Coronary artery bypass grafting with concomitant cardiac resynchronisation therapy in patients with ischaemic heart failure and left ventricular dyssynchrony

Evgeny Pokushalov a,*, Alexander Romanov a, Darya Prohorova a, Alexander Cherniavsky a, Kinga Goscinska-Bis b, Jaroslaw Bis b, Andrzej Bochenek b, Alexander Karaskov a

*State Research Institute of Circulation Pathology, Novosibirsk, Russian Federation
bMedical University of Silesia, Katowice, Poland

Abstract

Objective: We have tested the hypothesis that epicardial implantation of cardiac resynchronisation therapy (CRT) system during coronary artery bypass grafting (CABG) may be an additional treatment method, which can decrease the mortality and improve left ventricle (LV) systolic function in patients with ischaemic heart failure (HF) and LV dyssynchrony.

Methods: One hundred and seventy-eight consecutive patients with severe ischaemic HF and LV dyssynchrony were enrolled in two groups: CABG alone (n = 87) and epicardial CRT implantation during CABG (n = 91). The primary end point of the study was the comparison of mortality between two groups at 18 months of follow-up.

Results: Twenty-three patients (26.1%) in the CABG group died at 18 months of follow-up compared with nine (10%) in CABG + CRT group (log-rank test, p = 0.006). The Cox regression analysis revealed that LV dyssynchrony (hazard ratio (HR) 2.634 (1.206–5.751), p = 0.015) was the independent predictor of all-cause death and HF hospitalisation. LV systolic function, dyssynchrony signs and quality of life did not change significantly post-CABG compared to pre-CABG data in CABG group patients. On the contrary, echocardiography revealed an improved LV ejection fraction (42 ± 1.9 vs 28 ± 2.7; p < 0.001), smaller LV end-systolic volume (120 ± 57.5 vs 164 ± 61.4; p = 0.04) and improved LV systolic function in the CABG + CRT group compared with the CABG group. In the CABG + CRT group, more patients improved by two NYHA classes (NYHA, New York Heart Association; 49 vs 0; p = 0.028), had a longer 6-min-walk test distance (452 ± 65 vs 289 ± 72; p < 0.001) and a better quality of life (22.9 ± 5 vs 46.4 ± 11; p < 0.001) compared with the CABG group.

Conclusion: For majority of the patients with ischaemic HF 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 and quality of life and is associated with low mortality at 18 months of follow-up.

© 2010 European Association for Cardio-Thoracic Surgery. Published by Elsevier B.V. All rights reserved.

Keywords: Ischaemic heart disease; Heart failure; Myocardial perfusion; Resynchronisation

1. Introduction

Coronary artery bypass graft (CABG) surgery improves prognosis in patients with ischaemic heart failure and angina [1,2]. However, approximately one-third of the patients are diagnosed with left ventricular (LV) dyssynchrony, which, as a rule, remains even after surgical revascularisation [3]. LV dyssynchrony can worsen prognosis for advanced systolic heart failure, and, therefore, requires to be corrected [4,5]. Correction of dyssynchrony with the help of biventricular pacing has proved to be efficient in these patients – improving symptoms, left ventricular ejection fraction (LVEF) and survival rate [6]. However, all the major trials exhibit a history of 8–10% failure rate for the placement of the LV lead via the transvenous route [6,7]. This is why we suggest that performing surgical revascularisation concomitant with epicardial cardiac resynchronisation therapy (CRT) system implantation is the procedure of choice for this category of the patients. Some authors showed 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 [8,9]. However, these isolated findings were collected only in a limited number of patients with a short follow-up period.

Thus, the objective of this study was the comparative evaluation of mortality, LV function and clinical data in patients with severe ischaemic heart failure, undergoing
CABG alone or CABG combined with concomitant epicardial implantation of a CRT system.

