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Coronary Artery Bypass Grafting with and without Concomitant Epicardial Cardiac Resynchronization Therapy in Patients with Ischemic Cardiomyopathy: A Randomized Study

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ABSTRACT

Background: Epicardial implantation of a cardiac resynchronization therapy (CRT) system during coronary artery bypass grafting (CABG) may be an additional treatment method for improving left ventricle (LV) systolic function and dyssynchrony in patients with ischemic heart failure.

Objective: The objective was to compare the long-term results in patients with severe ischemic heart failure who underwent CABG alone or CABG combined with concomitant epicardial implantation of a CRT system.

Methods: One hundred sixty-four consecutive patients with severe ischemic heart failure and LV dyssynchrony were enrolled into 2 groups: CABG alone (n = 80) and epicardial CRT implantation during CABG (CABG + CRT) (n = 84). This prospective, randomized, and single-blind study was designed to compare clinical and echocardiography data after 6, 12, and 18 months of follow-up.

Results: In the CABG group, LV systolic function, dyssynchrony signs, and quality of life did not change postoperatively, compared with preoperative data. In contrast, these parameters significantly improved in the CABG + CRT group. The 2 treatment groups did not differ with respect to postoperative improvement in Canadian Cardiovascular Society class (P = .68). The improvement in the New York Heart Association functional class was much more pronounced in the CABG + CRT group than in the CABG group (P = .029). In the CABG group, 21 patients (26.2%) had died by the 18-month follow-up, compared with 9 patients (10.7%) in the CABG + CRT group (P = .012, log-rank test).

Conclusion: Epicardial implantation of a CRT system concomitantly with CABG facilitates the early postoperative period, improves LV systolic function, improves the quality of life, and decreases LV dyssynchrony. Moreover, mortality in the CABG + CRT group was significantly lower than in the CABG group.

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INTRODUCTION

Numerous large randomized studies have demonstrated that cardiac resynchronization therapy (CRT) is presently a highly efficacious therapy for patients with severe heart failure [Abraham 2002; Bradley 2003; Bax 2005]. In most patients, heart failure is caused by ischemic heart disease [Kaesemeyer 1994], and many patients need surgical revascularization. However, the impact of coronary artery bypass grafting (CABG) on mortality, quality of life, the course of heart failure symptoms, and left ventricle (LV) dyssynchrony still has not been adequately studied.

We hypothesized that epicardial implantation of a CRT system during CABG could be an additional treatment method that could improve systolic function, improve the quality of life, and eliminate the signs of LV dyssynchrony in patients with ischemic heart failure. Some investigators have demonstrated the beneficial effect of epicardial implantation of a CRT system during CABG on the course of heart failure, compared with patients who were treated with CABG alone [Bis 2007; Goscinska-Bis 2008]; however, these isolated findings were collected only for a limited number of patients and only for a short follow-up period.

Thus, the objective of this study was to compare the long-term results in patients who had severe ischemic heart failure and underwent CABG alone or CABG combined with concomitant epicardial implantation of a CRT system.

METHODS

We enrolled 164 patients with ischemic heart failure in this study. Inclusion criteria were the following:

- New York Heart Association (NYHA) functional class III or IV;
- LV ejection fraction ≤35%;
- Failure of modern medical therapy (angiotensin-converting enzyme inhibitors, β-blockers, and diuretics) within 3 months before enrollment in the study;
- Evidence of dyssynchrony based on at least one of the following criteria: QRS interval >120 milliseconds; Cardiac Resynchronization-Heart Failure (CARE-HF) study criteria (aortic preejection delay >140 milliseconds, interventricular mechanical delay >40 milliseconds,

Table 1. Methods of Clinical Examination of the Study Patients before and 6, 12, and 18 Months after the Surgery*

	Baseline (n = 164)	6 Months (n = 144)	12 Months (n = 134)	18 Months (n = 134)
Physical examination	×	×	×	×
Case history	×	×	×	×
Prescribed medical therapy	×	×	×	×
MLwHFQ score	×	×	×	×
Electrocardiography	×	×	×	×
NYHA functional class	×	×	×	×
CCS functional class	×	×	×	×
Standard laboratory tests	×	×	×	×
6-Minute walk test	×	×	×	×
Echocardiography + TDI	×	×	×	×
Stress echocardiography†	×			
Coronary angiography†	×			
CRT programming (for CABG + CRT group)‡		×	×	×

*MLwHF score indicates Minnesota Life with Heart Failure Questionnaire score; NYHA, New York Heart Association; CCS, Canadian Cardiac Society; TDI, tissue Doppler imaging; CRT, cardiac resynchronization therapy; CABG, coronary artery bypass grafting.

†Coronary angiography and stress echocardiography may be repeated if indicated.

