International Heart and Vascular Disease Journal
Volume 3, Number 7, September 2015
Journal of the Cardioprogress Foundation

Biventricular pacing: current trends and future strategies

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Summary

Biventricular pacing has become an accepted therapeutic modality for medically refractory congestive heart failure (CHF). This new pacing strategy also known as cardiac resynchronization therapy (CRT) synchronizes ventricular contraction, which consequently results in improved pumping efficiency, enhanced left ventricular (LV) filling, and reduction in the severity of the mitral regurgitation. Biventricular pacing has substantially altered the natural course of ventricular failure, exerting its physiological impact through favorable ventricular remodeling, with a reduction in LV volumes and improvement in ejection fraction (EF). Despite this success of CRT and the recent expansion of its role in the treatment of patients with CHF, there remain many inherent limitations to the technology and its delivery. A significant minority of patients (about 30%) continue to remain non-responsive to this pacing strategy. This review will highlight biventricular pacing in its present form, will elaborate on strategies to enhance response to CRT, and outline future trends and synergies towards maximizing the potential benefit of CRT.

Key words

Heart failure, cardiac resynchronization therapy

Introduction

Biventricular pacing has become an accepted therapeutic modality for patients with medically refractory congestive heart failure (CHF). This new strategy of stimulation also known as intimate resynchronization therapy (CRT), synchronizes ventricular contraction which consistently results in improvement of pumping efficiency, to filling left ventricular (LV) and to reduction of a degree of mitral regurgitation. Biventricular stimulation has essentially changed natural course of ventricular failure, showing the physiological influence by means of favorable ventricular remodeling, with

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reduction of volumes of LV and improvement in ejection fraction (ФВ) [1]. This in turn, results in long-term clinical improvement, such as to the improved quality of a life, reduction of quantity of hospitalization concerning the improvement of heart failure (HF) and to reduction of total mortality [2, 3]. Standard indications for biventricular pacing which originally included patients with severe HF and signs of systolic dysfunction (EF ≤35%), with violations of intraventricular conduction and symptoms of HF (III and IV functional classes (EF) EF according NYHA classification), now tends to expansions for inclusion of patients with moderate symptoms of EF — I and II EF according NYHA) [4, 5].

Despite of success of CRT and expansion of its role in treatment of patients with CHF, there are many inherent restrictions of use of this technology still. A significant number of patients (~ 30%) continue to remain "non-responders" to such strategy of stimulation [1, 2, 6]. The present review will open to clinical physicians biventricular stimulation in its current form, will specify the strategy of increase in response on CRT, and will depict in general the future tendencies and joint actions of doctors to increase in potential benefit from CRT.

Physiology of CRT

Electric sequence of heart activation and CRT.

Electric sequence of heart activation is the important, determining factor of the coordinated cardiac contraction and relaxation and full cardiac function. Frustration in electric activation of heart, such as left bundle branch block Gis (LBBBG) in most cases can cause the asynchronous and detained reduction of lateral wall of LV, thus, reducing mechanical energy efficiency of the heart resulting in HF.

It is important to note, that intraventricular conduction disorders may lead directly to HF or can again exist as an integral part of the process of cardiac remodeling which complicate coincidence of severe cardiomyopathies. Ventricular Remodeling by HF is progressing process, which includes the degenerate and irreversible changes occur in the tissue, cellular and subcellular levels [7]. The described changes include: cardiomyocyte hypertrophy, regional changes in protein expression, necrosis, inflammation, fibrotic lesion of the conduction system of the ventricles, as a result is broken formation and dissemination of the pulse [8, 9]. Besides disturbances in the conduction system and the degree of asynchrony can be result of significant influence on a myocardium, because of presence of

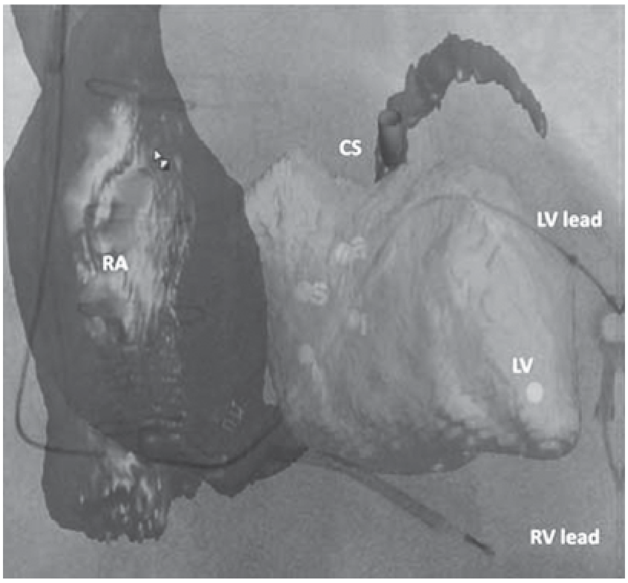

Fig. 1. United image (computed tomography + fluoroscopy).

