Hemodynamics and Prognosis after Primary Cardiac Resynchronization System Implantation Compared to "Upgrade" Procedures

HERBERT NÄGELE, M.D.,* JULIA DODECK, M.D.,* STEFAN BEHRENS, M.D.,* MOJGAN AZIZI, M.D.,* SANDRA HASHAGEN, M.D.,* CHRISTINE EISERMANN, M.D.,* and MARIA A. CASTEL, M.D.†

From the *St. Adolfstift, Reinbek, Medical Department, Reinbek, Germany; and †Hospital Clinic, Thorax Institute, Barcelona, Spain

Introduction: *Left bundle brunch block (LBBB) and right ventricular stimulation (RVS) may be associated with asynchrony and heart failure. Differences between these two entities and their response to cardiac resynchronization therapy (CRT) are not well defined.*

Methods: *Patients receiving CRT from 1999 to 2006 were analyzed for cardiac events and prognosis separated between primary implants for LBBB (n = 221) and upgrades from RVS (n = 107). A subgroup of 105 patients (LBBB = 69; RVS = 36) was studied in more detail (New York Heart Association [NYHA], quality of life, brain natriuretic peptide, peakVO2, left ventricular ejection fraction [LVEF], wedge pressure, Cardiac Index, QRS, left-right preejection period using pulsed wave doppler, septum-lateral wall motion delay using tissue doppler imaging) at baseline and after 1 year.*

Results: *Age (68.4 ± 11 years vs 68.7 ± 15 years, n. s.), NYHA class (3.1 vs 3.1, n. s.), LVEF (26.4 vs 28.1, n. s.), and clinical parameters were comparable between LBBB and RVS. The latter group consisted of more patients with chronic atrial fibrillation (14% vs 37%, P = 0.03). After 1 year, NYHA class (−0.8 ± 0.8 vs −0.6 ± 0.8, n. s.), LVEF (+13.7 ± 14% vs +8.7 ± 10%, n. s.), and clinical parameters improved similarly. After a median follow-up of 2.33 ± 1.8 years in the LBBB versus 2.43 ± 1.9 years in the RVS group, there was no difference in long-term prognosis or cardiac events in the total cohort (5-year event rate, 53% vs 55%, P = n. s.).*

Conclusion: *Upgrade patients showed similar baseline parameters and response to CRT as to primary implants. No difference in events or long-term prognosis could be observed. (PACE 2008; 31:1265–1271)*

heart failure, cardiac resynchronization, prognosis, right ventricular stimulation

Introduction

Cardiac resynchronization therapy (CRT) reduces symptoms and mortality in patients with left bundle branch block (LBBB) and severe chronic heart failure.[1,2] In the majority of large randomized studies, primary implantation of a CRT device was used as therapeutic intervention.

The published data are relatively limited thus far whether patients with heart failure, conventional pacemakers, and permanent right ventricular stimulation (RVS) will benefit in a similar way from an upgrade to biventricular pacing. Chronic right ventricular apical pacing leads to paradoxical septal motion and apical perfusion defects.[3] Accordingly, only biventricular pacing, but not right ventricular pacing, improves systolic function, and reduces both mitral regurgitation and left ventricular (LV) volumes in patients with heart failure and electromechanical delay.[4,5] Previous studies have demonstrated acute or short-term improvement of LV function and asynchrony parameters after upgrade of chronically stimulated RV patients to a CRT system.[6,7]

To our knowledge, no publication comparing the long-term prognosis of patients upgraded from RVS compared to patients with primary CRT implants has thus far been published. Therefore, we analyzed data from our cohort of CRT patients in an effort to obtain this information. In addition, we wanted to compare the response for CRT in both groups in terms of clinical and hemodynamic changes.

