Biventricular Pacemakers (Cardiac Resynchronization Therapy) for the Treatment of Heart Failure

Medical Policy

Section: Medicine
Original Policy Date: 12:2013
Last Review Status/Date: Reviewed with literature search 12:2013

Issue: 12:2013

Disclaimer

Our medical policies are designed for informational purposes only and are not an authorization, or an explanation of benefits, or a contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the coverage. Medical technology is constantly changing, and we reserve the right to review and update our policies periodically.

Description

Cardiac resynchronization therapy (CRT), which consists of synchronized pacing of the left and right ventricles, is intended to treat patients with heart failure and dyssynchronous ventricular contractions. Treatment involves placement of a device that paces both ventricles and which coordinates ventricular pacing to maximize cardiac pumping function and left ventricular ejection fraction (LVEF).

It is estimated that 20–30% of patients with heart failure have intraventricular conduction disorders resulting in a contraction pattern that is not coordinated and a wide QRS interval on the electrocardiogram (ECG). This abnormality appears to be associated with increased morbidity and mortality. Biventricular pacemakers using 3 leads (1 in the right atrium and 1 in each ventricle) have been investigated as a technique to coordinate the contraction of the ventricles, thus improving patients’ hemodynamic status. Two strategies are being explored: incorporating biventricular pacing into automatic implantable cardiac defibrillators and the development of stand-alone biventricular pacemakers.

One stand-alone biventricular pacemaker (InSync® Biventricular Pacing System, Medtronic) has received approval by the U.S. Food and Drug Administration (FDA) for the treatment of patients with New York Heart Association (NYHA) class III or IV heart failure, on a stable pharmacologic regimen, who also have a QRS duration of 130 msec or longer and a left-ventricular ejection fraction (LVEF) of 35% or less. Biventricular pacemakers have also been combined with automatic implantable cardiac defibrillators (ICDs). Both Guidant (CONTAK CD® CRT-D System) and Medtronic (InSync® ICD Model 7272) have received FDA approval for combined cardiac resynchronization therapy defibrillators for patients at high risk of sudden cardiac death due to ventricular arrhythmias and who have NYHA Class III or IV heart failure with LVEF of 35% or less, QRS duration 130 msec or longer (120 msec or longer for the Guidant device), and remain symptomatic despite a stable, optimal heart failure drug therapy.
In September 2010, the FDA expanded the indications for cardiac resynchronization therapy (CRT) to include patients with class I and II heart failure. In addition to NYHA class I/II heart failure, indications for CRT in mild heart failure include a LVEF of less than 30% and a QRS duration of 130 msec or greater.

In 2005, the InSync Sentry system received FDA approval through the supplemental premarket approval (PMA) process. This combined biventricular pacemaker/ICD is also equipped to monitor intrathoracic fluid levels using bioimpedance technology, referred to as OptiVol Fluid Status monitoring. Bioimpedance measures, defined as the electrical resistance of tissue to flow of current, are performed many times per day using a vector from the right ventricular coil on the lead in the right side of the heart to the implanted pacemaker devices; changes in bioimpedance reflect intrathoracic fluid status and are evaluated based on a computer algorithm. For example, changes in a patient’s daily average of intrathoracic bioimpedance can be monitored; differences in the daily average compared to a baseline are reported as the OptiVol Fluid Index. It has been proposed that these data may be used as an early warning system of cardiac decompensation or to provide additional feedback enabling a physician to further tailor medical therapy. Policy No. 2.02.24 addresses the use of external bioimpedance devices to noninvasively assess cardiac output.

Policy

Biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (i.e. a combined biventricular pacemaker/ICD) may be considered medically necessary as a treatment of heart failure in patients who meet all of the following criteria:

**New York Heart Association Class III or IV**
- Left ventricular ejection fraction ≤ 35%
- Sinus rhythm
- QRS duration of ≥ 120-130* msec, and
- Patients treated with a stable pharmacological medical regimen prior to implant, such as an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin receptor blocker) and a beta blocker, digoxin, and/or diuretics

**New York Heart Association class II**
- Left ventricular ejection fraction ≤ 30%
- Sinus rhythm
- QRS duration of ≥ 120–130* msec, and
- Patients treated with a stable pharmacological medical regimen prior to implant, such as an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin receptor blocker) and a beta blocker (or angiotensin receptor blocker), digoxin, and/or diuretics

* The FDA-labeled indications for QRS duration vary by device. For some devices, FDA approval is based on QRS duration of ≥ 130 (e.g., InSync® device) while for others it is based on QRS duration ≥ 120msec (e.g., CONTAK CD® CRT-D System). These differences in QRS
duration arise from differences in the eligibility criteria in the trials on which the FDA approval is based.

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker/ICD) are considered investigational as a treatment for patients with NYHA class I heart failure.

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker/ICD), are considered investigational as a treatment for heart failure in patients with atrial fibrillation.

An intrathoracic fluid monitoring sensor is considered investigational as a component of a biventricular pacemaker.