Note: The figure shows the calculated integrated image of the heart, tomography plus fluoroscopy. Coronary sinus (CS), left ventricle (LV), right atrium (RA); right ventricular electrode (RV lead), left ventricular electrode (LV lead). Truong, et al. [36].

scarring, fibrosis, and an ischemia, which aggravate the nature of intraventricular conduction.

During the CRT, the stimulation of the right ventricle (RV) and left ventricular (LV) (figure 1), produce two wave front ventricularthat which begin in LV and RV, raising its side, and heading in opposite directions toward each other. Advantage of CRT is in effective merger of the two wave fronts of depolarization; synchronizing walls of LV. Full synchronous electric activation of LV can be achieved further by change of time of distribution of stimulating pulses on atrioventricular and interventricular conduction system of the heart parts [10, 11].

Mechanical dyssynchrony

Inexactness of QRS complex, which has been written down with the help of surface ECG to predict the answer on CRT, due to the complexity and the different levels of electrical and mechanical dyssynchrony in heart damage. Dyssynchrony can exist at various levels, and can be atrial, atrioventricular, interventricular, intraventricular, and intramural (figure 2) [10]. The majority of researches have emphasized the importance of intraventricular dyssynchrony, as a primary factor promoting progressing of HF, and as predictor of response on CRT. Echocardiographic (ECG) research methods have filled l this gap of knowledge by better understanding of the anatomical and functional aspects of cardiac pathology substrate of HF. M — mode, two-dimensional ECG, three-dimensional

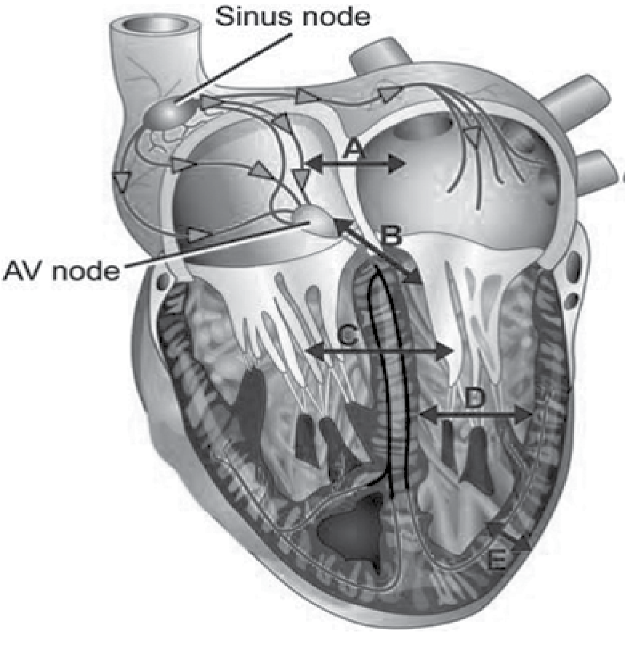

Fig. 2. Levels of mechanical dyssynchrony.

Note: The figure shows the levels of dyssynchrony in heart: (A) interatrial, (B) atrioventricular, (C) interventricular, (D) intraventricular and (E) intramural.

ECG and Tissue Doppler Visualization (TDV) provide the best understanding of a level of an initial parameter of dyssynchrony, sharp responses and symptoms favorable remodeling in response to CRT.

TDV facilitates measurement of dyssynchrony, estimating a direction and travel speed wall infarction in different segments of the LV [11]. The difference of speed of time of rise up to maximal in various segments can be appreciated, and many single-site researches have shown good attributes of the answer on CRT. However, with TDV, passive movement of a myocardium cannot be distinguished between active reductions that take place at an estimation of the patient with ischemic cardiomyopathy, which can have segments with myocardial scar changes. Besides that, TDV still remains prevailing two-dimensional (2D) ECG technology, and demands high frequency of the staff, and it limits the sanction and quality of the image.