Methods

The study was approved by the ethics committee of Bad-Segeberg, Germany (reference number 164/04). We analyzed data from a cohort comprised of all patients undergoing CRT system implantation in the years 1999–2006 (n = 328) at the hands of one single implanter (H.N.) in two centers (University Hospital Hamburg-Eppendorf and St. Adolfstift, Reinbek). Patients were selected for implantation according to standard criteria

Address for reprints: Herbert Nägele, M.D., St. Adolfstift, Reinbek, Medical Department, Hamburger Str. 41, D-21465 Reinbek, Germany. Fax: +49-40-7280-2729; e-mail: herbert_naegele@yahoo.de

Received March 29, 2008; revised May 8, 2008; accepted July 5, 2008.

(New York Heart Association [NYHA] III or IV despite optimal medical therapy, QRS interval width either spontaneous or stimulated >130ms, and left ventricular ejection fraction <35%). Two separate groups were defined: (1) primary implants for LBBB (n = 221) and (2) upgrades from RVS (n = 107). All patients were followed either directly in our outpatient clinic or by referring physicians, from whom data of cardiac events were collected at regular intervals. Telephone calls with patients or relatives provided missing information. Cardiac events were defined as death due to a cardiac reason (sudden death, heart failure death), heart transplantation, or hospitalization due to a cardiac reason (congestive heart failure decompensation, arrhythmia). Nonresponder patients were defined as patients remaining in NYHA classes III–IV despite optimized biventricular pacing and a complete heart failure therapy regimen consisting of at least ß-blockers, ACE inhibitors, or AT1 antagonists, and diuretics for at least 3 months. In 3 consecutive years of the study period we performed a more detailed investigation in a subgroup of the total cohort consisting of 105 consecutive new patients from the years 2004–2006 (LBBB = 69; RVS = 36). They were studied in regard to parameters of heart failure at rest and during exercise (NYHA stage, quality of life, brain natriuretic peptide, peak oxygen consumption, left ventricular ejection fraction, pulmonary capillary wedge pressure, cardiac index). Right heart catheterization results were obtained at rest and during exercise at a standard load of 25 W during 5 minutes. Arterial pressures were directly measured by additional cannulation of radial arteries. Furthermore, asynchrony parameters were measured using a VIVID seven dimension machine (GE Healthcare, Chalfont St. Giles, UK). The following parameters of asynchrony were measured: QRS width, the difference of left-right preejection period (DPEP) using pulsed wave doppler, and septum-lateral wall motion delay using tissue doppler (SLWMD) at baseline and after 1 year. Investigation after 1 year was chosen in order to exclude possible medical and placebo effects; furthermore, data collected at the 1-year time point afford more accurate identification of responders versus nonresponders. Pacemaker or defibrillator implantations with coronary sinus leads were performed with standard techniques via left or right cephalic or subclavian veins.

Statistics

Differences in the results of clinical and hemodynamic data were checked for significance by means of Student's *t*-tests for matched and nonmatched pairs. Nonparametric data were checked for significance by the Wilcoxon test. For multiple comparisons between and within groups, analysis of variance was performed (ANOVA). All data are expressed as mean ± SD. According to the sample size of n = 325 and a distribution of 0.48:1.0 (RVS: LBBB), the study was powered enough to detect at least moderate differences between groups as measured by a *t*-test.[8] Survival rate was calculated by Kaplan-Meier analysis and the log-rank test (Winstat 3.1, Kalmia Inc. [Cambridge, MA, USA] and SPSS for Windows 6.1, SPSS, Inc., Chicago, IL, USA).

Results

In 90/107 patients (84%) of the RVS group, total atrioventricular (AV) block was the indication for the first conventional pacemaker implantation. In the remaining 17 patients, sick sinus syndrome with unavoidable RV stimulation was the underlying rhythm disturbance. Of RVS patients 87/107 had preexisting dual-chamber pacemakers and the remaining 20 patients had single-chamber pacemakers. The median time of RV stimulation prior to upgrade procedures was 2.8 ± 2.4 years. Information on the ejection fraction prior to conventional implantation was available in only a few patients. The rate of ventricular stimulation in the upgrade group prior to conversion to CRT was 96% ± 4 according to results of pacemaker interrogation. Among RVS, 38/107 patients had permanent atrial fibrillation (bradyarrhythmia) with a slow ventricular escape rhythm. In three patients, the complete obstruction of veins by inserted pacemaker leads was an operation hindrance. In these patients, contra lateral insertion of the coronary sinus lead with a suprasternal subcutaneous connection was performed. An example is given in Figure 1. This patient had an occlusion of the right subclavian vein in the region of preexisting pacemaker leads. Upgrade to CRT was performed by contra lateral insertion of the coronary sinus lead and a presternal connection by subcutaneous tunneling to the right-sided pacemaker battery. Redundant lead material could therefore be avoided.