‡CRT device programming has to be performed before the patient is discharged and again according to the control dates.

delayed activation of posterolateral LV wall); dyssynchrony evidence obtained with tissue tracking and tissue synchronization imaging (TSI) methods;

- Indications for CABG according to the American College of Cardiology/American Heart Association guidelines for CABG surgery [Eagle 2004; Cleland 2005].

Exclusion criteria included the following:

- Failure to provide informed consent;
- Previous heart surgery;
- Noncardiac illness with a life expectancy of <1 year;
- Noncardiac illness with a substantial operative mortality rate;
- Previous heart, kidney, liver, or lung transplantation.

This study was approved by the local ethics committee and conducted in compliance with the protocol and in accordance with study standard operating procedures. These procedures are designed to ensure adherence to good clinical practice, as described in the following documents concerning medical research in humans: ICH Harmonized Tripartite Guidelines for Good Clinical Practice 1996, Directive 91/507/EEC, The Rules Governing Medicinal Products in the European Community, and the Declaration of Helsinki. All patients signed an informed-consent form for participation in the study.

Table 1 summarizes the methods of the patients' examinations before and at 6, 12, and 18 months after the surgery.

Study Design and End Point

The study was a prospective, randomized, and single-blind investigation and was designed to compare 2 treatment methods: (1) CABG and (2) CABG plus CRT. After the patients signed the informed-consent form, they were randomized into 2 groups to undergo either CABG alone and modern medical therapy (n = 80) or CABG plus implantation of a CRT system during the surgery with the use of epicardial leads and modern medical therapy (n = 84). The patients were randomized with an electronic randomization system. Table 2 summarizes the characteristics of the patients.

The primary end point of the study was a comparison of the mortality for the 2 groups. The secondary end points were echocardiography data and Doppler imaging data, NYHA functional class, quality of life, duration of intensive care unit (ICU) stay, mean time of inotropic support, and the cardiac index 2 days after the operation.

Echocardiography and Tissue Doppler Imaging

Studies were performed with available echocardiographic equipment (Vivid 7D; GE Vingmed Ultrasound, Horten, Norway). Global LV function was assessed by using the modified biplane Simpson rule to measure LV end-diastolic and end-systolic volumes and the LV ejection fraction [Van de Veire 2007].

An M-mode recording from the parasternal short-axis view (at the level of papillary muscles) can be used to obtain the septal-to-posterior wall motion delay, and a cutoff value of ≥130 milliseconds was proposed as a marker of intraventricular dyssynchrony [Bax 2005].

Interventricular dyssynchrony can be evaluated by pulsed-wave Doppler echocardiography for assessing the extent of interventricular mechanical delay, which is defined as the time difference between the left and right ventricular preejection intervals. A delay ≥40 milliseconds has been proposed as a marker of interventricular dyssynchrony [Bax 2004a].

Table 2. Clinical Characteristics of the Patients Enrolled in the Study*

	All Patients (n = 164)	CABG Group (n = 80)	CABG + CRT Group (n = 84)
Age, y	62.4 ± 8	65 ± 4	63 ± 5
Male sex, %	89	92	90
6-mWT, m	249 ± 48	265 ± 34	244 ± 52
NYHA FC	3.4 ± 0.3	3.5 ± 0.4	3.3 ± 0.2
CCS FC	2.5 ± 0.4	2.6 ± 0.5	2.6 ± 0.3
LVEF, %	29 ± 2.7	30 ± 2.5	28 ± 2.2
EDV, mL	229 ± 54.2	228 ± 52.2	232 ± 49.4
ESV, mL	149 ± 65.9	147 ± 64.7	149 ± 67.7
No. of MIs	3.0 ± 0.5	2.8 ± 0.6	2.9 ± 0.7
QRS, ms	139 ± 29	142 ± 27	137 ± 29
LBBB, %	79.4	76	83
MLwHF score, points	65.8 ± 18	64.2 ± 18	65.3 ± 21
MR, grade	1.75 ± 0.4	1.7 ± 0.5	1.8 ± 0.6

*Data are presented as the mean ± SD where indicated. CABG indicates coronary artery bypass grafting; CRT, cardiac resynchronization therapy; 6-mWT, 6-minute walk test; NYHA FC, New York Heart Association functional class; CCS FC, Canadian Cardiac Society functional class; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume of left ventricle; ESV, end-systolic volume of left ventricle; MI, myocardial infarction; LBBB, left bundle branch block; MLwHF, Minnesota Life with Heart Failure Questionnaire; MR, mitral regurgitation.

Color-coded tissue Doppler imaging was performed by using the apical 4-chamber view to assess longitudinal myocardial regional function. Gain settings, filters, and the pulse repetition frequency were adjusted to optimize color saturation. Sector size and depth were optimized for the highest possible frame rate. In the basal septal and lateral segments, the time from the beginning of the QRS complex to peak systolic velocity (Ts) was measured; the delay in systolic velocities was considered to reflect LV dyssynchrony, as has previously been described [Bax 2004b].

