Intraoperative Evaluation of Myocardial Viability by Nitroglycerin-induced Improvement in Regional Left Ventricular Function Assessed by Transesophageal Echocardiography

Takashi Watanabe, M.D.

Summary

The aim of this study was to assess whether intraoperative transesophageal echocardiography with nitroglycerin infusion could identify viable myocardium. Twenty-eight patients with coronary artery disease with regional dysfunction underwent transesophageal echocardiography during bypass surgery. A transgastric left ventricular cross-sectional image at the mid-papillary level was obtained and divided into four segments for wall motion analysis. Forty-four segments were graded as asynergic. Nitroglycerin was then given intravenously with an initial infusion rate of 1 μg/kg/min, followed by an increase in dose up to 3 μg/kg/min. Functional improvement with nitroglycerin was observed in 33 of 44 asynergic segments, while 11 remained unchanged. Follow-up transthoracic echocardiography was performed at 15.9 ± 5.5 days after surgery. A segment was defined as viable when wall motion was better than or equal to severe hypokinesis at baseline or follow-up. Forty-three of 44 asynergic segments at baseline were defined as viable; these were the same segments demonstrating wall thickening with nitroglycerin. In particular, four of 5 akinetic segments at baseline demonstrated viability at follow-up, which had been predicted with nitroglycerin. Transesophageal echocardiography with nitroglycerin correctly identified viability (p < 0.05). No adverse hemodynamic effect was observed. Intraoperative transesophageal echocardiography with nitroglycerin appears to be a safe, noninvasive, feasible, and widely available method to identify myocardial viability under the condition supported by cardiopulmonary bypass. (Jpn Heart J 36: 593–603, 1995)

Key words: Intraoperative transesophageal echocardiography Myocardial viability Coronary artery bypass grafting Nitroglycerin

The distinction between myocardial fibrosis and asynergic but viable myocardium is important for the selection of target vessels in coronary artery bypass grafting (CABG) in patients with impaired left ventricular func-
An accepted standard method for evaluation of myocardial viability is delayed thallium-201 scintigraphy. But if reliable information on viability can be obtained with echocardiography, it would be a very valuable tool having low cost, widespread availability, and environmental safety. A recent study suggests that viable myocardium can be identified by dobutamine-echocardiography. Nitroglycerin (NTG) has also frequently been used to elicit a response that might prove myocardial viability. In patients with critically stenosed coronary arteries, the administration of a positive inotropic agent may increase myocardial demand producing myocardial ischemia, while NTG administration usually results in a favorable alteration of the myocardial oxygen supply: demand ratio. In patients with a poor acoustic window, transthoracic examination is not always feasible and endocardial borders are sometimes not completely defined, while transesophageal echocardiography provides high-quality images. In addition, intraoperative evaluation just before the procedure provides the most accurate and up-to-date information, which may contribute to the final decision-making regarding target vessels during CABG.

Therefore, intraoperative transesophageal echocardiography was performed together with NTG in 28 patients with ventricular dysfunction undergoing CABG. The present study demonstrates the hemodynamic effects of intravenous NTG, and also suggests the possibility of evaluating myocardial viability with intraoperative NTG-transesophageal echocardiography.

**Patients and Methods**

Twenty-eight patients (24 men and 4 women, age range 31 to 79 years, mean 62.9 ± 8.7) with angiographically proven coronary artery disease and left ventricular dysfunction were studied. Patients were selected from 104 consecutive patients who had received coronary artery bypass graft surgery (CABG) at Juntendo University Hospital from November 1992 to July 1993. Patients with recent myocardial infarction or unstable angina were excluded (Table I). Previous myocardial infarction had occurred in 18 patients. The site of myocardial infarction was anterior in 9 patients and inferior in 9. Average left ventricular ejection fraction, calculated from biplane contrast ventriculography, was 66.2 ± 13.2%. Coronary angiography demonstrated significant stenosis (≥ 50% reduction in luminal diameter in the left main trunk and ≥ 75% in other coronary arteries) of 2 vessels in 4 patients, 3 vessels in 17, and the left main trunk in 7. Administration of beta blockers was discontinued ≥ 12 hours before the operation, and no patient was receiving beta blockers at the time of the intraoperative transesophageal echocardiographic study. Informed consent was obtained from each patient.
Table I. Patients’ Profile (n = 28)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male : female</td>
<td>24 : 4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31 – 79 (62.9 ± 8.7)</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>18 (64.3%)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>37 – 89 (66.2 ± 13.2)</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td></td>
</tr>
<tr>
<td>left main trunk</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>2</td>
<td>4 (14.3%)</td>
</tr>
<tr>
<td>3</td>
<td>17 (60.7%)</td>
</tr>
<tr>
<td>No. of grafts</td>
<td>2 – 5 (2.7 ± 0.8)</td>
</tr>
</tbody>
</table>

Horizontal View

Posterior wall

Septal wall

LV

Lateral wall

Anterior wall

Figure 1. Four-segment model used for assessment of wall motion by transesophageal echocardiography. LV = left ventricle.