Despite of promising results in small works when two multicenter prospective researches were carried out, ECG methods unconvincing predicted the answer on CRT. Researches PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) [12] and [13] were multicenter, developed for an estimation of efficiency of parameters of dyssynchrony in definition of the answer on CRT; in researches [13] — by the patients with narrow complexes of QRS. Research PROSPECT was not randomized, prospective, observant research, which involved 426 patients who underwent implantation of the device according to the selection criteria. Before implantation the patients were investigated for dyssynchrony by different methods, for an estimation of intra- and interventricular dyssynchrony by using of the M-mode and TDV. The 6-month's final points including the incorporated clinical report have been analyzed: Death rate from all reasons, hospitalization concerning worsening of HF, a class on NYHA, the general inspection of the patient, and 15%-s' reduction of the end-systolic volume of the left ventricle (LV CSR) in comparison with an initial condition. Despite of training on a workplace on purchase of skills of standard diagnostics and results of three main laboratory blind studies, there was not any ECG parameter of reaction on CRT.

Research [13] randomized, multicenter research executed for an estimation of parameters suitability of dyssynchrony in the forecast of the answer on CRT by the patients with narrow complexes of QRS. 250 patients with HF III or IV FC on NYHA, EF ≤35% and duration QRS <130 msec were randomized on groups with CRT and without CRT. Dyssynchrony has been determined with help of M — mode of ECG and TDV parameters. For 6 months of research these two groups had no distinctions in final points as a result of increase in peak consumption of oxygen, at least, on 1.0 ml / kg of weight in body / minutes. While these two researches have not defined parameters dyssynchrony to predict CRT, that is distinct from the big number of smaller researches which to some extent have shown some optimism concerning advantage of CRT. It, probably, occurred because of differences in study design, weak and doubtful final points, methods, which have been used for reception of results as well as variability and bad standardization. Now it is known that Research (EchoCRT) is in a stage of realization, for studying the above mentioned problems by patients with narrow complexes QRS [14].

Newer echocardiographic techniques using speckle tracking for measurement of a beam spectrum develop as good parameters of studying predictors of response to CRT. Until now, the method speckle tracking has been checked up only in randomized, small research [15]. For tracking speckle-tracking use, advantage of interference in a beam of ultrasound, which creates small color defects of the digital image on two-dimensional, an echo to images (figure 3).

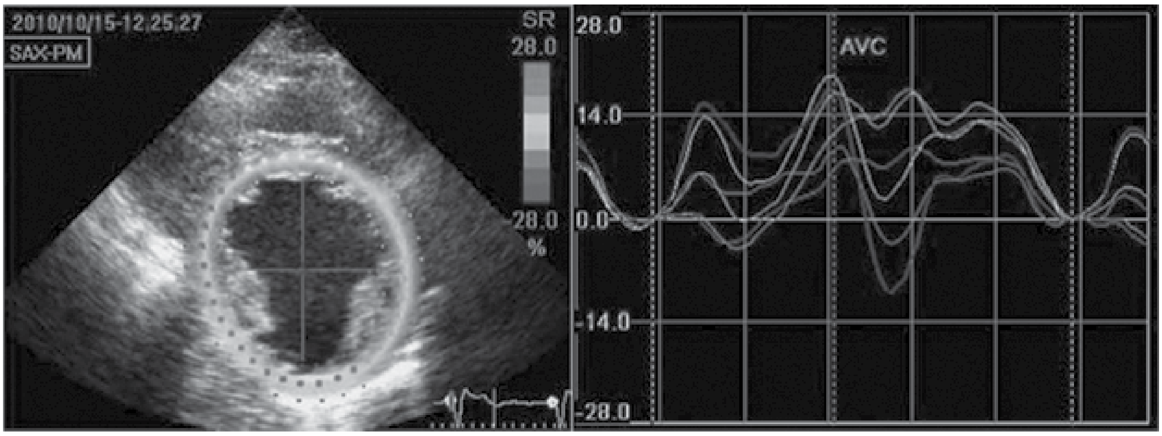

Fig. 3. Tracking speckle-tracking strain imaging.

Note: the left panel shows the two-dimensional images; the right panel shows the curve of segmental strain in time for the left ventricle.

Other methods, such as magnetic resonance tomography (MRT) and computer tomography (CT) of heart offer an opportunity of association of measurements of dyssynchrony for presence of the scars in the myocardium, and studying the anatomy of the coronary veins for implantation of left ventricular electrode. Small researches have shown promising results. Unfortunately, still there is not present big multicenter researches, which have estimated the above-stated technologies of diagnostics.

Researches devoted CRT

Heavy HF

Some thousand patients with heavy HF III and IV FC (NYHA) have been investigated in randomized, controllable, clinical researches with indisputable proofs of that CRT improve the clinical forecast of illness. Below it will be briefly discussed 4 researches in which patients with HF from moderate up to a heavy degree have been included, with obvious behavioral problems (wide complex QRS ≥120 ms) and low EF LV (≤35%) which have helped to strengthen role of CRT at such population of patients.

