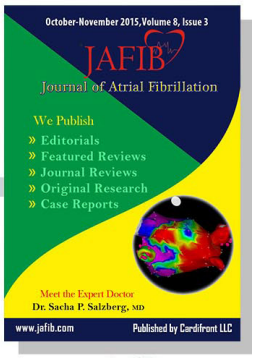
JAFIB
Featured Review
Journal of Atrial Fibrillation



www. jafib.com

Haemodynamic Alterations Induced By Cardiac Pacing: Is Clinical Evaluation Sufficient Or Do We Need Long-Term Device Monitoring?

Gerrit Frommeyer, MD, Florian Reinke, MD, Lars Eckardt, MD.

Division of Electrophysiology, Department of Cardiovascular Medicine, University of Münster, Münster, Germany.

Abstract

Cardiac pacing may induce haemodynamic alterations. RV pacing may have deleterious effects including a decrease of LV function as well as an increase of heart failure hospitalizations and mortality. Biventricular pacing is established in patients with heart failure and left bundle branch block or chronic AV block to improve haemodynamics. In the future, device optimization employing quadripolar leads or multisite pacing may further increase the rate of responders. However, cinical evaluation represents the most important tool to recognize the necessity for device optimization. Device algorithms are not yet successfully established to replace clinical and echocardiographic evaluation.

Introduction

Cardiac pacing may induce haemodynamic alterations. RV pacing may have deleterious effects including a decrease of LV function as well as an increase of heart failure hospitalizations and mortality. Biventricular pacing is established in patients with heart failure and left bundle branch block or chronic AV block to improve haemodynamics. In the future, device optimization employing quadripolar leads or multisite pacing may further increase the rate of responders. However, cinical evaluation represents the most important tool to recognize the necessity for device optimization. Device algorithms are not yet successfully established to replace clinical and echocardiographic evaluation.

Right Ventricular Pacing

Permanent cardiac pacing is the treatment of choice for patients with chronic high-degree atrio-ventricular (AV) block or symptomatic sick sinus syndrome (SSS).[1] Most regularly the right ventricular (RV) pacing electrode is placed in the RV apex (RVA). However, various clinical studies have suggested that electrode placement in the RVA may induce a dyssynchronous contraction. This may further result in a reduction of left ventricular (LV) function, myocardial perfusion defects and severe heart failure. A negative effect of RV pacing was proven in a large cohort study of 11.426 patient who underwent pacemaker implantation.[2] The authors reported a significant increase of heart failure events such as hospitalization or death due to heart failure.[2] In a cohort of 304 patients permanent RV pacing was associated with heart failure in 26% of these patients.[3] In a small group of 43 patients who were chronically paced due to complete AV block exercise myocardial scintigraphy was performed to assess myocardial perfusion in combination with radionuclide ventriculography to assess left ventricular function.[4] This study revealed a relevant incidence of myocardial perfusion defects that were associated with apical wall motion abnormalities and a reduced global LV function.[4] Apart from an increased risk of heart failure hospitalizations an increased occurrence of atrial fibrillation in the presence of ventricular desynchronization due to RV pacing has also been observed.[5] In the DAVID-trial which included a total of 506 patients with implantable cardioverter-defibrillator (ICD) dual-chamber pacing was associated with an increased occurrence of the combined end point of death or hospitalization for heart failure as compared with patients who received a single-chamber ICD for backup pacing.[6] The benefits of atrial pacing as compared with ventricular pacing in patients with SSS have already been confirmed in a study of 225 patients with a follow-up over 8 years.[7] In this study, the authors described a significantly higher survival, less atrial fibrillation, fewer thromboembolic complications and less heart failure in patients who underwent atrial pacing as compared with patients who were paced in the RV.[7]

The negative effects described in these studies are the result of several mechanisms. RVA pacing induces an abnormal electrical and mechanical activation of the ventricles.[8] The conduction of the

Key Words:
Cardiac Pacing, Right Ventricular Pacing, Cardiac Resynchronization Therapy, Quadripolar Leads, Multisite Pacing.