2. Methods

2.1. Study design

Between March 2006 and June 2009, 178 consecutive patients with ischaemic heart failure, who fulfilled the inclusion/exclusion criteria, were recruited to the study. Inclusion criteria comprised (1) III—IV New York Heart Association (NYHA) functional class; (2) LVEF ≤ 35%; (3) failure of optimal medical therapy (angiotensin-converting enzyme (ACE) inhibitors, β-blockers and diuretics) within 3 months before enrolment into the study; (4) evidence of dyssynchrony based on at least one of the following criteria: QRS > 120 ms, Cardiac Resynchronisation in Heart Failure (CARE-HF) criteria aortic pre-ejection delay > 140 ms, interventricular mechanical delay > 40 ms, delayed activation of postero-lateral LV wall or dyssynchrony evidence based on tissue tracking (TT) and tissue synchronisation image (TSI) methods; and (5) indications for CABG according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for CABG surgery. The following exclusion criteria were applied: (1) failure to provide informed consent; (2) previous heart surgery; (3) non-cardiac illness with a life expectancy of less than 1 year; (4) non-cardiac illness imposing substantial operative mortality; and (5) previous heart, kidney, liver or lung transplantation.

This study was approved by the local Ethic Committee and conducted in compliance with the protocol and in accordance with standard operating procedures of the study. These procedures are designed to ensure adherence to Good Clinical Practice (GCP), as described in the following documents: 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, concerning medical research in humans. All patients signed the Informed Consent Form for participation in the study.

The study was prospective, randomised and single blind, and was designed to compare two treatment methods: (1) CABG and (2) CABG + CRT.

The patients were randomly allocated to two groups, namely CABG group in which the patients were treated by CABG alone combined with optimal medical therapy (n = 87), and CABG + CRT group in which the patients were treated by CABG + implantation of CRT system during the surgery with the use of epicardial leads and optimal medical therapy (n = 91). Randomisation was done using an electronic system. Clinical characteristics of the patients are presented in Table 1.

2.2. Primary and secondary end points

The primary end point of the study was comparison of mortality rate between two groups at 18 months of follow-up. The secondary end points included identification of the predictors of all-cause death and heart failure hospitalisation, comparison of echocardiography data and Doppler imaging data, NYHA functional class, quality of life, duration of stay in the intensive care unit (ICU), mean time of inotropic support and cardiac index 2 days after operation.

2.3. Follow-up

The baseline assessment included clinical evaluation, standard laboratory analyses, angina (Canadian Cardiovascular Society (CCS) score) and quality of life (Minnesota Living with Heart Failure Questionnaire (MLwHF) score). All patients underwent a 6-min walking test to evaluate their exercise capacity, 24-h Holter monitoring to assess ventricular arrhythmias, echocardiography and Doppler imaging to assess LV function and coronary angiography.

Clinical and laboratory evaluation of all patients was performed at 6, 12, and 18 months after initiation of the study.

2.4. Echocardiographic and tissue Doppler imaging studies

Studies were performed with available echocardiographic equipment (VIVID 7D, GE Vingmed Ultrasound AS, Horten, Norway) using the following technology: tissue tracking (TT) and tissue synchronisation image (TSI) methods. These methods were performed at 6, 12, and 18 months after initiation of the study. The following basic echocardiographic parameters were measured:

- LVEF (%);
- L VEF (%);
- EDV L V (ml);
- ESV L V (ml);
- LBBB (%).

Table 1
Clinical characteristics of the patients enrolled into the study.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex (%)</th>
<th>6-mWT (m)</th>
<th>NYHA FC</th>
<th>CCS FC</th>
<th>LVEF (%)</th>
<th>EDV L V (ml)</th>
<th>ESV L V (ml)</th>
<th>Number of MI</th>
<th>LBBB (%)</th>
<th>MLwHF (points)</th>
<th>MR (grade)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>62.8 ± 7</td>
<td>90</td>
<td>252 ± 49</td>
<td>3.4 ± 0.2</td>
<td>2.6 ± 0.4</td>
<td>29 ± 2.5</td>
<td>229 ± 52.4</td>
<td>162 ± 64.7</td>
<td>3 ± 0.4</td>
<td>79.8</td>
<td>64.8 ± 17</td>
<td>1.77 ± 0.3</td>
<td>0.12</td>
</tr>
</tbody>
</table>

