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MATTHIEU GRAS

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Cardiac resynchronization therapy and ventricular fusion: Evaluation by non-invasive mapping

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TABLES DES MATIERES

Serment d'Hippocrate…… Page 7

Remerciements…… Page 8

Abreviations…… Page 10

Abstract ……..…… Page11

Introduction…… Page 14

Methods……... Page 15

Study population

Device implantation

AdaptivCRT

Outcomes

Statistical analysis

Results……. Page 18

Baseline characteristics

Epicardial activation

Dyssynchrony index

Isochronal Surfaces

CRT Response

Discussion……... Page 22

Limitations……. Page 27

Conclusion…….. Page 28

References…….. Page 29

Tables and Figures……..... Page 32

Supplemental data…… Page 46

SERMENT D'HIPPOCRATE

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De mes chers condisciples
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ABREVIATIONS LIST

CRT: Cardiac Resynchronization Therapy

LV: Left Ventricle

LBBB: Left Bundle Block Branch

RV: Right Ventricle

ECM: Electrocardiographic mapping

BiV: Biventricular

EF: Ejection Fraction

LVEF: Left Ventricular Ejection Fraction

VEU: Ventricular Electrical Uncoupling

RVTAT: Right Ventricular Total Activation Time

LVTAT: Left Ventricular Total Activation Time

QRSd: QRS duration

CT: Computerized Tomography

ABSTRACT

Background

Cardiac resynchronization therapy (CRT) is recommended in selected patients with chronic heart failure and wide QRS, leading to clinical benefits in approximately 70% of cases. AdaptivCRT algorithm allows CRT using fusion between of left ventricular only pacing and right ventricular intrinsic conduction. This study aimed to evaluate changes in ventricular activation sequences during conventional CRT (biventricular pacing) and with AdaptivCRT algorithm.

Method

Electrocardiographic mapping (ECM) using a 252 thoracic electrodes jacket was used to collect unipolar body surface potentials. Acquisitions of unipolar signals were obtained and further combined with cardiac thoracic scan in a way to produce 3D color coded activation maps during intrinsic cardiac rhythm, biventricular pacing and AdaptivCRT.

Results

Twelve patients were investigated, all of them presenting with left ventricular ejection fraction ≤35% and typical left bundle branch block. Baseline ventricular activation patterns were similar in all patients. Right ventricular activation patterns were similar during intrinsic rhythm and AdaptivCRT, but different during biventricular pacing. LV activation patterns were comparable in most patients during biventricular pacing and AdaptivCRT. Ventricular electrical uncoupling (VEU) was improved during biventricular pacing (-17 ms, IQR -27 – -2) and AdaptivCRT (-27 ms, IQR -31 – -21), when compared to intrinsic rhythm (-53 ms, IQR -60 – -43), ($p<0.01$ and $p<0.01$, respectively). VEU index were not different between AdaptivCRT and biventricular pacing ($p=0.10$). Areas of late RV activation (<80 ms) were larger during AdaptivCRT (100%, IQR 95.6 – 100) than biventricular pacing (89.1%, IQR 64.6 – 98.3), ($p=0.03$).

Conclusion

AdaptivCRT algorithm allows for faster and more homogeneous RV activation than biventricular pacing, while keeping similar benefits on left ventricular activation and offering potential additional battery longevity.

RESUME

Introduction

Le traitement par resynchronisation cardiaque est indiqué chez les patients insuffisants cardiaques avec QRS larges sur l'ECG. Les bénéfices de la resynchronisation cardiaque sont observés chez 70% des patients implantés. L'algorithme AdaptivCRT permet une resynchronisation cardiaque par fusion entre une stimulation ventriculaire gauche et la dépolarisation intrinsèque du ventriculaire droit. Notre étude vise à comparer l'activation électrique biventriculaire entre une stimulation biventriculaire conventionnelle et l'algorithme AdaptivCRT.

Méthode

Des cartographies non-invasives d'activation biventriculaire ont été réalisées en rythme spontané, stimulation biventriculaire et stimulation mono ventriculaire gauche seule (AdaptivCRT) à l'aide du système CardioInsight (ECVUE, CardioInsight Technologies Inc, Medtronic). L'acquisition des signaux unipolaires grâce à un gilet doté de 252 électrodes a permis la réalisation des cartes d'activation.

Résultats

Douze patients ont été analysés présentant tous une fraction d'éjection ventriculaire gauche ≤35% ainsi qu'un bloc de branche gauche. Les profils d'activation ventriculaire en rythme spontané sont comparables. Les profils d'activation ventriculaire droite sont identiques en rythme spontané et avec l'algorithme AdaptivCRT, mais différent en stimulation biventriculaire. Les profils d'activation ventriculaire gauche semblent comparables en stimulation biventriculaire et avec l'algorithme AdaptivCRT. Les index de désynchronisation (VEU) en stimulation biventriculaire (53 ms, IQR -60 – -43), ou AdaptivCRT (27 ms, IQR -31 – -21) sont supérieurs à ceux analysés en rythme spontané (-17 ms, IQR -27 – -2), ($p<0.001$ et $p<0.001$, respectivement). Il n'y avait pas de différence de VEU entre les patients avec stimulation biventriculaire et AdaptivCRT ($p=0.10$). Les surfaces de dépolarisation tardive du ventricule

droit était plus élevées en stimulation biventriculaire (10.85%, IQR 0.7 – 27.1) comparées à celles documentées avec AdaptivCRT (0.1%, IQR 0 – 1.3), (p=0.02).

Conclusion

L'algorithme AdaptivCRT permet d'obtenir une activation ventriculaire droite plus rapide et plus homogène que la stimulation biventriculaire, tout en conservant des bénéfices semblables sur la resynchronisation du ventricule gauche, et en offrant une longévité de batterie potentiellement plus longue.

INTRODUCTION

Heart failure is one of the leading causes of death worldwide. Cardiac resynchronization therapy (CRT) is recommended by current guidelines (1, 2) in patients with drug-refractory heart failure, low LV EF ≤35% and wide QRS, with a goal to reduce overall mortality, improve clinical symptoms and quality of life (3–8).

Despite this therapy has been developed for more than 25 years, we still observe a 30% rate of patients who do not respond to CRT (5). In this context, many efforts have been performed to optimize the device settings (9) and to reach a better understanding of CRT electrophysiological effects, in a way to further improve outcomes in this population. Over the last few years, improvement of device capabilities and development of new algorithms dedicated to CRT, helped to reach a better heart failure management with better clinical outcomes (10–12). AdaptivCRT (Medtronic, Inc., Mounds View, Minnesota) is a recent algorithm which allows permanent fusion between spontaneous right ventricular activation through the His Purkinje system and left ventricular pacing in patients with left bundle branch block (LBBB). Previous meta-analysis suggest that LV-only pacing can be at least as efficient as biventricular pacing, without differences in mortality (13).

Nevertheless, electro-anatomical patterns obtained during AdaptivCRT have never been investigated. A better understanding of the mechanisms of delayed myocardial activation and contraction patterns leading to dyssynchrony is of key importance to improve individual CRT delivery. Electrocardiographic mapping (ECM) is a new technique that enables non-invasive analyses of epicardial electrical activation, using high-resolution mapping during a single cardiac cycle. This study aimed to compare ventricular electrophysiological substrate and electrical ventricular dyssynchrony in CRT patients with cardiac resynchronization with or without fusion, using a non-invasive mapping approach.

METHODS

Study population

We conducted a prospective monocentric study from July 2018 to July 2019 in the cardiology department of TOURS university hospital. All patients ≥ 18 years old, implanted with a Medtronic CRT device between March 2015 and July 2019, were identified from the local database of CRT patients. According to guidelines, following criteria were required before implantation: New York Heart Association functional (NYHA) class II, III or IV (ambulatory) despite optimal medical therapy ; left ventricular ejection fraction ≤35% ; wide QRS >120 ms with typical LBBB morphology on 12-lead EKG (14). Patient's information were collected, including comorbidities, medical history, and events during hospitalisation or follow-up. Response to CRT was defined as an increase of LVEF ≥ 10% and an improvement of NYHA functional ≥ 1. All of patients gave written consent before inclusion in the study. Patient with permanent AF, AV block, valvular replacement, or non-specific intraventricular conduction disturbances were excluded.

Device implantation

Right ventricular lead was implanted at the RV apex and LV lead ideally in a latero-basal position. All LV leads were quadripolar leads manufactured by Medtronic (model 4398 – 88 cm length). Final position was determined on chest X-ray (LAO and RAO projections). CRT pacing parameters and LV pacing polarity were selected on an individual basis and left to the discretion of the physician.

AdaptivCRT

AdaptivCRT algorithm (Medtronic, Inc., Mounds View, Minnesota) allows for automatic adjustment of atrio-ventricular and inter ventricular delays. LV-only pacing is synchronized to right ventricular intrinsic activation through the His Purkinje system when AV conduction is normal (< 200 ms during sinus rhythm, < 250 ms during atrial pacing). AV conduction is measured from the onset of the far-field electrogram sensed by the atrial lead, to the onset of the

far-field electrogram sensed by the right ventricular lead. The algorithm switches from LV only pacing to biventricular pacing when the device detects either abnormal AV conduction, high rate (>100 bpm) or atrial fibrillation. Periodical measurements allow the algorithm to switch between LV-only or biventricular pacing (AV delays/60 seconds, P wave/16hours, QRS duration/16 hours). Left ventricular pacing occurs after 70% of the intrinsic AV interval, as measured during the previous cardiac cycle, or at least 40 ms before intrinsic QRS ***(Figure 1).*** During biventricular pacing, the AV delay is adjusted to pace the ventricle 30 ms after the end of the P wave, or at least 50 ms prior to intrinsic RV activation (12), ***(Figure 1)***

Outcomes

Study outcomes were collected prospectively. Biventricular epicardial activation maps were acquired using a non-invasive high-resolution ECM system (EVCUE, CardioInsight Technologies Inc., Cleveland, OH, USA). Jackets with 252 thoracic electrodes were used to collect unipolar body surface potentials in each patient and combine them with cardiac thoracic scan to produce 3D activation maps. This novel method has been previously used in canine hearts and in humans (15, 16). Thoracic computerized tomography (CT) scan was performed to precisely identify the position of each electrode relative to the epicardial surface. A strictly similar Sensor Array configuration was used during the acquisition of activation maps. In a way to reach high consistency in the imaging resolution and quality, the CT scan parameters were set to meet at least the following requirements: 3 mm slice thickness, 64 slices and cardiac gating. Field of view started 5 cm above the shoulder line to the bottom of Sensor Array and from mid-arm to mid-arm laterally, in a goal to include the entire torso. We further performed cardiac segmentation, to well separate the heart cavities and the great vessels. Electrical and imaging data were then combined and computed on the CardioInsight™ workstation, using the CardioInsight™ application and automated algorithms, to obtain epicardial unipolar electrogram and ventricular activation maps. Data were acquired during intrinsic rhythm, biventricular pacing and LV only pacing (AdaptivCRT). QRS duration was determined by plotting unipolar signals

analyzed by the ECM system, considering the time-interval from the onset of the earliest electrogram to the final return to the isoelectric line recorded on the latest electrogram.

