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Comprehensive cardiac resynchronization therapy optimization in the real world

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Abstract

Background: *Cardiac resynchronization therapy (CRT) reduces morbidity and mortality in patients suffering from chronic heart failure (CHF). Optimal device programming is crucial for maximum patient benefit. The goal of the present study was to assess device settings from CHF patients undergoing CRT optimization in a "real world" setting, and to delineate parameters most frequently requiring adjustment.*

Methods: *All patients who underwent CRT device implantation in the Cardiology Clinic at the University Hospital Zurich between January 2011 and September 2012 and in whom follow-up was available were included in this analysis.*

Results: *A total of 170 CHF patients were included in this analysis. True biventricular pacing was present in 44% of all patients, while QRS fusion was detected in 49.9%. The majority of the patients presented with suboptimal atrioventricular (AV) delays requiring adjustment. AV delays were therefore shortened due to the presence of QRS fusion in 53.3% and 38.1% of patients (sAV and pAV, respectively) or prolonged because of truncation of the A wave in the left ventricular inflow pulse wave Doppler measurement (17.5% and 28.4% for sAV and pAV, respectively). In contrast, interventricular delay (VV delay) was rarely changed (11.9%).*

Conclusions: *In our "real world" cohort, a substantial proportion of patients presented to their first post-operative consultation with suboptimal device settings. Our data indicate that the opportunity to optimize device settings is frequently wasted in the "real world", underlining the necessity for expert device follow-up to deliver optimal care to this challenging group of heart failure patients.* (Cardiol J 2014; 21, 3: 316–324)

Key words: heart failure, cardiac resynchronization therapy, integrative device follow-up

Introduction

Cardiac resynchronization therapy (CRT) has become a cornerstone in the treatment of chronic heart failure (CHF) [1, 2]. Indeed, several clinical trials observed a reduction in morbidity and mortality as compared to medical therapy alone in patients suffering from symptomatic left ventricular (LV) dysfunction (LV ejection fraction [LVEF] ≤ 35%) with a prolonged QRS duration (≥ 120 ms).

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Nevertheless, almost 30% of patients do not exhibit an improvement in clinical symptoms or hemodynamic parameters after CRT implantation (so-called "non-responders") [3]. This lack of improvement may be due to pre-implantation characteristics such as large areas of scar tissue due to coronary artery disease or a lack of mechanical dyssynchrony [4]. Suboptimal LV lead position further represents a reason for a lack of benefit [4]. Additionally, however, some patients do not respond to CRT due to suboptimal CRT device settings, impairing LV filling (atrioventricular [AV] dyssynchrony) and/or persistent LV dyssynchrony [5].

At the University Hospital of Zurich, we implemented a standard protocol by which every patient with a CRT device undergoes a complete device optimization 3–6 months after implantation and again on a yearly basis or if clinically deemed necessary. The goal of the present study was to summarize clinical presentation, echocardiographic findings, and device settings from CHF patients undergoing CRT optimization in this "real world" setting, unraveling the amount of patients presenting with suboptimal settings, as well as the parameters most frequently requiring adjustment. We provide a rationale for the necessity of implementing a routine protocol for the integrated management of these complex CHF patients, including expert device management.

Methods

Study population and CRT implantation

All patients with a CRT device receiving their first device follow-up in our specialized device clinic from January 1st 2011 until September 2012 were prospectively included. The study was approved by the cantonal ethics committee Zurich. Mean time from implantation to optimization was 2.9 months (Table 1). Indications for CRT implantation were based on current guidelines [1]. CRT devices were implanted by a standard procedure under local anesthesia. Devices and leads from Biotronik, Boston Scientific/Guidant, Medtronic and St. Jude Medical were used. For implantation of the LV lead, percutaneous placement into a lateral or postero-lateral vein was attempted whenever possible. If no suitable vein branch was available, epicardial lead implantation was performed.

Table 1. Demographics at implantation.