Tissue tracking provides a color-coded display of myocardial displacement, which allows for easy visualization of LV dyssynchrony and the region of latest activation. TSI is a parametric imaging tool derived from 2-dimensional tissue Doppler images. It automatically calculates Ts in every position in the image with reference to the QRS interval. The TSI algorithm detects positive velocity peaks within a specified time interval, and the color coding ranges from green (earliest) to red (latest) within this interval. With the user-defined event-timing tool, the time from the onset of the QRS complex to the aortic valve opening and closure was first measured in a separately recorded pulsed Doppler spectrum. A quantitative measurement tool allows the calculation of the median Ts within a 6-mm sample volume manually positioned within the 2-dimensional TSI image [Van de Veire 2007].

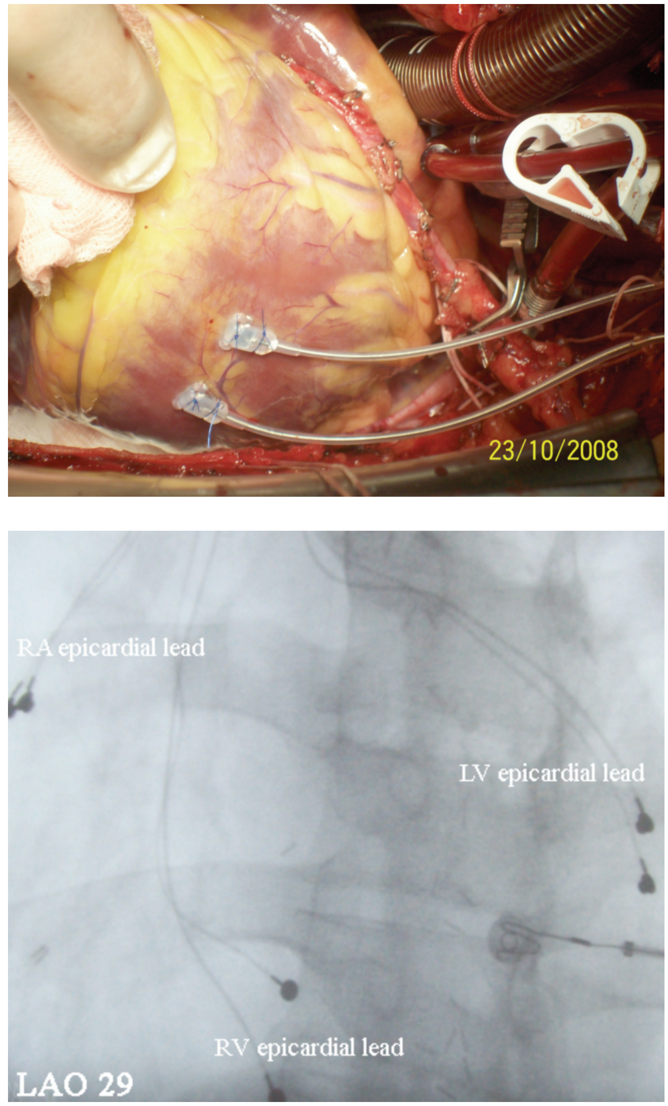

Figure 1. A, Implantation of an epicardial lead into the left ventricle. B, Radiographic image of the 3 implanted leads. RA indicates right atrium; LV, left ventricle; RV, right ventricle.

Surgical Details

All patients under cardiopulmonary bypass (CPB) underwent conventional CABG. In most cases, blood cardioplegia was used. In the CABG plus CRT group, 3 epicardial leads (CapSure Epi; Medtronic Minneapolis, MN, USA) were implanted after the main stage of the surgery. The leads were placed in the posterior-lateral area of the LV (posterior to the obtuse edge artery and 2 to 3 cm apically). The absence of great vessels and the presence of scar and adipose tissue in this area were the prerequisites. Lead placement on the right ventricle was in the area of the anterior wall close to the apex, and implantation on the right atrium was in the appendage area. The lead poles were positioned at a distance of 1 to 1.5 cm. All leads were fixed by Prolene 5-0 suture. During the reperfusion period after removal of the aortic clamp, sensitivity