Research MUSTIC (Multisite Stimulation in Cardiomyopathies) is one of the first among researches in which studied influence of CRT by 67 patients with heavy HF, normal sinus rhythm and duration of QRS> 150 ms. It was blind, randomized, controlled, crossover study, comparing clinical reaction of patients for the period inactive CRT of stimulation with active CRT stimulation 3 months during each period. By patients who have finished both phases of research, atrio-biventricular stimulation has considerably improved exercise tolerance, quality of a life and has reduced quantity of hospitalization concerning HF [16]. A multicenter, randomized, clinical research MIRACLE (Multicenter InSync Randomized Clinical Evaluation) randomized 453 patients with HF III and IV FC (NYHA) to CRT with optimum pharmacological treatment against only one optimum pharmacological therapy [1]. Other criteria of inclusion were EF LV ≤35% and duration QRS≥130 ms. Significant improvement of symptomatic — FC HF (NYHA) both quality of a life, and the functional status — 6 minutes a distance of walking is marked. These improvements were accompanied by increase of ventricular remodeling and reduction of risk by 40% of the incorporated final points, such as death, quantity of hospitalization concerning heavy HF by patients with CRT. Other sign research was influence of CRT on morbidity and mortality in HF — CARE-HF (Cardiac Resynchronization in Heart Failure) in which 813 patients participated. They had III and IV FC HF (NYHA) and have shown advantage of CRT of optimal medical therapy [3]. It is revealed 37% reduction of relative risk in final points, such as hospitalization concerning cardiovascular event, general death rate. It is interesting, that criteria of inclusion for this research were a little more strict: besides EF LV <35%, it was necessary, that the patients had wider complexes QRS ≥150 ms or QRS 120–149 ms with additional presence of mechanical dyssynchrony, determined with help of ECG. Research COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) in comparison of medical therapy, stimulation and defibrillation by patients with HF was the biggest tribal, executed with participation of patients with HF [2]. In total 1520 patients with III and IV FC HF NYHA, EF LV <35%, and QRS> 120 ms were randomized on groups with optimum medical therapy (OMT), biventricular stimulation (CRT-P) +OMT and biventricular stimulation with defibrillator (CRT-D) + OMT. Patients with CRT-E and CRT-D have shown significant reduction of number of hospitalization concerning worsening of CH with additional reduction of death rate at CRT-D. However in research it was impossible to compare CRT-E with CRT-D, thus, there was open an important question concerning a choice of an adequate kind of the device.

Easy and moderate HF

Early research works, such as 'Intimate resynchronization therapy for treatment of HF by patients with ventricular disturbances in behavior and malignant ventricular tachyarrhythmia (CONTAK-CD) and «Effects of cardiac resynchronization on disease progression by patients with diastolic dysfunction of LV» (MIRACLE ICD–II), with a study of CARE-HF, have shown, that CRT can be effective in group of patients with less heavy HF [17–19]. Proofs of favorable remodeling of LV marked the opposite in both researches by patients with symptoms of HF II FC (NYHA). These results further have been checked up in researches REVERSE-HF (REsynchronization reVerses Remodeling in Systolic left ventricular dysfunction) [5], MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) [4] and RAFT (Resynchronization/Defibrillation for Ambulatory Heart Failure Trial) [20].

610 patients with EF LV <40 %, duration of complex QRS ≥120 ms, I and II FC HF (NYHA), randomized to CRT+ or CRT- participated in research REVERSE-HF. In this research, it was presented differences in duration of the remote supervision between patients in Europe and Northern America, which were observed within 2 years and one year accordingly. A primary final point in this research was the percent of patients, which worsened a clinical total point (which included the quantity of hospitalization concerning deterioration HF, transition in other group of research or deterioration FC (NYHA) points on quality of a life). Preliminary set secondary final point there were changes in EDV LV. During 12 months of research, there was no significant distinction in primary final points: a parity of patients with the worsened result though significant reduction of EDV LV- was observed at CRT+. During 24 months in the European cohort, 19 % at CRT + vs 34 % at CRT- there was the deterioration of total clinical reaction (p=0,01). Amazing reduction of EDV LV was observed in CRT+ — 27.5 + 31,8 ml / m2 vs 2.7 + 25.8 ml / m2 at CRT-.

