Background: Measurement of QRS duration (QRSd) on surface electrogram (ECG) is the main tool, together with left bundle branch block (LBBB), to select patients (pts) which will benefit from cardiac resynchronisation therapy (CRT). This value is accepted as an undeniable fact but neither guidelines nor randomised studies which support evidence of CRT (even single centres of individual practitioners) use standardised measurements of QRSd.

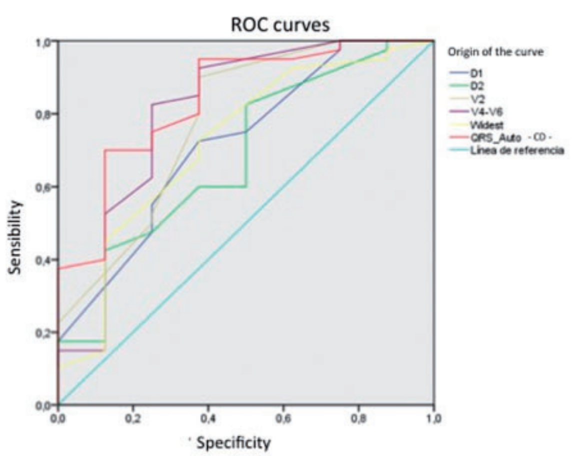
Purpose: To assess reliability and precision of different measurement methods of QRSd.

Methods: 56 consecutive patients with LBBB with one available ECG with at least 6 simultaneous leads were evaluated in our Arrhythmia outpatient clinic (age 69,5 ±11,4 years, 48,2% male, 63% without structural heart disease and 16 patients with left ventricular ejection fraction < 35%). We registered the computerized determination of QRSd value (CD-QRS) obtained from the electrocardiograph as well as measurements obtained from 2 different observers and using 4

methods: a) QRSd in individual leads, b) mean QRSd from V4-6, c) longest QRSd, d) global measurement (from earliest QRS begin to the latest J-point on precordial leads, considered as reference). We analysed intraclass correlation coefficient (ICC), diagnostic odds ratio (DOR) and receiver operating characteristic (ROC)curves.

Results: ICC between global QRSd and other methods showed good agreement measures (never excellent) for V2 (0.76, confidence interval (CI): 0,62-0,85), CD-QRS (ICC 0,74; CI: 0,59-0,85), mean in V4-6 (ICC 0.72; CI: 0.57-0.83) y longest QRSd (ICC 0.69; IC: 0.42-0.75). Agreement measures were moderate for lead I (ICC 0,61; CI: 0,42-0,75) and specially for lead II (ICC 0.58; CI: 0.38-0.73). Similar trends were observed in interobserver ICC. In the ROC curves, CD-QRS showed the greatest area under the curve (AUC) (0.841) followed by the mean in V4-6 (0.683) for a threshold point of 130ms (Figure).

Conclusions: QRSd varies significantly between different leads and different measurement methods, these could a potential risk of exclusion of CRT for patients who could benefit. The CI-QRS was the measurement method which most related to the global QRSd, followed by the mean in V4-6 and V2. The routine use of lead II is not recommended. Accurate measurement of QRSd should be standardised to improve patient selection for CRT and interpretation of research results.



Abstract P319 Figure. ROC curves for QRSd estimation methods

P320

End-systolic septum strain: a multi-modality strain parameter that accurately predicts cardiac resynchronization therapy response

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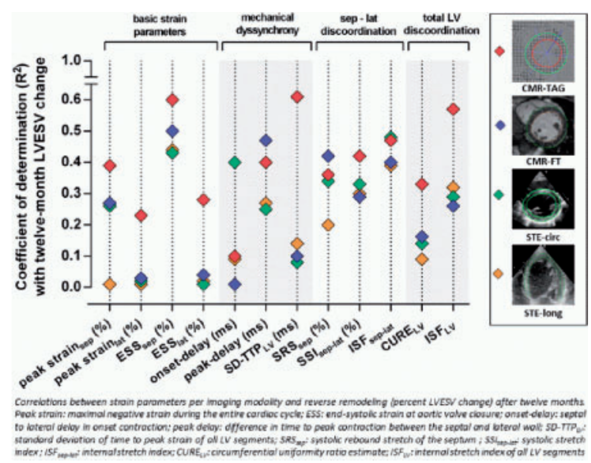
Objectives: This study aims to compare predictive performance of different strain parameters and evaluate results per imaging modality to predict cardiac resynchronization therapy (CRT) response.

