



Role of Quantitative Gated SPECT in Predicting Response to Cardiac Resynchronization Therapy

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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LIST OF CONTENTS

| Title | Page No. |
|---|----------|
| List of Tables | i |
| List of Figures | iv |
| List of Abbreviations..... | viii |
| Introduction..... | - 1 - |
| Aim of the Work | 4 |
| Review of Literature | |
| ▪ Heart Failure | 5 |
| ▪ Role of CRT in Patients with Heart Failure..... | 27 |
| ▪ Assessment of Ventricular Mechanical Dyssynchrony | 57 |
| Patients and Methods | 82 |
| Results | 95 |
| Discussion..... | 133 |
| Summary | 144 |
| Conclusion | 147 |
| Recommendations | 148 |
| Study Limitations | 149 |
| References | 150 |
| Arabic Summary | |

LIST OF TABLES

| Table No. | Title | Page No. |
|------------------|---|----------|
| Table 1: | New York Heart Association (NYHA) classification | 8 |
| Table 2: | Etiology of HF | 10 |
| Table 3: | Symptoms & signs of HF | 11 |
| Table 4: | Recommendations of CRT implantation..... | 23 |
| Table 5: | ESC guidelines..... | 25 |
| Table 6: | Comparison of echocardiographic methods to quantify left ventricular dyssynchrony | 66 |
| Table 7: | New York Heart Association (NYHA) classification | 84 |
| Table 8: | The Minnesota Living with Heart Failure questionnaire. | 87 |
| Table 9: | Distinguishing ischemic from non-ischemic cardiomyopathy using nuclear imaging..... | 89 |
| Table 10: | Demographic data of total cases | 95 |
| Table 11: | Shows risk factor distribution among patients | 96 |
| Table 12: | NHYA class and life style score in all patients | 98 |
| Table 13: | Medication among all patients..... | 99 |
| Table 14: | ECG parameters & EF by echocardiography in all patients | 100 |
| Table 15: | Shows baseline MPI study of the patients. | 101 |
| Table 16: | Lead position & its concordance with latest activation segment & scar..... | 102 |

LIST OF TABLES cont...

| Table No. | Title | Page No. |
|------------------|--|----------|
| Table 17: | Compares baseline and follow up NYHA class and quality of life score in all patients. | 105 |
| Table 18: | Baseline and follow up gated SPECT parameters in all patients. | 107 |
| Table 19: | EF improvement in responders and non-responders. | 108 |
| Table 20: | Demographic data of both groups. | 110 |
| Table 21: | Risk factor distribution in both subgroups. | 111 |
| Table 22: | Baseline NYHA class & MLHFQ score in responders and non-responders. | 113 |
| Table 23: | Follow up NYHA class & MLFHQ score in both groups. | 114 |
| Table 24: | Baseline and follow up NYHA class & MLHFQ score among responders group. | 115 |
| Table 25: | Baseline and follow up NYHA class & MLHFQ score in the non-responder group. | 115 |
| Table 26: | Medications given to patients in both groups. | 116 |
| Table 27: | QRS duration and morphology as well as EF in both groups. | 117 |
| Table 28: | Baseline MPI data in both groups. | 118 |
| Table 29: | Baseline total perfusion defect (TPD) in both groups. | 119 |
| Table 30: | Follow up gated SPECT parameters in both groups. | 120 |

LIST OF TABLES cont...

| Table No. | Title | Page No. |
|------------------|--|----------|
| Table 31: | Baseline and follow up gated SPECT parameters in the responder group. | 121 |
| Table 32: | Baseline and follow up gated SPECT parameters in the non-responder group. | 122 |
| Table 33: | Lead concordance with latest activation segment & scar in both groups..... | 123 |
| Table 34: | The degree of change of different parameters in both groups. | 125 |
| Table 35: | The correlation between studied parameters and the Δ change in EF. | 126 |
| Table 36: | Univariate analysis for independent predictors for CRT responders. | 130 |
| Table 37: | Cut off point for PSD | 131 |
| Table 38: | Cut off point for PHB..... | 132 |