Premedication consisted of diazepam, 0.1 mg/kg, orally, 90 minutes before surgery, and morphine, 0.2 mg/kg, IM, 60 minutes before surgery. Before induction of anesthesia, a radial arterial line and electrocardiographic monitor were put in place. Anesthesia was maintained with fentanyl (50 to 100 µg/kg) and midazolam (0.2 to 0.3 mg/kg), and muscle relaxation was achieved with vecuronium bromide (4 mg). After anesthetic induction, a thermodilution pulmonary artery catheter was inserted, and cardiac output (CO) and pulmonary capillary wedge pressure (PCWP) were measured. A 5.0-MHz transesophageal echocardiographic probe was then inserted and connected to a Hewlett-Packard 77025A ultrasound imaging system (Hewlett-Packard Co., Andover, MA, USA). The probe was positioned to obtain optimal transgastric left ventricular cross-sectional images at the mid-papillary level. Two-dimensional transesophageal echocardiographic images with electrocardiography were recorded continuously on videotape at baseline. The left ventricle was divided into four segments: anterior, lateral, posterior, and septal wall (Figure 1). Segmental wall motion was evaluated as follows: 1. normal — normal wall motion and systolic thickening; 2. mildly hypokinetic — mild reduction in endocardial motion and systolic thickening; 3. severely hypokinetic — marked reduction in endocardial motion and systolic thickening; 4. akinetic — virtual absence of inward motion and systolic
thickening; 5. dyskinetic — paradoxical wall motion away from the center of the left ventricle in systole, or systolic thinning, or both. After recording of echocardiographic images, the probe was positioned to obtain a left ventricular four-chamber view, and pulsed wave Doppler ultrasound examination was performed. Mitral flow velocity was recorded with a pulsed wave technique together with the electrocardiogram. The sample volume was placed between the tips of the mitral leaflets where the maximal flow velocity in early diastole was obtained. Peak mitral flow velocities, in early diastole and at atrial contraction, were measured in order to calculate E/A. The NTG was then given intravenously preceding surgical incision. The initial NTG infusion rate was 1 μg/kg/min, followed by an increase in dose of up to 3 μg/kg/min, until systolic blood pressure decreased. Again two-dimensional transesophageal echocardiographic images and mitral flow velocity were recorded as NTG-induced results. At the same time, CO and PCWP were measured to study the hemodynamic effects of intravenous NTG. Videotapes were analyzed by 2 experienced independent observers unaware of the clinical data. Of the total of 224 segments graded as baseline studies and NTG-induced results, both observers reached the same decision in 206 segments (92%), whereas in the remaining segments a split decision was resolved by discussion. Also, systolic and diastolic wall thickness in all segments was measured to obtain the rate of wall thickening (RWT), which is calculated as follows.

\[
RWT = \frac{\text{systolic wall thickness} - \text{diastolic wall thickness}}{\text{diastolic wall thickness}} \times 100
\]

At operation, an attempt was made to revascularize all major vessels with 50% or greater stenosis. In 28 patients, 76 stenosed vessels eventually received a graft (2.7 ± 0.8 grafts per patient). Myocardial protection consisted of core cooling to 25 to 28°C with iced saline solution in the pericardial well as topical cooling, and cold cardioplegia infused every 15 to 30 minutes.

Follow-up transthoracic echocardiography was obtained in all patients at an average of 15.9 ± 5.5 days after CABG. All patients underwent successful CABG. No patients had clinical evidence of perioperative myocardial infarction, nor was any patient receiving inotropic drugs at the time of this echocardiographic evaluation.

Statistics: Twenty-eight patients and 112 segments were enrolled in the study. Hemodynamic variables were assessed using Student’s t-test for paired data. Statistical analysis of diagnostic value of viability was performed with Fisher’s exact probability test. A \( p \) value < 0.05 was considered statistically significant. Values are given as mean ± standard deviation unless otherwise stated.
RESULTS

Hemodynamic effects of intravenous NTG: The pre-NTG and post-NTG hemodynamic changes are shown in Table II. In all 112 segments enrolled in this study, RWT increased significantly with NTG infusion. In 28 patients, E/A demonstrated a significant increase. BP and PCWP decreased significantly. On the other hand, no significant changes were noted in cardiac index (CI) and HR.