Research MADIT-CRT included 1820 patients from> 110 centers in Europe and Northern America. By surveyed it should be EF LV <30 % and duration QRS> 130 ms and FC I or II HF (NYHA). Patients were randomized on groups of patients with implantable cardioverter-defibrillators (ICDs) and with CRT-D devices. Almost by 2/3 patients in research MADIT-CRT was QRS> 150 ms and 80 % of patients had II FC HF NYHA. Essential distinctions were observed by 17,2 % of patients in group SRT-D vs 25,3 % of patients in group IKD on the tested incorporated final points of death and quantity of hospitalization concerning weighting of HF (p <0,001). The opposite remodeling it was studied for tracking an outcome of illness with reduction of EDV LV by 57 ml in group SRT-D vs 18 ml in group IKD (p <0,001). 41 %-s' reduction of risk of hospitalization concerning HF in group MADIT-CRT vs 53 %-s' reductions of time of the first hospitalization concerning deterioration HF in research REVERSE has been revealed. It is interesting, that by women the smaller quantity of hospitalization concerning weighting HF and general death rate with improved by the opposite remodeling of LV was observed in comparison with sick men [21].

Recently executed research RAFT included 1798 patients with II and III FC HF during the 40-month's period. Primary results by quantity of death and/or hospitalization in connection with deterioration of HF are marked by 33,2 % of patients in group SRT-D vs 40,3 % in group IKD. At stratification on weight HF it has been revealed reduction by 27 % of relative risk in primary final points in group of patients with II FC HF has been revealed. Despite of advantage of CRT, substantial growth of a level of early adverse events it has been marked in this group. It is interesting, that CRT rendered independent useful influence both on mortality and on quantity of hospitalization concerning deterioration of HF in group of patients with II FC HF NYHA [20]. It is remarkable, that in all three above mentioned researches, strengthened reaction on biventricular stimulation was observed at patients with wider QRS (> 150 ms) and by those patients by whom it was observed morphology QRS on type LBBBG.

Maximal increase in reaction on SRT

Despite of these obvious advantages, there are some unresolved questions, and most actual of them is that up to 1/3 patients do not answer and do not receive effective advantage from SRT. Because of high prevalence, disease and death rate by CHF and high cost of treatment it is impossible to underestimate value of increase of the maximal reaction of all patients on SRT. Selection of the correct patient and understanding of differences between patients can predict distinctions in reaction on SRT, the use of the approaches determined for the patient, for implantation of an electrode in LV, with adequate programming the device and corresponding postoperative observation can raise the efficiency of implantation and the answer on SRT.

Morphology QRS, electric activation and comorbidity

After an establishment of the reason resulted in deterioration function of LV and choice OMT, selection of patients on SRT still depends on presence of wide complex QRS on a superficial electrocardiogram. Duration of complex QRS as "the sacred Grail" used for selection of patients and the forecast of the answer on SRT seems to be the super-simplified attribute. Value of duration of QRS complex decreases in connection with that there are patients with the big duration of complex QRS and minimal mechanical dyssynchrony, while there are patients with narrow complexes QRS and significant mechanical dyssynchrony [22]. The big duration of complex QRS can be an attribute of heavy cardiomyopathy and, in spite of the fact that in cases where the best choice of treatment of SRT, this attribute can not reserve natural current of illness. Other approaches investigating bases "SRT the caused changes" in duration QRS on an electrocardiogram, morphology QRS, were not able to predict structure of electric activation of ventricles, but can have some ability to predict response on SRT [23, 24].

Work [10] allows to assume, that it can be the significant difference of the clinical answer by the patients with LBBBG and without LBBBG. As a rule, by LBBBG the sequence of electric activation is distributed aside tops with a delay of distribution in lateral and poster-lateral parts of LV. As the delay of distribution of electric activation is accompanied by a delay of mechanical activation in the same territory, and the choice of a lateral wall for implantation of an electrode in LV is intuitive. Especially even by classical LBBBG when there is a high level of heterogeneity of activation in structures of LV, accompanied with distinction of the functional block. Results of recent works assume, that by patients with morphology QRS on type nonLBBBG, in group of patients with uncertain infringements of intraventricular conduction there is more the worse result, while by the patients with the right bundle branch block Gis (RBBBG) the results are the worst [25–27]. Patients with RBBBG, probably, do not answer on SRT, the same as the patients with LBBBG, so as by these patients there is no dyssynchrony of LV, suitable for SRT [28]. In addition, patients with RBBBG usually have the accompanying dysfunction of RV, the increased pressure in pulmonary arteries, and more expressed infringements of carrying out. In spite of the fact that only the quarter of patients with RBBBG can have infringements of passage of LV, comparable with LBBBG, almost 50 % from them have some delay, which is possible for correcting by SRT [29]. The reduced response on SRT in group of patients without LBBBG can be explained by insufficient changes in a technique of implantation of an electrode, despite of the changed features of front wave of depolarization. By the patients with RBBBG is doubtful, whether really the leading part of an electrode in LV is necessarily to synchronize heart or adequately designed pulse of stimulation from electrode RV can correspond to synchronization.