Men [years]	130/170 (76.5%)
New implantation	129/170 (75.9%)
CRT upgrade	41/170 (24.1%)
Time implantation — optimization [months]	2.9 ± 5
Age at implantation [years]	62.8 ± 12.5
Ischemic cardiomyopathy	75/169 (44.4%)
CRT-D	156/170 (91.8%)
Sinus rhythm at implantation	107/167 (64.1%)

CRT — cardiac resynchronization therapy

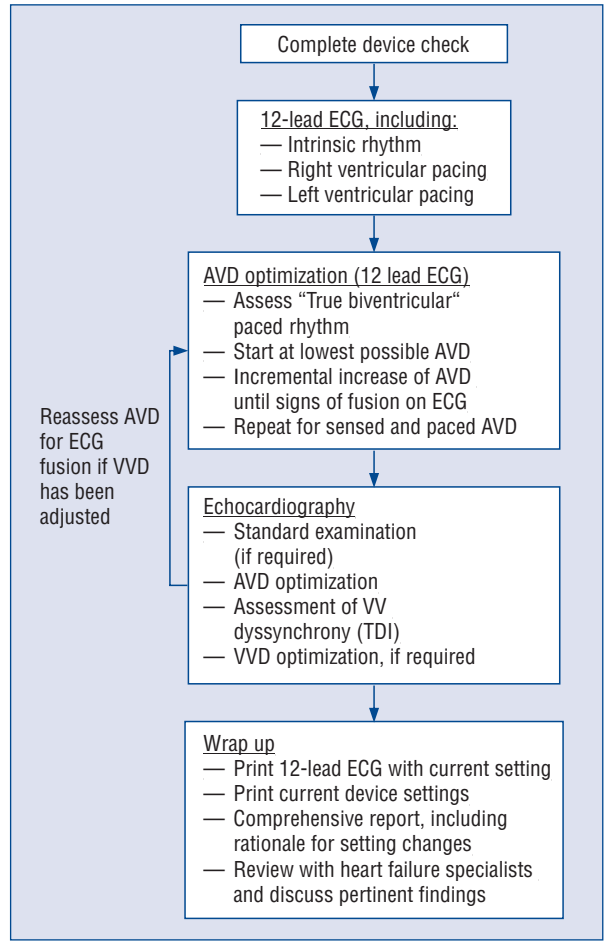

Figure 1. Cardiac resynchronization therapy patient follow-up algorithm as implemented at the University of Zurich. See text for details, AVD — atrioventricular delay; VVD — interventricular delay.

Follow-up protocol

We implemented a standard protocol by which every patient with a CRT device underwent a comprehensive and standardized device follow-up and optimization procedure (Fig. 1). After a complete clinical assessment by a heart failure specialist, a comprehensive device follow-up was performed

by implantable electronic cardiac device specialists (JS/DH), including complete check of the system with 12-lead electrocardiogram (ECG), and review of all brady- and tachycardia parameters. Subsequently, a complete echocardiographic exam was performed (Vivid E9, GE), followed by optimization of the AV- and interventricular (VV) delay if necessary. AV delay optimization was performed starting at a long AV-delay without intrinsic conduction. The AV-delay was then progressively shortened in steps of 20 ms until truncation of the A-wave was observed. Then, the AV-delay was prolonged in 10 ms steps until the optimal separation of E/A wave without truncation of the A-wave was reached, which was considered the optimal AV-delay.

Results

Study population

A total of 170 CHF patients were included in this prospective analysis. Baseline demographic data at implantation, as well as clinical characteristics at time of follow-up are summarized in Table 1. The majority of patients were men (76.5%), and had a cardiovascular risk profile typical of a real-world CHF cohort as previously shown [6]. All patients were on optimal medical therapy including angiotensin converting enzyme-inhibitors or angiotensin-II-blockers (95.2%), beta-blockers (93.5%) and diuretics (86.3%) prior to implantation. Furthermore, more than 50% of patients were treated with an aldosterone antagonist (55.4%) in addition to standard diuretic therapy, and received anti-arrhythmic treatment with either digitalis (13.1%) or amiodarone (17.9%) (Table 2).

Table 2. Clinical parameters at time of optimization.

