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Medical Policy

Subject:	**Wireless Cardiac Resynchronization Therapy for Left Ventricular Pacing**		
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Description/Scope

This document addresses wireless cardiac resynchronization therapy (CRT) for left ventricular (LV) pacing. Wireless CRT for LV pacing has been proposed as an alternative to conventionally delivered CRT as a treatment of heart failure. Currently, no device has been approved by the U.S. Food and Drug Administration (FDA).

Note: For additional information, please see:

- **CG-SURG-63 Cardiac Resynchronization Therapy with or without an Implantable Cardioverter Defibrillator for the Treatment of Heart Failure**
- **SURG.00033 Cardioverter Defibrillators**
- **SURG.00150 Leadless Pacemaker**

Position Statement

Investigational and Not Medically Necessary:

Wireless CRT for left ventricular pacing is considered investigational and not medically necessary for all indications, including heart failure.

Rationale

Wireless CRT for LV Pacing

Wireless CRT for LV pacing has been proposed as an alternative to conventional CRT; however, there have been a limited number of studies published in the peer-reviewed literature addressing the use of this technology.

This Medical Policy provides assistance in understanding Healthy Blue’s standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue’s Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

In 2013, Auricchio and colleagues published the results of a study that investigated the safety and performance of the WiCS®-LV system, now known as the WiSE™ CRT System (EBR Systems, Inc., Sunnyvale, CA). The authors evaluated the technology in 3 individuals in three different circumstances: an individual with an implanted cardioverter defibrillator (ICD) upgraded to CRT, another individual with an implanted CRT defibrillator (CRT-D) with exit block in the coronary sinus (CS) lead, and a third individual with an implanted CRT-D who was a non-responder. At 6 months post-procedure, all 3 individuals retained capture, New York Heart Association (NYHA) functional class "significantly changed (Pre: III in two patients, and IV in one patient; Post: I in one patient, II in one patient, and II–III in one patient), and LV ejection fraction increased from 23.7+3.4% to 39+6.2% (p<0.017)" (Auricchio, 2013). The results of this study are limited by the low quality design including small sample size, lack of blinding, and no control group.

Auricchio and colleagues reported on the Wireless Stimulation Endocardially for CRT (WiSE-CRT) study (2014). This multicenter, prospective, and observational feasibility study was designed to enroll 100 individuals in up to 12 centers; however, 17 individuals were enrolled from 6 centers. Of the 17 individuals enrolled, 13 (76.5%) individuals received device implants. Reasons for device implantation included: individuals with failed CS lead implantation for CRT (n=7); individuals with an implanted CRT device and were not responding to CRT (n=2); and individuals with an implanted pacemaker or implantable cardioverter-defibrillator who met the standard indications for CRT (n=8). The primary endpoints were biventricular pacing capture on 12-lead electrocardiogram (EKG) analysis at 1 month and serious adverse events. Secondary endpoint was evaluation at 6 months. At 1 month, biventricular pacing was recorded in 83% (n=10) of the individuals and at 6 months, it was recorded in 92% (n=11) of the individuals. One individual had a non-functional device due to battery depletion at the 6-month follow-up. Serious adverse event rate at 1 month was 35%. This included three peri-operative pericardial effusions (18%), one of which resulted in death (6%). At the 6-month follow-up, 8 individuals (66%) had a NYHA functional class change, and LV ejection fraction significantly increased by 6 points (p<0.01). Limitations to this study include small sample size, and no control group or blinding.

In 2017, Reddy and colleagues published the outcomes of the Safety and Performance of Electrodes implanted in the Left Ventricle (SELECT-LV) study, which was a prospective, multicenter, non-randomized trial that investigated the safety and performance of the WiSE-CRT system in individuals (n=35) who had a standard indication for CRT, but failed conventional CRT [difficult CS anatomy (n=12; 34%), failure to respond to conventional CRT (n=10; 29%), high CS pacing threshold or phrenic nerve capture at low