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; LBBB: left bundle branch block; MR: mitral regurgitation; number of MI: quantity of myocardial infarction; MLwHF: Minnesota life with Heart Failure Questionnaire score.
Norwegian Global LV function was assessed by measuring LV end-diastolic and end-systolic volumes (EDV and ESV) and LVEF, using the modified biplane Simpson’s rule.

Using an M-mode recording from the parasternal short-axis view (at the level of papillary muscles), the septal-to-posterior wall motion delay can be obtained, and a cut-off value of 130 ms or more was proposed as a marker of interventricular dyssynchrony.

Interventricular dyssynchrony can be evaluated by pulsed-wave Doppler echocardiography assessing the extent of interventricular mechanical delay defined as the time difference between left and right ventricular (RV) pre-ejection intervals; a delay of 40 ms or more has been proposed as a marker of interventricular dyssynchrony.

Colour-coded tissue Doppler images (TDIs) was performed using the apical four-chamber view to assess longitudinal myocardial regional function. Gain settings, filters and pulse repetition frequency were adjusted to optimise colour saturation. Sector size and depth were optimised 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 (TSI) was measured; the delay in systolic velocities was considered to reflect LV dyssynchrony, as described previously.

TT provides a colour-coded display of myocardial displacement, allowing for easy visualisation of LV dyssynchrony and the region of latest activation.

TSI is a parametric imaging tool derived from two-dimensional TDIs. It automatically calculates TSI, 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 colour coding ranges from green (earliest) to red (latest) within this interval. Using the user-defined event-timing tool, time from 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 TSI within a 6-mm sample volume manually positioned within the two-dimensional TSI image.

2.5. Surgical details

All patients under cardiopulmonary bypass (CPB) underwent conventional CABG. In most cases, blood cardioplegia was used. In the CABG + CRT group, three bipolar epicardial leads (CapsureEpi, Medtronic Inc, Minneapolis, USA) were implanted following the main stage of the surgery. In LV, the leads were placed in the posterior—lateral area (posterior to obtuse edge artery and 2—3 cm apical). 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 anterior wall close to the apex, and implantation on the right atrium was in appendage area. The lead poles were positioned at a distance of 1—1.5 cm. All leads were fixed by Prolene 5/0 suture. In reperfusion period after removal of aortic clamp, sensitivity parameters and stimulation threshold were measured for each lead. Connector part of the leads was further advanced through the second or third intercostal spaces to the formed subcutaneous pocket in the left subclavicular area and connected to the CRT device (Insync III, Medtronic Inc, Minneapolis, USA; Fig. 1).

2.6. Statistical analysis

Sample size (n = 178 per both group), with α < 0.05, power 80% and proportion difference of 15%, was calculated using log-rank test of survival in two groups followed up for a fixed time.

Results are expressed as mean values (standard deviation (SD)) for continuous parameters or as numbers and percentages for categorical ones. Continuous variables were compared by repeated-measures analysis of variance (ANOVA), t-test and Wilcoxon—Mann—Whitney tests. Categorical variables were compared by Pearson’s chi-square test or Fisher’s exact test. Two-sided paired and unpaired Student’s t-test or Pearson correlation coefficient was used as appropriate. Cox regression analysis was performed to determine the independent predictors of all-cause death and heart failure hospitalisation. Survival curves were calculated and plotted using the Kaplan–Meier method with the log-rank test. A value of p < 0.05 was considered to be statistically significant.