Clinical parameters	
Height [m]	1.7 ± 0.1
Weight [kg]	82 ± 18.5
Body mass index [kg/m^2]	28.4 ± 5.9
Systolic BP [mm Hg]	116.1 ± 17.3
Diastolic BP [mm Hg]	73 ± 11.7
NYHA class:	
NYHA I	24/134 (17.9%)
NYHA II	54/134 (40.3%)
NYHA III	20/134 (14.9%)
NYHA IV	1/134 (0.7%)
Medication	
Beta-blocker	157/168 (93.5%)
ACE-I/ARB	160/168 (95.2%)
Aldosterone antagonist	93/168 (55.4%)
Other diuretics	145/168 (86.3%)
Digitalis	22/168 (13.1%)
Amiodarone	30/168 (17.9%)
CCB	11/168 (6.5%)
Nitrates	11/168 (6.5%)
Lipid lowering treatment	103/168 (61.3%)
Aspirin	84/168 (50%)
Clopidogrel	12/168 (7.1%)
Oral anticoagulation	84/168 (50%)

ACE-I/ARB — angiotensin-converting-enzyme inhibitors/angiotensin II receptor blockers; BP — blood pressure; CCB — calcium channel blocker; NYHA — New York Heart Association classification

Echocardiographic and electrocardiographic parameters at follow-up

Most patients demonstrated a reduced LVEF (mean 37.3 ± 11.1%) and a dilated LV (end-diastolic volume index 88.4 ± 41.6 mL/m^2; Table 3). Of note, parameters of dyssynchrony at this time mainly demonstrated values within our lab's predefined normal values (interventricular mechanical delay — IVMD < 40 ms, tissue Doppler imaging — $TDI_{septal\text{-}lateral}$ < 60 ms, $TDI_{anteroseptal\text{-}posterolateral}$ < 60 ms), with an IVMD of 17.5 ± 27.7, as well as 32.7 ± 46.8 ms and 33.5 ± 46.3 ms for septal-lateral and anteroseptal-posterolateral delay assessed by TDI, respectively. The mean intrinsic QRS duration was 150 ± 26.6 ms with an ECG pattern of left bundle branch block in the majority of cases (59.5%), and an average PQ interval of 184.7 ± ± 27.6 ms (Table 4). At the time of implantation and at the first follow-up, most patients were in sinus rhythm (65.9%). While 65.3% of the patients had the same rhythm at our follow-up visit, a minority of patients switched from atrial fibrillation to sinus rhythm (2.4%) and vice versa (4.8%).

Device settings and intervals at the time of optimization

True biventricular pacing was present in nearly half of the patients at the time of optimization (44.7%), while QRS fusion could be detected in 39.4% of cases (Table 5, Fig. 2). At the time of optimization, average sensed AV (sAV) delay was 110.5 ± 19 ms and paced AV (pAV) 136.5 ± 23.4 ms. QRS fusion, as diagnosed by 12-lead surface ECG, began to appear at an average sAV of 103.9 ± ± 37.1 ms and an average pAV of 136.5 ± 23.4 ms, respectively.

A biventricular pacing rate of more than 95% was present in 85.8% of patients from the studied cohort. The main reason for a low biventricular pacing percentage was either atrial fibrillation or

Table 3. Echocardiography at optimization.

LVEF [%]	37.3 ± 11.1
LVEDD [mm]	6.2 ± 1.1
LVESD [mm]	4.9 ± 1.3
EDV [mL]	169.5 ± 79.2
EDV index [mL/m^2]	88.4 ± 41.6
ESV [mL]	110.8 ± 71.5
ESV index [mL/m^2]	58.8 ± 38.3
Diastolic dysfunction:	
No diastolic dysfunction	92/168 (54.8%)
Grade I	7/168 (4.2%)
Grade II	1/168 (0.6%)
Grade III	0/168 (0%)
Mitral regurgitation:	
Minimal	88/167 (52.7%)
Mild	59/167 (35.3%)
Moderate	13/167 (7.8%)
Severe	4/167 (2.4%)
LAESD [mm]	4.7 ± 0.9
RV: Area D [cm^2]	16.2 ± 5.1
Fractional shortening RV [%]	39.7 ± 12.1
TAM [mm]	18.3 ± 4.9
RV/RA-pressure gradient [mm Hg]	27.9 ± 11.6
RA size	5 ± 0.9
Dyssynchrony assessment:	
RV-PEP [ms]	118.1 ± 31.3
LV-PEP [ms]	135.5 ± 31.5
IVMD	17.5 ± 27.7
TDI SL	32.7 ± 46.8
TDI AS-IL	33.5 ± 46.3
Diastolic filling time/RR-interval	49.5 ± 32.1

AS-AL — anteroseptal-posterolateral; EDV — end-diastolic volume; ESV — end-systolic volume; IVMD — interventricular mechanical delay; LAESD — left atrium end-diastolic diameter; LV — left ventricle; LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-diastolic diameter; PEP — preejection period; RV — right ventricle; RA — right atrium; SL — septal lateral; TDI — tissue Doppler imaging; TAM — tricuspid annular movement

Table 4. Electrocardiogram parameters.

