Current Status and Advances in Left Ventricular Endocardial Pacing Therapy

qingshan tian[1], Houde Fan[1], Zhiping Xiong[1], and Zhenzhong zheng[1]

[1]First Affiliated Hospital of Nanchang University

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Abstract

Nowadays, more and more heart failure patients need to be treated with cardiac resynchronization therapy (CRT). Traditional epicardial pacing has a high implantation failure rate and non-response rate, while left ventricular endocardial pacing therapy exactly overcomes these disadvantages, especially leadless endocardial pacing therapy has a broad application prospect.

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Qingshan Tian[a1],Ph.D, Houde Fan[b1],MD.,Zhiping Xiong[c], MD., Zhenzhong Zheng[d],Ph.D

[a]Department of Cardiology, The First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Street, Nanchang, 330006, Jiangxi, People's Republic of China, tqs576342580@sina.com

[b]Department of ultrasonography, The First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Street, Nanchang, 330006, Jiangxi, People's Republic of China, fhd15297728858@sina.com

[c]Department of Cardiology, The First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Street, Nanchang, 330006, Jiangxi, People's Republic of China, xzp1157650042@sina.com

[d]Department of Cardiology, The First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Street, Nanchang, 330006, Jiangxi, People's Republic of China, zzz567890123@sina.com

[1]The first two authors contributed equally to this work.

Corresponding author:Zhenzhong Zheng,Ph.D. Department of Cardiology, The First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Street, Nanchang, 330006, Jiangxi, People's Republic of China, zzz567890123@sina.com

Qingshan Tian ORCID iD : 0000-0001-8448-4257

Zhenzhong Zheng ORCID iD : 0000-0002-1730-8138

Abstract: Nowadays, more and more heart failure patients need to be treated with cardiac resynchronization therapy (CRT). Traditional epicardial pacing has a high implantation failure rate and non-response rate, while left ventricular endocardial pacing therapy exactly overcomes these disadvantages, especially leadless endocardial pacing therapy has a broad application prospect.

Keywords: heart failure, cardiac resynchronization therapy, left ventricular pacing, endocardial pacing

Introduction

Cardiac resynchronization therapy (CRT) is an excellent treatment for heart failure after medical and surgical therapy. It can increase the ejection fraction, improve cardiac function, and improve quality of life in most heart failure patients with wide QRS waves (>150.00 ms). The therapeutic effect is more pronounced in patients with a significant decrease in the ejection fraction (left ventricular ejection fraction, LVEF <30.00%).[1,2] Conventional CRT is paced by epicardial veins that enter the left ventricle mainly through the coronary sinus, but there is still an implantation failure rate of approximately 5% and a non-response rate of 20.00-30.00% in clinical practice.[3,4] The reasons for this may include abnormal anatomical structures, contrary to physiological sequence, limited selection of pacing sites, and diaphragm stimulation, among others. LV endocardial pacing is a new technique based on traditional CRT with advantages such as multientry pacing, multispot pacing, a low arrhythmia rate, and less phrenic nerve stimulation. In recent years, a number of studies have shown better maneuverability through LV endocardial pacing and better recovery of cardiac function after surgery.[5-9] Endocardial pacing can also be used to achieve good results in patients with failed epicardial pacing. However, LV endocardial pacing also has the disadvantage of causing endocardial infection, thromboembolism, and increased mitral valve damage. With the development of science and technology and the increased awareness of pacing therapy, wireless pacing has been applied for clinical treatment; wireless pacing has the advantages of wired endocardial pacing but can effectively avoid its shortcomings. Currently, endocardial pacing is used relatively little in clinical practice, and the long-term safety and efficacy of endocardial pacing still needs to be validated by large-scale clinical data, but it can be an effective treatment for patients with heart failure. This article focuses on the advantages and disadvantages of endocardial pacing with and without wires.