Directional activation maps were analyzed using color coding from red to blue, corresponding from early to late isochronal surfaces.

Ventricular activation times (VAT) were calculated automatically from QRS onset complex to the maximal negative slope of each unipolar electrogram, after exclusion of the pacing artefact. An epicardial breakthrough site was defined as the earliest location identified on the isochrone maps. A line of slow conduction was recorded whenever the activation timing of adjacent points on either side of this line differed ≥ 40 milliseconds (ms).

Were measured:

- Right Ventricular Total Activation Time (RVTAT) defined as the time duration (ms) between the earliest and the latest activated sites of right ventricular activation.
- Left Ventricular Total Activation Time (LVTAT) defined as the time duration (ms) between the earliest and the latest activated sites of left ventricular activation.
- Ventricular Electrical Uncoupling (VEU) defined as the time difference (ms) between mean right and left ventricular activation times. A negative value is due to left ventricular uncoupling from the right whereas a positive value reflects right ventricular uncoupling from the left.
- Percentages of very early (<40 ms), early (40 to 80 ms and <80 ms), late (80 to 120 ms) and very late (>120 ms) depolarized epicardial surfaces were also calculated among right ventricle, left ventricle and both (RV + LV).

Statistical analysis

Qualitative variables are described as counts and percentages. Quantitative variables are described as median value and interquartile range. Non-parametric tests (Wilcoxon paired test and Mann Whitney test) were performed for comparison of variables between groups. Statistical significance was defined by p-value <0.05. Statistical analyses were performed using XLSTAT 2019 software.

RESULTS

Baseline characteristic

Out of 246 CRT patients initially identified, 234 were excluded from the study because of various reasons (AF, AV block, valvular replacement, death, absence of informed consent …). The final population consists in 12 CRT patients including 8 responders to CRT and 4 non-responders ***(Figure 2).*** Patient's characteristics are summarized in ***Table 1***. Median age was 68 years-old (IQR 62 – 70). All patients but one had non-ischemic cardiomyopathy. The median LVEF improved from 28% (IQR 22 – 34) at baseline, to 40% (IQR 32 – 50), ($p<0.01$) after CRT implantation. The median QRS duration during intrinsic rhythm (149 ms, IQR 142 – 159) was longer compared to biventricular pacing (98 ms, IQR 89 – 111) or AdaptivCRT (108 ms, IQR 96 – 119), ($p<0.01$ and $p<0.01$ respectively). QRS duration was not different during biventricular compared to AdaptivCRT ($p=0.09$), ***(Table 2, 3, 4)***

Epicardial activation

Epicardial activation maps are depicted according to the different pacing mode. Intrinsic rhythm in all patients was characterized by an initial breakthrough in the right ventricular antero-sepal area. Ventricular activation then spread towards the apex and late activation was observed in the lateral or posterior left ventricular wall ***(Figure 3)***. During biventricular pacing, various patterns of ventricular activation were observed. Initial breakthrough was documented either at the RV apex (patient #3, #5, #6, #7, #10, #11) or on the RV lateral wall (patient #1, #2, #4, #8, #9, #12). Ventricular activation then spread radially in the RV with various speed of activation depending on patients. RV wall activation could be either fast (patient #1, #2, #4 #5, #9, #10) or slow (patient #3, #6, #7, #11, #12) or both in patient#8**.** A second initial breakthrough was observed in the LV with eccentric ventricular front of activation ***(Figure 4).***

All patients with LV only pacing (AdaptivCRT) had RV anteroseptal breakthrough followed by eccentric ventricular front of activation occurring in the postero-lateral wall of the LV (example: Patients #2), ***(Figure 5)***

Dyssynchrony index

Dyssynchrony index is expressed by changes in ventricular electrical uncoupling (VEU) and summarized in ***Table 2, 3 and 4***. VEU was significantly improved during biventricular pacing (-17 ms, IQR -27 – -2) and AdaptivCRT (27 ms, IQR -31 – -21) when compared to intrinsic rhythm (53 ms, IQR -60 – -43), (p=0.01 and p=0.01, respectively).

Isochronal Surfaces

Very early activation

Areas of activation are expressed in percentage and summarized in ***Table 2, 3 and 4.***

There was a trend towards a larger area of biventricular activation <40 ms during intrinsic rhythm (52.6%, IQR 49.5 – 57.9) than during biventricular pacing (39.6%, IQR 30.8 – 55.8) or LV only pacing with AdaptivCRT algorithm (47.4%, IQR 42.6 – 52.0), (p=0.14 and p=0.11, respectively). Area of right ventricular activation <40 ms was larger during intrinsic rhythm (83.9%, IQR 81.1 – 91.0) than biventricular pacing (43.6%, IQR 22.0 – 77.2) or LV only pacing with AdaptivCRT (67.5%, IQR 59.6 – 78.5), (p<0.01 and p<0.01, respectively). Area of left ventricular activation <40 ms was smaller during intrinsic rhythm (25.7%, IQR 18.7 – 30.1) than biventricular pacing (38.8%, IQR 25.2 – 44.9). There was a trend towards a smaller area of LV activation <40 ms during intrinsic rhythm compared to AdaptivCRT (31.4%, IQR 25.0 – 38.5), (p=0.08).

Early Activation from 40 to 80 ms

Area of bi-ventricular activation from 40 to 80 ms was smaller during intrinsic rhythm (22.0%, IQR 18.9 – 27.5) than biventricular pacing (35.5%, IQR 28.9 – 42.5) or LV only pacing with AdaptivCRT (43.5%, IQR 31.2 – 49.5), (p<0.01 and p<0.01, respectively). Area of right ventricular activation from 40 to 80 ms was smaller during intrinsic rhythm (12.9%, IQR 8.2 – 18.1) than biventricular pacing (23.3%, IQR 20.7 – 36.5) or LV only pacing with AdaptivCRT (29.9%, IQR 17.3 – 40.3), (p=0.02 and p=0.02, respectively)

There was a trend towards smaller area of LV activation from 40 to 80 ms during intrinsic rhythm (28.4%, IQR 23.8 – 36.4) than biventricular pacing (39.9%, IQR 29.5 – 54.1), (p=0.06).

Area of LV activation from 40 to 80 ms during intrinsic rhythm was smaller than LV only pacing with AdaptivCRT algorithm (48.7%, IQR 39.1 – 60.7), (p<0.01). Areas of biventricular activation from 40 to 80 ms in intrinsic rhythm (17.1%, IQR 14.6 – 18.9) and biventricular pacing (20.2%, IQR 1.6 – 29.2) were not different (p=0.84).

Early Activation under 80 ms

Area of biventricular activation was smaller during intrinsic rhythm (74.3%, IQR67.3 – 79.4) than LV only pacing (88.6%, 83.4 – 95.4), (p<0.01). No statistical difference of biventricular activation was documented between intrinsic rhythm and biventricular pacing (78.9%, IQR 68.4 – 98.4), (p=0.42). Area of RV activation was larger during intrinsic rhythm (99.8%, IQR 97.1 – 100) than biventricular pacing (98.1%, IQR 64.6 – 98.3), (p=0.04). No statistical difference of RV activation was documented between intrinsic rhythm and LV only pacing (100%, IQR 95.6.4 – 100), (p=0.62). Area of LV activation was smaller during intrinsic rhythm (55.4%, IQR 44.9 – 60.0) than AdaptivCRT. There was a trend towards smaller area of LV activation during intrinsic rhythm (55.4%, IQR 44.6 – 60.0) than biventricular pacing (70.2%, IQR 57.3 – 80.3), (p=0.05). There was a trend towards larger area of biventricular activation during LV only (88.1%, IQR 83.4 – 95.4) pacing than biventricular pacing (78.9%, IQR 68.4 – 98.4), (p=0.11). RV activation was significantly larger during LV only pacing (100%, IQR 95.6 – 100) than biventricular pacing (89.1%, IQR 64.6 – 98.3), (p=0.03) than biventricular pacing. There was a trend towards larger area of LV activation during LV only pacing (82.1%, IQR 10.0 – 99.4) than biventricular pacing (70.2%, IQR 57.3 – 80.3).

Late and very late activations

There was a trend towards smaller area of bi-ventricular activation from 80 to 120 ms during intrinsic rhythm compared to LV only pacing with AdaptivCRT (8.7%, IQR 3.3 – 17.2), (p=0.08). Areas of right ventricular activation from 80 to 120 ms were smaller during intrinsic rhythm (0.1%, IQR 0 – 1.9) than biventricular pacing (10.9%, IQR 0.7 – 27.1), (p=0.03). Areas of RV activation during intrinsic rhythm and LV only pacing with AdaptivCRT (0.1%, IQR 0 – 1.3) were not different (p=0.44). There was a trend towards a larger area of left ventricular

activation from 80 to 120 ms during intrinsic rhythm (27.6%, IQR 23.1 – 35.1) than biventricular pacing (19.7%, IQR 2.0 – 30.6) or LV only pacing with AdaptivCRT (19.2%, IQR 1.3 – 31.2), (p=0.20 and p=0.15, respectively). No ventricular activation was observed over 120 ms during biventricular pacing and LV only pacing (AdaptivCRT).

Ventricular activation during biventricular pacing and AdaptivCRT

There was a trend towards larger area of RV activation <40 ms during LV only pacing with AdaptivCRT algorithm (67.5% IQR 59.6 – 78.5) compared to biventricular pacing (43.6% IQR 22.0 – 77.2), (p=0.13). There was a trend towards smaller area of LV activation <40 ms during LV only pacing with AdaptivCRT algorithm (31.4% IQR 25.0 – 38.5) compared to biventricular pacing (38.8% IQR 25.2 – 44.9), (p=0.17). There was a trend towards larger area of LV activation from 40 to 80 ms during LV only pacing with AdaptivCRT algorithm (48.7%, IQR 39.1 – 60.7) compared to biventricular pacing (39.9% IQR 29.5 – 54.1), (p=0.17). There was a trend towards larger area of biventricular activation <80 ms during LV only pacing (88.1%, IQR 83.4 – 95.4) than biventricular pacing (78.9%, IQR 68.4 – 98.4), (p=0.11). RV activation <80 ms was significantly larger during LV only pacing (100%, IQR 95.6 – 100) than biventricular pacing (89.1%, IQR 64.6 – 98.3), (p=0.03). There was a trend towards larger area of LV activation <80 ms during LV only pacing (82.1%, IQR 10.0 – 99.4) than biventricular pacing (70.2%, IQR 57.3 – 80.3). There was a trend towards smaller area of biventricular activation from 80 to 120 ms during LV only pacing with AdaptivCRT algorithm (8.7% IQR 3.3 – 17.2) compared to biventricular pacing (20.2%, IQR 1.6 – 29.2), (p=0.14). Area of RV activation from 80 to 120 ms was smaller during LV only pacing with AdaptivCRT algorithm (0.1%, IQR 0 – 1.3) than biventricular pacing (10.9%, IQR 0.7 – 27.1), (p=0.02).

CRT Response

Electrical and mechanical outcomes documented in CRT responders versus non-responders during intrinsic and paced rhythm are summarized in ***Table 5.*** CRT response was documented in 8 patients (67%), while 4 patients (33%) remained non-responders (patient #1, #6, #8, #12).

