The Effect of Myocardial Surgical Revascularization on Left Ventricular Late Potentials

Levent Can, M.D.,* Meral Kayıkçioğlu, M.D.,* Halil Halil, M.D.,†
Hakan Kültürsay, M.D., F.E.S.C.,* Harun Evrengül, M.D.,*
Kamil Kumanlioğlu, M.D.,‡
and Cüneyt Türkoglu, M.D., F.A.C.C., F.E.S.C.*

From the *Department of Cardiology, Ege University School of Medicine, Izmir, Turkey;
†Department of Cardiology, Ege Sağlık Hospital, Izmir, Turkey, and ‡Department of Nuclear
Medicine, Ege University School of Medicine, Izmir, Turkey

Background: The presence of ventricular late potentials (LP) is an important indicator for the development of ventricular tachyarrhythmias due to ischemic heart disease. The effect of myocardial revascularization on LP has remained controversial. The purpose of this study was to determine whether complete myocardial surgical revascularization (CABG) documented by myocardial perfusion scintigraphy might alter the substrate responsible for LP.

Methods: Prospectively, enrolled patients undergoing elective CABG were evaluated with thallium-201 myocardial perfusion scintigraphy and signal-averaged ECG pre- and postoperatively. SAECG recordings were obtained serially: before, 48–72 hours and 3 months after CABG. LPS were defined as positive if SAECG met at least two of Gomes criteria. Scintigraphies were performed pre- and 3 months postoperatively for determination of the success of revascularization. Changes observed in SAECG recordings after CABG were compared between those with and without successful revascularization.

Results: CABG resulted in successful revascularization in 23 patients and was unsuccessful in 17 (no change or deterioration of the perfusion defects). Preoperative SAECG values were not different between groups except for RMS values. The incidence of LP decreased significantly postoperatively in patients with improved myocardial perfusion, whereas there were no changes in patients who did not have postoperative perfusion improvement (McNemar test, $P < 0.05$).

Conclusions: LPs disappear following the elimination of myocardial ischemia by complete surgical revascularization. Persistence of ischemia following CABG usually results in the persistence of late potentials. The incidence of ventricular arrhythmias is expected to be unchanged in these patients and they should be reevaluated for reinterventions.

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The signal-averaged electrocardiogram (SAECG) is a noninvasive, computerized surface electrocardiographic recording that can detect delayed low amplitude cardiac signals (late potentials) in the terminal portion of the QRS complex or within the ST segment.^{1–3} These late potentials, which reflect de-

layed ventricular activity in ischemic zone, are believed to be the marker of potential reentrant circuits in coronary artery disease.^{4,5} Successful coronary artery bypass grafting (CABG) can improve myocardial function and diminish myocardium at risk, thus preventing development of life-

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Address for reprints: Levent Can, M.D., Mavişehir Pamukkale 05, No. 94 Daire:55, Karsiyaka, Izmir, Turkey. Fax: +90232 3746618; E-mail: can@bornova.ege.edu.tr

threatening ventricular arrhythmias.⁶ The presence of late potentials on the early postoperative signal-averaged electrocardiography was also found to be an independent predictor of life-threatening tachyarrhythmias.⁶

Thallium-201 single photon emission computed tomography (SPECT) is a reliable method to detect the success of revascularization early after CABG.^{7,8} It is also useful in predicting the outcome after CABG.⁹ Our purpose in this prospective study was to determine whether complete myocardial revascularization may alter the substrate responsible for late potentials.

METHODS

Patients

Forty-two patients (mean age: 54 ± 7 , range 32 to 61 years) with chronic coronary artery disease and angina pectoris referred for CABG, were prospectively evaluated by thallium-201 myocardial perfusion scintigraphy and SAECG recordings 24-48 hours before, and 3 months after the attempted surgery at our university hospital. The diagnosis of coronary artery disease was documented by coronary angiography in all patients. The number of diseased vessels was determined by counting the major coronary arteries with at least 50% luminal diameter stenosis. Left ventricular ejection fraction was determined by contrast ventriculography before and by echocardiography 3 months after CABG. No patient had a history of presyncope, syncope or sustained ventricular tachyarrhythmias before CABG. None of them were receiving antiarrhythmic medication. Exclusion criteria were: (1) presence of intraventricular conduction delay (QRS > 120ms), bundle branch block, atrial fibrillation, or pacemaker dependency; (2) history of myocardial infarction; (3) history of previous revascularization procedures; (4) other CABG concomitant cardiac surgery (i.e., valve replacement therapy, aneurysmectomy); (5) presence of a noise level > 0.5 μ V in the composite lead of the SAECG; and (6) the presence of electrolyte derangement before and after CABG. Informed consent was obtained from all participants. The study protocol was approved by the local ethic committee. All patients underwent CABG using standard operative techniques. Patients were divided into two groups according to the changes observed in the postoperative thallium-201 scintigraphy compared

with the preoperative images. The first group consisted of patients with improvement in thallium-201 scans, and the second group included patients showing no change or deterioration in thallium images after CABG.