Background: Myocardial strain imaging is a potential tool to improve patient selection for CRT. Various strain parameters have been proposed as predictors of CRT response measuring regional timing differences (dyssynchrony) or inefficient contraction patterns (discoordination). Also, multiple imaging modalities are presently available including CMR tagging (CMR-TAG), CMR feature tracking (CMR-FT) and speckle tracking echocardiography (STE). Despite promising results for multiple parameters and different modalities, a systematic comparison between parameters and methods is lacking.

Methods: Twenty-seven patients, prospectively enrolled in the MARC study, underwent both CMR- and echocardiographic examination before CRT implantation. Strain analysis was performed in the circumferential (CMR-TAG, CMR-FT and STE-circ) and longitudinal (STE-long) orientation. Different subsets of strain parameters were measured including regional strains, measures of dyssynchrony, and discoordination. After twelve months, CRT response was measured by the echocardiographic change in left ventricular end-systolic volume.

Results: Twenty-six patients (age 65±9 year, 58% men) completed follow-up. Mean LVESV change was -29±27% with 17 (65%) patients showing ≥15% reduction in LVESV. Each subset of strain parameters was strongly related to CRT response when using the reference CMR-TAG technique with best results for dyssynchrony (SD-TTPLV R2 0.61) and discoordination (ISFLV: R2 0.57) including all LV segments. However, these measures showed wide variability between imaging modalities with less favorable results for CMR-FT and STE. In contrast, regional end-systolic septal strain (ESSsep) showed a consistent high correlation with LVESV change for all modalities (CMR-TAG R2 0.60; CMR-FT R2 0.50; STE-circ R2 0.43; and STE-long R2 0.44).

Conclusions: Both measures of dyssynchrony and discoordination were strongly related to CRT response when using the CMR-TAG reference technique. However, CMR-FT and STE showed less favorable results for these parameters. In contrast, the end-systolic septal strain marker (ESSsep) showed a consistently high correlation with CRT response irrespective of modality.



Abstract P320 Figure.

P321

Effect of biventricular pacing on ventricular remodeling in asymptomatic heart failure patients with ischemic cardiomyopathy

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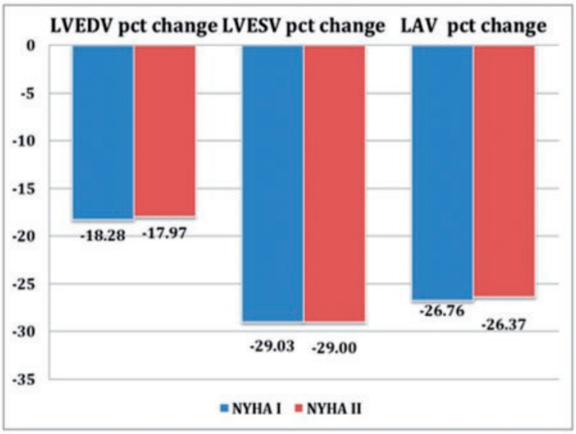
Background: Since introduction of cardiac resynchronization therapy (CRT) in clinical practice, reversal of remodeling has been identified as one of the key elements of beneficial response. Data on reverse remodeling (RR) to CRT in asymptomatic heart failure(HF) patients (pts) are however scarce. We sought to evaluate echocardiographic RR to CRT-D in pts enrolled in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) Trial, by baseline New York Heart Association (NYHA) Class I vs. II.

Methods: MADIT-CRT trial enrolled pts with reduced left ventricular ejection fraction (LVEF)≤30% and prolonged QRS≥130ms, pts with non-ischemic cardiomyopathy (CM) and NYHA Class II, or ischemic CM and either a NYHA class I or II. Of the 999 pts with ischemic CM, 265 (26.5%) were classified as NYHA class I, 152 of them had a CRT-D. Among the NYHA Class II ischemic subjects, 446 pts were implanted with CRT-D. Echocardiographic images were obtained both at enrollment and at 1-year follow-up analyzed by a central core laboratory. End points were changes in left ventricular end-diastolic and end-systolic volumes, LVEF and left atrial (LA) volume at 1-year.