Disclosures:
None.

Corresponding Author:
Dr. med. Gerrit Frommeyer
Abteilung für Rhythmologie
Department für Kardiologie und Angiologie
Universitätsklinikum Münster
Albert-Schweitzer Str. 33
D-48149 Münster

electric wave front moves through the myocardium and does not use the HIS-Purkinje conduction system. As a result, the excitation is conducted slowly. This leads to a heterogeneous electrical activation of the myocardium and can be compared to the pathological condition of left bundle branch block.[9] Mechanistically, this condition is characterized by a breakthrough of the electrical activation at the interventricular septum. The inferoposterior base of the LV is the region with the latest activation.[10-12] Apart from the electrical activation pattern, the mechanical activation pattern of the LV is also altered by RVA pacing.[8] The abnormal contraction pattern leads to less effective contractions with haemodynamic consequences.[13]

The described deleterious effect of RVA pacing led to investigations on different sites of pacing that are accompanied by more beneficial effects on LV contraction.[14] The RV septum has been identified as a possible pacing site with improved haemodynamics as compared with RVA pacing.[15]

A large meta-analysis of 9 prospective studies suggested superior haemodynamic effects of pacing sites in the right ventricular outflow tract (RVOT) as compared with electrode position in the RVA. Midterm or longterm effects were only seen in two of the 9 studies included in this analysis.[16] Another systematic review and meta-analysis of randomized controlled trials suggested beneficial effects of non-apical vs. RVA pacing leading to an increased LV ejection fraction. However, the trials included in this meta-analysis provided inconclusive results regarding exercise capacity, functional New York Heart Association (NYHA) class, quality of life and survival.[17]

His-bundle pacing may also be considered as another alternative and may be the most physiologic option. In a crossover design comparison his-bundle pacing and biventricular pacing led to an equivalent response to cardiac resynchronization therapy. Of note, his-bundle pacing induced a narrowing of the QRS-complex despite the presence of left bundle branch block.[18]

Biventricular Pacing

Biventricular pacing is generally recognized to improve clinical outcomes and to reduce heart failure hospitalizations and mortality in patients with chronic and symptomatic heart failure despite optimal medical therapy. In a large meta-analysis, cardiac resynchronization therapy (CRT) with biventricular pacing led to a decrease in hospitalizations by 37% and a decrease of mortality by 22% as compared with controls.[19] The underlying mechanisms for the haemodynamic amelioration induced by CRT are attributed to the correction of electrical and mechanical dyssynchrony. Various clinical studies have underlined the beneficial effects of CRT in patients with severe heart failure and left bundle branch block. In addition, single left ventricular pacing has also been evaluated as a potential beneficial therapy in patients with heart failure. Auricchio et al. reported an increased aortic pulse pressure in patients with severe heart failure and wide left bundle branch block in the presence of left ventricular pacing employing an epicardial left ventricular lead.[20] An enhanced contractile function by left ventricular pacing at the site of the greatest electrical delay was also described in other small cohorts of heart failure patients.[21,22] In a recent meta-analysis of randomized controlled trials which compared biventricular to LV pacing a similar improvement of the clinical status was described. However, the authors reported a trend toward superiority of biventricular pacing over LV pacing for reverse remodeling and LV function.[23] In another systematic review including 630 patients of randomized controlled trials biventricular and LV pacing appeared to achieve similar effects regarding all-cause mortality and hospitalizations.[24] Of note, biventricular pacing was superior to conventional right ventricular pacing in patients with AV block and LV systolic dysfunction regarding death from any cause, urgent visit for heart failure or intravenous therapy. Furthermore, the LV end-systolic volume index was increased.[25]