---

**Coding Issues**

In 2003, CPT introduced separate codes for biventricular pacing. Note that CPT “dual chamber” codes describe combined right atrial and right ventricular electrode placement. CPT “biventricular” codes describe the additional placement of a left ventricular electrode via the cardiac vein. A left ventricular pacing lead is placed in the marginal branch of the coronary sinus and into a cardiac vein to allow for biventricular pacing for cardiac resynchronization. CPT notes the following:

“A single chamber pacemaker system includes a pulse generator and one electrode inserted in either the atrium or the ventricle. A dual chamber pacemaker system includes a pulse generator and one electrode inserted in the right atrium and one electrode inserted in the right ventricle. In certain circumstances, an additional electrode may be required to achieve pacing of the left ventricle (biventricular pacing). In this event, transvenous cardiac vein placement of the electrode should be separately reported using code 33224 or 33225."

- 33224 Insertion of pacing electrode, cardiac venous system, for ventricular pacing, with attachment to previously placed pacemaker or pacing cardioverter-defibrillator pulse generator (including revision of pocket, removal, insertion, and/or replacement of generator).
- 33225 Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of pacing cardioverter-defibrillator or pacemaker pulse generator (including upgrade to dual chamber system (list separately in addition to code for primary procedures)

Use 33225 in conjunction with 33206, 33207, 33208, 33212, 33213, 33214, 33216, 33217, 33221, 33222, 33230, 33231, 33233, 33234, 33235, 33240, and 33249.

Thus, CPT describes 33225 as an “add-on” code to other pacing or pacing cardioverter-defibrillator procedures.
Rationale

This policy was created in July 1999 and updated periodically with literature review. The most recent update covers the period from February 2011 through February 2012.

LITERATURE REVIEW

Biventricular pacemakers and combined biventricular pacemakers/cardiac defibrillators

Efficacy of CRT in advanced heart failure (New York Heart Association [NYHA] Class III/IV)

Use of biventricular pacemakers with or without accompanying implantable cardiac defibrillator (ICD) for selected patients with advanced heart failure is supported by a large body of clinical trial evidence. For patients with the following characteristics, this treatment receives a class I recommendation in the 2005 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the diagnosis and management of patients with heart failure, (1) supported by the “A” level of evidence:

- Left-ventricular ejection fraction \( \leq 35\% \)
- Sinus rhythm
- New York Heart Association (NYHA) functional class III or IV despite optimal medical therapy
- Cardiac dyssynchrony as defined as a QRS >120 msec
- No contraindications for biventricular pacing

The current ACC/AHA guideline is accompanied by a review of the evidence, which states that more than 4,000 patients have been evaluated in randomized, clinical trials (RCTs) and that these trials establish benefit for CRT in this patient population in improving functional status and exercise capacity.

A 2009 TEC Assessment of cardiac resynchronization therapy (CRT) in mild heart failure (2) summarized 5 of the larger trials of CRT for advanced heart failure, showing that CRT improves quality of life (QoL) and functional status for patients with class III and class IV heart failure. Four of the 5 trials reported improvements in functional status for the CRT group. Similarly, 4 of the trials reported QoL measures, with all 4 showing significant improvements for the CRT group. Hospitalizations were reduced in 2 of the 4 trials, with an additional 2 trials reporting no difference in hospitalizations. The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, (3) which had the highest enrollment and the longest follow-up, reported a significant improvement in mortality. The other trials reported lower mortality for the CRT group, which did not reach statistical significance.

A systematic review of 9 RCTs of CRT in class III/IV heart failure was published in 2004. (4) This quantitative analysis revealed the following conclusions: 1) improvement of 3.5% in left-ventricular ejection fraction (LVEF); 2) improved QoL, with weighted mean difference on the Minnesota Living with Heart Failure Questionnaire of 7.6 points (0–100 scale); 3) improved functional capacity and a reduction in all-cause mortality of 21%. This analysis also found some evidence that cardiac morphology may be improved, suggesting that CRT may prevent, delay,
or even reverse the changes in morphology resulting from chronic heart failure (reverse remodeling).

**Efficacy of CRT in mild heart failure (NYHA Class I/II)**

Evaluation of CRT in mild heart failure was originally based on a 2009 TEC Assessment. (2) There is less evidence on treatment of mild heart failure compared to that for advanced heart failure, but clinical trial evidence is available. At least 4 RCTs enrolling over 3,000 patients, with follow-up ranging from 6 months to 2.4 years, have been published to date. A summary of the major RCTs in mild heart failure is provided.