During intrinsic rhythm, there was a trend towards larger area of biventricular activation from 40 to 80 ms in patients who did not respond to CRT (25.3%, IQR 22.5 – 28.2), compared to responders (20.8%, IQR 16.5 – 23.4), (p=0.15)

During biventricular pacing, there was a trend towards smaller area of biventricular and RV activation from 40 to 80 ms in patients who did not respond to CRT (28.3%, IQR 25.8 – 32.5; 32.6%, IQR 26.5 – 39.8; respectively) than those who respond to CRT (39.7%, IQR 32.7 – 47.0; 46.5%, IQR 37.1 – 59.3; respectively), (p=0.21 and p=0.21, respectively). There was a trend towards smaller area of biventricular and RV activation from 40 to 80 ms in patients who did not respond to CRT (60.6%, IQR 54.7 – 72.4; 57.4%, IQR 46.9 – 74.1; respectively) than those who respond to CRT (88.4%, IQR 77.9 – 98.4; 96.7%, IQR 80.8 – 98.3; respectively), (p=0.17 and p=0.23, respectively). Patients who did not respond to CRT had longer LVTAT (89 ms, IQR 87 – 95) than those who respond to CRT (76 ms, IQR 74 – 83), during biventricular pacing (p=0.04).

During LV only pacing (AdaptivCRT), there was a trend towards larger area of RV activation from 80 to 120 ms in patients who did not respond to CRT (1.7%, IQR 0.3 – 4.4) than those who responded to CRT (0%, IQR 0 – 0.2), (p=0.08).

DISCUSSION

AdaptivCRT algorithm, a potential option to improve CRT response

Non response to CRT therapy remains an issue in daily practice and there was no clear improvement over the last few years. Numerous clinical situations may explain CRT failure consisting in atrial fibrillation with either electronic tachycardia or loss of biventricular capture, frequent premature ventricular beats, LV lead dysfunction and/or suboptimal positioning (17). Furthermore, causes for CRT failure may be more complex in advanced cardiomyopathies, including electrophysiological abnormalities with ventricular lines of block or slow conduction areas (18). To improve CRT response and efficacy, AdaptivCRT algorithm was developed and evaluated through a prospective and randomized trial. This study reported on the safety and non-inferiority of LV only pacing compared to biventricular pacing with echocardiographic optimization (19). Further study described a lower overall mortality and cardiac mortality in patients treated by AdaptivCRT (20). Furthermore, the use of the algorithm was associated with lower readmission rate after heart failure hospitalization, as well as lower risk of atrial fibrillation, as described in other studiers (10, 11, 21–23).

To our knowledge, this is the first study which compares ventricular activation sequences in patients treated either by conventional biventricular pacing, or fusion between right ventricular intrinsic conduction and LV only pacing, using the AdaptivCRT algorithm. Thanks to the CardioInsight technology (ECVUE, CardioInsight Technologies Inc, Medtronic), our study describes the precise electrical activation patterns of patients with typical LBBB who are treated either by conventional biventricular pacing or LV only pacing (AdaptivCRT).

Dyssynchrony index according to ventricular rhythm

QRS duration reflects total ventricular activation but does not provide information about intra right or LV dyssynchrony, as well as dyssynchrony between RV and LV. Biventricular pacing and LV only pacing both reduced QRS duration but no statistical difference was observed between these two pacing modes. We did not documented any difference of QRS duration

between CRT responders and those who did not respond to CRT neither during intrinsic rhythm nor biventricular pacing, nor LV only pacing.

In our study we did consider VEU to analyze dyssynchrony, a parameter which was already used in previous trials (18, 24). Ploux and colleagues observed that VEU was strongly associated with CRT clinical response and a more powerful predictor than 12-lead ECG (25). In our study, the median VEU was -53 ms (IQR -60 – -43) in patients with LBBB while the mean VEU was -76±24 in previous study (18). We documented a median VEU of -27 ms (IQR -31 – -21) during biventricular pacing when Varma and colleagues reported a "comparable" mean value of -31±32 (18). In our study, biventricular pacing and LV only pacing both improved the VEU dyssynchrony index, traducing improvement on ventricular synchrony. No statistical difference was observed in the median VEU between biventricular pacing or LV only pacing, suggesting a comparable impact achieved by these two different pacing modes. Furthermore, we did not observed any difference of VEU index between CRT responders and non-responders neither during intrinsic rhythm nor biventricular pacing, nor LV only pacing. VEU remains a controversial dyssynchrony index. According to Varma and colleagues, this index did not predict CRT clinical response and did correlate to QRS duration (18).

Changes in ventricular activation patterns and isochronal surfaces

Ventricular activation during intrinsic rhythm

Patients with typical LBBB had a uniform pattern of ventricular activation, resulting in a "U-shaped" activation wave front from the RV anteroseptal area to the postero-lateral LV wall. This pattern has already been observed in previous studies, using endocardial or epicardial approach. (14, 24, 26, 27)

Dyssynchronization seemed to be linked to LV activation pattern because different areas of activation were observed over time in the LV, suggesting intraventricular dyssynchrony ***(Figure 6)***. RV activation pattern was not dyssynchronized, suggesting interventricular uncoupling from the LV ***(Figure 7 and 8)***. Our study documented that very early activation was linked to the right

ventricle process during intrinsic rhythm, while LV activation was not involved **(Figure 3, 6, 7 and 8).**

Otherwise CRT responders seemed to be more dyssynchronized during intrinsic rhythm than those who did not respond to CRT **(Table 5).** This latter suggests that responders to CRT were more likely to benefit from CRT possibly due to higher dyssynchronization at baseline. Varma and colleagues observed regions of slow conduction and lines of slow conduction from base to apex orientation in LBBB patients, a process that may delay LV activation. Number and characteristic of these functional lines may differ according to the cardiac underlying disease. These individual variations might explain the various clinical benefits observed during CRT (18).

Ventricular activation during biventricular pacing

We observed different patterns of activation during biventricular pacing. Initial breakthrough started at the RV apex or the RV lateral wall. Electrical activation and isochrone maps showed heterogeneous RV activation during biventricular pacing. Previous studies reported that electrical and mechanical activation sequences during biventricular pacing were patient specific (28, 29).

Furthermore, biventricular areas were less dyssynchronized in patients with biventricular pacing than those with intrinsic rhythm ***(Figure 6)***. Biventricular pacing improved ventricular synchrony by lowering LV late activation. Thus, improvement of cardiac resynchronization seems to be linked with resynchronization of LV activation ***(Figure 8).*** On the other hand, RV activation was slower and delayed when compared to intrinsic rhythm ***(Figure 7).***

Otherwise, CRT non-responders still had late activation during biventricular pacing. CRT response could be improved by an increase of very early activation areas or a reduction of late activation ***(Table 5).*** This latter suggests that good understanding of the electrophysiological substrate appears to be of major importance to improve CRT response.

LV only pacing activation pattern (AdaptivCRT)

Patients with LV only pacing have an initial breakthrough in the RV anteroseptal area, followed by ventricular activation in the LV postero-lateral wall. This sequence suggests a natural activation through the His Purkinje system together with proper LV pacing from a delayed activated area. We also documented homogeneous RV activation during LV only pacing, similar to what is observed at baseline with LBBB.

RV activation seemed to be more uniform and began much earlier, as suggested by a higher percentage of early activation < 80 ms during LV only pacing when compared to biventricular pacing ***(Table 4).*** This latter suggests a faster and homogeneous RV activation in patient with LV only pacing ***(Figure7).*** In the study by Varma, RV activation was delayed during RV pacing or biventricular pacing, but not during to intrinsic rhythm or LV only pacing (30). In our study, patients with LV only pacing had similar benefits on LV synchrony than those with biventricular pacing ***(Figure 8).***

Otherwise, we did not observed electrical difference between patients who responded to CRT and those who did not responded to CRT during LV only pacing ***(Table 5).*** Dissociation between clinical response and electrical outcomes could be explained by dissociation between electrical and mechanical activation. Relationships between mechanical and electrical activation remain complex. Dawoud and colleagues used non-invasive cardiac mapping and cardiac magnetic resonance tissue tracking to evaluate LV dyssynchrony (31). In their study, a small minority of CRT non responder had discordance between electrical and mechanical activation.

Perspectives and additional benefit

This study shows that effective resynchronization can be achieved during either biventricular pacing or LV only pacing. AdaptivCRT allows proper CRT delivery using automatic adaptation of LV only pacing. Furthermore, the use of natural intrinsic conduction, cycle by cycle, rather than RV pacing, may be helpful to improve battery longevity. These strategies of non-invasive cardiac imaging could be useful for selected patients with heart failure but are complex and not without cost (32).

LIMITATIONS

Our study is limited by a small number of subjects and may not characterize typical patients implanted with a CRT device. Observation of ventricular activation was performed at different times intervals after CRT device implantation and LV reverse remodeling may differ between patients. Isochrone maps and ECVUE provide epicardial activation data without any information on endocardial or septal activation.

CONCLUSION

Non-invasive cardiac mapping is helpful to reach a better understanding of CRT delivery, and to analyze the mechanisms of CRT failure. Our study documented uniform patterns of ventricular activation in patients with LBBB with intraventricular and interventricular dyssynchrony. RV activation is heterogeneous during biventricular pacing and homogeneous during both intrinsic rhythm and LV only pacing (AdaptivCRT). The RV activation process seems to be of key importance to reach biventricular very early (40 ms) activation. Left ventricular activation is similar during biventricular pacing and LV only pacing (AdaptivCRT). Biventricular pacing and AdaptivCRT are both capable to correct for the late LV segmental activation usually observed during intrinsic rhythm. AdaptivCRT allows for more homogeneous RV activation than biventricular pacing, while keeping similar benefits on left ventricular activation patterns together with potential additional battery longevity

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Figure legends

Figure 1: AdaptivCRT Algorithm (Gerasimos Filippatos and al)

Figure 2: Flow chart

Figure 3: Epicardial activation and isochrone maps in patient #4 with intrinsic rhythm.

Figure 4: Epicardial activation and isochrone maps in patient #2, #7 and #8 with bi-ventricular pacing.

Figure 5: Epicardial activation and isochrone maps in patient #2 with LV-pacing only (AdaptivCRT).