outputs (n=5; 14%), CS lead dislodgment or lead failure (n=3; 9%), prior infection or upper extremity venous occlusion (n=3; 9%), or other (n=2; 6%)]. The WiSE-CRT system was successfully implanted into 33 (97.1%) individuals for LV endocardial wireless pacing. The primary endpoints were biventricular pacing capture on EKG analysis at 1 month, and device-related complications from implant to 24 hours post-implant and from 24 hours post-implant to 30 days. Biventricular pacing capture was achieved in 33 individuals (97%). Due to defective transmitters, 2 of the 33 (5.7%) individuals did not achieve biventricular pacing. There were 3 (8.6%) individuals with device-related events within 24 hours. One individual died as a result complications from cardiac arrest due to ventricular fibrillation during the electrode implant procedure. Prior to the introduction of the sheath into the left ventricle, another individual experienced embolization of the electrode to the left tibial artery during the exchange of the dilator and the catheter. The third individual required surgical repair after the formation of a femoral artery fistula. There were 8 (22.9%) individuals with device-related events between 24 hours and 30 days. These events included stroke (basilar artery) in conjunction with warfarin noncompliance (n=1), femoral pseudoaneurysm (n=2), pocket hematoma (generator) (n=1), suspected infection (generator site) (n=3), and death following ventricular fibrillation during the initial implant procedure as previously described (n=1). The secondary endpoints, which were evaluated at 6 months, were change in the clinical composite score (all-cause mortality, heart failure hospitalization, NYHA functional class, and global assessment), and change in echocardiographic left ventricular end-systolic volume (LVESV), left ventricular end-diastolic volume (LVEDV), and left ventricular ejection fraction (LVEF). The clinical composite score improved in 28 (84.8%) individuals. This change was largely driven by an improvement in NYHA functional class (n=22; 66.7%) and an improvement in quality of life scores (n=23; 69.7%). "Using the responder criteria for LVESV (≥ 15% relative reduction), LVEDV (≥ 10% relative reduction), and LVEF (≥ 5% absolute increase), positive echocardiographic responses to CRT were observed in 52% (n=3), 40% (n=10), and 66% (n=21) of patients, respectively" (Reddy, 2017). This study resulted in serious adverse events in a third of treated individuals. Furthermore, interpretation of study results is limited by a small sample size, lack of blinding, and no control group.

LV Endocardial Pacing

LV endocardial pacing (LVEP) presents a possible alternative to conventional CRT. There are several techniques with multiple variations that achieve LVEP, such as the atrial transeptal approach and the trans-ventricular apical approach. While the majority of studies on this alternative are case series, there have recently been some larger studies assessing LVEP.

In 2016, Morgan and colleagues released the results of the ALternate Site Cardiac ResYNChronization (ALSYNC) study, which was an international multicenter prospective study that assessed the safety and efficacy of LVEP using a single-incision, pectoral, atrial transseptal approach. Between March 2011 and July 2013, individuals who had either a failed previous conventional LV lead implantation, suboptimal CS anatomy, or were a CRT non-responder were enrolled in the study (n=138). The primary objective was freedom from complications greater than or equal to 70% related to the lead, the lead delivery system, or the implant procedure at the 6-month follow-up. Complications were defined as "any transseptal implant tool, transseptal implant procedure, or LVEP lead-related adverse event resulting in patient death, confirmed stroke, termination of significant device function, or any invasive intervention (including administration of intramuscular and parental fluids)" (Morgan, 2016). Of the 138 individuals enrolled in the study, LVEP lead implantation was performed in 132 individuals. Of those individuals who were not included in the results analysis, two were excluded from the analysis due to left superior vena cava, one died before the planned implant, and three did not have an implant due to thrombus in the left atrium. LVEP lead implantation was successful in 118 individuals (89%; 95% confidence interval [CI], 83–94%). The primary objective, freedom from complications as previously defined, was 82.2% at 6 months (95% CI, 75.6–88.8%). Adverse events included 5 post-procedure strokes (95% CI, 1.1–6.3), 14 transient ischemic attack (TIA) episodes observed in 9 individuals (95% CI, 3.6–17.6), and 23 deaths during study follow-up due to heart failure, renal failure, pulmonary failure, cancer, and sudden cardiac death (mortality rates at 6, 12, and 24 months after first implant attempt were 8.3%, 14.4%, and 18.4%, respectively). None of the deaths were due to a primary objective complication. Clinical outcomes during follow-up assessments at 6 months included 55% of individuals with a reduction in LV end-systolic volume (LVESV) of at least 15% ($p<0.0001$), 59% of individuals with an improvement of at least one NYHA class ($p<0.0001$), 33% of individuals with an improvement of mitral valve regurgitation by at least one class ($p=0.035$), 64% of individuals with at least a 5% absolute increase in LVEF ($p<0.0001$), and 44% of individuals with at least a 60 meter increase in the six-minute walking test ($p=0.004$). While this study did not have a control group and randomization, it did show significant results that demonstrate clinical feasibility of LVEP as an alternative to conventional CRT.