**MADIT-CRT trial.** The largest trial published to date was the Multicenter Automatic Implantation Trial – Cardiac Resynchronization (MADIT-CRT) trial, (5) a single-blind trial that randomized 1,820 patients with NYHA class I/II heart failure to an ICD alone or an ICD-CRT device. The MADIT-CRT trial reported a reduction for the ICD-CRT group on the primary outcome, i.e., death or acute heart failure exacerbation. The primary endpoint was reached by 17.2% of patients in the ICD-CRT group compared to 25.3% of patients in the ICD-alone group. The first component of the composite outcome, acute heart failure events, occurred in 22.8% of patients in the ICD-alone group compared with 13.9% of patients in the ICD-CRT group (relative risk reduction [RRR] 39%, absolute risk reduction [ARR] 8.9%, number needed to treat [NNT]:11.2). This difference in acute heart failure events accounted entirely for the difference on the primary composite outcome. The death rate was similar between groups.

A follow-up publication from the MADIT-CRT trial was published in 2011 and analyzed the reduction in recurrent heart failure events. (6) This analysis supplemented the original MADIT-CRT outcome of time to first heart failure event, by comparing total heart failure events during an average follow-up of 2.6 years. Over this time period, there was a 38% relative reduction in heart failure events in the CRT group (hazard ratio [HR] 0.62, 95% confidence interval [CI]: 0.45-0.85, p=0.003). On subgroup analysis, the benefit was evident in patients with left bundle branch block (HR: 0.50, 95% CI: 0.33-0.76, p=0.001) but not in patients without left bundle branch block (HR: 0.99, 95% CI: 0.58-1.69, p=0.96).

**RAFT trial.** A second, large RCT was the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial or (RAFT) (7) trial, which randomized 1,798 patients with class II/III heart failure to ICD-CRT or ICD alone, with a mean follow-up 40 +/- 20 months. Unlike most previous trials, this trial did not confine enrollment to patients with sinus rhythm but allowed patients with atrial arrhythmias to participate. However, the number of patients who were not in sinus rhythm was only 12.8% (229/1,798). The RAFT trial was included in a 2011 TEC Assessment. On formal quality assessment as part of the TEC Assessment, this trial met all quality indicators and was given a “good” quality rating.

The primary outcome, death from any cause or hospitalization for heart failure, was reduced in the ICD-CRT group compared to the ICD-alone group (33.2% vs. 40.3%, respectively; p<0.001). There were significant reductions in both individual components of the primary outcome, overall mortality (20.8% vs. 26.1%, p=0.003) and hospitalizations (19.5% vs. 26.1%, all respectively, p<0.001). When restricted to patients with NYHA class II heart failure, the improvements in the outcomes of mortality and hospitalizations remained significant. The mortality for class II patients in the ICD-CRT group was 15.5% versus 21.1% in the ICD-alone group (HR: 0.71, 95% CI: 0.56-0.91; p<0.006). Hospitalizations for class II patients occurred in 16.2% of patients in the
ICD-CRT group compared to 21.1% in the ICD-alone group (HR: 0.70, 95% CI: 0.55-0.89, p<0.003).

Subgroup analyses from the RAFT trial reported that female gender, QRS duration equal to or greater than 150 msec, LVEF less than 20%, and QRS morphologic features were predictive of benefit. Of these factors, the QRS duration was the strongest factor. Patients with a QRS duration equal to or greater than ≥150 msec had a relative risk (RR) for the primary outcome of approximately 0.50, compared with a RR of approximately 1.0 for patients with a QRS duration less than 150 msec (p=0.003 for difference between RRs). There was a trend for greater improvement in patients with sinus rhythm compared to patients with atrial arrhythmias, but this difference did not reach statistical significance.

**REVERSE trial.** The Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) trial (8) enrolled a total of 610 patients, all of whom received a CRT device. Patients were randomized to CRT-ON or CRT-OFF for a period of 12 months in double-blind fashion. The primary outcome was a composite measure that classified patients as improved, unchanged, or worse. There were no significant differences reported on this primary outcome. There was a decrease in hospitalizations for heart failure in the CRT-ON group (4.1%, 17/419) compared with the CRT-OFF group (7.9%, 15/191). Changes in functional status, as measured by the 6-minute walk, were similar between groups. Quality of life, as measured by the Minnesota Living with Heart Failure Questionnaire, was also similar between groups.

**MIRACLE ICD trial.** The Multicenter InSync ICD Randomized Clinical Evaluation MIRACLE ICD study (9) was the smallest of the 3 studies, enrolling 186 patients with class II heart failure and an indication for an ICD in an unblinded fashion. Patients were randomized to ICD/CRT-ON versus ICD/CRT-OFF and followed for 6 months. There was no difference in the primary outcome of peak oxygen uptake between groups. There were also no differences reported between groups on the secondary outcomes of functional status, as measured by the 6-minute walk, QoL, as measured by the Minnesota Living with Heart Failure Questionnaire, and NYHA heart failure class.