LIST OF FIGURES

| Fig. No. | Title | Page No. |
|-------------------|---|----------|
| Figure 1: | Key Elements of Modern Use of CRT in heart failure patients | 29 |
| Figure 2: | The novel pacing approaches in CRT | 45 |
| Figure 3: | Rates of non-response to cardiac resynchronization therapy depending on the measure used in controlled trials and large observational studies of cardiac resynchronization therapy, each represented by a bar | 53 |
| Figure 4: | Tissue tracking at the apical 4-chamber view | 60 |
| Figure 5: | DTI demonstrating strain in a synchronous patient (panel A) and in a heart failure patient with LBBB (panel B) | 61 |
| Figure 6: | Strain rate imaging at the apical 4-chamber view (time to peak negative systolic strain rate in this patient is dyssynchronous) | 62 |
| Figure 7: | TSI from the 3 standard apical views demonstrating color coding of time to peak velocity data from a patient with dyssynchrony | 63 |
| Figure 8: | Panel A: Normal synchrony, with time volume curves converging at a near-single time point (Philips Q Lab) | 64 |
| Figure 9: | Speckle-tracking images demonstrating synchrony in a healthy individual (panel A) and severe dyssynchrony in a heart failure patient with LBBB (panel B) | 65 |
| Figure 10: | Processing steps of multi –harmonic phase analysis tool | 68 |

LIST OF FIGURES CONT...

| Fig. No. | Title | Page No. |
|-------------------|---|----------|
| Figure 11: | Illustration of using phase analysis to assess left ventricular dyssynchrony | 69 |
| Figure 12: | 58 year-old man had past history of CAD the phase analysis shows left Ventricular synchrony (PHB 30°, PSD 6.7°)..... | 73 |
| Figure 13: | 59 year -old women had past history of MI..... | 73 |
| Figure 14: | Example of phase analysis in non-responder A, and responder B patient to CRT | 78 |
| Figure 15: | Comprehensive method for CRT selection | 79 |
| Figure 16: | The characteristics of LBBB and RBBB, (2017) | 85 |
| Figure 17: | Basics of ECG- Interpretation of waves and intervals (2016) | 86 |
| Figure 18: | The site of latest mechanical activation was assessed on GMPS studies, (b) and related to the LV lead position on fluoroscopy (a) | 92 |
| Figure 19: | Distribution of male & female in all cases. | 96 |
| Figure 20: | Distribution of risk factors among all patients..... | 97 |
| Figure 21: | Distribution of ICM & NICM among all patients..... | 97 |
| Figure 22: | Medications among all patients..... | 99 |
| Figure 23: | QRS morphology among all patients..... | 100 |
| Figure 24: | Distribution of latest activation segments assessed by SPECT. | 103 |
| Figure 25: | Lead positioning by fluoroscopy. | 103 |

LIST OF FIGURES CONT...

| Fig. No. | Title | Page No. |
|-------------------|---|----------|
| Figure 26: | Lead position & its concordance with the latest activation segment..... | 104 |
| Figure 27: | Lead position & its concordance with scar position. | 104 |
| Figure 28: | Baseline NYHA class in all patients. | 106 |
| Figure 29: | Baseline and follow up MLHFQ score in all patients..... | 106 |
| Figure 30: | Baseline and follow up gated SPECT parameters in all patients. | 107 |
| Figure 31: | Percentages of Responders and non-responders. | 109 |
| Figure 32: | EF improvement in responders and non-responders. | 109 |
| Figure 33: | Gender distribution in both groups..... | 110 |
| Figure 34: | Distribution of the type of cardiomyopathy in both groups..... | 112 |
| Figure 35: | Baseline NYHA class in both groups. | 113 |
| Figure 36: | Follow up NYHA class in both groups. | 114 |
| Figure 37: | QRS Morphology in both groups..... | 117 |
| Figure 38: | Baseline MPI data in both groups..... | 119 |
| Figure 39: | Baseline total perfusion defect (TPD) in both groups. | 120 |
| Figure 40: | Follow up gated SPECT parameters in both groups. | 121 |
| Figure 41: | Lead position and its concordance with latest activation segment in both groups. | 124 |