Gamble and collagues (2018) performed a systematic review and meta-analysis evaluating the benefits and risks of LVEP as an alternative to conventional CRT. The literature search yielded 23 studies published between 1999 and 2016 with a total of 384 individuals. There were 5 case reports, 15 case series, 2 retrospective case series, and 1 prospective clinical trial, which was the ALSYNC study that was previously described. While most individuals in the studies had a history of a failed CS implant of an LV lead for CRT, 10% of individuals were non-responders to CRT. The LVEP techniques used in the studies were trans-atrial septal (n=20), trans-ventricular apical (n=1), and trans-ventricular septal (n=2). Sixteen studies reported

clinical response outcomes, defined as improvement of at least one NYHA class, for 262 individuals (68%). Of the 262 individuals, 191 individuals (73%) had a positive clinical response; however, due to the wide and uneven distribution of the range of reporting between studies, the meta-analysis estimate of reponse was 82% (95% CI, 71-89%). No significant difference in clinical response was found between LVEP techniques (p=0.2). A significant difference in clinical response was found between the ALSYNC study (59%) and the remainder of the studies (92%) (p=0.02), which may be due to the the large number of non-responders to CRT in the ALSYNC group. Non-responders to CRT are less likely to show improvement due to various reasons such as comorbidities. Another possible reason for the significant difference in clinical response found between the ALSYNC study and the remaining studies is smaller studies typically have less bias-resistant designs. In regards to thromboembolic complications, which were reported by all studies, "the rate of stroke was 2.5 events per 100 patient years (95% CI, 1.5–4.3), and TIA 2.6 (1.1–6.1). The mortality rate was 4.5 (1.5–13.6) per 100 patient years" (Gamble, 2018). No significant difference was found in relation to complications and LVEP technique (p=0.7). The authors noted that clinical response rates and complication rates in this meta-analysis were comparable to other studies, including a large meta-analysis, on conventional CRT. While the sample size of this meta-analysis is small, which limits available data for analysis, the data shows that LVEP results in similar clinical reponse outcomes and complication rates making LVEP a viable alternative to conventional CRT.

Summary

Published studies evaluating the WiSE CRT system have included a small sample size, no method of randomization, and an absence of a comparison control group. In addition, high rates of serious adverse events including death, and questions relating to generarlizablity (for example, procedure feasibility outside of academic research institutions) are outstanding. Individuals who are not candidates for or have failed conventional CRT may be eligible for LVEP, which has demonstrated comparable results with conventional CRT. Additional well-designed studies are required to demonstrate long-term safety and efficacy of wireless CRT for LV pacing for heart failure. Currently, no device has been approved by the U.S. Food and Drug Administration (FDA) for provision of wireless CRT for LV pacing.

Background/Overview

Wireless CRT for LV pacing has been proposed as an alternative to conventionally delivered CRT through transvenous LV lead positioning as a treatment of heart failure. Devices that provide wireless CRT for LV

pacing are co-implanted with a pacemaker, ICD, or CRT device. An implanted pulse transmitter senses the right ventricular pacing signal from the co-implanted device. This prompts the transmitter to generate ultrasound that is detected by an electrode implanted on the LV endocardial wall, which converts the ultrasound to an electrical pacing pulse creating LV stimulation.

