



Revascularization of dysfunctional but viable myocardium needs to be careful about postoperative rhythm disturbance after off-pump coronary artery bypass grafting: an uncontrolled observational retrospective clinical study

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Myocardial viability is one of important factors to determine clinical outcomes after off-pump coronary artery bypass grafting. We hypothesized that the revascularization of nonviable myocardium might show the different features of myocardial reperfusion postoperatively as compared with viable myocardium. Patients who underwent off-pump coronary artery bypass grafting for 2 years were retrospectively reviewed. Viable group (V group, n=159) and nonviable group (N group, n=24) were divided using preoperative single photon emission-computed tomography. The postoperative complication was evaluated by 1) occurrence of rhythm disturbance (atrial fibrillation/flutter or ventricular tachycardia), 2) use of continuous epinephrine, and 3) intra-aortic balloon pump insertion. Intubation time and intensive care unit (ICU) stay were also documented. Demographic data (gender, age, ejection fraction, and New York Heart Association [NYHA] classification) showed no difference. N group showed higher incidence of rhythm disturbance. Although intubation time showed no difference, ICU stay of N group was longer than V group. Revascularization of non-myocardium was associated with higher incidence of rhythm disturbance and longer ICU stay as compared with viable myocardium.

Keywords: Coronary artery bypass; Myocardial reperfusion; Postoperative complications

INTRODUCTION

Differentiation of viable from nonviable myocardium in patients with coronary artery disease is important for consideration of revascularization. Some patients with coronary artery disease and severe left ventricular dysfunction will ben-

efit from myocardial revascularization and revascularization of viable myocardium can be expected to improve regional and global function, left ventricular ejection fraction, and symptoms of coronary artery disease as compared with non-viable myocardium [1-3]. Therefore, various imaging methods including thallium-201 (²⁰¹Tl) and single photon emission-

computed tomography (SPECT) are applied to identify the presence of viable but ischemic myocardium in patients with ischemic left ventricular dysfunction [4,5].

“Viable” means that the myocardial cell is metabolically active and exhibits contractility. The myocardium in patients with coronary artery disease may be viable, nonviable, or dysfunctional, but viable myocardium may present as “hibernating” [6] or “stunned” [7]. After revascularization, viable and dysfunctional myocardium can usually recover normal myocardial function. However, nonviable myocardium generally does not recover normal function.

Patients with coronary artery disease conventionally undergo revascularization of viable and dysfunctional but viable myocardium. However, nonviable myocardium sometimes also undergoes revascularization. We hypothesized that revascularization of nonviable myocardium might show different features after myocardial reperfusion postoperatively, as compared those in viable myocardium. Therefore, the aim of this study was to investigate postoperative adverse outcomes in nonviable myocardium compared to viable myocardium after revascularization in patients who undergo off-pump coronary artery bypass (OPCAB) grafting.

MATERIALS AND METHODS

Study population

After obtaining Institutional Review Board of Seoul National University Hospital (Seoul, Korea) and obtaining informed consent from each subject, 333 patients who underwent OPCAB grafting for 2 years were retrospectively reviewed. Of the

333 patients identified, we only included those (n=183) who underwent valve surgery using cardiopulmonary bypass in Fig. 1. The viable group (V group, n=159) and nonviable group (N group, n=24) were assessed using preoperative SPECT.

Assessment of viability using single photon emission-computed tomography

Rest ^{201}Tl -dipyridamole stress $^{99\text{m}}\text{Tc}$ -sestamibi gated 24-h ^{201}Tl redistribution SPECT was performed before OPCAB surgery as in a previous study protocol [8].

Two-Dimensional echocardiography

Standard transthoracic echocardiography was performed. Left ventricular ejection fraction was calculated from conventional apical 2-chamber and 4-chamber views using the biplanar Simpson method [9].