LIST OF FIGURES CONT...

| Fig. No. | Title | Page No. |
|-------------------|---|----------|
| Figure 42: | Lead position and its concordance with scar in both groups..... | 124 |
| Figure 43: | The degree of change of different parameters in both groups..... | 125 |
| Figure 44: | Correlation between PHB and EF change. | 127 |
| Figure 45: | Correlation between PSD and EF change..... | 127 |
| Figure 46: | Correlation between ESV and EF change..... | 128 |
| Figure 47: | Correlation between MLFHQ score and EF change..... | 128 |
| Figure 48: | Receiver-operating characteristic curve analysis of gated myocardial perfusion SPECT for phase standard deviation (PSD) for prediction of response to cardiac resynchronization therapy..... | 131 |
| Figure 49: | Receiver-operating characteristic curve analysis of gated myocardial perfusion SPECT for phase histogram bandwidth (PHB) for prediction of response to cardiac resynchronization therapy..... | 132 |

LIST OF ABBREVIATIONS

| Abb. | Full term |
|----------------|---|
| ACCF/AHA | American College of Cardiology Foundation / American Heart Association |
| ACEIs..... | Angiotensin-converting enzyme inhibitors |
| ALT..... | Alanine aminotransferase |
| AMI..... | acute myocardial infarction |
| ANP..... | A-type natriuretic peptide |
| ARNI..... | Angiotensin receptor neprilysin inhibitor |
| AST..... | Aspartate aminotransferase |
| AV..... | Atrioventricular |
| BB..... | Beta-blockers |
| bpm..... | Beats per minute |
| BVP..... | Biventricular pacing |
| CCM..... | Cardiac contractility modulation |
| CMD..... | Cardiac mechanical dyssynchrony |
| CRT..... | Cardiac resynchronization therapy |
| CT..... | Computed tomography |
| DCM..... | Dilated cardiomyopathy |
| DENSE..... | Displacement encoding with stimulated – echo |
| DPD..... | Diphosphono-1,2-propanodicarboxylic acid |
| DTI..... | Doppler tissue imaging |
| ECG..... | Electrocardiography |
| EF..... | Ejection fraction |
| eGFR..... | Estimated GFR |
| ESC..... | European society of cardiology |
| GGTP..... | Gamma-glutamyltransferase |
| HF..... | Heart failure |
| LGE..... | Late gadolinium enhancement |
| LV EF | Left ventricular ejection fraction |
| LV..... | Left ventricular |
| LVMD | LV mechanical dyssynchrony |
| LVP..... | Left ventricular pacing |
| MEC..... | Mechano-Electric Coupling |

LIST OF ABBREVIATIONS CONT...