Except of duration, QRS there are other clinical characteristics, which can influence on ventricular remodeling and an outcome of illness. It is important to recognize, that presence of RV dysfunction, pulmonary hypertension, rumen severe myocardial damage and a marked increase in heart can influence the clinical answer on SRT [30, 31]. In addition coexisting accompanying pathologies, such as a terminal stage of renal failure, an anemia, severe coronary artery disease, etc. can influence the answer at SRT [32]. Though the majority of researches has shown, that patients with ischemic and with not ischemic cardiomyopathies receive the profit from SRT, the tendency of reception of good reaction on SRT was observed in not ischemic group of patients [4, 33, 34].

Reception of images for increase in patient — specific approaches

Reception of the image is an integral part of treatment with use of SRT. Visualization is necessary at all three stages of treatment, i.e. before procedure (for selection and planning of implantation), during procedure (implantation of the device) and after procedure (supervision and optimization). Unfortunately, any unique technique of visualization cannot guarantee performance of all these three aspects of treatment. As the majority of methods of visualization gives the additional information relative cardiac structure (fluoroscopy, CT of coronary venous anatomy) and functions (ECG for mechanical dyssynchrony), the combination of some from these technologies can help to facilitate a choice of the patient and planning of procedure [35]. Preprocedural estimation of mechanical dyssynchrony, and intraprocedural integration with venous cartography can be useful strategy, but still there is a necessity of improvement in order it will be more practical, reliable and checked up in the future. Conceptually intended stimulation sounds very attractive because the data from small retrospective researches have shown, that stimulation in a place of maximal dyssynchrony and avoiding of the scar area can lead to the best results. Though ECG would be seemed natural suitable for use during procedure to demonstrate the most backward segments, for carrying out LV electrode, is forces heavy and technically causing a pressure technique.

Not combined methods of visualization, such as CT and MRT have an ability to give the information, thus eliminating the requirement for methods of the integrated image [36]. Multidetector CT can provide with the important information on anatomy of coronary veins, contractile function of LV and mechanical dyssynchrony, just as integrated information concerning the relation of a venous branch with a segment of dyssynchrony and/or scar [18, 33]. MRT is strenuously studied its ability to calculate more precisely dyssynchrony, and to improve selection of patients [37]. Now, efforts on application of MRT also are focused in development of new methods to characterize architecture and ultrastructure myocardial fibers, as well as the three-dimensional image of a pressure of a myocardium. MRT, however, remains the urgent offer by this category of patients taking place in bad condition, many of which already have earlier implanted devices.

Strategy of stimulation: whether can we achieve the greater success?

Biventricular stimulation improves synchronism of reduction of LV through stimulation late activated its areas. A usual method of implantation of LV electrode is trans-venous, as a result with accommodation it in one of branches of veins of coronary sine (CS). As soon as vascular access will be achieved, the stimulating electrode canceled by directing introducer and moves ahead through it to branches of CS of the second or third order. Still there are contradictions concerning the best location of an electrode and a choice between optimum anatomic position. The question on place criteria of implantation, or in a segment with maximal mechanical dyssynchrony, or area of the maximal electric delay, is still discussed. The current tendencies continue to remain simplified and specify, that LV electrode will be placed in optimum according anatomy place of stimulation (usually determined as lateral and poster-lateral wall of LV) [38]. However insufficiently favorable clinical answer by almost 1/3 patients receiving CRT, offers restrictions in this approach to a choice of place of stimulation. Complex interaction between unpredictable character of activation of LV, frequently a casual choice of a final place of stimulation (dictated by presence of suitable venous branch), and the changes caused by stimulation of RV in electric and mechanical structure of activation LV could be a potential explanation of high percent of the patients who are not answering on CRT (even by patients with anatomically optimal position of LV electrode). It is little known about segmentary influence of localization of LV electrode within the limits of the elected substrata. Recently finished work has shown, that apical implantation of LV electrode is connected with the worse results of CRT; preferable arrangement of LV electrode at the basis / on the average segments of the ventricle, can improve results [39]. These results have been recently proved in the analysis of research MADIT-CRT [40].