Figure 6: Area of biventricular depolarisation according to ventricular rhythm

Figure 7: Area of right ventricular depolarisation according to ventricular rhythm

Figure 8: Area of left ventricular depolarisation according to ventricular rhythm

Table 1: Baseline characteristics

	#1	#2*	#3*	#4*	#5*	#6	#7*	#8	#9*	#10*	#11*	#12	
Age	56	69	68	79	64	62	61	67	54	69	74	77	67.7 (IQR 61.8-70.3)
Man	N	Y	Y	N	N	Y	Y	Y	N	Y	N	Y	7/12 (58%)
Ischaemic cardiomyopathy	N	Y	N	N	N	N	N	N	N	N	N	N	1/12 (8%)
Non ischemic cardiomyopathy	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11/12 (92%)
NYHA pre CRT	2	2	2	3	3	2	3	2	3	2	3	2	-
NYHA post CRT	1	1	1	1	2	2	2	2	2	1	1	1	-
Diabetes melitus	Y	Y	N	N	N	Y	N	N	N	N	Y	N	4/12 (33%)
Tabaco	Y	Y	N	N	Y	N	N	Y	Y	N	N	N	5/12 (42%)
HTA	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	10/12 (83%)
LV lead position	LB	LM	LB	LB	LM	LM	LM	LB	LB	LB	LM	LM	-
LVEF (%) before CRT	31	19	32	34	17	25	34	23	34	24	34	20	28.0 (IQR 22.3-34.0)
LVEF (%) after CRT	36	29	55	50	33	26	45	34	45	53	50	25	40.5 (IQR 32.0-50.0)
VTDVG index	77	83	49	56	45	18	53	64	52	54	46	74	53.5 (IQR 48.3-66.5)
TAPSE (mm)	17	22	22	18	17	20	21	21	24	20	17	19	20,0 (IQR 17.8-21.3)
Loop Diuretics	Y	Y	N	N	N	N	N	Y	Y	Y	Y	Y	7/12 (58%)
CRT Responder	N	Y	Y	Y	Y	N	Y	N	Y	Y	Y	N	8/12 (67%)

Patients with (*) are CRT responders whereas the other are not.

Table 2: Electrical and mechanical outcomes between patients with intrinsic rhythm and biventricular pacing

	Intrinsic Rhythm (median, IQR)	Biventricular pacing (median, IQR)	p
QRSd (ms)	149 (142 – 159)	98 (89 – 111)	<0.01
RVTAT (ms)	43 (36 – 54)	70 (51 – 79)	0.03
LVTAT (ms)	97 (81 – 108)	83 (75 – 88)	0.03
VEU (ms)	-53 (-60 – -44)	-17 (-27 – -2)	<0.01
Area (%) of Ventricular activation < 40 ms	52.6 (49.5 – 57.9)	39.6 (30.8 – 55.8)	0.14
Area (%) of Ventricular activation from 40 to 80ms	22.0 (18.9 – 27.5)	35.5 (28.9 – 42.5)	<0.01
Area (%) of Ventricular activation < 80 ms	74.3 (67.3-79.4)	78.9 (68.4-98.4)	0.42
Area (%) of Ventricular activation from 80 to 120 ms	17.1 (14.6 – 18.9)	20.2 (1.6 – 29.2)	0.84
Area (%) of Ventricular activation >120 ms	7.6 (3.8 – 15.6)	0 (0 – 0)	<0.01
Area (%) of RV activation < 40ms	83.9 (81.1 – 91.0)	43.6 (22.0 – 77.2)	<0.01
Area(%) of RV activation from 40 to 80 ms	12.9 (8.2 – 18.1)	23.3 (20.7 – 36.5)	0.02
Area(%) of RV activation < 80 ms	99.8 (97.1-100)	89.1 (64.6-98.3)	0.04
Area (%) of RV activation from 80 to 120 ms	0.1 (0 – 1.9)	10.9 (0.7 – 27.1)	0.03
Area (%) of RV of activation >120 ms	0 (0 – 0)	0 (0 – 0)	0.79
Area (%) of LV activation < 40ms	25.7 (18.7 – 30.1)	38.8 (25.2 – 44.9)	<0.01
Area (%) of LV activation from 40 to 80 ms	28.4 (23.8 – 36.4)	39.9 (29.5 – 54.1)	0.06
Area (%) of LV activation < 80ms	55.4 (44.9-60.0)	70.2 (57.3-80.3)	0.05
Area (%) of LV activation 80 to 120 ms	27.6 (23.1 – 35.1)	19.7 (2.0 – 30.6)	0.20
Area(%) of LV activation >120 ms	14.8 (6.9 – 30.0)	0 (0 – 0)	<0.01

Table 3: Electrical and mechanical outcomes between patients with intrinsic rhythm and AdaptivCRT

	Intrinsic Rhythm (median, IQR)	AdaptivCRT (median, IQR)	p
QRSd (ms)	149 (142 – 159)	107 (98 – 111)	<0.01
RVTAT (ms)	43 (36 – 54)	64 (48 – 70)	0.06
LVTAT (ms)	97 (81 – 108)	82 (73 – 96)	0.05
VEU (ms)	-53 (-60 – -44)	-27 (-31 – -21)	<0.01
Area (%) of Ventricular activation < 40 ms	52.6 (49.5 – 57.9)	47.4 (42.6 – 52.0)	0.11
Area (%) of Ventricular activation from 40 to 80ms	22.0 (18.9 – 27.5)	43.5 (31.2 – 49.5)	<0.01
Area (%) of Ventricular activation < 80 ms	74.3 (67.3-79.4)	88.6 (83.4-95.4)	<0.01
Area (%) of Ventricular activation from 80 to 120 ms	17.1 (14.6 – 18.9)	8.7 (3.3 – 17.2)	0.08
Area (%) of Ventricular activation >120 ms	7.6 (3.8 – 15.6)	0 (0 – 0)	<0.01
Area (%) of RV activation < 40ms	83.9 (81.1 – 91.0)	67.5 (59.6 – 78.5)	<0.01
Area(%) of RV activation from 40 to 80 ms	12.9 (8.2 – 18.1)	29.9 (17.3 – 40.3)	0.02
Area(%) of RV activation < 80 ms	99.8 (97.1-100)	100 (95.6-100)	0.62
Area (%) of RV activation from 80 to 120 ms	0.1 (0 – 1.9)	0.1 (0 – 1.3)	0.44
Area (%) of RV of activation >120 ms	0 (0 – 0)	0 (0 – 0)	0.37
Area (%) of LV activation < 40ms	25.7 (18.7 – 30.1)	31.4 (25 – 38.5)	0.08
Area (%) of LV activation from 40 to 80 ms	28.4 (23.8 – 36.4)	48.7 (39.1 – 60.7)	<0.01
Area (%) of LV activation < 80ms	55.4 (44.9-60.0)	82.1 (70.0-99.4)	<0.01
Area (%) of LV activation 80 to 120 ms	27.6 (23.1 – 35.1)	19.2 (1.3 – 31.2)	0.15
Area(%) of LV activation >120 ms	14.8 (6.9 – 30.0)	0 (0 – 0)	<0.01

Table 4: Electrical and mechanical outcomes between patients with biventricular pacing and AdaptivCRT

	Biventricular pacing (median, IQR)	AdaptivCRT (median, IQR)	p
QRSd (ms)	98 (89 – 111)	108 (96 – 119)	0.09
RVTAT (ms)	70 (51 – 79)	64 (48 – 70)	0.27
LVTAT (ms)	83 (75 – 88)	82 (73 – 96)	0.86
VEU (ms)	-17 (-27 – -2)	-27 (-31 – -21)	0.10
Area (%) of Ventricular activation < 40 ms	39.6 (30.8 – 55.8)	47.4 (42.6 – 52.0)	0.45
Area (%) of Ventricular activation from 40 to 80ms	35.5 (28.9 – 42.5)	43.5 (31.2 – 49.5)	0.30
Area (%) of Ventricular activation < 80 ms	78.9 (68.4-98.4)	88.6 (83.4-95.4)	0.11
Area (%) of Ventricular activation from 80 to 120 ms	20.2 (1.6 – 29.2)	8.7 (3.3 – 17.2)	0.14
Area (%) of Ventricular activation >120 ms	0 (0 – 0)	0 (0 – 0)	-
Area (%) of RV activation < 40ms	43.6 (22.0 – 77.2)	67.5 (59.6 – 78.5)	0.13
Area(%) of RV activation from 40 to 80 ms	23.3 (20.7 – 36.5)	29.9 (17.3 – 40.3)	0.90
Area(%) of RV activation < 80 ms	89.1 (64.6-98.3)	100 (95.6-100)	0.03
Area (%) of RV activation from 80 to 120 ms	10.9 (0.7 – 27.1)	0.1 (0 – 1.3)	0.02
Area (%) of RV of activation >120 ms	0 (0 – 0)	0 (0 – 0)	-
Area (%) of LV activation < 40ms	38.8 (25.2 – 44.9)	31.4 (25.0 – 38.5)	0.17
Area (%) of LV activation from 40 to 80 ms	39.9 (29.5 – 54.1)	48.7 (39.1 – 60.7)	0.17
Area (%) of LV activation < 80ms	70.2 (57.3-80.3)	82.1 (70.0-99.4)	0.05
Area (%) of LV activation 80 to 120 ms	19.7 (2.0 – 30.6)	19.2 (1.3 – 31.2)	0.85
Area(%) of LV activation >120 ms	0 (0 – 0)	0 (0 – 0)	-

Table 5: Electrical and mechanical outcomes in CRT responders versus non-responders according to underlying intrinsic or paced rhythm