Signal-Averaged Electrocardiography

The SAECGs were obtained three times in all participating patients. Recordings were performed 24–48 hours before, 36–72 hours and 3 months after the CABG operation. Time domain signal-averaged recordings were performed using a high resolution electrocardiograph (1200 EPX, Arrhythmic Research Technology; Austin, TX, USA) in accordance with the recommended standards for analysis of ventricular late potentials on SAECGs.³ Briefly, signal averaging was performed in a patient at rest using the three standard orthogonal bipolar X, Y, and Z leads. About 200 QRS complexes were amplified, averaged, filtered with a 40-Hz high-pass filter, and combined into a vector magnitude $X^2 + Y^2 + Z^2$ according to the method described by Gomes.¹⁰ The noise level was tried to be held under 0.5 μ V during all recordings. The onset and offset of the QRS complex were determined by an algorithm that calculated the total QRS duration (QRSd), the root mean square voltage of the last 40 ms (RMS 40) of the QRS complex, and the duration of the terminal low (< 40 μ V) amplitude signals (LAS 40) of the QRS complex. The presence of late potentials was defined as present if the SAECG met two of three of the following criteria: filtered QRSd > 114ms, RMS 40 < 20 μ V, or LAS 40 > 38 ms.

Thallium-201 Scintigraphy

To assess the changes in late potentials and their relationship with the success of revascularization, exercise thallium-201 scintigraphy was performed according to the symptom-limited Bruce protocol to traditional endpoints (severe fatigue, moderate angina, or > 2 mm ST segment depression). To avoid blunting the heart rate response and to maximize the test sensitivity, all beta blocking drugs, nitrates and calcium antagonists were withdrawn for a period of 24 to 72 hours before the test, depending on each agent's duration of action. Thallium-201 imaging was obtained on average 2 days before and 3 months after the attempted CABG. For both studies radionuclide investigations were based on the combination of stress/redistribution

thallium SPECT. Patients were injected with 3 mCi (111 mBq) thallium-201 at peak exercise 1 minute before finishing the treadmill test. SPECT images for thallium's myocardial uptake were obtained within 5 minutes after the termination of the exercise and 3 hours later for redistribution images. Recordings were done by Sophy-DST gamma camera equipped with a low-energy, all purpose collimator. The detector collected data through a 180° arc from 45° right anterior oblique to the 45° left posterior oblique position. Images were reconstructed using a hamming filter and projected in short axis, vertical and horizontal long-axis views in a side by side display. The coding of the thallium data was blinded with regard to clinical and SAECG data. Thallium scans were coded according to a 10-segment system as follows: vertical long axis (anterior, inferior, apical), horizontal long axis (septal, lateral, apical), and short axis (apical, lateral, inferior, septal). Thallium-201 activity in each segment was scored as 3 (normal), 2 (mildly reduced), 1 (moderately reduced), or 0 (severely reduced or absent). A segment was considered abnormal if its score was ≤ 2 . Stress images were compared with redistribution images to evaluate the presence or absence of reversible or fixed defects. Reversible perfusion defects were defined as abnormal segments with an increment of tracer uptake >1 grade at the redistribution phase compared with the stress phase. Myocardial ischemia was considered in segments with reversible perfusion defects. Ischemia (redistribution) was interpreted in the presence of more than 25% reversibility.

The pre- and postoperative thallium-201 images were compared in order to define the success of the surgical revascularization. Patients were grouped according to the changes observed in scintigraphic data after CABG as follows: patients with improvement, patients without any change in perfusion, and patients showing deterioration. Improvement was defined as loss of at least one of the segmental defects. If the preoperative thallium defects were remained the same after CABG or while one segment was improving, a new defect was appearing in a previously normal segment it was accepted as "no change." Patients who showed new segmental defects after CABG without any change in their previous defects were accepted as the "deteriorated group."

STATISTICAL ANALYSIS

All values are expressed as mean $\pm$ standard deviation, with statistical significance set at the 0.05 level. Student *t*-test was used for evaluation of continuous variables in the two groups and Fisher's exact test for proportions when appropriate. Chi-square analysis and Student unpaired *t*-test were used to compare variables between groups for univariate analysis. Paired Student *t*-test was performed to compare SAECG variables before and after CABG. Changes in the frequency of late potentials were compared with the McNemar test according to the changes observed in postoperative thallium-201 images.