Baseline characteristics of the patients were shown in Table I. Except for a somewhat greater presence of atrial fibrillation (P = 0.03) and a broader QRS complex width (P < 0.001) in the RVS group there was no significant difference between patients receiving a primary implant versus upgrade. The rate of patients receiving a CRT defibrillator was comparable between the groups, as was the responder rate, defined as patients improving at least one NYHA class during the first observation year. In Table II, we made a subanalysis after stratification for the presence of chronic atrial fibrillation. QRS width and QRS interval shortening after CRT remained different in primary implants versus upgrade patients. Once again, no significant difference was found with regard to patient characteristics such as underlying disease, the rate of

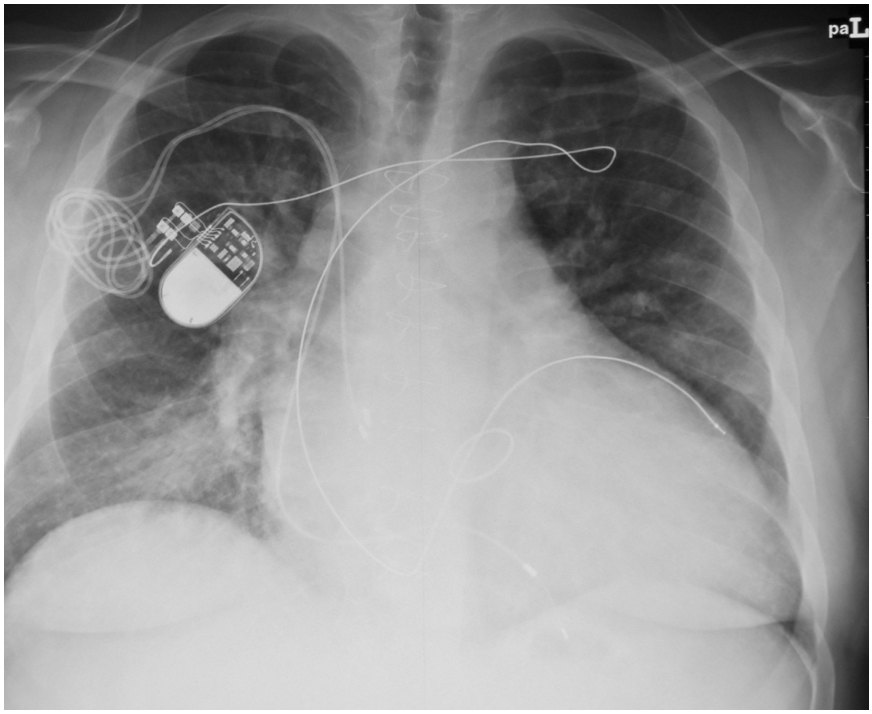


Figure 1. *An X-ray example of a patient with occlusion of the right subclavian vein in the region of preexisting pacemaker leads. Upgrade to CRT was performed by contra lateral insertion of the coronary sinus lead and its presternal connection to the right-sided pacemaker battery. Redundant lead material could therefore be avoided.*

responders, or change in NYHA class over time. After 1 year, there was a similar significant improvement in both groups with regard to asynchrony and heart failure parameters (Table III, LBBB vs RVS). These results were comparable and were not different between both groups (Table III, pre vs 1 year). The only significant difference was a greater reduction of the QRS complex in the upgrade group ($P = 0.01$) and a somewhat better augmentation of the mean arterial blood pressure in the primary implant group ($P = 0.03$). Figure 2 shows an illustrative example of a patient who was stimulated for 10 years with right ventricular pacing only (VVIR-ICD). He has dilated cardiomyopathy, chronic atrial fibrillation, and a third-degree AV block without any ventricular escape rhythm. After upgrade to CRT (biventricular VVIR), his heart size on X-ray decreased, and his clinical status, as well as echo parameters, clearly improved.

