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Influence of the atrio-ventricular delay optimization on the intra left ventricular delay in cardiac resynchronization therapy

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Abstract

Background: Cardiac Resynchronization Therapy (CRT) leads to a reduction of left-ventricular dyssynchrony and an acute and sustained hemodynamic improvement in patients with chronic heart failure. Furthermore, an optimized AV-delay leads to an improved myocardial performance in pacemaker patients. The focus of this study is to investigate the acute effect of an optimized AV-delay on parameters of dyssynchrony in CRT patients.

Method: 11 chronic heart failure patients with CRT who were on stable medication were included in this study. The optimal AV-delay was defined according to the method of Ismer (mitral inflow and trans-oesophageal lead). Dyssynchrony was assessed echocardiographically at three different settings: AVD_{OPT} ; $AVD_{OPT}-50$ ms and $AVD_{OPT}+50$ ms. Echocardiographic assessment included 2D- and M-mode echo for the assessment of volumes and hemodynamic parameters (CI, SV) and LVEF and tissue Doppler echo (strain, strain rate, Tissue Synchronisation Imaging (TSI) and myocardial velocities in the basal segments)

Results: The AVD_{OPT} in the VDD mode (atrially triggered) was 105.5 ± 38.1 ms and the AVD_{OPT} in the DDD mode (atrially paced) was 186.9 ± 52.9 ms. Intra-individually, the highest LVEF was measured at AVD_{OPT} . The LVEF at AVD_{OPT} was significantly higher than in the $AVD_{OPT}-50$ setting ($p = 0.03$). However, none of the parameters of dyssynchrony changed significantly in the three settings.

Conclusion: An optimized AV delay in CRT patients acutely leads to an improved systolic left ventricular ejection fraction without improving dyssynchrony.

Background

Asynchronous myocardial contraction in heart failure is associated with poor prognosis. Recent studies have shown an acute and sustained hemodynamic improve-

ment after biventricular pacing (BVP), reversal of LV-remodelling, an increased quality of life, a reduction of symptoms of heart failure, and an improvement of exercise tolerance [1-7].

Table 1: Patient characteristics

Age _(mean ± SD)	63.2 ± 11.7
Gender (m/f) _(n/n%)	7(63.6)/4(36.4%)
Coronary artery disease _(n/n%)	4 (36.4%)
Dilated Cardiomyopathy _(n/n%)	7 (63.6%)
Left-ventricular ejection fraction _(mean ± SD)	27.3% ± 11.9
Interval in months between stress testing and ICD implantation (months) _(mean ± SD)	11.9 ± 12.9
location of the CS – electrode	
lateral	6 (54%)
posterolateral	4 (36.4%)
anterolateral	1 (9%)
diabetes mellitus _(n/n%)	6 (54%)
medication	
ACE inhibitors _(n/n%)	9 (82%)
ARB _(n/n%)	2 (18%)
Beta-blockers _(n/n%)	10 (91%)
Digitalis _(n/n%)	8 (73%)
Diuretics _(n/n%)	11 (100%)
spironolactone _(n/n%)	8 (73%)

ARB = Angiotensin-receptor blockers;

CS = coronary sinus

The optimization of the AV delay in DDD pacemaker patients is generally recommended and is performed in clinical practice. A variety of invasive and non-invasive methods were assessed in the past [8-15]. Recent studies have shown that also in CRT patients, invasively (dP/dt) [16-19] and non-invasively measured hemodynamic parameters (stroke volume) [20,21] are modified according to the programmed AV delay. A hemodynamically optimal AV delay can be defined.

Ismer's method of AV delay optimization [22] is validated for biventricular as well as right ventricular DDD pacing.

Tissue Doppler Imaging (TDI) is an evaluated tool in clinical practice to identify myocardial dyssynchrony. TDI (including strain and strain rate) imaging measures regional wall motion velocities and can accurately quantify regional left ventricular function [24].

Strain measures compression and distension of myocardial segments ("deformation imaging") and strain rate imaging expresses strain changes per time interval [25]. TSI (Tissue Synchronization Imaging) utilizes color-coded time-to-peak tissue Doppler velocities and visualizes segments of dyssynchrony in real-time by superimposing these temporal motion data on 2D echo images. [26,27].

These new techniques could potentially improve patient selection and guidance of implantation and programming of the devices for BVP. There is a variety of methods to determine dyssynchrony as summarized elsewhere [28].

There are no published data on the correlation of parameters of dyssynchrony and programming of the optimal AV interval. Aims of our study were therefore to investigate the influence of an optimized AV delay determined by the method of Ismer et al. [22] on dyssynchrony.