RESULTS

Clinical characteristics: 42 patients (4 women, 38 men) were included initially in the study. Two men died postoperatively from respiratory problems at the days 2 and 3. A total of 137 grafts were bypassed. The mean number of diseased coronary vessels was 2.8 ± 0.6 . The mean global ejection fraction was $48\% \pm 8\%$. The study population was divided into two groups according to the success of revascularization determined by the changes observed in postoperative SPECT images. The first group consisted of 23 patients with successful revascularization who showed improvement, and the second group included 17 patients with unsuccessful revascularization who had no changes or increase in the number of defects in the thallium images after CABG. Baseline characteristics of all patients and groups are listed in Table 1. No significant difference in clinical characteristics (including left ventricular ejection fraction) or cardiac medication use was evident preoperatively between the groups. Three (7.5%) patients had postoperative non-Q wave myocardial infarction (creatinine kinase MB > 50 IU/L). All patients were asymptomatic during the first 2 months following CABG. In the third month physical examination, 3 patients were suffering from angina pectoris.

SAECG findings are listed in Table 2. There was no overall difference between the pre- and postoperative third day SAECG recordings. But the changes between pre- and postoperative third months' SAECGs of the study population were significant ($P < 0.05$, McNemar Test). Preoperatively 15 (37.5%) patients had positive late potentials. On the third day of operation, 11 (73.3%) of them were

Table 1. Patient Characteristics

	All Patients (n = 40)	Unsuccessful Revascularization (n = 17)	Successful Revascularization (n = 23)
Age	53 ± 7	53 ± 9	54 ± 7
Gender (M/F)	36/4	14/3	22/1
Risk factors			
Smoking	27 (68%)	11 (65%)	16 (70%)
Hyperlipidemia	15 (38%)	7 (41%)	8 (35%)
Diabetes Mellitus	8 (20%)	2 (12%)	6 (26%)
Family history	14 (35%)	8 (47%)	6 (26%)
Obesity	22 (55%)	11 (65%)	12 (52%)
Hypertension	11 (28%)	5 (29%)	6 (26%)
Ejection fraction (preop.)	48.1 ± 8.3	44.9 ± 13.4	49.6 ± 8.2
Lesion location			
Left anterior descending	40 (100%)	17 (100%)	23 (100%)
Circumflex	33 (83%)	10 (59%)	23 (100%)
Right coronary artery	32 (80%)	11 (65%)	21 (91%)

None of the variables were statistically different between groups.

late potential positive. In the third month SAECG recordings, only 4 patients remained late potential positive. In 2 patients, late potentials became positive on the third month SAECG. Among the quantitative SAECG variables of the study population, there were no differences between the preoperative and immediate postoperative SAECGs, while the QRS duration and LAS 40 values decreased significantly ($P = 0.04$ and 0.009 , respectively) and there was a significant increase in RMS values ($P = 0.001$) in the third month SAECG recordings.

The effect of revascularization on the incidence of late potentials is shown in Figure 1. The inci-

dence of late potentials in patients with successful revascularization was higher than the unsuccessful group (52% vs 18%, $P = 0.06$) at baseline recordings. The RMS 40 values were also more abnormal at baseline before surgery among patients with subsequent successful revascularization (45.3 ± 22.4 vs 26.0 ± 19.4 ms [$P < 0.05$]). Among patients with improved thallium-201 imagings, the mean QRS duration and RMS 40 changed significantly at the postoperative third month SAECG recordings [QRS, 104.4 ± 16.1 ms before to 95.9 ± 12.3 ms after [$P = 0.000$]; RMS 40, 26.0 ± 19.4 ms before to 50.2 ± 28.9 μ V after [$P = 0.009$]]. Patients with

Table 2. SAECG Parameters

	All Patients	Unsuccessful Revascularization (n = 17)	Successful Revascularization (n = 23)	P Value*
Total QRSd (ms)				
Baseline	101.9 ± 15.9	98.8 ± 16.5	104.4 ± 16.1	Ns
Postoperative	99.3 ± 19.4	94.7 ± 17.1	101.9 ± 18.2	Ns
3 rd month	93.5 ± 12.0	94.1 ± 12.6	95.9 ± 12.3	Ns
LAS 40 (msec)				
Baseline	33.5 ± 15.5	30.4 ± 18.0	37.8 ± 13.3	Ns
Postoperative	32.3 ± 13.5	28.5 ± 15.1	37.0 ± 12.7	Ns
3 rd month	26.8 ± 11.7	26.1 ± 15.4	27.2 ± 8.5	Ns
RMS 40 (μ V)				
Baseline	33.9 ± 22.4	45.3 ± 22.4	26.0 ± 19.4	0.006
Postoperative	37.7 ± 23.3	50.7 ± 24.7	31.8 ± 19.9	0.01
3 rd month	52.1 ± 19.8	55.4 ± 22.2	50.2 ± 28.9	Ns

