 심전도 변화양상, 도관 개존율의 차이는 통계적으로 유의하지 않았다. 다변량 분석 결과 양군간의 수술 후 심근 무운동성을 일으킬 수 있는 위험요소로 수술전 심실 구출률이 통계적으로 의미가 있었으나 원위부 문합개수, 도관폐쇄 여부는 통계적 의미가 없었다.

무심폐기 관상동맥우회로술을 시행받은 환자에서 심근 무운동성이 새롭게 발견된 환자들의 심전도 변화 양상, 심근효소 수치, 도관 폐쇄 여부는 무운동성이 발생하지 않은 군과 비교하여 차이가 없었다. 이는 수술후 발생하는 무운동성(akinesia)은 수술 중 심장 거상 또는 저혈압 등에 의해 초래된 심근손상에 기인한 것으로 생각된다.

핵심되는 말 : 관상동맥 우회로 수술, 심근효소, 심근수축력

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