**Systematic Reviews.** Numerous systematic reviews and meta-analyses have been published on CRT for heart failure. (4, 10-15) The majority compare CRT to medical management and report that outcomes are improved for patients with advanced heart failure and for patients with mild heart failure. For example, a meta-analysis of 25 trials of CRT was published in February 2011 by Al-Majed et al. (11) This study focused on the analysis of trials with class I/II heart failure patients, identifying 6 trials treating 4,572 patients. There was a significant mortality benefit associated with CRT on combined analysis (6 trials, 4,572 participants; RR 0.83 [95% CI: 0.72 to 0.96]). This mortality benefit was driven largely by the results of the RAFT trial, which had the most number of events and was given the greatest weight in combined analysis. There was also a significant reduction in heart failure hospitalizations associated with CRT use (4 trials, 4,349 participants; RR, 0.71 [CI: 0.57 to 0.87]). There were no significant benefits reported for quality of life, functional status, or progression to more advanced stages of heart failure.

**Adverse Effects of CRT placement**

Complications in the main RCTs were not uniformly reported; however, each trial contained some information on short- and long-term complications. Short-term complication rates ranged from 4–22%, with lead dislodgement and hematoma at the access site most common. Long-
term complications were reported by 2 of the trials, (8, 9) with rates of 16% and 35%. The majority of these long-term complications were lead dislodgement.

A systematic review and meta-analysis was published in 2011 that focused on complications from CRT treatment. (16) This review included 7 trials of CRT treatment that reported on in-hospital mortality and complications related to device placement. In all 7 CRT trials, the device was placed percutaneously without a thoracotomy. In-hospital mortality occurred at a rate of 0.3%, and 30-day mortality was 0.7%. The most common complications were related to placement of the left ventricular (LV) lead. Lead dislodgement occurred in 5.9% of patients. Other LV lead placement complications included coronary vein dissection in 1.3% and coronary vein perforation in 1.3%. Pneumothorax occurred in 0.9% of patients, and hematoma at the insertion site occurred in 2.4% of patients.

Conclusions. There is a large body of clinical trial evidence that supports the use of CRT in patients with NYHA class III/IV heart failure. These trials establish that CRT treatment leads to reduced mortality, improved functional status, and improved QoL.

For patients with milder heart failure, at least 4 RCTs of CRT have been published in the literature. A mortality benefit was reported by one of the 4 trials, the RAFT trial. This trial was free of major bias and reported a fairly large absolute difference in overall mortality of 5.3%. None of the other 3 RCTs reported a mortality difference. While 2 of the other 3 trials were underpowered to detect differences in mortality, the MADIT-CRT was approximately the same size as the RAFT trial and did not show any improvement in mortality. It is possible that the sicker patient population and longer follow-up in RAFT accounted for the mortality difference. Among other outcome measures, hospitalizations for heart failure showed consistent improvements, but quality of life and functional status did not.

Use of CRT in patients with atrial fibrillation

There is controversy about whether CRT leads to health outcome benefits for patients with atrial fibrillation. Many experts feel that if CRT is to be used, it needs to be combined with ablation of the atrioventricular node, in order to avoid transmission of atrial impulses through the node that might result in rapid ventricular rates, thus undermining the efficacy of CRT.

An RCT was published in 2011 (17) that compared CRT to right ventricular pacing alone in patients with atrial fibrillation. A total of 186 patients had atrioventricular nodal ablation and implantation of a CRT device. Patients were then randomized to echo-optimized CRT or right-ventricular pacing alone and followed for a median of 20 months. The primary outcome measure was a composite of death from heart failure, hospitalization for heart failure, or worsening heart failure. This combined endpoint occurred in 11% of the CRT group compared with 26% of the RV pacing group (HR: 0.37, 95% CI: 0.18-0.73, p=0.005). For the individual outcome measures, there was not a significant reduction in mortality (HR: 1.57, 95% CI: 0.58-4.27, p=0.37), but there were significant reductions in hospitalizations (HR: 0.20, 95% CI: 0.06-0.72, p=0.013) and worsening heart failure (HR: 0.27, 95% CI: 0.12-0.58, p=0.37). There were no differences in outcomes on subgroup analysis, including analysis by ejection fraction, NYHA class, and/or QRS duration.

A systematic review published in 2011 (18) compared outcomes of CRT in patients with and without AF. This analysis included 23 observational studies enrolling 7,495 patients, of whom 1,912 had AF. Outcomes in patients with AF were less favorable on all measures. This included overall mortality (Relative risk [RR]: 1.5, 95% CI: 1.08 to 2.09, p=0.015), nonresponse to CRT.
(RR: 1.32, 95% CI: 1.12 to 1.55, p=0.001), change in the Minnesota Living with Heart Failure QoL score (mean difference -4.1, 95% CI: -1.7 to -6.6, p=0.001), and change in the 6-minute walk distance (mean difference -14.1 meters, 95% CI: -28.2 to 0.0, p=0.05). Five studies compared outcomes of patients with AF who had AV nodal ablation to patients who did not have ablation. Pooled analysis from these studies indicated that AV nodal ablation was associated with a lower rate of non-response (RR: 0.40; 95% CI: 0.28 to 0.58, p<0.001).