All data are expressed as mean ± SD; * for comparison of successful versus unsuccessful group. LAS 40 = low amplitude signals; QRSd = QRS duration; RMS 40 = root-mean square voltage of terminal 40 ms of QRS complex.

Figure 1. The effect of surgical revascularization on the classification of the signal-averaged electrocardiogram. Although the percentage of patients with late potentials was higher before CABG in the group with successful revascularization ($n = 23$), at month 3 follow-up (F/U) the unsuccessful group ($n = 17$) had a higher percentage of patients with late potentials.

unsuccessful revascularization also had significant changes in the mean QRS duration and LAS 40 values on the third month recordings (QRS, 99.8 ± 16.5 ms before to 94.1 ± 12.6 ms after [$P = 0.03$]; LAS 40, 30.4 ± 18.0 ms before to 26.1 ± 15.4 ms after [$P = 0.000$]).

Changes observed in the frequency of late potentials in patients with successful revascularization were statistically significant ($P = 0.008$, McNemar Test); twelve patients (52.1%) had late potentials at baseline, of whom 11 lost them 3 months after CABG, while 1 patient remained positive, eleven

patients (late potential negative) had no change, and none had a change from normal to abnormal (Fig. 2). Among the patients with unsuccessful revascularization, preoperative late potentials were positive in 3 (17.6%) patients who remained positive 3 months after CABG, whereas 2 (11.7%) had a change from normal to abnormal, and 12 (late potential negative) had no change 3 months later. These changes were not statistically significant ($P = 1.0$, McNemar Test).

DISCUSSION

Ventricular late potentials are high frequency, low amplitude signals in the terminal portion of the QRS complex that can be detected during sinus rhythm on the body surface by SAECG recordings.¹¹ They correspond to fragmented activation of ventricular tissue and are thought to originate from areas of slow and inhomogeneous conduction within diseased myocardial regions.¹² These low amplitude waveforms are also thought to represent delayed activation of damaged myocardium that serves as an arrhythmogenic substrate.¹³ CABG is an increasingly used therapeutic modality in the management of coronary artery disease. The effect of successful coronary revascularization on ventricular arrhythmogenic substrate has remained controversial.¹⁴ Some reports have described a net beneficial effect,¹⁴ while others revealed no effect

Figure 2. The effect of surgical revascularization on the classification of the signal-averaged electrocardiogram in individual patients with successful (A) and unsuccessful revascularization (B). As shown, the late potential (LP) changes observed at 3 month after surgery (POST) were significant in the successful group.

after CABG.¹⁵ Several causes such as graft occlusion and reperfusion, may be implicated in the development of increased ventricular ectopy after CABG. Despite successful surgical revascularization, patients with a previous myocardial infarction are more prone to new ventricular arrhythmias.¹⁶ The SAECG variables are related to the degree of slow conduction in the potential reentry circuit and the presence of late potentials is thought to reflect ventricular electrical instability.⁶ Besides offering an insight into the mechanism of postoperative ventricular arrhythmias, the examination of the SAECG characteristics before and after CABG may also be helpful in evaluating the prognosis. Frieligsdorf et al.¹⁷ evaluated the use of late potentials for the prediction of ventricular arrhythmias in the short- and long-term follow-up after CABG. In their study patients with late potentials before CABG, showed a markedly higher risk of developing serious ventricular arrhythmias in the perioperative period than patients without late potentials. In another study, Elami et al.⁶ had evaluated the value of abnormal late potentials on SAECG in identifying patients at risk of developing ventricular tachycardia or ventricular fibrillation in the early postoperative period after CABG. The presence of late potentials and low cardiac output in 72 postoperative patients was found to be the independent predictor of life-threatening tachyarrhythmias. Similarly, Lacroix et al.,¹⁸ had obtained SAECG of 100 patients in order to assess their prognostic value and evolution after CABG. They had obtained SAECG 24 hours before, 9 days after, and then followed up for 4 years. Their results showed that late potentials persist after CABG in 2/3 patients. Their interpretation was that the low incidence of postoperative sudden death could be attributed to the favorable overall effects of revascularization rather than on the arrhythmogenic substrate. Also Terada et al.¹⁹ has studied 21 patients after myocardial infarction with positive late potentials who had at least one occluded infarct related artery. They have investigated the presence of late potentials on the day of CABG and 1 week after surgery. According to their data, in patients with positive late potentials late after myocardial infarction, grafting to the infarct artery eliminated the late potentials soon after CABG.