Small retrospective researches have shown, that stimulation of a place of maximal dyssynchrony can strengthen the reverse remodeling and, hence, improve the forecast of illness. In all these researches, an estimation of the relation an electrode / segment was a retrospective assumption without true integration of image [41]. This approach is limited now to features of anatomy of veins. As CRT is the form of electric therapy for synchronization of chaotic electric activation of heart, is meaningful to try to designate the purpose of implantation of LV electrode the area of the maximal electric delay [38]. Some invasive and non-invasive methods of visualization have been offered for definition of the area of LV with the latest electric activation. In spite of the fact that three-dimensional contactless endocardial LV charting it provides the exact characteristic of sequence of electric activation of LV remains impractical for its performance during implantation of LV electrode. The more practical strategy is intraprocedural use of intraintimate electrogramme, measurement of an electric delay on LV electrode for individual implantation of LV electrode. The electric delay is calculated as a difference of time between the beginning of complex QRS on a superficial electrocardiogram and detectable signal of maximum delays on LV electrode. This delay is corrected with beginning of QRS (registered simultaneously with LV), expressing it as percent from initial duration of QRS [42]. Stimulation of heart in zones with the big electric delay on LV electrode has been connected with improved sharp hemodynamic answer and an outcome of illness. Good venous angiogram is the important part of procedure of implantation as the detailed venous map helps to outline various accessible variants. Improving technologies (smaller on the size and multipolar electrodes) will allow the doctor who is carrying out implantation to choose specific "not cicatrized" zones in an optimum anatomic place of position or within the limits of segments with a significant electric mechanical delay. Recent efforts on electric mapping of venous system for definition of presence of zones of cicatricial changes and a degree of an electric delay can be executed by use of new electro-anatomic methods of visualization.

Though location of RV stimulating electrode, always goes down to the status of an electrode of the second order, it is remarkable, that it can influence the front of a wave depolarization of LV and, hence, on resynchronization. The previous work has shown, that changes of RV electrode can change the sequence of activation of LV the same as also mechanics of LV [43]. There are data that the relation RV/LV can influence an outcome of illness in its turn. However, based on existence of the various reasons of a substratum of dyssynchrony, localizations LV electrode, sizes of LV and it is probable, that presence or absence of scar, homogeneous position of RV electrode is improbable, and, that the identical effect will take place. Actually, there is a big requirement of definition of individual approaches for each patient which should be estimated prospectively.

Taking into account restrictions usual trans-venous way of implantation, have been offered some alternative approaches of implantation. There is some potential at newer endocardial and epicardial approaches that can change the field of play [44, 45]. Biventricular endocardial stimulation has yielded promising results with high clinical and improved hemodynamic parameters of LV in comparison with epicardial biventricular stimulation [46]. Endocardial stimulationcan provide more physiological electric activation when electric activation begins in endocardium and is distributed to epicardium [47]. Some methods have been offered, namely: transaortic, transseptal through interatrial or interventricular partitions and transapikalny. Transseptal approaches through subclavian vein can lay a way, which will combine endocardial implantation of LV electrode with usual implantation of the device. Researches of last time informed, that individually based approach with regular testing has shown many places of optimum implantation of LV electrode which strongly differed from usual installation of an electrode through CS, to stimulation of a lateral wall and methods of implantation under control of ECG. Research has shown, that when it is necessary to optimize a site of an electrode, there is a significant difference between various patients [42]. This research has presented certificates that the best place of stimulation of LV is not only specific to each patient, but also that it is difficult to determine beforehand given place. However, some questions concerning a problem of safety, such as thromboembolism or an infection of endocardial electrode demanding extraction, it is necessary to discuss [48]. Last preliminary work also has shown, that bench ventricular excitation using two separate LV electrodes, placed in coronary venous system, can improve clinical and ECG results [49]. The further researches, however, have confirmed the superiority and safety of any multiplace or endocardial stimulations over conventional methods.

By 8–10% of the patients carrying implantation of biventricular pacemaker, implantation of LV electrode is not possible for the various reasons: impossibility of cannulation CS, absence of the suitable venous branches, insufficient stability of an electrode, stimulation of phrenic nerve, etc. Surgical epicardial implantation of LV electrode is a method of a choice by these patients. Some surgical methods have been offered for epicardial implantation of LV electrode, which include such methods as front or side mini thoracotomy, VATS technique and robotic systems of implantation [44]. Especially it is developed the modern conservative percutaneous directions with a technique of implantation of an electrode under xiphoid process. The most important questions of this approach should be still addressed to strategy of fixing of an electrode, and mechanisms of implantation in order that the epicardial electrode casually has not damaged vessels of a coronary arterial channel.

Postimplant supervision: strengthening of opportunities of the patient, the doctor and the device

The modern condition of supervision of the patient after implantation of the device falls short in several areas, in particular: optimization of AV and VV intervals, discussion of the diagnostic information of the implanted device, use of these data for stratification of risk of the patient, optimization of medicinal therapy and, that is even more important, early definition and treatment of patients non-responders.