In general, CRT led to important reductions in each asynchrony variable in both patients with previous RV pacing and those with intrinsic LBBB. The magnitude of these changes in measures of asynchrony was also not different between the two groups.

Table I.

Baseline Characteristics of CHF Patients Receiving Primary CRT Implants for LBBB (n = 221) Versus Upgrade to CRT from RV Stimulation (n = 107)

	LBBB	RVS	P
Mean age (years)	68.4 ± 11	68.7 ± 15	NS
Median observation time	2.33 ± 1.8	2.43 ± 1.9	NS
NYHA II/III/IV	21/188/24	10/85/18	NS
Male (%)	80	92	NS
Height (cm)	171.0 ± 8	174.8 ± 7	NS
Weight (kg)	78.3 ± 9	79.1 ± 8	NS
Permanent atrial fibrillation (%)	14%	37%	0.03
QRS-interval length (ms)	168.3 ± 24	187.1 ± 28	<0.001
CAD (%)	53	49	NS
LVEF (%)	26.4 ± 9	28.1 ± 6	NS
LVEDD (mm)	63 ± 9	65 ± 13	NS
BNP	635 ± 350	600 ± 380	NS
Responder (%)	87	76	NS
Defibrillator	66%	68%	NS

Table II.

Baseline Characteristics of CHF Patients Receiving Primary CRT Implants (LBBB, n = 221) Versus Upgrade from Existing RV Stimulation (RVS, n = 107), Stratified for the Presence of Sinus Rhythm (SR) or Chronic Atrial Fibrillation (AF)

	LBBB and SR	LBBB and AF	RVS and SR	RVS and AF	P
N	189	32	69	38	
Responder (%)	84	81	78	74	NS
Male (%)	72	88	93	85	NS
CAD (%)	47	45	46	56	NS
Age (years)	67.5 ± 11	68.6 ± 15	68.8 ± 12	69.8 ± 13	NS
Weight (kg)	78.7 ± 9	77.3 ± 9	78.3	79.1 ± 8	NS
Defibrillator (%)	66	65	70	69	NS
Mean obs. time	2.2 ± 1,5	2.3 ± 1.7	2.1 ± 1,9	2.4 ± 1.2	NS
NYHA II/III/IV	11/169/9	3/24/5	5/55/9	3/30/5	NS
Delta-NYHA 1year	−0.9 ± 0.6	−0.3 ± 0.9	−0.4 ± 0.7	−0.7 ± 0.8	NS
QRS-interval (ms)	165 ± 29	165 ± 30	185.3 ± 33	188.3 ± 32	<0.001 LBBB vs RVS
Delta-QRS (ms) 1 year	−24.7 ± 14	−23.3 ± 17	−36.7 ± 16	−34.9 ± 15	<0.001 LBBB vs RVS