Rhythm at optimization	
SR	112/170 (65.9%)
SR, AVB III°, without ventricular escape	15/170 (8.8%)
SR, AVB III°, with ventricular escape	6/170 (3.5%)
AF with AV conduction	20/170 (11.8%)
AF, AVB III°	7/170 (4.1%)
AF post AV node ablation	6/170 (3.5%)
PQ intrinsic	184.7 ± 27.6
QRS intrinsic	150 ± 26.6
Bundle branch block:	
No block	14/163 (8.6%)
LBBB	97/163 (59.5%)
RBBB	13/163 (8%)
AVB III°	36/163 (22.1%)
Development of rhythm	
Unchanged	109 (65.3%)
AF → SR	4 (2.4%)
AF → PM	2 (1.2%)
SR → AF	8 (4.8%)
SR → PM	4 (2.4%)
PM upgrade	41 (24%)

AF — atrial fibrillation; AV — atrioventricular; AVB — atrioventricular block; LBBB — left bundle branch block; RBBB — right bundle branch block; PM — pacemaker; SR — sinus rhythm

frequent ventricular extrasystoles. At the time of follow-up, mean programmed VV delay was 8.5 ± 14.4 ms (LV first).

Left ventricular lead settings

In a third of all cases, lead pacing configuration was "true" bipolar from the LV lead tip (LvTip) to the LV ring (LvRing; 34.1%) or between LvTip to the right ventricular lead ring (RvRing; 28.2%, Table 6). In every fifth patient, the pacing vector was between the LvTip and the coil of the right ventricular lead (RvCoil; 23.5%). With these configurations, only a minority of patients (n = 7, 4.2%) were suffering from diaphragmatic capture (4.2%), which was solved in all cases by reprogramming.

Optimization of CRT settings after implantation

In the majority of all patients who underwent CRT device implantation, the programmed AV intervals were deemed suboptimal during follow-up and were subsequently reprogrammed (Table 7). AV delays were shortened (sAV delay in 53.3%, pAV delay in 38.1% of the patients) mainly due to the presence of QRS fusion on the 12-lead ECG. In contrast, the AV delay was prolonged in only 17.5% and 28.4% (sAV and pAV, respectively), mostly due to truncation of the A wave in the LV inflow pulse wave Doppler measurement. In 77 patients (45% of the entire cohort), some degree of QRS fusion was accepted in order to allow for better LV filling.

In contrast to the adjustments of the AV interval, the VV delay was left unchanged in the majority of patients (88.1%). The main reason for a change in VV delay was intraventricular dyssynchrony observed on TDI (82.4%).

Thirty three (19.4%) patients in our cohort suffered from atrial fibrillation. By virtue of this, AV optimization was impossible in these patients and VV optimization greatly impaired. Of our patients with atrial fibrillation, 20 (61%) had intrinsic con-

Table 5. AV/VV settings at optimization.

Pacing at optimization:	
True biventricular stimulation	76/170 (44.7%)
Fusion	67/170 (39.4%)
Pseudofusion	3/170 (1.8%)
Atrial fibrillation	23/170 (13.5%)
AV delays:	
sAV (at interrogation)	110.5 ± 19
pAV (at interrogation)	136.5 ± 23.4
Begin QRS fusion (sAV)	103.9 ± 37.1
Begin QRS fusion (pAV)	174.3 ± 42.7
Intraatrial delay (pAV-sAV)	71.9 ± 28.2
No fusion (AV block)	33 (19.4%)
Dynamic AV delay on	78/164 (47.6%)
Situation at sensed AV delay 120 ms:	
Pure biventricular stimulation	58/140 (41.4%)
Fusion	72/140 (51.4%)
Intrinsic rhythm/Pseudofusion	8/140 (5.7%)
Status before optimization:	
A-wave truncation	38/147 (25.9%)
QRS fusion	39/147 (26.5%)
Both A-wave truncation and QRS fusion	31/147 (21.1%)
VV (at interrogation) [ms]	8.5 ± 14.4
Biventricular pacing (average) [%]:	94.3 ± 13.3
≥ 97%	112 (67.9%)
< 97%	53 (32.1%)
< 95%	40 (24.2%)
< 90%	23 (13.9%)
≤ 85%	16 (9.7%)
Reason for low biventricular pacing (< 95%):	
Atrial fibrillation	18/39 (46.2%)
VES	13/39 (33.3%)
Intrinsic conduction	3/39 (7.7%)
Other	4/39 (10.3%)
Device manufacturer:	
Medtronic	31/170 (18.2%)
St. Jude Medical	49/170 (28.8%)
Biotronik	79/170 (46.5%)
Boston Scientific	10/170 (5.9%)