There are interesting data, which suggest, that adjustment and optimization of AV interval can lead to increase of hemodynamic efficiency, however, there is an insufficient information on influence of this optimization on character of electric activation. The maximal improvement of systolic functions of LV is reached by short, AV interval, which allows the full capture of ventricles by two fronts of a wave of excitation caused by stimulation [50]. Exact value of this AV delay which improves synchronism, is a variable, being specific to each patient.

Recently it has been shown [32], that essential percent of not answering on biventricular stimulation can actually benefit from optimization AV of an interval. Whether AV optimization is necessary for each patient during implantation of the device, it is disputably, though it seems evident, that patients will require optimization of these intervals because of a significant degree of distinctions of position of atrial, RV and LV electrodes, and because of significant distinctions between patients on a principal cause of disease, and because of presence of cicatricial changes of myocardium. Till now the final conclusion is still absent, even that in researches FREEDOM and SMART-AV it has been assumed that "brilliant" parameters of adjustment can work only well [51, 52]. In both researches there were significant restrictions in their design, the group has been appreciated, the decision on performance of research has been preliminary accepted, and force of research has been calculated.

One more factor, which influences on activation of ventricle during time of biventricular stimulations, is the delay of time of interventricular (VV) activation. Modern devices SRT have an opportunity of programming of VV interval of the stimulation, allowing simultaneous or consecutive stimulation LV-RV with a various degree of preexcitation of LV or RV. These adjustments together with adjustments of AV interval can make set of examples of ventricular repolarization, offering by the patients with intraventricular conduction disturbances with intact AV conduct, the certain degree of the control of three fronts of the activation going from BBBG and from RV and LV of electrodes. Though at the majority of patients, simultaneous RV–LV stimulation results in good hemodynamic results, preexcitation of LV before RV, apparently, further optimizes synchronism, and increases systolic function of LV by the patients [53]. It is necessary to note, that others randomized researches have not shown significant clinical effect from programming an interval of VV delay [54, 55].

Devices SRT write down and provide with the detailed information about activity of the patient, frequency of intimate reductions, independent electric activity, transthoracic resistance and the nearest future events, they also provide with the hemodynamic data in real time [56, 57]. Occurrence of remote monitoring of implanted devices has enabled automatic transfer of the outpatient information in real time concerning frequency of intimate reductions, physical activity, the beginning of development of interstitial pulmonary edema (measurement transthoracic resistance), etc. through the Internet. Continuation of work on improvement of technology of a sensor control has allowed transfer through a global network of such important parameters, as arterial pressure, weight, saturation of blood by oxygen, etc. The control of these patients and their devices over the Internet provides an opportunity for various adjacent experts to transfer the data of the patient, and provide more personalized form of treatment. The Strategies based on the control by the sensors will continue to grow and will be addition for simplification of stratification of risk, will allow predicting early risk of acute decompensation, will allow to automate therapeutic interventions, and will improve outcomes of illness.

The multidisciplinary approach in treatment and supervision of these patients, apparently, becomes a new direction in the future. More often, patients not answering on therapy usually pay to themselves attention by aggravation of HF or by increase in quantity of hospitalization; one of the purposes of the integrated multidisciplinary approach is the early revealing of a problem with Preventive medication regimen modification or parameters of adjustment of the device, for the prevention of acute decompensated disease. Teamwork of experts of all disciplines (electrophysiology, HF and experts on visualization) can facilitate adequate selection of patients with SRT, optimization of SRT device and careful titration of medicamentous therapy in postimplantation period. Despite of understanding, that the multidisciplinary model would provide improvement of the control over the patient, influence of such integrated services should be still appreciated in the future.

Conclusion

Now biventricular stimulation is recognized as safe and effective therapeutic strategy for treatment of patients with refractory to medicamentous therapy 3CH. Implanted SRT devices through synchronized stimulation of RV and LV can improve contractility of the sick heart and thus change natural current of illness. Though biventricular stimulation rendered the big influence on treatment of patients with HF, its full potential is not realized yet. For the following some years, understanding of mechanical ventricular dyssynchrony for the reasons resulted in it and the answer on SRT depending on a place of stimulation will be improved. Wider opportunity of application of innovative forms of stimulation ventricular (s) by the patients with HF will be presented at narrow and wide complexes QRS. The big uniformity in definition of the answer on SRT both early definition and treatment not answering on SRT of the patients will improve its applicability and, hence, profitability.

Conflict of interest: None declared

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