Table 3. The Sensing and Pacing Parameters*

	During Implantation	6 Months	12 Months	18 Months	*P*†
RA pacing threshold, V	1.2 ± 0.4	0.9 ± 0.2	0.8 ± 0.4	0.9 ± 0.6	.73
RA sensing threshold, mV	3.9 ± 1.8	>2.8	>2.8	>2.8	NS
RA impedance, Ω	815 ± 223	593 ± 138	608 ± 112	611 ± 126	.39
RV pacing threshold, V	1.2 ± 0.5	0.9 ± 0.4	0.7 ± 0.2	0.67 ± 0.2	.08
RV sensing threshold, mV	11.9 ± 4.2	10.9 ± 3.4	10.7 ± 2.9	11.2 ± 2.2	.82
RV impedance, Ω	1184 ± 297	648 ± 112	632 ± 118	638 ± 126	.68
LV pacing threshold, V	0.85 ± 0.6	0.72 ± 0.2	0.55 ± 0.1	0.57 ± 0.2	.09
LV sensing threshold, mV	14.2 ± 7	10.2 ± 3.2	10.1 ± 2.5	9.9 ± 1.2	.78
LV impedance, Ω	1198 ± 328	635 ± 131	618 ± 128	621 ± 136	.64

*Data are presented as the mean ± SD. Pacing thresholds and impedance are measured at 0.5 milliseconds. RA indicates right atrium; NS, not statistically significant; RV, right ventricle; LV, left ventricle.

†6 Months versus 18 months.

Table 4. Patient Characteristics in the Early Postoperative Period*

	CABG Group (n = 51)†	CABG + CRT Group (n = 54)†	*P*
Mean time in ICU, d	3.9 ± 0.5	2.5 ± 0.5	.038
CI before operation, mL/min per m^2	2.4 ± 0.8	2.3 ± 0.5	.22
CI second day after operation, mL/min per m^2	2.4 ± 0.5	4.2 ± 0.4	.01
Mean time of lung ventilation, h	15.2 ± 7.4	14.9 ± 5.5	.62
Mean time of inotropic support, d‡	2.5 ± 0.5	1.2 ± 0.4	.037
Mean duration of IABP, h§	44.2 ± 21.4 (n = 27)	35.2 ± 19.4 (n = 29)	.04

*Data are presented as the mean ± SD. CABG indicates coronary artery bypass grafting; CRT, cardiac resynchronization therapy; ICU, intensive care unit; CI, cardiac index; IABP, intra-aortic balloon pump.

†Data of patients with inserted IABP are not included.

‡Inotropic support consisted of adrenaline (0.05 μg/kg per minute) and/or dopamine (5 μg/kg per minute).

§Data for patients with inserted IABP.

parameters and the stimulation threshold were measured for each lead. The connector part of the leads was further advanced through the second or third intercostal spaces to the formed pocket in the left subclavicular area and connected to the CRT device (InSync III; Medtronic; Figure 1).

Statistical Analysis

Results are expressed as mean values (±SD) for continuous parameters or as numbers and percentages for categorical ones. Continuous variables were compared by repeated-measures analysis of variance, the Student *t* test, and the Wilcoxon-Mann-Whitney tests. Categorical variables were compared with the Pearson chi-square test or the Fisher exact test. In addition, multivariable logistic regression was used to determine independent relationships. Survival curves were calculated and plotted according to the Kaplan-Meier method and analyzed with the log-rank test. A *P* value <.05 was considered statistically significant.

RESULTS

Surgical Procedure

The day before surgery, an intra-aortic balloon pump (IABP) was inserted in 27 patients (33.7%) of the CABG group and in 29 patients (34.5%) of the CABG plus CRT group. There were no significant differences between the 2 groups in the number of conduits, duration of aorta cross-clamping, or CPB duration. In the CABG and CABG plus CRT groups, the mean number of conduits was 3.5 ± 1.3 and 3.4 ± 1.2, respectively (*P* = .82). The mean durations of aorta cross-clamping in the CABG and CABG plus CRT groups were 52 ± 12 minutes and 56 ± 9 minutes, respectively (*P* = .49). The mean CPB times in the CABG and CABG plus CRT groups were 102 ± 22 minutes and 108 ± 19 minutes, respectively (*P* = .84).

In the CABG plus CRT group, the mean time required for implanting 3 epicardial leads was 6.2 ± 1.2 minutes, which extended the aorta cross-clamping period and CPB time by a mean of 2.2 ± 0.4 minutes and 6.2 ± 1.2 minutes, respectively. The LV epicardial lead was implanted during aorta cross-clamping, whereas the right ventricular and right atrial epicardial leads were implanted only at the time of CPB after the aorta cross-clamp had been removed. Values for sensitivity parameters and stimulation thresholds of CRT systems are summarized in Table 3.