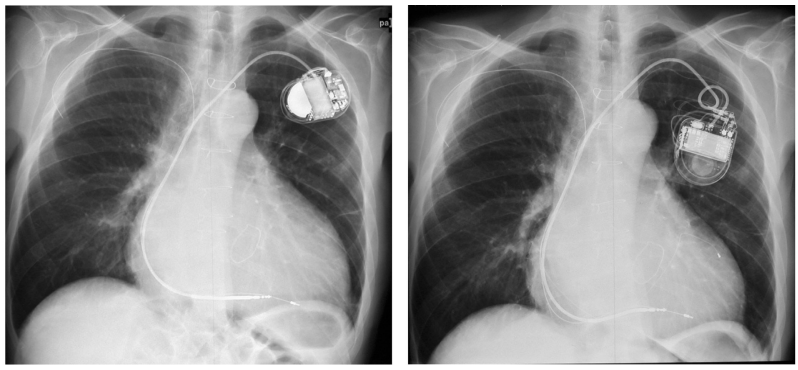
The median follow-up time was 2.33 ± 1.8 versus 2.43 ± 1.9 years in the primary implant versus the upgrade group. As to overall prognosis (Fig. 3) during this follow-up, no significant difference could be observed between RVS patients and patients with spontaneous LBBB and sinus rhythm. Because of the higher number of atrial fibrillation in the RVS group, a second analysis was done, stratifying the groups according to the presence of chronic atrial fibrillation (Fig. 4). Interestingly, there was absolutely no difference in terms of prognosis between RVS patients after upgrade to CRT, whether atrial fibrillation was present or not. In contrast, CRT patients with spontaneous LBBB and chronic atrial fibrillation had a somewhat worse prognosis midterm compared to their counterparts with sinus rhythm. After 3 years, freedom from death or heart transplantation (HTx) was 83% in the LBBB group with sinus rhythm versus 62% in LBBB patients with atrial fibrillation. Both curves merged after 5 years. Cardiac events were not different between RVS and spontaneous

Table III.

Results of the Subgroup with Detailed Analysis (Baseline vs 1 Year) CRT Implantation for Spontaneous LBBB: n = 69; CRT Implantation for RVS; n = 36)

	LBBB	RVS	P Pre vs 1 year	P LBBB vs RVS
NYHA	−0.84 ± 0.8	−0.55 ± 0.8	<0.005	NS
LWHFQ	−9.8 ± 27	−6.9 ± 33	=0.009	NS
BNP (pg/mL)	−366 ± 600	−341 ± 580	<0.005	NS
Peak VO2/ml/min×kgKG)	+1.6 ± 1.3	+2.4 ± 0.7	=0.04	NS
LVEF (%)	+13.7 ± 14	+8.7 ± 10	<0.003	NS
QRS (ms)	−23.7 ± 14	−35.3 ± 15	=0.004	0.01
DPEP (ms)	−12 ± 13	−10 ± 28	=0.001	NS
SLWMD (ms)	−41 ± 27	−26 ± 26	0.04	NS
PCWP (mmHg)	−6 ± 8	−9 ± 7	<0.003	NS
PCWP 25 W (mmHg)	−6 ± 10	−8 ± 10	<0.003	NS
CI (l/min × kgKG)	+0.4 ± 0.6	+0.7 ± 0.6	<0.003	NS
CI 25 W (l/min × kgKG)	+0.3 ± 0.6	+0.6 ± 0.6	<0.01	NS
MAP (mmHg)	+3 ± 11	+4 ± 12	<0.01	NS
MAP 25 W (mmHg)	+12 ± 11	+5 ± 12	<0.001	0.03

Abbreviations: NYHA = New York heart association; LWHFQ = living with heart failure score; BNP = brain natriuretic peptide; VO2 = oxygen uptake; LVEF = left ventricular ejection fraction; QRS = QRS width (ms); DPEP = delta-preejection period; SLWMD = septum-lateral wall delay; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; MAP = mean arterial pressure.



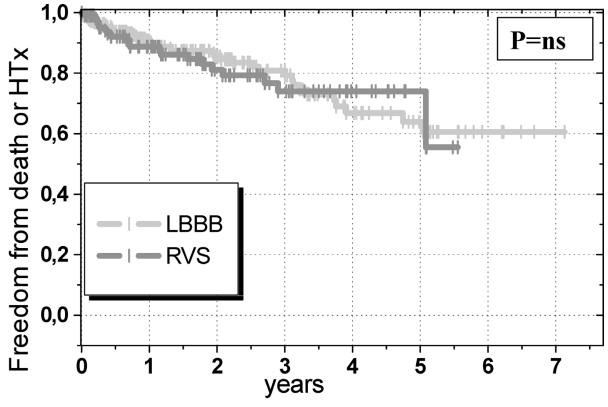
	Pre upgrade to CRT	12 month post upgrade to CRT
NYHA	3	2
LVEF (%)	16	37
LVEDV (ml)	294	193
LVEDD (cm)	8.0	7.4