	Intrinsic rhythm			Biventricular Pacing			AdaptivCRT		
	CRT Non Responders (median, IQR) N=4	CRT Responders (median, IQR) N=8	p	CRT Non Responders (median, IQR) N=4	CRT Responders (median, IQR) N=8	p	CRT Non Responders (median, IQR) N=4	CRT Responders (median, IQR) N=8	p
QRSd (ms)	149 (143-159)	149 (142-159)	1	106 (101-111)	90 (87-111)	0.50	103 (91-116)	108 (100-119)	0.56
RVTAT (ms)	48.5 (45.25-53.0)	39 (29-52)	0.28	70 (64-84)	62 (46-79)	0.50	64 (60-67)	59 (47-71)	0.79
LVTAT (ms)	101 (96-103)	89 (78-121)	0.68	89 (87-95)	77 (74-83)	0.04	90 (82-95)	77 (73-98)	0.93
VEU (ms)	-46 (-51 – -44)	-58 (-65 – -45)	0.50	-17 (-24 – -8)	-15 (-28 – -2)	0.79	-22 (-26 – -20)	-30 (-32 – -22)	0.44
Area (%) of Ventricular activation < 40 ms	50.0 (48.5- 52.1)	55.0 (51-58)	0.39	28.9 (23.4-42.1)	45.6 (34-55.8)	0.36	50.3 (44.9-53.8)	46.2 (42.3-51.1)	0.46
Area (%) of Ventricular activation from 40 to 80ms	25.3 (22.5-28.2)	20.8 (16.5-23.4)	0.15	28.3 (25.8-32.5)	39.7 (32.7-47.0)	0.21	43.5 (37.0-47.5)	41.2 (31.2-51.1)	0.80
Area (%) of Ventricular activation < 80 ms	78.6 (75.2-79.4)	73.3 (66.8-76.2)	0.57	60.6 (54.7-72.4)	88.4 (77.9-98.4)	0.17	91.0 (83.5-96.9)	88.1 (83.4-95.4)	0.80
Area (%) of Ventricular activation from 80 to 120 ms	16.9 (15.3-17.4)	17.7 (14.5-21.2)	0.61	40.5 (28.9-44.6)	12.0 (1.6-21.7)	0.17	11.2 (7.4-16.5)	7.6 (0.9-17.2)	0.56
Area (%) of Ventricular activation >120 ms	5.0 (3.8-10.2)	11.6 (3.5-15.6)	1	0 (0-1.05)	0 (0-0)	-	0 (0-0)	0 (0-0)	-
Area (%) of RV activation < 40ms	83.2 (78.7-88.1)	85.6 (81.9-91.0)	0.69	31.6 (19.4-51.6)	60.6 (25.2-78.1)	0.36	64.95 (60.7-69.5)	72.0 (56.9-80.9)	0.68
Area(%) of RV activation from 40 to 80 ms	13.9 (7.6-21.1)	12.9 (8.2-15.8)	0.56	22.1 (20.7-25.5)	29.9 (19.4-41.7)	0.46	30.8 (25.8-36.8)	28.1 (12.7-43.0)	0.80
Area(%) of RV activation < 80 ms	99.8 (98.4-99.9)	99.5 (97.1-100)	0.46	57.4 (46.9-74.1)	96.7 (80.8-98.3)	0.23	98.4 (95.6-99.9)	100 (95.6-100)	0.47
Area (%) of RV activation from 80 to 120 ms	0.2 (0-19)	0.1 (0-1.9)	1	44 (26.7-52.9)	5.7 (0.7-15.1)	0.14	1.7 (0.3-4.4)	0(0-0.2)	0.08
Area (%) of RV of activation >120 ms	0 (0-0.05)	0 (0-0)	1	0 (0-0.2)	0 (0-0)	-	0 (0-0)	0 (0-0)	-
Area (%) of LV activation < 40ms	23.5 (19.8-27.4)	25.7 (18.5-32.1)	0.93	28.9 (23.8-39.5)	39.1 (35.0-44.9)	0.46	37.1 (32.9-39.57)	27.0 (22.0-38.2)	0.36
Area (%) of LV activation from 40 to 80 ms	32.2 (27.3-38.5)	26.7 (22.0-34.7)	0.46	32.6 (26.5-39.8)	46.5 (37.1-59.3)	0.21	48.2 (36.5-59.9)	48.7 (43.8-60.7)	0.68
Area (%) of LV activation < 80ms	60.3 (54.1-63.5)	51.2 (44.8-56.6)	0.56	64.4 (50.3-82.2)	90.9 (77.3-98.1)	0.30	88.3 (72.1-99.7)	79.9 (70.0-99.0)	0.57
Area (%) of LV activation 80 to 120 ms	27.6 (22.7-32.1)	28.4 (23.1-37.4)	0.80	35.7 (17.9-48.0)	11.2 (2.0-23.4)	0.30	19.2 (11.6-27.9)	20.7 (1.3-31.2)	0.93
Area(%) of LV activation >120 ms	9.3 (7.4-17.8)	22.2 (6.25-30.0)	1	0 (0-1.7)	0 (0-0)	-	0 (0-0)	0 (0-0)	-

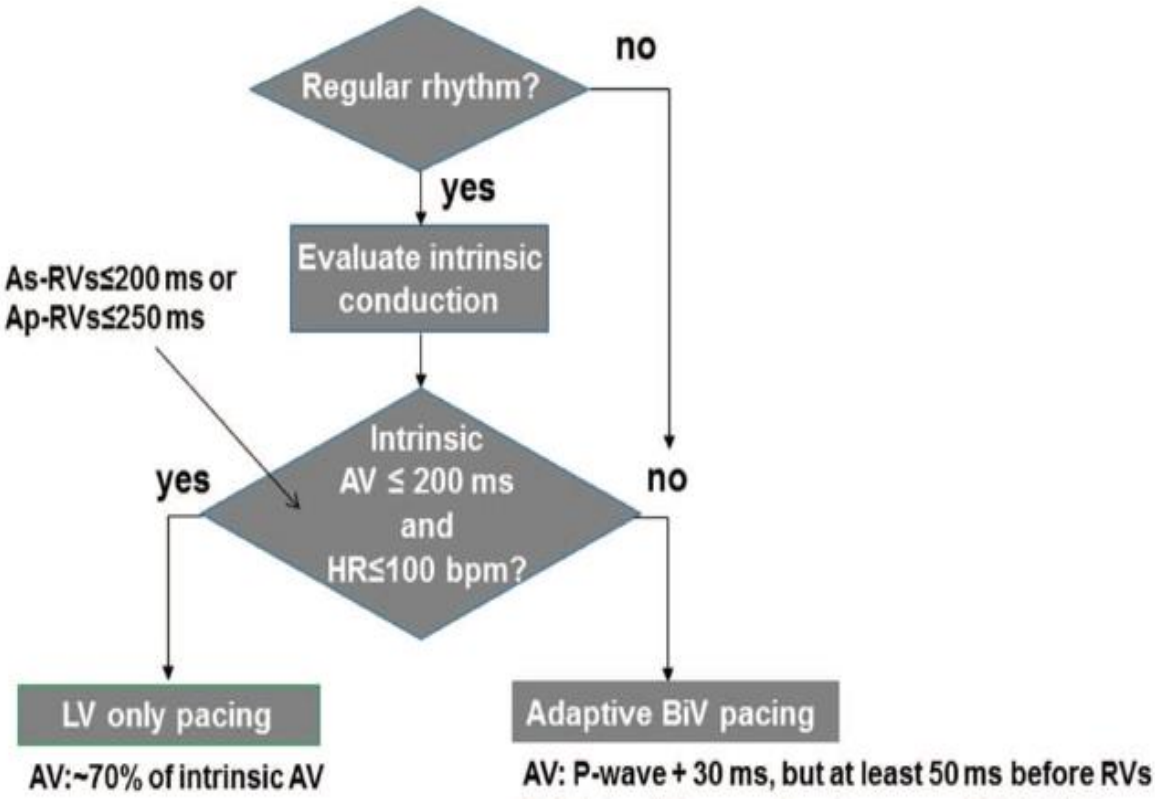

Figure 1: AdaptivCRT algorithm (Gerasimos Filippatos and colleagues)

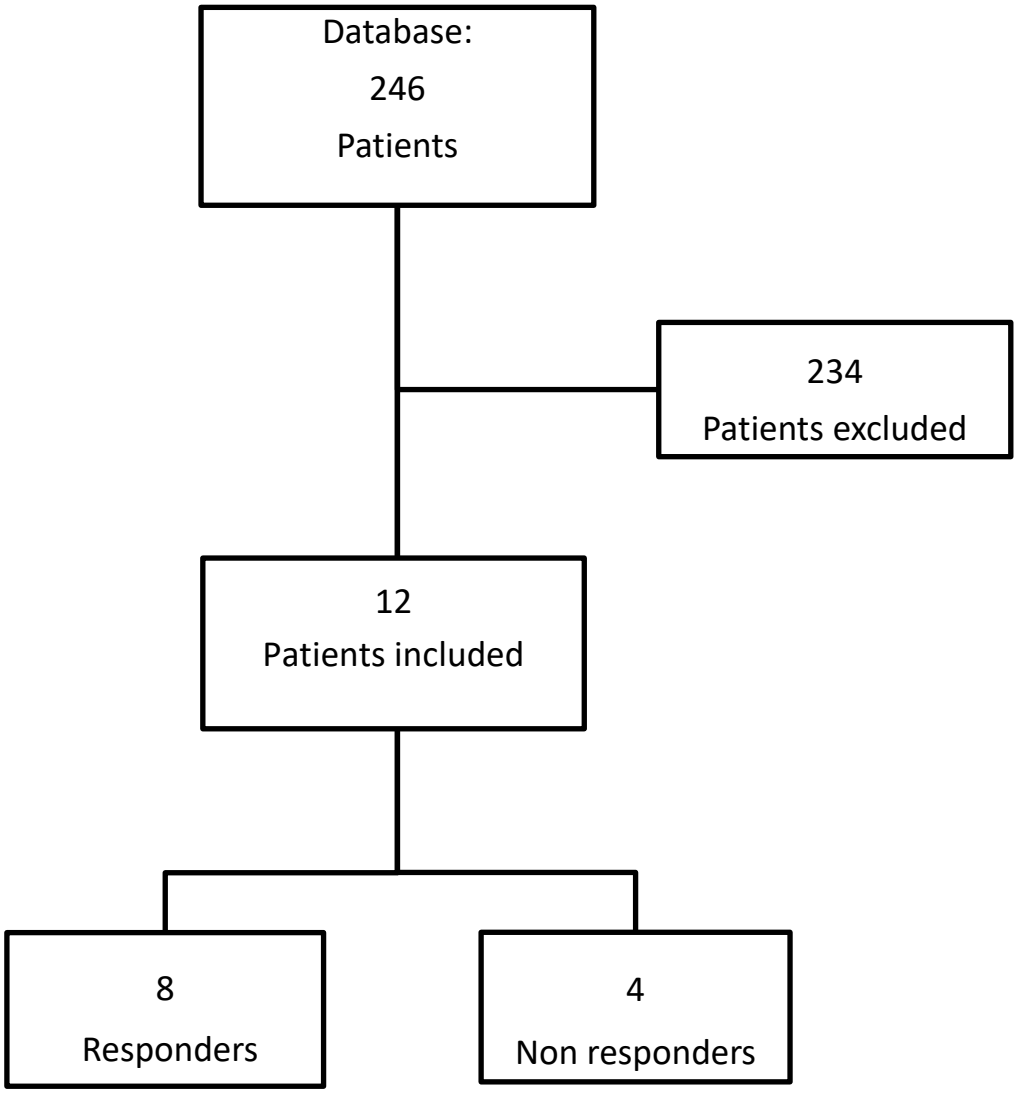

Figure 2: Flow chart

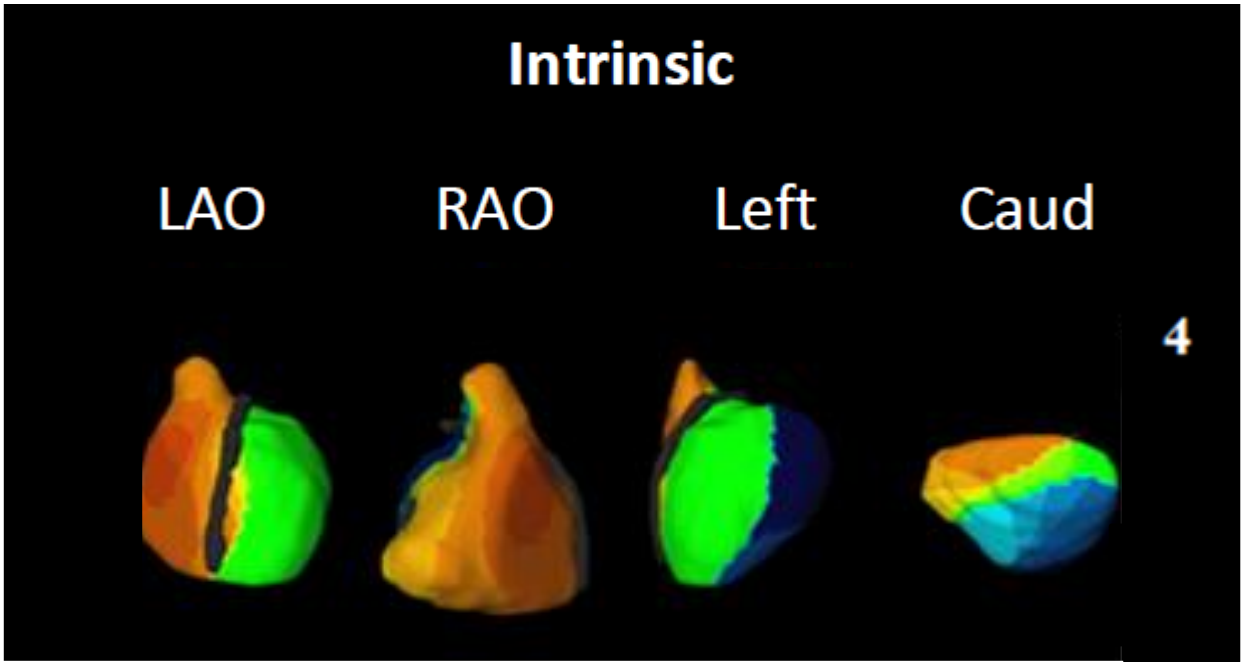

Figure 3: Epicardial activation and isochrone maps of patient #4 with LBBB intrinsic rhythm.