A second systematic review that evaluated the role of AV node ablation in patients with atrial fibrillation (AF) treated with CRT was published in 2012. (19) This review included non-randomized studies that reported outcomes of CRT and medical therapy. Six studies were included, enrolling a total of 768 patients, 339 of whom underwent atrioventricular (AV) node ablation and 429 who did not. AV nodal ablation was associated with improvements in the outcomes of all-cause mortality (RR: 0.42; 95% CI: 0.26 to 0.68), cardiovascular mortality (RR: 0.44, 95% CI: 0.24 to 0.81), and change in NYHA class (mean difference -0.34, 95% CI: -0.56 to -0.13, p=0.002).

Conclusions. There is insufficient evidence to determine whether CRT improves outcomes for patients with AF and heart failure. One systematic review of observational studies suggests that patients with AF do not achieve the same degree of benefit as do patients with sinus rhythm. However, this comparison does not determine whether patients with AF have a greater benefit from CRT compared to medical therapy. For patients with AF who are undergoing CRT, one RCT and a systematic review of non-randomized studies conclude that, when CRT is used in patients with AF, AV nodal ablation is associated with improved outcomes compared to no AV nodal ablation.

Selecting patients for CRT treatment

For patients who meet indications for CRT treatment, there is a large variability in the magnitude of response. Some patients do not respond at all, while others have very substantial benefit. As a result, there is interest in better defining the clinical features that predict response in order to better target therapy toward those who will benefit most.

The Predictors of Response to Cardiac Resynchronization Therapy (PROSPECT) study (20) was a prospective, multicenter study that evaluated the ability of echocardiographic parameters to predict response to CRT. Results of this trial indicated that the 12 individual echocardiographic parameters varied widely in their ability to predict response. (21) The sensitivity of these individual measures ranged from 6-74% and the specificity ranged from 35-91%. The authors concluded that it was unlikely that these echocardiographic measures could improve patient selection for CRT.

Ventricular dyssynchrony. A small randomized controlled trial (RCT) that compared outcomes of CRT in patients with ventricular dyssynchrony versus those without was published in 2011. (22) A total of 73 patients with class II/IV were evaluated, 44 of whom were found to have dyssynchrony on echocardiography. These 44 patients were randomized to a combined CRT-defibrillator or a defibrillator alone. Outcomes measures were peak O2 consumption (VO2max), NYHA class, and echocardiographic parameters. At 6 months of follow-up, more patients in the CRT group had an increase of at least 1 mL/kg/min in VO2max (62% vs. 50%, p=0.04). There were significant within-group improvements in NYHA class and echocardiographic measures, but the between-group comparisons with the no-CRT group did not reach statistical significance.
Several observational studies of patients who meet criteria for treatment have shown that measures of dyssynchrony measured by various methods are correlated with treatment response, as defined by improvements in left ventricular end-systolic volume, ejection fraction, or clinical criteria. (23) Although correlations have been found, studies vary due to the method used to measure dyssynchrony, the cutoff value used, and the criteria used for clinical response. Without clinical trial evidence, it is not possible to determine which method and which cutoff will select patients who otherwise meet criteria for therapy who would be better off without a biventricular pacemaker.

**QRS duration.** One RCT was identified that selected patients who had a narrow QRS complex on EKG and echocardiographic evidence (Doppler and M-mode) of dyssynchrony. (24) The Resynchronization Therapy in Normal QRS Trial [RethinQ study] randomized 172 patients to receive a CRT device, turned on or not, and followed up for 6 months. CRT-treated patients were not more likely to have improvement than non-CRT patients (46 vs. 41%, respectively, met endpoint of improvement in exercise capacity [peak VO2]). A subset of patients with QRS duration greater than or equal to 120–130 msec showed improvement (p=0.02), whereas patients with QRS less than 120 msec did not (p=0.45). This study confirmed that patients with a QRS duration less than 120 msec do not benefit from CRT.

A meta-analysis was published in 2011 that evaluated whether patients with modest prolongations of the QRS complex benefited from CRT. (25) This study identified 5 trials enrolling 5,813 patients that reported on outcomes stratified by QRS duration. There was some variability in the definition of QRS categories, but the authors were able to categorize studies into those with moderately prolonged QRS, generally 120-149 msec, and severely prolonged QRS, generally 150 msec or greater. For patients with a moderately prolonged QRS, there was no significant benefit for CRT in reducing composite outcomes of adverse cardiac events (Risk ratio [RR]: 0.95, 95% CI: 0.82 to 1.10, p=0.49). In contrast, for patients with a severely prolonged QRS, there was a 40% relative reduction in the composite outcomes (RR: 0.60, 95% CI: 0.53 to 0.67, p<0.001). There were no differences in outcomes on sensitivity analysis according to NYHA class and implantable cardiac defibrillator (ICD) status.