Figure 2. *An X-ray example of a patient with chronic atrial fibrillation without ventricular escape rhythm. Left figure: preupgrade, right figure: 12 months after upgrade of the existing RV pacing system (VVI-ICD) to a biventricular defibrillator. After upgrade to CRT his heart size on X-ray decreased, his clinical status and his echo parameters improved clearly (see below).*

LBBB patients (Fig. 5). The occurrence of cardiac events in the total cohort after 5 years was 53% for LBBB versus 56% for RVS patients (P = n. s.).

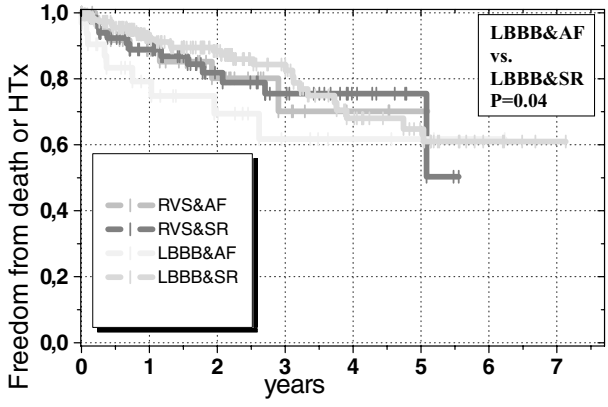
Discussion

We found overall similar improvements induced by CRT for patients having a primary



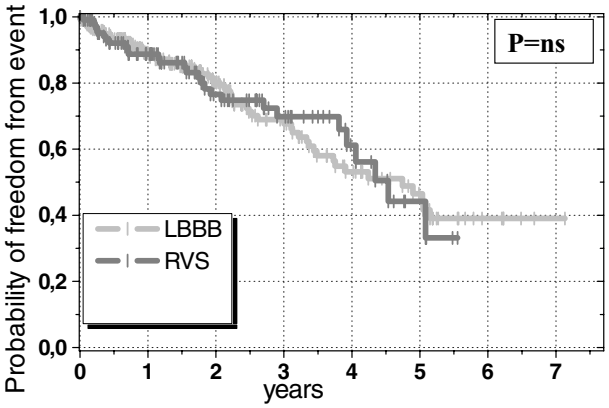
LBBB	221	136	94	57	32	19	7	4
RVS	107	76	45	28	13	5		

Figure 3. *Freedom from death or HTx in CRT patients with upgrade from RVS (n = 107) versus primary implantation in LBBB (n = 221).*



RVS & AF	38	29	17	8	4	1		
RVS & SR	69	48	29	21	10	4		
LBBB &AF	32	19	14	8	4	2		
LBBB & SR	189	118	81	49	29	18	6	2

Figure 4. *Freedom from death or HTx in CRT patients with primary implantation and LBBB versus upgrade from RVS stratified to the presence of atrial fibrillation. RVS and AF = Upgrade and chronic atrial fibrillation, n = 38; RVS and SR = Upgrade and sinus rhythm, n = 69; LBBB and AF = Primary implant and atrial fibrillation, n = 32; LBBB and SR = Primary implant and sinus rhythm, n = 189.*