AV — atrioventricular; sAV — sensed AV; pAV — paced AV; VV — interventricular; VES — ventricular extrasystoles

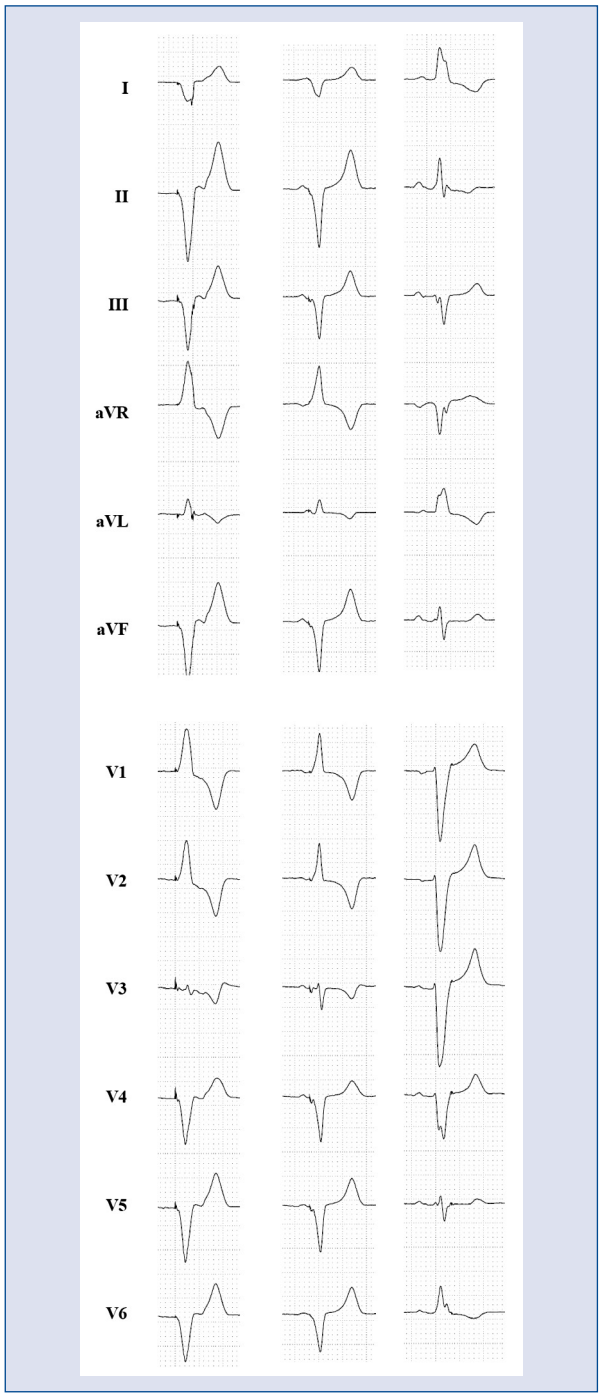

Figure 2. Twelve-lead electrocardiograms (ECGs) of a patient presenting for cardiac resynchronization therapy optimization. "True" biventricular pacing (VVI 90 bpm, left panel), intrinsic rhythm (right panel) and rhythm at follow-up (middle panel) are shown. Note the significant degree of QRS fusion as demonstrated by 12-lead ECG with the current device settings. QRS fusion is best appreciated in I, aVL and V3, indicating the necessity for comprehensive 12-lead ECG analysis in the follow-up of these patients.

duction, whereas 7 (21.2%) and 6 (18.2%) patients had no intrinsic AV conduction or had undergone AV node ablation, respectively (Table 4).

Discussion

The aim of the present study was to give an overview on CRT settings at the time of device implantation and to demonstrate the potential for optimization by comprehensive assessment during

Table 6. Left ventricular lead parameters.