Potential Of Quadripolar Leads For Haemodynamic Device Optimization

Pacing the LV at the latest activated site is predictive of a most optimal increase in contractility.[26] Standard haemodynamic device optimization involves optimization of the atrioventricular delay as well as the interventricular delay. Some devices present algorithms for atrioventricular or interventricular delay optimization albeit echocardiographic optimization is commonly recognized to be superior for haemodynamic outcome.[27] The development of multipolar pacing leads for placement in the coronary venous system can be regarded as one of the most important advancements of the last years. These leads have been evaluated in various clinical studies. An improved haemodynamic response associated with higher responder rates of biventricular pacing was reported for quadripolar leads as compared with unipolar or bipolar leads in a cohort of 27 patients.[28] Tools for non-invasive haemodynamic analysis to assess haemodynamic response are measurement of cardiac output, blood pressure, total periphery resistance, LV diameters and volumes as well as stroke volume.[29] A large multicenter study including 418 patients showed significantly lower rates of lead-related problems as well as reduced procedural and fluoroscopic times for system implantation.[30] In addition, a trend to a lower risk of surgical LV lead revision and a lower incidence of dislodgment was descirbed.[31] A lower rate of hospilatizations for heart failure and LV surgical lead revision for quadripolar leads as has also been reported in a cohort of 193 patients.[31] Furthermore, the employment of quadripolar leads enables the clinician to perform haemodynamic vector personalization and thereby increase the rate of responders of cardiac resynchronization therapy.[32] In single-center studies, echocardiographic optimization in the presence of quadripolar leads resulted in a significant improvement of functional NYHA class and LV ejection fraction over a period of 6 months.[33]

Apart from quadripolar leads, multisite pacing also represents a promising perspective to increase the rate of responders. A significant reduction of echocardiographic dyssynchrony by multisite pacing has been described in a population of 52 patients.[34] Multisite pacing can be achieved by placement of multiple pacing leads within the coronary sinus and its tributaries or by employing a quadripolar (or multipolar) lead to deliver pacing stimuli at different sites of the same vein.[35]

Conclusions

Cardiac pacing regularly induces haemodynamic alterations. RV pacing is associated with deleterious effects including a decrease of LV function and an increase of hospitalizations and mortality. Biventricular pacing is an established therapy in patients with heart failure and left bundle branch block or chronic AV block to improve haemodynamics. In the future, device optimization employing quadripolar leads or multisite pacing may further increase the rate of responders. However, clinical evaluation represents the most important tool to recognize the necessity for device optimization. Device algorithms are not yet successfully established to replace

clinical and echocardiographic evaluation.