3. Results

3.1. Study population

The study included 178 patients with chronic ischaemic heart disease and severe heart failure. Clinical characteristics of the patients in both groups were not significantly different (Table 1). In addition, they received virtually identical medical therapy (nitrates in 100%, ACE enzyme inhibitors in 94%, diuretics in 100%, oral anti-platelets in 85.4% and oral anticoagulants in 14.6% patients with paroxysmal atrial fibrillation (AF) or β-blockers in 91% of patients). The type and the dose of medication did not change during the 18-month follow-up (excluding nitrates doses). Interventricular dyssynchrony was diagnosed in all 178 patients (100%), whereas interventricular dyssynchrony was present in 142 patients (79.7%).

3.2. Procedural data

The day before surgery, an intra-aortic balloon pump (IABP) was inserted in 27 (31.1%) CABG group patients and in 29 (31.9%) CABG + CRT group patients. There was no significant difference in the number of conduits, duration of aorta cross-clamping or CPB between the two groups. Complete revascularisation of all stenosed lesions was obtained in 146 (82.1%) patients. In the CABG and CABG + CRT...
groups, the average conduits number were 3.5 ± 1 and 3.4 ± 1, respectively (p = 0.72). Average duration of aorta cross-clamping in the CABG group and CABG + CRT group was 52 ± 13 min and 56 ± 11 min, respectively (p = 0.68). Average time of CPB in the CABG and CABG + CRT groups was 104 ± 26 min and 112 ± 17 min, respectively (p = 0.32).

In the CABG + CRT group, the time required for implantation of three epicardial leads was 6.8 ± 1.3 min, extending the aorta cross-clamping period and CPB time by 2.3 ± 0.6 min and 6.8 ± 1.4 min, respectively. LV epicardial lead was implanted during aorta cross-clamping, while RV and right atrial (RA) epicardial leads were implanted only at the time of bypass after the aorta cross-clamp was taken off. In all patients, pacing and sensing parameters remained stable during the follow-up period. No case of exit block was observed.

3.3. Adverse events in early postoperative period

In the early postoperative period, re-operation for bleeding was required for seven CABG patients and five CABG + CRT patients. Two CABG patients needed dialysis because of renal failure, and another CABG patient needed extended lung ventilation because of microfocal stroke and re-operation due to mediastinitis.

3.4. Primary end point

There were five deaths in the early postoperative period. In the CABG group, one patient died due to ventricular fibrillation 4 days after operation and three patients died due to progression of heart failure. In the CABG + CRT group, one patient died due to perioperative myocardial infarction.

At 6 months of follow-up, 10 (11.4%) CABG patients and four (4.4%) CABG + CRT patients died. During 6–12 months of follow-up, eight (9.1%) CABG patients and three (3.3%) CABG + CRT patients died.

Finally, in the CABG group, 23 patients (26.4%) died at 18-month follow-up compared with nine (9.9%) in the CABG + CRT group and CABG + CRT patients. Two CABG patients needed dialysis because of renal failure, and another CABG patient needed extended lung ventilation because of microfocal stroke and re-operation due to mediastinitis.

3.5. Secondary end points

Immediately after termination of the surgery, all patients were admitted to ICU. Average time of residence in ICU for the CABG group patients was 3.9 ± 0.6 days, and for the CABG + CRT group patients it was 2.5 ± 0.5 days (p < 0.001). In the CABG group, the cardiac index after surgery did not differ from preoperative value (2.4 ± 0.8 vs 2.3 ± 0.6; p = 0.56). In the CABG + CRT group, this value significantly increased and reached 4.1 ± 0.4 compared to the baseline of 2.3 ± 0.6 (p < 0.001). It should be noted that these data do not cover the patients with IABP. In the CABG + CRT patients, the course of early postoperative period was more favourable in terms of some parameters. In the CABG group patients, the time of inotropic support was 2.6 ± 0.5 days compared to 1.2 ± 0.4 days in the CABG + CRT group patients (p = 0.02; Table 2).