Revascularizations

OPCAB surgeries were all performed using the same techniques. Graft harvesting was performed with internal mammary arteries and gastroepiploic arteries. The patients in the nonviable group were excluded when revascularization did not include nonviable myocardial areas. Anticoagulation was provided by intravenous heparin after graft harvesting and activating clotting time was maintained above 300 seconds during revascularizations. To control motion of the beating heart, a mechanical stabilizer (Octopus; Medtronic Inc., Minneapolis, MN, USA) and a heart positioner (Starfish; Medtronic Inc.) were used. Intravenous protamine was slowly dripped to reverse anticoagulation after revascularization.

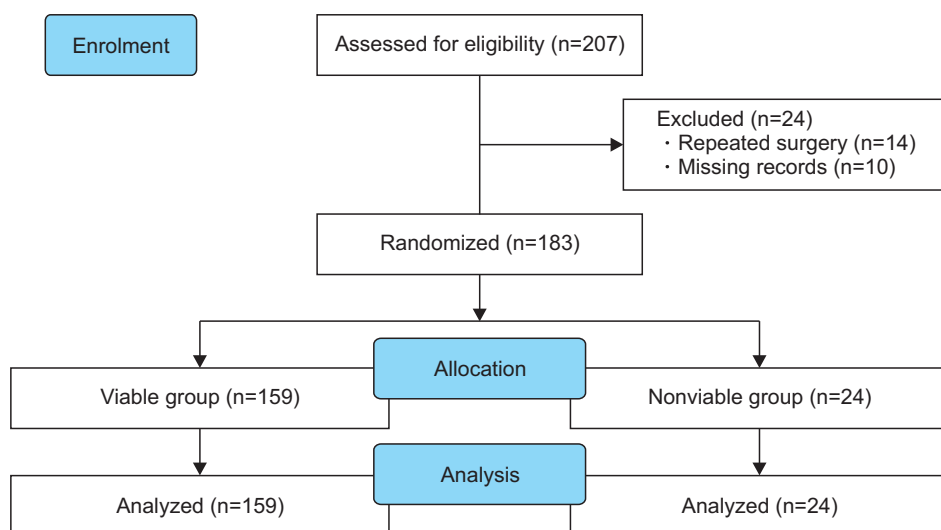


Fig. 1. CONSORT flow diagram in this study.

Hemodynamic strategies

Standardized intraoperative and postoperative hemodynamic management was performed. Hypotension (mean blood pressure <65 mmHg) was managed with volume replacement, phenylephrine, ephedrine, or vasopressin. Persistent hypertension (systolic blood pressure >150 mmHg) was controlled by increasing the anesthetic depth, administration of nitroglycerin, or a Ca^{2+} channel blocker. Tachycardia (heart rate >100 beats/min) was treated by increasing the depth of anesthesia, administration of β blocker, or a Ca^{2+} channel blocker. Bradycardia (heart rate <40 beats/min) was treated with glycopyrrolate or atropine. Low cardiac output (cardiac index <2.0 L/min/m²) was treated with dobutamine or milrinone. Epinephrine was used to treat hemodynamic instability with dobutamine above 15 $\mu\text{g/kg/min}$. When hematocrit decreased to less than 25%, red blood cells were transfused.

Intra-aortic balloon pump

An intra-aortic balloon pump (IABP) was inserted for intractable ventricular arrhythmia post-myocardial infarction, heart failure refractory to medical therapy, or cardiogenic shock, and for hemodynamic support for high-risk coronary artery bypass grafting (left ventricular ejection fraction $\leq 35\%$, left main stem coronary artery stenosis $\geq 70\%$, and unstable angina despite optimal medical therapy) [10,11].

Rhythm

Continuous electrocardiogram (ECG) monitoring was performed from the start of surgery to admission to the intensive care unit (ICU). A 12-lead ECG was recorded if arrhythmia was suspected. Atrial fibrillation was defined as an irregular narrow complex rhythm (in the absence of bundle branch block), with absence of discrete P waves. Atrial flutter was defined as the presence of coarse “saw-tooth” flutter waves with an atrial rate of 250 to 350 beats/min [12]. Ventricular tachycardia was defined as a ventricular rate greater than 120 beats/min, with 5 or 10 consecutive ventricular premature depolarizations [13].