Left ventricular pacing configuration:	
LvTip-LvRing	58/170 (34.1%)
LvRing-LvTip (inverse bipolar)	5/170 (2.9%)
LvTip-RvRing	48/170 (28.2%)
LvRing-RvRing	9/170 (5.3%)
LvTip-RvCoil	40/170 (23.5%)
LvRing-RvCoil	7/170 (4.1%)
Unipolar	1/170 (0.6%)
Diaphragmatic capture:	
No diaphragmatic capture	161/168 (95.8%)
Diaphragmatic capture, resolved with reprogramming	7/168 (4.2%)
Diaphragmatic capture, not amenable to programming changes	0/168 (0%)
Threshold left ventricle [V]	1.3 ± 0.8
Threshold left ventricle [ms]	0.5 ± 0.2
Left ventricular sensing [mV]	12.6 ± 8.6
Left ventricular impedance [Ohm]	644.4 ± 228.3

Lv — left ventricle Rv — right ventricle

Table 7. Changes during optimization.

Change in sensed AV delay	
Unchanged	39/137 (28.5%)
Shortened	73/137 (53.3%)
Lengthened	24/137 (17.5%)
Changes in paced AV delay	
Unchanged	45/134 (33.6%)
Shortened	51/134 (38.1%)
Lengthened	38/134 (28.4%)
Reason for AV delay change	
ECG fusion	56/97 (57.7%)
LV inflow truncation	23/97 (23.7%)
LV inflow fusion	14/97 (14.4%)
Visual LV filling	3/97 (3.1%)
Other	1/97 (1%)
Status after optimization	
A-wave truncation	22/147 (15%)
QRS fusion	47/147 (32%)
Both A-wave truncation and QRS fusion	34/147 (23.1%)
Change in VV delay	
Unchanged	118/168 (70.2%)
LV earlier	13/168 (7.7%)
RV earlier	5/168 (3%)
Dyssynchronous, not improvable	30/168 (17.9%)
Reason for VV delay changes	
Visual	3/17 (17.6%)
Tissue Doppler imaging	14/17 (82.4%)

AV — atrioventricular; ECG — electrocardiogram; LV — left ventricle; RV — right ventricle; VV — interventricular

follow-up in an integrative device clinic. In view of the substantial discrepancy between programmed parameters and optimal values, our data indicate that this opportunity is frequently missed in the "real world", providing a rationale for the necessity of protocol-oriented expert follow-up and optimization procedures for these patients.

AV delay optimization and QRS fusion

Whether and how AV intervals should regularly be evaluated and adjusted remains a matter of debate [7–9]. In various preliminary studies, optimization of the AV delay has been demonstrated to significantly increase hemodynamic response, New York Heart Association (NYHA) class, LVEF and B-type natriuretic peptide level in the short-time follow-up [10–14]. In contrast, the recently published SmartDelay determined AV Optimization: A comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (SMART-AV) trial implied otherwise. In this study, CRT device recipients were randomized to a fixed empirical AV delay of 120 ms, an echocardiographically optimized AV delay or a device-based AV optimization algorithm (SmartDelay) [15]. The primary endpoint, LV end-systolic volume at 6 months after implantation did not differ between the 3 groups. As discussed by the authors, it may be possible that the observed acute beneficial hemodynamic effects after CRT implantation are not sufficient enough to result in an improvement of hard clinical endpoints. On the other hand, the follow-up period of only 6 months may have been too short to evaluate such endpoints.

Furthermore, it has to be kept in mind that the optimal AV delay may have a high variability among CRT patients [5, 16]. As such, data from SMART-AV do not imply that individual patients with suboptimal AV delay may not profit from an optimization procedure. Indeed, this has been substantiated most recently in a subanalysis from MADIT-CRT, in which patients with short AV-delays (notably < 120 ms) had a superior outcome compared to those with longer AV delays [17]. Our data demonstrate that programming an empirical setting of 120 ms for the sensed AV delay was suboptimal in terms of true biventricular stimulation in the vast majority of patients (57.1%), and 8 (5.7%) patients even demonstrated entirely intrinsic conduction or pseudofusion (and hence loss of biventricular pacing) at this setting. Furthermore, a subanalysis of the Clinical Evaluation on Advanced Resynchronization (CLEAR) pilot study revealed that systematic CRT optimization was

associated with a higher percentage of improved patients based on the composite endpoint (all-cause mortality, heart failure-related hospitalization, NYHA functional class, and quality of life score), fewer deaths and fewer hospitalizations [18]. These data clearly indicate a role for CRT optimization over standard programming in all patients.