Reference

1. European Society of C, European Heart Rhythm A, Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, Cleland J, Deharo JC, Delgado V, Elliott PM, Gorenek B, Israel CW, Leclercq C, Linde C, Mont L, Padeletti L, Sutton R, Vardas PE. 2013 esc guidelines on cardiac pacing and cardiac resynchronization therapy: The task force on cardiac pacing and resynchronization therapy of the european society of cardiology (esc). Developed in collaboration with the european heart rhythm association (ehra). Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2013;15:1070-1118
2. Freudenberger RS, Wilson AC, Lawrence-Nelson J, Hare JM, Kostis JB, Myocardial Infarction Data Acquisition System Study G. Permanent pacing is a risk factor for the development of heart failure. The American journal of cardiology. 2005;95:671-674
3. Zhang XH, Chen H, Siu CW, Yiu KH, Chan WS, Lee KL, Chan HW, Lee SW, Fu GS, Lau CP, Tse HF. New-onset heart failure after permanent right ventricular apical pacing in patients with acquired high-grade atrioventricular block and normal left ventricular function. Journal of cardiovascular electrophysiology. 2008;19:136-141
4. Tse HF, Lau CP. Long-term effect of right ventricular pacing on myocardial perfusion and function. Journal of the American College of Cardiology. 1997;29:744-749
5. Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL, Lamas GA, Investigators MOST. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline qrs duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation. 2003;107:2932-2937
6. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, Kutalek SP, Sharma A, Dual C, Investigators VVIIDT. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: The dual chamber and vvi implantable defibrillator (david) trial. Jama. 2002;288:3115-3123
7. Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet. 1997;350:1210-1216
8. Prinzen FW, Peschar M. Relation between the pacing induced sequence of activation and left ventricular pump function in animals. Pacing and clinical electrophysiology : PACE. 2002;25:484-498
9. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony implications for therapy. Journal of the American College of Cardiology. 2009;54:764-776
10. Vassallo JA, Cassidy DM, Miller JM, Buxton AE, Marchlinski FE, Josephson ME. Left ventricular endocardial activation during right ventricular pacing: Effect of underlying heart disease. Journal of the American College of Cardiology. 1986;7:1228-1233
11. Rodriguez LM, Timmermans C, Nabar A, Beatty G, Wellens HJ. Variable patterns of septal activation in patients with left bundle branch block and heart failure. Journal of cardiovascular electrophysiology. 2003;14:135-141
12. Auricchio A, Fantoni C, Regoli F, Carbucicchio C, Goette A, Geller C, Kloss M, Klein H. Characterization of left ventricular activation in patients with heart failure and left bundle-branch block. Circulation. 2004;109:1133-1139
13. Prinzen FW, Hunter WC, Wyman BT, McVeigh ER. Mapping of regional myocardial strain and work during ventricular pacing: Experimental study using magnetic resonance imaging tagging. Journal of the American College of Cardiology. 1999;33:1735-1742
14. Mond HG, Gammage MD. Selective site pacing: The future of cardiac pacing? Pacing and clinical electrophysiology : PACE. 2004;27:835-836
15. Mond HG, Vlay SC. Pacing the right ventricular septum: Time to abandon apical pacing. Pacing and clinical electrophysiology : PACE. 2010;33:1293-1297
16. de Cock CC, Giudici MC, Twisk JW. Comparison of the haemodynamic effects of right ventricular outflow-tract pacing with right ventricular apex pacing: A quantitative review. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2003;5:275-278
17. Shimony A, Eisenberg MJ, Filion KB, Amit G. Beneficial effects of right ventricular non-apical vs. Apical pacing: A systematic review and meta-analysis of randomized-controlled trials. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2012;14:81-91
18. Lustgarten DL, Crespo EM, Arkhipova-Jenkins I, Lobel R, Winget J, Koehler J, Liberman E, Sheldon T. His-bundle pacing versus biventricular pacing in cardiac resynchronization therapy patients: A crossover design comparison. Heart rhythm : the official journal of the Heart Rhythm Society. 2015;12:1548-1557
19. McAlister FA, Ezekowitz J, Hooton N, Vandermeer B, Spooner C, Dryden DM, Page RL, Hlatky MA, Rowe BH. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: A systematic review. Jama. 2007;297:2502-2514
20. Auricchio A, Stellbrink C, Block M, Sack S, Vogt J, Bakker P, Klein H, Kramer A, Ding J, Salo R, Tockman B, Pochet T, Spinelli J. Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. The pacing therapies for congestive heart failure study group. The guidant congestive heart failure research group. Circulation. 1999;99:2993-3001
21. Kass DA, Chen CH, Curry C, Talbot M, Berger R, Fetics B, Nevo E. Improved left ventricular mechanics from acute vdd pacing in patients with dilated cardiomyopathy and ventricular conduction delay. Circulation. 1999;99:1567-1573
22. Blanc JJ, Bertault-Valls V, Fatemi M, Gilard M, Pennec PY, Etienne Y. Midterm benefits of left univentricular pacing in patients with congestive heart failure. Circulation. 2004;109:1741-1744
23. Liang Y, Pan W, Su Y, Ge J. Meta-analysis of randomized controlled trials comparing isolated left ventricular and biventricular pacing in patients with chronic heart failure. The American journal of cardiology. 2011;108:1160-1165
24. Boriani G, Gardini B, Diemberger I, Bacchi Reggiani ML, Biffi M, Martignani C, Ziacchi M, Valzania C, Gasparini M, Padeletti L, Branzi A. Meta-analysis of randomized controlled trials evaluating left ventricular vs. Biventricular pacing in heart failure: Effect on all-cause mortality and hospitalizations. European journal of heart failure. 2012;14:652-660
25. Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfesee L, Shinn T, Sutton MS, Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block Trial I. Biventricular pacing for atrioventricular block and systolic dysfunction. The New England journal of medicine. 2013;368:1585-1593
26. Zanon F, Baracca E, Pastore G, Fraccaro C, Roncon L, Aggio S, Noventa F, Mazza A, Prinzen F. Determination of the longest intrapatient left ventricular electrical delay may predict acute hemodynamic improvement in patients after cardiac resynchronization therapy. Circulation. Arrhythmia and electrophysiology. 2014;7:377-383
27. Kamdar R, Frain E, Warburton F, Richmond L, Mullan V, Berriman T, Thomas G, Tenkorang J, Dhinoja M, Earley M, Sporton S, Schilling R. A prospective comparison of echocardiography and device algorithms for atrioventricular and interventricular interval optimization in cardiac resynchronization therapy. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal

of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2010;12:84-91

28. Osca J, Alonso P, Cano O, Sanchez JM, Tejada D, Andres A, Sancho Tello MJ, Olague J. The use of quadripolar left ventricular leads improves the hemodynamic response to cardiac resynchronization therapy. Pacing and clinical electrophysiology : PACE. 2014
29. Santini L, Legramante J, Condemi F, Santucci L, Panattoni M, Crobeddu P, Sergi D, Forleo G, Romeo F. Non-invasive hemodynamic analysis in cardiac resynchronization therapy patients wearing quadripolar left ventricular leads: The importance of pacing electrode selection. Minerva cardioangiologica. 2014;62:449-459
30. Forleo GB, Di Biase L, Panattoni G, Mantica M, Parisi Q, Martino A, Pappalardo A, Sergi D, Tesauro M, Papavasileiou LP, Santini L, Calo L, Tondo C, Natale A, Romeo F. Improved implant and postoperative lead performance in crt-d patients implanted with a quadripolar left ventricular lead. A 6-month follow-up analysis from a multicenter prospective comparative study. Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing. 2014
31. Forleo GB, Di Biase L, Bharmi R, Dalal N, Panattoni G, Pollastrelli A, Tesauro M, Santini L, Natale A, Romeo F. Hospitalization rates and associated cost analysis of cardiac resynchronization therapy with an implantable defibrillator and quadripolar vs. Bipolar left ventricular leads: A comparative effectiveness study. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2015;17:101-107
32. Trolese L, Biermann J, Hartmann M, Schluermann F, Faber TS, Bode C, Asbach S. Haemodynamic vector personalization of a quadripolar left ventricular lead used for cardiac resynchronization therapy: Use of surface electrocardiogram and interventricular time delays. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2014;16:1476-1481
33. Calo L, Martino A, de Ruvo E, Minati M, Fratini S, Rebecchi M, Lanzillo C, Fagagnini A, Borrelli A, De Luca L, Sciarra L. Acute echocardiographic optimization of multiple stimulation configurations of cardiac resynchronization therapy through quadripolar left ventricular pacing: A tailored approach. American heart journal. 2014;167:546-554
34. Rinaldi CA, Kranig W, Leclercq C, Kacet S, Betts T, Bordachar P, Gutleben KJ, Shetty A, Keel A, Ryu K, Farazi TG, Simon M, Naqvi TZ. Acute effects of multisite left ventricular pacing on mechanical dyssynchrony in patients receiving cardiac resynchronization therapy. Journal of cardiac failure. 2013;19:731-738
35. Rinaldi CA, Burri H, Thibault B, Curnis A, Rao A, Gras D, Sperzel J, Singh JP, Biffi M, Bordachar P, Leclercq C. A review of multisite pacing to achieve cardiac resynchronization therapy. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2015;17:7-17