Follow-up changes in clinical data in both the groups are summarised in Table 3. Both groups showed a significant reduction in angina and NYHA functional class. The CCS angina class did not differ in both the groups. In contrast, improvement in NYHA functional class was significantly different, greater improvement was observed in CABG + CRT group (2.2 ± 0.7 vs 3.5 ± 0.3; p < 0.001). The distance covered by the patients during a 6-min walking test increased in the CABG group compared to baseline (289 ± 72 vs 265 ± 32; p = 0.09) and in the CABG + CRT group compared to the CABG group (452 ± 65 vs 289 ± 72; p < 0.001).

The MLwHF score was significantly greater in the CABG group compared to baseline (46.4 ± 11 vs 63.2 ± 19; p = 0.04) and in the CABG + CRT group compared to the CABG group (22.9 ± 5 vs 46.4 ± 11; p < 0.001).

The LVEF increased in both the groups, but significantly more in the CABG + CRT group (p < 0.001). The LV volumes (EDV and ESV) decreased only in the CABG + CRT group. LV dyssynchrony showed a significant correlation with the change
The concomitant CRT implantation. Results proved better dyssynchrony correction in patients undergoing CABG surgery.

4.1. Main findings

in both LV ESV ($r = 0.48$; $p < 0.001$) and LVEF ($r = -0.58$; $p < 0.001$) between baseline and 12-month follow-up.

The number of segments with dyssynchrony by TT and TSI, as well as delay of systolic contraction in these segments, did not change significantly after operation compared to baseline level in the CABG group. In the CABG + CRT group, there was a significant reduction in the number of such segments and delay of systolic contraction in these segments. Results are shown in Table 4.

In the 18-month follow-up period, re-admission to the hospital for heart failure was required for six (6.6%) CABG group patients and 19 (21.9%) CABG group patients, and four of them received cardioversion due to AF.

Patients in the CABG group who died after surgery had significantly greater LV dyssynchrony ($p < 0.001$). Other baseline clinical and echocardiographic variables were similar. Forty-two clinical events (48.3%) occurred in 87 CABG patients compared with only 15 events (16.5%) in 91 CABG + CRT patients ($p < 0.001$, Fisher’s exact test). Median event-free survival was significantly longer in the CABG + CRT patients ($p < 0.01$). In Cox regression analysis, LV dyssynchrony (hazard ratio (HR) 2.634 (1.206—5.751), $p = 0.015$) was identified as the independent predictor of all-cause death and heart failure hospitalisation (Table 5).

3.6. Impact of surgery on dyssynchrony

The LV dyssynchrony before CABG correlated significantly with the dyssynchrony after CABG ($r = 0.86$; $p < 0.001$). Only 23 (26.4%) of 87 patients with significant LV dyssynchrony before CABG surgery showed minor dyssynchrony after CABG. On the contrary, 63 patients (73.4%) did not have changes of dyssynchrony signs after CABG. Six (6.9%) of 87 patients had worsening LV dyssynchrony after CABG.

4. Discussion

4.1. Main findings

In this research, we studied the advantages of LV dyssynchrony correction in patients undergoing CABG surgery by the concomitant CRT implantation. Results proved better effectiveness of the CABG and CRT combination compared to the CABG procedure alone only in patients with severe ischaemic heart failure and ventricular dyssynchrony. Main findings can be summarised as follows: (1) the presence of dyssynchrony after CABG was associated with increased mortality; (2) CABG surgery alone insignificantly resynchronised the LV contraction pattern in most of the patients; (3) CABG surgery with CRT significantly reduced dyssynchrony and improved long-term prognosis; and (4) LV dyssynchrony after CABG emerged as an independent predictor of long-term survival and heart failure hospitalisation.

These results suggest the necessity of the routine diagnostics of LV dyssynchrony and its correction in patients with systolic heart failure undergoing CABG.