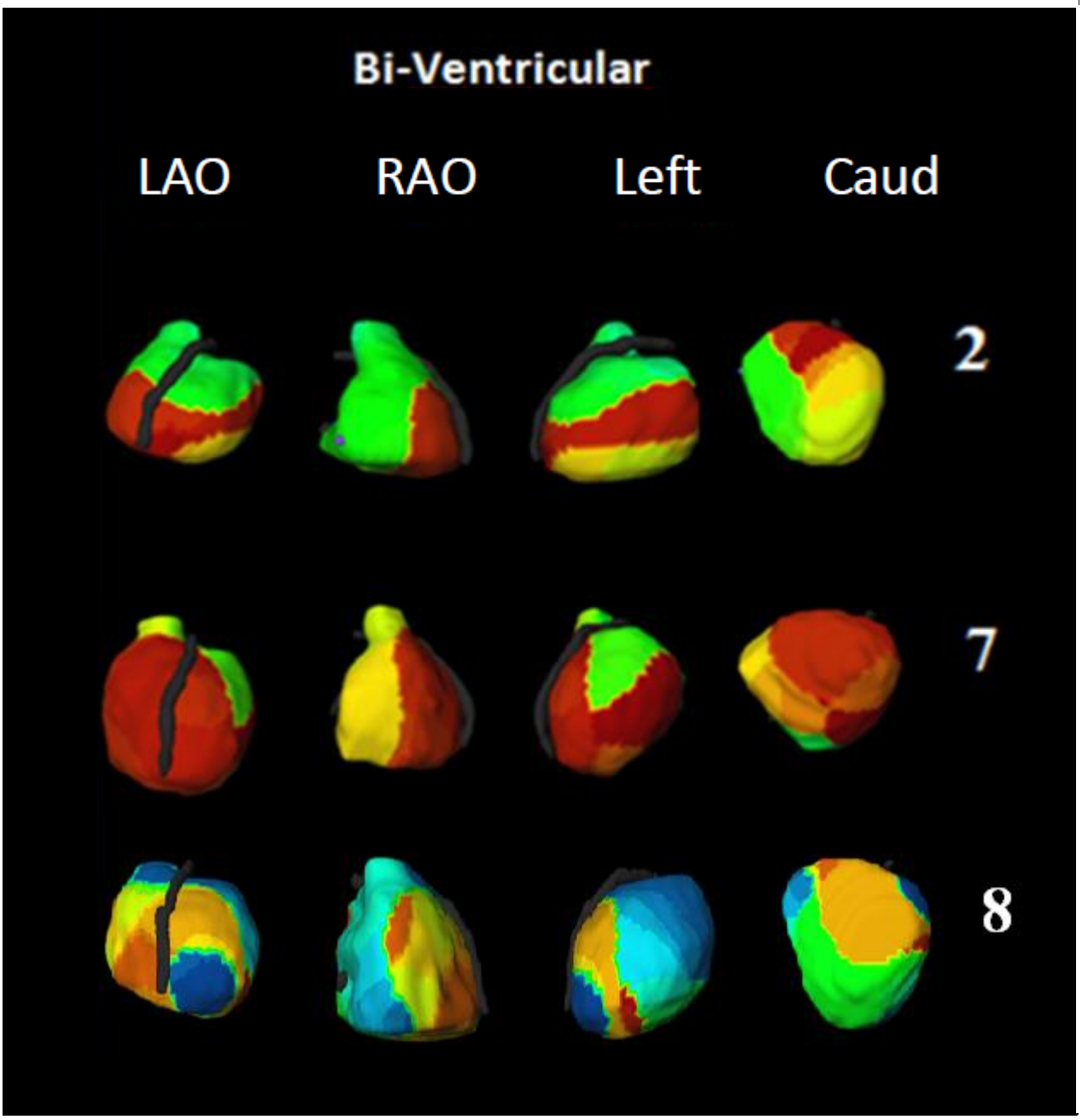

Figure 4: Epicardial activation and isochrone maps of patient #2, #7 and #8 with biventricular pacing.

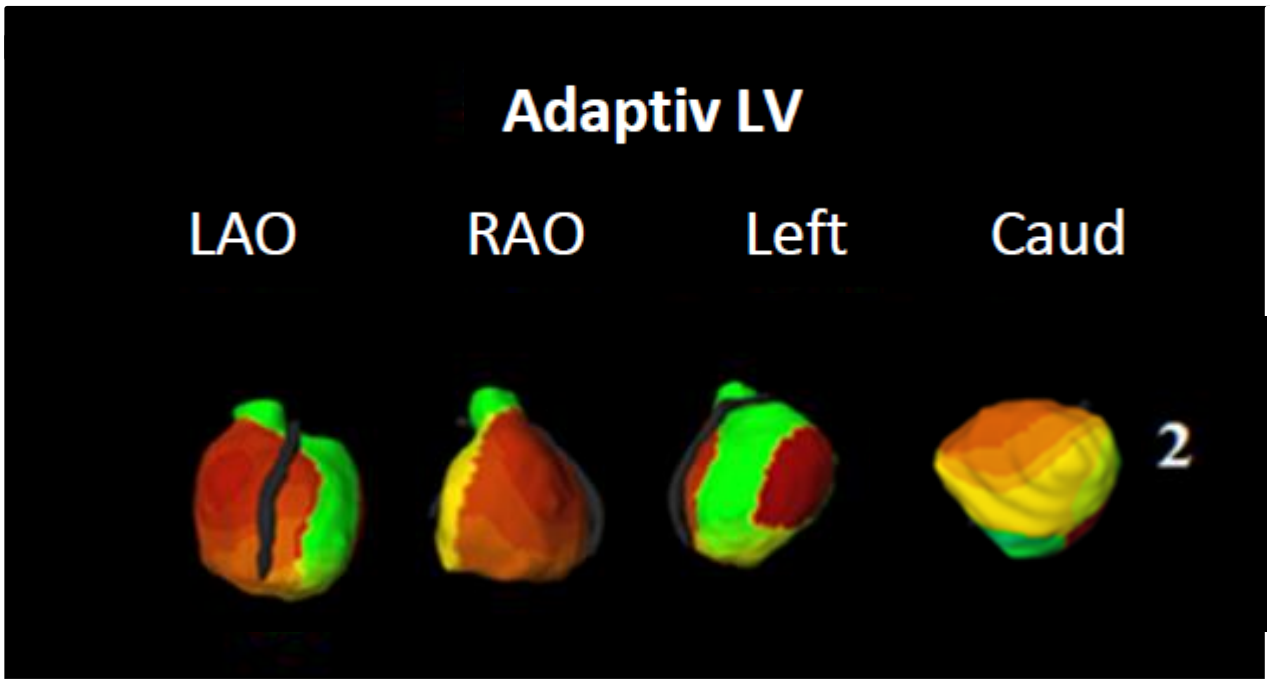

Figure 5: Epicardial activation and isochrone maps of patient #2 with LV only pacing (AdaptivCRT).