Early Postoperative Period

Immediately after termination of surgery, all patients were admitted to the ICU. The mean time of residence in the ICU was 3.9 ± 0.5 days for patients in the CABG group and 2.5 ± 0.5 days for patients in the CABG plus CRT group

Table 5. Course of Clinical Data in the 2 Groups at 6, 12, and 18 Months after Surgery*

	Baseline		6 Months		12 Months		18 Months		
	CABG (n = 80)	CABG + CRT (n = 84)	CABG (n = 66)	CABG + CRT (n = 78)	CABG (n = 59)	CABG + CRT (n = 75)	CABG (n = 59)	CABG + CRT (n = 75)	P
CCS FC	2.6 ± 0.5	2.6 ± 0.3	1.5 ± 0.6†	1.6 ± 0.4†	1.8 ± 0.4†	1.8 ± 0.7†	1.9 ± 0.6†	1.8 ± 0.8†	.68
NYHA FC	3.5 ± 0.4	3.3 ± 0.2	2.7 ± 0.6	2.1 ± 0.8†‡	2.9 ± 0.8	2.2 ± 0.6†‡	2.9 ± 0.6	2.2 ± 0.8†‡	.029
6-mWT, m	265 ± 34	244 ± 52	376 ± 131	429 ± 124†‡	319 ± 63	445 ± 82†‡	292 ± 74	449 ± 69†‡	.003
MLwHF score, points	64.2 ± 18	65.3 ± 21	52.8 ± 23	40.6 ± 17†§	41.5 ± 9	32.9 ± 8†§	45.9 ± 11	22.4 ± 6†§	.001
Change in NYHA class in relation to the baseline:									
No change, n (%)			31 (47)	5 (6.4)§	34 (57.6)	3 (4)§	44 (74.6)	3 (4)§	
Improvement by 1 class, n (%)			29 (43.9)	19 (24.4)	22 (37.3)	24 (32)	15 (25.4)	27 (36)	
Improvement by 2 classes, n (%)			6 (9.1)	54 (69.2)§	3 (5.1)	48 (64)§	0 (%)	45 (60)§	

*Data are presented as the mean ± SD where indicated. *P* values reflect comparison of the differences between CABG plus CRT group and the CABG group over time. CABG indicates coronary artery bypass grafting; CRT, cardiac resynchronization therapy; CCS FC, Canadian Cardiac Society functional class; NYHA FC, New York Heart Association functional class; 6-mWT, 6-minute walk test; MLwHF, Minnesota Life with Heart Failure Questionnaire.

†$P < .01$ versus baseline.

‡$P < .05$ versus CABG group.

§$P < .001$ versus CABG group.

($P = .038$). In the CABG group, the mean postoperative cardiac index did not differ from the preoperative value (2.4 ± 0.8 versus 2.4 ± 0.5, $P = .22$). In the CABG plus CRT group, the cardiac index increased significantly postoperatively to 4.2 ± 0.4, compared with the baseline value of 2.3 ± 0.5 ($P = .01$). Notably, these data do not include the patients with an IABP. In the CABG plus CRT group, the course of the early postoperative period was more favorable with respect to some parameters. The mean time of inotropic support was 2.5 ± 0.5 days in the CABG group and 1.2 ± 0.4 days in the CABG plus CRT group ($P = .037$) (Table 4).

Clinical Results

The 2 treatment groups did not differ with respect to postoperative improvement in Canadian Cardiovascular Society angina class. In contrast, the 2 groups were significantly different with regard to improvement in functional class (assessed with NYHA criteria): Functional class improvement was much more pronounced in the CABG plus CRT group than in the CABG group (Table 5).

In the CABG group, the mean postoperative Minnesota Living with Heart Failure Questionnaire (MLwHF) score decreased, compared with the preoperative score (52.9 ± 23 points versus 64.2 ± 18 points; $P = .032$). This score remained lower when it was measured 12 and 18 months later (41.5 ± 9 and 45.9 ± 11 points, respectively; $P < .05$ versus baseline).

In the CABG plus CRT group, the MLwHF score was decreased significantly at 6 months postoperatively (40.6 ± 17 points versus 65.3 ± 21 points, $P = .018$). The decline in MLwHF score was maintained at 12 and 18 months after surgery (32.9 ± 8 and 22.4 ± 6 points, respectively; $P < .01$ versus baseline).

Echocardiography and Doppler Imaging

In the CABG group, the ejection fraction, the end-diastolic volume, and the end-systolic volume were not changed postoperatively compared with the preoperative values. In the CABG plus CRT group, on the contrary, the values for these parameters improved.

The number of segments with dyssynchrony according to tissue tracking and TSI, as well as the delay of systolic contraction in these segments, was not changed postoperatively in the CABG group, compared with the baseline values. Patients in the CABG plus CRT group had a significant reduction in the number of such segments and a significant delay of systolic contraction in these segments as assessed by TSI (Table 6, Figure 2).

Serious Adverse Events

There were 3 deaths in the early postoperative period. In the CABG group, 1 patient died from ventricular fibrillation 4 days after the operation, and another patient died from progression of heart failure 5 days after the operation. In the CABG plus CRT group, 1 patient died from a perioperative myocardial infarction. In addition, reoperation for bleeding was required in the early postoperative period for 4 CABG patients and 2 CABG plus CRT patients. Two CABG patients needed dialysis because of renal failure, and another CABG patient needed both extended lung ventilation for microfocal stroke and reoperation for mediastinitis.