Results: In pts with NYHA class I, CRT-D was associated with a mean reduction in LVEDV of -18.28%, similar to pts with NYHA class II (-17.97%, p=0.823). Additionally, there was a significant reduction in LVESV in both NYHA I and NYHA II ischemic pts (NYHA I: -29.03%, NYHA II: -29.00%, p=0.993), indicating similar degrees of LV volume reduction 1 year after CRT-D implantation. LA volumes were also significantly lower after CRT-D in both NYHA classes (Figure). LVEF significantly improved in both NYHA classes with CRT-D (NYHA I: 9.8±5.1% vs. NYHA II: 10.0±4.9%, p=0.694).

Conclusions: In MADIT-CRT, asymptomatic (NYHA class I) and moderately symptomatic HF pts (NYHA class II) with ischemic CM demonstrated similar degrees of echocardiographic RR to CRT-D. Therefore, it seems debatable to exclude NYHA class I pts with ischemic CM from CRT.



Abstract P321 Figure. Echo changes in pts with CRT-D, 1y

P322

Is physiologic preservation of microcirculation important for functional recovery after CRT?

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Background: Cardiac implantable electronic devices changed the treatment of patients with systolic heart failure. Although, CRT has become a mainstay in heart failure management, 40% of patients failed to respond to therapy.

Purpose: The aim of the study was to assess predictive significance of residual coronary flow reserve (CFR) as the marker of preserved microcirculation, and existing or provoked functional dyssynchrony, for an improvement of left ventricular function after cardiac resynchronization therapy (CRT).

Methods: The study was prospective and enrolled 51 consecutive patients meeting the recommended criteria for cardiac resynchronization therapy, with or without ischemic heart disease. Before CRT, functional dyssynchrony (apical rocking and septal flash as the most robust and most easiest to parameters use) was assessed at rest and at peak dobutamine stress (20 mcg/kg/min). CFR was measured noninvasively with transthoracic echocardiography during hyperemia induced with adenosine (140mcg/kg/min for 1 min). The patients were followed up over a 12 month period, after CRT implantation. Responders were defined as the patients showing improvement in quality of life by at least 1 NYHA class, and an increase in EF greater than 5%, as established by objective measurement.

Results: After a 12 months follow up, out of 51 patients enrolled in our study, there were 30 responders (58.8%) and 21 nonresponders (41.2%). Based on the univariate regression analysis, the most significant predictors of responders are: the cardiomyopathy type (ischaemic or non-ischaemic dilated), p=0.028, presence of LBBB (p=0.005), apical rocking at rest and during DSE (AR p=0.025 and ARdob 0.002), septal flash during DSE (SF dob p=0.045), a delta variation of WMSI rest-stress $\geq$ 0.20 (ΔWMSI $\geq$0.20 p=0.003) and CFR before CRT implantation (CFR before CRT p=0.001). Multivariate regression analysis identified apical rocking during DSE (ARdob p=0.001) and CFR before CRT implantation (CFR before CRT p= 0.0001) as independent predictors of recovery. By applying ROC analysis, the CFR $\geq$ 1.79 measured before the cardiac resynchronization pacemaker implantation identifies responders with sensitivity of 82% and specificity of 78% (area under the curve = 0.78; 95% CI 0.626-0.938; P<0.002),

Conclusion: Based on our results, it may be concluded that mechanical dyssynchrony, as septal flash and apical rocking at rest and/or provoked with low dose dobutamine indicate the patients most likely to improve with resynchronization. Furthermore, patients with severely compromised coronary flow reserve, CFR $\leq$ 1.79, show no significant recovery of left ventricular function. Our results demonstrate that, preserved coronary microcirculation demonstrated by adequate CFR response is significant physiological prerequisite for functional recovery after CRT treatment.

P323

Response to cardiac resynchronization therapy is determined by intrinsic electrical substrate rather than by its modification

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Background: In systolic heart failure patients, electrocardiographic mapping (ECM) can be used to express electrical activation by magnitude and direction of the activation delay vector (ADV). The aim of the present study was to investigate to what extent the response to cardiac resynchronization therapy (CRT) is determined by baseline ADV (considered as the electrical substrate), ADV modification by biventricular and left ventricular (LV) pacing and by optimization of LV pacing site.