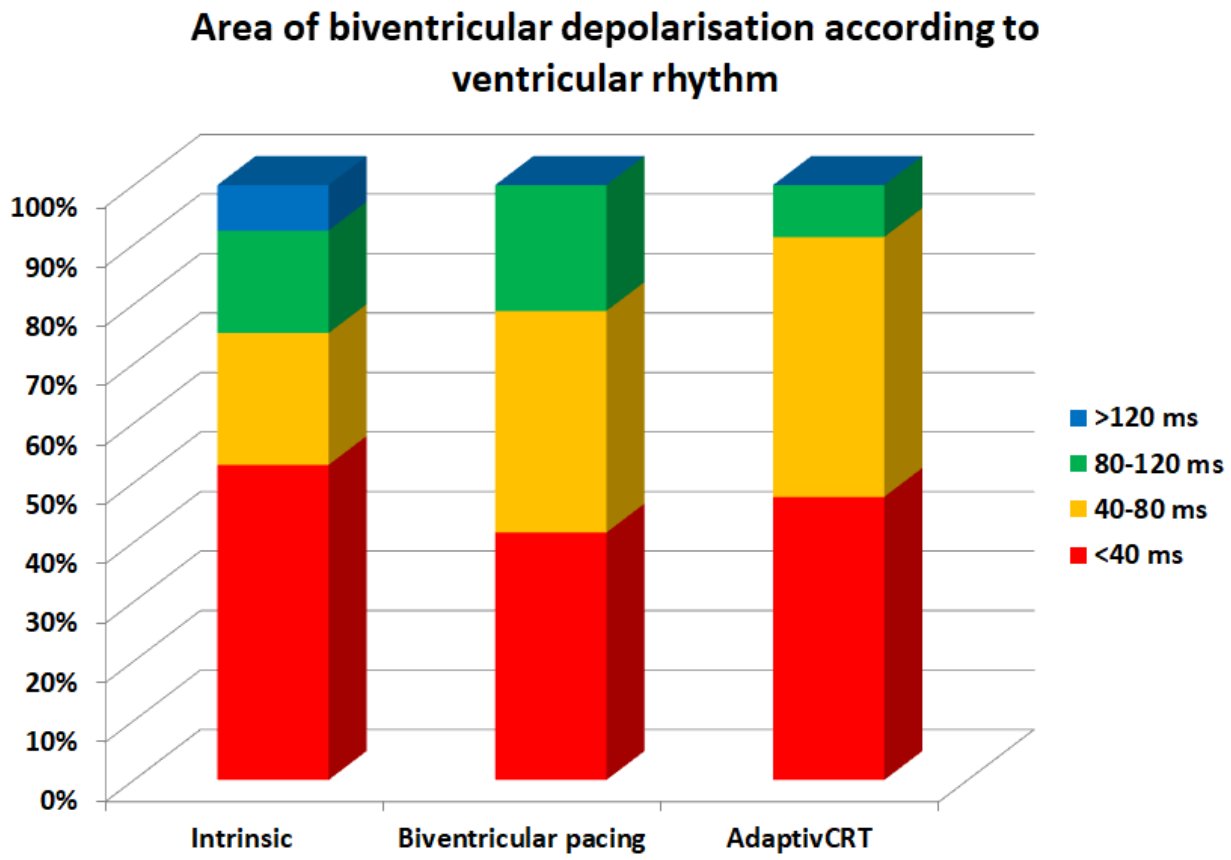

Figure 6: Area of biventricular depolarisation according to ventricular rhythm

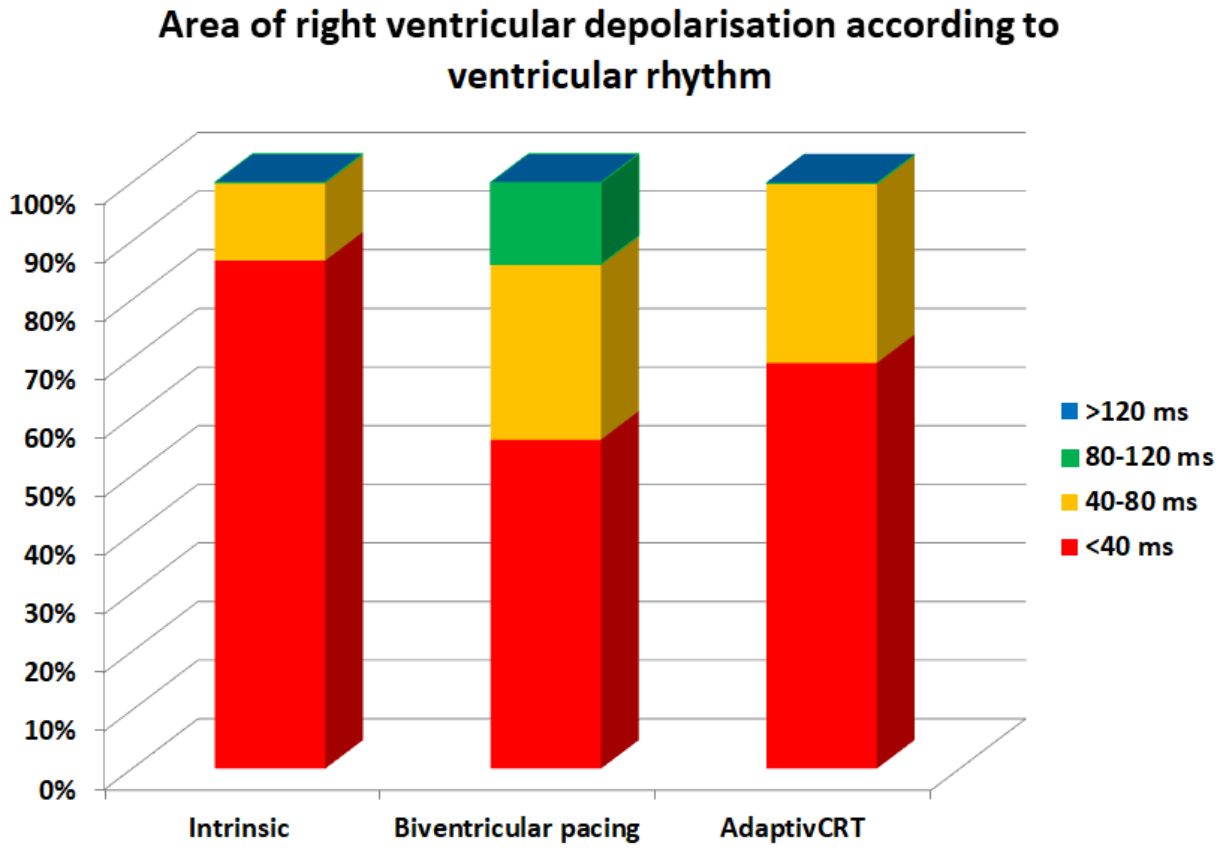

Figure 7: Area of right ventricular depolarisation according to ventricular rhythm

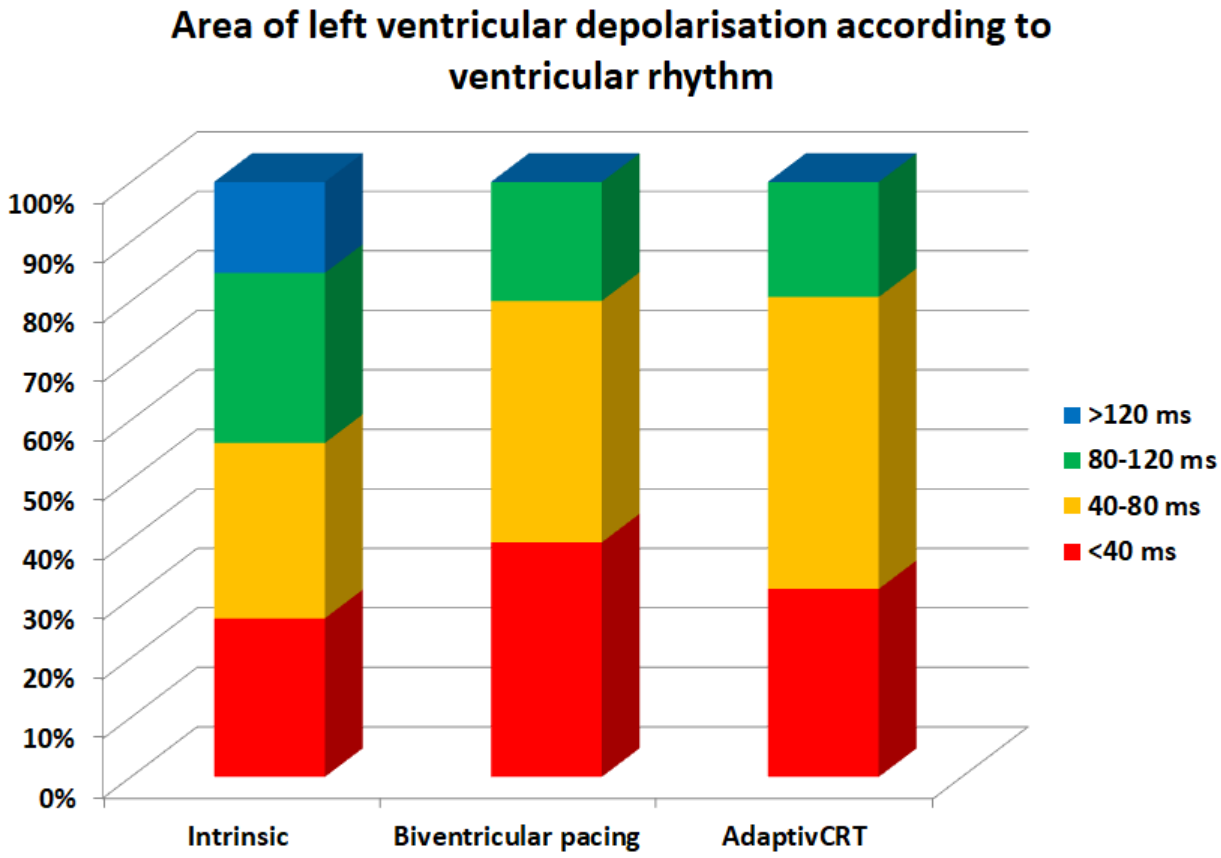

Figure 8: Area of left ventricular depolarisation according to ventricular rhythm

SUPPLEMENTAL DATAS

Table 6: Electrical outcomes of patients with intrinsic rhythm

	#1	#2*	#3*	#4*	#5*	#6	#7*	#8	#9*	#10*	#11*	#12
QRSd (ms)	134	146	174	144	136	146	152	180	129	154	182	152
RVAT (ms)	46	41	76	18	13	51	37	43	32	44	118	63
LVAT (ms)	88	79	146	82	70	99	95	102	112	112	164	107
VEU (ms)	-42	-38	-70	-64	-57	-48	-58	-59	-42	-68	-46	-44
Area (%) of Ventricular activation < 40 ms	57.9	56.6	48.1	40.0	58.2	50.1	57.9	44.3	51.9	60.4	53.2	49.9
Area (%) of Ventricular activation from 40 to 80ms	21.9	30.6	15.8	27.4	16.7	27.8	22.1	22.7	21.8	4.6	19.7	29.3
Area (%) of Ventricular activation < 80 ms	79.8	87.2	63.9	67.4	74.9	77.9	80.0	67.0	73.7	65.0	72.9	79.2
Area (%) of Ventricular activation from 80 to 120 ms	17.1	10.7	15.8	17.1	22.5	18.1	18.2	11.1	10.5	34.8	20.8	16.7
Area (%) of Ventricular activation >120 ms	3.3	0.8	20.6	15.5	4.0	4.0	1.8	22.6	15.8	14.0	9.2	6.0
Area (%) of RV activation < 40ms	96,0	82.1	76.2	82.2	92.6	72.3	89.0	80.8	81.2	94.0	90.4	85.5
Area(%) of RV activation from 40 to 80 ms	4.0	17.9	15.1	14.7	7.4	27.4	11.0	19.0	18.8	3.2	8.5	8.8
Area(%) of RV activation < 80 ms	100	100	91.3	96.9	100	99.7	100	99.8	100.0	97.2	98.9	94.3
Area (%) of RV activation from 80 to 120 ms	0	0	9.6	0.1	0	0.3	0	0	0	2.7	1.6	6.6
Area (%) of RV of activation >120 ms	0	0	0	3.0	0	0	0	0.2	0	0	0	0
Area (%) of LV activation < 40ms	26.6	31.6	26.1	1.0	33.9	29.6	25.3	18.4	17.4	33.6	18.8	20.3
Area (%) of LV activation from 40 to 80 ms	36.1	44.5	19.5	37.3	21.1	28.3	33.8	24.3	24.9	22.2	28.5	45.7
Area (%) of LV activation < 80ms	62.7	76.1	45.6	38.3	55.0	57.9	59.1	42.7	42.3	55.8	47.3	66.0
Area (%) of LV activation 80 to 120 ms	31.3	23.4	19.5	37.4	40.3	34.4	37.2	19.3	22.5	23.3	38	23.8
Area(%) of LV activation >120 ms	6.1	1.6	37.8	28.3	7.1	7.8	3.7	39.7	35.2	25.5	18.8	10.7

Patients with (*) are CRT responders whereas the other are not.