Extubation and discharge from intensive care unit protocols

Extubation criteria included temperature greater than 36°C, urine output 0.5 mL/kg/h or greater, and chest tube drainage less than 100 mL/h [14]. Before extubation, all patients received

0.2 mg/kg of morphine. All patients were monitored for vital signs, pain scores, and sedation levels. For breakthrough pain, an additional bolus of 5 mg morphine was injected.

With return of adequate response to commands, pH 7.3 or greater, pulse oximetry (SpO_2) 95% or greater at fraction of inspired oxygen (FiO_2) ≤ 0.5 , arterial carbon dioxide tension (PaCO_2) ≤ 55 mmHg, and adequate respiratory effort, patients were extubated.

With return of adequate cardiac stability with no hemodynamically significant arrhythmia, $\text{SpO}_2 \geq 90\%$ at an $\text{FiO}_2 \leq 0.5$ by face mask, no intravenous inotropic or vasopressor therapy, chest tube drainage less than 50 mL/h, urine output greater than 0.5 mL/kg/h, and no seizure activity, patients were transferred out of the ICU.

Statistics

All data were expressed as average median (range) or number (%). Statistical analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). The chi-square test was used to analyze categorical data. Based on distribution of variables, continuous variables were compared by means of a nonparametric (Wilcoxon signed-rank sum) test. A p-value less than 0.05 was considered statistically significant.

RESULTS

During a 2-year period, patients who underwent OPCAB were retrospectively evaluated. The patients were divided into two groups using preoperative SPECT: a viable group (V group, n=159) and nonviable group (N group, n=24).

Table 1 summarizes demographic characteristics of the 183 patients. There were no significant differences between the 2 groups in demographic data, preoperative New York Heart Association (NYHA) classification, preoperative echocardiographic data, coexisting disease, and current medications.

Use of continuous epinephrine, use of IABP, and intubation time were similar in the 2 groups (Table 2). However, the incidence of rhythm disturbances including atrial fibrillation/flutter and ventricular tachycardia was significantly higher in the N group (odds ratio=2.43) than in the V group ($p < 0.05$) (Table 2). ICU stay was also significantly longer in the N group than in the V group ($p < 0.05$) (Table 2).

Table 1. Patients' demographic characteristics

Characteristic	Viable group (n=159)	Nonviable group (n=24)
Gender		
Male	105 (66.0)	17 (70.8)
Female	54 (34.0)	7 (29.2)
Age (y)	67 (42–80)	68.5 (45–78)
Ejection fraction	52.5 (34–68)	51 (30–68)
New York Heart Association classification	II (I–IV)	II (I–IV)
Smoking	50 (31.4)	8 (33.3)
Underlying disease		
Hypertension	129 (81.1)	19 (79.2)
Diabetes mellitus	70 (44.0)	8 (33.3)
Dyslipidemia	70 (44.0)	5 (20.8)
Percutaneous coronary intervention history	40 (25.2)	11 (45.8)
Coronary artery bypass graft surgery history	0	5 (20.8) ^a
Current medication		
Alpha blocker	30 (18.9)	11 (45.8)
Angiotensin receptor blockers	89 (56.0)	3 (12.5)
Angiotensin-converting-enzyme inhibitor	10 (6.3)	3 (12.5)
Beta blocker	89 (56.0)	13 (54.2)
Calcium channel blockers	89 (56.0)	11 (45.8)
Aspirin	89 (56.0)	11 (45.8)
Plavix	30 (18.9)	5 (20.8)

Values are presented as number (%) or median (range). ^ap<0.05, viable group vs. nonviable group.

DISCUSSION

We investigated the relationship between myocardial viability and myocardial reperfusion injury. A higher incidence of rhythm disturbance and longer ICU stay can occur with revascularization of nonviable myocardium as compared with revascularization of viable myocardium.