Table 2: Measurement of the components of the optimal AV delay according to Ismer et al. [22]

pacemaker-related interatrial conduction interval (IACT)	VDD pacing: MA-LA measured between right-atrial sense-event marker (MA) and the beginning of left-atrial deflection (LA) in oesophageal electrogram DDD pacing: SA-LA measured between right-atrial pacing stimulus (S _A) and the beginning of left-atrial deflection (LA) in oesophageal electrogram
left-atrial electromechanical action (LA-EAC _{long})	Measured during unphysiologically long programmed AV delay between the beginning of left-atrial deflection (LA) in oesophageal electrogram and the end of the left-atrial contribution (EAC) in transmitral flow.
left-ventricular electromechanical latency period (Sv-EAC _{short})	Measured during unphysiologically short programmed AV delay between ventricular pacing stimulus (Sv) and the end of the left-atrial contribution (EAC) in transmitral flow.

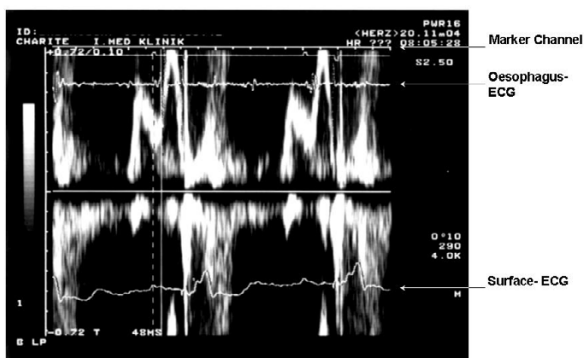


Figure 1
Measurement of the IACT in the VDD - Mode = MA-LA. MA = right atrial sensing marker (see marker channel). LA = left atrial deflection (see oesophageal ECG). In this particular patient the IACT is 48 ms.

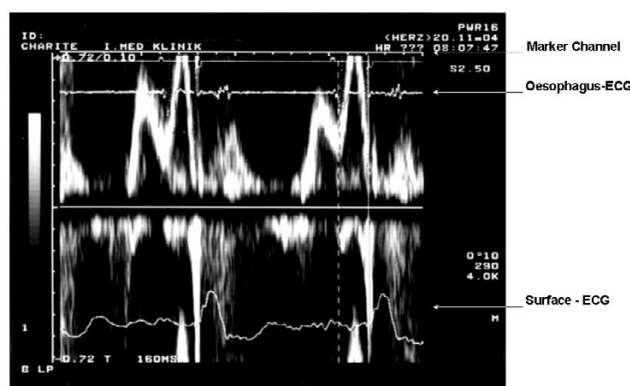


Figure 2
Assessment of the left-atrial electromechanical action = LA-EAC_{long}. LA = left atrial deflection (see oesophagus-ECG). EAC_{long} = the end of the A-wave in an unphysiologically long AV-intervall. In this particular patient the LA-EAC_{lang} is 160 ms

Methods

Patients

11 chronic heart failure patients of our clinic were included in this study. All patients had a biventricular ICD (pre-implantation NYHA III-IV, EF < 35%, QRS width > 120 ms). Clinical characteristics are demonstrated in Table 1. Patient exclusion criteria were as follows: atrial fibrillation, pacemaker malfunction and oesophageal diseases, NYHA IV, prosthetic mitral valve replacement.

AV delay: components and optimization

For the AV delay optimization we used the method proposed by Ismer et al [22].

This approach needs the placement of a bi-polar oesophageal electrode to provide a filtered left-atrial electrogram (LAE). We applied a 5F oesophagus electrode (Osypka TO2/5F, order no. TA12991101, Rheinfelden, Germany). Filtered oesophageal electrogram and telemetric real-time pacemaker markers provided by the programmer's analogue output were superimposed on the display of transmitral flow velocity on the Doppler-echo system (Figure 1). The simultaneous recording of transmitral flow, the left atrial oesophageal electrogram and the real-time sense-event markers, allow determining the components of the optimal AV delay (Table 2, Figure 1 and 2).

Based on these measurements, optimal AV delays were calculated for VDD (atrial-triggered) and DDD (atrial-paced) mode using the equations:

$$AVD_{OPT\ VDD} = MA-LA + LA-EAC_{long} - Sv-EAC_{short}$$

and

$$AVD_{OPT\ DDD} = SA-LA + LA-EAC_{long} - Sv-EAC_{short}$$

Echocardiography

Echocardiography to assess dyssynchrony was performed subsequently under three pacemaker settings: optimal AV delay (AVD_{OPT}), optimal AV delay minus 50 ms (AVD_{OPT}-50), optimal AV delay plus 50 ms (AVD_{OPT}+50).