**Conclusions.** The optimal selection of patients for CRT treatment remains an active area of investigation. The presence of dyssynchrony on echocardiography may risk stratify patients, but is not a good discriminator of responders versus non-responders. In contrast, a QRS duration of greater than 150 msec, or the presence of left bundle branch block, appears to discriminate well between responders and non-responders and represents another potential factor on which patients may be selected for CRT treatment. The evidence on this question is primarily from subgroup analyses of RCTs but is consistent across multiple studies and is supported by quantitative pooling of these subgroup analyses in a meta-analysis.

**Combined automatic implantable cardiac defibrillators/biventricular pacemakers/intrathoracic fluid monitors**

Adding intrathoracic fluid status monitoring has been proposed as a more sensitive monitoring technique of the fluid status leading to prompt identification of impending heart failure, permitting early intervention and, it is hoped, a decreased rate of hospitalization. There is a lack of evidence from RCTs on the efficacy of fluid monitoring compared to usual care. The available evidence consists of uncontrolled studies that evaluate the correlation of fluid status information with cardiac events.
A prospective cohort of 558 patients from 34 centers identified the number of "threshold crossing events" and the percent of days with such events as predictors of hospitalization for severe heart failure using multivariate regression. (26) Over a mean of 326 days, 953 threshold crossing events in 351 patients resulted in 63 hospitalizations among 49 patients. Each subsequent event was associated with a 36% increased risk of hospitalization; however, the extent to which the presence of threshold crossing events influenced the decision to hospitalized is not known.

A similar retrospective study, that evaluated “threshold crossings” as a predictor of arrhythmogenic events, was published in 2011. (27) This analysis included 282 patients with NYHA class III or IV heart failure followed for a mean of 10 months. Patients were categorized into those that had “threshold crossings” (n=145, 51%) and those that did not (n=137, 49%). Tachyarrhythmic events were more common in patients with threshold crossings than in patients without (3,241 vs. 1,484 events, p<0.0001).

Medtronic, the manufacturer of the OptiVol™ Fluid Status Monitoring feature of the InSync Sentry system, has announced several ongoing clinical trials of the device as follows. The Optilink HF trial (28) is designed to evaluate fluid status monitoring with the OptiVol™ device combined with wireless transmission through the CareLink Network. Patients with NYHA class II or III heart failure are eligible, and the target enrollment is 1,000 patients. The primary outcome is a composite of all-cause death or cardiovascular hospitalization. The trial is scheduled to report the first results in May 2014.

The Medtronic Impedance Diagnostics in Heart Failure (MID-HeFT) study was a retrospective study designed to investigate the feasibility of predicting heart failure hospitalization based on intrathoracic bioimpedance and to validate impedance measurements as a surrogate measure of pulmonary congestion based on pulmonary capillary wedge pressure. The device that was used was a modified pacemaker and thus was not incorporated into a biventricular pacemaker/ICD. A total of 9 abstracts are derived from this study. One abstract included 33 patients. (29) Among the 10 patients with 26 hospitalizations for heart failure during an 18-month follow-up, thoracic bioimpedance gradually decreased prior to the hospitalization, in many instances before the onset of clinical symptoms.

The Fluid Accumulation Status Trial (FAST) is a prospective trial investigating the use of the algorithm used to analyze the collected bioimpedance data. The early results of this trial have been presented at the 13th Heart Failure Society meeting in September 2009. (30) Data presented at that time reported that fluid monitoring was more sensitive in predicting acute heart failure exacerbations, compared to weight monitoring. To date, there have not been any publications in the peer-reviewed literature on this study, and no data on other health outcomes is available at this time.

The Sensitivity of the InSync Sentry for Prediction of Heart Failure (SENSE-HF) study is designed to prospectively evaluate the sensitivity of the OptiVol fluid trends feature in predicting heart failure hospitalizations with signs and/or symptoms of pulmonary congestion and then to define OptiVol clinical guidelines for patient management. The SENSE-HF study was completed in March 2009. Baseline characteristics of the PARTNERS-HF study (31) have been published; study outcomes have not been published in the peer-reviewed literature.

The Combined Heart Failure Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalization (PARTNERS-HF) is a prospective, nonrandomized postmarketing study
conducted in up to 100 U.S. centers that was completed in March 2008. (32) The goal of the trial is to characterize the relationship between a variety of diagnostic data derived from the implanted biventricular/ICD devices. Data from this study were presented at the 2008 Annual Heart Failure Society Meeting. Researchers reported at this time that patients with a fluid index that crossed threshold were twice as likely to develop acute heart failure events, compared to patients whose fluid index did not cross the threshold.

Conclusions. The evidence is not sufficient to determine whether intrathoracic fluid monitoring improves outcomes for patients who receive a CRT device. The available evidence indicates that intrathoracic monitoring may be a more sensitive measure for predicting heart failure exacerbations compared to weight monitoring. However, there is no published data that report improved outcomes associated with fluid monitoring. Although numerous trials have been undertaken, as of April 2012, there were no RCT publications in the peer-reviewed literature that report on outcomes and/or the utility of intrathoracic fluid monitoring in the management of patients with heart failure.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 8 academic medical centers while this policy was under review in 2012. There was consensus agreement with the medically necessary statements. For patients with class I heart failure, there was mixed input as to whether CRT should be medically necessary. Regarding the duration of the QRS complex, there was acknowledgement that the literature supported use mainly in patients with a QRS greater than 150 msec, but most reviewers disagreed with restricting CRT use to patients with a QRS greater than 150 msec because that was not currently the accepted standard of care. For patients with atrial fibrillation, the input was mixed on whether biventricular pacing improves outcomes.