Evaluation of viability: Of 112 myocardial segments in the 28 patients, 44 were graded as asynergic at the baseline study. Of these 44 segments, 33 showed improvement in regional wall motion after administration of NTG, and 11 remained unchanged (Figure 2). In a follow-up study of the 44 asynergic segments, 33 showed improved wall motion, 7 remained unchanged, and 4 demonstrated deteriorated wall motion (Figure 3). A segment was defined as viable when baseline regional wall motion, or follow-up regional wall motion, was better than

<table>
<thead>
<tr>
<th>Table II. Hemodynamic Effects of Nitroglycerin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic variables</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>RWT (%)</td>
</tr>
<tr>
<td>E/A</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
</tr>
<tr>
<td>HR (beats/min.)</td>
</tr>
<tr>
<td>CI (lit/min./m²)</td>
</tr>
</tbody>
</table>

RWT = rate of wall thickening; SBP = systolic blood pressure; PCWP = pulmonary capillary wedge pressure; HR = heart rate; CI = cardiac index

normal

mild hypokinesis

severe hypokinesis

akinesis

(n=44) baseline nitroglycerin

![Diagram showing changes with nitroglycerin infusion in asynergic segments at baseline study.](image-url)
Figure 3. Changes in asynergic segments between baseline and follow-up study.

Table III. Comparison between the Segments Demonstrating Systolic Wall Thickening with Nitroglycerin and Segments Defined as Viable

<table>
<thead>
<tr>
<th></th>
<th>Viability (Viability)</th>
<th>($p &lt; 0.05$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Wall thickening</td>
<td>(+)</td>
<td>43</td>
</tr>
<tr>
<td>with nitroglycerin</td>
<td>(-)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>43</td>
</tr>
</tbody>
</table>

Figure 4. Individual changes in five akinetic segments between baseline, nitroglycerin-infused and follow-up study.
Figure 5. Example of improvement in left ventricular wall motion with intraoperative nitroglycerin transesophageal echocardiography. At baseline study, the end-diastolic phase (a) shows mildly reduced wall thickness (arrowheads) in the posterior wall. At the end-systolic phase (b), no inward wall motion was observed. During nitroglycerin infusion, the end-diastolic phase (c) showed the same wall thickness, whereas, the end-systolic phase (d) demonstrated systolic wall thickening.

or equal to severe hypokinesis. In the 44 asynergic segments, 43 segments were defined as viable, these were the same segments demonstrating systolic wall thickening with NTG infusion (Table III). Transesophageal echocardiography with NTG correctly identified viability \( (p < 0.05) \). In particular, of the 5 akinetic segments at the baseline study, 4 demonstrated viability upon follow-up study, which had been predicted with NTG-induced improvement in regional wall motion (Figure 4). An example of NTG-induced improvement in regional wall motion is shown in Figure 5.

**DISCUSSION**

The identification of viable myocardium is important for selection of target vessels in CABG, especially in patients with severe left ventricular dysfunction. An accepted clinical standard for myocardial viability is delayed thallium-201 scintigraphy. An ideal technique for detecting myocardial viability is still to be defined. The possibility of obtaining reliable information on viability by means of echocardiography is attractive because of its low cost, widespread availability, and environmental safety (no radionuclides). Recent studies suggest that viable
myocardium can be identified using transthoracic two-dimensional echocardiography together with low-dose dobutamine infusion. In patients with a poor acoustic window, transthoracic examination is not always feasible and endocardial borders are sometimes not completely defined. On the other hand, transesophageal echocardiography provides excellent quality cross-sectional images of the left ventricular cavity in most patients undergoing either cardiac or noncardiac surgery.