4.2. Electrical and mechanical dyssynchrony

Not all the patients with heart failure show increase in LVEF and improvement in quality of life after CABG procedure [10]. It is linked with the fact that one-third of these patients show LV dyssynchrony, which as a rule, does not disappear after CABG [3]. As a result, there are no opportunities for adequate LV function improvement. It is important to distinguish electrical and mechanical dyssynchrony as two fundamentally different types of dyssynchrony in patients with ischaemic heart failure. Electrical dyssynchrony is caused by disorders of electrical activation propagation as a uniform high-velocity wave front through the myocardial Purkinje network. It usually takes place in dysfunctional areas of ischaemic myocardium with preserved viability, where defects of the velocity and direction of electrical propagation form regions of both early and delayed ventricular contraction [11,12]. The delayed segments accommodate contractile force and volume, reducing systolic function [13]. Mechanical dyssynchrony is caused by impaired regional contractility and wall motion abnormalities associated with myocardial ischaemia. Hypokinetic wall motion, on the other hand, may result in delayed motion as an intrinsic property of injured myocardium independent of electrical activation [12,14]. However, ischaemic myocardium, as a rule, is concomitant with both mechanical and electrical types of dyssynchrony, which are autonomous and either of the types can be more or less apparent.
Some studies reveal that CABG alone can in some cases improve LV systolic function in patients with chronic myocardial ischaemia [1,2]. The mechanism by which CABG improves LV function is only partially understood. It is hypothesised that surgical revascularisation may improve myocardial contractility by promoting myocardial perfusion [8,12,13]; in other words, it is possible that revascularisation can positively influence mechanical dyssynchrony by improving myocardial contractility. However, partial reduction in LV dyssynchrony (mechanical dyssynchrony) did not lead to a significant LVEF growth (average 3.5 ± 7.3%), supposed due to the fact that residual electrical activation propagates disorders (electrical dyssynchrony).

4.3. Cardiac resynchronisation therapy-pacing versus cardiac resynchronisation therapy-defibrillator

The CARE-HF study demonstrated that total mortality after CRT was reduced by 36% at 29 months of follow-up compared with medical therapy. Although CARE-HF did not compare cardiac resynchronisation therapy-pacing (CRT-P) with cardiac resynchronisation therapy-defibrillator (CRT-D) directly, it provided strong evidence in support of the potential for CRT-P alone to reduce mortality of HF patients significantly. On the other hand, CRT-P impact on potentially life-threatening arrhythmias remains an unsettled question and sudden death still accounted for 32% of all deaths in CRT-treated patients [6].

The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial demonstrated that CRT decreases the combined risk of death or first hospitalisation in patients with advanced heart failure and QRS prolongation. Although there was no significant difference in overall mortality between CRT-P and CRT-D, however, sudden death was reduced by 63% with CRT-D therapy. Even though the COMPANION trial was not designed to compare CRT therapy with CRT-D therapy, the findings of the present study demonstrate a positive therapeutic association with CRT-D with regard to sudden-death risk reduction [15].

The data regarding prophylactic implantation of implantable cardioverter defibrillator (ICD) in ischaemic heart failure patients are controversial. The CABG-Patch trial demonstrated that there was no evidence of improved survival among patients with coronary heart disease, a depressed LVEF and an abnormal signal-averaged electrocardiogram in whom a defibrillator was implanted prophylactically at the time of elective coronary bypass surgery. However, the further analysis of the mechanisms of death in this trial revealed that ICD therapy reduced arrhythmic death by 45% without significant effect on non-arrhythmic deaths. Because 71% of the deaths were non-arrhythmic, total mortality was not significantly reduced [16].

On the contrary, the results of the MADIT-II trial (Multi-center Automatic Defibrillator Implantation Trial II (MADIT-II)) showed that that in patients with a prior myocardial infarction and advanced LV dysfunction, prophylactic implantation of a defibrillator improves survival and should be considered as a recommended therapy [17]. However, the further analysis of MADIT-II trial showed that patients enrolled more than 6 months after coronary revascularisation demonstrated a significantly higher survival rate after ICD

---

Table 4: The course of echocardiography and Doppler cardiology in both groups after the surgery.