Summary

Evidence from clinical trials and systematic reviews supports the benefit of CRT treatment for patients with NYHA class III/IV heart failure. For this group, there are improvements in mortality, functional status and quality of life. As a result, CRT treatment may be considered medically necessary for patients with NYHA class III/IV heart failure who have an ejection fraction <35%, sinus rhythm, a QRS duration of at least 120 msec, and who are treated with an optimal pharmacologic regimen.

For patients with milder heart failure, RCT evidence from at least one large, high-quality trial reports a mortality benefit for patients with class II heart failure, but other RCTs do not report a mortality benefit. Several studies report a decrease in hospitalizations for class II patients, but no studies provide evidence of treatment benefit on functional status or QOL outcomes. Despite the lower level of evidence available for mild compared to advanced heart failure, it can be concluded that the benefit of CRT outweighs the risk for these patients. Therefore, CRT treatment may be considered medically necessary for class II heart failure patients who meet other clinical criteria for treatment. The evidence on class I heart failure is not sufficient to permit...
conclusions, as only a small number of class I patients have been included in some of the trials, and no benefit has been demonstrated for this specific subgroup. As a result, CRT is considered investigational for class I heart failure.

Treatment of patients with atrial fibrillation and heart failure is controversial. Available evidence establishes that patients with heart failure probably do not derive the same magnitude of benefit as do patients with sinus rhythm and that CRT with AV nodal ablation is probably superior to CRT without AV nodal ablation in patients with heart failure. However, the evidence is insufficient to determine whether CRT treatment is superior to no treatment for this patient group. In addition, clinical input in 2012 was mixed as to whether patients with atrial fibrillation should be treated with CRT. Therefore, CRT remains investigational for patients with atrial fibrillation.

The optimal selection of patients for CRT treatment remains uncertain. Accumulating evidence indicates that benefit is concentrated in patients with a QRS duration of greater than 150 msec. This factor offers a potential method to better select patients for CRT and potentially avoid treatment in patients who will not benefit. Clinical input in 2012 demonstrated support for continued use of QRS threshold of 120 msec, rather than restricting treatment to patients with QRS greater than 150 msec. Other factors for selecting patients, such as ventricular dyssynchrony on echocardiography, have not been shown to be good discriminators of responders versus non-responders.

Practice Guidelines and Position Statements

Guidelines for device-based treatment of cardiac rhythm abnormalities were published jointly by ACC/AHA/HRS in 2008. (33) These guidelines included the following recommendations on CRT for heart failure:

Class I recommendations

- For patients who have LVEF [left ventricular ejection fraction] less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, and sinus rhythm, CRT with or without an ICD is indicated for the treatment of NYHA functional Class III or ambulatory Class IV heart failure symptoms with optimal recommended medical therapy. (Level of Evidence: A)

Class IIa recommendations

- For patients who have LVEF less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, and AF, CRT with or without an ICD is reasonable for the treatment of NYHA functional Class III or ambulatory Class IV heart failure symptoms on optimal recommended medical therapy. (Level of Evidence: B)

- For patients with LVEF less than or equal to 35% with NYHA functional Class I or II symptoms who are receiving optimal recommended medical therapy and who have frequent dependence on ventricular pacing, CRT is reasonable. (Level of Evidence: C)

Class IIb recommendations

- For patients with LVEF less than or equal to 35% with NYHA functional Class I or II symptoms who are receiving optimal recommended medical therapy and who are
undergoing implantation of a permanent pacemaker and/or ICD with anticipated frequent ventricular pacing, CRT may be considered. *(Level of Evidence: C)*

The 2005 AHA/ACC guidelines (34) suggest that patients with atrial fibrillation (AF) and complete atrioventricular (AV) block may benefit from CRT. A prospective cohort of 162 patients indicated for CRT with permanent AF found that CRT without AV ablation was associated with less favorable outcomes than CRT with AV ablation. (35) Response to pacing was defined as 85% biventricular capture at 2 months and 42% of patients responded; non-responders underwent ablation. Evidence of reverse remodeling (reduction of left ventricular end-systolic volume [LVESV] of ≥10% from baseline at 6 and 12 months) was 3 times more likely in ablated compared to nonablated patients. Controlled trials addressing this issue are underway and are needed before recommending the “ablate and pace” pathway that would render many patients pacemaker dependent.

References:


2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Cardiac resynchronization therapy for mild congestive heart failure. TEC Assessments 2009; Volume 24, Tab 8.