In patients with critically stenosed coronary arteries (with reduction in coronary blood flow so severe at rest as to produce sustained regional contractile dysfunction), the administration of a positive inotropic agent (even at low doses) may merely increase myocardial demand in the setting of exhausted coronary flow reserve, thereby producing myocardial ischemia and persistent regional dysfunction. In contrast, NTG administration usually results in a favorable alteration of the myocardial oxygen supply: demand ratio. Intravenous NTG has been used for the treatment of intraoperative episodes of myocardial ischemia, and also for the prevention of ischemic episodes during the perioperative period, in patients with coronary artery disease. NTG has frequently been used in patients with ischemic heart disease to elicit a response that might characterize functional viability, such as improvement of abnormal wall motion in asynergic ischemic segments. An experimental study also showed that the degree of NTG-induced potentiation of segmental cardiac function was closely associated with the extent of myocardial necrosis in the particular ventricular segment, inducing a conclusion that two-dimensional echocardiography coupled with an NTG potentiation test might be useful for assessing the viability of ischemic myocardium. The potential mechanisms involve reducing ventricular loading, altering the myocardial oxygen supply-to-demand ratio, and redistributing blood flow to ischemic zones.

In the study, regions that exhibited improvement in systolic function during NTG infusion were viable. In contrast, regions that remained akinetic during NTG infusion had persistent regional akinesis in the postoperative study. BP and PCWP were significantly decreased by NTG. BP decreased to 97.8 ± 10.7 mmHg, which seemed clinically acceptable. CI and HR were unchanged despite a marked reduction in filling pressures, indicating improved ventricular function. RWT increased significantly, which also indicated improved systolic function. A significant increase was observed in E/A, demonstrating improved diastolic function. Thus, NTG administration has no adverse effect on perioperative hemodynamics. Also, administration during operation is considered relatively safe under a condition supported by surgical back-up with cardiopulmonary bypass.

An acceptable evaluation of viability is not always obtained preoperatively
in some situations without the availability of scintigraphy, time to spare, and so on. Intraoperative use of transesophageal echocardiography can afford the final opportunity of evaluation. In this study, the decisions were made for the first time to revascularize two coronary arteries supplying the two akinetic segments according to the results of intraoperative transesophageal echocardiography with NTG. The additional advantage of intraoperative use is that any patient may tolerate the esophageal probe under anesthesia. A study showed that in some patients transesophageal examination was interrupted due to the patient’s intolerance of the esophageal probe. Intraoperative transesophageal echocardiography with NTG thus demonstrates images just before the procedure, providing the most accurate and up-to-date information of myocardial viability, and contributing to the final decision-making regarding target vessels during CABG.

**Study limitations:** The first limitation of this study is comparing myocardial segments imaged by 2 different approaches, namely transesophageal intraoperatively, and transthoracic postoperatively. An attempt was made to minimize this problem by using a 4-segment model in which both techniques can demonstrate almost the same cross-sectional images reflecting the supply of the three main coronary arteries. A further limitation is the possible negative effect of surgery on wall motion. There may be a possibility that viable segments are defined as nonviable by baseline and follow-up studies, which can be improved by CABG. However, the akinetic segments throughout this study also demonstrated a defect in delayed thallium-201 scintigraphy performed preoperatively. A potential limitation of the study may be the subjective and qualitative evaluation of regional wall motion. However, the diagnostic accuracy may not be increased by quantitative methods, which are time-consuming and still result in endocardial and epicardial signal dropouts, because image quality appears markedly reduced after digitization of end-diastolic and end-systolic still frames with commercially available software. In addition, the human eye naturally integrates space and time, and its discriminatory power is very difficult to match and virtually impossible to surpass. Different examiners have different eyes, but there is excellent concordance between experienced observers after a limited learning curve. Therefore, qualitative image analysis of wall motion remains the current standard with minimal interobserver variability.

**Clinical implications**

This study indicates that intraoperative transesophageal echocardiography with NTG appears to be a safe, noninvasive, feasible, cost-effective and widely available method to identify myocardial viability under the condition supported
by cardiopulmonary bypass in patients with left ventricular dysfunction. Accurate intraoperative evaluation of myocardial viability may contribute to the final decision-making regarding target vessels during CABG. However, this study involved only five akinetic segments and short-term follow-up periods. Thus, the application of intraoperative NTG-transesophageal echocardiography for the identification of myocardial viability is a potentially exciting approach, but one that clearly requires further study.

ACKNOWLEDGMENT

The author is grateful to Dr. Yasuyuki Hosoda, M.D. for guiding of the study, to Dr. Yoshinari Niimi, M.D. for help in collecting clinical studies, and to Dr. Shiro Sasaguri, M.D. for his capable review of the paper.

REFERENCES

7. Dumanski JG, Ritman EL, Davis GD, Gau GT, Rutherford BD, Frye RL: Regional left ventricular wall dynamics before and after sublingual administration of nitroglycerin. Am J Cardiol 36: 419, 1975
echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. Circulation 88: 430, 1993