Similar to these previous studies, the main purpose of our study was to document the effect of surgical revascularization on ventricular late potentials. We used thallium-201 SPECT for the eval-

uation of the success of surgical revascularization. Exercise thallium-201 SPECT has been shown to provide prognostic information after CABG.^{8,9} To the best of our knowledge, there is no study correlating the myocardial perfusion abnormalities to SAECG following CABG. We investigated whether alterations in myocardial perfusion directly affected the formation of ventricular late potentials. At the third month control thallium-201 imaging myocardial perfusion defects disappeared in 23 patients, worsened in 4 patients, and did not change in 13. We grouped patients according to the changes observed in postoperative thallium imaging: successful (nonischemic) group and unsuccessful (ischemic) group. Except for the preoperative RMS 40 values, there were no significant differences between the groups' SAECG variables. The baseline characteristics of the groups including left ventricular ejection fraction were also similar. The incidence of late potentials was also not statistically different before surgery (12/23 for the successfully revascularized group and 3/17 for the unsuccessful group, $P = 0.06$). As the groups are not randomized and are formed according to the results of myocardial perfusion image there cannot be a selection bias. The changes observed in the incidence of late potentials in the successful group 3 months after CABG was statistically significant, however this significant change was not observed in unsuccessfully revascularized patients. The late potentials disappeared in all patients except one in the successful group while presence of late potentials increased in the unsuccessful group. Better reperfused myocardial perfusion seemed to be reflecting an electrically more stable myocardium.

There are several other studies that have examined the effect of CABG on the quantitative variables of the SAECG. Borbala et al.⁴ have studied the effect of CABG on late potentials in 40 patients with chronic coronary artery disease. They have taken SAECG recordings before and within the first 10 days following CABG and found that patients with previous myocardial infarction have a higher rate of late potentials and the incidence of late potentials did not change significantly after CABG. In their study except the mean QRSd, which was shorter after CABG, SAECG variables were not changed. Their results were similar to our immediate recordings after CABG. Our first recordings after CABG also revealed no difference from the baseline SAECG values, which might be related to the perioperative hemodynamic instability. Their

interpretation was that the reported increase after CABG in ventricular arrhythmias was not probably related to a change in the arrhythmogenic substrate for ventricular reentry but was associated with changes in the arrhythmogenic milieu. In another study, Savelieva et al.²⁰ have recorded SAECGs before and 14 days after surgery in 119 patients and observed that the appearance of ventricular late potentials after CABG occurred in relation to the improvement of myocardial function. Their results may suggest that myocardial ischemia with prolonged wall-motion abnormalities is a possible mechanism in the occurrence of late potentials. All of these studies have included patients with previous myocardial infarctions. However, patients with known infarction were excluded from our study, in order to evaluate the ischemic but noninfarcted segment changes in thallium-201 imaging after CABG.

The type of the revascularization may also be important on the arrhythmogenic substrate. Richard et al.²¹ have studied the SAECG in 148 patients undergoing either CABG (64 cases) or coronary balloon angioplasty (84 cases). Two criteria of the SAECG were significantly modified after surgery: QRS duration ($P < 0.05$), and RMS 40 ($P < 0.01$). After bypass surgery, 71% of patients with an abnormal SAECG preoperatively had shown normal SAECG compared with 25% after angioplasty (non-significant). Their observations may support the hypothesis of a favorable modification of the arrhythmogenic substrate after myocardial revascularization, especially surgery.

Study Limitations

Although most of the patients after surgery had improved thallium-201 uptake and none had any symptoms or clinical events to suggest graft occlusion, we cannot be sure as to the continued patency of the grafts because repeat angiographies were not performed. This is the major limitation of our study.

CONCLUSIONS

Late potentials disappear following the elimination of myocardial ischemia by complete surgical revascularization. The persistence of myocardial ischemia following surgical intervention usually also results in the persistence of late potentials. As the incidence of ventricular arrhythmias is ex-

pected to be unchanged in these patients, they should be reevaluated for reinterventions. The routine use of pre- and postoperative SAECG evaluation in all patients undergoing elective CABG is advocated. Additionally SAECG may be used as a noninvasive method in simple means of predicting the success of revascularization, and may help in selecting which patients require detailed invasive reinterventions or investigations.

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