In the 18-month follow-up, readmission to the hospital for heart failure was required for 2 patients (4.3%) in the CABG plus CRT group and for 9 patients (20%) in the CABG group, 2 of whom received cardioversion because of atrial fibrillation.

Table 6. The Course of Echocardiography and Doppler Echocardiography Data in the 2 Groups after Surgery*

	Baseline		2 Weeks		6 Months		12 Months		18 Months		
	CABG (n = 80)	CABG + CRT (n = 84)	CABG (n = 78)	CABG + CRT (n = 83)	CABG (n = 66)	CABG + CRT (n = 78)	CABG (n = 59)	CABG + CRT (n = 75)	CABG (n = 59)	CABG + CRT (n = 75)	*P*
Quantity of segments by TT, n	2.4 ± 1.2	2.5 ± 1.4	2.5 ± 1.6	0.9 ± 0.6†‡	2.5 ± 1.3	0.9 ± 0.4†‡	2.3 ± 1.4	0.8 ± 0.5†‡	2.6 ± 1.2	0.9 ± 0.4†‡	.0001
Quantity of segments with systolic delay by TSI, n	5.2 ± 2.2	4.9 ± 1.9	4.4 ± 1.8	1.2 ± 0.6†‡	4.4 ± 2.1	1.2 ± 0.5†‡	4.5 ± 1.8	1.1 ± 0.6†‡	4.5 ± 1.9	1.2 ± 0.4†‡	.0001
Time of systolic delay in these segments by TSI, ms	429 ± 102	442 ± 98	441 ± 119	241 ± 78†‡	432 ± 112	242 ± 72†‡	445 ± 122	239 ± 79†‡	444 ± 102	242 ± 59†‡	.001
QRS interval, ms	142 ± 27	137 ± 29	136 ± 26	122 ± 16†§	137 ± 25	124 ± 12†§	135 ± 27	122 ± 15†§	134 ± 25	121 ± 16†§	.028
IVD, ms	56 ± 14	59 ± 15	56 ± 18	33 ± 12†‡	57 ± 16	35 ± 12†‡	55 ± 12	32 ± 14†‡	55 ± 15	29 ± 17†‡	.019
SPWMD, ms	75 ± 22	72 ± 19	74 ± 24	54 ± 22†§	72 ± 24	55 ± 22†§	74 ± 25	52 ± 20†§	72 ± 21	49 ± 22†§	.048
LVEF, %	30 ± 2.5	28 ± 2.2	31 ± 3.8	30 ± 3.5	31 ± 3.2	40 ± 2.4†§	30 ± 2.7	41 ± 1.9†§	29 ± 2.5	42 ± 1.7†§	.022
EDV, mL	228 ± 52	232 ± 49	229 ± 56	214 ± 38	225 ± 48	212 ± 42	227 ± 52	210 ± 40	228 ± 47	211 ± 37	.086
ESV, mL	147 ± 64	149 ± 67	144 ± 68	148 ± 64	142 ± 62	132 ± 59	144 ± 59	129 ± 62	146 ± 62	132 ± 58	.041

*Data are presented as the mean ± SD. *P* values reflect comparison of the differences between the CABG plus CRT group and the CABG group over time. CABG indicates coronary artery bypass grafting; CRT, cardiac resynchronization therapy; TT, tissue tracking; TSI, tissue synchronization imaging; IVD, interventricular delay; SPWMD, septal-to-posterior wall motion delay; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume of left ventricle; ESV, end-systolic volume of left ventricle.

†$P < .01$ versus baseline.

‡$P < .001$ versus CABG group.

§$P < .05$ versus CABG group.

By the 6-month follow-up, 12 CABG patients (15%) and 5 CABG plus CRT patients (5.9%) had died. Between the 6-month and 12-month follow-ups, 7 CABG patients (8.75%) and 3 CABG plus CRT patients (3.6%) died.

A total of 21 patients (26.2%) in the CABG group had died by the 18-month follow-up, compared with 9 patients (10.7%) in the CABG plus CRT group (P = .012, log-rank test; Figure 3).

DISCUSSION

An increase in LV ejection fraction and an improvement in the quality of life are not observed after CABG in all patients with heart failure [Velazquez 2007]. In our study, we have demonstrated the advantage of the combined use of CABG and CRT in a large number patients with ischemic heart failure and evidence of LV dyssynchrony and with long-term follow-up. In addition, the mortality in the CABG plus CRT group was significantly lower than that in the CABG group. The principal concept of this study is that CABG alone neither eliminates dyssynchrony nor improves LV systolic function. Accordingly, in this patient category, it is reasonable to approach the problem of dyssynchrony through concomitant implantation of a CRT system.