A viable myocardium has metabolic activity and contractility, which means that myocardial cells are alive. Viable myocardium is divided into viable and dysfunctional but viable myocardium that presents as “hibernating” or “stunned” myocardium. “Hibernating myocardium” is a state of permanently impaired left ventricular and myocardial function at rest because of decreased coronary blood flow. However, if the myocardial oxygen supply/demand relationship is favorably changed by revascularization, left ventricular and myocardial function can be partially or completely restored to normal [6]. “Stunned myocardium” is a state of contractile

Table 2. Viability and clinical data

Clinical data	Viable group (n=159)	Nonviable group (n=24)
Rhythm disturbance	30 (18.9)	11 (45.8)
Use of continuous epinephrine	20 (12.6)	7 (29.2)
Use of intra-aortic balloon pump	34 (21.4)	7 (29.2)
Intubation time (h)	18 (9–87)	19 (13–165)
Intensive care unit stay (h)	25 (16–95)	40 (21–329)

Values are presented as number (%) or median (range).

dysfunction resulting from an ischemic insult and myocardial necrosis [7]. Theoretically, dysfunctional but viable myocardial muscle has the potential to recover contractility. After revascularization, dysfunctional but viable, hibernating or stunned myocardium can become normal. Therefore, evaluation of myocardial viability is important.

The standard of reference for determining the presence of viable but ischemic myocardium in a dysfunctional myocardial region is improved myocardial function following revascularization or evidence of preserved glucose uptake on positron emission tomography (PET) or SPECT [15,16]. PET is not always available in most hospitals, and postoperative evaluation of viability is not useful for preoperative decision-making. In clinical practice, therefore, SPECT has emerged as the most commonly used technique for viability evaluation in patients with coronary artery disease and decreased left ventricular function. For SPECT imaging, ²⁰¹Tl and ^{99m}Tc-sestamibi are the most frequently used radiopharmaceuticals. We also evaluated myocardial viability using PET.

Myocardial reperfusion injury can cause paradoxical damage to the process of restoring blood flow to the ischemic myocardial region [17]. This injury accelerates progression to arrhythmia, functional impairment, and cell death. In addition, when performing surgery, an attempt may be made to revascularize nonviable myocardium according to the patient's condition. However, the complications caused by reperfusion injury are more likely to occur. Clinically, myocardial reperfusion injury presents as hemodynamic instability, rhythm disturbances such as atrial fibrillation, atrial flutter, or ventricular tachycardia, or failure of revascularization.

Atrial fibrillation is a common complication of coronary artery bypass grafting and has been reported to occur in 5% to 50% of cases, with a median of 25% [18]. It is generally a self-limiting arrhythmia, but is associated with prolonged hospitalization, postoperative stroke, and hemodynamic compro-

mise, particularly in patients with decreased left ventricular function [18]. Nevertheless, one-third of cardiac hospitals do not use routine prophylactic management and less than one-half of patients receive postoperative β -blockade.

A higher incidence of rhythm disturbance leads to prolonged ICU stay [19]. Our research showed the same results. Patients with coronary artery disease are often elderly and have underlying diseases such as cerebrovascular accident, hypertension, diabetes mellitus, renal disease, and dyslipidemia. These patients have a high risk of hospitalization-related complications. Although OPCAB surgery is preferred over conventional on-pump coronary artery bypass grafting for various reasons [20], the most important is to reduce hospital stay. However, revascularization of nonviable myocardium can increase the length of hospital stay and hospitalization-related complications. This study showed that revascularization of nonviable myocardium was associated with higher incidence of rhythm disturbance as compared with that following revascularization of viable myocardium. In other words, revascularization of nonviable myocardium was associated with a higher incidence of reperfusion injury as compared with that following revascularization of viable myocardium.

In conclusion, revascularization of nonviable myocardium is associated with a higher incidence of myocardial reperfusion injury, which is associated with a longer ICU stay.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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