LBBB	221	136	94	57	32	19	7	4
RVS	107	76	45	28	13	5		

Figure 5. *Freedom from cardiac events (death, heart transplantation, or the need of hospitalization due to cardiac causes) in CRT patients with upgrade from RV stimulation (n = 113) versus primary implantation (n = 233).*

implantation as compared to patients receiving an upgrade procedure after chronic RVS (Tables II and III). These results are in agreement with several other studies[6,7,9,10] and extend their findings to the central hemodynamic response and prognostic data (Figs. 3–5). Both earlier reports and our findings imply that biventricular pacing synchronizes mechanical activation in different myocardial regions in patients upgraded from RV pacing as well. In terms of exercise hemodynamics, research has shown that different modes of ventricular stimulation alter the *in vivo* force-frequency relation of CHF patients. In contrast to single-site RV pacing, contractile function improves with increasing heart rates during biventricular stimulation. This effect may contribute to the enhanced exercise capacity during CRT and could provide a functional benefit over single-site pacing in patients.[11] This supports our findings of improved hemodynamics, especially augmentation of the mean arterial pressure at exercise (Table III). Our results showed no significant difference in heart failure parameter change after CRT, with the exception of a more pronounced shortening of the QRS interval in the RVS group. In this regard, the initial QRS width (either spontaneous or evoked) as a surrogate parameter of asynchrony[12] was significantly broader in the RVS group. This could suggest some difference in asynchrony induced by RVS in contrast to "spontaneous asynchrony."

Upon closer examination, there are indications that spontaneous LBBB patients may respond better than does the RVS group (Table III). The reason of this trend remains unclear. Perhaps patients with preexisting pacemakers are somewhat more ill at the offset; notably significantly more atrial fibrillation existed in the RVS group (Table I), suggesting that atrioventricular coupling plays a role in successful CRT. The possible interference of atrial fibrillation was investigated in more detail and these data are shown in Table II. QRS width and QRS interval shortening after CRT remained different in primary implants versus upgrade patients, irrespective of the presence of atrial fibrillation. No significant difference was found with regard to patient's characteristics such as underlying disease, the rate of responders, or change in NYHA class over time in relation to atrial fibrillation. In contrast to primary CRT implantations, there was also no difference in prognosis between upgraded patients with or without atrial fibrillation (Fig. 4). One can speculate that our upgraded patients had nearly no spontaneous rhythm and therefore received a 100% CRT delivery. In primary implants with LBBB and chronic atrial fibrillation, residual intrinsic rhythm may disturb successful resynchronization even when a ventricular sensing reaction was activated (as was routine practice in our patients). Clearly these patients represent a subgroup in which the benefit of CRT was limited. A full suppression or even AV node ablation should be discussed in this group.

Other mechanisms may also play a role in the effects of RV system upgrade, such as a reduction of ventricular[13] and supraventricular[14] arrhythmia frequency. However, we have no data to prove this assumption.

The most important finding in our study is a lack of difference in hard end points of overall prognosis or the cardiac event rate between patients with primary CRT implants compared to upgrade patients (group primary implantation vs upgrade, Figs. 3–5). From these findings, a similar efficacy of CRT in both entities can be extrapolated. These results on survival and cardiac event rates are important in our means, because randomized studies in regard to upgrade procedures are still not available.

As procedural aspects, implantation success, and clinical response to CRT were comparable for patients undergoing *de-novo* versus upgrade procedures,[7,14,15] patient selection for upgrading can be the same as for new CRT implantation. Particularly, patients with rapid HF progression under RV stimulation should be considered as upgrade candidates.[16,17] Prospective studies for the optimal timing of CRT upgrade may be useful, to be performed at times of battery replacement when signs of heart failure are present. Even

primary CRT implantation in patients with an indication for conventional RVS should be considered. In summary, CRT can be offered to patients with RVS similar to the practice current for LBBB patients.

Limitations

The study is limited by its retrospective nature and by the fact that only a subgroup of patients was studied hemodynamically and echocardiographically in more detail.