Echocardiography was performed on the Vivid 5 and Vivid 7 Dimension (GE Vingmed Ultrasound, Horton, Norway) machines. The TDI and strain analysis were performed in an off-line work station. The LVEF was assessed by area-length method in the apical four chamber view. The CI and the SV were calculated from the systolic velocities measured by PW-Doppler in the aortic outflow tract. Strain rate, tissue Doppler velocities were measured in the basal segments of the apical four-, three- and two-chamber views.

Statistics

Values are expressed as mean ± standard deviation (SD). Groups were compared by parametric or non-parametric tests (t-tests and Wilcoxon-Mann-Whitney tests, respectively). Statistical significance was assumed at a value of P < 0.05. Statistical analysis was performed with the SPSS 12 software package (SPSS; Chicago, Ill, USA).

Results

Optimal AV delay

In all patients, we could define an optimal AV delay in the VDD and the DDD modes respectively. The AVD_{OPT} in VDD mode was 105.5 ± 38.1 ms and the AVD_{OPT} in the DDD pacing mode was 186.9 ± 52.9 ms. The results are summarized in Table 3. As expected, the mean optimal AV delay was lower in the VDD than in the DDD mode.

Table 3: AVD_{OPT} VDD = optimal AV delay for atrially triggered (VDD) and atrially paced (DDD) modes

patient	AVD _{OPT} VDD	AVD _{OPT} DDD
1	60	172
2	78	154
3	96	204
4	92	132
5	92	144
6	122	174
7	136	216
8	64	128
9	84	180
10	168	252
11	168	300
	105,5 ± 38,1 ms	186,9 ± 52,9 ms

ARB = Angiotensin-receptor blockers; CS = coronary sinus

Echocardiography was performed subsequently under three pacemaker settings: AVD_{OPT}, AVD_{OPT}-50, AVD_{OPT}+50. All patients had continuous biventricular stimulation even under AVD_{OPT}+50.

2D and TDI echocardiography

The LVEF with AVD_{OPT} was 28% (± 12%), with an AVD_{OPT}-50 20% (± 7%, p= 0.03 compared to AVD_{OPT}), with an AVD_{OPT}+50 23% (± 7%, p = 0.11 compared to AVD_{OPT}). The heart rate did not change significantly in the different settings (AVD_{OPT}: 65,4/min, AVD_{OPT}-50: 65,6/min, AVD_{OPT}+50: 65,8 ms). The hemodynamics (SVI, CI, LVEF) and the TDI derived data are listed in Table 4. There was no significant difference of the amount of segments with dyssynchrony in TSI in the three settings. The maxi-

mal delay in the basal segments in the apical two-, three- and four-chamber views measured by TSI and strain did not differ in the AVD_{OPT}, AVD_{OPT}+50 and AVD_{OPT}-50 setting.

Discussion

Optimal AV delay

To date, Ismer's method for the optimal AV delay was applied to patients with DDD pacemakers and normal left ventricular function [22,23]. This is the first study to assess the optimal AV delay by Ismer's method in patients with reduced left ventricular function. In our CRT patients, an optimal AV delay according to Ismer's method could be defined. This is the only method that allows separate measurement of the three AV-delay components: i.e., the pacemaker-related interatrial conduction time, the left-atrial electromechanical action, and the left-ventricular latency period. The benefits of this method, however, are offset by the necessity for placement of an oesophageal electrode. This requirement explains why only a few medical centres have applied this method in clinical practice and in most cases for purposes of scientific investigation only.

Our results concerning the AVD_{OPT} in the VDD mode (105.5 ± 38.1 ms) are in agreement with the results of other studies on AVD_{OPT} in CRT patients: Butter [16] determined an AVD_{OPT} of 100 ms in 30 patients, Auricchio [17] an AVD_{OPT} of 112 ± 33 ms in 41 patients and Kass [18] an AVD_{OPT} of 125 ± 49 ms. A study that was recently published by Porciani [29] found an AVD_{OPT} during simultaneous biventricular pacing of 97 + 27 ms.

In the literature, there are no published data on AVD_{OPT} in DDD mode. Therefore, our AVD_{OPT} in DDD mode of 186.9 ± 52.9 ms cannot be compared to other studies.