Moreover, the mean interatrial delay was markedly longer (71.9 ± 28.2 ms; Table 5) than the standard programmed difference between sensed and paced AV delay (usually 30–40 ms) found in the default settings, further supporting an individualized approach to AV delay programming.

The majority of our patients (> 70%) underwent reprogramming of the AV delay. One of the most important parameters to guide AV delay optimization is the level of true biventricular pacing or, vice versa, the degree of QRS fusion as a result of intrinsically conducted ventricular excitation [19–21]. In our cohort, 45.3% of patients presented with an AV delay too long to avoid any QRS fusion. However, whether some degree of ventricular fusion may be clinically beneficial remains a matter of debate, as a certain amount of QRS fusion has been shown to improve hemodynamics [22–24]. Fusion allows for intrinsic excitation of the right ventricle via the normal-conducting right bundle branch which may result in improved right ventricle contraction [25]. A recent study further demonstrated that the maximal rate of LV pressure increase (dP/dt) was higher in LV pacing combined with intrinsic conduction as compared to biventricular pacing [22]. Based on these data, we accepted some degree of QRS fusion in order to allow for optimal LV filling in those cases where it was impossible to shorten the AV delay to the point of complete loss of QRS fusion (Fig. 2). Importantly, intrinsic conduction and pseudofusion could entirely and sustainably be avoided in all patients presenting with these findings.

VV delay optimization

For various reasons, VV delay optimization appears to be less important as compared to AV delay optimization. Even though an improvement in hemodynamic conditions has been observed after optimization of VV intervals [26–28], other randomized trials failed to find a beneficial effect [29, 30]. The latter may, at least in part, be due to the fact that VV delay optimization was performed in the majority of patients on top of AV delay optimization. In a small study investigating the effect of simultaneous AV and VV time optimization, an additional but smaller beneficial effect of VV delay optimization was found [31]. In our cohort, only a minority of patients underwent VV optimization, mainly due to the fact that it was not deemed necessary due to satisfying echocardiographic dyssynchrony parameters and, coherently, visual impression of synchronous LV contraction. In patients who were optimized, the indication was mainly driven by TDI values during echocardiographic evaluation. Conversely, 30 (17.9%) patients were dyssynchronous either visually or by TDI measurements, but could not be corrected by advancing left or right ventricle activation. As a result, and due to the lack of clear evidence for a benefit, VV optimization is only performed in special cases in our institution.

CRT in patients with atrial fibrillation

19.4% of patients in our cohort suffered from atrial fibrillation. These patients pose a challenge in CRT as the uncoordinated and often rapid intrinsic conduction often results in a substantially impaired rate of biventricular pacing (< 95%). Indeed, atrial fibrillation was the main reason for a low percentage of biventricular pacing in our cohort. Pharmacologically, amiodarone has been shown to be most effective and safe for rhythm control in atrial fibrillation patients with heart failure [32], and, as a consequence, is frequently used to increase the percentage of biventricular stimulation. If the medical therapy is insufficient, AV nodal ablation is recommended as the next step [33]. In our cohort, 39.4% of patients with atrial fibrillation ultimately had no intrinsic AV conduction and, consequently, had a high degree of biventricular pacing.

Limitations of the study

Our study has some inherent limitations. Data are only collected from a single tertiary care center, and may hence not be generalizable to other healthcare settings. We do, however, believe that most interpretations and statements characteristically reflect the situation of "real world" CRT patients, and are therefore important for therapy optimization of these individuals. The study is further limited by the fact that we focused on the necessity and possibilities for CRT optimization, and as such did not assess clinical or echocardiographic outcome in these patients, which was beyond the scope of this study. However, evidence is accumulating as indicated above that empirical AV delay programming cannot generally be recommended [17]. As such, our data do indicate that specialist follow-up of CRT recipients is of crucial importance in order to provide optimal care for these complex patients, which was the primary aim of the current study.

Conclusions and perspective

In our "real world" cohort, a substantial proportion of patients presented with suboptimal device settings. Data from previous studies demonstrate that device optimization is associated with improved outcome [17, 18]. Yet, our data indicate that this opportunity is frequently missed in daily clinical practice, underlining the necessity for expert follow-up to deliver optimal care to this challenging group of heart failure patients in order for them to benefit most of their devices.

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