References

1. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, et al., for the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronisation therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004; 350:2140–2150.
2. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L, et al., for the Cardiac Resynchronisation — Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronisation on morbidity and mortality in heart failure. N Engl J Med 2005; 352:1539–1549.
3. Lee MA, Dae MW, Langberg JJ, Griffin JC, Chin MC, Finkbeiner WE, O'Connell JW, et al. Effects of long-term right ventricular apical pacing on left ventricular perfusion, innervation, function and histology. J Am Coll Cardiol 1994; 24:225–232.
4. Yu CM, Lin H, Fung WH, Zhang Q, Kong SL, Sanderson JE. Comparison of acute changes in left ventricular volume, systolic and diastolic functions, and intraventricular synchronicity after biventricular and right ventricular pacing for heart failure. Am Heart J 2003; 145:E18.
5. Hay I, Melenovsky V, Fetics BJ, Judge DP, Kramer A, Spinelli J, Reister C, et al. Short-term effects of right-left heart sequential cardiac resynchronization in patients with heart failure, chronic atrial fibrillation, and atrioventricular nodal block. Circulation 2004; 110:3404–3410.
6. Horwich T, Foster E, De Marco T, Tseng Z, Saxon L. Effects of resynchronization therapy on cardiac function in pacemaker patients "upgraded" to biventricular devices. J Cardiovasc Electrophysiol 2004; 15:1284–1289.
7. Eldadah ZA, Rosen B, Hay I, Edvardsen T, Jayam V, Dickfeld T, Meininger GR, et al. The benefit of upgrading chronically right ventricle-paced heart failure patients to resynchronization therapy demonstrated by strain rate imaging. Heart Rhythm 2006; 3:435–442.
8. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Res Methods 2007; 39:175–191.
9. Witte KK, Pipes RR, Nanthakumar K, Parker JD. Biventricular pacemaker upgrade in previously paced heart failure patients–improvements in ventricular dyssynchrony. J Card Fail 2006; 12:199–204.
10. Duray GZ, Israel CW, Pajitnev D, Hohnloser SH. Upgrading to biventricular pacing/defibrillation systems in right ventricular paced congestive heart failure patients: Prospective assessment of procedural parameters and response rate. Europace 2008; 10:48–52. Epub 2007 Dec 12.
11. Vollmann D, Lüthje L, Schott P, Hasenfuss G, Unterberg-Buchwald C. Biventricular pacing improves the blunted force-frequency relation present during univentricular pacing in patients with heart failure and conduction delay. Circulation 2006; 113:953–959.
12. Bleeker GB, Schalij MJ, Molhoek SG, Verwey HF, Holman ER, Boersma E, Steendijk P, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. Cardiovasc Electrophysiol 2004; 15:544–549.
13. Ermis C, Seutter R, Zhu AX, Benditt LC, VanHeel L, Sakaguchi S, Lurie KG, et al. Impact of upgrade to cardiac resynchronization therapy on ventricular arrhythmia frequency in patients with implantable cardioverter-defibrillators. J Am Coll Cardiol 2005; 46:2258–2263.
14. Yannopoulos D, Lurie KG, Sakaguchi S, Milstein S, Ermis C, VanHeel L, Benditt DG. Reduced atrial tachyarrhythmia susceptibility after upgrade of conventional implanted pulse generator to cardiac resynchronization therapy in patients with heart failure. J Am Coll Cardiol 2007; 50:1246–1251.
15. Baker CM, Christopher TJ, Smith PF, Langberg JJ, De Lurgio, Leon AR. Addition of a left ventricular lead to conventional pacing systems in patients with congestive heart failure. Pacing Clin Electrophysiol 2002; 25:1166–1171.
16. Leon AR, Greenberg JM, Kanuru N, Baker CM, Mera FV, Smith AL, Langberg JJ, et al. Cardiac resynchronization in patients with congestive heart failure and chronic atrial fibrillation; Effect of upgrading to biventricular pacing after chronic right ventricular pacing. J Am Coll Cardiol 2002; 39:1258–1263.
17. Shimano M, Tsuji Y, Yoshida Y, Inden Y, Tsuboi N, Itoh T, Suzuki H, et al. Acute and chronic effects of cardiac resynchronization in patients developing heart failure with long-term pacemaker therapy for acquired complete atrioventricular block. Europace 2007; 9:869–874.