The criteria for concomitant implantation of a CRT system after various types of cardiosurgical operations in patients with pronounced heart failure have been addressed in only a few publications [Bax 2004a; Bis 2007; Goscinska-Bis 2008]. The study by Bis et al demonstrated a significant decrease in heart failure symptoms and improvement in functional status for the patients who underwent concomitant CRT implantation during CABG. The number of patients participating in this study was limited, however, and statistically significant results were obtained only because of a crossover design [Bis 2007; Goscinska-Bis 2008].

As expected, our results showed that CABG alone is insufficient for elimination of dyssynchrony. Concomitant use of CABG and a CRT system proved to be efficacious. We clearly saw an improvement in LV contractile function compared with patients in whom only CABG was performed.

There have been no prospective randomized comparisons of surgical epicardial lead implantation versus transvenous implantation of leads in the coronary sinus; however, these 2 approaches have been compared in a number of articles [Navia 2005]. For example, Mair et al [2005] published the results of a retrospective comparison of lead implantation in the coronary sinus versus a left minithoracotomy. A number of negative aspects of transvenous implantation were shown. For example, implantation of the lead into an appropriate area was achieved in only 70% of the patients, and the long-term LV stimulation threshold was much higher than with epicardial implantation [Mair 2005].

Some researchers select the optimum LV lead position for epicardial implantation by stimulating various areas monitored by Doppler echocardiography immediately after the onset of CPB [Goscinska-Bis 2008]. Bypass and revascularization can alter the activation sequence of LV segments,

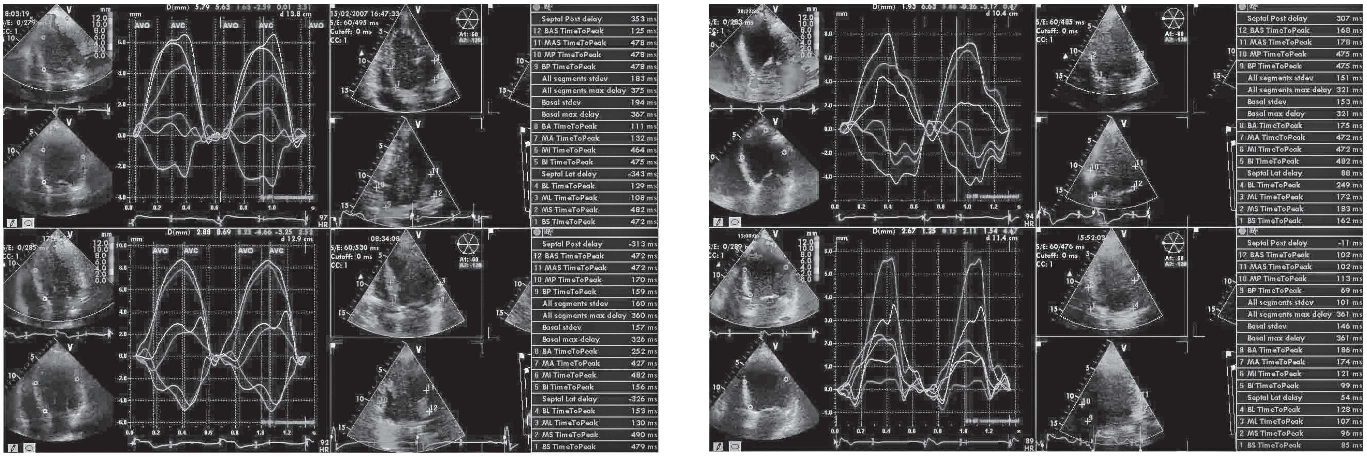

Figure 2. A, Example of Doppler echocardiography data obtained with tissue tracking and tissue synchronization imaging (TSI) methods in a CABG group patient before (upper half) and 18 months after (lower half) the surgery. B, Example of Doppler echocardiography data obtained with tissue tracking and TSI methods in a patient in the CABG plus CRT group before (upper half) and 18 months after (lower half) the surgery.