Table 4: Hemodynamic and Tissue Doppler Echocardiography parameters in the AVD_{OPT}, AVD_{OPT}-50 and AVD_{OPT}+50 modes.

	Hemodynamics			p
	AVD _{OPT}	AVD _{OPT} -50	AVD _{OPT} +50	
SV [ml]	89,2 (± 27.7)	89,7 (± 36.9)	95,3 (± 36.9)	n.s.
LVEF	0,28 (± 0.12)	0,20 (± 0.07)*	0,23 (± 0.07)**	*0.03 / **0.11
CI	3,0 (± 0.9)	3,2 (± 0.8)	3,4 (± 0.9)	n.s.
HR	65,4 (± 8.8)	65,6 (± 9.4)	65,8 (± 9.4)	n.s.
	Tissue Doppler			p
	AVD _{OPT}	AVD _{OPT} -50	AVD _{OPT} +50	
TDI max. delay in basal segments [ms]	122,9 (± 95,6)	125,0 (± 109,2)	131,7 (± 85,2)	n.s.
TSI segments with asynchrony	2,08 (± 1,24)	2,27 (± 1.19)	2,41 (± 1.43)	n.s.
Strain max. delay in basal segments [ms]	148,3 (± 74.9)	167,5 (± 90.2)	151,7 (± 54.1)	n.s.
Strain [%]				
4AC lateral	13,7 (± 6,5)	14,5 (± 9,8)	13,4 (± 9,8)	n.s.
4 AC septal	15,6 (± 7,3)	13,9 (± 9,3)	15,0 (± 9,8)	n.s.
A2C anterior	16,8 (± 9,7)	17,2 (± 10,5)	16,1 (± 9,1)	n.s.
A2C inferior	20,0 (± 11,5)	15,0 (± 11,4)	16,1 (± 9,8)	n.s.
A3C anterior	19,7 (± 9,5)	12,4 (± 9,7)	18,1 (± 9,8)	n.s.
A3C interior	19,1 (± 9,8)	14,1 (± 12,7)	19,2 (± 10,1)	n.s.

Hemodynamics

Intra-individually, the patients had the best LVEF under optimal AV-delay compared to the +50 and -50 ms settings. The LVEF is significantly higher in the AVD_{OPT} setting than in the AVD_{OPT} -50 setting. Obviously the formation of "cannon waves" seen with a shorter AV interval (AVD_{OPT} -50) had a more negative hemodynamic effect than the diastolic mitral regurgitation seen with longer AV delays (AVD_{OPT} +50). The hemodynamically unfavourable effects of "cannon waves" are described since the beginning of pacemaker therapy and are also termed "pacemaker syndrome". It is generally accepted that an adequate pacemaker programming can avoid this [30]. Toda et al. [31] could show in his studies that the mean LVEF in AVD_{OPT} is higher than in prolonged AV delays. However, he found no significant difference.

Dyssynchrony

Changes of dyssynchrony can be seen immediately, as seen in studies that have examined on/off comparisons in CRT patients [32]. However, an optimized AV interval does not change the markers of dyssynchrony. The reason for the improved hemodynamic situation under AVD_{OPT} seems to be the better left ventricular filling and not the altered dyssynchrony.

Limitations

This study included only a small number of patients. There was no follow-up examination of the patients.

Conclusion

This study confirmed that an optimized AV delay improves the left ventricular ejection fraction. Acutely, the optimized AV delay does not influence left ventricular dyssynchrony. Whether a long-term AVD_{OPT} leads to changes in left ventricular dyssynchrony via an improved LVEF and reverse remodelling can only be speculated. This has to be addressed in future studies with a long-term observation interval.

Abbreviations

AVD_{OPT} optimal AV delay

AVD_{OPT}-50 optimal AV delay -50 ms

AVD_{OPT}+50 optimal AV delay + 50 ms

CRT Cardiac Resynchronization Therapy

DCM Dilated Cardiomyopathy

EMD Electromechanical Delay

IVMD Inter-ventricular mechanical delay

LBBB Left Bundle Branch Block

SRI strain rate imaging

TDI Tissue Doppler Imaging

TSI Tissue Synchronization Imaging

VDD atrially triggered mode

DDD atrially paced mode

EAC the end of the A-wave

LVEF Left ventricular ejection fraction

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

CM and FK have equally contributed to this publication. CM, BI, FK and ACB have designed and performed the study and have written the manuscript. HJB, CAN and GB have participated in the study design and coordination and have helped to draft the manuscript. All authors read and approved the final manuscript.

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