Table 7: Electrical outcomes of patients with Bi-ventricular pacing

	#1	#2*	#3*	#4*	#5*	#6	#7*	#8	#9*	#10*	#11*	#12
QRSd (ms)	90	109	118	85	90	120	87	104	91	80	122	108
RVAT (ms)	73	80	73	33	51	115	79	66	38	49	87	58
LVAT (ms)	85	82	76	59	87	109	77	88	71	75	89	89
VEU(ms)	-12	-2	-3	-26	-36	6	2	-22	-33	-26	-2	-31
Area (%) of Ventricular activation < 40 ms	69.5	44.8	34.4	58.0	46.4	24.8	23.4	19	79.6	55.1	32.8	32.9
Area (%) of Ventricular activation from 40 to 80ms	30.5	33.6	63.1	42	29.8	38.4	55.9	26.1	18.6	44	37.3	25
Area (%) of Ventricular activation < 80 ms	100	78.4	97.5	100	76.2	63.2	79.3	45.1	98.2	99.1	70.1	57.9
Area (%) of Ventricular activation from 80 to 120 ms	0	22.9	5	0	26.1	38.5	21.3	50.7	1.8	0.9	19	42.5
Area (%) of Ventricular activation >120 ms	0	0	0	0	0	0	0	4.2	0	0	12.2	0
Area (%) of RV activation < 40ms	78.8	44.7	18.0	76.6	82.5	15.9	22.4	20.6	99.1	76.4	26.1	42.5
Area(%) of RV activation from 40 to 80 ms	21.2	37.7	79.6	21.4	13.3	33.4	53.5	19	0	23.6	36.1	22.9
Area(%) of RV activation < 80 ms	100	82.4	97.6	98.0	95.8	49.3	75.9	39.6	99.1	100	62.2	65.4
Area (%) of RV activation from 80 to 120 ms	0	18.2	3.8	0	7.6	54.3	24.3	52.4	0.9	0	14.1	0
Area (%) of RV of activation >120 ms	0	0	0	0	0	0	0	0.8	0	0	23.9	35.6
Area (%) of LV activation < 40ms	61.7	44.7	45.5	38.8	20.1	32.1	23.8	18.4	79.6	39.4	38.7	25.6
Area (%) of LV activation from 40 to 80 ms	38.3	30.3	52.5	61.2	40.4	44.1	60.0	25.4	18.3	59.0	39.4	26.9
Area (%) of LV activation < 80ms	100	75.0	98.0	100	60.5	76.2	83.8	43.8	97.9	98.4	78.1	52.5
Area (%) of LV activation 80 to 120 ms	0	27.1	5.2	0	40.9	23.8	17.2	49.4	2.1	1.6	22.1	47.5
Area(%) of LV activation >120 ms	0	0	0	0	0	0	0	6.8	0	0	1.8	0

Patients with (*) are CRT responders whereas the other are not.

Table 8: Electrical outcomes of patients with Left-only pacing (AdaptivCRT)

	#1	#2*	#3*	#4*	#5*	#6	#7*	#8	#9*	#10*	#11*	#12
QRSd (ms)	88	111	126	120	105	125	97	114	90	101	118	93
RVAT (ms)	64	55	78	17	48	77	43	64	63	68	93	47
LVAT (ms)	85	74	101	66	79	95	74	95	98	98	69	71
VEU (ms)	-21	-19	-23	-49	-31	-18	-31	-31	-35	-30	24	-24
Area (%) of Ventricular activation < 40 ms	52.7	44.8	34.6	45.5	50.8	57.4	46.9	36.0	76.6	51.8	23.8	47.9
Area (%) of Ventricular activation from 40 to 80ms	47.3	49.2	50.4	32.2	28.2	28.7	53.0	39.7	22.9	33.1	67.3	48.0
Area (%) of Ventricular activation < 80 ms	100	94.0	85.0	77.7	79.0	86.1	99.9	75.7	99.5	84.9	91.1	95.9
Area (%) of Ventricular activation from 80 to 120 ms	8.5	6.3	15.8	22.3	21.2	13.9	0.7	24.3	0.5	0.9	8.9	4.1
Area (%) of Ventricular activation >120 ms	0	0	0	0	0	0	0	0.8	0	0	0	0
Area (%) of RV activation < 40ms	66.6	61.8	42.2	86.9	88.5	78.3	19.4	52.8	78.9	68.4	6.5	63.3
Area(%) of RV activation from 40 to 80 ms	33.4	38.1	57.8	13.1	11.5	18.7	24.5	47.0	1.1	31.6	76.1	28.1
Area(%) of RV activation < 80 ms	100	99.9	100	100	100	97.0	100	99.8	80.0	100	82.6	91.4
Area (%) of RV activation from 80 to 120 ms	0.3	0.7	0	0	0	3	0	0.2	0	0	17.4	8.6
Area (%) of RV of activation >120 ms	0	0	0.8	0	0	0	0	0	0	0	0	0
Area (%) of LV activation < 40ms	41.6	26.6	27.4	6.1	22.8	38.9	40.3	25.7	50.0	38.2	38.3	35.3
Area (%) of LV activation from 40 to 80 ms	58.4	60.6	45.2	48.5	39.5	38.0	80.5	32.0	48.9	34.3	61.0	64.3
Area (%) of LV activation < 80ms	100	87.2	72.6	54.6	62.3	76.9	99.9	57.7	98.9	72.5	99.3	99.6
Area (%) of LV activation 80 to 120 ms	15.3	12.8	28.9	45.4	38	23.1	1.4	42.1	1.1	28.6	0.7	0.4
Area(%) of LV activation >120 ms	0	0	1.5	0	0	0	0	1.4	0	0	0	0

Patients with (*) are CRT responders whereas the other are not.

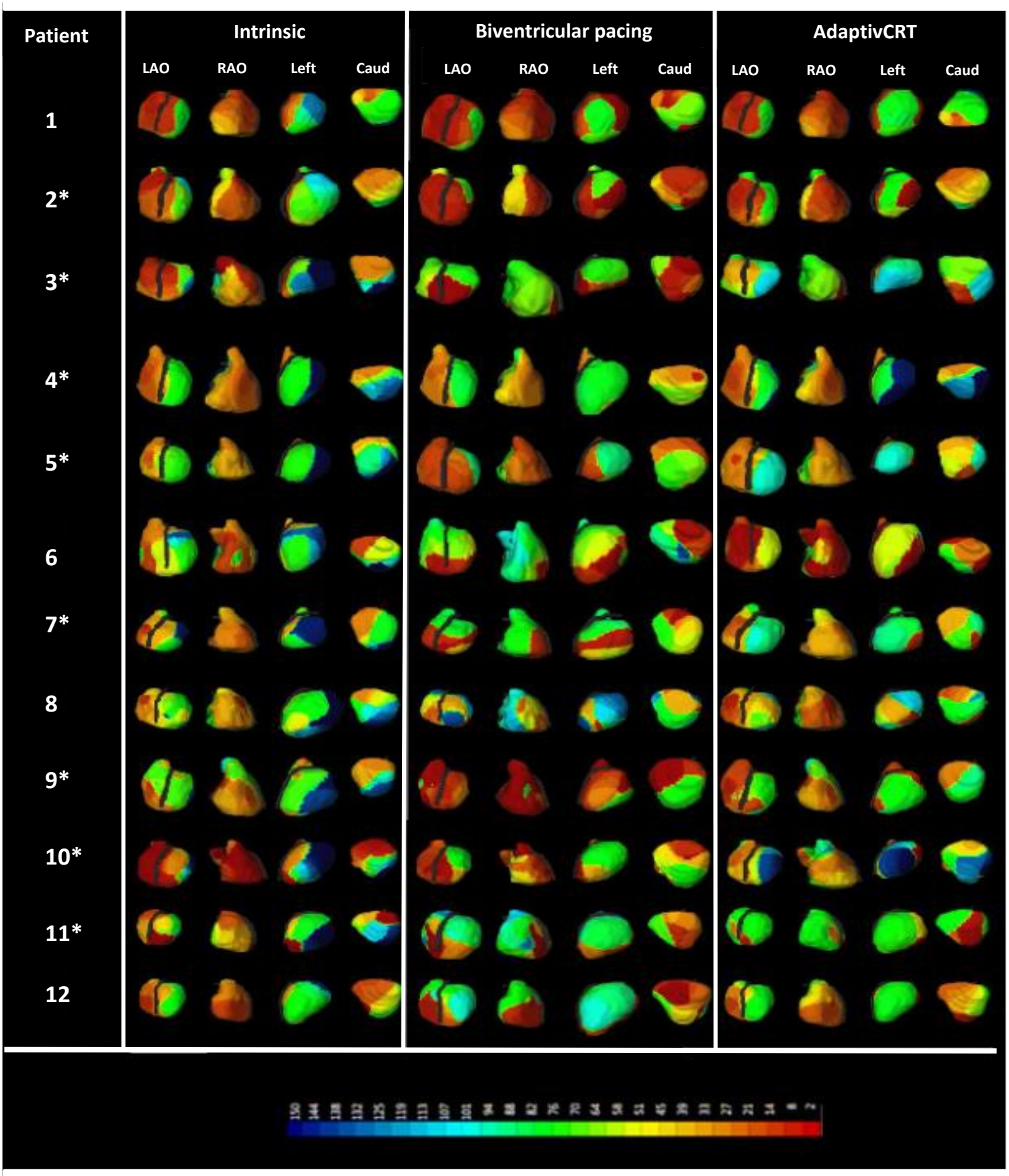

Figure 9: Epicardial activation and isochrone maps of patients with LBBB intrinsic rhythm (left), Biventricular pacing (center) or LV-pacing only (right). Patients with (*) are CRT responders whereas the other are not.

Vu, le Directeur de Thèse

Vu, le Doyen

De la Faculté de Médecine de Tours

Tours, le

GRAS Matthieu

52 Pages – 8 tableaux – 6 figures – 3 graphiques

Résumé :

Le traitement par resynchronisation cardiaque est indiqué chez les patients insuffisants cardiaques avec QRS larges sur l'ECG. Les bénéfices de la resynchronisation cardiaque sont observés chez 70% des patients implantés. L'algorithme AdaptivCRT permet une resynchronisation cardiaque par fusion entre une stimulation ventriculaire gauche et la dépolarisation intrinsèque du ventricule droit. Notre étude vise à comparer l'activation électrique biventriculaire entre une stimulation biventriculaire conventionnelle et l'algorithme AdaptivCRT dans cette population. Des cartographies non-invasives d'activation biventriculaire ont été réalisées en rythme spontané, stimulation biventriculaire et stimulation mono ventriculaire gauche seule à l'aide du système CardioInsight (ECVUE, CardioInsight Technologies Inc, Medtronic) Douze patients ont été analysées dont 7 hommes et 5 femmes.

Les profils d'activation ventriculaire en rythme spontané sont comparables. Il existe des différences d'activation ventriculaire droite chez les patients resynchronisés par stimulation bi-ventriculaire. Les profils d'activation ventriculaire gauche semblent comparables en cas de stimulation biventriculaire ou avec l'algorithme AdaptivCRT. Le VEU des patients resynchronisés par stimulation bi-ventriculaire ou AdaptivCRT sont supérieurs à celui des patients en rythme spontanée ($p<0.01$ et $p<0.01$, respectivement). Il n'y avait pas de différence de VEU entre les patients avec stimulation biventriculaire et AdaptCRT. La surface de dépolarisation précoce du ventricule droit était plus élevée chez les patients resynchronisés par stimulation bi-ventriculaire par rapport à ceux avec AdaptivCRT. L'algorithme AdaptivCRT permettrait une activation ventriculaire droite plus rapide et plus homogène avec des bénéfices semblables sur la resynchronisation du ventricule gauche et une augmentation de la longévité de la batterie.

Mots clés : Resynchronisation cardiaque, AdaptivCRT, Fusion ventriculaire, Cartographie non invasive, CardioInsight

Jury :

Président du Jury : Professeur Dominique BABUTY

Directeur de thèse : Docteur Nicolas CLEMENTY

Membres du Jury : Professeur Laurent FAUCHIER,
Professeur Denis ANGOULVANT,
Docteur Thibaud GENET

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