Definitions

Congestive heart failure (CHF) or heart failure: A condition in which the heart no longer adequately functions as a pump. As blood flow out of the heart slows, blood returning to the heart through the veins backs up, causing congestion in the lungs and other organs.

New York Heart Association (NYHA) Definitions:
The NYHA classification of heart failure is a 4-tier system that categorizes subjects based on subjective impression of the degree of functional compromise; the four NYHA functional classes are as follows:

- **Class I - patients with cardiac disease but without resulting limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain; symptoms only occur on severe exertion.**
- **Class II - patients with cardiac disease resulting in slight limitation of physical activity; they are comfortable at rest; ordinary physical activity (e.g., moderate physical exertion such as carrying shopping bags up several flights of stairs) results in fatigue, palpitation, dyspnea, or anginal pain.**
- **Class III - patients with cardiac disease resulting in marked limitation of physical activity; they are comfortable at rest; less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.**
- **Class IV - patients with cardiac disease resulting in inability to carry on any physical activity without discomfort; symptoms of heart failure or the anginal syndrome may be present even at rest; if any physical activity is undertaken, discomfort is increased.**

Ventricular fibrillation (Vfib or VF): A condition in which the heart's electrical activity becomes disordered. When this happens, the heart's lower (pumping) chambers contract in a rapid, unsynchronized fashion (the ventricles "quiver" rather than beat) and the heart pumps little or no blood.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
0515T	**Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and interpretation, when performed; complete system (includes electrode and generator [transmitter and battery])**
0516T	**Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and interpretation, when performed; electrode only**
0517T	**Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and interpretation, when performed; pulse generator component(s) (battery and/or transmitter) only**
0518T	**Removal of only pulse generator component(s) (battery and/or transmitter) of wireless cardiac stimulator for left ventricular pacing**
0519T	**Removal and replacement of wireless cardiac stimulator for left ventricular pacing; pulse generator component(s) (battery and/or transmitter)**
0520T	**Removal and replacement of wireless cardiac stimulator for left ventricular pacing; pulse generator component(s) (battery and/or transmitter), including placement of a new electrode**
0521T	**Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording, and disconnection per patient encounter, wireless cardiac stimulator for left ventricular pacing**
0522T	**Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, including review and report, wireless cardiac stimulator for left ventricular pacing**

ICD-10 Diagnosis

All diagnoses

References

Peer Reviewed Publications:

1. **Auricchio A, Delnoy PP, Butter C, et al. Feasibility, safety, and short-term outcome of leadless ultrasound-based endocardial left ventricular resynchronization in heart failure patients: results of the wireless stimulation endocardially for CRT (WiSE-CRT) study. Europace. 2014; 16(5):681-688.**
2. **Auricchio A, Delnoy PP, Regoli F, et al. First-in-man implantation of leadless ultrasound-based cardiac stimulation pacing system: novel endocardial left ventricular resynchronization therapy in heart failure patients. Europace. 2013; 15(8):1191-1197.**
3. **Gamble JHP, Herring N, Ginks M, et al. Endocardial left ventricular pacing for cardiac resynchronization: systematic review and meta-analysis. Europace. 2018; 20(1):73-81.**
4. **Morgan JM, Biffi M, Gellér L, et al. ALternate Site Cardiac ResYNChronization (ALSYNC): a prospective and multicentre study of left ventricular endocardial pacing for cardiac resynchronization therapy. Eur Heart J. 2016; 37(27):2118-2127.**
5. **Reddy VY, Miller MA, Neuzil P, et al. Cardiac resynchronization therapy with wireless left ventricular endocardial pacing: the SELECT-LV study. J Am Coll Cardiol. 2017; 69(17):2119-2129.**

Government Agency, Medical Society, and Other Authoritative Publications:

1. **Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013; 62(16):e147-239.**

Websites for Additional Information

1. **National Heart, Lung and Blood Institute. Heart failure. Available at: http://www.nhlbi.nih.gov/health/dci/Diseases/Hf/HF_WhatIs.html. Accessed on January 14, 2019.**

Index

WiCS-LV System
WiSE CRT System

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
New	03/21/2019	Medical Policy & Technology Assessment Committee (MPTAC) review. Initial document development.