| Abb. | Full term |
|------------------------|---|
| <i>MPI</i> | <i>Myocardial perfusion imaging</i> |
| <i>MR</i> | <i>Mitral regurgitation</i> |
| <i>MRAs</i> | <i>Mineralocorticoid / aldosterone receptor antagonists</i> |
| <i>MRI</i> | <i>Magnetic resonance imaging</i> |
| <i>n-3 PUFAs</i> | <i>n-3 polyunsaturated fatty acids</i> |
| <i>NHANES</i> | <i>National Health and Nutrition Examination Survey</i> |
| <i>NOACs</i> | <i>Non-vitamin K antagonist oral anticoagulants</i> |
| <i>NPs</i> | <i>Natriuretic peptides</i> |
| <i>NYHA</i> | <i>New York Heart Association</i> |
| <i>OMC</i> | <i>Mechanical contraction</i> |
| <i>OMR</i> | <i>Onset of mechanical relaxation</i> |
| <i>OMT</i> | <i>Optimal medical therapy</i> |
| <i>PET</i> | <i>Positron emission tomography</i> |
| <i>PHB</i> | <i>Phased histogram bandwidth</i> |
| <i>PSD</i> | <i>Phase standard deviation</i> |
| <i>QALYs</i> | <i>Quality-adjusted life-years</i> |
| <i>QGS</i> | <i>Quantitative Gated SPECT</i> |
| <i>QOL</i> | <i>Quality of life</i> |
| <i>RBB</i> | <i>Right bundle branch</i> |
| <i>RBBB</i> | <i>Right bundle branch block</i> |
| <i>RV</i> | <i>Right ventricular</i> |
| <i>SPECT</i> | <i>Single photon emission computed tomography</i> |
| <i>SVR</i> | <i>Surgical ventricular reconstruction</i> |
| <i>TDI</i> | <i>Tissue Doppler imaging</i> |
| <i>TIBC</i> | <i>Total iron binding capacity</i> |
| <i>TOE</i> | <i>Transoesophageal echocardiography</i> |
| <i>TSI</i> | <i>Tissue synchronization imaging</i> |
| <i>TTE</i> | <i>Transthoracic echocardiography</i> |

INTRODUCTION

Cardiac resynchronization therapy (CRT) is an established therapeutic option for patients with drug-refractory advanced heart failure and ventricular conduction delay (*Abraham et al., 2002*). The merits of CRT have been demonstrated in terms of morbidity and mortality in several randomized clinical trials. Traditionally, a wide QRS complex, in addition to QRS morphology, has served to identify appropriate response to CRT. However, current selection criteria may not reliably portray the magnitude of CRT-remediable LV contraction dyssynchrony, as approximately 30% of patients selected with current selection criteria according to contemporary guidelines do not respond to CRT, a serious limitation for this invasive and costly endeavor (*Cleland et al., 2005*).

One of the possible explanations of CRT non-response is that a wide QRS complex may reflect interventricular rather than intraventricular dyssynchrony (*Boogers et al., 2009*). In addition, a low correlation exists between LV mechanical dyssynchrony and electrical dyssynchrony manifested as prolonged QRS duration, as the QRS duration is an indirect correlate but not a direct reflection of mechanical dyssynchrony, which is the real substrate. Thus, assessment of mechanical dyssynchrony might serve as a better predictor of response to CRT than QRS duration (*Haghjo et al., 2007; Uebleis et al., 2012*).

Several myocardial imaging techniques have been utilized to identify mechanical dyssynchrony, including echocardiography with tissue Doppler imaging (TDI), strain (rate) imaging, speckle tracking or three dimensional-derived parameters, magnetic resonance imaging (MRI), and nuclear imaging with single photon emission computed tomography (SPECT) (*Bax et al., 2005; Henneman et al., 2007*).

Gated SPECT is a widely available technique that enables assessment of both perfusion and left ventricular functional parameters with low inter- and intra-observer variability in a single investigation. Recently, phase analysis on gated SPECT has been evaluated for the assessment of LV dyssynchrony and Quantitative Gated SPECT (QGS) algorithm (Cedars-Sinai) has been expanded to provide quantitative parameters for the assessment of LV mechanical dyssynchrony (LVMD) based on the Fourier phase histogram of the LV in which phase histogram band width (PHB) and (PSD) phase standard deviation have been identified as valid markers of LVMD. In addition to preexisting mechanical dyssynchrony, location and extent of scarred myocardium and the position of the left ventricular (LV) pacing lead have been suggested to influence the response to CRT (*Chen et al., 2010; Trimble et al., 2008*). Indeed, the region of LV pacing and the area of latest mechanical activation, seem to be important factors in the prediction of outcome to CRT (*Deplagne et al., 2009; Becker et al., 2007*).