<table>
<thead>
<tr>
<th>Time</th>
<th>CABG</th>
<th>CABG + CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>n = 87</td>
<td>n = 91</td>
</tr>
<tr>
<td>2 weeks</td>
<td>2.5 ± 1.1</td>
<td>2.6 ± 1.5</td>
</tr>
<tr>
<td>6 months</td>
<td>5.1 ± 2.4</td>
<td>4.8 ± 2.2</td>
</tr>
<tr>
<td>12 months</td>
<td>2.5 ± 1.4</td>
<td>2.6 ± 1.5</td>
</tr>
<tr>
<td>18 months</td>
<td>2.5 ± 1.4</td>
<td>2.6 ± 1.5</td>
</tr>
<tr>
<td>1.1 2.6</td>
<td>1.5 2.5</td>
<td>1.8 0.8</td>
</tr>
</tbody>
</table>
implantation, whereas no survival benefit was found in the group enrolled 6 months or less after revascularisation [18].

The question regarding benefits of CRT-D comparing with CRT-P is now under debate and survival advantage of CRT-D versus CRT-P has not been adequately addressed.

4.4. CABG concomitant with epicardial CRT system implantation

Large multicentre trials have demonstrated the efficacy of CRT as a method of treatment of severe heart failure with ventricular dyssynchrony [6]. But, at the same time, several clinical trials evaluating the effect of chronic CRT indicated the lower benefit of CRT for ischaemic patients presenting with dyssynchrony compared to patients with dilated cardiomyopathy of other origin [6,19,20]. This phenomenon in patients with ischaemic heart disease can be explained by the fact that CRT implantation allows to reach full reduction of electrical dyssynchrony but does not help to fully reduce mechanical dyssynchrony caused by impaired regional contractility and wall motion abnormalities as a result of myocardial ischaemia in viable myocardium. It can also be explained by the presence of non-viable myocardium. This hypothesis is confirmed by the recent Bleeker et al. study that found that achievement of mechanical synchrony is of paramount importance for the response to CRT; electrical activation is not a critical determinant of wall motion delay, the intrinsic contraction properties of diseased myocardium ultimately prevent mechanical synchrony [21].

Our results suggest that the aetiology of cardiomyopathy should be integrated into the evaluation of mechanical and electric dyssynchrony of patients referred for surgical revascularisation. In the presence of both mechanical and electric dyssynchrony, as in the current study, these patients could benefit from a combined procedure of surgical revascularisation concomitant with CRT system implantation.

The criteria for concomitant implantation of a CRT system after various types of cardiosurgical operations in patients with pronounced heart failure were addressed only in a few publications [8,9]. The study by Bis et al. demonstrated a significant decrease in heart failure symptoms and functional status improvement in the patients who underwent concomitant CRT implantation during CABG. However, the number of patients participating in this study was limited, and statistically significant results were obtained only due to a cross-over design [8,9].

In the present study, we used echocardiographic criteria for defining dyssynchrony. In most large multicentre trials of CRT published to date, as well as in the ACC/AHA and European Society of Cardiology (ESC) guidelines for CRT, wide QRS complexes are implemented as criteria for dyssynchronous contraction [6,8,15]. However, there is growing evidence that electrocardiographic parameters do not always correlate with dyssynchrony [16]. Moreover, patients with normal QRS duration and the presence of mechanical dyssynchrony identified in echocardiography may also benefit from CRT [22]. Therefore, echocardiography is becoming a useful tool for assessing dyssynchrony in clinical practice.

This research has a number of limitations, as we did not perform prospective randomised comparisons of surgical epicardial lead implantation versus transvenous implantation of leads in the coronary sinus. However, these two approaches have been compared in a number of articles [23]. A number of negative aspects of transvenous implantation were shown. For example, implantation of the lead into an appropriate area was achieved only in 70% of the patients, and the long-term LV stimulation threshold was much higher compared with epicardial implantation [24].