1. LV endocardial pacing with leads

1.1 Advantages of lead endocardial pacing

1.1.1 Multipath pacing without vascular constraints

LV epicardial pacing can be performed with a guidewire through the coronary sinus and pacing in the epicardial vasculature with a single pacing entry; endocardial pacing can be performed through the septum, interventricular septum, aorta, and apex, with a wide selection of access paths:(1) Room separation method: In 1998, Jais et al[10] performed the first LV endocardial pacing via a combined upper and lower vena cava inflow via the septum, but pacing via the internal jugular vein or femoral vein inflow via the septum is still the most common.[11,12] (2) Room interval method: In 2013, Gamble et al[13] reported for the first time a case of transventricular LV endocardial pacing with significant improvement in cardiac function and no complications after the procedure. Betts et al[14] punctured the interventricular septum via the subclavian vein using a puncture needle, radiofrequency needle, and radiofrequency energy wire; the success rate was high, the duration was short, rapid localization of the radiofrequency energy wire was achieved, and the LVEF improved by 14.00 ± 8.00%. While transient intraoperative ventricular tachycardia occurred. there were no postoperative complications, such as perforation or endocardial infection. Intraventricular septal puncture does not involve passing through the mitral valve, so this procedure can be considered in patients with associated mitral valve dysfunction. As puncture may damage the myocardium and the conduction system of the heart, it may cause ventricular arrhythmia, hematoma formation, or cardiac compression due to ventricular perforation. (3) Arterial approach: transarterial access has been used in animal studies. Reinig et al [15] paced the apical left ventricle by puncturing the porcine carotid artery, and after 6 months of follow-up, the pacing threshold increased, the LVEF was normal, and there was no significant aortic regurgitation or thromboembolism. Zabek et al[16]paced patients with a second-degree atrioventricular(AV) block with a guidewire through the subclavian artery into the left ventricle, but pacing remained poor at the maximal amplitude. A right bundle branch block (RBBB) on electrocardiography, echocardiography and computed tomography (CT) suggested that the wire was located in the apical part of the left ventricle, and there was no thrombus or valve damage after removal of the wire. Sosdean et al[17] reported that puncture of the subclavian vein led to perforation of the aortic arch, and then the wire was passed through the aortic valve into the left ventricle for pacing. The electrocardiogram suggested a RBBB, and the wire was found to be located in the left ventricle by cardiac ultrasound. The wire was not removed, and no thrombosis occurred after 12 months of oral anticoagulation medication with normal pacing parameters. Dry cough and limb weakness due to nerve irritation by the guidewire have been reported clinically, and passage of the guidewire through the aortic valve into the left ventricle has been found.[18,19] (4) Apical puncture: Transapical approach pacing, which does not involve passage through the valve structures of the heart, does not cause valve damage, and allows pacing from anywhere in the endocardium directly into the left ventricle. Kassai et al[20,21] performed transthoracic LV apical percutaneous wire implantation with good pacing and no surgical complications ,such as valve infection or pericardial effusion, on follow-up. Mihalcz et al[22] found a significant improvement in cardiac function by apical puncture pacing compared with epicardial pacing(LVEF:39.70 +- 12.50 vs 26.00 +- 7.80%, P $<$ 0.01; New York Heart Association (NYHA) class:2.20 +- 0.40 vs 3.50 +- 0.40, P $<$ 0.01). Transapical puncture allows direct adjustment or replacement of the guidewire in the event of dislocation or infection and does not cause damage to the valve.

1.1.2 Multisite pacing facilitates selection of the optimal pacing site

The cardiac veins are relatively straight, and with greater cardiac pacing activity, epicardial pacing is prone to wire dislocation, which limits the choice of pacing sites. Endocardial pacing is not limited by blood vessels, and the wire can reach any part of the ventricular wall, which in combination with the use of spiral electrodes allows for more precise pacing. The choice of the pacing site varies from individual to individual, with a more pronounced increase in the LVEF with the use of sites further away from the ventricular scar and conduction block region.[23,24] Therefore, adjusting the pacing site is important for cardiac function recovery. Osca et al[25]found that multipoint LV pacing (MPP) increased LVEF by 38.40+-1.80% and the cardiac index (CI) by 34.70+-5.10% and significantly improved LV function compared with conventional CRT. With improvements in pacemaker technology and increased awareness of CRT, combined with MPP pacing and the unrestricted site of endocardial pacing, the therapeutic effects of LV endocardial pacing will be further enhanced.

1.1.3 Low arrhythmia prevalence and low complex discrete polarity

Normal cardiac electrical conduction is propagated from the endocardium to the epicardium, and intravenous (lV) endocardial pacing can take full advantage of fibrillary network agitation, with short ventricular depolarization times and low transmural complex dispersion, consistent with physiological pacing. The sequence of agitation during epicardial pacing can be completely reversed, reversing the normal LV transmural agitation, resulting in delayed depolarization and repolarization and a significantly prolonged QT interval. Cabanelas et al[26]reported sympathetic storms after epicardial pacing in women with severe heart failure due to valvular heart disease, under optimal medical therapy. Tayeh et al[27] found a significant prolongation of the QTc interval after epicardial pacing (498.90 +- 50.80 vs 476.20 +- 41.60 msec, P $<$ 0.01). Prolongation of the decomplexation time and QT interval is an important factor in the development of sudden cardiac death and malignant arrhythmias.