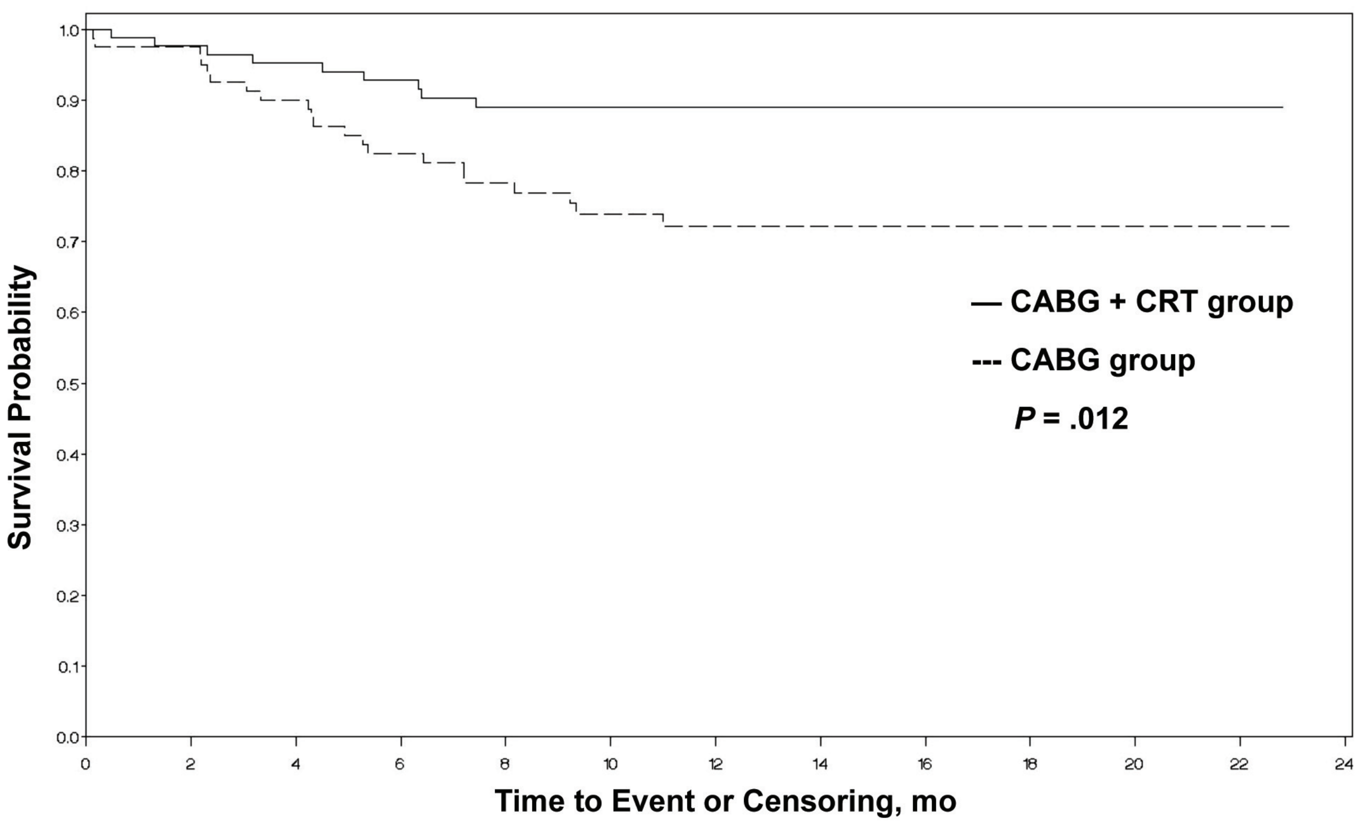

Figure 3. Kaplan-Meier curves of survival in the 2 groups after the surgery.

however, and accurate determination of the implantation site before the main stage of surgery seems questionable. On the basis of these considerations, we routinely implanted epicardial leads on the posterior-lateral LV in all patients, and all patients showed a positive response. Lead implantation in this area is reasonable, because this area is in contraposition to the interventricular septum and contains minimum vessels and epicardial fat [Chung 2008].

Current indications for CRT use a wide QRS complex as the marker of interventricular dyssynchrony; however, many studies that have been based on the width of the QRS complex have shown a rather high nonresponder percentage—from

20% to 30% [Abraham 2002; Bax 2002; Steendijk 2004]. The Doppler echocardiography methods used by many researchers to reveal LV dyssynchrony have varied, but the data to date are controversial regarding the use of Doppler echocardiography for selecting patients for CRT [Ellenbogen 2005; Chung 2008]. Because this issue is still unresolved, we took into consideration both the width of the QRS complex and Doppler echocardiography results in our study; however, our study did not answer the question of whether one of the methods or their combination is more advantageous than another.

Data are limited on the acute impact of CRT on the postoperative course of heart failure. We demonstrated a considerable increase in the cardiac index in the patients with CRT in the early postoperative period. This improvement significantly facilitated the patient's course during this period and allowed earlier discharge from the hospital.

Our study does not answer the question of how CRT affects patients with LV dyssynchrony who undergo aneurysmectomy in addition to CABG. Mizuno et al demonstrated a considerable decrease in cardiac failure symptoms and improvement of LV function in patients who underwent CABG combined with remodeling of the LV cavity and epicardial implantation of a CRT system [Mizuno 2003]. It was impossible in this study, however, to differentiate the effect of surgical intervention from the effect of CRT on the course of heart failure.

In conclusion, in patients with ischemic cardiomyopathy and evidence of LV dyssynchrony, CABG neither eliminates dyssynchrony nor improves systolic function. Epicardial implantation of a CRT system concomitant with CABG facilitates patient management in the early postoperative period, improves LV systolic function, improves the quality of life, and is associated with low mortality during long-term follow-up.

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