Besides, we did not select the optimum position for the LV lead for epicardial implantation by stimulation of various areas monitored by Doppler echocardiography immediately after the onset of bypass [8]. However, bypass and revascularisation can alter the activation sequence of LV segments, and accurate determination of the implantation site before the main stage of surgery seems questionable. Based on this, we routinely implanted epicardial leads on the posterior—lateral LV in all patients, and all patients showed a positive response. Lead implantation to this area is reasonable, because this area is in contraposition to the interventricular septum and contains minimum vessels and epicardial fat [25].

We restricted our study to implantation of CRT-P devices, and it is possible that the inclusion of implanting CRT-D devices within the present study could reduce the risk of sudden death.

In conclusion, in most number of patients with ischaemic 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 and quality of life and is associated with low mortality during follow-up.

References


[26] Hawkins N, Petrie M, MacDonald M, Hogg K, McMurray JJ, \textit{et al.} Is there any role for a ventricular lead on the left lateral wall, and we did it in the majority of the cases. Of course, there were some patients who had a scar area or a fat area, and we tried to implant the left ventricle lead to the posterior wall. Of course, there were some patients who did not have a scar area or a fat area, and we tried to implant the left ventricle lead to the posterior wall.

[27] Sutton MG, Pippart T, Hilpisch KE, Abraham WT, Hayes DL, Chinchoy E. Sustained reverse left ventricular structural remodeling with cardiac resynchronization at one year is a function of etiology: quantitative Doppler echocardiographic evidence from the multicenter InSync Randomized Clinical Evaluation (MIRACLE). Circulation 2006;113:266—72.


Appendix A. Conference discussion

Dr A. Diegeler (Bad Neustadt, Germany): In the manuscript you could nicely show that you could improve in those groups with additional asynchronous therapy the six-minute walk test, the ejection fraction, mortality, and New York Heart Classification. Most astonishing for me was that in the control group there was no improvement of all these parameters. The only improvement you could show in this control group was a slight improvement in angina. Thus, apart from the question whether coronary bypass surgery in those patients makes any sense, I have three questions. First, I did not find in your exclusion criteria that scar formation was an issue. In your study, what impact did the location of a scar have? You showed a mean of three myocardial infarctions in your patients, therefore you must have had some patients with significant scar formation. How did the presence or location of the scar formation impact your outcome?

Second, how many of the patients in the control group compared to the study group reached the maximum medical therapy for heart failure? Could you follow those patients exactly to establish that they take the drugs or not?

Third question, you should have some non-responders in the treatment group. Did you find some clues in a subgroup of those non-responders that they have the same discouraging outcome as those in the control group?

Dr Romanov: Of course, we have some non-responders in the active group. Unfortunately, we had many patients with ischaemic heart failure, and when we started to include these patients in this study, we examined about 500 patients, and only a third of them had signs of dyssynchrony. And concerning medical therapy, all patients included in the study received the modern medical therapy three months before including them in the study and during follow-up. Of course, in the CABG group there were some patients who had an increase of ejection fraction, but in the majority of cases their ejection fraction and all parameters of left ventricle function, also on TDI data, didn’t change. Our suggestion is that this is the influence of preoperative dyssynchrony. Maybe the patients who will plan to undergo CABG without signs of dyssynchrony can have better results. This is our suggestion.

Mr R. Asclonne (Bristol, UK): Perhaps I can ask you a quick question. It is really about the methodology of LV lead positioning. Apparently the percutaneous approach can often be problematic, leading to failure in terms of positioning the lead at the right place. Surgically this is potentially an advantage. What was your rationale for epicardial lead positioning? Was it based on anatomy only or epicardial mapping?

Dr Romanov: We think that epicardial mapping is good in some cases, but for a clearer group we tried to implant the left ventricle lead to the posterolateral wall, and we did it in the majority of the cases. Of course, there were some patients who had a scar area or a fat area, and we tried to implant the leads to the posterior wall.