Methods and Results: ECM was used to acquire electrical activation maps in 79 systolic heart failure patients (4 RBBB, 12 QRS <120ms, 23 non-specific conduction delay [NICD] and 40 left bundle branch block [LBBB]). 67 patients (QRS>120 ms) underwent CRT implantation and in 26 patients multiple LV pacing sites were tested. ADV was calculated from locations and depolarization times of 2000 virtual epicardial electrodes. CRT response was defined as $\geq$10% LVdP/dtmax increase (24/57 acute responders) and a composite clinical score at 6 months (36/55 chronic responders). During intrinsic conduction, ADV direction was similar in patients with QRS<120 ms, NICD and LBBB, pointing towards the LV free wall, while ADV magnitude was larger in LBBB patients (117$\pm$25 ms) than in patients with NICD (70$\pm$29 ms, P<0.05) and QRS<120ms (52$\pm$14 ms, P<0.05). Intrinsic ADV accurately predicted the acute (AUC = 0.93) and chronic (AUC 0.90) response to CRT. In contrast, the change in ADV by CRT only moderately predicted response (highest AUC 0.76). LV pacing site optimization had limited effects on acute response.

Conclusion: The baseline electrical substrate, adequately measured as ADV, strongly determines acute and chronic CRT response, while the extent of its modification by conventional CRT or by varying LV pacing sites has limited influence.

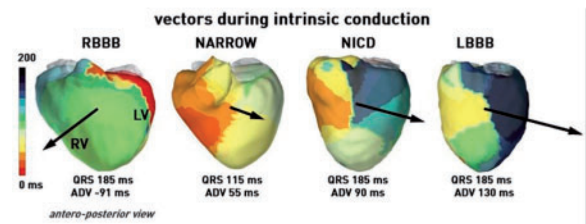

Figure 1. Electrocardiographic activation time maps with activation delay vector (ADV) during intrinsic conduction in NYHA III heart failure patients with right bundle branch block (RBBB), narrow QRS complex (NARROW), non-specific intraventricular conduction delay (NICD) and left bundle branch block (LBBB). ADV amplitudes and QRS widths are presented for each patient. LV = left ventricle. RV = right ventricle.

Abstract P323 Figure.

P324

Optimal MRI-based left ventricular lead placement for cardiac resynchronization therapy in patients with an ischemic cardiomyopathy: a retrospective analysis

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Background: CRT is a proven therapy for patients with chronic heart failure. However, a substantial amount of patients undergoing CRT implantation do not respond significantly. The percentage of non-responders to CRT is higher in patients with ischemic cardiomyopathy in contrary to non-ischemic patients. It is suggested that the lead is positioned in a dyssynchronous area without scar to optimize outcome.

Purpose: In this feasibility study we evaluate the relation of LV lead position with respect to the infarcted area and area of time-to-peak circumferential strain of the LV wall to CRT response using a fully MRI-based approach in patients with ischemic cardiomyopathy.

Methods: Three main variables were identified retrospectively in 32 patients: the position of infarcted area, defined with late gadolinium enhanced cardiac MRI (1), the area of time-to-peak circumferential strain, defined by using cardiac MRI cine images using feature tracking strain analysis (2), and the current LV lead position on fluoroscopy. The ideal pacing target was defined as an area of the LV with lowest as possible scar transmurality and with the highest time-to-peak circumferential strain. Distance from the target segment to the current LV lead position was scored: within (group 1), adjacent (group 2) or remote (group 3) on a 36 segment cardiac bullseye (fig 1 B,C). The relation between these scores and echocardiographic response to CRT, defined as $\geq$15% LVESV reduction at six months follow-up, was determined. LV scar burden was determined to see if this is an independent variable predicting response in this study population.

Results: The study was made up of 18 CRT non-responders (94% male, 66.7% left bundle branch block (LBBB), 33.3% intraventricular conduction delay (IVCD), median LVEF 27.6%) and 14 responders (64% male, 93% LBBB, 7% IVCD, median LVEF 21.5%). In seven patients the LV lead was positioned within the target area (group 1), in seventeen adjacent to the target area (group 2), and in eight remote from the target area (group 3). The percentage responders was 86% in group 1, 41% in group 2 and 13% in group 3. A significant difference was seen between the percentage responders in group 1 and group 3 (p=0.010). No significant differences were seen between group 1 and 2, nor between group 2 and 3. Data are presented in fig 1 A. Scar burden showed a significant relation with LVESV change (correlation coefficient 0.408, p=0.020) and response to CRT (p=0.044), but no significant differences were seen in scar burden between group 1, 2 and 3.