35. Gasparini M, Auricchio A, Regoli F et al. Four-year efficacy of cardiac resynchronization therapy on exercise tolerance and disease progression: the importance of performing

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>33208</td>
<td>Insertion or replacement of permanent pacemaker with transvenous electrode(s); atrial and ventricular</td>
</tr>
<tr>
<td></td>
<td>33211</td>
<td>Insertion or replacement of temporary transvenous dual chamber pacing electrodes (separate procedure)</td>
</tr>
<tr>
<td></td>
<td>33213</td>
<td>Insertion or replacement of pacemaker pulse generator only; dual chamber</td>
</tr>
<tr>
<td></td>
<td>33224</td>
<td>Insertion of pacing electrode, cardiac venous system, for ventricular pacing, with attachment to previously placed pacemaker or pacing cardioverter-defibrillator pulse generator (including revision of pocket, removal, insertion and/or replacement of generator)</td>
</tr>
<tr>
<td></td>
<td>33225</td>
<td>Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of pacing cardioverter-defibrillator or pacemaker pulse generator, including upgrade to dual chamber system (list separately in addition to code for primary procedures)</td>
</tr>
<tr>
<td></td>
<td>33233</td>
<td>Removal of permanent pacemaker pulse generator only</td>
</tr>
<tr>
<td></td>
<td>33228</td>
<td>Removal of permanent pacemaker pulse generator with replacement of pacemaker pulse generator; dual lead system (new code 1/1/12)</td>
</tr>
<tr>
<td>ICD-9 Procedure</td>
<td>00.50</td>
<td>Implantation of cardiac resynchronization pacemaker without mention of defibrillation, total system [CRT-P]</td>
</tr>
<tr>
<td></td>
<td>00.51</td>
<td>Implantation of cardiac resynchronization defibrillator, total system [CRT-D]</td>
</tr>
<tr>
<td></td>
<td>00.52</td>
<td>Implantation or replacement of transvenous lead [electrode] into left ventricular coronary venous system</td>
</tr>
<tr>
<td></td>
<td>00.53</td>
<td>Implantation or replacement of cardiac resynchronization pacemaker, pulse generator only [CRT-P]</td>
</tr>
<tr>
<td></td>
<td>00.54</td>
<td>Implantation or replacement of cardiac resynchronization defibrillator, pulse generator device only [CRT-D]</td>
</tr>
<tr>
<td>ICD-9 Diagnosis</td>
<td>428</td>
<td>Heart failure, code range</td>
</tr>
<tr>
<td>HCPCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD-10-CM (effective 10/1/13)</td>
<td>I50.20 – I50.9</td>
<td>Congestive heart failure, code range</td>
</tr>
<tr>
<td>ICD-10-PCS (effective 10/1/13)</td>
<td>Surgical, heart and great vessels, insertion, percutaneous, pacemaker lead, code by body part (right atrium, left atrium, right ventricle, or left ventricle)</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>02H63MA, 02H73MA, 02HK3MA, 02HL3MA</td>
<td>Surgical, heart and great vessels, insertion, percutaneous, defibrillator lead, code by body part (right atrium, left atrium, right ventricle, or left ventricle)</td>
<td></td>
</tr>
<tr>
<td>02H63ME, 02H73ME, 02HK3ME, 02HL3ME</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, pacemaker single chamber, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63P0, 0JH60P0</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, pacemaker single chamber rate responsive, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63P1, 0JH60P1</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, pacemaker dual chamber, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63P2, 0JH60P2</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, cardiac resynchronization pacemaker pulse generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63P3, 0JH60P3</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, defibrillator generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63P4, 0JH60P4</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, cardiac resynchronization defibrillator pulse generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63PA, 0JH60PA</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, contractility modulation device, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH63PY, 0JH60PY</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, chest, other cardiac rhythm related device, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83P0, 0JH80P0</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, pacemaker single chamber, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83P1, 0JH80P1</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, pacemaker single chamber rate responsive, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83P2, 0JH80P2</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, pacemaker dual chamber, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>0JH83P3, 0JH80P3</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, cardiac resynchronization pacemaker pulse generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83P4, 0JH80P4</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, defibrillator generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83P5, 0JH80P5</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, cardiac resynchronization defibrillator pulse generator, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83PA, 0JH80PA</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, contractility modulation device, code by approach (percutaneous or open)</td>
<td></td>
</tr>
<tr>
<td>0JH83PY, 0JH80PY</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, abdomen, other cardiac rhythm related device, code by approach (percutaneous or open)</td>
<td></td>
</tr>
</tbody>
</table>

**Type of Service**: Cardiology  
**Place of Service**: Inpatient

**Index**
- Biventricular Pacing
- Congestive Heart Failure, Pacemakers
- Dual Chamber Pacing, Congestive Heart Failure
- Intrathoracic Fluid Monitoring with Biventricular Pacing
- Pacing, Biventricular
- Resynchronization, Cardiac