1.1.4 Low phrenic nerve stimulation, low pacing threshold

The left phrenic nerve is close to the pericardium and distributed in the diaphragm, and the lateral and posterior veins are close to the septal nerve, which causes spastic contraction of the diaphragm during epicardial pacing due to stimulation of the phrenic nerve by the electric field and other factors. In epicardial pacing clinical studies.[28,29] the incidence of phrenic nerve stimulation ranges from 10.00% to 40.00%, and the incidence of clinical symptoms of phrenic nerve stimulation ranges from 9.00% to 14.00%. The pacing threshold varies at different pacing sites and may be elevated postoperatively, which may require a second surgery due to phrenic nerve stimulation or elevated thresholds. Endocardial pacing away from the phrenic nerve and the ability to select sites with low pacing thresholds for pacing can reduce the occurrence of secondary procedures.

1.2. Defects in LV endocardial pacing

LV endocardial pacing is primarily associated with the risk of infection, embolization, and mitral valve damage. The implantation of endocardial pacing leads may cause infective endocarditis and the formation of superfluous lead growths. The removal of lead infection may lead to mitral valve damage and the detachment of superfluous growths, which may cause cerebral artery embolism and other complications, as well as the activation of endogenous coagulation, which increases the incidence of thromboembolic events. There have been clinical reports of thrombosis caused by accidental entry of wires into the left ventricle due to septal defects and transient ischemic attacks caused by self-withdrawal of anticoagulants after endocardial pacing.[30] Long-term oral anticoagulants use should be weighed against the advantages and disadvantages of bleeding and thrombotic events.

2 LV endocardial pacing without leads

2.1 Leadless LV endocardial pacing, which includes ultrasonic energy-mediated leadless pacing, magnetic energy-mediated leadless pacing and pacing with miniature leadless devices, can reduce various complications caused by the lead, including lead infection, dislocation, mitral regurgitation, and the formation of superfluous lead growths. At the same time, it has many advantages for endocardial pacing, including less phrenic nerve stimulation, physiological agitation, and more pacing sites. The pacing threshold is low. The use of miniature wireless pacemakers also has the unique advantage of eliminating the need for a capsule bag; additionally, the operation is simple, the incision is small, there is no risk of capsule bag infection, and there is less impact on postoperative life.

2.2 Ultrasound energy-mediated wireless pacing: Pacing of the heart is performed using pulse dispensers, ultrasound generators, and wireless endocardial electrodes with ultrasound receivers. Echt et al[31] studied the use of ultrasonic wireless pacemakers in pigs, selected 30 sites for pacing, and achieved a pacing threshold of 1.80+-0.90 V with simultaneous pacing of both ventricles. Auricchio et al[32] implanted an ultrasound wireless pacemaker in 17 patients with a pacing threshold of 1.60+-1.00V and a LVEF of 31.00%+-7.00%, which significantly improved cardiac function. Seifert et al[33] showed that the LV end-diastolic volume decreased by >15.00% and the LVEF increased significantly (6.70+-7.60) in 39 patients at the 6 month postoperative follow-up compared with the preoperative period.

2.3 Magnetic energy-mediated wireless pacing

Magnetic energy-mediated pacing is similar to ultrasound-mediated pacing in that the generator emits magnetic energy to a receiver, which is then converted to electrical energy for pacing. Wieneke et al[34] successfully converted a magnetic field of 1.50 mT to a voltage pulse of 0.60-1.00V/0.40 ms in a porcine model and demonstrated the feasibility of magnetic energy-mediated pacing for the first time, with a high energy conversion rate and a long pacemaker service life. It has not yet been applied in clinical trials and its safety and feasibility need to be further confirmed.

2.4 Miniature wireless pacemakers: As there is energy loss in the conversion of ultrasound and magnetic energy, miniature wireless pacing devices have integrated batteries in the pulse generator, which significantly extends the battery life and reduces the complications associated with arrhythmias, making it the most promising pacing method. Miniature wireless pacemakers were first researched using nuclear energy for pacing, with a lifespan of up to 20 years, and with the application of microchips to pacemakers, the size of pacemakers has decreased significantly. Koruth et al[35] successfully implanted a miniature pacemaker using a sheep model with an intraoperative pacing threshold of 1.20+-0.70 V and a follow-up threshold of 0.70+-0.20 V after 3 months.

3 Summary and outlook

LV endocardial pacing has many advantages over epicardial pacing, including physiological pacing, a low pacing threshold, less phrenic nerve stimulation, and multipath pacing. With the development of wireless pacing, the advantages of endocardial pacing will be further highlighted, especially with the development of microwireless pacemakers, and endocardial pacing will be more widely used. Although there are still many problems to be solved, with the deepening of the understanding of pacing and the continuous progress of science and technology, we believe that more patients will be satisfied with the treatment.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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